



Chirurgie cardiaque mini-invasive : du concept à l'évaluation d'une instrumentation spécifique

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DESCHAMPS

RESUME .

Ce travail reprend les études d'évaluation d'une plateforme instrumentale dédiée à la chirurgie mitrale mini-invasive vidéo-assistée, et du télémanipulateur Da Vinci pour la réalisation d'anastomose mammaire interne / IVA à thorax fermé.

1) Evaluation du Portaclamp. Nous avons participé à l'étude pilote multicentrique étudiant la sécurité et l'efficacité de ce système de clampage original. Cette étude clinique a porté sur 20 patients opérés de chirurgie cardiaque sous CEC et a confirmé la simplicité d'utilisation du système, son efficacité et l'absence de morbidité ou complication induite. *Early experience with a new aortic clamping system designed for port access cardiac surgery: The Portaclamp. Heart Surgery Forum 2004, 7: E240-E244.*

De façon concomitante, dans une étude expérimentale chez le porc, les effets histologiques sur la paroi de l'aorte des trois techniques de clampage utilisées en chirurgie mini-invasive (l'endo-clamp, le clamp métallique type Chitwood et le Portaclamp) ont été analysés. L'étude a porté sur 15 porcs. L'analyse histologique a révélé une atteinte majeure de l'endothélium aortique induite par l'endo-clamp ; des lésions non spécifiques de la média externe et de l'adventice ont été observées indépendamment du clamp utilisé et de façon similaire. *Comparison between 3 aortic clamps for video-assisted cardiac surgery : A histological study in a pig model. Heart Surgery Forum 2006, 9: E657-E660.*

2) Evaluation du Portapleg. Le Portapleg est un dispositif auto-suturent de cardioplégie antérograde constitué principalement d'un clip en Nitinol restant implanté sur l'aorte. Nous avons été investigateur principal de l'étude pilote multicentrique non comparative, non aveugle et non randomisée intitulée « *Performances in vivo du système Portapleg* » et comprenant l'inclusion de 40 patients sur quatre centres européens afin d'évaluer la sécurité et la fonctionnalité du dispositif. Le critère principal était le temps de saignement du site de ponction après injection de Protamine. Dans notre centre, une étude par angio scanner de l'aorte avant décharge et à trois mois a été incluse au protocole. Cette étude ancillaire sur 20 patients a été rapportée de façon indépendante avec comme critère secondaire la position du clip en Nitinol sur l'aorte. Le système a montré son efficacité hémostatique dans tous les cas sans événement secondaire. L'analyse par angio scanner a montré que le clip en Nitinol était bien ancré

sur l'aorte dans tous les cas avec cependant une position asymétrique dans 5 cas. A trois mois, l'étude radiologique a confirmé la stabilité du clip dans sa position initiale.

Self-sealing antegrade cardioplegia system for video-assisted cardiac surgery : Preliminary results. Innovations 2007; 2:209-212.

3) Evaluation du Mitrax's. C'est un cône en plastique polymère auto ajustable et auto expansible, qui repousse de façon symétrique et concentrique les parois de l'oreillette. Une étude prospective de son efficacité a été réalisée chez 62 patients opérés de chirurgie mitrale vidéo-assistée de façon consécutive. L'indice de satisfaction (de 1 à 5) a été élevé (en moyenne 4.6), témoin d'une exposition optimale de la valve mitrale avec une vision endoscopique ou directe de la valve mitrale jugée excellente. Cette évaluation a montré les avantages du Mitrax's : simplicité d'utilisation, absence de distorsion de la valve mitrale et de déformation des parois de l'oreillette gauche, absence de distorsion de la valve aortique. Elle a montré également les limites du dispositif liées à la standardisation des tailles, avec une exposition incomplète de la totalité de l'anatomie de la valve en cas d'inadéquation entre la taille de l'oreillette et la taille de l'anneau mitral. ***Evaluation of a new left atrial retractor for minimally invasive mitral valve surgery. J Thorac Cardiovasc Surg 2011; 141: 297-299.***

Ces études ont montré qu'il était possible d'améliorer la faisabilité et la reproductibilité de la chirurgie mitrale mini-invasive vidéo-assistée grâce à une plateforme instrumentale adaptée à un micro environnement chirurgical ; elles ont contribué à sa diffusion.

4) Analyse comparative des techniques mini-invasives de revascularisation de l'IVA par pontage mammaire (Port Access, MIDCAB, TECAB).

Une étude prospective sur 10 ans a été conduite afin d'évaluer de façon comparative les résultats des trois techniques de chirurgie coronaire mini-invasive utilisées pour la revascularisation isolée de l'IVA et correspondantes à trois concepts différents : le PACABG (Port-Access coronary surgery), le plus invasif mais reproduisant le mieux la technique classique de pontage coronaire avec anastomose sur cœur arrêté ; le TECAB (totally endoscopic coronary artery bypass grafting), le moins invasif à thorax fermé sans CEC et à cœur battant ; le MIDCAB (minimally invasive direct coronary artery bypass), avec un caractère invasif intermédiaire puisque sans CEC et à cœur battant, mais à thorax ouvert, après prélèvement mammaire par vidéo ou robot-assistance.

Cette étude a porté sur 160 patients. Malgré ces limites, étude non randomisée et sur des périodes d'inclusion différentes, les résultats ont montré, à trois mois, un taux de réintervention sur l'IVA, artère cible pontée, significativement plus élevé dans le groupe

TECAB : PA-CABG, 0% ; MIDCAB, 1.8% ; TECAB, 10% ; $p < 0.01$. Ces différences observées ont souligné et confirmé une intuition chirurgicale : la perméabilité précoce des anastomoses réalisées sur cœur arrêté est meilleure que celles réalisées sur cœur battant ; la perméabilité précoce des anastomoses réalisées manuellement en vision directe est meilleure que celles réalisées avec robot-assistance à thorax fermé.

Néanmoins, au début de notre expérience TECAB, la technique d'anastomose utilisée était identique à la celle des procédures MIDCAB ; les premiers échecs de perméabilité après TECAB nous ont conduit à modifier cette technique d'anastomose et de passer du surjet continu Gortex 8/0 aux points séparés Uclip en Nitinol. Cette évolution technique, au rythme de l'évolution technologique, a fait disparaître les problèmes anastomotiques mais ne nous a pas mis à l'abri de trois cas d'occlusion fonctionnelle du pédicule mammaire avec anastomose perméable, témoin de la difficulté d'orienter ou de vérifier le pédicule mammaire au cours d'une procédure à thorax fermé. A trois ans, les taux actuariels de survie sans réintervention étaient : PA-CABG, 100% ; MIDCAB, 98 ± 5 % ; TECAB, 88 ± 8 % ; $p < 0.05$. Cette différence observée était directement liée aux échecs précoces de perméabilité.

Cette étude nous a conduit à considérer la procédure MIDCAB vidéo ou robot –assistée comme technique chirurgicale de référence pour la revascularisation isolée de l'IVA, compte tenu du surcoût induit par la technique PA-CABG et du taux plus élevé des échecs primaires avec la technique TECAB.

Is there an optimal minimally invasive technique for left anterior descending coronary artery bypass? J Cardiothorac Surg 2011; 6: 37.

Conclusion. Ce travail résume une expérience sur plus de 10 ans, dans un domaine en évolution constante dépendant des progrès technologiques et de la volonté de la communauté chirurgicale. La chirurgie mitrale vidéo-assistée a atteint une phase de maturité après 15 ans d'effort. La chirurgie cardiaque robotique est encore en phase de maturation ; son avenir dépend probablement de systèmes plus légers et moins onéreux, hybrides, associant colonne vidéo 3D et instruments motorisés, et de systèmes d'anastomose automatique performants.

TITLE .

Mini-Invasive Cardiac Surgery : From the Concept to The Evaluation of Dedicated Implements.

SUMMARY .

This thesis is based on the evaluation studies of an instrumental platform dedicated to video assisted minimally invasive mitral valve surgery, and of the robotic Da Vinci system in LAD bypass with mammary artery in a closed chest approach.

1) Evaluation of Portaclamp. We took part in the multicenter pilot study to demonstrate the safety and the efficacy of a new aortic cross clamping concept for use in port access cardiac surgery. Twenty patients underwent various cardiac operations under cardiopulmonary bypass and aortic cross clamping with Portaclamp. This clinical study showed that the clamping system is safe, fast and easy and does not generate undue morbidity. *Early experience with a new aortic clamping system designed for port access cardiac surgery : The Portaclamp. Heart Surgery Forum 2004, 7: E240-E244.*

Concurrently, an experimental study was undertaken in a pig model, comparing the Portaclamp, Endoclamp and a metallic clamp, to assess in 3 groups of 5 pigs each, the histological traumatic effects of the aortic clamps used in video-assisted cardiac surgery. In the Endoclamp group, severe lesions of the intima were observed on the clamping spot. Only spongy lesions located on the external third of the media were observed with a random distribution in aortic samples without difference between groups. *Comparison between 3 aortic clamps for video-assisted cardiac surgery: A histological study in a pig model. Heart Surgery Forum 2006, 9: E657-E660.*

2) Evaluation of Portapleg. Portapleg is an auto-suturing system dedicated to antegrade cardioplegia delivery, and based on a Nitinol clip acting as a staple and left implanted on the aortic wall after the retraction of the cardioplegia canula. We were principal investigator of the multicenter pilot study for the assessment of “**the performances of Portapleg system in vivo**” with the enrolment of 40 patients. The primary end point was the puncture bleeding time after reversal of heparin by protamine. In our center, a CT scan was performed to record the position of the Nitinol clip onto the aorta before discharge from the hospital and three months after surgery. This ancillary study was reported separately and the secondary end point was the Nitinol clip position on the aorta. The closure of the puncture aortic hole and the

primary end point were obtained in all cases. The procedure did not generate undue morbidity and there was no device-related adverse event. The CT scan analysis demonstrated a good anchoring of the clip onto the aortic wall even if the clip was observed in an asymmetric position in 3 patients; 3 months after surgery, the position of the clip remained stable, and secondary end point was obtained in all cases. ***Self-sealing antegrade cardioplegia system for video-assisted cardiac surgery: Preliminary results. Innovations 2007; 2:209-212.***

3) Evaluation of Mitrax's. The Mitrax's retractor is a pattern cut polymer sheet, self-expanding and auto-adjusting, which once deployed, generates a conical volume. It works as an "expander" and maintains the left atrium wide open in a symmetrical way. The effectiveness of Mitrax's was evaluated in 62 patients who consecutively underwent a video-assisted mitral valve procedure. The global satisfaction index (from 0 to 5) was 4.6 ± 0.5 , demonstrating the effectiveness of the device which provides optimal exposure and excellent direct vision; easy to use, no distortion of the mitral apparatus, no atrial folds, and no aortic valve distortion are the main advantages of Mitrax's. Size standardization is its main drawback and may involve mismatch with an incomplete exposure of the mitral valve when a small left atrium is associated with a dilated annulus. ***Evaluation of a new left atrial retractor for minimally invasive mitral valve surgery. J Thorac Cardiovasc Surg 2011; 141: 297-299.***

These studies demonstrated that it is possible to make the technique of minimally invasive video-assisted mitral valve surgery easier and more reproducible with an instrumental platform adapted to a surgical micro environment. They have contributed to its diffusion.

4) Comparative analysis of minimally invasive techniques for LAD revascularization with mammary artery graft (Port Access, MIDCAB, TECAB). In a prospective study, we have analysed the results of three minimally invasive techniques used for the revascularization of isolated LAD lesion, corresponding to three different concepts: Port-Access surgery (PA-CABG), the most invasive technique, based on on-pump CABG with mini-thoracotomy and hand-sewn anastomosis; totally endoscopic coronary artery bypass grafting (TECAB), the less invasive technique, based on off-pump and closed chest surgery with robotic assisted anastomosis; minimally invasive direct coronary artery bypass (MIDCAB) based on off-pump CABG with mini-thoracotomy,

hand-sewn anastomosis, and video or robotic assistance for mammary harvesting. Over a decade, 160 patients were included; there was no randomization and inclusion according to the technique performed was period related. At 3-month postoperatively, the end-point of LAD reintervention were PA-CABG, 0%; MIDCAB, 1.8%; TECAB, 10%; $p=0.01$. This significant difference confirmed a surgical intuition: Anastomoses done on arrested heart have better patency than those done on beating heart; hand-sewn anastomoses under direct vision have better patency than closed chest robotic assisted anastomoses. However, modifications of the anastomosis technique allowed to improve the patency in TECAB group: after the occurrence of post-anastomotic dysfunction cases, distal LAD occlusion during anastomosis was abandoned and this type of failure disappeared; anastomotic dysfunction disappeared also when we changed from running suture to uclips suture which provided a 100% patency. Nevertheless, we have observed three cases of LITA occlusion with an opened LAD anastomosis, showing the difficulty to guide and to check the mammary graft in a closed chest procedure. At 3-year, reintervention-free survival was significantly lower in the TECAB group: PA-CABG, 100% ; MIDCAB, $98\pm5\%$; TECAB, $88\pm8\%$; $p<0.05$. The difference was directly related to primary bypass failures.

This study confirmed that minimally invasive LAD grafting was safe and effective. TECAB is associated with a higher rate of early bypass failure and reintervention. MIDCAB is still the most reliable surgical technique for isolated LAD grafting and the least cost effective. ***Is there an optimal minimally invasive technique for left anterior descending coronary artery bypass? J Cardiothorac Surg 2011; 6: 37.***

Conclusion. This report sums up an experience over a decade in a surgical field in persistent progress according to the improvement of the technology and the will of the surgical community. Video-assisted mitral valve surgery is now established as a new standard, after 15 years of effort. Robotic cardiac surgery is making good progress; its future is maybe depending on lighter and less expansive systems, as hybrid concept with the association of 3D column and motor driven instruments. The occurrence of efficient anastomotic devices would be useful too.

MOTS-CLES – KEY WORDS.

Cardiac Surgery, Minimally invasive Surgery, Robotic Surgery, Mitral Valve Surgery, Coronary Bypass Grafting, MIDCAB, TECAB, Port Access, New Technology.

INTITULE DU LABORATOIRE.

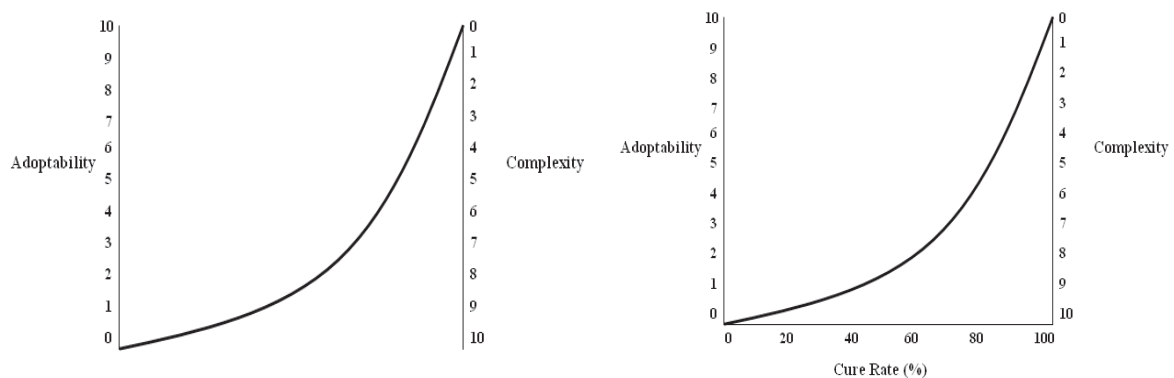
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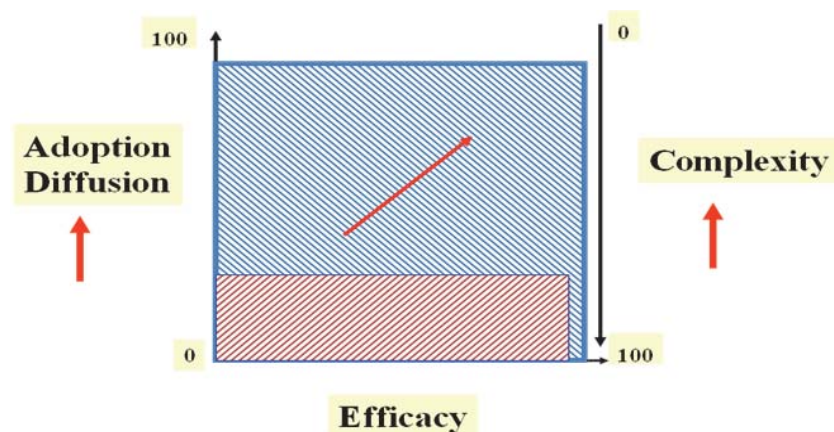
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INTRODUCTION.

Il existe une relation étroite entre la complexité d'une nouvelle technologie et son taux d'adoption ou d'utilisation ; relation qui n'est pas influencée par l'efficacité de la technique elle-même. Ainsi, si une nouvelle technique, même très efficace, est trop complexe, elle demeure peu utilisée avec une diffusion limitée.



Diminuer la complexité d'un nouveau concept ou d'une technique est donc nécessaire afin de la rendre accessible et reproductible par le plus grand nombre. Cela passe souvent par une amélioration des outils nécessaires à sa réalisation.

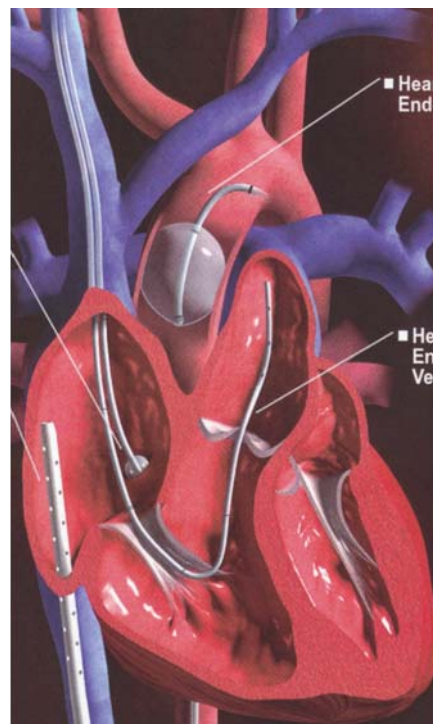
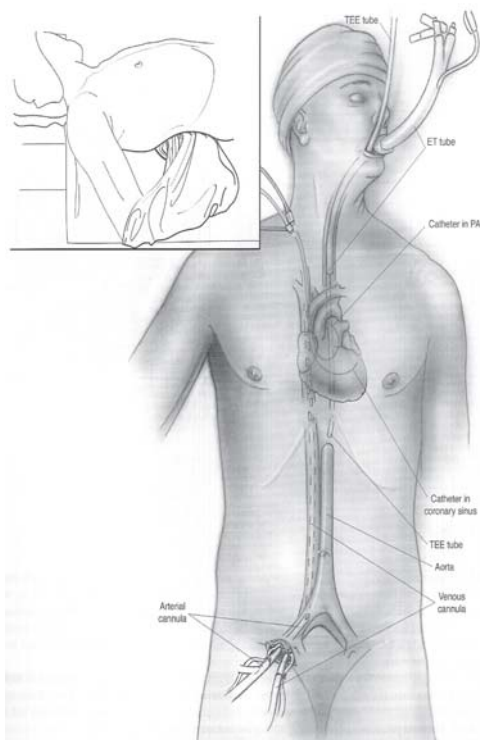


En chirurgie cardiaque, les techniques mini-invasives ont été développées à la fin des années 1990 et nous avons été parmi les premières équipes en Europe à les utiliser et à les évaluer. Tout d'abord pour la chirurgie de la valve aortique et nous avons exploré l'intérêt de la mini-sternotomie comme voie d'abord pour le remplacement valvulaire

aortique en alternative à la sternotomie totale (1,2); puis pour la chirurgie mitrale ou plus globalement la chirurgie atriale gauche ou droite, dès que la plateforme « Port-Access » a été disponible sur le marché européen (3).

Le concept initial reconnu sous cette appellation « Port-Access », et utilisant la plateforme prénommée repose sur 3 principes (4):

- Réaliser le geste de chirurgie cardiaque par une mini-thoracotomie centrée sur la lésion à traiter, en alternative à une sternotomie médiane,
- Conduire la CEC, le clampage aortique et la cardioplégie à partir des vaisseaux fémoraux grâce à des canules artérielles et veineuses spécifiques et un ballon d'occlusion endo-aortique ou « endo-clamp »,
- Optimiser le geste chirurgical par la vidéo-assistance et l'utilisation d'une instrumentation endoscopique spécifique.

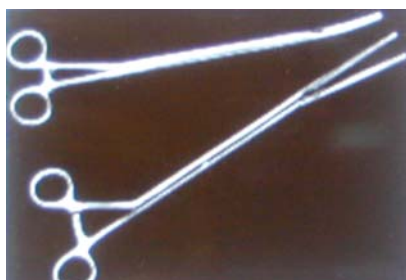


Cette technique s'est avérée performante, permettant de miniaturiser la voie d'abord chirurgicale (5) et nous l'avons appliquée dès 1997 (6) à la chirurgie atrio-ventriculaire valvulaire (mitrale ou tricuspide), tumorale (myxome ou fibroélastome), ou septale (CIA). Après une période d'engouement de la communauté chirurgicale et malgré des résultats encourageants (7,8) sans augmentation du risque opératoire, sans altération du résultat anatomique des gestes réparateurs et avec un bénéfice esthétique évident,

l'intérêt pour cette technique a décliné conduisant parfois à l'arrêt des programmes dans certains centres, et cela pour 3 raisons principales en plus d'un certain conservatisme de la profession et du manque de formation des chirurgiens cardiaques aux techniques de vidéo-chirurgie :

- La complexité de la CEC endo-vasculaire,
- Un risque vasculaire inhérent à l'endo-clamp avec un taux de dissection aortique rétrograde d'environ 1%,
- Un surcoût par procédure d'environ 1500 euros.

Si la technique « Port-Access » est devenue confidentielle au début des années 2000 et ne restait pratiquée que dans quelques centres, elle avait donné naissance au concept plus général de chirurgie mitrale mini-invasive vidéo-assistée qui a vite connu un regain d'intérêt grâce au développement d'un clamp métallique trans-thoracique (9), dit clamp de « Chitwood », permettant de s'affranchir de l'endoclamp, de sa morbidité vasculaire, de sa complexité et de son coût. Comme beaucoup d'équipe travaillant dans cette nouvelle direction de la chirurgie cardiaque, nous avons très rapidement adopté cet instrument dédié et continué à n'utiliser l'endoclamp que dans des indications très spécifiques comme les réinterventions.

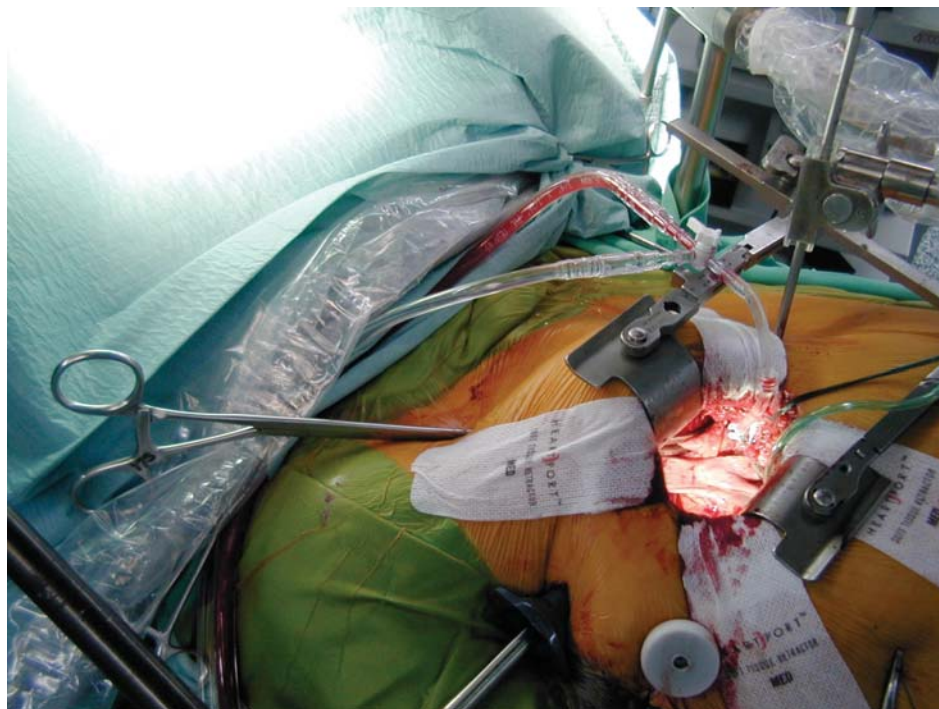


Le grand mérite de cette évolution technique a été de rendre accessible et reproductible la technique de chirurgie mitrale mini-invasive vidéo-assistée et de favoriser sa diffusion et son adoption. Néanmoins ce clamp présente plusieurs inconvénients :

- un clamping asymétrique avec risque de pincement ou d'écrasement de la paroi de l'aorte,

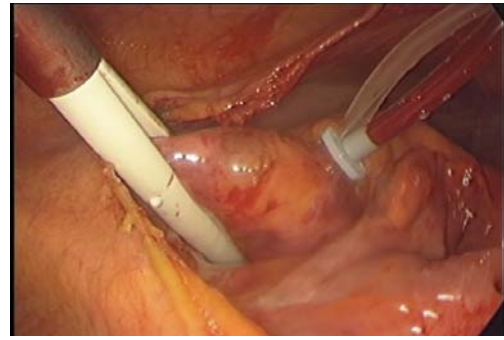
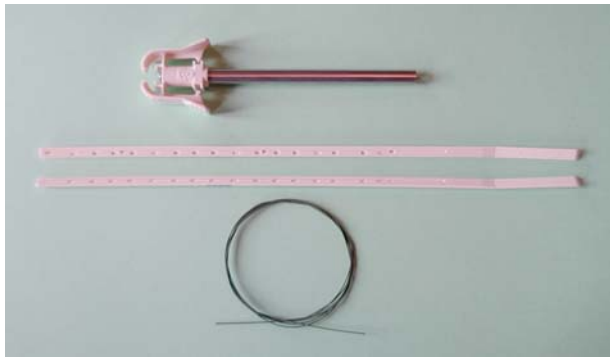
- une extrémité fine et traumatisante avec un risque de plaie ou de contusion de l'auricule gauche et/ou de l'artère pulmonaire droite,
- un encombrement extérieur important avec des possibilités de conflits soit avec la caméra soit avec les mains du chirurgien,

L'utilisation de ce clamp et le retour d'une certaine façon aux techniques traditionnelles de clampage de l'aorte a reposé le problème de l'accès à l'aorte ascendante pour le positionnement de la canule de cardioplégie, avec son risque hémorragique difficile à contrôler dans un mini- environnement, et souvent considéré comme un obstacle à la diffusion de la technique.

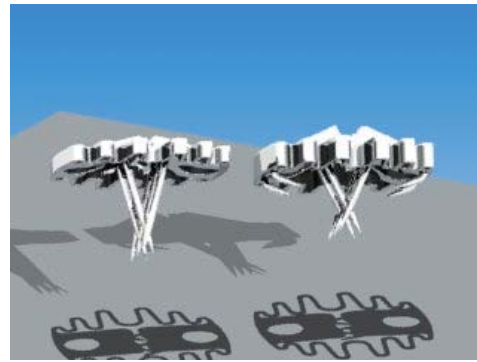


Les inconvénients relatifs de ce système de clampage et de cardioplégie nous ont conduits à participer à l'évaluation clinique de nouveaux outils dédiés:

- un nouveau clamp original et non traumatisant, le « Portaclamp »,

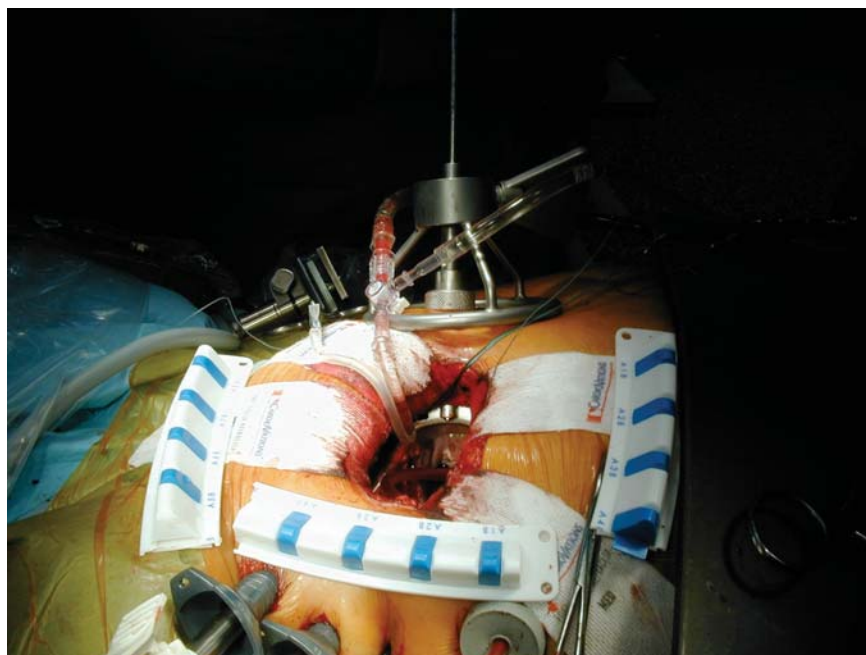


- un système de clip auto-suturent pour la canule aortique de cardioplégie, le « Portapleg ».



Un autre problème inhérent à la voie d'abord utilisée, relevé par tous les chirurgiens et que nous avons identifié dès le début de notre expérience, est la difficulté d'exposition de la valve mitrale au cours de cette chirurgie vidéo-assistée. Le matériel ancillaire d'écarteur mitral dédié et à disposition, est constitué d'une palette intra-atriale tenue par un axe trans-thoracique, réalisant par traction vers le haut une élévation non seulement du septum inter-atrial pour l'exposition de la valve mitrale, mais également des parois latérales et postérieure de l'oreillette gauche qui viennent comme un rideau cacher la valve mitrale et rendent son accès plus difficile (10). Ces écarteurs ont également l'inconvénient de déformer l'anatomie de la valve mitrale, ce qui compromet son analyse pour une chirurgie réparatrice, et de créer une certaine distorsion de la

valve aortique, obligeant à changer l'exposition en cas de perfusion itérative de cardioplégie.



Les inconvénients relatifs de ce système d'écarteur mitral nous ont conduits à participer au développement et à l'évaluation clinique d'un système innovant et original d'exposition de la valve mitrale le « MitraXs ».

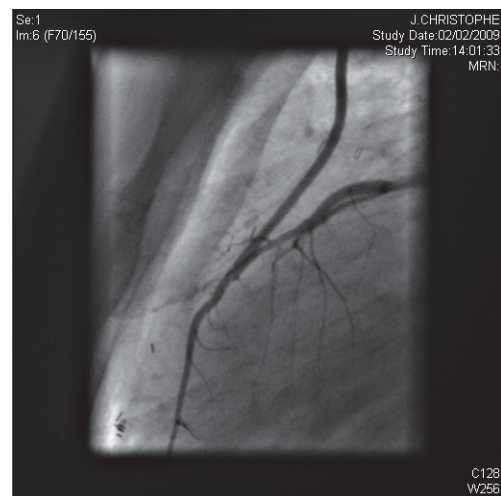


Ce travail reprend les études et les publications scientifiques réalisés sur cette thématique dont le but initial était de développer et/ou d'évaluer des outils spécifiques, dédiés à la chirurgie mitrale mini-invasive, susceptibles d'apporter une solution ou une amélioration à des problèmes identifiés et non résolus auxquels les chirurgiens faisaient

face tous les jours et s'adaptaient par nécessité. L'objectif était de rendre cette technique plus accessible et plus reproductible pour une meilleur diffusion et adoption.

De façon concomitante à ces travaux en chirurgie valvulaire mini-invasive, nous avons également développé un programme mini-invasif en chirurgie coronaire pour les revascularisations par greffon mammaire de l'IVA. Tout d'abord avec la plateforme « Port-Access », pour des revascularisations par mini-thoracotomie sous CEC et cœur arrêté (11), puis selon la technique « MIDCAB » (minimally invasive direct coronary artery bypass) pour des revascularisations par mini-thoracotomie sans CEC et à cœur battant (12), afin de s'affranchir de la plateforme « Port-Access » et de son surcoût. En 2003, notre service a été doté d'un robot chirurgical Da Vinci que nous avons utilisé de façon préférentielle pour la chirurgie des coronaires sans CEC, à cœur battant avec pour objectif la réalisation de pontage coronaire mammaire totalement endoscopique ou TECAB (totally endoscopic coronary artery bypass), concept ultime en chirurgie mini-invasive (13,14).



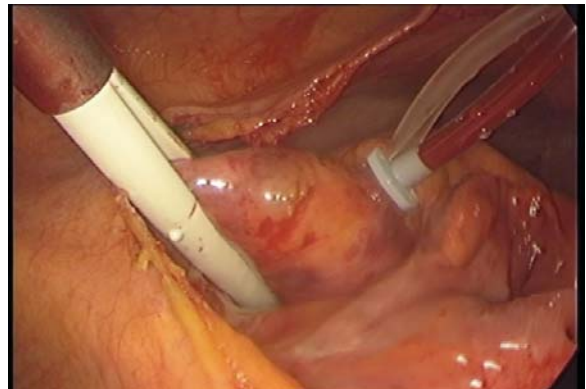


La chirurgie coronaire robot-assistée nous a ainsi conduits à une adaptation des outils disponibles à ce nouvel environnement chirurgical. Nous avons utiliser et adapter les

techniques de sutures développés de façon spécifique pour la chirurgie coronaire sans CEC à cœur battant (shunt coronaire, technique de clampage proximal, système de stabilisation par succion), ce qui nous a permis dès le début de notre expérience d'atteindre notre objectif et de réaliser en clinique le premier TECAB trois semaines après l'acquisition du robot, puis de réaliser le premier cas publié de double pontage mammaire TECAB (15). Ultérieurement nous avons introduit les anastomoses robot-assistées par Uclips afin de pallier aux inconvénients des anastomoses par suture continue en surjet. In fine, sur les bases et les acquis d'une même plateforme technique nous avons pu comparer les résultats cliniques des anastomoses robot-assistées par voie endoscopique et des anastomoses manuelles par mini-thoracotomie, avec ou sans CEC, dans une population homogène de patients afin de déterminer si une technique mini-invasive de revascularisation isolée de l'IVA était optimale. Cette étude est également rapportée dans ce travail.

Partie 1. Evaluation du « Portaclamp ».

Le Portaclamp a été développé par la société Cardio Life Research (CLR) à partir d'une idée originale du Dr Didier Decannière. Il a été conçu pour un clampage de l'aorte ascendante direct, trans-thoracique et atraumatique en alternative à l'endo-clamp ou au clamp métallique type Chitwood. Il comporte deux baguettes identiques en plastique polymère et de section semi-lunaire qui sont introduites de façon séquentielle par un port thoracique 11 mm et positionnées de part et d'autre de l'aorte au niveau du sinus de Theile. Leur partie proximale au contact de l'aorte est atraumatique et délimitée par un ergot externe de repérage. L'effet de clampage vasculaire est obtenu par un mandrin métallique introduit autour d'elles puis poussé progressivement jusqu'au contact des ergots délimitant leur zone de clampage. Initialement ces deux baguettes pouvaient être chargées sur un guide introduit préalablement dans le sinus de Theile et autour des gros vaisseaux, afin de faciliter leur placement ; cette technique de positionnement a été rapidement abandonnée car compliquée et peu utile.



Nous avons participé à l'étude pilote multicentrique étudiant la sécurité et l'efficacité de ce système de clampage. Cette étude clinique a porté sur 20 patients opérés de chirurgie cardiaque sous CEC et a confirmé la simplicité d'utilisation du système, son efficacité et l'absence de morbidité ou complication induite. *Early experience with a new aortic clamping system designed for port access cardiac surgery: The Portaclamp. Heart Surgery Forum 2004, 7: E240-E244.*

Early Experience with a New Aortic Clamping System Designed for Port Access Cardiac Surgery: The PortaClamp

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Dr. de Cannière



ABSTRACT

Background: We report a clinical study to demonstrate the feasibility and safety of a new aortic crossclamping concept for use in port access cardiac surgery. The limited access to the aorta in minimally invasive cardiac surgery mandates specific clamping modalities, which entail specific limitations, drawbacks, and costs. Therefore a new autoguided, extravascular, and atraumatic clamping system (PortaClamp) was developed to facilitate port access surgery while potentially avoiding the complications and costs inherent to endoluminal clamping or "blind" crossclamping.

Methods: Twenty patients underwent various cardiac operations under cardiopulmonary bypass and aortic crossclamping with the PortaClamp between February and September 2003. The method of aortic clamping is described and the operative course and clinical outcome of the patients are reported as surrogates of feasibility and safety.

Results: The average time to position the clamp was 196 ± 75 seconds. Crossclamping through a 10-mm port or incision was achieved successfully, enabling cardiac arrest throughout the procedure in every patient. No patient presented with cardiovascular accident or transient ischemic attack, aortic dissection, or hematoma. Intensive care unit times were 12 ± 3 hours; length of stay was 7.2 ± 1.1 days.

Conclusion: From this early experience we conclude that the PortaClamp system is safe and can effectively be used to crossclamp the aorta inexpensively to facilitate port access cardiac surgery. Further comparative studies with the existing systems are warranted to confirm that the atraumatic design provides further benefit.

INTRODUCTION

Despite increasing evidence that port access surgery is a beneficial option in numerous indications [Casselman 2003], its rate of adoption remains low in the surgical community. This situation has multiple causes.

First, most of the operations can be performed with satisfactory results through sternotomies. It is difficult to demonstrate much incremental added value to the existing mature and efficient procedures, such that the benefits of port access are regarded by some surgeons as marginal or insufficient to change their practice in the absence of large-scale randomized studies.

Second, cardiopulmonary bypass and cardiac arrest themselves require experience and carry inherent risks and costs [Wimmer-Greinecker 1999] in the port access environment. Thus the additional investment in time and energy in the development of the skills required by the port access technique itself for a given intervention (eg, mitral repair, atrial-septal defect closure) is regarded by many as a step back. If femoral cannulation can easily be performed, aortic crossclamping and cardioplegia delivery are made awkward by the limited access to the ascending aorta.

These disadvantages have led to the design of purpose-built devices. Aortic clamping is performed either with an endovascular balloon (EndoClamp Cardioversions; Ethicon, Cornelia, GA, USA or Remote Access Perfusion cannula; Estech, Danville, CA, USA) or with the Chitwood clamp (Scanlan International, St. Paul, MN, USA) [Aybeck 2000]. The endovascular balloons necessitate continuous monitoring, may generate specific life-threatening complications, and are associated with a significant increase in operative cost [Wimmer-Greinecker 1999]. The Chitwood clamp represents a cost-effective and readily available alternative but requires a remote and partially blind maneuver to crossclamp the aorta, a procedure that carries the risk of injuring a cardiac structure without direct access to bail out. Because of these drawbacks, an alternative clamping system has been designed to enable safe, easy, and steady extraluminal crossclamping of the aorta with the objective of avoiding the specific difficulties and risks of the existing systems. Here we describe the PortaClamp and report our early clinical experience with this device.

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METHODS

Between February and September 2003, 20 patients underwent various cardiac procedures on cardiopulmonary bypass with aortic crossclamping and cardioplegia (Table). We report the surgical procedure, operative times, and patient outcomes. All patients provided written informed consent in concordance with a protocol approved by the ethics committee of Erasme Hospital at Brussels University.

Surgical Procedures

With the patient under general anesthesia with transesophageal echocardiography (TEE) monitoring, a sternotomy ($n = 4$), ministernotomy ($n = 3$), or right anterolateral minithoracotomy ($n = 13$) is performed and cardiopulmonary bypass instituted either centrally or peripherally. A 5-mm port (Thoracoport, US Surgical, Norwalk, CT, USA) is positioned in the 2nd or 3rd intercostal space laterally behind the anterior axillary line. The PortaClamp guidewire is inserted through this port in the transverse sinus through a small (2–3 cm) pericardial incision between the aorta and the superior vena cava (SVC) (unless the pericardium had been widely opened in the case of central cannulation). The guidewire is pushed into the sinus (eventually with the help of a forceps in the vicinity of the SVC) perpendicularly to the axis of the aorta, until it pops up along the anterior aspect of the pulmonary artery (PA) and aorta (Figure 1). The proximal end of the guidewire is retrieved and pulled back through the same port with a shafted forceps while the distal end is pushed forward. At this point in time the guidewire encircles the aorta and pulmonary artery and the Thoracoport is eventually withdrawn (Figure 1). After cardiopulmonary bypass is instituted, 2 clamping jaws are inserted sequentially in front of and behind the aorta. Those clamping jaws follow the guidewire as they present with an axial lumen in which the 2 free ends of the guidewire are threaded (Figure 2). The clamping jaws are

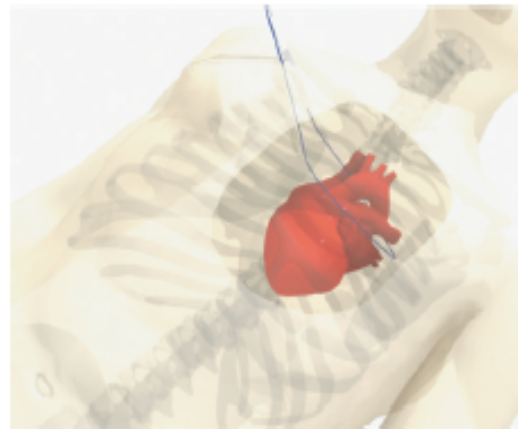


Figure 1. Procedural step 1: guidewire positioned around aorta and pulmonary artery.

pushed freely around the aorta, and eventually also around a part of the PA without risk of damaging any cardiovascular structure. A marking shows the surgeon that the clamping position has been reached. A cylindrical squeezing tube (Figure 3) is placed around the 2 clamping jaws and gently slid toward the aorta until it reaches a stop, to crossclamp the vessel (Figures 4 and 5). The guidewire does not play any role in the clamping mechanism and is left loose to avoid a strangulation effect of the PA. The unclamping is performed by gently withdrawing the squeezing tube. The jaws have been designed to ensure a homogenous clamping force and pressure along the clamping area and to avoid the "crab forceps effect," which is encountered with the Chitwood clamp and other external clamps. A broader and smoother clamping surface enables the delivery of a smaller clamping pressure to the aortic wall for any given clamping force.

Antegrade cardioplegia was delivered through a regular cardioplegic needle (DLP standard aortic root cannula;

Procedures and Demographics

Procedure	
Coronary artery bypass graft/sternotomy	3
Aortic valve replacement/sternotomy	1
Aortic valve replacement/ministernotomy	3
Mitral valve repair/right minithoracotomy	9
Atrial-septal defect/right minithoracotomy	2
Myxoma/right minithoracotomy	1
Demographics	
Sex, M/F	13/7
Age	71.2 \pm 8.6 y
Peripheral atheroma	6
Diabetes	5
Hypertension	7
Renal failure	3
Crossclamp time	65 \pm 28 min
Cardiopulmonary bypass time	82 \pm 35 min
Intensive care unit time	16.8 \pm 12 h
Length of stay	7.2 \pm 2.1 d



Figure 2. Clamping jaws with the axial lumen in which the 2 ends of the guidewire are threaded.



Figure 3. Clamping ("squeezing") tube with locking handle.

Medtronic, Tolochenaz, Switzerland) that was eventually inserted through the working incision: small anterolateral thoracotomy or sternotomy. The needle was secured by a purse string pledgetted suture and a tourniquet. No bleeding occurred at the puncture site.

RESULTS

Four cases were performed with sternotomy in order to verify the adequacy of the clamping function with the ability to convert the procedure in the event of a device malfunction or complication such as aortic hematoma or dissection. The next 16 cases were performed through right minithoracotomies ($n = 13$) or ministernotomies ($n = 3$). The time to position the clamp, including the port placement, pericardial incision, guidewire, and jaws insertion and clamping decreased steeply from 370 to 127 seconds with increasing experience (mean 196 ± 75 seconds). Satisfactory crossclamping, as demonstrated by a complete heart arrest throughout the entire clamping period, was achieved in every single case without need for repositioning. In only 1 case a recurrence of some electrical activity during crossclamp occurred and mandated reiteration of antegrade cardioplegia. The completeness of occlusion was further verified by direct vision in cases of proximal aortotomy (4 aortic valve replacement and 3 coronary artery bypass grafts necessitating proximal venous



Figure 4. PortaClamp in place during mitral valve surgery.



Figure 5. Schematic representation of the clamping mechanism in place.

anastomosis performed on the crossclamped aorta). TEE and visual inspection of the aortic clamping site at the end of operation showed no lesion or even marking of the aortic wall at the site of clamping. All the patients recovered uneventfully. No complications occurred in this group, namely no patient experienced transient ischemic attack or stroke. Mean intensive care unit stay was 0.7 ± 0.5 days, mean length of hospital stay was 7.2 ± 2.1 days.

COMMENT

The present pilot study shows that port access aortic crossclamping is feasible, stable, and reproducible with the new dedicated PortaClamp system. This procedure does not generate undue morbidity.

The clamping maneuver is safe, fast, and easy and does not require a long learning process. To the best of our knowledge it has been reported only once in the literature as a technology enabling a new minimally invasive approach to aortic valve replacement [Gersak 2003].

The limited access to the aorta in port access cardiac surgery has mandated the design of new clamping modalities because the insertion of a "classical" clamp was impossible. New technologies developed include endoluminal clamping systems and the Chitwood clamp. Those systems have demonstrated their usefulness and validity as platforms enabling port access cardiac surgery [Casselman 2003], but they carry specific complications and drawbacks.

The endoaortic clamping mode entails specific risks for the benefit of exerting its action without necessitating a direct intrathoracic introduction. Those specific risks are rupture of the dedicated aortic cannula (Heartport), endocamp balloon rupture, balloon migration toward the left ventricle or toward the brachiocephalic trunk, and aortic dissection. Besides those specific risks, which are due to the catheterization technique, there is a risk of particulate embolism into the systemic circulation as in any clamping modality [Barbut 1994].

Balloon rupture is an event that is reported in almost every Heartport series [Hesselvik 1999]. The consequence of a bal-



Figure 6. Crab forceps effect of articulated clamp.

loon rupture is a sudden restart of the heart leading to either an immediate replacement of the balloon, which is risky and technically challenging and performed only by several experienced teams in the world, or an urgent conversion to sternotomy in order to crossclamp the aorta and readminister cardioplegia. In the Estech system, the balloon is part of the cannula, and its rupture leads to an untreatable situation because the cannula cannot be removed and the heart, eventually opened, cannot be restarted. In this case urgent conversion is the only option. There are no clear-cut figures to determine the exact incidence of these complications with either endoballoon system (Heartport or Estech).

Because of the compliance of the aortic wall and/or a pressure decrease in the endocamp, the endoaortic balloon can migrate and occlude the brachiocephalic trunk [Grocott 1998, Schneider 1998]; the monitoring of this complication, which may provoke ischemia to one hemisphere of the brain, requires specific invasive insertion of a intraarterial catheter in the radial artery in every single patient.

Aortic dissection may be the Achilles heel of endovascular clamping; the incidence of this rare but catastrophic complication of endovascular clamping has been part of the driving force to develop an alternative such as the PortaClamp. The endoarterial maneuvers such as sequential guidewires and retrograde introductions coupled with the retrograde blood flow are prone to tear apart the fragile monocellular intimal layer or atheromatous plaques and trigger aortic dissection.

A higher incidence of aortic dissection is classically reported when endocamp is used. It has been reported to be as high as 3.9% in early series by Mohr and colleagues [Mohr 1998]. More recently Vanermen et al [2000] reported 2 aortic dissections (1 lethal) in a series of 121 patients who underwent minimally invasive mitral valve repair (1.65 % compared to an expected 0.1 % [Hagl 2000]).

The Chitwood thoracoscopic clamping mode also entails specific risks, which balance the benefit of enabling a minimally invasive, eventually endoscopic, intervention. Those risks are inherent to the difficulty of adequately positioning the forceps without visualization of the entire aortic and pul-

monary artery structures and the crab forceps effect (Figure 6). If the clamp is positioned too deeply, there is a risk of hurting the PA; if the clamp is not positioned deeply enough, the aorta is insufficiently crossclamped, making it impossible to perform the operation or leading to insufficient heart protection during the operation.

Felger et al [2001], presenting their experience of minimally invasive mitral valve repair with the Chitwood clamp, reported the occurrence of 1 stroke in a series of 124 patients (0.8%). This figure corresponds to the expected incidence of stroke reported in the STS (Society of Thoracic Surgeons) database. Specific complications have been recorded only as case reports.

The above-mentioned risks, coupled with a significant cost increase and the need for the entire surgical team to undergo a complex learning processes, have contributed to a relatively low adoption of port access techniques. We therefore felt there was a need to develop an alternative clamping method that would be fast, safe, reliable, and cost-effective. The guided feature of the PortaClamp avoids the risk of damaging the vascular structures adjacent to the clamping zone of the aorta (ie, the SVC, main PA, and right PA), which is not the case with the currently available technologies for aortic occlusion. The PortaClamp brings the surgeon back to the well known paradigm of extraluminal crossclamping, obviating the need for invasive monitoring of the right radial artery pressure and the necessity of continuous monitoring and specific attention paid to the clamping throughout the operation. The results of the present study using the PortaClamp show that clamping is feasible, reproducible, and does not generate undue mortality or morbidity. We believe that it greatly facilitates port access cardiac surgery by enabling the surgeon to focus on the objective of the intracardiac maneuver. Only redo cases in which adhesions preclude the passage of the guidewire cannot be dealt with by the method. Further data is required to demonstrate that the atraumatic design providing a more homogenous clamping force and a broader clamping area throughout the clamping zone leads to a lower incidence of injury to the aortic wall.

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De façon concomitante, notre équipe a réalisée sous ma direction et dans le cadre de l'unité INSERM E0226 du Pr Ovize, une étude expérimentale chez le porc afin d'analyser les effets histologiques sur la paroi de l'aorte des trois techniques de clampage utilisées en chirurgie mini-invasive : l'endo-clamp, le clamp métallique type Chitwood et le Portaclamp. L'étude a porté sur 15 porcs. L'analyse histologique a révélé une atteinte majeure de l'endothélium aortique induite par l'endo-clamp ; des lésions non spécifiques de la média externe et de l'adventice ont été observées indépendamment du clamp utilisé et de façon similaire. ***Comparison between 3 aortic clamps for video-assisted cardiac surgery : A histological study in a pig model. Heart Surgery Forum 2006, 9: E657-E660.***

Comparison between 3 Aortic Clamps for Video-Assisted Cardiac Surgery: A Histological Study in a Pig Model

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ABSTRACT

Objectives. To assess histological traumatic effects of aortic clamps used in video-assisted surgery, an experimental study was undertaken in a pig model, comparing the Portaclamp, Endoclamp, and a metallic clamp.

Material and Methods. In 3 groups of 5 pigs each, the descending aorta was exposed through a posterolateral left thoracotomy. External clamps (Portaclamp and metallic clamp) were positioned at the middle of the aorta. Endoclamps were inserted at the top of the descending aorta through a small purse and inflated lower. After 60 minutes of clamping, the clamp was removed and the animal reperused for 60 minutes. It was then sacrificed and the descending aorta was harvested for blind histological study using hematoxylin-eosin staining of 4 samples per animal: A, before the clamping spot; B, at the clamping spot; C, after the clamping spot; D, a remote sample as control.

Results. In the Portaclamp and metallic clamp groups, there were no lesions of the intima in all aortic samples. In the Endoclamp group, severe lesions of the intima were observed on the clamping spot: endothelium crushing with flattening of cell nucleus (3/5) or endothelium stripping with vanishing of cell nucleus all gathered in 1 point (2/5). Only spongy lesions (clearance between fibers) located on the external third of the media and moderate inflammatory lesions of the adventice were observed with a random distribution in aortic samples without difference between groups.

Conclusions. This study reveals the impressive lesions of the aortic intima due to the Endoclamp. The nonspecific lesions observed in media or adventice may be related to the surgical trauma of the procedure.

INTRODUCTION

Since the mid 1990s, video-assisted cardiac surgery has gained interest along with the development of new cardiopulmonary bypass (CPB) techniques and, more recently, robotic assistance. Mitral and septal surgery, as well as coronary surgery, became possible with the introduction of endo-CPB systems that allow cardiac assistance and arrest, owing endovascular aortic clamping to fluoroscopy- or transesophageal echocardiography (TEE)-guided balloons [Galloway 1999]. In parallel, standard femoro-femoral CPB is still used, and in this case, aortic clamping is performed with a solid body transthoracic clamp passed through a port [Chitwood 1997]. Although some studies have already compared the different clamping techniques effect on postoperative morbidity and mortality, there is no analysis of the direct effect of the different clamping techniques upon the aortic tissue itself [Reichenspurner 2005].

The aim of the present study was to analyze the effect of 3 different vascular clamps used in video-assisted cardiac surgery on the aortic wall in an experimental model in a pig.

MATERIAL AND METHODS

Animals

Adult pigs weighing approximately 35 kg were used. All animals received human care in compliance with the "Guide for the Care and Use of Laboratory Animals" published by the US National Institutes of Health (NIH Publication No. 85-23, revised 1996). The experimentation did not receive support from any company.

General Surgical Preparation

Pigs were premedicated with 0.25 mL/kg intramuscular 2% xylazine (Rompun; Bayer HealthCare, West Haven, CT, USA). Venous access was obtained through a 24-gauge IV catheter placed in a marginal ear vein. Anesthesia was induced and maintained using intravenous nesdonal (20 mg/kg and 20 mg/kg per hour, respectively). A continuous perfusion of hydroxyethyl amidon (6%, 15 mL/h) was started and maintained throughout the experiment. After general heparinization (500 U/kg), the animals were ventilated through a standard tracheal intubation at a rate of 3.5 L/min and 60%

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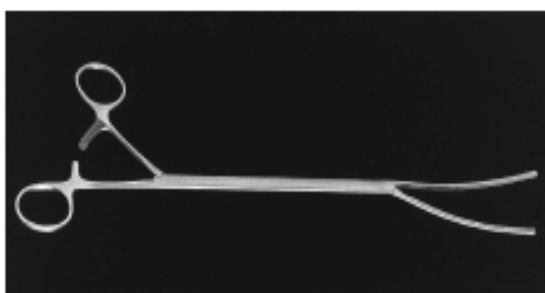


Figure 1. View of the crocodile-like jaws of the Chitwood clamp.

oxygen fraction. The expired partial CO_2 was measured after equilibration. A 20-gauge catheter was placed in the right carotid artery after exposition for continuous monitoring of systemic mean arterial pressure (MAP) and heart rate (BPM). Another catheter was inserted through the internal jugular vein for central venous pressure control. A posterolateral left thoracotomy was performed in the eighth intercostal space and the ninth rib was removed for better exposure. The descending aorta was dissected. A prosthetic 10-mm Dacron shunt was placed between the proximal and the distal segments of the descending aorta to avoid hemodynamic instability during clamping. These end-to-side sutures were made under lateral clamping, using 4/0 polypropylene sutures. The clamp was positioned between the 2 lateral anastomosis of the shunt in a no-touch aortic region, and the aorta was totally occluded.

Experimental Protocol

Pigs were randomized into 3 experimental groups of 5 animals each. In the metallic clamp group (TTC), pigs were

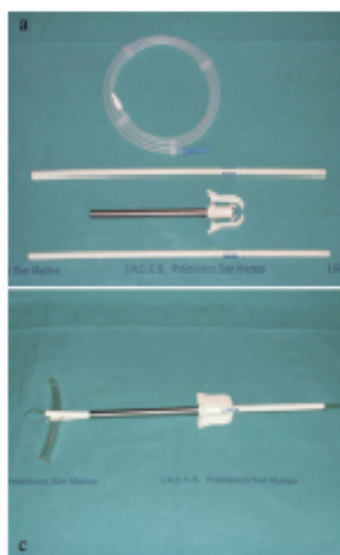


Figure 2. View of the Portaclamp. Note the guide wire that allows easy positioning through the transverse sinus.

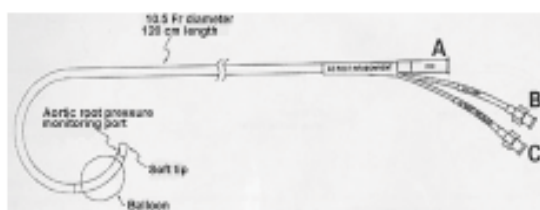


Figure 3. View of the Endoclamp. Two versions allowing direct or femoral clamping are available.

subjected to 60 minutes of aortic occlusion with a Chitwood clamp (Scanlan, St. Paul, MN, USA; Figure 1), followed by 60 minutes of reperfusion. In the Portaclamp group (PTC), animals had 60 minutes of aortic occlusion using the endoscopic Portaclamp (Cardiolife Res, Leuven, Belgium; Figure 2), then 60 minutes of reperfusion. In the Endoclamp group (ENDO), an Endoclamp (Cardioventions, Somerville, NJ, USA; Figure 3) was inserted at the top of the descending aorta through a purse string. It was then inflated between the 2 lateral anastomosis with an inflation pressure maintained between 280 and 350 mmHg. Occlusion and reperfusion were comparable to the 2 previous groups.

Histological Analysis

At the end of the reperfusion period, the animals were sacrificed and the descending aorta was harvested for blind histological analysis, using hematoxylin-eosin staining. The analyses concerned all the circumference of the aortic wall and were made on 4 samples per animal: 1 cm before the clamping place (A), at the clamping place (B), 1 cm after the clamping place (C) and a remote sample as control (D). Histological examinations were focused on the aortic intima, media, and adventice. Samples were classified as normal, stripping, or crushing for the endothelium, normal or spongy for the media, and normal or inflammatory for the adventice.

RESULTS

No significant difference existed between the 3 groups concerning the weight of the animal and the diameter of the aorta. All the procedures were driven until the end of the reperfusion period.

Intima Lesions

We did not observe lesions of the intima in the TTC and PTC groups. In the ENDO group, the intima was normal for points A, C, and D in all animals. At point B, 3 animals presented with endothelium crushing (Figure 4) and 2 had endothelium stripping (Figure 5). We did not observe intima rupture in any case.

Media/Adventice Lesions

Spongy lesions, defined as clearance between fibers, located on the external third of the media, were observed regardless of animal, clamping technique, or location. Moderate inflammation of the adventice was noted with random distribution, without difference between groups and location.

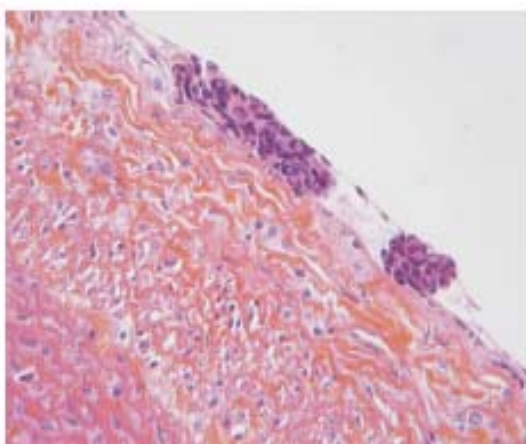


Figure 4. Microscopic aspect of the endothelium in the ENDO group. The endothelial cells are stripped and gathered in 1 point (ES lesions).

We did not observe media break or adventice hematoma. Data are reported in Table 1. The average of normal media in every group is reported in Table 2.

DISCUSSION

Video-assisted cardiac surgery has become a routine technique since the mid 1990s, allowing for the development of different types of interventions, coronary as well as valvular. Because the access to the great vessels is reduced, 2 different strategies were adopted for aortic clamping, endovascular occlusion balloons (Endoclamp; Cardioversions) or transthoracic port-adapted solid clamps [Chitwood 1997; Galloway 1999]. Yet each technique has its own inconveniences. The use of the Endoclamp was associated with aortic dissection in the beginning of the international experience, and solid transthoracic clamps oblige the surgeon to perform cardioplegia in the aortic root through the tiny access space [Chitwood 1997;

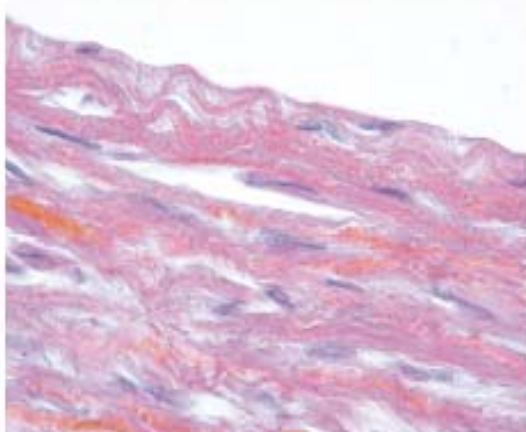


Figure 5. Crushing of the endothelial cells in microscopy. Cell nuclei appear to be flattened (EC lesions).

Table 1. Comparison between Groups for Media/Adventice Lesions*

Animals	Media/Adventice Samples			
	A	B	C	D
TTC group				
1	S/I	S/I	N/I	S/I
2	N/N	N/N	S/N	S/N
3	N/N	S/N	N/I	S/I
4	N/N	S/N	S/I	N/N
5	S/I	N/N	S/I	N/N
PTC group				
6	S/N	N/N	S/N	S/N
7	S/N	S/I	S/I	S/I
8	S/I	N/N	S/I	S/I
9	S/I	S/I	S/I	S/I
10	S/N	N/N	S/N	S/N
ENDO group				
11	N/N	S/I	N/I	N/N
12	S/I	S/N	S/N	N/I
13	N/I	N/N	S/I	S/I
14	S/N	N/N	N/I	N/N
15	N/N	S/I	N/N	S/I

*There was no significant difference among animals, clamping technique, or location of the examined segment. A is a sample taken from a section 1 cm before the clamping zone; B, at the clamping zone; C, 1 cm after the clamping zone; D, remote sample. TTC indicates metallic transthoracic clamp; S, sponge; I, inflammatory; N, normal; PTC, Portadamp; ENDO, endovascular balloon clamp.

Galloway 1999]. Some recent studies have compared the 2 different approaches effect on morbidity [Reichenspurner 2005]. But to our knowledge, there is no reported study dealing with the direct impact of these different clamping techniques on the aorta itself. This experimental study was carried out to analyze the histological lesions on the aortic tissue caused by the different clamps.

In our study, the use of the transthoracic clamps (TTC and PTC animals) did not promote endothelial injury. Fur-

Table 2. Comparison of the Different Normal Samples between the 3 Groups, in Media and Adventice*

	Samples			
	A	B	C	D
No. of normal media				
TTC group	3/5	2/5	2/5	2/5
PTC group	0/5	3/5	0/5	0/5
ENDO group	3/5	2/5	3/5	3/5
No. of normal adventice				
TTC group	3/5	4/5	1/5	3/5
PTC group	3/5	3/5	2/5	2/5
ENDO group	3/5	3/5	2/5	2/5

*A is a sample 1 cm before the clamping zone; B, at the clamping zone; C, 1 cm after the clamping zone; D, remote sample. TTC indicates metallic transthoracic clamp; PTC, Portadamp; ENDO, endovascular balloon clamp.

thermore, the lesions of the external layers of the aorta were not specific. The Chitwood clamp is a "lobster pincer" clamp that does not apply the same pressure equally over the jaws. This could theoretically promote aortic wall injury at the proximal segment of the clamping zone as the distal part of the clamp is less aggressive. Furthermore, the tip of the clamp is responsible for pulmonary artery and left atrial appendage injuries when used in a blind technique [Felger 2001]. In opposition, the Portacamp applies the same pressure equally over the jaws. It is a wire-guided clamp and clamping marks on both jaws avoid collateral lesions during clamping [de Canniere 2004]. In both groups, we did not observe major lesions of the aortic layers such as trans-sections or local dissections. Furthermore, the lesions of the media and the adventice were not specific and were randomly observed in all groups. This could be related to the manipulation of the aortic segments during the surgical procedure.

In the ENDO group, major modifications of the endothelium were observed. We had either stripping or crushing lesions at the clamping zone with no specific damage on the other aortic layers. The endo-aortic clamping technique requires a long learning curve [Casselman 2003]. In the beginning of the international experience, some aortic dissections due to vascular injuries in association with retrograde arterial perfusion were described [Galloway 1999]. Reichenspurner et al have recently reported no difference upon mortality and morbidity between transthoracic clamping using a Chitwood technique and endovascular clamping in a prospective study [Reichenspurner 2005]. Nevertheless, the endovascular clamping technique is useful in case of reoperations that limit the access to the aorta. Mueller et al have analyzed the aortic endothelial lesions using an intra-aortic balloon pump in an experimental model in calves [Mueller 2000]. They found that the endothelium was damaged at the inflation zone facing the balloon. Yet endothelial regeneration could be obtained after 14 days with no sequel. This model is the

nearest to the one we describe here, even if in our approach the compression of the aortic wall by the balloon is permanent during 60 minutes and not intermittent.

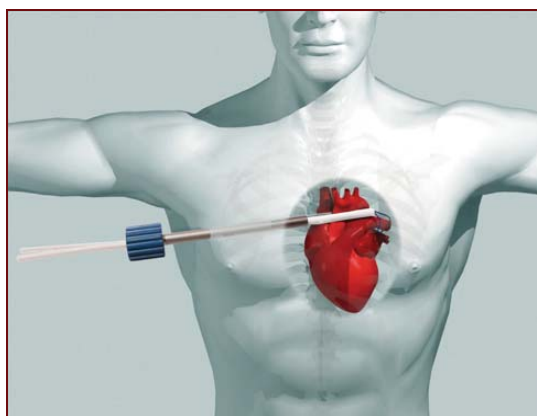
In conclusion, aortic clamping for minimally invasive cardiac surgery can be performed safely with a range of different clamps, external or endovascular. The lesions consecutive to the clamping are basically located at the endothelium in endovascular approach. An experimental study concerning long-term lesions after clamping could be interesting for analyzing the recovery of the endothelium. Both transthoracic and endovascular techniques can widen the operative armamentarium.

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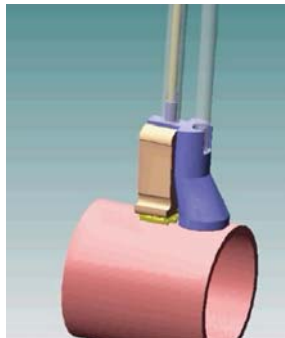
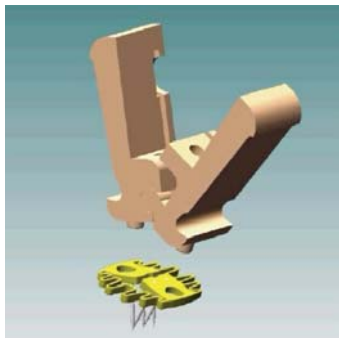
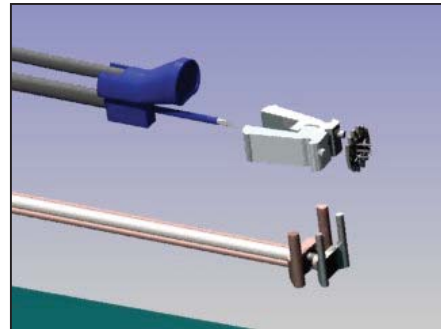
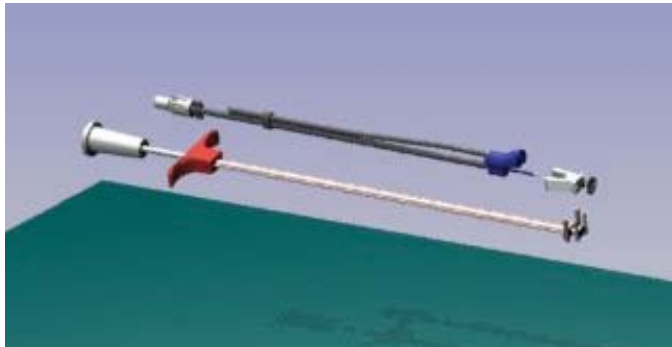
Ces deux études ont permis de valider le concept du Portaclamp et son efficacité sans démontrer un bénéfice réel par rapport au clamp type Chitwood, bien que le clampage symétrique et la largeur des mors plaident en sa faveur, en particulier dans les réinterventions et les aortes fragiles, comme nous l'avons observé ultérieurement.

Une évolution a ensuite été développée avec la partie distale des deux baguettes souple et flexible, associée à un mandrin en deux parties détachables ; système particulièrement adapté à la chirurgie robot-assistée.

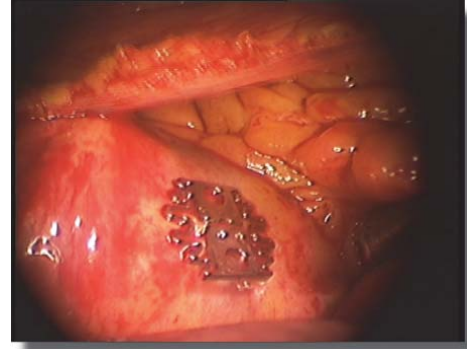
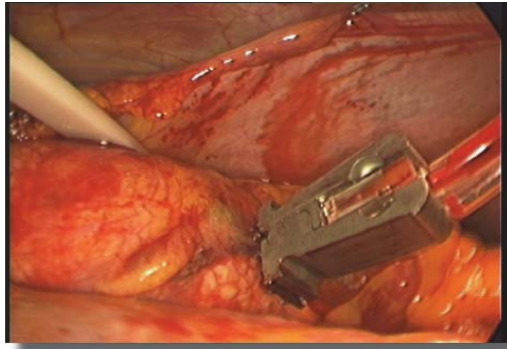


Partie 2. Evaluation du « Portapleg ».

Le Portapleg est un dispositif auto-suturent de cardioplégie antérograde en chirurgie cardiaque. Le but du système Portapleg est d'éviter une suture manuelle sur l'aorte pour maintenir l'aiguille de cardioplégie puis assurer l'étanchéité au niveau du point de ponction sur l'aorte. L'aiguille de cardioplégie est maintenue au contact de l'aorte pendant toute la procédure par un système de ventouse externe ; en fin de procédure lors du retrait de l'aiguille de cardioplégie, un clip auto-suturent en nitinol est libéré et assure l'étanchéité du point de ponction.



Le système Portapleg est donc constitué principalement d'un clip de suture qui reste implanté sur l'extérieur de l'aorte après retrait de l'aiguille de cardioplégie. Ce clip en Nitinol assure une compression des lèvres de la ponction laissée par l'aiguille et assure un contrôle de l'hémorragie et la cicatrisation du site.



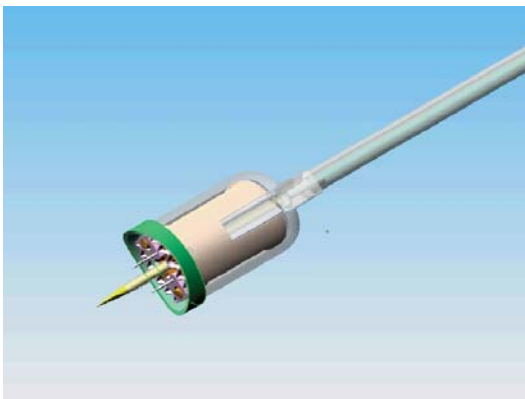
Le Portapleg a été développé par la société CLR et nous avons participé aux études pré-cliniques sur modèle in vitro d'aorte de cadavre pressurisée et sur modèle animal porcin dans le cadre de l'école de chirurgie de l'université Claude Bernard Lyon 1. Nous avons été investigateur principal de l'étude pilote multicentrique non comparative, non aveugle et non randomisée intitulée « *Performances in vivo du système Portapleg* » et comprenant l'inclusion de 40 patients sur quatre centres européens afin d'évaluer la sécurité et la fonctionnalité du dispositif. Le critère principal était le temps de saignement du site de ponction après injection de Protamine. Dans notre centre, une étude par angio scanner de l'aorte avant décharge et à trois mois a été incluse au protocole. Notre série personnelle de 20 patients a été rapportée de façon indépendante avec comme critère secondaire la position du clip en Nitinol sur l'aorte. Dans cette série, le système Portapleg a été utilisé dans douze procédures de pontages coronaires par sternotomie et dans huit procédures de chirurgie mitral video-assistée par mini-thoracotomie. Le système a montré son efficacité hémostatique dans tous les cas sans événement secondaire. L'étude par angio scanner a montré que le clip en Nitinol était bien ancré sur l'aorte dans tous les cas avec cependant une position asymétrique dans 5

cas. A trois mois, l'étude radiologique a confirmé la stabilité du clip dans sa position initiale.

Cette étude a validé le concept de clip auto-suturent sur l'aorte. Le système Portapleg nous a semblé une bonne réponse pour rendre l'administration antérograde de la cardioplégie plus simple et plus accessible pendant les procédures vidéo-assistées.

Self-sealing antegrade cardioplegia system for video-assisted cardiac surgery : Preliminary results. Innovations 2007; 2:209-212.

Ultérieurement une évolution du système a été proposée afin de le rendre moins encombrant, plus maniable et d'optimiser sa stabilité sur l'aorte pendant la procédure, avec une cloche d'aspiration concentrique et non plus latérale.



Nous avons réalisé sur cadavre les tests de conformité de cette nouvelle version qui est malheureusement restée au stade de prototype.

Self-Sealing Antegrade Cardioplegia System for Video-Assisted Cardiac Surgery: Preliminary Results

Olivier Jegaden, Thomas Sassard, Loïc Boussel, and Fadi Farhat

(*Innovations* 2007;2: 209–212)

Video-assisted cardiac surgery has gained in interest along with the development of new cardiopulmonary techniques and more recently, robotic assistance. However, their rates of adoption remain low in the surgical community because they require experience and carry inherent risks and costs. The endocardiopulmonary bypass (CPB) technique,^{1,2} standard femoro-femoral CPB, and direct aortic clamping through a port with either a metallic clamp³ or the atraumatic Portacamp (Cardio Life Research, s.a., Louvain-la-neuve, Belgium)^{4,5} have facilitated video assisted cardiac operations. However, cardioplegia delivery is made awkward by the limited access to the ascending aorta and preparing purse-string sutures and tying knots with shafted instruments through a small incision using video monitoring is difficult, and any technical mishap may be difficult to control.

We have designed an antegrade cardioplegia delivery system (Portapleg Cardio Life Research, s.a., Belgium). It requires no sutures, and the aortic puncture is closed automatically as it is removed. We report our preliminary clinical experience with this device.

METHODS

The objective of this study was to assess the safety, efficacy, and usability of the Portapleg system on patients undergoing sternotomy and minimally invasive cardiac surgery. It was an open-label, nonrandomized, unblinded pilot study. All patients provided written informed consent in concordance with a protocol approved by the ethics committee of our institution (Hospices civils de Lyon, Claude Bernard University).

Portapleg System

This system focuses on the material and the method of administration, with no change to the cardioplegia solution itself. Using a dedicated ancillary tooling, a dedicated can-

nula is placed onto the aortic root together with a surrounding prestrained device (AOSeal clip) that anchors itself by using pins penetrating the aortic tissue, coaxially to the cannula puncture site. The cardioplegia solution is administered in the usual way. A vacuum suction device (–400 mm Hg) in the hub of the cannula maintains the assembly onto the aorta during the course of surgery, allowing maintenance injection of cardioplegia and venting of the aorta. There is a specific handle-matching holder to help the remote implantation of the Portapleg assembly and the removal of the cannula (Figure 1). On retraction of the cannula, the tooling is releasing the radial constraints of the surrounding AOSeal clip that closes itself and compresses the tissue circling the puncture left by central cannula, achieving hemostasis. The AOSeal clip is made of Nitinol. It acts as a staple and is left implanted on the aortic wall (Figure 2).

Protocol

The Portapleg System was used for the administration of antegrade cardioplegia solution during arrested heart cardiac surgery performed using either sternotomy or mini-thoracotomy with video assistance. The main preoperative exclusion criteria were aortic valve surgery, emergency surgery, unstable clinical status, and short life expectancy. Diffuse aortic calcification was a perioperative exclusion criterion. The evaluation was focused on performances of the Portapleg AOSeal clip and its occlusion function on cardioplegia cannula retrieval. The primary end point was the puncture site bleeding time after reversal of heparin by protamine. Additional pursestring suture, AOSeal removal, and early reoperation for aortic bleeding were considered as device related adverse events. Before discharge from the hospital, a thoracic radiograph and a CT scan were performed to record the position of the AOSeal clip onto the aorta. Three months after surgery, each patient had a medical control visit and new thoracic radiograph and CT scan were performed. The secondary end point of the study was the AOSeal clip position on the aorta.

Surgical Procedures

Twenty patients were consecutively screened and enrolled in the study: 13 men and 7 women; mean age, 68 ± 7 years. Twelve patients underwent coronary artery bypass grafting (CABG) procedures through sternotomy and 8 patients underwent video assisted mitral valve surgery through mini-thoracotomy. In the CABG procedures, the Portapleg was implanted before CPB and left in place during all the

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FIGURE 1. Portapleg assembly, constituted by the AOSeal and its dedicated tooling, the canula, and its suction cup. It is loaded on its specific handle holder.



FIGURE 2. AOSeal is released on the aorta, closing the puncture aortic hole as a staple.

procedure to repeat cardioplegia and vent the aorta. The Portapleg was removed, and the AOSeal clip was released just after the aortic clamp removal and before completing the proximal anastomosis of the vein grafts before weaning CPB and using lateral aortic clamping. In mitral procedures, the Portapleg was implanted under femoral CPB. It was left in place for repeat cardioplegia and for antegrade low pressure coronary reperfusion just before the Portapleg removal and after the Portapleg removal, it was used for venting and deairing of the heart and removed and the AOSeal clip released just before weaning CPB.

RESULTS

In all cases, the implantation of the device was successful, allowing satisfactory antegrade cardioplegia administration. The



FIGURE 3. Portapleg holder assembly on the ascending aorta during CABG procedure through sternotomy. The suction cup is localized on the opposite of the assembly.

stability of the device upon the aorta and the efficacy of the suction cup during the procedure were assessed.

During CABG procedures through sternotomy, the mobilization of the heart to have access to coronary network involved occasionally a lateral movement of the Portapleg system, with a loss of the suction cup adhesion; the surgeon was informed immediately by the noise of the air inlet, and good adhesion was regained easily by manual repositioning. In no case was a backward motion of the AOSeal or of the canula observed (Figure 3). Aortic clamping time was 62 ± 17 minutes and CBP time was 77 ± 18 minutes. Distal anastomoses were 3 ± 0.7 per patient, most often with arterial grafts. Repeat cardioplegia was done in 75% of cases without problems, and aortic venting was efficient in all cases. The release of the AOSeal was done properly in all cases after aortic clamp removal; good anchoring of the pins in the aortic wall and close contact of the AOSeal clip to the aorta were obtained in all cases. Vein grafts were used for 3 patients; the proximal anastomosis was performed after aortic clamp removal and AOSeal release by using lateral aortic clamping between the AOSeal clip and the aortic root; no modification of the AOSeal clip stability was observed.

During video-assisted mitral valve surgery through mini-thoracotomy, the Portapleg system was far from the surgical field (Figure 4); the tubes of the system were localized at the upper part of the thoracotomy (Figure 5) and was protected from risk of motion during surgery. No case of displacement was observed. Aortic clamping time was 98 ± 25 minutes, and CBP time was 120 ± 45 minutes. Four patients had mitral valve replacement, three patients had mitral valve repair, and one patient had myxoma resection. Repeat cardioplegia and low-pressure reperfusion were achieved in all cases without problems; aortic venting for deairing was efficient in all cases. After checking the deairing efficiency by transesophageal echocardiography, the release of the AOSeal was achieved properly in all cases. For three patients, the AOSeal was asymmetrically implanted, with

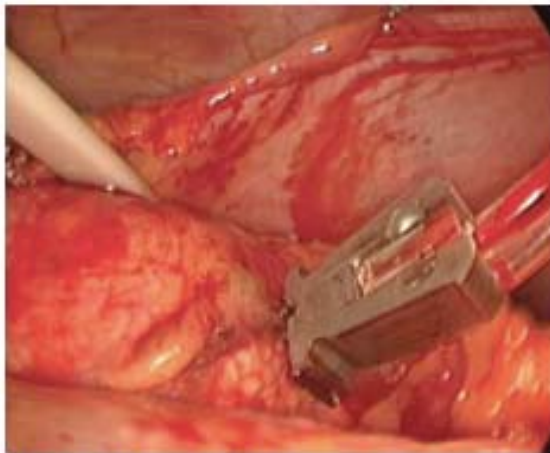


FIGURE 4. Portapleg holder assembly on the proximal aorta during video-assisted mitral valve surgery through mini-thoracotomy, with Portaclamp ready to be activated.

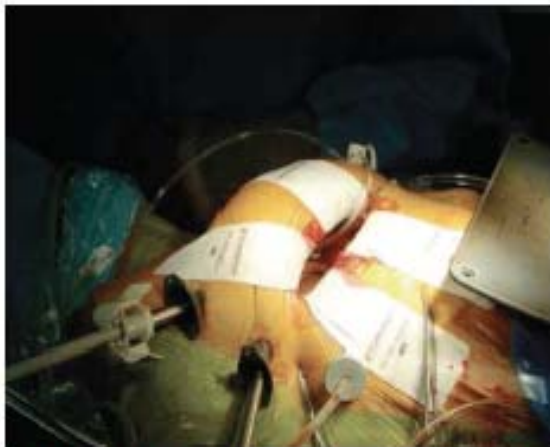


FIGURE 5. Portaclamp and Portapleg in place during video-assisted mitral valve surgery. The cardioplegia line and vacuum line are localized at the upper part of the working incision.

close contact on one side and far contact on the other side but with good anchoring of the pins in the aortic wall, and it was not necessary to modify the position of the AOSeal.

In all cases, we observed the same sequence concerning the efficacy of the AOSeal to close the aortic puncture site of the cannula: trivial bleeding just after the release of the AOSeal that stopped quickly and a recurrence of trivial bleeding at the weaning of CPB related to the increase of the arterial pressure that stopped again during the protamine perfusion. In two patients, the bleeding time was prolonged and stopped 13 and 5 minutes, respectively, after the end of protamine perfusion. In one patient, it was related to a platelets disorder known before surgery, and bleeding stopped after the transfusion of platelets concentrates planned before surgery; in the second case there was no specific

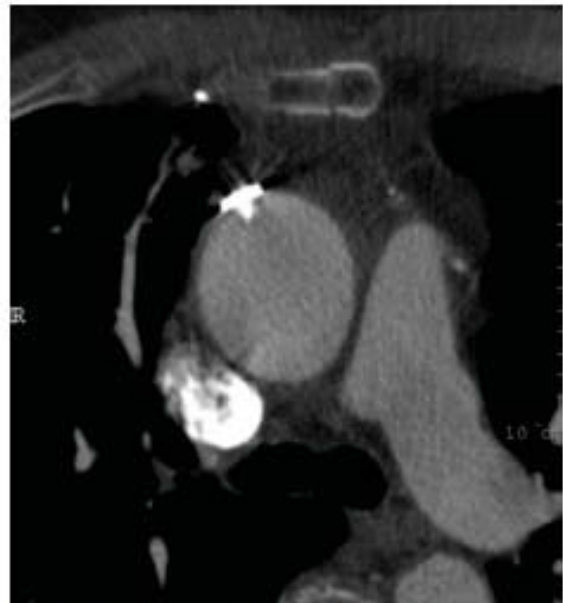


FIGURE 6. CT scan control showing a symmetric position of the AOSeal on the aorta, with pins penetrating into the aortic wall.

reason identified, probably a delayed effect of the heparin antagonization by protamine. This result was within the acceptance window of the protocol for primary end point. It is important to point out that 14 patients (70%) were given aspirin before surgery. There were no deaths, and no early reoperation was needed. Postoperative ventilation time was 8 ± 8 hours, ICU stay was 1.5 ± 1 day, and drain losses at 24 hours were 400 ± 150 mL. There was no particular postoperative event. Before discharge, all of the patients had thoracic radiography and CT scan to assess the position of the AOSeal clip and the aortic wall. In all cases, the AOSeal was well anchored in the aorta with pins penetrating in the aortic lumen (Figure 6); in five cases (CABG, 1; mitral valve surgery, 4), the AOSeal was observed in an asymmetric position (Figure 7). The aspect of the aorta was normal without any case of aortic hematoma or indirect sign of periaortic blood effusion. Hospital stay was 10 ± 4 days. All the patients had a clinical visit control 3 months after surgery, with a normal clinical examination; thoracic radiography and CT scan were performed again, and there was no modification of the data observed on the first radiologic controls, confirming the stability of the AOSeal in its initial position.

DISCUSSION

The concept of video-assisted mitral valve surgery through a mini-thoracotomy approach has been described for 10 years,¹⁻³ but it has not been widely accepted, possibly because of its complexity. The first endo-CPB technical concept was too complex, risky, and not cost-effective. The introduction of direct thoracoscopic clamping mode with a metallic aortic clamp was a good alternative.³ With Portaclamp, the drawbacks of the metallic clamp have disappeared



FIGURE 7. CT scan showing an asymmetric position of the AOSeal on the aorta, with pins remaining well anchored into the aortic wall.

and aortic thoracoscopic clamping has become atraumatic, safe, fast, and reliable.^{4–6} Thanks to these evolutions in aortic clamping mode, video-assisted cardiac surgery has gained interest and its adoption rate has increased.^{7,8} However, antegrade cardioplegia is delivered through a regular cardioplegia needle inserted through the working incision and secured onto the aortic root by a pursestring suture and a tourniquet as in conventional surgery, but the limited access to the ascending aorta through the mini-thoracotomy working incision makes it awkward and risky and remains a limiting factor for many surgeons.

The Portapleg system aims to make it easier and safer to administer antegrade cardioplegia when exposure of the ascending aorta is limited. The present pilot study shows that specifications of Portapleg, namely, one-shot implantation, good stabilization, and autosuturing closure, were achieved. This clinical evaluation was focused on the safety and the efficacy of the AOSeal, using both sternotomy and mini-thoracotomy surgical approaches.

The implantation of the Portapleg assembly is fast and easy and does not require a long learning process. The implantation was achieved before CPB in sternotomy patients, where it provided broad access to the ascending aorta. With mini-thoracotomy, the implantation was done under CPB as in our usual surgical protocol to improve the access onto the proximal aorta, and it resulted in a more lateral and proximal position, as shown by Figure 4 in comparison with Figure 3. We have observed that pin penetration was easier and deeper with systemic pressure than with CPB pressure. The lateral suction cup provided good stabilization of the Portapleg system, and when a lack of adhesion occurred

during coronary artery exposure, the pins of the AOSeal were anchored enough to avoid a backward motion. The injection and venting cannula functions operated properly in all cases.

The sequential steps for removal of the cannula and release of the AOSeal required careful attention. The release of the AOSeal was obtained easily in all cases. In a few cases, an asymmetric position of the clip was observed. This was mainly observed in video-assisted cases, possibly because its implantation under a lower CPB pressure resulted in less deep anchoring of the pins. Nevertheless, there was no failure of the Portapleg system, no additional suture was needed, and no AOSeal was either repositioned or removed.

The closure of the puncture aortic hole was obtained in all cases, with only trivial bleeding that stopped during protamine perfusion in 90% of the cases. In one case hemostasis was delayed and in one other case it was obtained after correction of coagulation disorder. The primary end point was obtained in 90% of cases and delayed in 10% without failure. The procedure did not generate undue morbidity, and there was no device-related adverse event.

The analysis of CT scan achieved before discharge demonstrated that there was no secondary risk of aortic bleeding or hematoma around the AOSeal anchored onto the aortic wall; the pins remained penetrating into the aortic lumen even if some AOSeals were observed in an asymmetric position. The analysis of the CT scan done 3 months after surgery demonstrated that the position of the clip remained stable, and secondary end point was obtained in all cases.

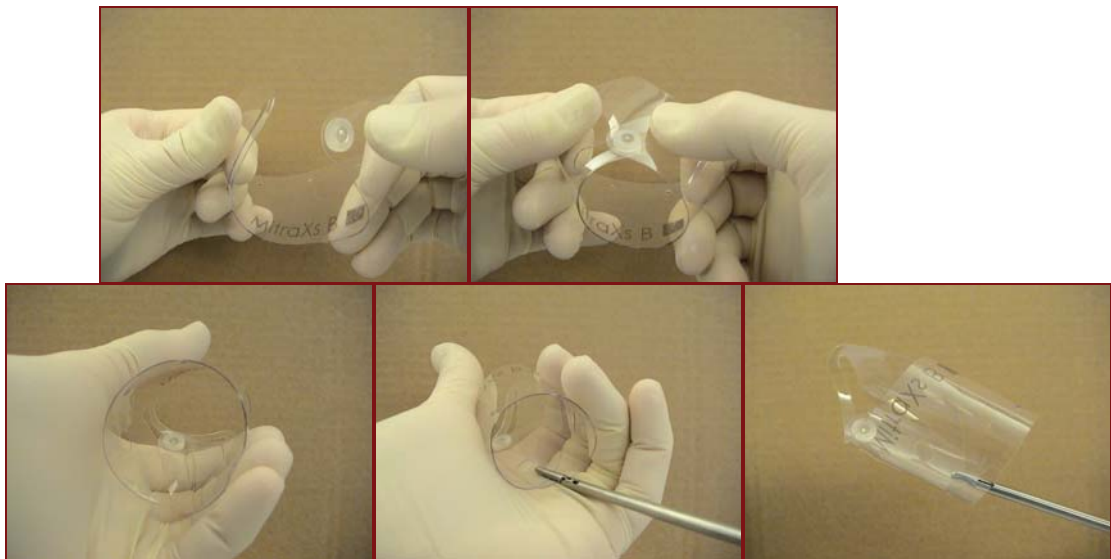
It is difficult to evaluate the incidence of surgical problems related to cardioplegia cannula aortic implantation in video-assisted cardiac surgery because it is rarely mentioned, but we know that it remains an obstacle for many surgeons to adopt this surgical concept. According to this pilot study, the Portapleg system is safe and effective and seems to be a good answer to make the antegrade cardioplegia administration more convenient in video-assisted cardiac surgery. We hope that when available, the Portapleg will contribute to improve the adoption rate of this surgical approach.

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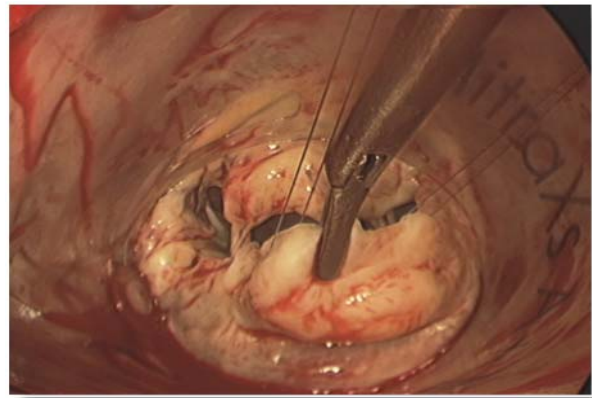
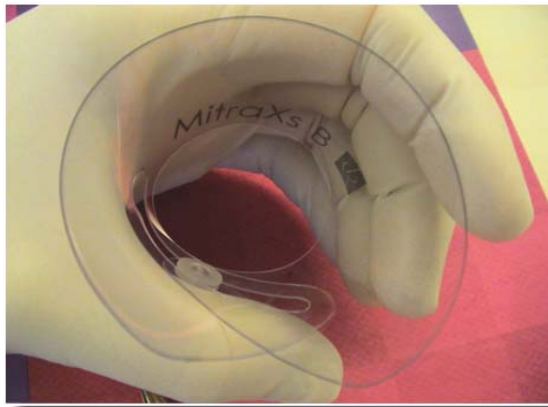
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Partie 3. Evaluation du « MitraXs».

Le Mitrax's a été développé en collaboration avec la société CLR à partir de notre idée originale. L'objectif était de concevoir un dispositif à usage unique permettant d'ouvrir la cavité de l'oreillette gauche sans exercer de traction sur les parois et sans support extra thoracique afin de pallier aux inconvénients des rétracteurs atriaux pré existants. Après une phase de conception puis d'essais de prototypes sur le cadavre dans le cadre de l'école de chirurgie de l'université Lyon 1, un produit définitif à usage clinique a été proposé et décliné en trois tailles en fonction des diamètres de l'oreillette gauche et de l'anneau mitral.



Mitrax's est un cône en plastique polymère auto ajustable et auto expansible, qui introduit dans l'oreillette gauche par l'orifice d'atriotomie, repousse de façon symétrique et concentrique les parois de l'oreillette ; il s'agit donc d'un écarteur plus que d'un rétracteur.



Une étude prospective de son efficacité a été réalisée chez 62 patients opérés de chirurgie mitrale vidéo-assistée dans notre équipe et de façon consécutive. L'indice de satisfaction (de 1 à 5) a été élevé (en moyenne 4.6), témoin d'une exposition optimale de la valve mitrale avec une vision endoscopique ou directe de la valve mitrale jugée excellente. Cette évaluation a montré les avantages du Mitrax's : simplicité d'utilisation, absence de distorsion de la valve mitrale et de déformation des parois de l'oreillette gauche, absence de distorsion de la valve aortique permettant de répéter les bolus de cardioplégie pendant la procédure sans modifier l'exposition de la valve mitrale. Elle a montré également les limites du dispositif liées à la standardisation des tailles, avec une exposition incomplète de la totalité de l'anatomie de la valve en cas d'inadéquation entre la taille de l'oreillette (trop petite) et la taille de l'anneau mitral (trop large). La mobilité du dispositif dans l'oreillette a permis de pallier à cet inconvénient en déplaçant le Mitrax's de façon séquentielle en fonction des différentes étapes du geste chirurgical.

Evaluation of a new left atrial retractor for minimally invasive mitral valve surgery.

J Thorac Cardiovasc Surg 2011; 141: 297-299.

Ce dispositif a été adopté par de nombreuses équipes en Europe et est systématiquement utilisé par notre équipe au cours des procédures mitrales vidéo-assistées.

Evaluation of a new left atrial retractor for minimally invasive mitral valve surgery

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Exposure of the mitral valve is a key success factor in minimally invasive mitral valve surgery (MIMVS) and a prerequisite for successful mitral valve repair.¹ We report the concept of a new left atrial retractor (MitraXs, St Jude Medical Inc, Minneapolis, Minn) dedicated to MIMVS. The effectiveness of the device was evaluated in a prospective series.

CLINICAL SUMMARY

The MitraXs retractor is a pattern-cut polymer sheet that once deployed and secured by a pivoting rivet generates a conical volume (Figure 1). The device is a self-expanding, auto-adjusting, single-use left atrial retractor that does not require a supporting arm. The retractor has 2 sizes (A and B) according to valve diameter and 2 lengths (regular or “+”) according to atrium depth to accommodate anatomic variations.

The introduction and deployment of the MitraXs device are key points. After the folding step, the MitraXs device is rolled and compressed from a conical shape to a cylinder with a reduced diameter creating a protruding triangular tab (Figure 1). By using a locking forceps, the MitraXs device is introduced via a minithoracotomy and an atriotomy, the tab with the rivet at the top loading the atrial septum first; then, with a clockwise rotation of a half turn, the device is progressively pushed into the left atrium in a screwing movement. When the MitraXs device is completely engaged in the left atrium, centered on the valve, with the rivet down in the posterior position, the forceps is released and the retractor deploys back into an optimal conical shape, working as an “expander” and maintaining the left atrium wide open in a symmetric manner.

The effectiveness of the MitraXs device was evaluated in 62 patients who consecutively underwent MIMVS during a 20-month period at the Louis Pradel Hospital. There

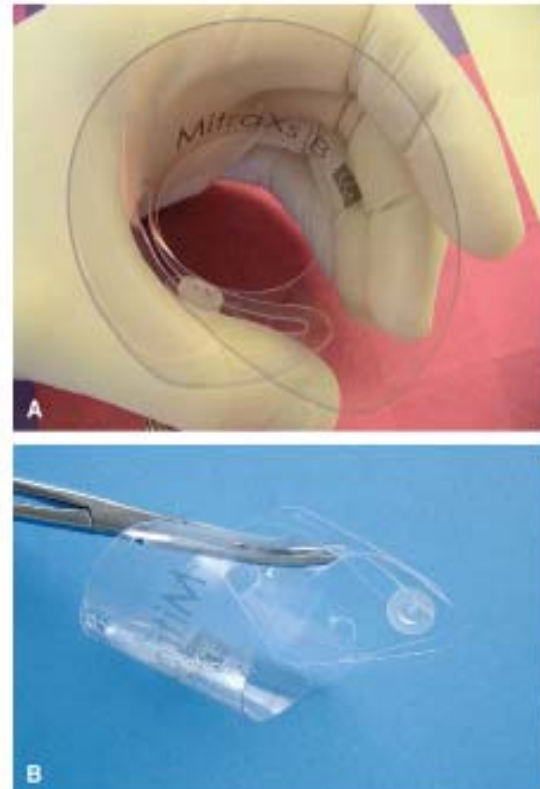


FIGURE 1. The MitraXs (St Jude Medical Inc, Minneapolis, Minn) is a self-supporting atrial retractor. A, In deployed position with 1 overmodulated pivoting rivet that makes its conical shape self-expanding and auto-adjusting. B, In rolled and compressed position, with triangular tab protruding out of the cylinder, which makes introduction into the left atrium easy.

were 21 female and 41 male patients with a mean age of 61 ± 17 years and a euroSCORE of 5.6 ± 2.8 . The operation was a redo in 6 cases, with previous mitral valve surgery in 4 patients and previous coronary artery bypass grafting in 2 patients. The origin of mitral valve lesions was rheumatic in 11 patients, degenerative in 45 patients, endocarditis in 2 patients, and bioprosthesis dysfunction in 4 patients. The surgical procedure was based on the principles of MIMVS with a transthoracic aortic clamp.² The MitraXs device was used in all cases as the primary indication for mitral valve exposure. The following were analyzed for each procedure: introduction of the retractor, size

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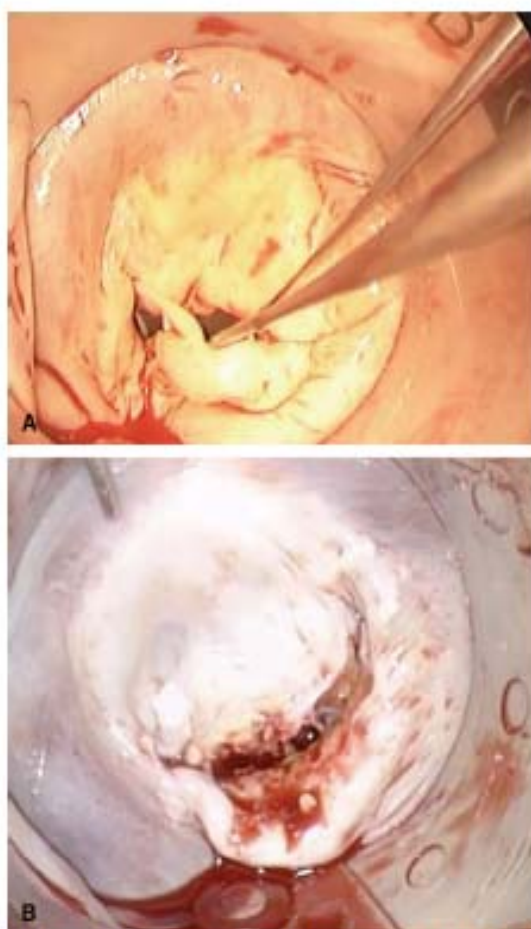


FIGURE 2. Intraoperative view. A, The mitral valve is nicely exposed without distortion, allowing easy and accurate analysis of the lesion. The left atrial muscle is homogeneously unfolded, providing space for suturing. B, The mitral valve is visualized in its entirety with a large working space, making en bloc valve resection possible. Note the asanguineous operative field with the vent back. The MitraXs device may prevent tissue fragments from falling into the pulmonary veins.

suitability, conversion to blade retractor, exposure of the mitral valve, distortion of the anatomy, working space available around the valve, access for endoscopic instruments, need of repositioning or additional sutures to improve exposure, video and direct vision, and extraction of the device. At the end of the procedure, the surgeon proposed a global satisfaction index from 0 to 5.

RESULTS

Mitral valve replacement was performed in 18 patients, and mitral valve repair was performed in 44 patients. An associated procedure was performed in 8 patients: myomectomy in 2 patients, atrial septal defect closure in 4 patients, and tricuspid valve repair in 2 patients. For mitral

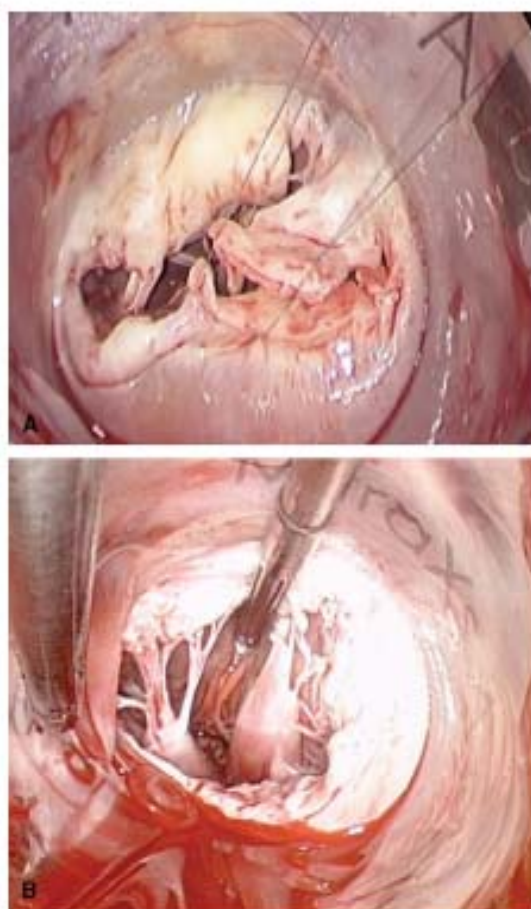


FIGURE 3. Intraoperative view. A, The MitraXs device is voluntarily centered on the posterior leaflet to make sliding plasty easier. Note the occluded area on anterior annulus that is accessible by sliding and repositioning. B, The MitraXs device is voluntarily pushed inside the mitral annulus to improve the exposure of papillary muscles for artificial chordae implantation.

valve repair, a posterior leaflet resection was performed in 28 patients and artificial chordae were used in 19 patients, mainly on the anterior leaflet; an annuloplasty using a complete semirigid ring was associated in all cases.

The introduction of the MitraXs device was fast and easy, with a mean placement time of 32 ± 8 seconds. There was a mismatch in 5 cases, and a smaller-sized MitraXs device was used. Size A was used in 34 patients (A, 21; A+, 13), and size B was used in 28 patients (B, 22; B+, 6). The MitraXs device was used in all procedures without an additional retractor or conversion to a different retractor. The exposure of the mitral valve, in regard to both leaflets and annulus, was estimated to be good to perfect in 47 cases, with the left atrial muscle homogeneously unfolded around the valve (Figure 2). In 15 cases of mitral valve repair, the

anterior part of the annulus was partially hidden; in 9 cases, the repair of the well-exposed mitral valve was performed first and repositioning was done for ring implantation in the occluded area (Figure 3, A), and in 6 cases, sutures for ring implantation were placed first using sequential repositioning to downsize the valve diameter enough to be included in the internal diameter of the MitraXs device. Repositioning was easily performed with hooks in a sliding movement. In all cases, there was no distortion of the valve anatomy, which made the analysis of valve dysfunction easy and reliable in repair procedures. In 8 patients, to improve accessibility to the papillary muscles for artificial chordae implantation, the MitraXs device was first pushed inside the annulus to throw back the posterior leaflet (Figure 3, B). The same technique was used in 2 patients for associated myectomy. In 4 patients, the MitraXs device (size+) slipped out of the left atrium during the procedure because of excessive traction on the annulus stitches, which progressively ejected the device; in 2 patients the device was successfully reintroduced into the left atrium, and in 2 patients the device was removed and ring implantation was finished without a retractor. An ideal straight line between the working port of the minithoracotomy and the plane of the mitral valve was obtained in most cases via a lateral thoracic approach; however, in 8 patients a "bayonet" effect was corrected using a traction stitch. In all patients, excellent direct vision was provided by the device. The vent placed in the pulmonary veins remained back without displacement or conflict. Repeat cardioplegia was performed with the MitraXs device in place, demonstrating no distortion of the aortic valve. In case of an associated right atrium approach for atrial septal defect or tricuspid surgery, the MitraXs device was used on the right side without the rivet engaged, working as a tent. Removal of the device was performed in a compressed cylindrical shape ($n = 51$) or a flat shape after the rivet release ($n = 11$). The global satisfaction index was 4.6 ± 0.5 . All patients had a good outcome and were discharged from the hospital.

DISCUSSION

Optimal exposure of the mitral valve is a key point in MIMVS. Since our program was started in 1997, we have

used the classic 2-piece blade retractor dedicated to such a procedure and observed its drawbacks related to the traction on the anterior leaflet with distortion of the mitral apparatus, the creation of atrial folds with large occluded areas, and the difficulty of not exposing the anterior annulus for ring implantation.³ The concept of the MitraXs device is based not on left atrial retraction but on left atrial expansion; thus, these drawbacks are not relevant. The association of a small left atrium with a dilated annulus was a difficult situation; the atrium diameter took the lead, and we had to accept a covered area in 24% of cases, no more than 10% on the anterior annulus. This drawback was offset by the freedom of the MitraXs device inside the left atrium, and repositioning was easy to modify the exposure according to the surgical stage. In the same manner, it was possible to focus the exposure on a specific area, such as the posterior annulus for sliding plasty or the papillary muscle for artificial chordae (Figure 3). In most cases, the MitraXs device provided optimal exposure and excellent direct vision. The global satisfaction index was high, demonstrating the effectiveness of the device; however, the MitraXs device has a few drawbacks. Size standardization may involve mismatch. Downsized or in case of excessive traction on annulus stitches, the MitraXs device may slip out of the left atrium.

CONCLUSIONS

The MitraXs is easy to use with excellent effectiveness. Since testing the device, we have adopted its use. According to our experience and the results of this series, the MitraXs makes the technique of MIMVS easier and more reproducible.

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Partie 4. Analyse comparative des techniques mini-invasives de revascularisation de l'IVA par pontage mammaire (Port Access, MIDCAB, TECAB).

Depuis le développement et les succès de la cardiologie interventionnelle, les indications de revascularisation chirurgicale isolée de l'artère inter ventriculaire antérieure (IVA) sont rares, le plus souvent après échec primaire ou secondaire de la cardiologie interventionnelle. Un effort important a été développé par la communauté chirurgicale pour réduire le caractère invasif de la revascularisation chirurgicale dans ce groupe spécifique de patient où la voie d'abord par sternotomie médiane semblait disproportionnée par rapport au geste de mono pontage coronaire par le pédicule mammaire interne gauche. En fonction de la technologie disponible et de son évolution notre approche chirurgicale mini-invasive dans ce groupe spécifique de patients a évolué sur deux périodes :

- Avant 2003 et l'acquisition du robot chirurgical Da Vinci, la procédure de référence était la technique Port-Access (PA-CABG) avec prélèvement vidéo-assisté du pédicule mammaire gauche et mini thoracotomie antérieure gauche pour une anastomose directe sous CEC et cœur arrêté avec clampage aortique par endoclamp. En cas de contre-indication à la CEC port access, une procédure MIDCAB était réalisée avec prélèvement vidéo-assisté du pédicule mammaire gauche et mini thoracotomie antérieure gauche pour une anastomose directe sans CEC à cœur battant, utilisant un stabilisateur myocardique externe puis endoscopique et un shunt coronaire systématiquement.
- Après 2003 et l'acquisition du robot chirurgical Da Vinci, la procédure de référence était la technique TECAB avec prélèvement robot-assisté du pédicule mammaire gauche et anastomose robot-assistée à thorax fermé sans CEC à cœur battant, utilisant un stabilisateur endoscopique et un shunt coronaire systématiquement. En cas de contre-

indication à une anastomose robot-assistée avant la procédure ou en cours de procédure, une procédure MIDCAB robot-assistée (RE-MIDCAB) était réalisée avec prélèvement robot-assisté du pédicule mammaire gauche et mini thoracotomie antérieure gauche pour une anastomose directe sans CEC à cœur battant, utilisant un stabilisateur myocardique endoscopique et un shunt coronaire systématiquement.

Une étude prospective sur 10 ans a été conduite dans ce groupe de patients afin d'évaluer de façon comparative les résultats des trois techniques de revascularisation chirurgicale mini-invasive utilisées et correspondantes à trois concepts différents :

- le PA-CABG, le plus invasif mais reproduisant le mieux la technique classique de pontage coronaire avec anastomose sur cœur arrêté,
- le TECAB, le moins invasif à thorax fermé sans CEC et à cœur battant,
- le MIDCAB, avec un caractère invasif intermédiaire puisque sans CEC et à cœur battant, mais à thorax ouvert, après prélèvement mammaire par vidéo ou robot – assistance.

Malgré les limites de cette étude, non randomisée, sur des périodes d'inclusion différentes, les résultats ont montré, à trois mois, un taux de réintervention sur l'IVA, artère cible pontée, significativement plus élevé dans le groupe TECAB : PA-CABG, 0% ; MIDCAB, 1.8% ; TECAB, 10% ; $p < 0.01$.

Ces différences observées ont souligné et confirmé une intuition chirurgicale :

- la perméabilité précoce des anastomoses réalisées sur cœur arrêté est meilleure que celles réalisées sur cœur battant,
- la perméabilité précoce des anastomoses réalisées manuellement en vision directe est meilleure que celles réalisées avec robot-assistance à thorax fermé.

Néanmoins, au début de notre expérience TECAB, la technique d'anastomose utilisée était identique à la celle des procédures MIDCAB ; les premiers échecs de perméabilité après TECAB nous ont conduit à modifier cette technique d'anastomose et de passer du

surjet continu Gortex 8/0 aux points séparés Uclip en Nitinol. Cette évolution technique, au rythme de l'évolution technologique, a fait disparaître les problèmes anastomotiques mais ne nous a pas mis à l'abri de trois cas d'occlusion fonctionnelle du pédicule mammaire avec anastomose perméable, témoin de la difficulté d'orienter ou de vérifier le pédicule mammaire dans un environnement thoracique fermé.

A trois ans, les taux actuariels de survie sans réintervention étaient : PA-CABG, 100% ; MIDCAB, 98 ± 5 % ; TECAB, 88 ± 8 % ; $p < 0.05$. Cette différence observée était directement liée aux échecs précoces de perméabilité.

Cette étude nous a conduit à considérer la procédure MIDCAB vidéo ou robot –assistée comme technique chirurgicale de référence pour la revascularisation isolée de l'IVA, compte tenu du surcoût induit par la technique PA-CABG et du taux plus élevé des échecs primaires avec la technique TECAB.

Is there an optimal minimally invasive technique for left anterior descending coronary artery bypass? J Cardiothorac Surg 2011; 6: 37.

RESEARCH ARTICLE

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Is there an optimal minimally invasive technique for left anterior descending coronary artery bypass?

Olivier Jegaden*, Fabrice Wautot, Thomas Sassard, Isabella Szymanik, Abdel Shafy, Joel Lapeze and Fadi Farhat

Abstract

Background: The aim of this retrospective study was to evaluate the clinical outcome of three different minimally invasive surgical techniques for left anterior descending (LAD) coronary artery bypass grafting (CABG): Port-Access surgery (PA-CABG), minimally invasive direct CABG (MIDCAB) and off-pump totally endoscopic CABG (TECAB).

Methods: Over a decade, 160 eligible patients for elective LAD bypass were referred to one of the three techniques: 48 PA-CABG, 53 MIDCAB and 59 TECAB. In MIDCAB group, Euroscore was higher and target vessel quality was worse. In TECAB group, early patency was systematically evaluated using coronary CT scan. During follow-up (mean 2.7 ± 0.1 years, cumulated 438 years) symptom-based angiography was performed.

Results: There was no conversion from off-pump to on-pump procedure or to sternotomy approach. In TECAB group, there was one hospital cardiac death (1.7%), reoperation for bleeding was higher (8.5% vs 3.7% in MIDCAB and 2% in PA-CABG) and 3-month LAD reintervention was significantly higher (10% vs 1.8% in MIDCAB and 0% in PA-CABG). There was no difference between MIDCAB and PA-CABG groups. During follow-up, symptom-based angiography ($n = 12$) demonstrated a good patency of LAD bypass in all groups and 4 patients underwent a no LAD reintervention. At 3 years, there was no difference in survival; 3-year angina-free survival and reintervention-free survival were significantly lower in TECAB group (TECAB, $85 \pm 12\%$, $88 \pm 8\%$; MIDCAB, 100% , $98 \pm 5\%$; PA-CABG, $94 \pm 8\%$, 100% ; respectively).

Conclusions: Our study confirmed that minimally invasive LAD grafting was safe and effective. TECAB is associated with a higher rate of early bypass failure and reintervention. MIDCAB is still the most reliable surgical technique for isolated LAD grafting and the least cost effective.

Background

For several decades, left internal thoracic artery (LITA) bypass grafting has been recognised as the gold standard for left anterior descending coronary artery (LAD) revascularization and its beneficial impact was demonstrated in conventional coronary artery bypass grafting (CABG). During the past decade, minimally invasive (MI) CABG, based on the lack of sternotomy approach, has been developed according to the evolution of technology and dedicated surgical tools, and it has been mainly performed in isolated LAD bypass grafting. Nowadays, MI-CABG brings together different surgical concepts: Port-Access surgery (PA-CABG) based on on-pump CABG with mini-thoracotomy and hand-sewn anastomosis,

minimally invasive direct coronary artery bypass (MIDCAB) based on off-pump CABG with mini-thoracotomy and hand-sewn anastomosis, and totally endoscopic coronary artery bypass grafting (TECAB) based on on-pump or off-pump surgery with robotic assisted anastomosis. These MI-CABG techniques have been compared to conventional CABG according to observational research because of the lack of randomized trial: the expected clinical results must be at worst as good as conventional CABG; the observational results are at best the same [1-3]. In the same way, these different MI-CABG techniques have never been compared together. In this series, we report our experience in minimally invasive LAD grafting with a comparative analysis between PA-CABG, MIDCAB and off-pump TECAB, in order to answer the question: is there an optimal minimally invasive technique for isolated LAD grafting?

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Methods

From January 1998 to December 2008, 160 eligible patients for elective LAD revascularization were referred to minimally invasive CABG surgery. There were 135 males and 25 females, mean age was 58 ± 11 years and Euroscore 1.7 ± 1.7 . There were two surgical periods: from January 1998 to September 2003, the intend-to-treat surgical procedure was either PA-CABG or MIDCAB depending on the patient's condition, and after the purchase of standard Da Vinci robotic system in September 2003, the intend-to-treat surgical procedure was either off-pump TECAB or robotic enhanced MIDCAB depending on the patient's condition. In this series, the patients were categorized into three groups according to the surgical procedure performed: PA-CABG ($n = 48$), MIDCAB ($n = 53$), TECAB ($n = 59$).

Port-Access group

The surgical technique was previously reported [3]. The video-assisted LITA harvesting was done through the anterior left mini-thoracotomy. The femoral approach for cardiopulmonary bypass was used and aortic clamping was done with the Endo-Aortic Clamp™ according to the concept of Port Access™ EndoCPB system. The coronary anastomosis was performed under direct vision with 8/0 Prolene running suture. PA-CABG was the intend-to-treat procedure in 48 patients free of peripheral atherosclerotic disease and it was done in all cases.

TECAB group

Off-pump TECAB was the intend-to-treat procedure in 78 cases with an auspicious anatomic condition based on preoperative angiography; however, 19 patients had a conversion to MIDCAB during the procedure and a complete TECAB surgery was performed in 59 patients. The TECAB surgical technique was previously reported [4] and intra-coronary shunt was used in all cases. Before January 2005, proximal and distal LAD occlusions were performed using 4-0 ePTFE sutures ($n = 11$), after only proximal LAD occlusion was done ($n = 48$). Before July 2006, the anastomosis was done with 8-0 ePTFE running suture ($n = 22$), after it was done with nitinol Uclips™ as interrupted sutures ($n = 37$).

MIDCAB group

MIDCAB was the intend-to-treat procedure as an alternative to PA-CAB in 17 patients with peripheral atherosclerotic disease. Robotic enhanced MIDCAB was the intend-to-treat procedure as an alternative to TECAB in 17 patients with an unfavorable anatomic condition and in 19 patients it was performed as a conversion of an intend-to-treat TECAB procedure (Table 1). In the first sub-group of 17 patients, the video-assisted LITA harvesting was done through the anterior left mini-

Table 1 Indications for robotic enhanced MIDCAB ($n = 36$)

	Intend-to-treat MIDCAB N = 17	Conversion from TECAB N = 19
Quality of LAD	9	8
Sequential graft indication	6	-
Intra-myocardial LAD	1	3
Pleural adhesions	-	3
Stabilizer failure	-	2
Limited anterior space	-	2
Septal back flow	-	1
Unstable angina	1	-

LAD, Left anterior descending coronary artery; MIDCAB, minimally invasive direct coronary artery bypass grafting; TECAB, totally endoscopic coronary artery bypass grafting. Note that all conversions except one (septal back flow) were decided before the anastomosis stage.

thoracotomy; myocardial stabilization was obtained with an Estech stabilizer; a proximal LAD occlusion was performed using 4-0 ePTFE sutures; the anastomosis was done under direct vision with intra-coronary shunt and 8-0 Prolene running suture. In patient with robotic enhanced MIDCAB ($n = 36$), after endoscopic LIMA harvesting, the pericardium was opened, the target vessel was identified, and the left anterior mini-thoracotomy was performed in the ideal position in front of the target anastomotic site. Myocardial stabilization was done using an Octopus TE endoscopic stabilizer (Medtronic Inc.), placed either before or after the mini-thoracotomy, and the anastomosis was performed according to the same rules with proximal LAD occlusion, intra-coronary shunt and running suture.

All the operations were performed with the patient's informed consent. Data was prospectively collected. Early patency was evaluated by an angiography or CT scan, systematically in the TECAB group, and only in cases of sequential LIMA graft or post-operative troponin level rise in other groups. All the patients had a stress ECG test during the 2-month post-operative period according to the rehabilitation protocol. Follow-up was made by mail enquiries and completed for all patients. During follow-up, only symptom-based coronary angiography was performed. Mean follow-up was 2.7 ± 0.1 years and cumulated follow-up was 438 years.

Data was accessed and analysed with statistical software. Categorical variables are expressed as number and percentage of patients and were analysed with the Fischer exact test or χ^2 test. Continuous variables were compared with a two-samples t-test. A log-rank test was used to compare Kaplan-Meier curves of survival and freedom from event.

Results

Patient populations were almost similar in the three groups (Table 2). However, in the MIDCAB group, the Euroscore was significantly higher, related to the significantly higher amount of females; in the TECAB group, sequential LITA graft to LAD and diagonal artery was significantly lower, related to the selection of the indications in this group (Table 1). In any group, there was no conversion from off-pump to on-pump procedure or to sternotomy approach. There was no difference in intervention time and complete revascularization between groups (Table 2). Intubation time was significantly lower after TECAB without any differences between PA-CABG and MIDCAB (Table 3). There was no difference between groups regarding ICU stay, Troponin level and blood loss.

Early post-operative outcome

Reoperation for bleeding was needed in eight patients: in one MIDCAB patient it was related to the anastomosis which was performed again as an early reintervention; in all other cases, only thoracic wall hemostasis was done and the bleeding source was not always found. In the TECAB group, there was a higher rate of reoperation for bleeding (8.5%) and a mini-thoracotomy was necessary to remove the blood clots in four patients (Table 3).

Post-operative myocardial infarction occurred in one PA-CABG patient, related to a septal artery occlusion and in two TECAB patients, related to an anastomosis dysfunction as demonstrated by angiography.

In the PA-CABG group, only two patients had a post-operative angiography control; in both cases, graft and anastomosis were patent with an occluded septal artery

Table 2 Preoperative and Intraoperative data

	PA-CABG N = 48	MIDCAB N = 53	TECAB N = 59
Mean age (years)	55 ± 9	61 ± 8	59 ± 12
Gender (M/F)	44/4	38/15 *	53/6
Angina CCSG (mean)	3 ± 0.3	2.9 ± 0.4	3 ± 0.3
LVEF (%)	58 ± 11	59 ± 8	57 ± 8
Euroscore	0.9 ± 1	2.3 ± 1.7 *	1.3 ± 1.6
Previous PCI	10 (21)	10 (19)	11 (18)
CPB time (min)	52 ± 15	-	-
Aortic clamp time (min)	34 ± 15	-	-
Intervention time (hrs)	3.2 ± 0.6	3.1 ± 0.7	3.4 ± 0.7
Sequential LAD+Diag	7 (15)	10 (19)	3 (5) *
Complete revascularization	35 (73)	38 (72)	42 (71)

Number of patients with (%): PA-CABG, Port-Access coronary artery bypass grafting; MIDCAB, minimally invasive direct coronary artery bypass grafting; TECAB, totally endoscopic coronary artery bypass grafting; CCSG, Canadian Cardiovascular Society Classification; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; CPB, cardio-pulmonary bypass; LAD, left anterior descending artery; Diag, diagonal artery. * p < 0.05.

Table 3 Early Postoperative results

	PA-CABG N = 48	MIDCAB N = 53	TECAB N = 59
Intubation time (hrs)	8 ± 4	7.2 ± 5.6	4.6 ± 2.4 *
ICU stay (days)	1.7 ± 2.7	1 ± 1.3	0.96 ± 0.8
Troponin (24 hrs, IU)	1.7 ± 2.4	2.1 ± 5	2.2 ± 10
Drainage (24 hrs, ml)	377 ± 245	408 ± 174	368 ± 159
Reoperation for bleeding	1 (2)	2 (3.7)	5 (8.5)
MI	1 (2)	0	2 (3.4)
Stroke	1 (2)	0	0
Reintervention	0	1 (1.8)	4 (6.8) *
Hospital stay (days)	7 ± 3	6.5 ± 1.5	5.5 ± 1.6 *
30-day mortality	0	0	1 (1.7)

Number of patients with (%): PA-CABG, Port-Access coronary artery bypass grafting; MIDCAB, minimally invasive direct coronary artery bypass grafting; TECAB, totally endoscopic coronary artery bypass grafting; ICU, intensive care unit; MI, myocardial infarction. * p < 0.05.

in 1 case. In the MIDCAB group, 13 patients had a postoperative control using either an angiography or CT scan, showing a 100% patency of grafts and anastomoses. In the TECAB group, two patients with post-operative myocardial infarction had angiography control showing anastomosis or post-anastomosis high-grade stenosis; all other patients had a CT scan control before discharge showing an asymptomatic LITA graft occlusion with patent anastomosis in 2 patients, confirmed by angiography. In these 4 patients a reintervention was successfully performed, using stenting done through the native coronary network or the LITA graft. In the TECAB group the patency rate was 93.2% (55/59) and reintervention (6.8%) was significantly higher (Table 3). One PA-CABG patient had a transient postoperative stroke. One TECAB patient died from arrhythmia after myocardial infarction despite reintervention. Hospital stay was significantly shorter in the TECAB group (Table 3).

Late post-operative outcome

There was a significant difference in follow-up between the three groups, related to the two surgical periods (Table 4).

In the PA-CABG group, there was no late death. Inferior myocardial infarction occurred in one patient and four patients had a recurrent angina (mean 4 ± 1.4 years postoperatively). In these 5 patients, coronary angiography demonstrated that the event was not related to the LAD bypass and two of them underwent a reintervention: 1 stenting on the right coronary artery and 1 surgical bypass to marginal and posterior descending coronary arteries. At follow-up, the CCS functional class was 1.1 ± 0.3.

Table 4 Late postoperative results

	PA-CABG	MIDCAB	TECAB
Mean follow-up (years)	3.9 ± 0.3	2.5 ± 0.3	1.8 ± 0.1
	*	*	*
3-year survival (%)	100	98 ± 5	96 ± 5
3-year angina-free survival (%)	94 ± 8	100	85 ± 12 *
3-year reintervention-free survival (%)	100	98 ± 5	88 ± 8 *

PA-CABG, Port-Access coronary artery bypass grafting; MIDCAB, minimally invasive direct coronary artery bypass grafting; TECAB, totally endoscopic coronary artery bypass grafting; * p < 0.05.

In the MIDCAB group, there were two late deaths from cancer (5 months and 8 years post-operatively). One patient had recurrent angina at 7-year post-operatively; coronary angiography demonstrated that the event was not related to the LAD bypass and the patient underwent a surgical reintervention to the marginal and right coronary arteries. At follow-up, the CCS functional class was 1.2 ± 0.14.

In the TECAB group, one patient committed suicide 6 months after surgery. Two patients had recurrent angina during the rehabilitation period (1 and 2 months post-operatively). Coronary angiography demonstrated that the event was related to the LAD bypass (1 occlusion of LITA, 1 post-anastomotic stenosis); both patients underwent a stenting of LAD. Six other patients had late recurrent angina (from 1 to 4 years post-operatively); in all these cases, coronary angiography demonstrated that the event was not related to the LAD bypass and one patient had a stenting of the right coronary artery. At follow-up, the CCS functional class was 1.1 ± 0.3.

At 3-year, there was no difference in survival between the three groups. However, 3-year angina-free survival and reintervention-free survival were significantly lower in the TECAB group (Table 4).

Discussion

Our study confirms minimally invasive CABG, regardless the technique used, is safe with a 0.6% early mortality, and effective with a 98 ± 2% 5-year survival, a 93 ± 6% 5-year freedom from reintervention and a 85 ± 9% 5-year freedom from angina. The early patency of LITA to LAD (94%, 77/82) is comparable to those of conventional on-pump CABG (91%) according to IMAGE trial [5] or off-pump CABG (92%) according to randomized trial [6]. All procedures were performed without conversion from off-pump to on-pump procedure or to sternotomy approach, and all LAD bypass failures could be treated by stenting.

We have analysed MI-CABG results between three different techniques developed during the past decade. PA-CABG is the most sophisticated procedure involving

on-pump surgery and endo-aortic clamping technique. In this group, we have observed very satisfactory early and late results, without any post-operative major event; symptom-based angiography demonstrated good graft and anastomosis patency in all cases. Results are comparable to those previously reported with this technique [7,8].

MIDCAB is the less demanding procedure and has gained widespread acceptance according to excellent results provided [9,10], which our series has confirmed. Only one case of reintervention occurred, related to early anastomosis bleeding. We have observed no differences in results between classical and robotic-enhanced MIDCAB. In this study, there was no difference in operative risks and mid-term results between PA-CABG and MIDCAB.

TECAB is controversial [2]; off-pump TECAB is the less invasive concept in LAD grafting, nevertheless results are not as good as expected. De Canniere [11] reported a 2.2% early mortality, a 92.1% early patency and a 4.1% reintervention rate at 30 days. In our series, early mortality was 1.7%, early patency was 93.2% and the reintervention rate before discharge was 6.8%. Two more patients underwent reintervention of LAD, 1 and 2 months postoperatively, after symptom-related angiography which showed LAD bypass dysfunction undetected by coronary CT scan before discharge. The actuarial freedom from angina and from reintervention were significantly lower in the TECAB group (Figure 1); it was directly related to a primary bypass failure which remains the main concern in the TECAB procedure. In our experience, modifications of the anastomosis technique allowed to improve the patency: after the occurrence of post-anastomotic dysfunction cases, distal LAD occlusion during anastomosis was abandoned and this type of failure disappeared; anastomotic dysfunction disappeared also when we changed from running suture to

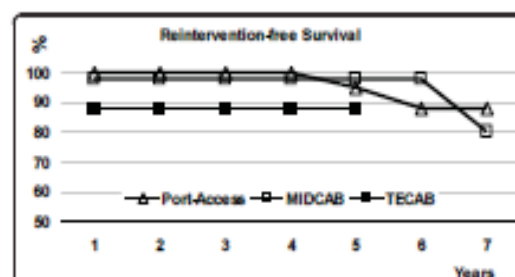


Figure 1 Actuarial reintervention-free survival according to the surgical technique performed. PA-CABG, Port-Access coronary artery bypass grafting; MIDCAB, minimally invasive direct coronary artery bypass grafting; TECAB, totally endoscopic coronary artery bypass grafting; p = 0.02 between TECAB and the two other techniques.

uclips suture which provided a 100% patency. Nevertheless, we have observed three cases of LITA occlusion with an opened LAD anastomosis: one seemed to be related to a twist of the graft, the two others remained unexplained. However, the rate of graft failure in the TECAB procedure is acceptable in comparison with classical coronary surgery; routine intraoperative completion angiography in classical CABG demonstrated that 7% of LAD-LITA grafts had a significant defect: 3% in the conduit and 4% at the distal anastomosis [12]. In our study, comparison of the patency between groups was not relevant because systematic assessment was not done in all groups; but there is no question regarding the end-point of LAD reintervention at 3 months (PACAB, 0%; MIDCAB, 1.8%; TECAB, 1.0%; $p = 0.01$). Nevertheless, there was no difference in mortality and survival between the three groups.

In all, reoperation for bleeding was high, specially in the TECAB group, demonstrating hemostasis is difficult in a minimally invasive environment and more in a closed chest procedure. In this series, from patients with an intent-to-treat TECAB procedure ($n = 78$), 24% had a conversion to MIDCAB procedure and from patients who underwent a TECAB procedure ($n = 58$), 7% had a thoracotomy during reoperation for bleeding. Nevertheless, hospital stay was significantly shorter in TECAB group.

There is no evidence in published data that on-pump TECAB (or Port-Access TECAB) procedure provides better results. In the multicenter European trial [11], there was no difference in 6-month freedom from MACE between on-pump and off-pump TECAB procedures; in the on-pump TECAB multicenter US trial [13], 3-month freedom from reintervention or angiography failure was 91% versus 90% in our series. Better results could be expected with the fourth arm Da Vinci system with the advantage of the robotic endostabilizer.

Our study has its limitations. Patients were not randomized and they were referred to one of the three MI techniques according to the evolution of the MI surgical concept in our team, to their condition and the quality of the target vessel. Inclusion in the MIDCAB group of conversions from an intent-to-treat TECAB procedure is also open to criticism; it was reasonable because all conversions except one were decided before the anastomosis stage and were mainly related to the quality of the LAD. All these bias contributed to include in the MIDCAB group the "worst" cases regarding target vessel quality, which did not have any impact on results, as good as in PA-CABG group and better than in TECAB group. An intention to treat analysis would provide the same results. A systematic post-operative assessment of LAD bypass was performed only after TECAB procedure and patency comparison between groups was not

relevant. In any case, the correlation between LAD bypass failure and recurrent angina is well known; in this study, all patients with angina recurrence underwent coronary angiography and comparison between groups was focused on reintervention events.

In conclusion, our study has confirmed minimally invasive CABG is safe and effective. If PA-CABG and MICAB provide results as good as conventional CABG, TECAB procedure is associated with a higher early rate of bypass failure and reintervention. Beyond the post-operative period, results are equivalent and stable regardless the surgical technique performed. According to these results, PA-CABG was abandoned considering its cost effectiveness [8] and patients for LAD grafting are referred either to robotic-enhanced MIDCAB or off-pump TECAB, mainly according to the quality of the target; but in any case of doubt or technical difficulty we don't hesitate to convert before the anastomosis stage, an intent-to-treat TECAB procedure to a MIDCAB procedure which remains the reference procedure for minimally invasive LAD grafting.

Authors' contributions

OL conceived of the study, and drafted the manuscript, PW participated in the design, TS IS AS JL participated in the surgery and data collection, FF participated in coordination and performed statistical analysis. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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Commentaires.

La plateforme Port-Access développée par la société Heart-Port a permis de valider le concept de chirurgie mitrale mini-invasive vidéo-assistée et c'est tout le mérite des pionniers dans ce domaine, en particulier Hugo Vanermen, Fred Mohr, et Randy Chitwood, compte tenu des volumes de patients opérés avec cette technique et des publications princeps qu'ils ont réalisés (16-18) ; mais cette plateforme n'a pas permis d'assurer la diffusion de cette technique du fait de sa complexité et de son coût, obstacles à son accessibilité et à sa reproductibilité.

Les travaux que nous avons réalisés dans ce domaine et rapportés dans ce document avaient pour objectifs d'évaluer une plateforme alternative et / ou complémentaire afin de simplifier la technique chirurgicale et de la rendre plus accessible et plus reproductible. Ces travaux ont démontré la sécurité et l'efficacité des dispositifs étudiés. L'absence d'étude clinique comparative ne nous a pas permis de montrer un bénéfice réel et objectif apporté par leur utilisation, néanmoins notre expérience chirurgicale nous a permis d'en souligner l'intérêt.

Le Portaclamp nous a semblé une bonne alternative au clamp métallique type Chitwood : moins dangereux du fait d'un clamage symétrique, d'extrémités plus larges et d'une zone effective plus large ; plus maniable également dans les thorax courts où l'articulation du clamp est encore dans la paroi lorsque le clamp atteint l'aorte, bloquant ainsi son ouverture et son bon positionnement. Dans les réinterventions, l'extrémité large et atraumatique du Portaclamp est utile pour libérer les adhérences péri-aortiques juste nécessaire à un bon positionnement. Nous avons adopté le Portaclamp très rapidement comme d'autres chirurgiens (19) et nous n'avons jamais observé dans notre expérience d'événement indésirable. Malheureusement la version initiale rigide a été retirée en faveur de la version souple ou Portaclamp Flex, qui du fait de la perte de

rigidité distale avait l'inconvénient d'induire un twist des deux parties proximales lors du clampage aortique, ce qui nous a paru dangereux et nous avons cessé rapidement de l'utiliser au profit du « bon » clamp de Chitwood malgré ses limites et inconvénients. Il faut souligné que la Méta-analyse réalisée en 2010 (20, cf annexe) a montré une plus faible fréquence des AVC et des complications vasculaires aortiques avec l'utilisation du clamp trans-thoracique comparativement à l'endoclamp.

Il est difficile d'évaluer l'incidence des complications ou incidents liés à la l'implantation de la canule de cardioplégie sur l'aorte, car cela est rarement voire jamais mentionné dans les études, mais nous savons que cela reste un obstacle pour de nombreux chirurgiens pour adopter la technique mini-invasive, du fait de la crainte d'un accident hémorragique sévère et difficile à contrôler par une voie d'abord limitée. L'étude pilote sur le Portapleg et notre série personnelle ont montré l'intérêt du système et de son clip auto-suturent, conduisant à l'accord des autorités de santé pour sa mise sur le marché. La version 2 du système a été testée et évaluée sur la cadavre mais n'a pas été développée par la société CLR.

L'écarteur Mitrax's a connu un grand intérêt parmi les chirurgiens impliqués dans un programme mini-invasif, du fait de sa simplicité et de l'exposition optimale de la valve mitrale qu'il permet, comme l'a démontré notre étude. Il est utilisé par de nombreux chirurgiens en Europe et représente un apport technique et instrumental indiscutable pour la technique (21).

En 2008, la société CLR avec laquelle nous avons travaillé en collaboration étroite pour l'évaluation des ces trois dispositifs dédiés à la chirurgie mitrale vidéo-assistée a été achetée par la société St Jude Medical dont la politique marketing sous l'égide des USA,

n'a pas permis de maintenir sur le marché ces produits à la hauteur de leur intérêt : la commercialisation du Portaclamp a été arrêté, le développement du Portapleg version 2 a été interrompu, seul le Mitrax's reste accessible aux chirurgiens préalablement utilisateurs du dispositif et il est vraisemblable que sa commercialisation sera arrêté dans les 12 ou 24 mois. Il n'en demeure pas moins que le Mitrax's garde une plus value d'efficience indiscutable, et pour confirmer l'intérêt du dispositif si cela était besoin, la société Medtronic vient de proposer un produit similaire, basé sur le même concept bien que plus complexe.

En définitive, cette collaboration étroite avec la société CLR et les travaux d'évaluation présentés dans ce document ont constitué une expérience très intéressante et nous ont permis de contribuer à la simplification et à la diffusion de cette technique, en complément du cours européen de chirurgie cardiaque mini-invasive (ECMICS) que nous avons monté en 2004 avec le Dr Rémi HOUEL et un groupe de chirurgiens experts européens (Dr De Cannière, Dr Munereto, Dr Birdi, Dr Diegeler) à Lyon dans le cadre de la FMC et de l'école de chirurgie de l'université Lyon 1, et au cours duquel à raison de deux séances par an, plus de 200 chirurgiens du monde entier ont complété leur formation pour cette technique qui est devenue avec le temps le nouveau standard pour la chirurgie mitrale (22, cf annexe) comme l'a souligné la conférence de consensus de l'ISMICS de 2010 (23, cf annexe). Les travaux et les recommandations de l'ISMICS (20,23) montrent que le bénéfice de la chirurgie mitrale mini-invasive par rapport à la chirurgie conventionnelle, est observé au prix d'un risque accru d'AVC et de complication vasculaire aortique qui disparaît avec l'utilisation d'un clamp trans-thoracique, de complications phrénique et pariétale au scarpa qui sont évitables avec certaines précautions techniques, et de temps opératoires plus longs qui se normalisent avec l'expérience.

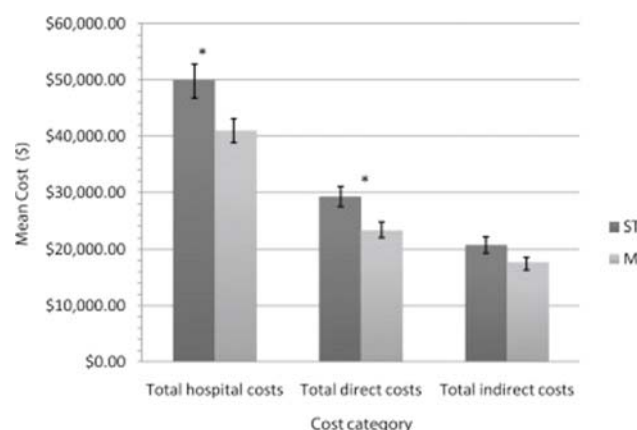
In patients with MV disease, minimally-invasive surgery is an alternative to conventional MVR/P [Class II b], given that there was:

- Comparable short term and long term mortality [Level B]
- Comparable in-hospital morbidity (renal, pulmonary, cardiac, pain perception, readmission rates) [Level B]
- Reduced sternal complications, volume of blood product transfusion, postop AF rate (18% vs 22%), ICU and hospital LOS, and time to return to normal activity [Level B]

However, this should be considered against the increased risk of

- Stroke (2.1% vs 1.2% for mini vs conv-MVR/P) [Level B],
- Aortic dissection (0.2% vs 0% mini- vs Conv MVR) [Level B],
- Phrenic nerve palsy [Level B],
- Groin complications [Level B],
- Increased XCL, CPB, and procedure time [Level B]

Cette contribution importante de l'ISMICS tend à clore près de 15 ans de controverses sur le sujet, d'autant qu'une étude récente a montré une réduction significative des coûts de procédure avec une approche mini-invasive (24).



La controverse autour de la chirurgie cardiaque robot-assistée reste par contre d'actualité en particulier dans la chirurgie des pontages coronaires. La technologie du télémanipulateur Da Vinci, avec la vision endoscopique 3D et l'endo-wrist instrumental a beaucoup séduit les chirurgiens impliqués en techniques mini-invasives, car il ouvrait

la voie à la chirurgie coronaire totalement endoscopique. Le concept et la faisabilité du TECAB ont été rapidement validés au début des années 2000 ; mais les études d'évaluation de la technique ont montré des résultats un peu décevant ou du moins pas à la hauteur des espérances : qu'il s'agisse de l'étude multicentrique européenne (25, cf annexe) avec une mortalité précoce de 2.2%, une perméabilité précoce de 92.1% et un taux de réintervention à 1 mois de 4.1%, ou de l'étude multicentrique nord américaine (26, cf annexe) avec un taux de réintervention ou d'échec de perméabilité de 9% à 3 mois, sans différence entre les techniques avec ou sans CEC. Comparés aux résultats de la chirurgie par sternotomie médiane de la STS data-base, ces résultats étaient acceptables, mais il nous a semblé important de les comparer aux techniques mini-invasives alternatives qui étaient largement utilisées et standardisées. Notre étude comparant TECAB, MIDCAB et Port-Access CABG dans la revascularisation isolée de l'IVA est la seule qui n'ait jamais été réalisée (27) et qui a eu le mérite malgré ses limites de confirmer la technique MIDCAB / ou RE-MIDCAB comme technique de référence pour ces indications. Cette étude nous a incité à ne pas hésiter à convertir une procédure TECAB en RE-MIDCAB au moindre doute de difficulté d'anastomose. L'amélioration de la technologie avec la dernière génération du Da Vinci, le quatrième bras et son stabilisateur endoscopique, a contribué sans doute à optimiser les résultats initiaux (28,29) qui ont cependant découragés de nombreuses équipes impliquées dans cette activité spécifique.

La possibilité de prélèvement mammaire bilatéral constitue un atout indiscutable du système Da Vinci et a ouvert la voie des procédures TECAB ou RE-MIDCAB avec multi-pontages mammaires. Bien que nous ayons été la première équipe à rapporté un TECAB bilatéral (15), notre expérience dans cette voie a été limitée du fait de la difficulté de la procédure anastomotique avec le système Da Vinci de première génération. Les résultats rapportés par J Bonatti (30) et R Dhawan (31, cf annexe) sont encourageants

mais révèlent néanmoins les limites de la technique avec un taux d'échecs primaires encore significatif. Notre intérêt pour la technique RE-MIDCAB avec multi-pontages demeure et nous travaillons actuellement au développement et à l'évaluation d'un système alternatif au Da Vinci, associant vision endoscopique 3D et endo-wrist instrumental pour le prélèvement mammaire bilatéral suivi d'une procédure RE-MIDCAB.

Conclusion.

Ce travail résume une expérience et une période formidable, personnelle mais aussi d'une équipe, sur plus de 10 ans, dans un domaine en évolution constante et dépendant des progrès technologiques et de la volonté de la communauté chirurgicale. La chirurgie mitrale vidéo-assistée a atteint une phase de maturité après 15 ans d'effort. La chirurgie cardiaque robotique est encore en phase de maturation ; son avenir dépend probablement de systèmes plus légers et moins onéreux, hybrides, associant colonne vidéo 3D et instruments motorisés, domaine que nous explorons actuellement, et de l'émergence de systèmes d'anastomose automatique performants (32).

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Review

Minimally invasive mitral valve surgery: a systematic review
and meta-analysisPaul Modi, Ansar Hassan, Walter Randolph Chitwood Jr.^{*}

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Summary

The mitral valve has been traditionally approached through a median sternotomy. However, significant advances in surgical optics, instrumentation, tissue manipulation, and perfusion technology have allowed for mitral valve surgery to be performed using progressively smaller incisions including the minithoracotomy and hemisternotomy. Due to reports of excellent results, minimally invasive mitral valve surgery has become a standard of care at certain specialized centers worldwide. This meta-analysis quantifies the effects of minimally invasive mitral valve surgery on morbidity and mortality compared with conventional mitral surgery and demonstrates equivalent perioperative mortality (1641 patients, odds ratio (OR) 0.46, 95% confidence interval 0.15–1.42, $p = 0.18$), reduced need for reoperation for bleeding (1553 patients, OR 0.56, 95% CI 0.35–0.90, $p = 0.02$) and a trend towards shorter hospital stays (350 patients, weighted mean difference (WMD) -0.73 , 95% CI -1.52 to 0.05 , $p = 0.07$). These benefits were evident despite longer cardiopulmonary bypass (WMD 25.81, 95% CI 13.13–38.50, $p < 0.0001$) and cross-clamp times (WMD 20.91, 95% CI 8.79–33.04, $p = 0.0007$) in the minimally invasive group. Case-control studies show consistently less pain and faster recovery compared to those having a conventional approach. Data for minimally invasive mitral valve surgery after previous cardiac surgery are limited but consistently demonstrate reduced blood loss, fewer transfusions and faster recovery compared to reoperative sternotomy. Long-term follow-up data from multiple cohort studies are also examined revealing equivalent survival and freedom from reoperation. Thus, current clinical data suggest that minimally invasive mitral valve surgery is a safe and a durable alternative to a conventional approach and is associated with less morbidity.

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Keywords: Surgical procedures; Minimally invasive; Thoracic surgery; Video-assisted; Mitral valve insufficiency

1. Introduction

Minimally invasive mitral valve surgery (MIMVS) does not refer to a single approach but rather to a collection of new techniques and operation-specific technologies. These include enhanced visualization and instrumentation systems as well as modified perfusion methods, all directed toward minimizing surgical trauma by reducing the incision size [1]. In the majority of cases, MIMVS has been performed through either a right anterior minithoracotomy or a hemisternotomy. The belief that this results in less surgical trauma, blood loss, transfusion and pain, which translates into a reduced hospital stay, faster return to normal activities, less use of rehabilitation resources, and overall healthcare savings, has driven this development. Scepticism surrounding MIMVS has focused on the potential 'trade-off' of incision size against the safety and exposure of established techniques with proven durable long-term results. Despite criticism over the last decade, various institutions have

adopted MIMVS and have published favorable results as single-center observational and comparative studies. A recent meta-analysis of minimal access aortic valve replacement suggested only marginal benefits for intensive care unit stay (ICU) and hospital stay over conventional surgery, despite longer operative times [2]. As yet, no such meta-analysis is available for MIMVS despite nearly 10 years of investigational data.

Changes in surgical indications, largely due to a better understanding of the natural history of organic mitral regurgitation and the increased use of repair techniques, have increased the number of minimally symptomatic patients with degenerative disease being referred for elective repair [3,4]. For MIMVS to become accepted widely, at least equivalent, if not better, short- and long-term outcomes must be demonstrated compared with sternotomy operations. This evidence should ideally come from large, multi-center prospective randomized controlled trials (RCT) that compare minimally invasive with conventional sternotomy-based mitral surgery. However, there are only two small RCTs, one of which reports data combined with minimally invasive aortic valve replacement [5,6]. The ability to conduct an effective RCT now would be compromised severely as patients and healthcare providers have preconceived notions

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about surgical approaches. This attitude would render patients unlikely to participate in a trial where randomization to sternotomy as a control cohort would be possible.

In the absence of large well-designed RCTs, data regarding short- and long-term outcomes are available from multiple case-control studies and observational studies. The aim of this report is to review the published randomized and nonrandomized comparative studies that compare minimally invasive endoscopic mitral valve surgery, excluding telemanipulation, to conventional approaches. Moreover, we integrate meta-analytical data to draw more useful conclusions about important short- and mid-term outcome metrics. Long-term outcomes are assessed using multiple large cohorts, to compare these to published sternotomy data.

2. Overview of the evolution of minimally invasive mitral valve surgery

In the mid-1990s, surgeons began to explore the potential advantages of minimizing incision size during cardiac surgery. Cosgrove and Cohn independently showed that mitral valve operations could be performed safely and efficiently using either parasternal or hemisternotomy incisions. Complications including slower healing, increased lung herniation, and less cosmetically appealing results led to the former being abandoned [7,8]. Carpentier performed the first video-assisted mitral valve repair through a minithoracotomy in February of 1996 [9]. Soon after, the East Carolina University group performed the first mitral valve replacement through a minithoracotomy, using video-direction, a transthoracic aortic clamp, and retrograde cardioplegia [10,11]. In 1997, we presented our first experience with 31 video-assisted mitral operations, reporting a 30-day mortality rate of 3.2% and no major complications [12]. In 1998, Mohr reported the Leipzig University experience using port-access (PA) technology, which was based on endo-aortic balloon occlusion (EABO) rather than direct aortic clamping [13].

The next major development was the introduction of a voice-controlled robotic camera arm (AESOP 3000, Computer Motion Inc., Santa Barbara, CA, USA) which allowed precise tremor-free camera movements with less lens cleaning. This technology translated into reduced cardiopulmonary bypass (CPB) and cross-clamp (XC) times [14,15], and enabled even smaller incisions with better valve and subvalvar visualization. The next evolutionary leap in endoscopic mitral surgery was the development of three-dimensional (3D) vision and computer-assisted telemanipulation that could transpose surgical movements from outside the chest wall to deep within cardiac chambers. Currently, the most widely used system is the Da Vinci® telemanipulation system (Intuitive Surgical Inc., Mountain View, CA).

3. Patients and methods

3.1. Literature search

The MEDLINE search strategy combined 'Cardiac surgical procedure' with the following MeSH terms: 'Surgical procedures, minimally invasive', 'Thoracic surgery, video-assisted',

'Endoscopy' AND with 'Mitral valve insufficiency', 'Mitral valve prolapse', and 'Mitral valve'. To reflect contemporary practice, the search was limited to the last 10 years and additional limits were English language citations and human subjects. The bibliographies of retrieved articles were searched for relevant articles. In addition, the 'related articles' function in PubMed was used as a further check of rigor. Where multiple cohort studies were published by a single institution, the largest or most informative study was included.

3.2. Inclusion criteria for meta-analysis

Intra-operative study variables included CPB and XC times, and postoperative ones were mortality, neurologic events (CVA), reoperation for bleeding, new atrial fibrillation (AF), intensive care unit (ICU) times, and hospital length of stay (LOS). The guidelines of the Meta-Analysis of Observational Studies in Epidemiology group were followed [16]. Both RCTs and case-control studies were used for the meta-analysis if they included at least one of the outcomes of interest. Reports presenting data for minimally invasive aortic and mitral valve surgery were only included if the mitral valve data were presented separately; studies reporting reoperative data were excluded from the meta-analysis. Studies in which data were not presented as mean and standard deviation (SD) or if this was not calculable were excluded from the analysis.

3.3. Statistical analysis

Meta-analyses were performed either using odds ratios (OR) or weighted mean differences (WMD) as the summary statistic for binary or continuous variables, respectively. The analyses were performed according to the recommendations of the Cochrane Collaboration and the Quality of Reporting of Meta-analyses guidelines [17]. An OR less than one or WMD less than one favors MIMVS over sternotomy. Random effects models were used as these assume variation between studies and are preferred for surgical data as selection criteria and risk profiles for patients differ between centers. Statistical significance was set at $p < 0.05$. Data were analysed using Review Manager version 4.2.10 (The Cochrane Collaboration, Oxford, England).

4. Results

We identified 43 published reports and of these there were two RCTs, 17 case-control studies, and 24 cohort studies. Of these studies, one RCT and ten case-control studies, published between 1998 and 2005, met the inclusion criteria (Table 1). Cohort patients numbered 2827, with 1358 in the MIMVS group and 1469 in the conventional sternotomy group. One comparative series was excluded [12] as more recent inclusive data from the same group were found [14]. One report contained data from the Society of Thoracic Surgeons (STS) database as the control arm and therefore was excluded [18]. One report presented results for mitral valve repair (MVP) and replacement (MVR) separately without presenting a combined group; the data for each were therefore analysed as independent studies [19]. The only randomized study included in the meta-analysis was by Dogan

Table 1
Studies comparing minimally invasive mitral valve surgery to sternotomy

Study, year, reference	Period	No. of patients		Valve	Approach	Design	Important findings
		MI	St				
Gower et al. (1998) [21]	N/A	21	20	MV	MT	CC	MI group had longer CPB times, better valvular/subvalvular visualization, returned to normal activity 5 weeks ahead of sternotomy patients
Asher et al. (1999) [29]	1/96–9/96	100	100	MV, AV	Not defined	CC	MI group had longer CPB/XC times, shorter hospital stay
Schneider et al. (2000) [27]	N/A	21	13	MV	MT	CC	MI group had longer CPB time, no difference in cerebral microembolic rate
Grossi et al. (2001) [20]	5/96–2/99	100	100	MV	MT	CC	Reported 1 year results: no difference in residual MR, freedom from reoperation or functional improvement between groups
Edgar et al. (2001) [14]	9/96–11/00	127	100	MV	MT	CC	Robotic direction with AESOP led to ↓ blood loss, ventilation and hospital stay compared to St group, and also ↓ CPB and XC times compared to manually directed videoscope
De Vaumas et al. (2003) [26]	N/A	10	10	MV	PS, 8–10cm	CC	PS group had longer CPB/XC times, ↑ blood loss
McCrath et al. (2003) [30]	3/90–10/00	214	87	MV	MT	CC	Reduced acute renal injury with MI approach
Gaudiani et al. (2004) [22]	1/97–12/02	205	616	MV	UHS, LHS, MT	CC	Shorter hospital stay for MI repair; less CVA for MI replacement
Mihaljevic et al. (2004) [24]	7/96–4/03	474	337	MV	LHS, PS	CC	MI group were lower risk patients. Low periop mortality in both groups (0.2% vs 0.3%). 5-year survival better for MI group (95% vs 86%, $p=0.03$)
Dogan et al. (2005) [5]	N/A	20	20	MV	MT	R	Intraoperative problem with EABO in 48%. No difference in markers of myocardial and cerebral injury, or pulmonary and neuropsychological tests between groups
Ryan et al. (2005) [19]	12/97–12/04	117	117	MV	MT	CC	MI group had longer CPB/XC times for repair; otherwise no differences
Colm et al. (1997) [8]	7/96–4/97	50	50	MV, AV	PS, UHS	CC	MI group had longer CPB and XC times, ↑ transfusion, greater patient satisfaction, less pain, faster return to normal activity, charges 20% less
Chilwood et al. (1997) [12]	5/96–3/97	31	100	MV	MT	CC	MI group had longer CPB/XC times, less transfusion, fewer re-explorations, reduced CVA, shorter ICU/hospital stays, reduced charges (↓27%) and costs (↓34%)
Reichenspumer et al. (1998) [18]	1/97–98	100	100	MV	MT	CC	Only difference was reduced AF in MI group
Grossi et al. (1999) [23]	1/94–12/98	111	259	MV, AV	MT	CC	Assessed patients ≥70 years old. MI group had lower sepsis/wound complications, less FFP, shorter hospital stay
Walthier et al. (1999) [32]	10/96–5/97	129	209	MV, AV, CABG	MT, UHS	CC	MT group approach had lower pain levels from day 3 onwards due to better thoracic stability
Hanano et al. (2001) [6]	4/97–12/98	21	27	MV, AV	PS 67%, UHS 29%, LHS 4%	R	No difference in CPB/XC times, transfusion requirements or SIRS between groups
Grossi et al. (2001) [25]	5/96–10/98	109	88	MV, AV	MT	CC	MI group had similar mortality, longer CPB times, shorter hospital stay, fewer transfusions and septic complications
Yanada et al. (2003) [28]	1/99–8/01	66	50	MV, AV	LHS	CC	MI group had longer CPB/XC times, less analgesics, less delirium, earlier food intake and Foley removal, and shorter ICU stay

Studies above the dotted line met the inclusion criteria for meta-analysis. AV, aortic valve; CC, case-control; CPB, cardiopulmonary bypass; CVA, cerebrovascular accident; EABO, endoaortic balloon occlusion; FFP, fresh frozen plasma; LHS, lower hemisternotomy; MI, minimally invasive; MT, minithoracotomy; MV, mitral valve; N/A, not available in text; PS, right parasternal; R, randomized; St, sternotomy; UHS, upper hemisternotomy; XC, cross-clamp.

et al. in which 20 patients in each arm were reported to have equivalent findings of ability to repair the valve, CPB and XC times, markers of myocardial and cerebral damage as well as pulmonary and neuropsychological tests [5]. Although the mean values for ventilation time, ICU time, hospital stay, and red blood cell transfusion were all lower in the MI group, these values did not reach statistical significance.

4.1. Mortality

Of the 11 comparative studies evaluating mortality, none found a significant difference between the minimally invasive

and conventional approaches [12,14,18–26]. In the largest study by Mihaljevic et al. 474 minimally invasive mitral operations (mostly lower sternotomy and right parasternal) were compared with 337 median sternotomy procedures. The perioperative mortality was 0.2% for the minimally invasive group and this compared favorably with 0.3% in the sternotomy cohort. However, the MIMVS patients were found to be a lower risk group (better ejection fraction, more repairs, less symptomatic) and no attempt was made to adjust for these differences [24]. Grossi et al. matched 88 patients undergoing minimally invasive aortic and mitral valve surgery over a 2.5-year period (through either a 2nd or 4th interspace incision) to

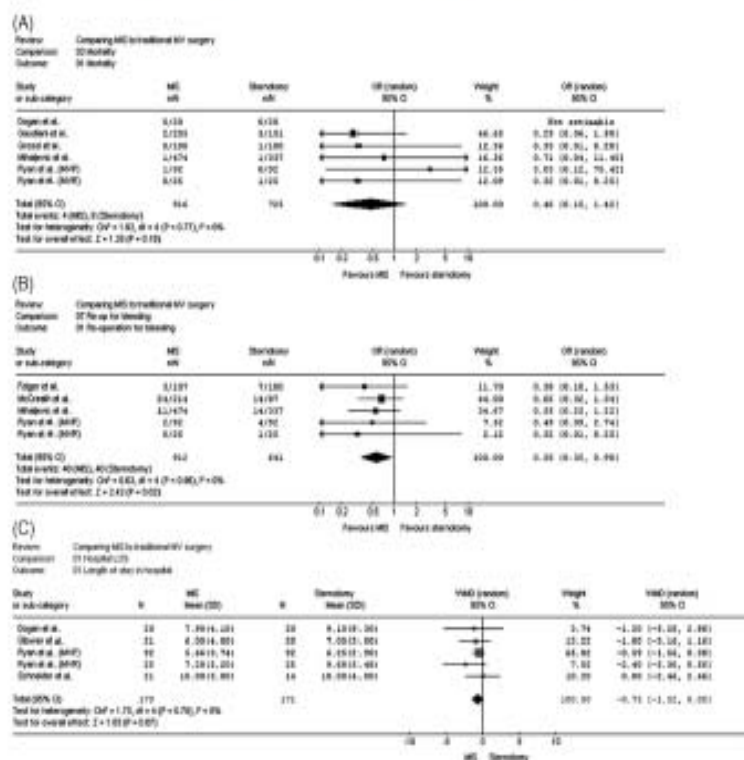


Fig. 1. Overall meta-analysis of perioperative mortality, reoperation for bleeding and hospital length of stay. The diamond represents the summary odds ratio (OR) from the pooled studies with 95% confidence intervals (CI) and is significant ($p \leq 0.05$) if it does not touch the central vertical line. Squares for each study show point estimates of treatment effect (OR) with the size of the square representing the weight attributed to each study; horizontal bars show 95% CI for these studies. *df*, degrees of freedom; MIS, minimally invasive surgery; MVR, mitral valve repair; MVR, mitral valve replacement.

patients having the same valve surgery via a sternotomy [25]. They demonstrated no significant difference in hospital mortality (3.7% vs 3.4%, respectively) between groups, even though mean CPB times were 30 min longer in the MI group. Six studies met the inclusion criteria for our meta-analysis and revealed no significant mortality difference between groups (1641 patients, OR 0.46, 95% CI 0.15–1.42, $p = 0.18$) (Fig. 1, Table 2).

4.2. Neurological events

Due to restricted access with minimally invasive cardiac operations, there continues to be concern that inadequate deairing can cause a higher incidence of neurological events. In

his early series, Mohr reported an 18% incidence of post-operative confusion; however, continuous CO_2 insufflation was not used as in more recent series [13]. Ten studies reported no difference in the incidence of stroke [14,18–21,23–27], while two showed a reduced incidence with a minimally invasive approach [12,22]. There was no significant difference in neurological events on meta-analysis of six eligible studies (1801 patients, OR 0.66, 95% CI 0.23–1.93, $p = 0.45$). Schneider et al. used trans-cranial Doppler to detect cerebral microemboli in 21 MIMVS patients undergoing endoaortic balloon occlusion with continuous CO_2 chest cavity insufflation. These were compared to 14 patients undergoing conventional mitral surgery [27]. They found no significant difference in the cerebral microembolic rate between either technique.

Table 2
Meta-analysis of outcomes

Outcome	No. of patients	No. of studies	OR/WMD (95% CI)	<i>p</i> value	Heterogeneity, χ^2	χ^2 , <i>p</i> value
Mortality	1641	6	0.46 (0.15 to 1.42)	0.18	1.82	0.77
Stroke	1801	6	0.66 (0.23 to 1.93)	0.45	6.77	0.24
CPB	871	8	25.81 (13.13 to 38.50)	<0.0001	27.05	0.0003
IC	671	7	20.91 (8.79 to 33.04)	0.0007	24.98	0.0003
Re-op for bleeding	1553	5	0.56 (0.35 to 0.90)	0.02	0.63	0.96
New onset AF	539	4	0.86 (0.59 to 1.27)	0.45	2.25	0.52
ICU stay	309	4	-0.36 (-0.80 to 0.08)	0.1	3.26	0.35
Hospital stay	350	5	-0.73 (-1.52 to 0.05)	0.07	1.75	0.78

AF, atrial fibrillation; CPB, cardiopulmonary bypass time; ICU, intensive care unit; IC, cross-clamp time.

4.3. Operative times

There were consistent findings that CPB and XC times were longer with a minimally invasive approach. There was evidence suggesting that parity can be achieved with experience while certain high volume centers report shorter operative times with MIMVS [24]. Of the 16 studies reporting cardiopulmonary bypass times, 10 described longer durations for MIMVS. Seven of 14 groups reported longer aortic cross-clamp times [6,8,12,14,18–30]. Meta-analysis of eligible studies showed significantly longer CPB (871 patients, WMD 25.81, 95% CI 13.13–38.50, $p < 0.0001$) and XC times (671 patients, WMD 20.91, 95% CI 8.79–33.04, $p = 0.0007$) with the minimally invasive approach.

4.4. Bleeding, transfusion and re-exploration

A reduction in postoperative hemorrhage and transfusion requirements has been suggested as a potential advantage of minimally invasive valve surgery. This benefit is important given the significant morbidity and mortality associated with transfusions and re-exploration for bleeding [31]. Four comparative studies reported blood loss volume with three utilizing a minithoracotomy [12,14,21] and one selecting a parasternal approach [26]. Few of these series met the inclusion criteria for the meta-analysis. Chitwood et al. demonstrated no difference in blood loss or blood product transfusions in 31 videoscopic mitral procedures compared with a conventional sternotomy, despite fewer re-explorations for bleeding [12]. The addition of a voice-activated robotic camera arm (AESOP 3000, Computer Motion, Inc., Galeta, CA) led to a reduction in blood loss as well as CPB and XC times. Nevertheless, there was no significant difference either in the percentage of patients receiving transfusions or the amount of blood products transfused [14]. In a consecutive series of 41 patients undergoing either port access ($n = 21$) or sternotomy ($n = 20$) mitral surgery, Glower et al. demonstrated no significant difference in chest tube drainage or transfusion requirements despite longer CPB times in the former [21].

Three of 10 studies showed reduced transfusion requirements with a minimally invasive approach, compared to conventional surgery [8,23,25] whilst the others showed no difference [6,12,14,19,21,26,32]. Too few studies met the inclusion criteria for meta-analysis (percent transfused, two studies; units transfused, three studies). In patients 70 years or older, Grossi et al. reported reduced plasma transfusions with a minimally invasive ($n = 111$) compared to a conventional ($n = 259$) approach [23]. However, the minimally invasive cohort had a lower preoperative risk profile (e.g. fewer redo operations), and there was no attempt to adjust for this baseline difference in the analysis. More convincing evidence came from a subsequent study by the same group that showed 13% fewer total transfusions with 1.8 fewer units of red blood cells using a minithoracotomy compared to a sternotomy [25]. Similar data from Cohn et al. confirm that patients undergoing minimally invasive valve surgery are transfused 1.8 units less compared to a conventional cohort [8].

Two of seven studies [12,14] demonstrated a reduced need for reoperation for bleeding with a minimally invasive approach [18,19,23,24,26]. Five studies met the inclusion

criteria for the meta-analysis that showed a significant reduction in reoperation for bleeding with a MI approach (1553 patients, OR 0.56, 95% CI 0.35–0.90, $p = 0.02$).

4.5. Atrial fibrillation (AF)

It has been suggested that a less traumatic surgical approach would be a less potent trigger of postoperative AF. Five of six studies, however, demonstrated this not to be the case [12,14,18,19,21,29], and on meta-analysis of four eligible studies, there was no significant difference between minimally invasive and sternotomy approaches (539 patients, OR 0.86, 95% CI 0.59–1.27, $p = 0.45$). Asher et al. addressed this question specifically in a cohort of 100 patients having elective primary minimally invasive aortic or mitral valve surgery and compared them to a matched control group undergoing a median sternotomy [29]. They found a similar prevalence of postoperative AF using either method, even when stratified for valve type. However, the PAIR registry reported a 10% incidence of new onset atrial fibrillation with the port access technique which is lower than that expected for sternotomy [33].

4.6. Septic complications

The incidence of septic wound complications is less with thoracotomy than median sternotomy. Of the three studies of mini-thoracotomy mitral valve surgery that reported wound complications compared to median sternotomy, Grossi et al. reported an incidence of 0.9% and 5.7% for mini-thoracotomy and sternotomy cases, respectively ($p = 0.05$) [25]. This increased to 1.8% and 7.7%, respectively, in elderly patients ($p = 0.03$) [23], whereas Felger et al. reported no significant difference [14].

4.7. Pain and speed of recovery

Of all the potential benefits of MIMVS, a reduction in pain and faster return to normal activity is the most consistent finding. All four studies that measured postoperative pain levels reported less compared to sternotomy [8,21,28,32] and both studies reporting time to return to normal activities noted a significant advantage for a minimally invasive approach [8,21]. In a nonrandomized study, Walther et al. reported equivalent pain for the first two postoperative days when a minithoracotomy approach was compared to sternotomy with a subsequent significant reduction of pain in the MI group from day 3 onwards, a difference which progressively widened with time [32]. Better stability of the bony thorax led to earlier mobilization and a faster return to activities of daily living. Glower reported that postoperative pain tended to resolve more quickly with a minimally invasive approach and that these patients returned to normal activity 5 weeks more rapidly than those having a median sternotomy (4 ± 2 weeks vs 9 ± 1 weeks, $p = 0.01$) [21]. Cohn's data is concordant with less pain in hospital and after discharge, less analgesic usage, greater patient satisfaction and a return to normal activity 4.8 weeks ahead of sternotomy patients [8]. Vanermen reported that 94% of his patients report no or mild postoperative pain, 99.3% feel they have an aesthetically pleasing scar, 93% would choose the same procedure again if

Table 3
Most recent observational cohort studies of minimally invasive mitral valve surgery

Study, year, reference	Institution/City	Period	No. of patients	Mortality (%)		Stroke (%)	
				MVP (%)	MVR (%)	MVP (%)	MVR (%)
Glower et al. (2000) [33]	PAIR	7/97–8/99	1059	1.6	5.5	2.6	2.8
Grossi et al. (2002) [37]	NYU	11/95–11/01	714	1.1	5.8	2.9	—
Soltész et al. (2007) [1] ^a	Brigham	7/96–2007	663	0.5	3.1	1	—
Chilwood et al. (2007) ^b	ECU	5/96–9/07	535	2.0	3.8	1.5	1.5
Casselman et al. (2003) [34]	Aalst	2/97–4/02	306	0.4	2.5	0.4	0
Cosgrove et al. (2003) [38]	Cleveland	1996–2002	1427	0.3	—	1.8	—
Wäthter et al. (2004) [39]	Leipzig	6/96–2004	1000	3.9	—	4.3	—
Mishra et al. (2005) [40]	New Delhi	9/97–12/04	430	0.5	—	0.5	—
Aybek et al. (2006) [41]	Frankfurt	7/97–5/04	241	3.3	—	0.8	—
Tornacca et al. (2006) [42]	Milan	10/99–12/03	104	0	—	0	—

ECU, East Carolina University; MVP, mitral valve repair; MVR, mitral valve replacement; NYU, New York University; PAIR, port access international registry; STS, Society of Thoracic Surgeons.

^a Includes data from Mihaljevic et al. [24].

^b Unpublished data.

Table 4
Summary data derived from above cohort studies compared to data from STS Fall 2007 report

		No. of patients	No. of studies	Summary data (%)	STS data (%)
Mortality	Repair	2176	6	1.1	1.5
	Replacement	979	5	4.9	5.5
	Overall	6253	10	2.0	3.3
Stroke	Repair	1226	4	1.6	1.9
	Replacement	778	3	2.3	3.2
	Overall	6290	10	2.2	2.5

Data for repair and replacement are derived from those studies where these variables are reported independently. Overall data are derived from all studies combined.

they had to have redo surgery and 46% are back at work within 3 weeks [34]. However, perhaps the most insightful piece of evidence for patient preference of MIMVS comes from two studies reporting that those who have had a MI approach as their second procedure all felt that their recovery was more rapid and less painful than their original sternotomy [14,35].

4.8. Hospital stay, costs and discharge disposition

Does a more rapid recovery translate into a shorter stay in hospital and therefore reduced costs? Eight of 14 studies reported less time in hospital with a MI approach [8,12,14,19,21–29,32]. Only five studies were eligible for meta-analysis and although the trend indicated this to be the case, the result was not statistically significant (350 patients, WMD -0.73 , 95% CI -1.52 to 0.05 , $p=0.07$) (Fig. 1). Chilwood, Cohn and Cosgrove equated this to a 34%, 20% and 7% cost saving, respectively [8,12,36]. Moreover, these patients had fewer requirements for post-hospital rehabilitation, which is a significant advantage in terms of healthcare savings

with 91% being discharged home compared to 67% with a conventional approach [8,24].

4.9. Intermediate- and long-term results

Comparing a consecutive cohort of 100 minithoracotomy mitral valve operations to the previous 100 sternotomy mitral valve procedures, Grossi et al. found comparable 1-year freedom from reoperation (96.8% vs 94.4%, $p=0.38$, respectively) with similar net improvement in functional class [20]. Mihaljevic et al. reported significantly better actuarial survival at 5 years for minimally invasive compared to sternotomy patients (95% vs 86%), but this may be explained by a lower risk profile [24]. Many of the cohort studies are temporally updated results from a few select high-volume centers such as the Cleveland Clinic, the Brigham and Women's Hospital, New York University, University of Leipzig, OLV Clinic (Aalst, Belgium) and East Carolina University. Therefore, only the most recent data from 10 cohorts with 6479 patients are considered, herein

Table 5
Studies reporting long-term results of minimally invasive mitral valve surgery

Study, year, reference	Institution	Survival	Freedom from re-operation
Gullelmos et al. (2000) [43]	Dresden	93.5% at 3.3 years	—
Casselman et al. (2003) [34]	Aalst	95.4 \pm 1.7% at 4 years	91 \pm 3.5% at 4 years
Grodish et al. (2003) [44]	Brigham	95% at 5 years	92% at 5 years
Wäthter et al. (2004) [39]	Leipzig	83% at 6.8 years	—
Mishra et al. (2005) [40]	New Delhi	99% at 3.2 years	99.3% at 3.2 years
Aybek et al. (2006) [41]	Frankfurt	90.7% at 6.3 years	96.2% at 6.3 years
Tornacca et al. (2006) [42]	Milan	100% at 2.3 years	95.2% at 4 years

(Table 3) [1,33,34,37–42]. The crude unadjusted mortality rates for the entire cohort are 1.1% for mitral valve repair and 4.9% for mitral valve replacement. The corresponding data from the Society of Thoracic Surgeons (STS) Fall 2007 report are 1.5% for MVP and 5.5% for MVR (Table 4). The neurological event rates for the entire cohort are lower than STS data. With regard to long-term survival, we found seven studies reporting from 100% survival at a mean of 2.3 years to 83% at 6.8 years postoperatively (Table 5) [34,39–44]. This compares favorably to 5-year survivals of 86.4% reported by the Mayo Clinic [45] and 82% reported by the Cleveland Clinic [46]. Five studies reported freedom from reoperation ranging from 99.3% at 3.2 years to 91% at 4 years [34,40–42,44]. The longest follow-up was 6.3 years with 96.2% freedom from reoperation. Again this compares favorably to the Mayo Clinic data which indicates a risk of reoperation of between 0.5% per year for isolated posterior leaflet prolapse to 1.64% per year for isolated anterior leaflet prolapse [45].

5. Special situations

5.1. Reoperative surgery

The greatest potential benefit of a right mini-thoracotomy is the avoidance of sternal re-entry and limited dissection of adhesions, avoiding the risk of injury to cardiac structures or patent grafts, and limiting the amount of postoperative bleeding [47]. This consistently translates into reduced blood loss, less transfusions and faster recovery. There are seven important studies (three case-control and four cohort) describing a right minithoracotomy approach for reoperative valve surgery [35,48–53] and one describing a left posterior approach [54] (Table 6).

The case-control studies all demonstrated superiority of the right mini-thoracotomy versus a reoperative sternotomy. The largest series from Sharony et al. demonstrated equal mortality (5% for isolated mitral operations), fewer wound infections, less blood product utilization, decreased hospital length of stay, and slightly more favorable mid-term

outcomes with a mini-thoracotomy approach for reoperative mitral and aortic valve surgery [48]. In 71 reoperative mitral valve operations of which 38 were done through a minithoracotomy, Bolotin et al. noted no difference in mortality or CPB times but significantly reduced intubation times, blood transfusion and hospital stay with a minimally invasive approach [49]. In a retrospective study from Duke University, patients undergoing a right mini-thoracotomy for redo mitral surgery had lower mortality, less blood loss and fewer transfusions than via a redo sternotomy or an anterolateral thoracotomy [50].

Vanermen recently reported 80 adults undergoing endoscopic MV and TV reoperative surgery with an operative mortality of 3.8% [51]. There was one intra-operative and two postoperative strokes. Survival at 1 and 4 years was $93.6 \pm 2.8\%$ and $85.6 \pm 6.4\%$ respectively, and there was one late reoperation at five years. At the University of Michigan, Bolling et al. used a 5–10 cm right anterior 5th interspace thoracotomy in 22 patients for reoperative mitral and tricuspid valve surgery with no 30-day mortality [35]. Patients were weaned from ventilation at a mean of 5 h and received 1.3 ± 1 units of blood. There were no re-explorations for bleeding. The important message from this study was that all patients interviewed considered that their recovery was more rapid and less painful than their original sternotomy.

Onnasch et al. reported 39 patients undergoing redo mitral valve surgery through a right minithoracotomy with a mortality of 5.1% [53]. One patient experienced transient hemiplegia due to migration of the aortic balloon endocatheter. This group concluded that a MI approach offers excellent exposure and minimizes the need for mediastinal dissection and optimizes patient comfort. Their updated series described 97 patients undergoing mitral reoperations since 1996 with an in-hospital mortality of 5.6% [52].

Finally, the New York University group have described a left posterior minithoracotomy approach in 40 patients in whom a right thoracotomy was precluded, e.g. right mastectomy/irradiation [54]. They concluded this approach to be a valuable option in complicated reoperative mitral

Table 6
Studies reporting a minithoracotomy approach for reoperative mitral valve surgery

Study, reference	Period	No. of patients		Valve	Design	Important findings
		MI	Conv			
Sharony et al. (2006) [48]	1995–2002	161	St 337	AV, MV	CC	Surgical approach not an independent risk factor for mortality. However, fewer wound infections, less blood product transfusion and shorter hospital stays for MI group
Bolotin et al. (2004) [49]	1/96–6/03	38	St 33	MV	CC	Shorter intubation and LOS, reduced blood transfusion
Burfeind et al. (2002) [50]	1985–2001	60	Th 37 St 155	MV ± TV	CC	Less bleeding, transfusion and mortality with minithoracotomy approach
Casselman et al. (2007) [51]	12/97–5/06	80	—	MI, TV	Cohort	Observed/expected mortality, 0.24. Four-year survival $85.6 \pm 6.4\%$. One reoperation at 5 years. 99% of patients preferred MI approach to prior sternotomy
Mesleis et al. (1998) [35]	12/96–10/97	22	—	MV ± TV or ASD	Cohort	No mortality, mean ventilatory support 5 h, mean blood transfusion 1.3 ± 1.0 units, mean LOS 5.9 days. All felt less pain and faster recovery than prior sternotomy
Wälther et al. (2006) [52]*	3/97–1996	97	—	MV	Cohort	Mortality 7.2% compared to registry data of 8.75%. Repair in 56%

ASD, atrial septal defect; AV, aortic valve; CC, case-control; Conv, conventional; LOS, length of stay; MI, minimally invasive; MV, mitral valve; St, sternotomy; Th, standard anterolateral right thoracotomy; TV, tricuspid valve.

* Updated results from a previous study [53].

procedures with acceptable perioperative morbidity and mortality.

5.2. Low ejection fraction

Previously considered by many as a contraindication to a minimally invasive approach, Mohr has treated 68 patients having a dilated cardiomyopathy ($EF 21 \pm 8\%$) with MI mitral valve repair and 11 with a replacement with an overall 8.8% mortality [52]. Severe pulmonary hypertension was present in 45.6%. Postoperatively, 6.3% developed renal failure and 7.9% had low cardiac output. Despite successful mitral valve repair, seven patients required transplantation during follow-up.

5.3. Elderly patients

Two studies have looked at the application of MI techniques specifically to elderly patients. Grossi et al. reviewed 111 patients undergoing MI valve surgery who were at least 70 years old and compared these to 259 patients having a sternotomy [23]. The MI group had a significantly lower incidence of sepsis and wound complications, required less frozen plasma transfusions, and had a shorter length of hospital stay. They concluded that this approach can be used safely in operations on the elderly population with excellent results. Also, Tabata et al. recently reported 123 cases of MI mitral valve repair in patients aged 70 years and older with 1.6% operative mortality as well as 5-year actuarial survival of 87% and 5-year freedom from reoperation of 93% [55].

6. Endo-aortic balloon occlusion versus transthoracic clamping

One of the most significant risks of endo-aortic balloon occlusion (EABO) is aortic dissection, and as a consequence, many surgeons have abandoned this technique. In the first FAIR report, the incidence of aortic dissection was 1.3% in the first half of the study compared to 0.2% in the second half, a difference attributable to experience, better techniques, and improved technology [56]. In comparison to transthoracic clamping (TTC), EABO is more expensive, and the clamp position is less stable. Proximal balloon dislodgement can cause innominate artery occlusion with neurological injury. Monitoring by transesophageal echocardiography and transcranial Doppler should be done routinely [57,58]. Balloon prolapse into the left ventricle can lead to inferior myocardial protection, ventricular distension or aortic valve injury.

There are three pertinent studies, all non-randomized consecutive series from Germany, demonstrating superiority of TTC over EABO. Onnasch et al. demonstrated a significantly higher risk of neurological complications with EABO (8.1% vs 1.8%, $p < 0.05$) and higher mortality (5.2% vs 3.1%, respectively). Mohr subsequently abandoned EABO for primary mitral valve procedures [59]. In 58 patients, Aybek et al. demonstrated similar results with faster operations, fewer technical difficulties, less blood loss and lower costs using the transthoracic clamp [60]. Reichenspurner et al. confirmed shorter operative times with TTC in 120 patients

and with fewer complications (reduced bleeding, wound problems and fewer femoral artery reconstructions) and he showed a reduction in costs of disposables by \$2800 [61].

7. Limitations of a minimally invasive approach

Clearly, there is a learning curve for the surgeon as well as the anesthetists, perfusionists and nursing teams. Mohr reported a high mortality (9.8%) in his early port access cases, partially procedure-related with two of 51 patients suffering an aortic dissection [13]. After simplification of the surgical procedure the mortality decreased to 3%. Vanermen demonstrated that ICU and hospital stays decrease with increasing experience [62].

There are potential vascular risks with femoral cannulation, especially with the larger port access femoral cannula. Groin seromas can be problematic but are kept to a minimum by dissection only of the anterior surface of the vessels as well as clipping lymphatics. When the pericardium is opened too posteriorly, phrenic nerve palsy has been reported and can be avoided by placing the pericardiotomy at least 3 cm anterior to it. Excessive tension by pericardial retraction sutures should be avoided. Although some have suggested that a small anterior thoracotomy is associated with equal or greater postoperative pain [63,64], there is good evidence as detailed above that it actually reduces postoperative discomfort and enhances recovery [21,25,65].

8. Conclusions

Over the last decade there has been a transformation in the way cardiac surgeons, cardiologists and patients decide the approach to cardiac therapies. Less invasive procedures are demanded but at the same time proven safety, efficacy and durability are expected. There is no prior level one evidence to justify switching to minimally invasive mitral valve surgery. All the reviewed evidence demonstrates that minimally invasive mitral valve surgery is associated with equal mortality and neurological events despite longer cardiopulmonary bypass and aortic cross-clamp times. However, there is less morbidity in terms of reduced need for reoperation for bleeding, a trend towards shorter hospital stay, less pain and faster return to preoperative function levels than conventional sternotomy-based surgery. This would be expected to translate into improved utilization of limited healthcare resources. With follow-up now of almost 7 years it is clear that long-term outcomes are equivalent to those of conventional surgery. Data for minimally invasive mitral valve surgery after previous cardiac surgery is limited but consistently demonstrates reduced blood loss, fewer transfusions and faster recovery compared to reoperative sternotomy. Almost all patients who undergo a minimally invasive mitral valve operation as their second procedure feel their recovery is more rapid and less painful than their original sternotomy.

As for the future, minimally invasive cardiac surgery is likely to become more widely adopted as growth in this niche market and cardiac surgery as a whole is often patient-driven, much in the same way that percutaneous intervention for multivessel

disease has been. That is, patients do not want a sternotomy and it is important as a surgical community that we realize this. However, despite enthusiasm, caution cannot be overemphasized as traditional cardiac operations still enjoy proven long-term success and ever-decreasing morbidity and mortality and remain our measure for comparison.

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Minimally Invasive Versus Conventional Open Mitral Valve Surgery

A Meta-Analysis and Systematic Review

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Objective: This meta-analysis sought to determine whether minimally invasive mitral valve surgery (mini-MVS) improves clinical outcomes and resource utilization compared with conventional open mitral valve surgery (conv-MVS) in patients undergoing mitral valve repair or replacement.

Methods: A comprehensive search of MEDLINE, Cochrane Library, EMBASE, CTSnet, and databases of abstracts was undertaken to identify all randomized and nonrandomized studies up to March 2010 of mini-MVS through thoracotomy versus conv-MVS through median sternotomy for mitral valve repair or replacement.

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Outcomes of interest included death, stroke, myocardial infarction, aortic dissection, need for reintervention, and any other reported clinically relevant outcomes or indicator of resource utilization. Relative risk and weighted mean differences and their 95% confidence intervals were analyzed as appropriate using the random effects model. Heterogeneity was measured using the I^2 statistic.

Results: Thirty-five studies met the inclusion criteria (two randomized controlled trials and 33 nonrandomized studies). The mortality rate after mini-MVS versus conv-MVS was similar at 30 days (1.2% vs 1.5%), 1 year (0.9% vs 1.3%), 3 years (0.5% vs 0.5%), and 9 years (0% vs 3.7%). A number of clinical outcomes were significantly improved with mini-MVS versus conv-MVS including atrial fibrillation (18% vs 22%), chest tube drainage (578 vs 871 mL), transfusions, sternal infection (0.04% vs 0.27%), time to return to normal activity, and patient scar satisfaction. However, the 30-day risk of stroke (2.1% vs 1.2%), aortic dissection/injury (0.2% vs 0%), groin infection (2% vs 0%), and phrenic nerve palsy (3% vs 0%) were significantly increased for mini-MVS versus conv-MVS. Other clinical outcomes were similar between groups. Cross-clamp time, cardiopulmonary bypass time, and procedure time were significantly increased with mini-MVS; however, ventilation time and length of stay in intensive care unit and hospital were reduced.

Conclusions: Current evidence suggests that mini-MVS maybe associated with decreased bleeding, blood product transfusion, atrial fibrillation, sternal wound infection, scar dissatisfaction, ventilation time, intensive care unit stay, hospital length of stay, and reduced time to return to normal activity, without detected adverse impact on long-term need for valvular reintervention and survival beyond 1 year. However, these potential benefits for mini-MVS may come with an increased risk of stroke, aortic dissection or aortic injury, phrenic nerve palsy, groin infections/complications, and increased cross-clamp, cardiopulmonary bypass, and procedure time. Available evidence is largely limited to retrospective comparisons of small cohorts comparing mini-MVS versus conv-MVS that provide only short-term outcomes. Given these limitations, randomized controlled trials with adequate power and duration of follow-up to measure clinically relevant outcomes are recommended to determine the balance of benefits and risks.

Key Words: Systematic review, Meta-analysis, Mitral valve surgery, Minimally invasive surgery.

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RATIONALE

Interest in minimally invasive cardiac surgery continues to grow rapidly. Although conventionally mitral valve surgery has been performed via a full incision through the sternum, a variety of technologies and techniques have enabled minimally invasive mitral valve surgery (mini-MVS) to be performed through one or more small incisions in the thorax with assisted vision using cameras. In some cases, robotic surgery may be used for mini-MVS. The goal of mini-MVS is to reduce the surgical trauma to the patient (presumably to reduce pain, scarring, and inflammatory response) while maintaining the proven surgical efficacy of the conventional open approach.

Some, but not all, studies suggest that favorable outcomes are achieved using the minimally invasive approach to mitral valve surgery. A comprehensive meta-analysis of available comparative studies (randomized and nonrandomized) is needed to better assess the risks versus benefits of mini-MVS versus conventional open mitral valve surgery (conv-MVS) through median sternotomy. One previous meta-analysis of mini-MVS by Modi et al¹ has been published. However, a number of relevant studies were not identified, and only some outcomes of interest were analyzed in the article. Therefore, we conducted a systematic review with meta-analysis to address the available evidence to date which compares mini-MVS via thoracotomy or parasternal approach with conv-MVS through median sternotomy.

OBJECTIVES

The objective of this systematic review with meta-analysis was to determine whether, in patients undergoing mitral valve surgery, mini-MVS improves postoperative complications and provides comparable or improved long-term clinical outcomes, quality of life, and cost-effectiveness compared with conv-MVS.

To answer this primary objective, the following sub-questions were prespecified to guide the systematic review:

1. Does mini-MVS reduce risk of death compared with conv-MVS?
2. Does mini-MVS reduce perioperative complications compared with conv-MVS?
3. Does mini-MVS improve quality of life, functionality, or other patient-reported outcomes?
4. Does mini-MVS reduce total costs, intensive care unit (ICU) and hospital length of stay, need for repeat cardiac surgery, readmissions, and is it cost-effective?

METHODS

This systematic review with meta-analysis of comparative studies was performed in accordance with state-of-the-art methodological recommendations for randomized and observational studies (ie, as per the "Quality of Reports of Meta-Analyses" and "Meta-Analysis of Observational Studies of Epidemiology," QUOROM and MOOSE guidelines, respectively)^{2,3} and according to a protocol that prespecified outcomes, search strategies, inclusion criteria, and statistical analyses.

Endpoints

Clinical endpoints of interest included postoperative all-cause mortality, stroke, myocardial infarction, atrial fibrillation, low cardiac output syndrome, need for antiarrhythmic drugs, need for pacemaker, reexploration for bleeding, major bleeding, transfusions, renal failure, heart failure, New York Heart Association (NYHA) class, reintervention for bleeding, reintervention for valvular repair or replacement, patient satisfaction, functionality, quality of life, cross-clamp time, duration of surgery, ICU length of stay, total hospital length of stay, costs, and cost-effectiveness.

Literature Search

A comprehensive literature search of MEDLINE, EMBASE, Cochrane CENTRAL, CTSnet, and databases of conference abstracts using keywords and variants was performed from the earliest available date to March 2010. Search terms included variants of "surgical procedures," "minimally invasive," "mitral valve," "thoracoscopic," and "robotic." No limits were placed on date, study design, or language. This was supplemented with hand search from the selected articles and review articles. Experts were contacted to solicit additional reports of published or unpublished clinical studies of mini-MVS.

Inclusion Criteria

To be eligible for inclusion in the systematic review and meta-analysis, studies had to be randomized or nonrandomized comparative studies comparing mini-MVS (performed via thoracotomy through port-access or keyhole, with either direct visualization or with camera or robotic assistance through lateral, parasternal, or xiphoid approaches) versus conv-MVS (performed via median sternotomy or parasternal approach). Published and unpublished studies were eligible in any language.

Data Extraction

Two authors extracted and verified by consensus the following data points: baseline demographics, surgical procedure details, and all clinically relevant or resource-related outcomes.

Data Analysis

Risk ratios (RRs) and their 95% confidence intervals (CIs) were calculated for discrete data. Weighted mean differences (WMD; 95% CI) were calculated for continuous data. Heterogeneity was explored through the Q-statistic and by calculating the heterogeneity (I^2). RR and WMD were calculated using the random effects model to provide a conservative analysis in the case of heterogeneity. When statistical heterogeneity was high ($I^2 > 75\%$), potential reasons for heterogeneity were explored. Because data from randomized trials were of greatest interest, subanalysis was planned for randomized controlled trials (RCTs) versus observational studies.

When possible, intention-to-treat was data analyzed. Statistical significance for overall effect was defined as $P < 0.05$ or a confidence that excluded the value 1.00 for RR and 0 for WMD. Data analysis was performed using Review Manager (REVMAN) 5 COCHRANE Collaboration software.

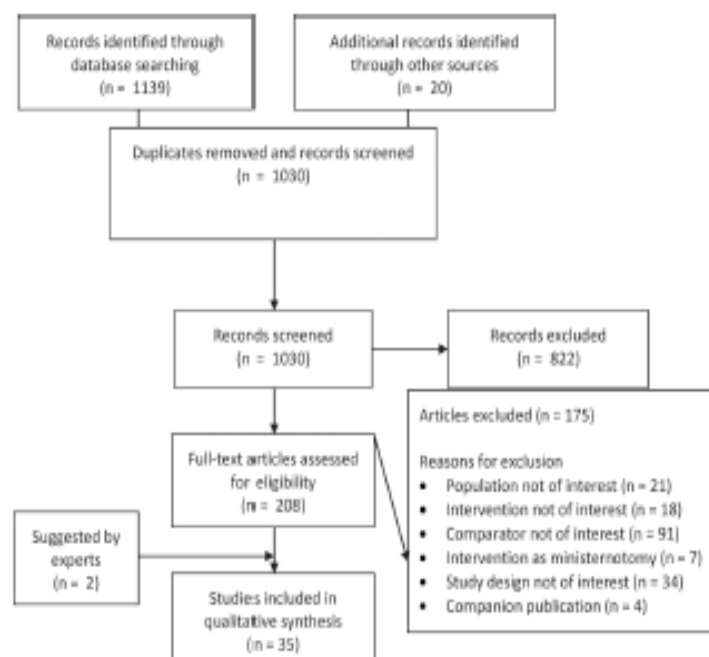


FIGURE 1. Study Identification.

RESULTS

Study Identification

Of over 1159 citations identified, 208 were identified as potentially relevant and were retrieved for full review. An additional two studies were identified by experts as potentially eligible studies. Of these, 35 studies met the inclusion criteria for the primary analysis of mini-MVS versus conv-MVS.^{4–38} Two of the included studies were RCTs^{12,13} and the remainder were nonrandomized studies (Fig. 1). Most of the non-RCTs were retrospective studies. Thirty-four of the studies were published between 1997 and 2010. One³⁷ of the two unpublished studies^{37,38} suggested by the experts was subsequently published before this manuscript was sent to press. Most of the studies were from the United States (n = 17), followed by Germany (n = 6), France (n = 2), Israel (n = 2), and one each from Austria, Yugoslavia, Slovenia, Japan, China, India, Egypt, and Turkey.

Eighteen studies used primarily endoaortic balloon clamping,^{5,7,12,17–20,22,23,25,27,29,30,32,33,35,36,38} whereas 13 studies used direct/transthoracic aortic clamping,^{8–11,13–15,21,24,28,31,34} and four studies used both endoaortic and transthoracic clamping.^{6,16,26,37} Three studies reported that posterior mitral valve repair was performed: 77% versus 73%,¹⁶ 75% versus 80%,²⁶ and 81% versus 80%¹⁹ for mini-MVS versus conv-MVS, respectively. No study provided separate data for anterior mitral valve repair versus posterior mitral valve repair. Three studies included only redo mini-MVS versus conv-MVS,^{3,4,25} whereas the remainder were of first-time, mixed redo or first-time, or did not report this information.

For studies that reported more than once on an identical or overlapping population, attempts were made to include only the most recent or most complete results. In many cases, it was difficult to determine whether series from the same centers (or involving overlapping authors, but from differing centers) provided distinct data or whether there was overlap between studies. In many nonrandomized studies, patient attrition was inadequately described, and crossover from intended mini-MVS to conv-MVS was rarely described. This does not guarantee that crossovers did not occur.

Patient Characteristics

Baseline characteristics are listed in Table 1. The patients in the mini-MVS group were younger on average by 1.6 (–2.7 to –0.4) years compared with conventional open mitral valve repair/replacement (MVR) (54.0 ± 12.4 years vs 55.8 ± 12.6 years, respectively). The percentage of females was similar for both groups (42%). The mini-MVS group had less baseline renal failure (1% vs 2%), less chronic obstructive pulmonary disease (11% vs 12%), and lower pulmonary artery pressures (42 vs 45 mm Hg) compared with the conv-MVS group. For other baseline characteristics, there were no statistically significant differences detected between mini-MVS and conv-MVS for most reported baseline characteristics; however, some characteristics were reported in only a few studies, and there was significant heterogeneity among the studies for a number of baseline characteristics. Although baseline patient characteristics were similar for randomized and nonrandomized studies, the small number and size of the randomized studies and the inconsistent reporting of baseline characteristics in nonrandomized studies precluded adequate power to confidently rule out whether potential differences exist.

TABLE 1. Patients' Characteristics Before Mitral Valve Repair or Replacement: Minimally Invasive Versus Conventional MVR

Outcome	Mean \pm SD/Incidence		n (N)	WMD (95% CI) or RR (95% CI)	P
	Mini-MVS	Conv-MVS			
Age (yr)	54.0 \pm 12.4	55.8 \pm 12.6	28 (14,677)	-1.57 (-2.72, -0.42)	0.007
Female	42%	42%	26 (14,595)	1.01 (0.92, 1.09)	NS
LVEF (%)	54.3 \pm 10.3	55.4 \pm 11.5	21 (12,374)	-1.56 (-3.50, 0.38)	NS
Mitral regurgitation	96%	95%	14 (11,081)	1.00 (0.99, 1.02)	NS
Mitral stenosis	17%	23%	8 (1,329)	0.85 (0.62, 1.15)	NS
Body weight (kg)	68.4 \pm 14.9	68.1 \pm 17.1	4 (776)	-0.17 (-2.46, 2.12)	NS
Diabetes	7%	7%	12 (11,326)	1.03 (0.84, 1.28)	NS
Heart failure	34%	33%	8 (10,848)	1.02 (0.85, 1.22)	NS
Hypercholestermia	21%	21%	4 (635)	1.04 (0.77, 1.40)	NS
Myocardial infarction	3%	5%	5 (951)	0.67 (0.26, 1.73)	NS
Stroke/CVA	3%	3%	5 (9,523)	0.88 (0.69, 1.12)	NS
Hypertension	49%	50%	9 (10,469)	0.91 (0.80, 1.03)	NS
Atrial fibrillation	21%	23%	4 (10,761)	0.79 (0.54, 1.16)	NS
PVD	9%	8%	4 (1,073)	1.05 (0.68, 1.61)	NS
Renal failure	1%	2%	6 (28,848)	0.47 (0.33, 0.67)	<0.0001
COPD	11%	12%	4 (9653)	0.57 (0.33, 0.98)	0.04
Pulmonary artery pressure (mm Hg)	42 \pm 15	45 \pm 20	2 (283)	-4.65 (-8.81, -0.48)	0.03

CI indicates confidence interval; Conv-MVS, conventional open mitral valve surgery; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; I^2 , heterogeneity; LVEF, left ventricular ejection fraction; Mini-MVS, minimally invasive mitral valve surgery; MVR, mitral valve replacement/repair; n, number of studies; N, number of patients; NS, not significant; PVD, peripheral vascular disease; RR, risk ratio; WMD, weighted mean difference.

All-Cause Mortality

All-cause mortality did not differ between minimally invasive and conventional open MVR (1.2% vs 1.5%; RR 1.03, 95% CI 0.75–1.42; 20 studies).^{5,6,8,12,13,15–19,21,26,28,31,32,34–38} Two RCTs involving 140 patients reported no mortality in minimally invasive and conventional open MVR.^{12,13} Subanalysis by endoaortic or transthoracic clamping also showed no significant difference for all-cause mortality between minimally invasive and conventional open MVR. There was no significant heterogeneity among the studies for this outcome (Fig. 2; Table 2).

Neurologic Outcomes Up to 30 Days

Stroke

Risk of stroke was significantly increased for mini-MVS compared with conv-MVS (2.1% vs 1.2%, RR 1.79, 95% CI 1.35–2.38; 11 studies).^{6,8,14,16,17,19,21,32,36–38} No RCTs reported stroke; however, subanalysis of two propensity comparison studies also showed significant increase of stroke in minimally invasive compared with conventional open MVR (1.9% vs 0.9%, RR 2.02, 95% CI 1.40–2.94; two studies). The results of these higher quality propensity-adjusted studies were consistent with the remainder of the cohort studies reporting on this outcome (Fig. 3; Table 2).

Subgroup analysis by endoaortic or transthoracic clamp suggested a consistent trend toward increased risk of stroke in the mini-MVS patients of the endoaortic clamp subgroup (RR 1.72, 95% CI 0.91–3.23; $P = 0.09$; five studies)^{17,19,32,36,38} and significantly increased risk of stroke in the studies reporting mixed use of endoaortic and transthoracic clamp (RR 1.84, 95% CI 1.33–2.55; three studies).^{6,16,37} whereas no such trend toward increased stroke existed in the studies using only

transthoracic clamp (RR 0.80, 95% CI 0.07–8.92; three studies).^{8,14,21} However, these results are constrained by the usual caveats associated with subanalysis of retrospective data. There was no significant heterogeneity among the studies for the overall as well as all the subgroup analyses (Fig. 4).

Transient Neuropathy

Transient neuropathy was not significantly different between mini-MVS and conv-MVS (RR 5.09, 95% CI 0.54–48.11; two studies).^{8,14} There was no significant heterogeneity among the studies, and no RCTs reported on this outcome.

Permanent Neurologic Deficit

Permanent neurologic deficit was not significantly different for mini- versus conv-MVS; however, only one observational study including 200 patients reported on this outcome and was underpowered to rule out the potential for clinically relevant difference.¹⁹

Pain

Available outcomes for pain included Visual Analog Scale (VAS) and use of analgesics. Meta-analysis of five observational studies involving 576 patients showed no significant difference in the VAS for pain between mini- and conv-MVS (WMD -0.07 points, 95% CI -0.25 to +0.11 points; five studies).^{21,23,33,34,38} There was no significant heterogeneity among the studies. Another observational study involving 41 patients reported similar postoperative pain between two groups, except that pain tended to resolve more quickly in minimally invasive than conventional open MVR.¹⁸ In addition, minimally invasive patients had less difficulty in coughing and getting out of the bed than patients who underwent conventional open MVR.

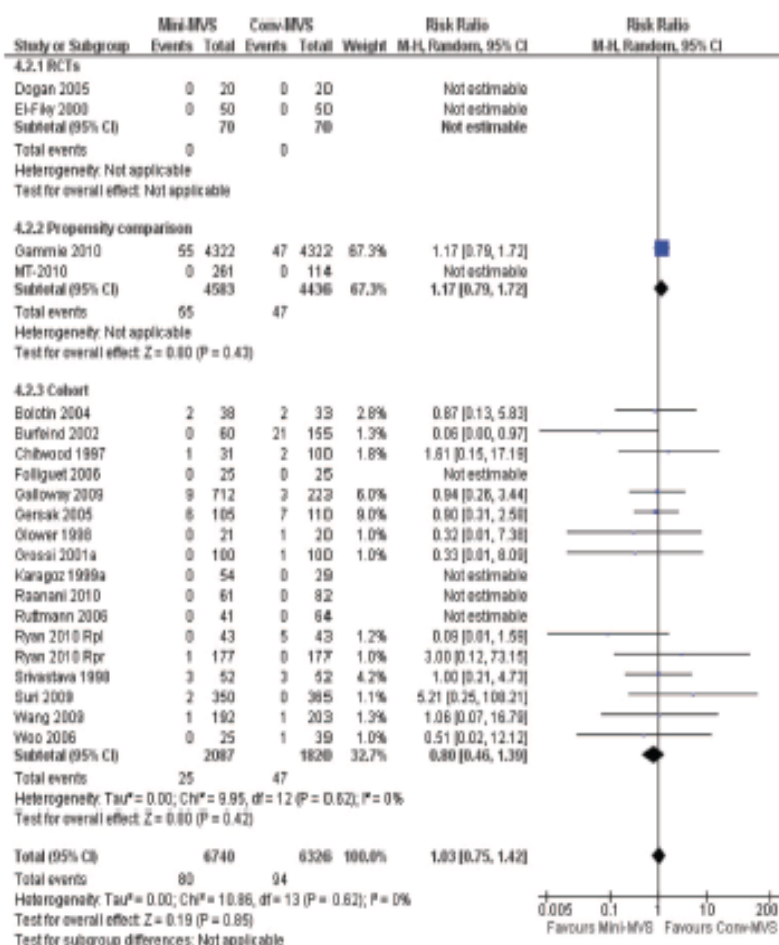


FIGURE 2. All-cause mortality up to 30 days. MVS, mitral valve surgery; RCT, randomized controlled trial.

An observational study involving 128 patients of thoracic clamping reported the use of analgesics and found that the total intake of acetaminophen/oxycodone (in milligrams) for the first 3 postoperative days was slightly less in the mini-MVS group compared with conv-MVS (WMD -3.35 mg, 95% CI -5.74 to -0.96 mg).⁴ However, there was no difference in the use of morphine in the first 3 postoperative days between mini- and conv-MVS in this study.⁴

Transfusions Up to 30 Days

RBC Units Transfused

Units of red blood cells (RBCs) transfused in the mini-MVS groups were significantly less than in the conv-MVS group (1.5 ± 1.8 U vs 3.5 ± 2.9 U, WMD -1.85 U, 95% CI -2.48 to -1.22 U; 10 studies).^{5,6,8,12,14,17,18,22,24,25} However, there was significant heterogeneity among the studies. The one

TABLE 2. All-Cause Mortality, Stroke up to 30 Days Postoperative

Outcome	Incidence		n (N)	WMD (95% CI) or RR (95% CI)	P	I ² (%)
	Mini-MVS	Conv-MVS				
All-cause mortality						
Overall	1.2%	1.5%	20 (13, 066)	1.03 (0.75, 1.42)	NS	0%
RCT	0%	0%	2 (140)	NE	NE	NA
Stroke						
Overall	2.1%	1.2%	11 (12, 655)	1.79 (1.35, 2.38)	<0.0001	0%

CI indicates confidence intervals; Conv-MVS, conventional open mitral valve surgery; I², heterogeneity; Mini-MVS, minimally invasive mitral valve surgery; n, number of studies; N, number of patients; NA, not applicable; NE, not estimable; NS, not significant; RCT, randomized controlled trial; RR, risk ratio; WMD, weighted mean difference.

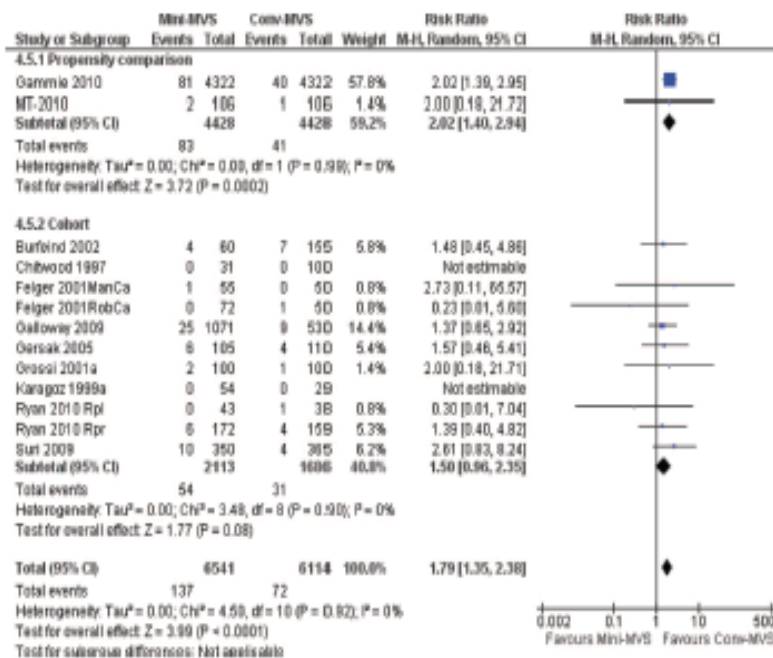


FIGURE 3. Stroke, up to 30 days postoperatively. Conv-MVS, conventional open mitral valve surgery; Mini-MVS, minimally invasive mitral valve surgery.

RCT that reported this outcome found no significant difference in the amount of RBCs transfused between groups (WMD -0.55 U, 95% CI -1.21 to $+0.11$ U) (Table 3).¹²

Patients Transfused RBCs

The percentage of patients receiving blood was similar for mini-MVS and conv-MVS groups (39% vs 42%, RR 0.97, 95% CI 0.81–1.17; seven studies).^{8,12,14,15,32,37,38} There was no significant heterogeneity among the studies (Table 3).

Units of Fresh Frozen Plasma Transfused

Significantly fewer units of fresh frozen plasma were transfused for mini-MVS compared with conv-MVS (0.3 ± 1.4 U vs 0.7 ± 1.5 U, WMD -0.44 U, 95% CI -0.81 to -0.08 U; two studies).^{12,14} There was no significant heterogeneity among the studies. One RCT reported the percentage of patient receiving fresh frozen plasma and found no significant difference between mini-MVS versus conv-MVS (20% vs 25%, RR 0.80, 95% CI 0.25–2.55; one RCT) (Table 3).¹²

Platelet Transfusion and Cryoprecipitate Transfusion

A single study reported platelet units transfused and showed a tendency toward lesser units of platelets transfused for mini-MVS versus conv-MVS (WMD 1.10 U, 95% CI -2.28 to 0.08 U; one study).¹⁴ This study also reported a tendency toward fewer units of cryoprecipitate transfused (WMD -1.10 U, 95% CI -0.21 to $+0.01$ U; one study) (Table 3).

The percentage of patients receiving platelets transfusion was significantly less with mini-MVS compared with

conv-MVS (16% vs 19%, RR 0.80, 95% CI 0.73–0.88; two studies).^{37,38} There was no significant heterogeneity between the studies. The percentage of patients receiving cryoprecipitate did not differ between groups (RR 3.0, 95% CI 0.12–72.8; one study) (Table 3).³⁸

Hemorrhagic or Chest Tube Drainage

Chest tube drainage was significantly decreased with mini-MVS versus conv-MVS (mean 578 ± 406 mL vs 871 ± 711 mL, WMD -266 mL, 95% CI -437 to -95 mL; 14 studies).^{5,6,8,11–15,17,18,21,24,31,34} The studies generally did not report whether chest tube drainage was serous or sanguineous. The two RCTs reporting this outcome together suggested no significant reduction in total drainage.^{12,13} There was significant heterogeneity among the studies for the overall as well for the RCTs and non-RCT subgroups considered alone (Table 3).

Reoperation for Bleeding

Reoperation for bleeding was not significantly different between mini-MVS and conv-MVS groups (3.5% vs 2.9%, RR 0.91 95% CI 0.59–1.41; 14 studies).^{6,8,12,14,15,21,26,28,32,34–38} There was no significant heterogeneity among the studies (Fig. 5; Table 3).

Cardiac Arrhythmia

Atrial fibrillation was significantly reduced with mini-MVS versus conv-MVS (18% vs 22%; RR 0.87, 95% CI 0.77–0.99; eight studies).^{7,8,14,18,32,36–38} There was no significant heterogeneity among the studies for this outcome. No randomized studies reported this outcome. Need for pacemaker implantation was not significantly different between mini-MVS and conv-MVS (RR 0.47, 95% CI 0.05–4.09; two

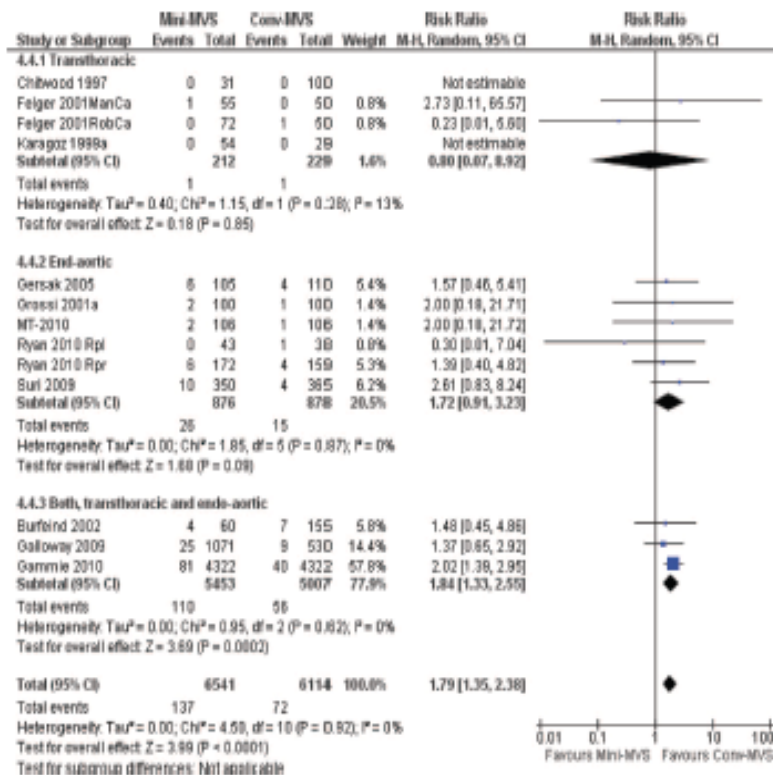


FIGURE 4. Stroke, subanalysis by transthoracic or endoaortic clamping up to 30 days postoperatively. Conv-MVS, conventional open mitral valve surgery; Mini-MVS, minimally invasive mitral valve surgery.

studies).^{5,12} Only one study, a RCT involving 40 patients, reported on ventricular fibrillation and found no statistically significant difference between mini- and conv-MVS (RR 0.33, 95% CI 0.01–7.72; Table 4).¹²

Aortic Dissection and Injury

Risk of aortic dissection was significantly increased for mini-MVS versus conv-MVS (0.2% vs 0%, RR 6.04, 95% CI 1.06–34.47; seven studies).^{5,10,20,26,32,36,37} There was no significant heterogeneity among the studies for this outcome. No RCTs reported this outcome. When aortic dissection and aortic injury (iatrogenic injury) were considered together, there was a significant risk of either dissection or injury for mini-MVS versus conv-MVS (RR 5.68, 95% CI 1.23–26.17; nine studies; Fig. 6; Table 4).^{5,8,10,20,26,28,32,36,37}

Cardiac Events In 30 Days

Perioperative Myocardial Infarction

Perioperative myocardial infarction was not significantly different between groups (0.5% vs 2.0%, RR 0.39, 95% CI 0.06–2.46; three studies).^{12,14,26} The one RCT that reported this outcome did not find a difference for myocardial infarction between groups.¹² There was no significant heterogeneity among the studies (Table 4).

Mitral Insufficiency

The proportion of patients with mitral insufficiency postoperatively was not significantly different between mini-MVS and conv-MVS groups (2.4% vs 2%, RR 1.16, 95% CI 0.38–3.57; five studies).^{12,15,21,28,38} One of the studies was an RCT, and it showed no significant difference between groups for mitral regurgitation.¹² There was no significant heterogeneity among the studies (Table 4).

Thromboembolic Events and Vascular Complications

There was no significant difference in the percentage of patients experiencing thromboembolic events or vascular complications between mini-MVS versus conv-MVS (0.3% vs 0.2%, RR 1.78, 95% CI 0.82–3.87; seven studies), and there was no significant heterogeneity among the studies.^{8,14,15,18,20,36,37} No RCT reported this outcome (Table 4).

Other Cardiovascular Outcomes

There was no difference in other cardiac outcomes including low cardiac output syndrome, cardiac tamponade, pericardial effusion, ventricular rupture, pericardiotomy syndrome, need for inotropes, and need for intra-aortic balloon pump implantation between groups; however, in most cases, only one or two studies reported these outcomes (Table 4).

TABLE 3. Transfusion of Blood and Plasma and Hemorrhage up to 30 Days Postoperative

Outcome	Mean \pm SD/Incidence		n (N)	WMD (95% CI) or RR (95% CI)	P	I ² (%)
	Mini-MVS	Conv-MVS				
Blood/RBC (U)						
Overall	1.5 \pm 1.8	3.5 \pm 2.9	10 (1,732)	-1.85 (-2.48, -1.22)	<0.00001	99%
RCT	0.5 \pm 0.8	1.1 \pm 1.3	1 (40)	-0.55 (-1.21, 0.11)	NS	NA
Blood/RBC (patients)						
Overall	39%	42%	7 (10,019)	0.97 (0.81, 1.17)	NS	42%
RCT	40%	40%	1 (40)	1.00 (0.47, 2.14)	NS	NA
Fresh frozen plasma (U)						
Overall	0.3 \pm 1.4	0.7 \pm 1.5	2 (267)	-0.44 (-0.8, -0.08)	0.02	0%
RCT	0.4 \pm 1.0	0.7 \pm 1.4	1 (40)	-0.27 (-1.0, 0.47)	NS	NA
Fresh frozen plasma (patients)						
Overall, RCT only	20%	25%	1 (40)	0.80 (0.25, 2.55)	NS	NA
Platelet (U)						
Overall	0.1 \pm 4.5	1.2 \pm 4.5	1 (227)	-1.10 (-2.28, 0.08)	NS	0%
Platelet (patients)						
Overall	16%	19%	2 (8,856)	0.80 (0.73, 0.88)	0.00001	0%
Cryoprecipitate (U)						
Overall	0.0 \pm 0.41	0.1 \pm 0.41	1 (227)	-0.10 (-0.21, 0.01)	NS	0%
Cryoprecipitate (patients)						
Overall	1%	0%	1 (212)	3.00 (0.12, 72.82)	NS	0%
Hemorrhage, chest tube drainage						
Overall	578 \pm 406	871 \pm 711	14 (1,703)	-265.97 (-436.62, -95.33)	0.002	100%
RCT	464 \pm 259	688 \pm 335	2 (140)	-234.46 (-674.04, 205.12)	NS	93%
Reoperation for bleeding						
Overall	3.5%	2.9%	14 (11,440)	0.91 (0.59, 1.41)	NS	25%
RCT	0%	5%	1 (40)	0.33 (0.01, 7.72)	NS	NA
Reoperation for any cause						
Overall, non-RCT	6.6%	5.5%	1 (8,644)	1.20 (1.01, 1.41)	0.03	NA

CI indicates confidence intervals; Conv-MVS, conventional open mitral valve surgery; I², heterogeneity; Mini-MVS, minimally invasive mitral valve surgery; n, number of studies; N, number of patients; NA, not applicable; NS, not significant; RBC, red blood cells; RCT, randomized controlled trial; RR, risk ratio; WMD, weighted mean difference.

Renal Events

No significant difference was found between mini-MVS versus conv-MVS for patients experiencing postoperative renal failure or insufficiency (RR 1.08, 95% CI 0.81–1.43; five studies), and there was no significant heterogeneity among the studies.^{8,14,22,26,37}

Pulmonary Events

There was no significant difference between groups for pneumonia, pleural effusion, pneumothorax, pneumonitis, or overall pulmonary complications, and these outcomes were generally reported by only one or two nonrandomized studies (Table 5).

Phrenic Nerve Palsy

Although the proportion of patients experiencing phrenic nerve palsy was significantly increased for mini-MVS compared with conv-MVS (3% vs 0%, RR 7.61, 95% CI 1.30–44.70; three studies, no heterogeneity among the studies), this result was limited by few studies reporting on the outcome, and presumably number of these studies had zero events.^{8,14,26} In some cases, there was prolonged impact on ventilation time and ICU stay, whereas in other cases the

clinical impact was limited to phrenic nerve elevation or was not described (Fig. 7; Table 5).

Gastrointestinal Events

There was no significant difference in gastrointestinal events between mini-MVS versus conv-MVS (1.3% vs 3%, RR 0.54, 95% CI 0.12–2.32; two studies).^{8,14} There was no statistically significant heterogeneity among the studies.

Infections and Mediastinitis

Sternal Infection

As expected, significantly fewer patients experienced sternal infections with mini-MVS compared with conv-MVS (0.04% vs 0.27%, RR 0.34, 95% CI 0.12–0.95; seven studies), and there was no heterogeneity across studies. Of the seven studies reporting this outcome,^{12–14,31,34,35,37} two were RCTs and together they suggested a trend toward reduction (Table 6).^{12,13} Although it seems counterintuitive that sternal wound infections could occur in mini-MVS, a total of two cases of sternal wound infections were reported in two studies involving 4377 patients.^{14,37} In both of these studies, robotic

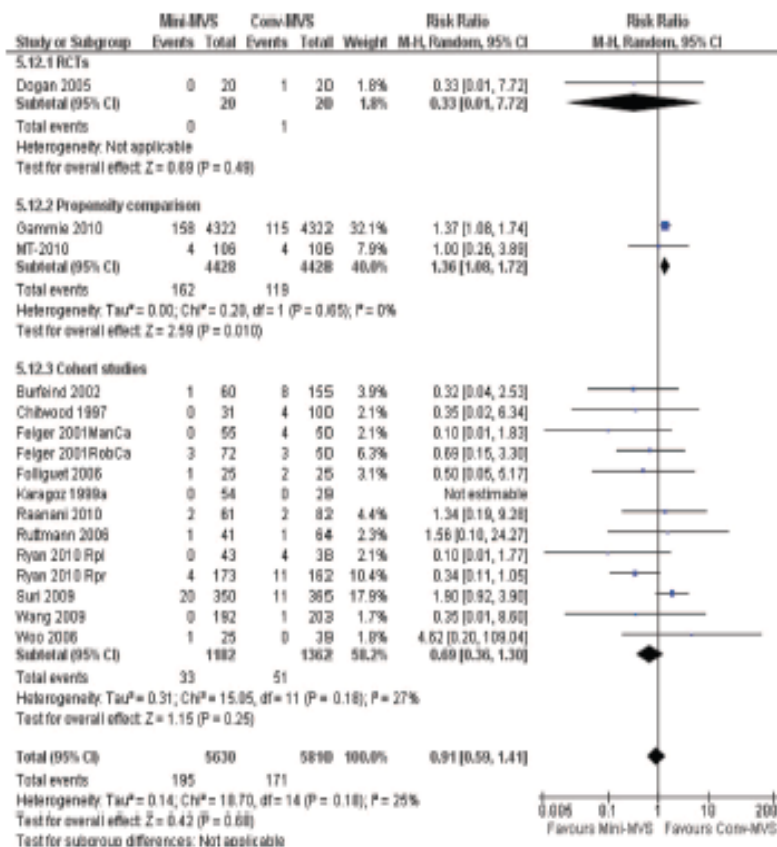


FIGURE 5. Reoperation for bleeding. Conv-MVS, conventional open mitral valve surgery; Mini-MVS, minimally invasive mitral valve surgery; RCT, randomized control trial.

assistance was used in at least a proportion of the patients in the mini-MVS group.

Mediastinitis

There was no significant difference in the risk of mediastinitis between mini-MVS and conv-MVS (2% vs 1%, RR 1.85, 95% CI 0.15–23.07; two studies). There was no statistically significant heterogeneity among the studies (Table 6).^{4,26}

Groin Infections, Hematoma, or Hydrocele

Groin infections, hematoma, and hydrocele were confined to mini-MVS, and none of these occurred in conv-MVS (2% vs 0%, RR 5.62, 95% CI 1.26–25.13; five studies).^{12,14,15,26,36} There was no statistically significant heterogeneity among the studies (Table 6).

Deep Infection and Wound Dehiscence

There was no significant difference between mini-MVS and conv-MVS for deep infection and wound dehiscence (0.7% vs 1.3%, RR = 1.09, 95% CI 0.12–10.20; three studies). There was statistically significant heterogeneity among the studies for the overall comparison (Table 6).^{16,31,32}

Superficial Infection and Keloid Formation

One observational study reported no significant difference in superficial infections (0% vs 5.8%, RR 0.14, 95% CI 0.01–2.70) and keloid formation (0% vs 3.8%, RR 0.20, 95% CI 0.01–4.07) between mini-MVS and conv-MVS (Table 6).³¹

Incision Length and Scar Dissatisfaction

Mean length of incision in the mini-MVS group was 6.3 ± 1.5 cm (reported in nine studies).^{5,6,8,12,18,23,25,34,36} However, one of these studies reported a disproportionately longer length of incision in mini-MVS (11.5 ± 0.7 cm), which does not reflect usual practice for mini-MVS.¹³ Only two studies reported the length of incision in both groups, and together they suggested that the mean incision length was significantly reduced for mini-MVS versus conv-MVS by >16 cm (8.4 vs 24.8 cm for mini- vs conv-MVS; WMD -16.35 cm, 95% CI -19.48 to -13.21 cm).^{18,34} There was a significant heterogeneity among the studies.

Patient Dissatisfaction With Scar

Significantly fewer patients were dissatisfied with their scar with mini-MVS versus conv-MVS (0% vs 19.2%, RR

TABLE 4. Cardiac, Aortic, and Thromboembolic Events Up to 30 Days Postoperative

Outcome	Incidence		n (N)	WMD (95% CI)/ RR (95% CI)	P	I ² (%)
	Mini-MVS	Conv-MVS				
Atrial fibrillation						
Overall	18%	22%	8 (10,437)	0.87 (0.77, 0.99)	0.03	25%
Ventricular fibrillation						
Overall, RCT	0%	5%	1 (40)	0.33 (0.01, 7.72)	NS	NA
Pacemaker implantation						
Overall	0%	2.5%	2 (171)	0.47 (0.05, 4.09)	NS	0%
RCT	0%	5%	1 (40)	0.33 (0.01, 7.72)	NS	NA
Aortic dissection						
Overall	0.2%	0%	7 (10,248)	6.04 (1.06, 34.5)	0.04	0%
Aortic dissection or injury						
Overall	0.2%	0%	8 (10,484)	5.68 (1.23, 26.17)	0.03	0%
Perioperative myocardial infarction						
Overall	0.5%	2%	3 (410)	0.39 (0.06, 2.46)	NS	0%
RCT	0%	0%	1 (40)	NE	NE	NA
Mitral insufficiency						
Overall	2.4%	2.0%	5 (490)	1.16 (0.38, 3.57)	NS	0%
RCT	0%	5%	1 (40)	0.33 (0.01, 7.72)	NS	NA
Pericardial effusion						
Overall	4.1%	2.0%	2 (123)	1.21 (0.11, 13.28)	NS	20%
RCT	0%	5%	1 (40)	0.33 (0.01, 7.72)	NS	NA
Cardiac tamponade						
Overall	0.5%	2.0%	1 (415)	0.33 (0.05, 2.12)	NS	0%
Pericardiotomy syndrome						
Overall	11.5%	2.4%	1 (143)	4.70 (1.01, 21.86)	0.05	NA
Ventricular rupture						
Overall	2%	0%	1 (83)	1.64 (0.07, 38.94)	NS	NA
Total thromboembolic events, ischemia and vascular complications						
Overall	0.3%	0.2%	9 (9,654)	1.78 (0.82, 3.87)	NS	0%

CI indicates confidence intervals; Conv-MVS, conventional open mitral valve surgery; P, heterogeneity; Mini-MVS, minimally invasive mitral valve surgery; n, number of studies; N, number of patients; NA, not applicable; NE, not estimable; NS, not significant; RCT, randomized controlled trial; RR, risk ratio; WMD, weighted mean difference.

0.05, 95% CI 0–0.79; one study) in the one observation study that reported this outcome (Table 6).³¹

Overall Complications

There was no significant difference between mini-MVS and conv-MVS for the percentage of patients who experienced no hospital complications (77% vs 80%, RR 0.92, 95% CI 0.65–1.28; two studies) (Table 6). There was significant heterogeneity among the studies, and no RCTs reported this outcome.^{10,26} When overall complications were defined as STS complications, there was no significant difference between mini-MVS versus conv-MVS for the percentage of patients with Society of Thoracic Surgeons (STS) defined complications (8.5% vs 9.4%, RR 0.90, 95% CI 0.38, 2.13; one study).³⁸

Quality of Life

One observational study reported that quality of life tended to improve similarly after mini-MVS and conv-MVS, with no significant difference between groups.³³

Repeat Procedure

There was no significant difference in the percentage of patients having repeat procedure between mini-MVS and conv-MVS (RR 0.61, 95% CI 0.12–3.25; one study) (Table 6).³⁶

Readmission Within 30 Days

There was no significant difference in the percentage of patients readmitted within 30 days between mini-MVS and conv-MVS (4.7% vs 9.0%, RR 0.53, 95% CI 0.24–1.15; one study) (Table 6).³⁶

Conversion to Sternotomy

Ten studies involving 866 patients undergoing minimally invasive MVR reported that 3.7% of the patients undergoing minimally invasive patients were converted to open sternotomy.^{5,8,12,14,15,18,19,21,36,38} In one RCT reporting this outcome, there was no incidence of conversion from planned mini-MVS to conv-MVS.¹²

Resource-Related Outcomes

Cross-Clamp Time

Cross-clamp time was significantly increased with mini-MVS versus conv-MVS (95 ± 39 minutes vs 74 ± 36 minutes, WMD 21.41 minutes, 95% CI 10.14 to 32.69 minutes; 24 studies).^{4,7,8,11–15,17,18,21,22,25–29,31,32,36–38} Another study³⁰ reported that in the beginning of the learning curve, cross-clamp time was 25 minutes longer in the mini-MVS group compared with conv-MVS. However, with experience

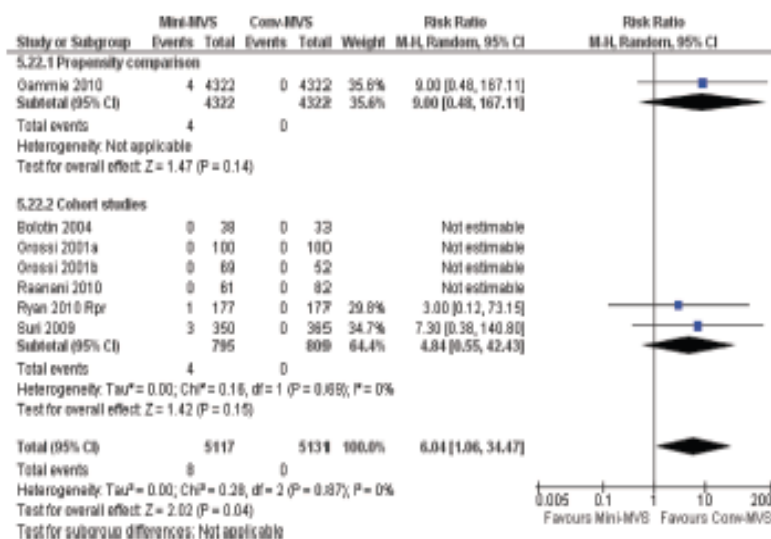


FIGURE 6. Aortic dissection. Conv-MVS, conventional open mitral valve surgery; Mini-MVS, minimally invasive mitral valve surgery.

cross-clamp time improved in their center but still remained 15% longer in the minimally invasive group. However, subanalysis of RCTs showed shorter cross-clamp time with mini-MVS versus conv-MVS (56 ± 16 minutes vs 60 ± 19 minutes, WMD -4.0 minutes, 95% CI -7.2 to -0.7 minutes; two RCTs), which is opposite to what the nonrandomized studies reported (Fig. 8; Table 7).^{12,13}

Cardiopulmonary Bypass Time

Cardiopulmonary bypass (CPB) time was significantly increased with mini-MVS versus conv-MVS (144 vs 111

minutes, WMD 33.0 minutes, 95% CI 18.9 to 47.1 minutes; 27 studies).^{4-8,11-15,17-19,21,22,25-29,31,32,34-38} There was significant heterogeneity across studies for this outcome. When subanalyzed, the two RCTs that reported this outcome also showed significantly increased CPB time with mini-MVS versus conv-MVS (Table 7).^{12,13}

Procedure Time

There was a significant increase in procedure time for mini-MVS compared with conv-MVS (4.5 vs 3.7 hours, WMD 0.79 hours, 95% CI 0.41 to 1.16 hours; 13

TABLE 5. Pulmonary Events Up to 30 Days Postoperative

Outcome	Incidence		n (N)	WMD (95% CI)/ RR (95% CI)	P	I ² (%)
	Mini-MVS	Conv-MVS				
Pneumonia						
Overall	1%	2.5%	4 (439)	0.62 (0.16, 2.39)	NS	0%
RCT	NR	NR	NA	NA	NA	NA
Phrenic nerve palsy/diaphragm elevation						
Overall	3%	0%	3 (501)	7.61 (1.30, 44.7)	0.02	0%
RCT	NR	NR	NA	NA	NA	NA
Mediastinitis						
Overall	2%	1%	2 (358)	1.85 (0.15, 23.07)	NS	28%
Pleural effusion						
Overall	1%	7%	2 (262)	0.37 (0.01, 21.87)	NS	73%
Prolonged ventilation						
Overall	7%	6%	1 (8644)	1.17 (1.00, 1.37)	NS	NA
Pneumonitis						
Overall	4%	5%	1 (104)	2.00 (0.19, 21.38)	NS	NA
Pneumothorax						
Overall	0%	5%	1 (40)	0.33 (0.01, 7.72)	NS	NA
Pulmonary complications						
Overall	8%	2%	1 (143)	3.36 (0.67, 16.75)	NS	NA

CI indicates confidence intervals; Conv-MVS, conventional open mitral valve surgery; I², heterogeneity; Mini-MVS, minimally invasive mitral valve surgery; n, number of studies; N, number of patients; NA, not applicable; NR, not reported; NS, not significant; RCT, randomized controlled trial; RR, risk ratio; WMD, weighted mean difference.

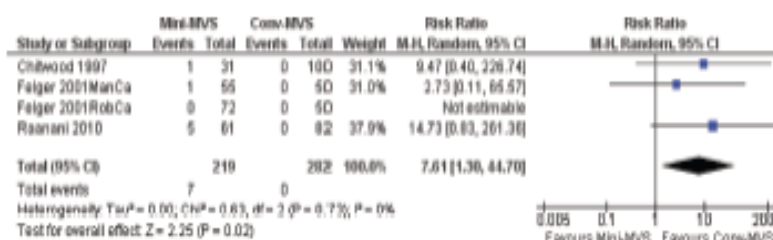


FIGURE 7. Phrenic nerve palsy/diaphragm elevation. Conv-MVS, conventional open mitral valve surgery; Mini-MVS, minimally invasive mitral valve surgery.

studies).^{5,6,12,14,15,18,21,25–27,34,37} The single RCT that reported this outcome showed no significant difference in procedure time between groups (WMD 0.24 hours, 95% CI –0.31 to +0.79 hours; one study).¹² There was significant heterogeneity among the studies for this outcome (Fig. 9; Table 7).

Length of Ventilation

Ventilation time was significantly reduced for mini-MVS compared with conv-MVS (12.6 vs 19.9 hours, WMD –2.07 hours, 95% CI –3.39 to –0.75 hours; 18 studies).^{5,7,8,11,12,14,15,17,18,27–29,31,32,34–37} There was significant het-

erogeneity across studies for this outcome. The one RCT that reported this outcome showed no difference in the length of ventilation between mini- and conv-MVS (WMD –3.0 hours, 95% CI –7.4 to +1.4 hours) (Table 7).¹²

Length of Stay in ICU

Length of stay in ICU was significantly reduced for mini-MVS versus conv-MVS (1.6 vs 2.4 days, WMD –0.50 days, 95% CI –0.68 to –0.32 days; 18 studies).^{5,7,8,11,12,14,15,17,21,24,27–29,31,33,35–37} There was significant heterogeneity for this outcome. The one RCT that reported

TABLE 6. Infection and Miscellaneous Events Up to 30 Days Postoperative

Outcome	Incidence		n (N)	WMD (95% CI)/ RR (95% CI)	P	I ² (%)
	Mini-MVS	Conv-MVS				
Sternal infections or instability						
Overall	0.04%	0.27%	7 (9574)	0.34 (0.12, 0.95)	0.04	0%
RCT	0%	2.9%	2 (140)	0.33 (0.04, 3.11)	NS	0%
Groin infection, hematoma, hydrocele						
Overall	2%	0%	5 (900)	5.62 (1.26, 25.13)	0.02	0%
RCT	15%	0%	1 (40)	7.00 (0.38, 127.32)	NS	NA
Deep infection, wound dehiscence						
Overall	0.7%	1.3%	3 (2420)	1.09 (0.12, 10.20)	NS	72%
RCT	NR	NR	NA	NA	NA	NA
Superficial infection						
Overall	0%	5.8%	1 (104)	0.14 (0.01, 2.70)	NS	NA
Patient dissatisfied with scar						
Overall	0%	19.2%	1 (104)	0.05 (0.00, 0.79)	0.03	NA
Keloid formation						
Overall	0%	3.8%	1 (104)	0.20 (0.01, 4.07)	NS	NA
Major hospital morbidity or mortality						
Overall	13%	11%	1 (8644)	1.17 (1.05, 1.31)	0.007	NA
Freedom from all hospital morbidity						
Overall	77%	80%	2 (343)	0.92 (0.65, 1.28)	NS	82%
Freedom from major hospital morbidity						
Overall	85.2%	92.7%	1 (143)	0.92 (0.82, 1.04)	NS	NA
Repeat procedure						
Overall	2.3%	4.5%	1 (440)	0.61 (0.12, 3.25)	NS	41%
Readmission within 30 days						
Overall	4.7%	9.0%	1 (392)	0.53 (0.24, 1.15)	NS	0%

CI indicates confidence intervals; Conv-MVS, conventional open mitral valve surgery; I², heterogeneity; Mini-MVS, minimally invasive mitral valve surgery; n, number of studies; N, number of patients; NA, not applicable; NS, not significant; RCT, randomized controlled trial; RR, risk ratio; WMD, weighted mean difference.

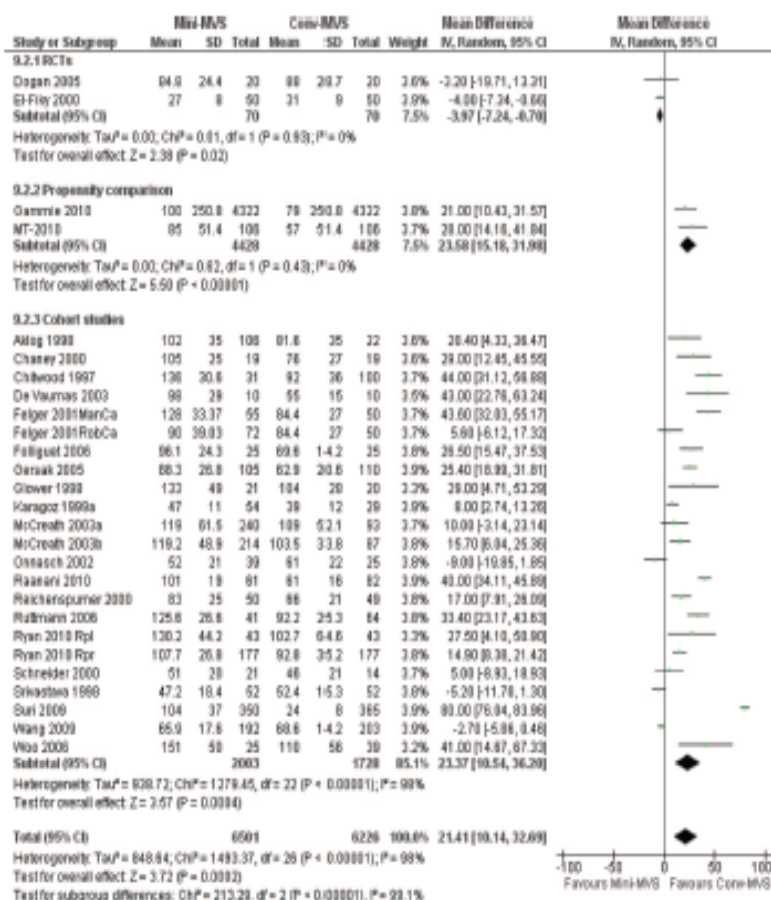


FIGURE 8. Cross-clamp time (minutes). Conv-MVS, conventional open mitral valve surgery; Mini-MVS, minimally invasive mitral valve surgery; RCT, randomized control trial.

this outcome showed no significant difference in the length of stay in ICU between mini- and conv-MVS (WMD -0.30 hours, 95% CI -0.92 to +0.32 hours) (Table 7).¹²

Length of Stay in Hospital

Length of hospital stay was significantly reduced with mini-MVS versus conv-MVS (mean 6.9 vs 8.9 days, WMD -1.60 days, 95% CI -2.09 to -1.11 days; 26 studies).^{4,5,7,8,10-15,17,18,21,24,26-29,31-38} Subanalysis of the two RCTs reporting this outcome showed no difference in the length of stay in hospital between groups (WMD -0.04 days, 95% CI -0.8 to +0.7 days; two studies).^{4,13} There was significant heterogeneity among the studies for this outcome (Fig. 10; Table 7).

Cost

A study from the United States reported that compared with patients undergoing conv-MVS, patients undergoing mini-MVS had lower mean hospital charges (WMD -\$11,430, 95% CI -\$12,420 to -\$10,440; one study), and lower mean hospital costs (WMD -\$9,160, 95% CI -9,870

to -8,460; one study).⁸ Operating room charges in this study were procedure based, and this may not have accounted for the time-dependent costs. This is an important consideration, because operating room time for mini-MVS was approximately 1.6 hours longer than conv-MVS in this study. This could have masked the time-dependent cost variances. Another study from Slovenia reported that patients undergoing mini-MVS had lower mean costs than patients undergoing conv-MVS (WMD -664 Slovenia tola, 95% CI -664 to -663 Slovenia tola) (Table 8).¹⁷ None of the studies provided a comprehensive cost-effectiveness analysis of the incremental costs and benefits of mini-MVS versus conv-MVS.

Long-Term Outcomes

All-Cause Mortality

Longer term risk of all-cause mortality was reported in few trials, and it did not show a significant difference between mini-MVS and conv-MVS at 1 year (0.9% vs 1.3%, RR 1.07, 95% CI 0.19 to 6.05; two studies).^{8,34} at 3 years (0.5% vs 0.5%, RR 1.06, 95% CI 0.07 to 16.79; one study)³⁴ and up to 9 years (0% vs 3.7%, RR 0.19, 95% CI 0.01

TABLE 7. Different Procedures-Related Timings and Stay

Outcome	Mean \pm SD		n (N)	WMD (95% CI) or RR (95% CI)	P	I ² (%)
	Mini-MVS	Conv-MVS				
Cross clamp time (min)						
Overall	95 \pm 39	74 \pm 36	24 (12,727)	21.41 (10.14, 32.69)	0.0002	98%
RCT	56 \pm 16	60 \pm 19	2 (140)	-4.0 (-7.2, -0.7)	0.02	0%
Cardiopulmonary bypass time (min)						
Overall	144 \pm 52	111 \pm 52	27 (13,213)	33.0 (18.9, 47.1)	<0.00001	99%
RCT	103 \pm 22	96 \pm 23	2 (140)	5.2 (0.8, 9.6)	0.02	0%
Procedure time (h)						
Overall	4.5 \pm 1.8	3.7 \pm 1.7	13 (10,284)	0.79 (0.41, 1.16)	<0.0001	96%
RCT	4.2 \pm 0.8	4.0 \pm 0.9	1 (40)	0.24 (-0.31, 0.79)	NS	NA
Length of ventilation (h)						
Overall	12.6 \pm 17.7	19.9 \pm 36.3	18 (11,434)	-2.07 (-3.39, -0.75)	0.002	84%
RCT	8.9 \pm 3.8	11.9 \pm 9.4	1 (40)	-3.00 (-7.44, 1.44)	NS	NA
Length of stay in ICU (d)						
Overall	1.6 \pm 1.7	2.4 \pm 2.4	18 (10,435)	-0.50 (-0.38, -0.32)	<0.0001	79%
RCT	1.3 \pm 0.9	1.6 \pm 1.1	1 (40)	-0.30 (-0.92, 0.32)	NS	NA
Hospital length of stay (d)						
Overall	6.9 \pm 4.2	8.9 \pm 5.1	26 (12,249)	-1.60 (-2.09, -1.11)	<0.00001	79%
RCT	7.5 \pm 3.1	8.1 \pm 5.2	2 (140)	-0.04 (-0.8, 0.7)	NS	0%

CI indicates confidence intervals; Conv-MVS, conventional open mitral valve surgery; I², heterogeneity; ICU, intensive care unit; Mini-MVS, minimally invasive mitral valve surgery; n, number of studies; N, number of patients; NA, not applicable; NS, not significant; RCT, randomized controlled trial; RR, risk ratio; WMD, weighted mean difference.

to 3.64; one study).²⁶ There was no significant heterogeneity among the studies, and no RCTs reported long-term mortality (Table 9).

Mitral Valve Leak or Insufficiency

No significant difference was found for the risk of long-term mitral valve leak between mini-MVS and conv-

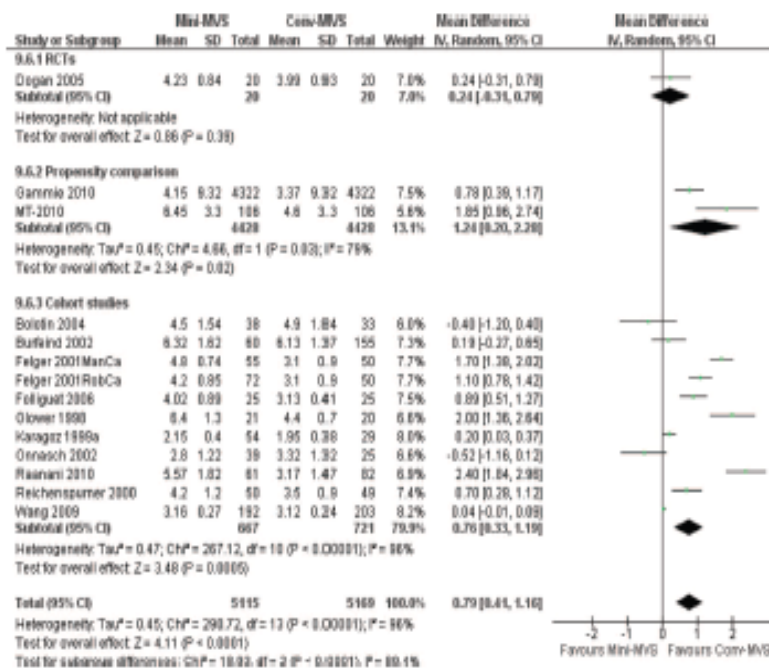


FIGURE 9. Procedure time (hours). Conv-MVS, conventional open mitral valve surgery; Mini-MVS, minimally invasive mitral valve surgery; RCT, randomized control trial.

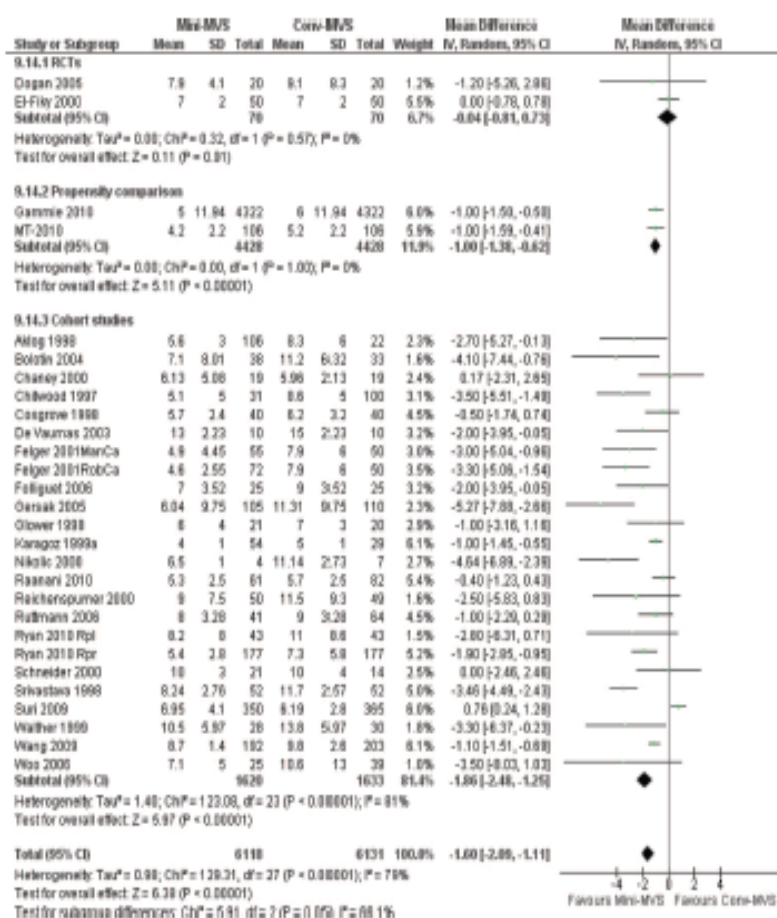


FIGURE 10. Length of stay in hospital (days). Conv-MVS, conventional open mitral valve surgery; Mini-MVS, minimally invasive mitral valve surgery; RCT, randomized control trial.

MVS (RR 9.5, 95% CI 0.4 to 226.7).^{8,21,24} There was significant heterogeneity among the studies, and no RCT reported long-term mitral valve outcomes. In addition, there was no significant difference in the grade of mitral insufficiency between mini-MVS and open-MVS (WMD 0.04, 95% CI -0.15 to +0.2).^{10,25,26} There was no significant heterogeneity among all these studies, and no RCT reported this outcome (Table 9).

Infective Endocarditis

There was no significant difference in the percentage of patients developing infective endocarditis between mini-MVS and open-MVS (0.5% vs 0.7%, RR 0.94, 95% CI 0.31–2.86; four studies).^{8,16,19,26} There was no significant heterogeneity among the studies, and no RCT reported this outcome (Table 9).

NYHA Classification

There was a small but significant decrease in NYHA class after 1 year for mini-MVS compared with conv-MVS (mean class 1.32 vs 1.52, WMD -0.26, 95% CI -0.27 to -0.25).^{10,26} There was no significant heterogeneity among the studies, and no RCT reported this outcome (Table 9).

neity among the studies, and no RCTs reported this outcome (Table 9).

Freedom From Valve-Related Reoperation

There was no significant difference in freedom from reoperation between groups at 1 year (RR 1.03, 95% CI 0.97 to 1.10; one study).¹⁰ However, at 8 years, there was significant improvement in freedom from reoperation for mini-MVS compared with conv-MVS (RR 1.04, 95% CI 1.01 to 1.08; one study).¹⁶ Freedom from valve-related reoperation was significantly improved when all studies evaluating this outcome at 1 to 8 years follow-up were combined (RR 1.04, 95% CI 1.01 to 1.06; three studies); however, differences in follow-up between groups challenge the validity of this finding.^{16,19,26} There was no significant heterogeneity among the studies, and no RCT reported this outcome (Table 9).

Return to Normal Activity

Return to normal activity was significantly faster for mini-MVS versus conv-MVS (6.3 vs 12.3 weeks, WMD

TABLE 8. Cost of Mini-MVS Versus Conv-MVS

Outcome	Mean \pm SD		n (N)	WMD (95% CI) or RR (95% CI)	P	I ² (%)
	Mini-MVS	Conv-MVS				
Hospital cost per patient ($\times 1000$)						
Overall	30.99 \pm 2.41	42.41 \pm 2.59	1 (131)	-11.43 (-12.42, -10.44)	<0.00001	NA
Hospital cost ($\times 1000$)						
Overall	17.88 \pm 1.7	27.05 \pm 1.91	1 (131)	-9.16 (-9.87, -8.46)	<0.00001	NA
Average total patient cost ($\times 1000$)						
Overall	2431.7 \pm 1.4	3095.3 \pm 1.4	1 (215)	-663.60 (-663.97, -663.23)	<0.00001	NA

CI indicates confidence intervals; Conv-MVS, conventional open mitral valve surgery; P, heterogeneity; Mini-MVS, minimally invasive mitral valve surgery; n, number of studies; N, number of patients; NA, not applicable; RR, risk ratio; WMD, weighted mean difference.

-4.96 weeks, 95% CI -6.39 to -3.52 weeks; three studies).^{4,18,34} There was significant heterogeneity across the studies for this outcome (Table 9).

Quality of Life

Quality of life was reported in only one observational study, and no significant difference was found in the change in quality of life between mini- and conv-MVS (Table 9).³³

Resource-Related Outcomes

No study provided the cost or cost-effectiveness of mini-MVS versus conv-MVS over the long-term period.

DISCUSSION

This systematic review with meta-analysis suggests that mini-MVS is associated with decreased hemorrhage, blood product transfusion, atrial fibrillation, chest wound infection, ventilation time, ICU stay, hospital length of stay, and reduced time to return to normal activity, without detected adverse impact on long-term need for valvular reintervention and survival (though this meta-analysis was underpowered for long-term outcomes). However, an increased risk of stroke, aortic dissection or aortic injury, phrenic nerve palsy, groin infections, and increased CPB, cross-clamp, and procedure time was found.

TABLE 9. Long-Term Outcomes

Outcome	Mean \pm SD/Incidence		n (N)	WMD (95% CI) or RR (95% CI)	P	I ² (%)
	Mini-MVS	Conv-MVS				
Mortality at 1 yr						
Overall	0.9%	1.3%	2 (526)	1.07 (0.19, 6.05)	NS	0%
Mortality at 3 yr						
Overall	0.5%	0.5%	1 (203)	1.06 (0.07, 16.79)	NS	NA
Mortality at 9 yr						
Overall	0%	3.7%	1 (143)	0.19 (0.01, 3.64)	NS	NA
Mitral valve leak						
Overall	0.4%	0%	3 (609)	9.5 (0.4, 226.7)	NS	NA ^c
Mitral insufficiency (scale of 0-3 or 0-4)						
Overall	0.82 \pm 0.47	0.75 \pm 0.52	3 (383)	0.04 (-0.15, 0.2)	NS	58%
RCT	NR	NR	NA	NA	NA	NA
Infective endocarditis						
Overall	0.5%	0.7%	4 (2,075)	0.94 (0.31, 2.86)	NS	0%
RCT	NR	NR	NA	NA	NA	NA
NYHA classification						
Overall	1.32 \pm 0.37	1.52 \pm 0.41	2 (343)	-0.26 (-0.27, -0.25)	<0.00001	0%
RCT	NR	NR	NA	NA	NA	NA
Freedom from valve related complications at 8 yr						
Overall	90%	86%	1 (1,601)	1.05 (1.01, 1.09)	0.03	NA
Freedom from reoperation						
Overall	95%	92%	3 (1,944)	1.04 (1.01, 1.06)	0.003	0%
RCT	NR	NR	NA	NA	NA	NA
Cerebral hemorrhage						
Overall	0.5%	0%	1 (395)	3.17 (0.13, 77.37)	NS	NA

CI indicates confidence intervals; Conv-MVS, conventional open mitral valve surgery; P, heterogeneity; Mini-MVS, minimally invasive mitral valve surgery; n, number of studies; N, number of patients; NA, not applicable; NYHA, New York Heart Association; NR, not reported; NS, not significant; RCT, randomized controlled trial; RR, risk ratio; WMD, weighted mean difference.

Perioperative Outcomes

Death

No significant differences in mortality were found in this meta-analysis. This result is similar to another systematic review,¹ which also found no difference in the overall mortality between mini-MVS and conv-MVS (odds ratio 0.46, 95% CI 0.15–1.42). Of note, an analysis of a large propensity-matched comparison study involving 8644 patients reported significant increase in the composite of major hospital morbidity or mortality with mini-MVS compared with conv-MVS (RR 1.17, 95% CI 1.05–1.32),³⁷ raising the potential for concern about the safety of the minimally invasive approach. Unfortunately, other studies did not report death and major complications as a composite outcome, and we were unable to provide a synthesis for this outcome across all studies. Given that the above-mentioned study is large and propensity matched (in comparison to many of the studies in this analysis being unmatched retrospective comparisons), it is important to keep this potential for increased overall adverse events in mind. On the other hand, some centers contributing data to this propensity-matched comparison study were low-volume centers. Further contemporary comparative studies should be conducted to measure the overall risk of death and complications.

Neurologic Events

Our meta-analysis showed increase in stroke in mini-MVS compared with conv-MVS (RR 1.79, 95% CI 1.35 to 2.38). In contrast, Modi et al¹ reported no difference in stroke between mini-MVS and conv-MVS (odds ratio 0.66, 95% CI 0.23–1.93). However, Modi included fewer studies in his meta-analysis and also included mini-sternotomy studies within the definition of mini-MVS. The cause of increased stroke with mini-MVS is not known and is beyond the scope of this meta-analysis. Potential hypotheses may be related to the restricted access and technically challenging de-airing and/or the increase in procedure time and CPB time. In our subgroup analysis of aortic clamping approach, we found that the majority of increased strokes occurred in the studies using endoaortic cross-clamping. In the studies using primarily transthoracic clamping, there was no excess of strokes. This raises the hypothesis that mini-MVS using the endoaortic clamp may pose greater risk for patients compared with the transthoracic approach. However, it must be stressed that there may be other unexplored factors that could contribute to the increased risk of stroke, and this hypothesis needs further testing in well-conducted, adequately powered comparative trials before the true association can be concluded.

Phrenic Nerve Palsy

Our meta-analysis showed significant increase in the risk of phrenic nerve palsy/diaphragm elevation for mini-MVS versus conv-MVS (3% vs 0%). This may be a potentially serious adverse effect; however, the details of the clinical significance and duration of the palsy were incomplete.^{8,14} In addition, it is important to note that a number of the studies failing to report specifically on this outcome may have had zero events, although we could not assume this for the meta-analysis. Therefore, the

interpretation of this result is limited by the small number of studies reporting on this outcome.

Pain and Functionality

It was anticipated that mini-MVS would be shown to induce less postoperative pain compared with conv-MVS. However, our meta-analysis found no significant difference in the VAS for postoperative pain between groups. Although the trend was toward reduction, the difference was very small with less than 1 point reduction on the VAS (WMD -0.07, -0.25 to 0.11 points on a 10-point VAS).^{21,23,33,34} Similarly, although intake of acetaminophen/oxycodone (in milligrams) was significantly less for mini-MVS compared with conv-MVS, the overall mean difference of 3 mg over the study period was very small and of questionable clinical relevance (WMD -3.35 mg, 95% CI -5.74 to -0.96 mg). There was no significant reduction in the use of morphine in the postoperative period.⁴ Therefore, although reduction in pain remains one of the key rationales for mini-MVS, it remains unproven by the current evidence base. Of all the studies published on mini-MVS versus conv-MVS, very few have reported on pain-related outcomes, and this should be an important part of any future research agenda. Meta-analysis of three studies showed faster return to normal activity of ~5 to 6 weeks (6.3 ± 4.8 weeks vs 12.3 ± 3.8 weeks) for mini-MVS versus conv-MVS.^{4,18,34}

Bleeding and Reoperation Outcomes

It is anticipated that the smaller incision of mini-MVS would lead to less hemorrhage; although there is concern that this could be counteracted by the longer procedure time required. Our meta-analysis showed a decrease in overall hemorrhage and chest tube drainage of ~300 mL for mini-MVS compared with conv-MVS. This translated into significantly less patients receiving RBC and platelet transfusions. However, there was no statistically significant difference in the percentage of patients undergoing reoperation for bleeding between minimally invasive and conventional open mitral valve surgery.^{6,8,12,14,15,21,26,28,32,34–38} In contrast, reoperation for any cause (bleeding or any other reason) was significantly increased by ~1% for mini-MVS versus conv-MVS (6.6% vs 5.5%, RR 1.20, 95% CI 1.01–1.41), although this was reported in just one study (propensity-matched comparison study involving 8644 patients).³⁷

Cardiac Outcomes

Our meta-analysis found a significant reduction in atrial fibrillation with mini-MVS compared with conv-MVS (absolute risk reduction 4%). This reduced risk of arrhythmia may be related to the less traumatic surgical approach used during mini-MVS resulting in lesser inducement of inflammatory mediators. Although atrial fibrillation was significantly reduced in our meta-analysis, there was no significant reduction in pacemaker implantation; however, this outcome was less commonly reported in the studies. Other cardiac outcomes of interest in our meta-analysis did not reach significant differences between groups, including myocardial infarction, left heart decompensation, hypotension, need for inotropes, in-

traaortic balloon pump implantation, ventricular rupture, cardiac tamponade, pericardial effusion, venous thromboembolism, arterial embolism, and in-hospital mitral insufficiency.

Aortic Events

Our meta-analysis showed a significant increased risk of aortic dissection or iatrogenic aortic injury; however, the absolute risk increase of 0.2% was small (0.2% vs 0% for mini- vs conv-MVS, RR 6.04, 95% CI 1.06 to 34.47). The reason for the increased risk of aortic dissection and aortic injury remains unclear (ie, differences in clamping or added difficulties in manipulating the aorta during minimally invasive surgery).

Other Clinical Complications

Our meta-analysis showed no significant difference for postoperative renal failure or renal dysfunction between groups. Because few studies measured the incidence of renal failure, the current evidence remains underpowered to safely rule out whether important differences may exist between mini-MVS and conv-MVS for this clinically relevant outcome.

Pulmonary events were not significantly different between groups, including pneumonia, pneumothorax, pneumonitis, mediastinitis, and pleural effusion. Similarly, gastrointestinal complications did not differ between groups.

Infections and Scar Length

As expected, our meta-analysis found a significant decrease in sternal infections and dehiscence, but an increase in groin infections, hematoma, or hydrocele. Incision length was significantly reduced by ~16 cm between groups, although these data were rarely provided for both groups in the studies and may not be reflective of the average practice difference between mini-MVS and conv-MVS. Only one study examined patient satisfaction with the scar and reported an improvement in satisfaction in patients undergoing mini-MVS compared with conv-MVS.

Overall Complications and Readmissions

Our meta-analysis showed no significance in the freedom from all hospital morbidity, quality of life, requirement of repeat procedure, and readmission within 30 days of postoperative period.

Conversions

Conversion to open sternotomy was reported in 3.7% of patients; however, relatively few studies reported this outcome (12 studies, including 866 patients). The absence of reporting on this outcome does not guarantee that no conversions occurred, and the concern remains that retrospective studies are less likely to ascertain this information because it would be difficult to determine retrospectively from patient charts whether patients who received open sternotomy were originally intended to receive mini-MVS. The inadvertent inclusion of converted patients in the conventional open MVS arm may unfairly bias the results of this meta-analysis toward favoring mini-MVS because converted patients tend to have

worse outcomes than patients undergoing their originally intended surgery.

Resource-Related Outcomes

Our meta-analysis found significantly increased cross-clamp time of ~20 minutes (95 ± 39 minutes vs 74 ± 36 minutes), increased CPB time of ~33 minutes (144 ± 52 minutes vs 111 ± 52 minutes), and increased procedure time of close to 1 hour (4.5 ± 1.8 hours vs 3.7 ± 1.7 hours) for mini-MVS versus conv-MVS. Ventilation time was reduced by 2 hours (12.6 ± 17.7 hours vs 19.0 ± 36.3 hours). Length of stay in ICU was reduced by 0.5 days (1.6 ± 1.7 days vs 2.4 ± 2.4 days), and hospital stay was significantly reduced by ~2 days (6.9 ± 4.2 days vs 8.9 ± 5.1 days) for mini-MVS versus conv-MVS. These results were of similar direction as in the systematic review by Modi et al,¹ although the analysis by Modi et al had insufficient power to detect the difference for some of these outcomes. There was significant heterogeneity for each of these outcomes, which is likely due to the different learning curves across the different centers.

It is notable that in the randomized trials, the differences between groups for procedure-related outcomes and length of stay were less stellar than in the observational studies. For example, the randomized trials suggested that cross-clamp time was slightly decreased by 4 minutes (rather than increased by 23 minutes as in the observational studies), procedure time did not differ significantly, and length of stay in ICU and hospital were not reduced significantly for mini-MVS versus conv-MVS. The differences between randomized trials (with comparable groups at baseline) and nonrandomized trials (with potentially important differences between groups at baseline) may be related to the differences in surgeon experience with mini-MVS, different settings, and patient selection criteria (which may unfairly bias the results of observational studies if different criteria are used for mini- vs conv-MVS). The lack of differences in the randomized trials may also be related to their small sample sizes ($n = 140$ in total).

Few studies reported on the relative cost of mini-MVS versus conv-MVS. One study each from the United States and Slovenia suggested that mini-MVS was associated with significantly lesser costs than conv-MVS. However, the relevance of these findings to other settings in other countries remains uncertain. In addition, these studies were cost analyses only and did not attempt to calculate the incremental cost-effectiveness of mini-MVS versus conv-MVS over the time horizon of a patient lifetime, or even over the midterm, by including follow-up costs during the midterm.^{8,17}

Longer Term Outcomes

Few studies provided long-term outcomes, and conclusions remain uncertain based on the results provided due to the paucity of data provided on completeness of follow-up in these studies. Of the studies that reported longer term outcomes (1 to 9 years of follow-up), there was no significant difference between groups for long-term mortality, quality of life, presence of mitral valve leak, grade of mitral insufficiency, risk of infective endocarditis, and need for reoperation. There was a small but significant decrease in NYHA

class (WMD -0.26 class, 95% CI -0.27 to -0.25 class) and decreased need for reoperation for mini- versus conv-MVS; however, the clinical relevance and generalizability are uncertain given that the reductions were small and were based on a single study.

Strengths and Limitations

This meta-analysis is based on a comprehensive search of several databases to identify all relevant comparative data, and it complies with the latest methodologic recommendations for comprehensive systematic reviews of observational and randomized studies. In addition, this meta-analysis reports on all available clinically relevant and resource-related outcomes, rather than selectively reporting only a few outcomes. However, this meta-analysis is limited by the type of studies and the quality of the data provided in those studies. Most studies in this meta-analysis were retrospective series that compared minimally invasive experience at one center with their own (or others') experience with conv-MVS. In some studies, the series for mini- and conv-MVS were non-contemporaneous series, and the more historic nature of the conventional group may bias the results toward favoring mini-MVS if more contemporary settings provide better outcomes in general (regardless of which procedure would have been provided). In addition, in many series the surgeons who performed mini-MVS were different than the surgeons who provided conv-MVS. Differences in skill sets and differences in progression through the learning curve could bias the results for or against mini-mitral. Improved characterization of the learning curve is also needed. Documentation of the improved procedure-related outcomes over time due to the learning curve effect has been reported in at least one study.³⁰ High-volume centers should perform comparative trials to determine whether better outcomes can be attained with experience.

Several outcomes were reported inconsistently across studies, including some of the most basic outcomes which would provide the rationale for mini-MVS including differences in pain, functionality, patient satisfaction, and quality of life. Also of key concern, most studies failed to provide data on outcomes beyond the patient's discharge from hospital.

Another significant limitation was the potential for overlap among the studies, which was difficult to ascertain in a number of cases due to insufficient reporting of dates of patient recruitment and repeated publications from the same authors or institutions. This issue requires further exploration to elucidate the independence among these patient sets. In addition, the largest data set comes from the STS database analysis by Gammie et al, and it may overlap significantly with some of the most recent studies from U.S. centers. Removing the smaller U.S. center studies from the graphs in the cases where both the study by Gammie et al and the potentially overlapping studies have reported on the same outcome did not have any material impact on the conclusions (because the weight of the study by Gammie et al was large, and the weight of the other singular studies was small). There are a number of U.S. studies that clearly did not overlap the study by Gammie et al because their date of recruitment was earlier than that covered by Gammie et al.

Implication for Practice and Further Research Required

Given the results of this imperfect evidence base, definitive conclusions regarding the overall benefit versus risk of mini-MVS versus conv-MVS are not possible. It seems that mini-MVS improves some important outcomes, but may increase the risk of other serious outcomes. Future studies should assess the volume-outcome relationship for mini-MVS versus conv-MVS. Further research should be encouraged. To ensure that any true differences between mini-MVS and conv-MVS can be detected, and that the magnitude of benefit versus risk can be measured objectively, adequately powered randomized trials should be undertaken to measure stroke, pain, patient satisfaction, overall major complications, need for reoperation, return to normal activity, and quality of life while in hospital and over the longer term. In addition, any future nonrandomized studies should increase validity through prospective and long-term follow-up for clinically important outcomes.

The authors are aware that recruitment for such a randomized trial may be perceived to be difficult in institutions where mini-MVS have been adopted before comparative evidence being available; however, this was equally true for other precedents in surgery, including the eventual conduct of randomized trials to test the widely accepted extracranial to intracranial (EC/IC) bypass to prevent ischemic stroke, even after it had been chosen as standard of care by many centres. Importantly, the eventual fair testing through randomized studies showed that EC/IC bypass surgery actually increased the risk of stroke compared with medical management.⁴⁰ Although some centers report excellent short- and long-term results, these reports are usually noncomparative case series with uncertainty regarding consecutive recruitment. On the other hand, the studies in this meta-analysis include a mixture of new and older studies, and the early parts of the learning curve may have contributed to the results. Future study should evaluate the volume-outcome relationship for mini-MVS.³⁰

CONCLUSIONS

Current evidence suggests that mini-MVS may be associated with decreased bleeding, blood product transfusion, atrial fibrillation, sternal wound infection, scar dissatisfaction, ventilation time, ICU stay, hospital length of stay, and reduced time to return to normal activity, without detected adverse impact on long-term need for valvular reintervention and survival beyond 1 year (although few studies reported long-term outcomes). However, these potential benefits for mini-MVS may come with an increased risk of stroke, aortic dissection or aortic injury, phrenic nerve palsy, groin infections/complications, and increased cross-clamp, CPB, and procedure time. Available evidence is largely limited to retrospective small cohort comparisons of mini-MVS versus conv-MVS that provide only short-term outcomes. Given these limitations, randomized controlled trials with adequate power and duration of follow-up to measure clinically relevant outcomes are recommended to determine the balance of benefits and risks.

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Minimally Invasive Versus Open Mitral Valve Surgery

A Consensus Statement of the International Society of Minimally Invasive Coronary Surgery (ISMICS) 2010

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Objective: The purpose of this consensus conference was to deliberate the evidence regarding whether minimally invasive mitral valve surgery via thoracotomy improves clinical and resource outcomes compared with conventional open mitral valve surgery via median sternotomy in adults who require surgical intervention for mitral valve disease.

Methods: Before the consensus conference, the consensus panel reviewed the best available evidence up to March 2010, whereby systematic reviews, randomized trials, and nonrandomized trials were considered in descending order of validity and importance. The accompanying meta-analysis article in this issue of the Journal

provides the systematic review of the evidence. Based on this systematic review, evidence-based statements were created for pre-specified clinical questions, and consensus processes were used to derive recommendations. The American Heart Association/American College of Cardiology system was used to label the level of evidence and class of each recommendation.

Results and Conclusions: Considering the underlying level of evidence, and notwithstanding the limitations of the evidence base (retrospective studies with important differences in baseline patient characteristics, which may produce bias in results of the evidence syntheses), the consensus panel provided the following evidence-based statements and overall recommendation:

In patients with mitral valve disease, minimally invasive surgery may be an alternative to conventional mitral valve surgery (Class IIb), given that there was comparable short-term and long-term mortality (level B), comparable in-hospital morbidity (renal, pulmonary, cardiac complications, pain perception, and readmissions) (level B), reduced sternal complications, transfusions, post-operative atrial fibrillation, duration of ventilation, and intensive care unit and hospital length of stay (level B). However, this should be considered against the increased risk of stroke (2.1% vs 1.2%) (level B), aortic dissection (0.2% vs 0%) (level B), phrenic nerve palsy (3% vs 0%) (level B), groin infections/complications (2% vs 0%) (level B), and, prolonged cross-clamp time, cardiopulmonary bypass time, and procedure time (level B). The available evidence consists almost entirely of observational studies and must not be considered definitive until future adequately controlled randomized trials further address the risk of stroke, aortic complications, phrenic nerve complications, pain, long-term survival, need for reintervention, quality of life, and cost-effectiveness.

Key Words: Minimally invasive, Mitral valve surgery, Consensus statement.

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Uptake of minimally invasive cardiac surgery continues to grow. The potential benefits of minimally invasive surgery include reduced pain and perioperative clinical complications, reduced length of stay, along with improved cosmetic results and patient satisfaction.^{1,3}

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Given the progression in popularity of minimally invasive mitral valve surgery (mini-MVS), and the increasing experience with the technique, mini-MVS has been adopted as standard of care by some, but not all, centers. Whether the purported benefits of mini-MVS translate into clinically important outcomes remains controversial, and there are conflicting opinions about whether minimally invasive surgery is ready for routine uptake in place of conventional open mitral valve surgery (conv-MVS) in selected patients or in the majority of patients who require surgical intervention for mitral valve disease. This article is intended to be read in light of the evidence provided in the accompanying systematic review published in this issue of the Journal.

METHODS

Purpose of the Consensus Conference

This consensus conference was held to clarify, for clinical practitioners and health care planners or administrators, the role of mini-MVS relative to conv-MVS in adults requiring surgical intervention for mitral valve disease. The growing practice of performing mitral valve surgery through the minimally invasive approach confirms the need for evidence-based recommendations, with careful deliberation of the balance of benefits versus risks. A secondary objective of this consensus conference was to identify the gaps in the evidence and suggest a future research agenda for mini-MVS.

Funding

Support for this consensus conference was provided by the International Society for Minimally Invasive Cardiothoracic Surgery (ISMICS), which has received unrestricted educational grants from industries that produce surgical technologies. Although ISMICS receives industry funding, no specific industry was linked with this consensus conference and did not involve direct funding from any device manufacturers. As in previous ISMICS consensus conferences, editorial independence was granted to the members of the expert panel, and the expectation was that the resulting consensus statements would be based on the best available evidence, with explicit acknowledgment of which recommendations were informed by evidence versus where opinion was required to create statements (when evidence was lacking).

Selection of Panel Members

Members of the consensus panel were invited to participate by the chair (V.F.) and facilitators of the consensus process. Members included representation from eight countries: eight cardiovascular surgeons (one from Israel, one from Switzerland, two from Germany, two from France, and two from the United States), one cardiac anesthesiologist, and one methodologist with expertise in health technology assessment and meta-analysis (Canada).

Defining the Clinical Question

Before the consensus conference, the consensus panel was asked to specify the clinical question, which involved defining each of the following considerations: patient population of interest, intervention of interest, valid comparator

group(s), and outcomes of interest.⁴ The clinical question was developed collaboratively with input from all consensus panel members and was finally stated as follows:

"Does minimally invasive mitral valve surgery via thoracotomy (mini-MVS) improve clinical and resource outcomes compared with conventional open mitral valve surgery through median sternotomy (conv-MVS) in adults requiring intervention for mitral valve disease?" Specifically, does mini-MVS compared with conv-MVS improve:

1. Perioperative and long-term morbidity and mortality
2. Pain, functionality, and quality of life (QOL)
3. Perioperative and long-term resource utilization.

Identifying Relevant Evidence

After the clinical questions had been defined, all published and unpublished evidence (presented at major meetings) with prespecified acceptable study designs was sought to inform this clinical question. Acceptable study designs included any randomized or nonrandomized comparative trial providing clinical or resource information for mini-MVS versus conv-MVS in adults requiring surgical intervention for mitral valve disease. Because there was no available comprehensive systematic review that included all relevant evidence to answer our clinical question, we conducted a full systematic review and meta-analysis of the evidence before the conference. The complete methodology and results of the systematic review has been described in another article in this issue of the Journal and should be consulted before reading the consensus statements provided here.⁵ In short, before the consensus conference, comprehensive searches of Cochrane, MEDLINE, EMBASE, and abstract databases were conducted to identify all randomized and nonrandomized comparative trials comparing mini-MVS with conv-MVS, and which reported clinical- or resource-related outcomes. Potentially relevant studies were circulated to the consensus panel for review and to assess agreement with the prespecified inclusion criteria and to determine whether any relevant trials were missed. Information related to baseline characteristics and outcomes was extracted by one author and verified by a second author. When appropriate, data were synthesized by valid meta-analytic techniques to provide more precise aggregate outcome estimates across multiple studies reporting the same outcome. Data that were not appropriate for statistical synthesis across trials were summarized qualitatively in tables and text to ensure all relevant data were addressed in the systematic review. The results of the systematic review and meta-analysis were used to populate evidence tables and forest plots to form the basis for discussions and support decision making for the consensus panel.

Reviewing and Presenting the Evidence

Before the consensus conference, each member of the consensus panel reviewed the selected randomized and nonrandomized studies related to the clinical questions. During the consensus conference meeting, the panelists were asked to address the following subquestions with the best available evidence:

1. When compared with conv-MVS, does mini-MVS reduce perioperative morbidity (stroke, myocardial infarction, ar-

- rhythmias, regurgitation, heart failure, transfusion, bleeding, reoperation for bleeding, renal failure, and infection) and mortality over the short term and long term?
- When compared with conv-MVS, does mini-MVS improve functionality, satisfaction, and QOL?
 - When compared with conv-MVS, does mini-MVS affect overall resource utilization (procedure time, length of stay, and overall costs)?

Applying the Evidence to Create Recommendations

Levels of Evidence and Grade of Recommendations

The methods were similar to previous consensus conferences hosted by ISMICS, (6–11) and the methodologic details are provided here for reader convenience. The evidence used to inform each clinical subquestion was classified according to the taxonomy suggested by AHA (American Heart Association)/American College of Cardiology (ACC), as outlined in Table 1. This classification categorizes the evidence based on study design and susceptibility to bias, wherein higher levels of evidence and grades are labeled to highlight their lesser likelihood for bias and increased confidence in “closeness to the truth.”^{4,12–15} Several systems of grading recommendations and labeling strength of the evidence exist. The AHA/ACC system was chosen for consistency with other guidelines (http://www.acc.org/clinical/manual/manual_index.htm; accessed April 19, 2004) (Tables 1 and 2). As recommended by guidelines,¹⁶ classification of the evidence and labeling recommendations should involve a group panel using a democratic voting process after adequate group discussion of the strength of the evidence.

Members of the panel considered the highest possible level of evidence to inform the clinical subquestions. Systematic reviews, meta-analyses, and randomized trials (level A evidence, Table 1) were considered preferentially to non-randomized clinical trials (level B evidence). When evidence from published or unpublished studies (from major meetings) to address the question was not available, expert opinion from the consensus panel members was required (level C evidence). In each case, the best available level of evidence was explicitly stated and subsequently interpreted in light of strengths and weaknesses before a statement of recommendation was made. It was generally agreed that recommendations with higher levels of evidence without heterogeneity should be interpreted with more confidence than recommendations based on lower levels of evidence or with heterogeneity, and that recommendations should be explicitly classified as per the ACC/AHA system (Table 2).

TABLE 1. Levels of Evidence

Level A	Data derived from multiple randomized clinical trials
Level B	Data derived from a single randomized trial, or non-randomized studies
Level C	Consensus opinion of experts

TABLE 2. Classes of Recommendations

Class I	Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective
Class II	Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment
IIa	Weight of evidence/opinion is in favor of usefulness/efficacy
IIb	Usefulness/efficacy is less well established by evidence/opinion
Class III	Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful

Consensus Process and the Role of Evidence Versus Opinion

After reviewing the available evidence during the consensus meeting, the consensus panel created draft statements for the subquestions. Further discussion of the strength, consistency, clinical significance, and relevance of the evidence occurred before final revisions and final agreement was made to the consensus statement (along with its appropriate Level of Evidence and Class of Recommendation) for each of the subquestions.

When limited evidence was found to inform a clinical subquestion, it was explicitly recognized that scientific information would need to be supplemented by the interpretations and opinions of the experts. Legitimate conflicts over differences in interpretation and value were resolved by discussion and majority consensus. Therefore, it is important to note that consensus was not always unanimous per se. This is particularly true for subquestions informed only by lower levels of evidence or heterogeneous evidence, where controversy was not allayed by clear evidence and where expert opinion was required to make a judgment.

After each subquestion had been addressed, the entire consensus panel reviewed the recommendations and their assigned grades of recommendations and proposed levels of evidence to address the overarching question of whether mini-MVS should be recommended as an alternative to conv-MVS in today's practice environment.

In summary, this consensus process sought to be evidence-based whenever evidence was available, while allowing for opinions to inform the judgment when the evidence was incomplete. The basis for the statement was labeled by a declarative level of evidence in order to understand whether the basis was evidence or opinion. Bringing experts together for a consensus process based as far as possible on evidence allowed for a carefully considered judgment of the evidence-based recommendations along with their certainties and uncertainties, but still remains imperfect given the limitations of the evidence and the need for filling in the gaps.

RESULTS

A systematic review and meta-analysis of the evidence performed by members of the consensus panel was used as the basis for the discussion of the evidence and formation of the recommendations. All available randomized and nonran-

domized comparative trials of isolated mini- versus conv-MVS were included in the systematic review.⁵

The systematic review with meta-analysis identified two randomized trials and 33 nonrandomized studies for a total of 35 studies comparing mini-MVS versus conv-MVS.¹¹ There was broad representation from a variety of countries in the included studies. Average age of patients at baseline was 55 years, 42% of whom were women. At baseline, mean ejection fraction was 55%, and approximately 7% of patients had diabetes, 22% had atrial fibrillation, 4% had previous myocardial infarction, and 3% had previous stroke. On average, 3.7% of patients required conversion from planned mini-MVS to conv-MVS, and it was not clear whether the individual studies excluded converted patients. We were unable to consider the impact of converted patients because of the lack of information about their outcomes in the studies.

There were some differences in baseline characteristics between groups when the studies were combined. Mini-MVS patients were slightly younger by 1.6 years than conv-MVS patients, and this difference was statistically significant [weighted mean difference (WMD) -1.57, 95% confidence interval (CI) -2.72 to -0.42 years]. In addition, mini-MVS patients were less likely to have renal dysfunction, chronic obstructive pulmonary disease, or elevated pulmonary artery pressures at baseline. These differences were generally driven by patient selection in the nonrandomized studies in this meta-analysis.¹¹ Please refer to the accompanying systematic review in this issue of the Journal for the baseline characteristics table.

For the following outcomes, heterogeneity across studies was observed in the meta-analysis for chest tube drainage, deep infection or dehiscence, bypass time, cross-clamp time, ventilation time, procedure time, length of stay, and time to return to normal activity. Nevertheless, much of the heterogeneity was less concerning because it was driven by uncertainty about the size of effect and not the direction of effect and therefore did not put into question the presence of significant benefit (when detected). The presence of heterogeneity was considered for each respective outcome during the consensus conference. The discussion and resulting evidence-based statements with assignment of levels of evidence and class of recommendation are given below for each clinical subquestion and for the overarching clinical question. The aggregate results from meta-analysis of randomized controlled trials (RCTs, level A) would have been preferred; however, because randomized trials were generally unavailable, aggregate results from nonrandomized evidence (non-RCTs, level B) were therefore required for most outcomes. Readers may consult the original publication for comprehensive reporting of both randomized and nonrandomized trials for all endpoints. For discrete outcomes, risk ratios (RRs) and their 95% CIs are reported. For continuous outcomes, the WMD (95% CI) is reported.

Question 1: Does Mini-MVS Compared With Conv-MVS Improve Perioperative Morbidity and Mortality?

Postoperative all-cause mortality was not significantly different between mini-MVS and conv-MVS in hospital or at

30 days (1.2% vs 1.5%, RR 1.03, 95% CI 0.75-1.42; 20 studies, level B). There was no difference between the RCTs and non-RCTs for this outcome, given that there were no deaths reported in either of the two RCTs.

Clinical outcomes that were improved with mini-MVS compared with conv-MVS included bleeding, units of red blood cells (RBCs), platelets and fresh frozen plasma transfused, postoperative atrial fibrillation, and (of course) sternal wound complications. Volume of bleeding, generally measured by chest tube drainage, was reduced with mini-MVS compared with conv-MVS by ~300 mL (WMD -255 mL, 95% CI -437 to -95 mL; 12 studies; level B). Volume of RBCs transfused was reduced by nearly two units (WMD 1.9 units, 95% CI -2.5 to -1.2 units, level B) for mini-MVS versus conv-MVS. However, the number of patients transfused RBCs was not significantly reduced. The volume of fresh frozen plasma transfused was reduced with mini-MVS versus conv-MVS, although the reduction was <0.5 unit (WMD -0.4 units, 95% CI -0.8 to -0.08 units, level B). The number of patients receiving platelet transfusion was reduced with mini-MVS versus conv-MVS, although the absolute reduction was small (16% vs 19%; RR 0.80, 95% CI 0.73-0.88; two studies, level B). The reasons for reduced bleeding are most likely associated with a smaller incision and less dissection of tissue and thus a smaller wound surface. Diffuse bleeding should therefore be less. There may, however, be a potential bias in that patients were also younger, and the threshold for transfusion may thus be different as lower hematocrit levels may have been accepted in younger patients. Transfusion data by age were unfortunately not available to test this hypothesis.

Mini-MVS was associated with a reduction in postoperative atrial fibrillation compared with conv-MVS (absolute risk reduction 4%). Whether this may be due to the reduced systemic inflammatory approach associated with the less traumatic minimally invasive approach remains to be proven. Reduction in atrial fibrillation with minimally invasive cardiac surgery has also been shown for other minimally invasive procedures including off-pump bypass surgery compared with on-pump bypass surgery.^{17,18} The reason for this difference in the new onset of atrial fibrillation remains uncertain. Perhaps, femoral vein cannulation is less likely to trigger fibrillation than direct right atrial cannulation, which is associated with more atrial manipulation. Limited dissection and manipulation of the heart and limited pericardiotomy may also play a role. Size of the left atrium as well as age differences may also be confounding factors. In addition, the studies did not clearly denote the number of patients who received concomitant surgical ablation for atrial fibrillation, and it is possible that this was performed more commonly in the conv-MVS group.

Although atrial fibrillation was significantly reduced (absolute risk reduction 4%) with mini-MVS compared with conv-MVS (RR 0.87; 95% CI 0.77 to 0.99; eight studies, level B), it is important to note that no reduction in pacemaker insertion was found (perhaps due to low power, as few studies consistently reported this outcome). It is also important to note that the finding of lesser postoperative atrial

fibrillation seems counterintuitive to the finding of increased risk of stroke in the mini-MVS group (see below).

Some adverse clinical outcomes were increased with mini-MVS compared with conv-MVS, including stroke (defined as neurologic deficits >24 hours), aortic dissection, phrenic nerve palsy, and groin wound/vasculature complications. The absolute risk increase of stroke for mini-MVS versus conv-MVS was 0.9% overall (2.1% vs 1.2%, RR 1.79, 95% CI 1.35–2.38; 13 studies, level B). In the two RCTs in the meta-analysis, stroke was not measured (or not reported). To select for higher quality nonrandomized studies to explore whether study design impacted the estimate of stroke risk, subanalysis of propensity-matched studies was performed. Subanalysis of two propensity comparison studies also showed significant increase of stroke of 1% with mini-MVS compared with conv-MVS (1.9% vs 0.9%, RR 2.02, 95% CI 1.40–2.94; two studies, level B). The results of these higher quality propensity-adjusted studies were consistent with the remainder of the retrospective unmatched cohort studies reporting on this outcome. Further exploration of the potential reasons for increased risk of stroke was performed by subanalyzing studies that reported using endoaortic clamp separately from those that reported using exclusively the transthoracic clamp.

The increased risk of stroke in the mini-MVS group compared with conv-MVS was numerically greater in the subgroup of mini-MVS studies that used endoaortic clamp exclusively (RR 1.72, 95% CI 0.91–3.23; $P = 0.09$; five studies, level B) or in studies that reported using endoaortic clamping in a proportion of included patients (RR 1.84, 95% CI 1.33–2.55; $P = 0.0002$; three studies, level B). In those studies in which transthoracic clamping was used exclusively, the risk was not increased, although this subgroup was underpowered (RR 0.80, 95% CI 0.07–8.92; $P = 0.9$; four studies, level B). In the studies using exclusively transthoracic clamping, there were only two strokes reported (one in each group). Because there was no heterogeneity across the trials for the outcome of stroke ($I^2 = 0\%$), we cannot conclude from these data that the difference in risk of stroke is related to the use of the endoaortic approach for clamping. More importantly, because these results are derived from observational studies, a causal link between mini-MVS and stroke cannot be definitively determined because important differences between patients in each group at baseline and/or differences in their treatment other than the type of surgery received may have biased the results. Clearly, this finding of potential for increased risk of stroke remains an important result to be explored further through trial designs adequate in size and duration to answer the question.

Potential reasons for the increased risk of stroke remain unknown, and have not been specifically studied. Some opinions (not yet supported by evidence) that may be important to consider for future hypothesis generation to guide future studies might include the following:

- Incomplete de-airing associated with the minimally invasive approach.
- Retrograde aortic flow with the potential of retrograde embolism from a calcified thoracic aorta or aortic arch.

- Use of CO₂ insufflation during mini-MVS to reduce the amount of detectable bubbles using transcranial Doppler.
- Failure to use an aortic root vent may potentially increase the risk of air emboli, leading some to recommend leaving the aortic root vent until the heart is fully beating and no more bubbles are seen on transesophageal echocardiography (TEE).
- To prevent retrograde embolism, it has been suggested that retrograde flow should be avoided in patients with an athermanous aorta or arterial cannulation may be performed via the axillary artery.
- Perhaps, prolonged cross-clamp time and cardiopulmonary bypass (CPB) time associated with mini-MVS contributes to the increased risk of stroke.

None of these factors has yet been proven to be the reason for increased risk of stroke, and these hypotheses require appropriate study.

Aortic dissections and iatrogenic aortic injuries were both increased with mini-MVS versus conv-MVS. Risk of aortic dissection, considered alone, was 0.2% versus 0% for the two groups, respectively (RR 6.04, 95% CI 1.06 to 34.47; six studies, level B). Similarly, when aortic dissections and injuries were considered as a composite endpoint, there was a significant increased risk with mini-MVS versus conv-MVS, although the absolute event rate was small (0.4% vs 0%, 5.68, 95% CI 1.23 to 26.17; eight studies, level B). It was not possible to determine the reasons for aortic dissections and iatrogenic aortic injuries from the information provided in the studies. No studies have been done to specifically inform this risk. Perhaps, increased incidence of aortic injury can be attributed to the learning curve associated with a change in aortic clamping techniques. If not monitored well, the endoaortic balloon can obstruct the truncus and lead to temporary malperfusion of the brain, and for this reason, it has been recommended to monitor both right and left radial artery pressures. Perhaps, retrograde cannulation of the femoral artery leads to increased risk of aortic injury which, with retrograde aortic flow, can predispose to aortic dissection. Some have suggested, therefore, that meticulous use of the Seldinger technique is important, and if there is any resistance for the guide wire, subclavian artery access should be chosen. These suggestions remain to be studied.

Risk of phrenic nerve palsy was higher with mini-MVS versus conv-MVS by an absolute increase of 3% (3% vs 0%, RR 7.6, 95% CI 1.3 to 44.7; three studies, level B). Some of the patients in the studies that reported phrenic nerve palsy experienced respiratory compromise and prolonged ventilation,^{19,20} whereas other patients experienced only diaphragm elevation¹ and/or were not described in sufficient detail to determine the clinical significance of the nerve palsy. It has been suggested that phrenic nerve palsy may result from extensive pull on the pericardial retraction sutures that are sometimes used for enhancing exposure of the left atrium. As a result, some have suggested that it is important to (1) cut the pericardium not too close to the phrenic nerve (≥ 3 cm away) and (2) not to place the retraction sutures close to the nerve and avoid excessive pull. Another potential source of phrenic nerve injury may be the use of a cryoprobe for concomitant

ablation therapy, as the probe can come in close proximity to the nerve and cause temporary palsy. Again, studies are needed to clarify these hypotheses.

Not surprisingly, sternal wound infections were significantly decreased with mini-MVS versus conv-MVS (0% vs 0.3%; RR 0.34, 95% CI 0.12 to 0.95; seven studies, level B). This is a result that is consistent with expectations, as the mini-MVS approach was by definition via a thoracotomy rather than via sternotomy, whereas the conv-MVS approach was by definition only via median sternotomy in this meta-analysis. As a corollary, the conv-MVS approach resulted in an absolute increase in the risk of groin infections/complications by 2% compared with conv-MVS (2% vs 0%, RR 5.62, 95% CI 1.26 to 25.135 studies, level B).

Other perioperative clinical outcomes did not differ between mini-MVS and conv-MVS, including renal complications (renal dialysis and renal dysfunction), pulmonary complications (pneumonia, pneumonitis, pleural effusion, and pneumothorax), cardiac outcomes (acute myocardial infarction, ventricular arrhythmias, mitral insufficiency, tamponade, pericardial effusion, heart failure, and thromboembolic events), reoperation for bleeding.

Statement

1. No difference was found in mortality (1.2% vs 1.5%) between mini-MVS and conv-MVS during the perioperative period and up to 30 days postoperatively (level B).
2. Risk of stroke was increased (2.1% vs 1.2%, number needed to harm = 111) with mini-MVS versus conv-MVS (level B).
3. Risk of aortic dissection was increased (0.2% vs 0%) with mini-MVS versus conv-MVS (level B).
4. Risk of phrenic nerve palsy was increased (3% vs 0%) with mini-MVS versus conv-MVS (level B).
5. Risk of groin infections/complications was increased (2% vs 0%) with mini-MVS versus conv-MVS (level B).
6. Risk of sternal complications was decreased (0% vs 0.3%) with mini-MVS versus conv-MVS (level B).
7. Volume of blood product transfusion was reduced (1.5 vs 3.5 RBC units) with mini-MVS versus conv-MVS (level B), but reoperation for bleeding was not different between groups (level B).
8. Risk of postoperative atrial fibrillation was reduced (18% vs 22%) with mini-MVS versus conv-MVS (level B).
9. There was comparable risk of other in-hospital morbidities (renal, pulmonary, cardiac, and readmission rates) for mini-MVS and conv-MVS (level B).
10. Longer term outcomes, including readmissions, need for reoperation, and survival at 1 to 8 years, were similar between mini-MVS and conv-MVS (level B); however, very few studies reported these outcomes.

Question 2: Does Mini-MVS Reduce Pain and Improve Functionality, Satisfaction, and QOL Compared With Conv-MVS?

Pain measured via VAS was not significantly reduced for mini-MVS versus conv-MVS (WMD -0.07 points, 95% CI

-0.25 to +0.11 points; five studies, level B) when measured postoperatively on day 1 through to discharge. Use of analgesics also did not differ between groups. However, few studies reported any outcomes related to pain and failure to find a difference may be due to underreporting. Nonetheless, it is interesting to note that in the studies where VAS was reported, the difference between groups (mean difference) and range of plausible differences (95% CI) was very small.

New York Heart Association class was slightly improved after 1 year for mini-MVS compared with conv-MVS (mean class 1.32 vs 1.52, WMD -0.26, 95% CI -0.27 to -0.25; two studies, level B), but the difference was small and based on two studies. The clinical relevance of this small incremental improvement between groups is uncertain.

There was no significant difference in freedom from reoperation between groups at 1 year (RR 1.03, 95% CI 0.97 to 1.10; 1 study, level B) based on one study only. However, at 8 years, there was significant improvement in freedom from reoperation for mini-MVS compared with conv-MVS (RR 1.04, 95% CI 1.01 to 1.08; one study, level B) based on one study only.

Return to normal activity was significantly faster for mini-MVS versus conv-MVS (6.3 vs 12.3 weeks, WMD -4.96 weeks, 95% CI -6.39 to -3.52 weeks; three studies, level B). There was significant heterogeneity across the studies for this outcome.

Time to return to normal activity was significantly improved with mini-MVS versus conv-MVS (WMD -5 weeks, 95% CI -6.4 to -3.5 weeks; three studies, level B). QOL was reported in only one observational study and showed no differences in the degree of improvement in QOL postoperatively between groups.

Mean incision length was 6.3 cm, and it was 16 cm shorter, on average, in the mini-MVS group compared with conv-MVS in the few studies that reported comparative data for this outcome (WMD -16 cm, 95% CI -19 to -13 cm, level B). One study measured patient dissatisfaction with the scar postoperatively and showed that significantly fewer patients were dissatisfied with the scar in the mini-MVS group versus conv-MVS (0% vs 19%, RR 0.05, 95% CI 0 to 0.79; 1 study, level B).

Statement

1. There was no difference in reported pain perception between mini-MVS and conv-MVS during the perioperative period and up to 30 days (level B).
2. Patient dissatisfaction with the scar postoperatively was reduced (0% vs 19%) with mini-MVS versus conv-MVS (level B); however, only one study reported this outcome.
3. New York Heart Association class improvement at 1 year was similar (mean class 1.32 vs 1.52) with mini-MVS and conv-MVS (level B).
4. Time to return to normal activity was significantly improved (6 vs 12 weeks) with mini-MVS compared with conv-MVS (level B).

5. There was a similar need for reoperation at 1 year between mini-MVS and conv-MVS (level B); however, few studies reported this outcome.
6. No difference was found for QOL between mini-MVS and conv-MVS (level B); however, only one study reported this outcome.

Question 3: When Compared With Conv-MVS, Does Mini-MVS Affect Overall Resource Utilization (Operating Room Time, Length of Stay, and Overall Costs)?

Although cross-clamp time, CPB time, and procedure time were increased with mini-MVS compared with conv-MVS, the ventilation time, and intensive care unit (ICU) and hospital length of stay were reduced. Cross-clamp time was increased by 21 minutes (WMD 21.41, 95% CI 10.14 to 32.69 minutes, level B), when all studies were considered in aggregate. In exploratory subanalyses, the increased cross-clamp time among observational studies was found mainly for repair but not for replacement. At least one study has reported a learning curve effect with earlier experience in mini-MVS requiring longer than later experience with mini-MVS, although in later experience, they still required a longer procedure time with the minimally invasive approach compared with conventional surgery.²¹ However, subanalysis of RCTs showed shorter cross-clamp time with mini-MVS versus conv-MVS (56 ± 16 minutes vs 60 ± 19 minutes, WMD -4.0 minutes, 95% CI -7.2 to -0.7 minutes), which is opposite to what the observational studies suggested. Cross-clamp time may be related directly to the experience of the centres. However, this hypothesis was not tested in our meta-analysis.

CPB time was significantly increased with mini-MVS versus conv-MVS (WMD 33.0, 95% CI 18.9 to 47.1 minutes; 27 studies, level B), when all studies were considered in aggregate. There was significant heterogeneity across studies for this outcome, and subanalysis of the two RCTs showed significantly reduced CPB time with mini-MVS versus conv-MVS (WMD -4 minutes, 95% CI -7 to -1 minutes), which is opposite to what the nonrandomized studies reported. The reasons for the discrepancy between randomized and nonrandomized studies remain uncertain. Often, the patient is put on CPB immediately after femoral cannulation even before the thoracotomy is made. This of course adds to the overall CPB time in mini-MVS.

Procedure time was significantly increased for mini-MVS compared with conv-MVS (WMD 0.79 hours, 95% CI 0.41 to 1.16 hours; 13 studies, level B) when all studies were considered together. There was significant heterogeneity among the studies for this outcome, but the heterogeneity was mostly due to the degree of increased procedure time rather than to differences in direction of effect. The single RCT that reported this outcome showed no significant difference in procedure time between groups (WMD 0.24, 95% CI -0.31 to +0.79 hours, one RCT, level B), although the trend was in the same direction and the study was likely underpowered.

Ventilation time was significantly reduced for mini-MVS compared with conv-MVS (12.6 vs 19.9 hours, WMD -2.07 hours, 95% CI -3.39 to -0.75 hours, 18 studies, level

B). The one RCT that reported this outcome showed no difference in the length of ventilation between mini- and conv-MVS (WMD -3.0, 95% CI -7.4 to +1.4 hours, level B) but may have been underpowered to detect a significant difference.

Length of stay in ICU was significantly reduced for mini-MVS versus conv-MVS (WMD -0.50 days, 95% CI -0.68 to -0.32 days, 18 studies, level B). No RCTs reported this outcome, and the heterogeneity among observational studies was generally not of concern given that the direction of effect was similar for most studies. Similarly, length of hospital stay was reduced with mini-MVS versus conv-MVS (WMD -1.60 days, 95% CI -2.09 to -1.11 days, 26 studies, level B). There was significant heterogeneity among the studies for this outcome, but the direction of effect was similar for most studies. Differences in patient discharge protocols and bed availability may account for differences in degree of reduction in length of stay. Subanalysis of the two RCTs reporting this outcome showed only a small numeric reduction in hospital length of stay that did not reach significance (WMD -0.04 days, 95% CI -0.8 to +0.7 days).

The overall impact on total costs remains uncertain. Although some centers have suggested cost savings with mini-MVS, this finding was not universal. It was not possible to combine costs reported in various studies across disparate countries, and synthesis of cost estimates was not possible because of heterogeneity. The incremental cost-effectiveness for mini- versus conv-MVS remains unstudied.

Statements

1. Cross-clamp time was longer (95 vs 74 minutes) for mini-MVS compared with conv-MVS (level B).
2. Cardiopulmonary bypass time was longer (144 vs 112 minutes) for mini-MVS compared with conv-MVS (level B).
3. Procedure time was longer (4.5 vs 3.7 hours) for mini-MVS versus conv-MVS (level B).
4. Ventilation time was shorter (13 vs 20 hours) for mini-MVS versus conv-MVS (level B).
5. Postoperative ICU stay (1.6 vs 2.4 days) and hospital stay (7 vs 9 days) were shorter for mini-MVS versus conv-MVS (level B).
6. Costs were reported in few studies, but with varied definitions and settings, generalizable conclusions regarding costs or cost-effectiveness were not possible.

Consensus Summary for Overarching Question

After discussion of each of the substatements for the three subquestions, the consensus panel discussed what should be the overall role of mini-MVS compared with conv-MVS in the current practice environment, to address the overarching question: does mini-MVS improve clinical and resource outcomes compared with conv-MVS? Because there are no studies that have examined a policy of routine mini-MVS versus conv-MVS as standard of care, the maximal level of evidence for this recommendation is level B. But, because the evidence was less well established for key clinical outcomes, and because there was some inconsistency of

opinion across the consensus panel, the recommendation was designated as Class IIb. In addition, there was much discussion about the limitations of the evidence and the fact that there have been no prospective randomized trials to establish the comparative effectiveness of the mini- versus conv-MVS. The current evidence base relies on retrospective reviews of experiences from a variety of centers, with varied levels of expertise, and there may be significant risk of publication bias as authors will be less likely to publish adverse outcomes when publishing their center's experience (and many centers have not published their experience at all). Notwithstanding these limitations, the panel discussed the fact that the review of the evidence was comprehensive and attempted to be objective in ascertaining all outcomes from all studies. The current evidence should guide our decision making, with full acknowledgment of the limitations and the need for future research to guide consensus updates in the future. Given this discussion, the panel suggested the following overarching recommendation:

Recommendation

In patients with mitral valve disease, minimally invasive surgery may be an alternative to conventional mitral valve surgery (Class IIb), given that there was:

1. Comparable short-term and long-term mortality (level B)
2. Comparable in-hospital morbidity (renal, pulmonary, cardiac complications, pain perception, and readmissions) (level B)
3. Avoidance of sternal complications (0 vs 0.3%), units transfused (1.5 vs 3.5 RBC units), postoperative atrial fibrillation (18% vs 22%), duration of ventilation, and ICU and hospital length of stay (level B).

However, this should be considered against the increased risk of:

4. Stroke (2.1% vs 1.2%) (level B)
5. Aortic dissection (0.2% vs 0%) (level B)
6. Phrenic nerve palsy (3% vs 0%) (level B)
7. Groin infections/complications (2% vs 0%) (level B)
8. Prolonged cross-clamp time, cardiopulmonary bypass time, and procedure time (level B).

DISCUSSION

Overall, the recommendations suggest that mini-MVS may have advantages with respect to reduced risk of bleeding, atrial fibrillation, and sternal infection but may increase the risk of stroke and groin infections/complications. For most other endpoints, no difference was found for either technique. However, the reliance on retrospective studies reduces the confidence in our findings, and some of the results may represent conservative estimates (especially if complicated patients crossed over to and were accounted for as conv-MVS, which is more likely to happen in retrospective studies where the original intent of the intended procedure may not be documented).

Statement on Future Research

This consensus statement must be interpreted in light of the fact that all recommendations were level B. Because only

two small randomized trials of mini-MVS have been published, and because there were insufficient events in these randomized trials to determine whether any differences might exist, none of the recommendations is based on level A evidence. Future evidence may change or further refine the statements within this consensus statement. Based on discussion of the limitations of the evidence base and key gaps in the available literature, the following areas were suggested by the consensus panel as priority areas for future research.

Trial Design

Future trials should be designed to compare mini-MVS versus conv-MVS rather than focusing on noncomparative case series only. Without a comparison to conventional open surgery, it is difficult to know whether mini-MVS is better, same, or worse than standard open mitral valve surgery with regard to the endpoints discussed here. Rates of repair versus replacement were inadequately studied in the existing studies and should be clarified in future comparative studies. Some series from experienced centers have shown repair rates exceeding 90% with minimally invasive techniques. However, these were noncomparative case series and provide insufficient proof of comparative outcomes and have been singularly underpowered to assess uncommon risks such as stroke.

Because of the potential implications of increased risk of stroke and because the retrospective nature of current studies raise questions of bias (which may change the results for worse or for better, and the balance of effect of bias remains unknown), adequately powered randomized trials are required to determine whether the risk of stroke truly differs between groups. Without randomized trials with baseline homogeneity in patient characteristics between groups, it will not be known whether this finding is real or whether it may be an artifact of differential patient selection and different intensities of reporting or follow-up in the observational studies included in the meta-analysis. Such a serious outcome requires a fair evaluation through randomized trials to definitively answer the question for future patients. The authors are aware that mini-MVS has been adopted as the standard of care in many centers and is also driven by patient desire that may provide a challenging environment for recruitment. Nonetheless, a randomized trial is possible despite these challenges and has been overcome in other areas of surgery where procedures have been adopted before developing an adequate evidence base.

In designing future randomized trials, careful attention to study design should be given. The process of randomization should be objective and concealed so that patients in each arm will be comparable and decisions to enroll patients are made under equipoise rather than having control over which patients are included in each arm of the study. Primary analysis of randomized studies, or any comparative analysis, should be made by intention-to-treat, with subsequent subanalysis of patients who crossover. This is equally important for prospective randomized studies as it is for nonrandomized retrospective studies, because patients who are intended to undergo mini-MVS and who are subsequently crossed over to

open surgery tend to have worse outcomes when compared with patients who were originally intended to undergo open surgery (without crossover). If these crossover patients are analyzed in the open surgery group, their results will unfairly bias the open surgical group. Therefore, for retrospective studies, extra effort should be applied to ascertaining whether patients in the open surgery group wrongly include patients who were originally intended to undergo minimally invasive surgery but were crossed over.

Future studies should also be of adequate duration to measure the most clinically relevant outcomes—long-term survival, patient functionality and QOL, and freedom from residual mitral insufficiency, and reoperation. Future studies from centers reporting their experience should ensure that any overlap with previous publications is declared.

Definitions

Efforts should be made to standardize definitions of mini-MVS. A variety of techniques have been used under the name of mini-MVS ranging from thoracotomy with small incision and videoscope used to assist vision, to thoracotomy with large incision and direct vision, and to mini-median sternotomy. Some mini-MVS have used totally robotic techniques, whereas others use robot-assisted techniques. Therefore, all future studies should explicitly define the mini-MVS procedure so that reviewers can understand what was done. Clear explanation of the access, cannulation site, occlusion technique, de-airing technique, and level of experience of the operators should be provided.

Outcomes

Because there is inadequate power in the existing small randomized trials (each with short-term follow-up), the majority of outcomes have not been adequately addressed. Although the balance of the evidence suggests that there may be some reduced risk of certain perioperative morbidities (transfusion, atrial fibrillation, mediastinitis, ventilation time, length of stay, and return to normal activity) and some increased risk of other perioperative morbidities (stroke, aortic dissection, phrenic nerve palsy, groin complications, increased cross-clamp and cardiopulmonary bypass time, and increased procedure time), these are based on nonrandomized trials with measurable selection bias. Therefore, all clinically relevant outcomes remain to be definitively proven in future adequately powered randomized trials that control for selection biases. In particular, outcomes that should be given high priority in future randomized trials include pain, QOL, functionality, return to normal function, survival, reoperation, long-term valvular function (with echo follow-up year by year), major adverse coronary events and overall resource utilization.

Strengths and Limitations

This consensus statement is based on a current and comprehensive systematic review of the evidence, with formal consensus processes that limited the role of opinion secondary to that of the evidence base. Care was taken to explicitly label the recommendations with the evidence available to inform it, and when evidence was unavailable, to

apply considered expert judgment to provide perspective for potential users of the statement. With this explicit evidence-based consensus process, it should be clear to the user how the recommendations were derived. The panel acknowledges that many large single center studies that report positive results with mini-MVS were excluded from this analysis because they were noncomparative case series without the ability to inform comparative efficacy versus conventional surgery. Thus, this analysis may not reflect contemporary practice because many experienced centers did not report comparative studies. Only two randomized trials have been published, and both of these date back to the earlier history of mini-MVS. Updated randomized trials involving experienced centers are necessary to elucidate the issue of stroke.

A notable strength of this consensus statement is its reliance on the evidence base, with comprehensive consideration of benefits, risks, and resource-related issues. The methodology undertaken and recommendations provided by this consensus conference are in agreement with current recommendations for developing consensus statements^{22,23} and guidelines.²⁴ To self-appraise our consensus statement against current standards for valid guidelines, we subjected our consensus process and recommendations to quality assessment checklists and found that most indicators of high-quality were met or exceeded.^{22,24} This is in contrast to the majority of existing guidelines, which rarely meet all of these recommended criteria.²⁴

Although a range of health care professionals and methodological expertise was represented on the consensus panel, some stakeholders were not represented. In particular, patients, administrators, and policymakers, were not invited to participate; however, patient-related outcomes including satisfaction and QOL were sought from published trials to address this perspective. It is unfortunate that patient satisfaction was infrequently reported in the studies. In addition, stakeholders from the manufacturing sector (ie, producers of technologies related to endoscopic and open surgery) were not included in the consensus and review process, to reduce the risk of bias that may result from direct manufacturer involvement.

Clinicians tend to overestimate the effectiveness of new interventions, especially if the intervention in question rests within the realm of their expertise.²⁵ In addition, there is a tendency for group decision-making processes to converge with compromises made to please all members, even for issues that are greatly polarized. To reduce this problem, experts in evidence-based decision-making and health technology assessment were invited to facilitate the discussion and to promote that the best available evidence should be the focus for discussion. Nonetheless, a key limitation was the absence of other surgeons on the consensus panel who are not strong proponents of mini-MVS. Most members were expert surgeons who perform mini-MVS, and this represents a significant limitation of breadth and balance of perspectives.

A further limitation of the evidence base on which these recommendations were made is the inconsistent management of patients who crossed over from mini-MVS to conv-MVS because of difficult morphology, intraoperative bleeding, he-

modynamic collapse, or other complications. In some studies, patients who crossed over were either excluded or accounted for in the conventional group. In many studies, no mention was made of how crossover patients were handled in the analysis. Studies that analyzed crossover patients may provide overestimations of benefit because the risk of crossover to conventional open surgery might not have been accounted for in the mini-MVS group (crossover patients tend to do worse, on average, than all other patients). Of trials that reported crossovers, there was an average of 3.4% of patients who required conversion to open surgery. The outcomes of patients who required conversion were not reported in the studies, and it was therefore not possible to separately analyze these patients. Most of the studies did not clarify how the converted patients were handled in the data analysis, and it is likely that many studies excluded converted patients from their analysis.

Finally, the lack of randomized trials to inform any of the consensus statements is a limitation that deserves discussion here. Although this limitation is common in surgery and is true of many consensus statements,²⁶ it does not provide reason to abandon the consensus statement. Rather, it should serve the purpose of explicitly defining the best available evidence to inform each statement. Even without the availability of an ideal evidence base, decisions must be made. In this case, the decisions need to be weighed with both the potential benefits and risks of mini-MVS. Because the studies were nonrandomized, usually retrospective series, there will be inherent biases in the patient selection. In particular, selection bias may increase the likelihood that patients with differing prognoses will be systematically chosen for mini-MVS rather than conv-MVS. Some of the significant differences found in the meta-analysis may be due to this selection bias. Because the magnitude of impact of this bias cannot be known, readers should bear in mind that the evidence base for statements labeled with level B may be an overestimation or underestimation of the overall magnitude of benefit. The consensus panel incorporated this uncertainty into their discussions and assigned the Class of Recommendation to reflect this uncertainty. It is hoped that future trials will be conducted to address these areas where only lower levels of evidence are available.

Feasibility and Training

Judgments about whether the affordability, feasibility, and uptake of mini-MVS (as a clinical or research program) depend on the local context and setting. Feasibility issues worth considering include time, skills, staff, training and equipment necessary to adhere to the recommendations, and the ability of local systems of care to implement them. Issues to consider when localizing these recommendations to specific settings include skills development programs, certification programs for mitral valve surgery, and local availability of equipment and supporting technologies. The learning curve for minimally invasive surgery is steep, and it should not be presumed that these evidence-based recommendations should be applied without consideration of individual skills development.

SUMMARY AND CONCLUSIONS

After review and discussion of the best available evidence, the following summary consensus recommendations were delineated.

In patients with mitral valve disease, minimally invasive surgery may be an alternative to conventional mitral valve surgery (Class IIb), given that there was

1. Comparable short-term and long-term mortality (level B)
2. Comparable in-hospital morbidity (renal, pulmonary, cardiac complications, pain perception, and readmissions) (level B)
3. Reduced sternal complications (0% vs 0.3%), transfusions (1.5 vs 3.5 RBC units), postoperative atrial fibrillation (18% vs 22%), duration of ventilation, and ICU and hospital length of stay (level B).

However, this should be considered against the increased risk of:

4. Stroke (2.1% vs 1.2%) (level B)
5. Aortic dissection (0.2% vs 0%) (level B)
6. Phrenic nerve palsy (3% vs 0%) (level B)
7. Groin infections/complications (2% vs 0%) (level B)
8. Prolonged cross-clamp time, cardiopulmonary bypass time, and procedure time (level B).

The available evidence consists almost entirely of observational studies and should not be considered definitive until future adequately controlled randomized trials further address the risk of stroke, aortic complications, phrenic nerve complications, pain, long-term survival, need for reintervention, QOL, and cost-effectiveness.

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Feasibility, safety, and efficacy of totally endoscopic coronary artery bypass grafting: Multicenter European experience

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See related editorials on pages 559 and 562.

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Objective: The invention of robotic systems has begun a new era of endoscopic cardiac surgery. Reports on totally endoscopic coronary artery bypass grafting are limited, however, and data regarding feasibility, safety, and efficacy are needed to determine this technique's position in the therapeutic armamentarium. This study describes the largest multicenter experience in the literature with robotic totally endoscopic coronary artery bypass grafting specifically addressing procedural feasibility, safety, and efficacy.

Methods: Between September 1998 and November 2002, a total of 228 patients with coronary artery disease were scheduled for totally endoscopic coronary artery bypass grafting with the da Vinci Surgical System (Intuitive Surgical Inc, Sunnyvale, Calif.) at five European institutions. Patients underwent totally endoscopic coronary artery bypass grafting with either an on-pump (group A, n = 117) or an off-pump approach (group B, n = 111). Patients underwent postoperative angiography or stress electrocardiography and were followed up for 6 months.

Results: Procedural feasibility was demonstrated through the completion of 164 successful totally endoscopic cases. Sixty-four patients (group C, 28%) had conversion to nonrobotic procedures. Conversion rates decreased with time. The overall procedural efficacy, as defined by angiographic patency or lack of ischemic signs on stress electrocardiography, was 97%. The incidence of major adverse cardiac events within 6 months was 5%.

Conclusion: Both on- and off-pump totally endoscopic coronary artery bypass grafting are feasible, with a conversion rate that diminishes with increasing experience. Conversion does not adversely affect outcome and thus constitutes a safe alternative. Although target vessel reintervention may be slightly higher than that reported for open coronary artery bypass grafting, graft patency and major adverse cardiac events for both approaches are comparable to those reported in the Society of Thoracic Surgeons database, demonstrating the safety and efficacy of the totally endoscopic coronary artery bypass grafting procedure.

The continuous refinement of coronary artery bypass grafting (CABG) has led to a mature and efficient procedure that provides excellent long-term results for selected patients, with low mortality.^{1,2} Standard CABG, however, is associated with significant invasiveness and large social, direct, and indirect costs.³ These limitations mandate further improvement. A novel procedure that uses robotic technology has been recently introduced into the operating room, enabling the performance of endoscopic coronary surgery.⁴ This procedure potentially offers the benefits of endoscopic surgery: avoidance of an aggressive chest incision, minimal

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CPB	= cardiopulmonary bypass
ECG	= electrocardiography
MACE	= major adverse cardiac event
STS	= Society of Thoracic Surgeons
TECAB	= totally endoscopic coronary artery bypass grafting

blood-air interface, and minimal risk of infection, with a better cosmetic result and faster recovery and return to routine activity. Robotic surgery represents a major paradigm shift and challenge for the operative team.⁵ It requires the development of new technical skills, communication patterns, and conversion and contingency modalities, as well as overall changes in operative planning.⁶⁻⁸ Since the world's first procedure at the end of 1998, only limited patient numbers have been reported from single-center series.

This report describes the largest multicenter experience to date with robotic totally endoscopic CABG (TECAB). It specifically addresses feasibility, safety, and efficacy while discussing the potential value and limitations of TECAB.

Materials and Methods

Between September 1998 and November 2002, a total of 228 patients aged 18 to 80 years (59.2 ± 10.1 years) with significant symptomatic coronary artery disease were selected to undergo TECAB with the da Vinci Surgical System (Intuitive Surgical Inc, Sunnyvale, Calif) at five European institutions. The patients were categorized into three groups: on-pump TECAB (group A, 1.9 ± 0.8), off-pump TECAB (group B, 1.9 ± 0.8), and conversions (group C, 2.0 ± 0.8). A conversion was defined as the need for an incision (sternotomy or minithoracotomy) before the completion of the endoscopic anastomosis. A reintervention, even during the same operative session, after the completion of the anastomosis has been regarded as a major adverse cardiac event (MACE). All patients underwent 6-month postoperative follow up. In considering patients suitable for a robotic operation, the following exclusion criteria were applied: evidence of severely calcified left anterior descending coronary artery, contraindications for peripheral cannulation (group A), morbid obesity, decompensated congestive heart failure, and acute renal failure.

Overall, the vast majority (90%) had single-vessel disease, with the target vessel for revascularization being the left anterior descending coronary artery in 86%, a diagonal branch in 3%, and the right coronary artery in 1%. The remaining patients received either a sequential left internal thoracic graft to the diagonal and left anterior descending arteries (6%) or a double thoracic graft to the left anterior descending artery and the circumflex artery, diagonal, or right coronary artery (4%). Sixty percent had a history of percutaneous intervention to the left anterior descending artery before TECAB, whereas 15% underwent TECAB as a part of a hybrid procedure. All institutions completed the majority of their

on-pump TECAB experience (group A) before proceeding to their off-pump TECAB experience (group B) and performed at least 30 cases. In group A, the left internal thoracic artery was harvested, the pericardium was opened, and the target vessel was identified before femoral cardiopulmonary bypass was instituted. The operative techniques have been described previously.^{9,10} In group A, the CABG was performed under endoaortic balloon clamping and cardioplegic arrest, with a running suture to anastomose the thoracic conduit to the target vessel. In group B, an endoscopic stabilizer was inserted through a subxyphoid port after the thoracic harvesting and pericardial opening for stabilization of the target vessel and performance of the anastomosis on the beating heart.

All the operations were performed after obtaining written informed consent from the patient, in accordance with the ethics committees of each participating institution.

Feasibility, Efficacy, and Safety Assessment

The feasibility of the procedure was assessed by the ability to successfully complete TECAB without the need for conversion to any kind of open-chest procedure. The rate, reasons, and evolution of conversions are described in Tables 1 and 2 and in Figure 1. The efficacy of the procedure was measured by postoperative angiography, stress electrocardiography (ECG), or both. Angiographic efficacy was defined with a modified FitzGibbon criteria of less than 50% stenosis of the distal anastomosis for a patent graft. A clinically negative stress test result for ECG, defined by the absence of angina and ST-wave changes, was used as a surrogate measure for graft patency. Procedural safety was measured by the incidence of MACEs within a 6-month postoperative period. MACE variables included all-cause mortality, myocardial infarction, and target vessel reintervention. Perioperative incidence of MACE was compared with that in a matched cohort from the Society of Thoracic Surgeons (STS) National Database for open chest procedures performed for isolated single-vessel disease between 2000 and 2002. To assess longer term recurrence of MACEs, a random sample of 100 patients was contacted during the reviewing period of the article, at an average follow-up of 3.5 years.

Data Collection, Entry, and Analysis

Data were abstracted from medical charts and covered a 6-month follow-up period for completion of the study. Clinical information was verified against medical records by three independent monitors. Once entered in a database and verified for accuracy, the data were accessed and analyzed with SAS (SAS Institute, Cary, North Carolina) statistical software.

Statistical Methods

The study was designed and powered to achieve an overall procedural efficacy of 94%, with a lower limit of the 95 percent confidence interval of at least 90%. All analyses were conducted according to an intent-to-treat principle. The data provided from the STS National Database used for perioperative comparisons of MACE frequency were based on a custom query of a patient population undergoing sternotomy CABG for isolated single-vessel disease. Patients were matched on the basis of age, sex, and preoperative risk factors. Although this comparison is provided as a baseline reference, it is not possible to draw meaningful statis-

TABLE 1. Intended totally endoscopic coronary artery bypass grafting procedures and conversions to alternate surgical modes and incisions

Intended total procedures	Nonconverted (TECAB)	Total converted	Conversion mode			
			Thoracotomy		Stemotomy	
			Arrested heart	Beating heart (MIDCAB)	Arrested heart (CABG)	Beating heart (OPCAB)
Group A (n = 117)	90 (77%)	27 (23%*)	6 (5.1%†)	14 (12%†)	4 (3.4%†)	3 (2.5%†)
Group B (n = 111)	74 (66.7%)	37 (33.3%*)	—	34 (30.6%†)	3 (2.7%†)	—
TECAB (n = 228)	164 (72%)	64 (28%)	—	—	—	—

All data represent numbers and percentages of patients. TECAB, Totally endoscopic coronary artery bypass grafting; MIDCAB, minimally invasive direct coronary artery bypass grafting; CABG, on-pump coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass grafting. *No statistically significant difference was seen in conversion rates between group A and group B ($P = .08$). †This is the percentage of attempted procedures among group A. ‡This is the percentage of attempted procedures among group B.

tical comparisons because of demographic differences of the two populations. Patients who did not undergo postoperative angiography or stress ECG were excluded from the efficacy analysis. Categorical variables are expressed as number and percentage of patients and were analyzed with the Fisher exact test or χ^2 test for association, with or without continuity correction.

Continuous variables were compared with a two-sample t -test. A log-rank test was used to compare Kaplan-Meier curves of freedom from MACE.

TABLE 2. Conversion reasons by procedure type

Reason for conversion	Conversions		
	Group A	Group B	Total
Total conversions	27	37	64
Cannulation	15	—	15 (23.4%)
Balloon failure (rupture or migration)	9	—	9 (14.1%)
Iliofemoral condition	6	—	6 (9.4%)
Patient conditions	3	22	25
Inability to locate and dissect LAD	3	8	11 (17.2%)
Ventricular tachycardia	—	1	1 (1.7%)
Inadequate LITA flow	—	1	1 (1.7%)
Hemodynamic instability	—	3	3 (4.8%)
Calcified LAD	—	7	7 (11%)
Body habitus	—	2	2 (3.1%)
Bleeding	6	8	14 (21.9%)
Anastomotic site	6	6	12 (18.8%)
LITA	—	1	1 (1.7%)
Right ventricle	—	1	1 (1.7%)
Inadequate stabilization	—	6	6 (9.4%)
da Vinci System failure	1	1	2 (3.1%)
Threshold of time on CPB reached	1	—	1 (1.7%)
Wrong target vessel	1	—	1 (1.7%)

All data represent numbers and percentages of patients. LAD, left anterior descending coronary artery; LITA, left internal thoracic artery; CPB, cardiopulmonary bypass.

Results

A total of 228 subjects were intended to undergo TECAB. One hundred sixty-four patients underwent completion of a totally endoscopic operation, whereas 64 patients (28%), denoted as group C, had intraoperative conversion to an alternate (nonrobotic) technique for completion of the procedure. The total numbers of patients, stratified by group and conversion mode, are shown in Table 1. There were no significant differences in conversion rate between groups A and B. The individual reasons for conversion among patients in group A and B are explained in Table 2. Most conversions in group A were due to cannulation, whereas conversion in group B occurred as the result of inadequate stabilization, inappropriate patient conditions, or bleeding at the anastomosis. The evolution of the conversion rates through discrete 6-month time intervals for the study period is shown in Figure 1. Twelve patients were unavailable for follow-up within the 6 month period.

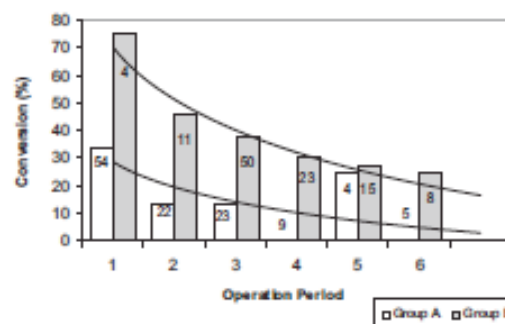


Figure 1. Operation period represents 6 discrete 8-month intervals in which on-pump (group A) and off-pump (group B) conversion rates are shown. Numbers in histogram represent total number of cases performed during period.

TABLE 3. Procedure efficacy as measured by angiography and stress electrocardiography

Patient group	Patients with angiography or stress test	Efficacy			Patients not assessed
		Per angiography	Per stress test	Per both angiography and stress test	
Group A (n = 90)	78	61/62 (98.4%)*	23/23 (100%)	84/85 (98.8%)	12
Group B (n = 74)	63	35/38 (92.1)†	24/25 (96)	59/63 (93.6)	11
Overall (A + B)	141	100	48	148	23
Group C (n = 64)	44	15/17 (88.2)‡	28/28 (100%)	43/44 (97.7%)	20

*Among 55 patients, 62 grafts were assessed. †Among 38 patients, 38 grafts were assessed. ‡Among 15 patients, 17 grafts were assessed. Mean CCSC score among 15 group A patients: preoperative, 1.9 ± 0.8 ; postoperative, 0.02 ± 0.2 . Mean CCSC score among 15 group B patients: preoperative, 1.9 ± 0.8 ; postoperative, 0.05 ± 0.2 . Mean CCSC score among 15 group C patients: preoperative 2.0 ± 0.8 , postoperative 0.06 ± 0.3 .

The efficacy of the TECAB procedure, as measured by the FitzGibbon definition of patency (<50% stenosis), was 96%, described in Table 3 for patients without conversion. Postoperative angiographic controls were not systematically performed except in the case of hybrid procedures. One hundred grafts were assessed in 93 patients who did not have conversion; 17 grafts were assessed in 15 patients who had conversion (group C). Among patients who did not undergo angiography, 48 had completed a stress ECG test. The overall efficacy of TECAB as assessed by stress test alone was 98%. The combined procedural efficacy, as defined for patients having had either test, was 97% for all patients undergoing TECAB. In patients who had conversion, the combined procedural efficacy was 97.7%. There were no statistically significant differences in procedural efficacy across the three groups.

The safety of the TECAB procedure is depicted in a series of Kaplan-Meier curves in Figure 2 for on- and off-pump procedures. There was no statistical differences in the 6-month freedom from MACE between groups A and B ($P = .64$), groups A and C ($P = .09$), and groups B and C ($P = .26$). The same was true when group B was compared with group C ($P = .26$). Perioperative safety of the proce-

cedure was further compared with open chest procedures from the STS National Database for isolated single-vessel disease between 2000 and 2002. This comparison was stratified by on- and off-pump procedures. Nine of 164 patients without conversion (5%) had a MACE within the 6-month postoperative period. Four of these events happened in group A (4%) and 5 in group B (7%). Among patients who had conversion, 3 of 64 had a MACE (5%). The rates of perioperative target vessel reintervention appear to be higher for all TECAB groups relative to those for open CABG as published in the STS National Database (Table 4); however, statistically meaningful conclusions cannot be drawn.

Overall, 3 patients without conversion (2%) died in the perioperative period. In group A, mortality was 1%. One patient died approximately 10 months after the operation from immunosuppressive therapy complications after kidney transplantation. In group B, mortality was 3%. One patient scheduled for a hybrid procedure died of an acute infarction in the territory of the circumflex artery before the planned percutaneous intervention could be performed. The cause of death and the patency of the left anterior descending artery bypass were confirmed at necropsy. One patient died of major, acute gastrointestinal bleeding with shock and cardiac arrest that led to postanoxic coma after cardiopulmonary resuscitation. Among patients who did not have conversion, mortality was 3%. The overall mortality of the three groups combined was 2.1%, versus a rate of 2.4% for open CABG.

Two patients (1%, 1 in group A and 1 in group B) had a myocardial infarction within 7 days after the operation. Myocardial infarction rates did not statistically differ across groups A and B and did not exceed the rates found with open CABG. Six patients underwent target vessel reintervention in the 6-month postoperative period. Five underwent surgical reintervention; the remaining patient underwent stent placement. Of the reinterventions, 2 occurred in group A, 3 in group B, and 1 in group C (2%, 4%, and 1%, respectively). There was no statistically significant difference in the incidence of target vessel reintervention. At a mean follow up of 3.5 years of 100 randomly selected

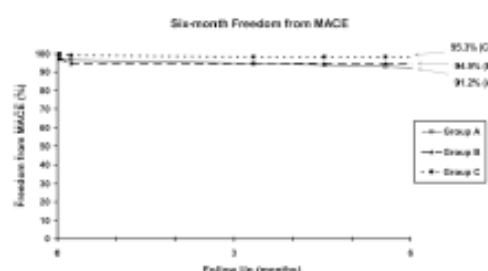


Figure 2. Kaplan-Meier curves for 6-month freedom from major adverse cardiac events (MACEs). Log-rank test shows no difference between groups A and B ($P = .64$), nor groups A and C ($P = .26$), nor groups B and C ($P = .09$).

TABLE 4. Major adverse cardiac events by procedure type

	Overall	Group A	Group B	Group C
Patient group				
No.	228	90	74	64
Total/STS National Database*	20:48	11:382	9:106	NA
All cause mortality				
Study, all causes	5 (2.1%)	1 (1.1%)	2 (2.2%)	2 (2.31%)
STS National Database	494 (2.4%)	279 (2.4%)	215 (2.4%)	—
Perioperative (<7 d) myocardial				
Study	2 (0.9%)	1 (1.1%)	1 (1.2%)	—
STS National Database	169 (0.8%)	92 (0.8%)	92 (0.8%)	—
Target-vessel reintervention (<30 d)				
Study	6 (2.6%)	2 (2.2%)	3 (4.1%)	—
STS National Database	60 (0.3%)	26 (0.2%)	34 (0.4%)	—

NA, Not available; STS, Society of Thoracic Surgeons. *Society of Thoracic Surgeons National Database 2000 through 2002 for single-vessel coronary artery bypass grafting on pump (vs A) and off-pump (vs B) with matched risk stratification.

patients, 4 had MACEs: 2 underwent percutaneous coronary intervention of a nontarget vessel, 1 had a myocardial infarction, and 1 had died from an unknown cause. No patient had undergone surgical target vessel reintervention.

Discussion

This study is limited by its retrospective nature and provision of only a 6-month follow up. It represents a multicenter collaboration in which 228 patients underwent TECAB. Its purpose was to demonstrate feasibility, efficacy, and safety of the endoscopic procedure on both the arrested and beating heart. A significant learning curve was observed. Patency rates and 6-month freedom from MACE revealed acceptable results which were comparable to those from the STS National Database. Although the institutions continue to perform TECAB, the period of September 1998 through November 2002 represents that in which the study took place and a sufficient sample size was obtained to study graft patency and safety of the procedure, as requested by the regulatory approval. Although patients in this study may in fact have had longer follow up available, the 6-month time frame was chosen as a reasonable point within which MACEs and graft patency would be assessed.

TECAB represents a new challenge, requiring development of technical ability to work in an endoscopic environment. A conversion strategy and contingency plan therefore must be choreographed to bring the operation back to the surgical standards in case of need.¹¹

In the on-pump group (group A), which required femoral cannulation and endoaortic balloon clamping, 55% of the conversions were related to cannulation issues and were related to neither the da Vinci system nor the endoscopic nature of the operation itself. The management and monitoring of the endoaortic balloon clamp were made awkward in the presence of the da Vinci system and generated significant "strategic" issues, such as the sequence of cannula

insertion and anticoagulation with regard to the robotic steps of the procedure. This contributed to an unexpectedly high rate of conversion for surgical teams with significant endoscopic CABG experience.^{12,13} Such conversions might have been categorized as intraoperative exclusions, never destined to be completed robotically, resulting in a significantly lower conversion rate; however, they are reported as conversions per our intent-to-treat principle and represent an evolutionary process.

In group B, 3 of 4 conversions were related to the target vessel (wall calcification, intramyocardial course, bleeding from the arteriotomy, and inadequate stabilization). It is likely that the small percentage of hemodynamic intolerance in group B (4.8%) was due to a combination of factors specific to this procedure: the coexistence of carbon dioxide insufflation and stabilization, coupled with some degree of hypoxemia in the event of single-lung ventilation with insufficient compensation, and a potentially longer period of target vessel occlusion.¹⁴ With the exception of hemodynamic instability, which may be present in a fixed percentage of cases, other reasons for conversion can be specifically addressed. A significantly improved endoscopic stabilizer has been a considerable asset for the global success of the procedure. Target vessel localization is improving with time with the development of endoscopic skills, and specific navigation software is currently under development to facilitate target vessel identification.¹⁵ Special silicone elastomer snares have been designed to minimize bleeding at the arteriotomy site. Conversion modalities were different in groups A and B (Table 1). Fourteen of 27 conversions in group A were performed off-pump through a lateral thoracotomy, whereas 34 of 37 patients in group B had conversion to a lateral thoracotomy off-pump procedure. This conversion modality, known as robotically enhanced minimally invasive direct coronary artery bypass grafting, is regarded by some authors as the best operation for single left anterior descending revascularization.¹⁶ It is note-

worthy that 54 of the 64 patients with conversions (84%) received a minimally invasive operation. Although the participating centers initially started with on-pump TECAB, this procedure was later abandoned in favor of off-pump TECAB in the case of single-vessel revascularization.

The efficacy of surgical revascularization can be addressed in different ways. The criterion standard is the angiogram demonstrating graft patency, eventually combined with a surrogate assessment of the functional completeness of revascularization confirming the adequacy of the therapeutic plan.¹⁷ The overall rate of TECAB procedural efficacy was 97%. It did not vary significantly between groups A and B, confirming that it is effective and within the expected range for a thoracic to left anterior descending graft.^{18,19} Furthermore, the postoperative outcomes of the patients are unchanged regardless of whether the procedure is endoscopic or converted to an alternate technique.

The specific skills that are required to perform an endoscopic anastomosis on an arrested heart can easily be developed on isolated animal hearts. Training on such models has taken place at each institution. On the other hand, theoretic concerns have been raised about the efficacy of off-pump TECAB.²⁰ The interposition of the robotic system introduces a delay between the surgical gesture and the motion of the telemanipulated instrument. This delay theoretically affects the precision of tasks performed on the beating heart, such as suture placement, so that even with an adequate visualization of the suture line, the quality of the anastomosis might be in question. This theoretic drawback cannot be solved unless perfect stabilization is achieved. It may also be overcome with the venue of anastomotic connectors that are currently under clinical development. The results of off-pump TECAB, however, as addressed through angiographic controls, have been shown to be satisfactory and to fall within the expected range for thoracic grafting.^{18,19} With confidence limits of combined efficacy ranging from 91% to 100%, off-pump TECAB is a viable therapeutic option.

The assessment of procedural safety shows that the incidence of MACE was similar between groups. Direct comparison of the overall incidence of MACE with that in the STS database is difficult because of the unknown multiplicity of coexisting adverse events among patients in the STS database. This comparison is for information purposes until prospective, randomized procedures are available. It needs to be mentioned that it takes place in the learning curve of TECAB, that the STS cohort is matched for the on and off pump cases but includes only single bypasses and that the patients of the TECAB cohort may have been followed up more closely, so that the comparison may be the worse case scenario for TECAB. Mortality and myocardial infarction are not affected by the endoscopic approach versus the STS database. On the other hand, concerns regarding a potentially higher incidence of target vessel reintervention for

endoscopic procedures must be weighed against the benefits of a minimally invasive approach. In the longer term, the place of the totally endoscopic procedures in the therapeutic armamentarium against coronary artery disease will also require comparison to the existing alternatives of CABG such as the robotic-enhanced minimally invasive direct CABG or ACAB.¹⁶

Conclusions

Although endoscopic CABG represents a major paradigm change, leading to difficulties that must not be underestimated, the results of this study demonstrate that on-pump and off-pump TECAB are feasible, with a conversion rate that diminishes with increasing experience. Conversion does not adversely affect outcome and thus constitutes a safe alternative. Although the rate of target vessel reintervention may be slightly higher than that reported for open CABG, graft patency and major adverse cardiac events for both approaches are comparable to those reported in the STS database and demonstrate that TECAB is a safe and effective procedure. Future prospective studies and longer follow-up may address the benefits of successful TECAB with respect to conventional CABG.

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Results of the Prospective Multicenter Trial of Robotically Assisted Totally Endoscopic Coronary Artery Bypass Grafting

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Background. Robotic technology has been proven safe and efficacious in the performance of mitral valve repair and atrial septal defect repair. This report describes a Food and Drug Administration-sanctioned multicenter study of the safety and efficacy of the da Vinci system (Intuitive Surgical, Inc, Mountain View, CA) for totally endoscopic coronary artery bypass (TECAB) surgery.

Methods. Patients requiring left anterior descending (LAD) coronary artery revascularization were eligible. The procedure was performed with femoro-femoral cardiopulmonary bypass (CPB), endoaortic balloon occlusion, and thoracoscopy. All aspects of the procedure were performed with the robotic system, from internal mammary artery harvest to coronary anastomosis.

Results. Ninety-eight patients requiring single-vessel LAD revascularization were enrolled at 12 centers. Thirteen patients (13%) were excluded intraoperatively (eg, failed femoral cannulation, inadequate working space). In 85 patients (69 men, age 58 ± 10 years) who underwent

TECAB, CPB time was 117 ± 44 minutes, cross-clamp time was 71 ± 26 minutes, and hospital length of stay was 5.1 ± 3.4 days. There were five (6%) conversions to open techniques. There were no deaths or strokes, one early reintervention, and one myocardial infarction (1.5%). Three-month angiography was performed in 76 patients, revealing significant anastomotic stenoses ($> 50\%$) or occlusions in 6 patients. Overall freedom from reintervention or angiographic failure was 91%.

Conclusions. Robotic TECAB was accomplished with no mortality, low morbidity, and angiographic patency and reintervention rates comparable with published data. Although the use of CPB was a limitation of the technique, this experience represents a step toward more advanced procedures, such as multivessel or off-pump TECAB.

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Computer (robotic) enhancement has emerged as a potential facilitator of minimally invasive surgical procedures. Initial applications of this technology were limited to providing enhanced (including voice-activated) endoscopic camera control [1] during minimal access procedures. A more advanced iteration of this technology is represented by the da Vinci surgical system (Intuitive Surgical, Sunnyvale, CA), a computerized telemanipulator that allows a surgeon to control two or three "wristed" endoscopic instruments from an operating console, while viewing the operative field through a three-dimensional endoscopic camera. Two Food and Drug Administration (FDA)-sanctioned

Investigational Device Exemption (IDE) trials have validated the safety and efficacy of this device for mitral valve repair [2] and atrial septal defect closure [3].

Loulmet and colleagues [4] and Falk and colleagues [5] have described the technique of totally endoscopic coronary artery bypass (TECAB), in which the da Vinci robotic surgical system is used to perform an entire coronary bypass procedure (including coronary anastomosis) in a closed chest environment. Notwithstanding the feasibility demonstrated by these and other pioneering investigators [6-8], the TECAB operation has not been subjected to evaluation in a clinical trial. This report describes the results of a multicenter, FDA-sanctioned IDE trial investigating the safety and efficacy of arrested-heart, single-vessel TECAB.

Dr Argenziano discloses that he has a financial relationship with Intuitive Surgical.

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Table 1. Inclusion Criteria

1. Suitable candidate for nonemergent, first time single vessel LIMA to LAD myocardial revascularization. Eligibility will be determined through preoperative coronary angiography conducted prior to enrollment of each patient or
Suitable candidate for undergoing a combination of stent placement or percutaneous transluminal coronary angioplasty (PTCA) and LIMA to LAD myocardial revascularization (hybrid approach)
2. Subjects between the ages of 18 and 80 years (inclusive)
3. Willingness and ability to provide informed consent, and undergo the prescribed follow-up regimen

LAD = left anterior descending; LIMA = left internal mammary artery.

Material and Methods

Trial Design

Patients with single-vessel coronary artery disease involving the left anterior descending (LAD) coronary artery referred for surgical revascularization were eligible for this study. The study protocol was approved by the FDA as IDE #G010011 in December 2001, and the multicenter trial began enrolling patients in January 2002. The protocol was also approved by the Institutional Review Board of each participating institution. Between January 2002 and July 2004, 98 patients were enrolled at 12 institutions. All patients gave informed consent for totally endoscopic coronary artery bypass surgery using the da Vinci robotic surgical system.

Training Protocol

All investigators participating in the trial were required to undergo a stepwise training program before enrolling patients in the trial. By requiring the demonstration of proficiency at each training level before allowing continuation to the next level, the minimum level of technical proficiency was standardized. The stages of the TECAB training requirements were the following: stage 1 – basic da Vinci surgical system training; stage 2 – robotically assisted IMA mobilization; stage 3 – minimally invasive cardiopulmonary bypass (CPB) experience; stage 4 – TECAB specific training; stage 5 – TECAB training cases.

Inclusion and Exclusion Criteria

Patients were considered eligible for enrollment in the trial if deemed appropriate candidates for nonemergent, first time single-vessel left internal mammary artery (LIMA) to left internal descending (LAD) myocardial revascularization. Complete inclusion and exclusion criteria are listed in Tables 1 and 2.

Procedure Details

General anesthesia is established with double-lumen intubation, to allow for selective lung ventilation. External defibrillator patches are placed on the chest, and the patient positioned supine with the left chest elevated 30 degrees with the aid of a small bolster under the left chest. The femoral vessels are exposed. After establishment of single left lung ventilation, the three trocars of the da Vinci robotic system are inserted into the left hemithorax, with carbon dioxide (CO₂) insuff-

lation to a pressure of 6–14 mm Hg. The robotic system is used to harvest the LIMA from the subclavian vein to the internal mammary artery (IMA) bifurcation, and to open the pericardium and identify the target vessel. After systemic heparinization, the distal LIMA is skeletonized and clipped distally. The LIMA is divided, spatulated, and prepared. Next, the femoral artery is cannulated with an endoaortic balloon cannula system, and the balloon is positioned in the ascending aorta with transesophageal echocardiographic guidance. The femoral vein is cannulated with a long venous cannula that is directed into the right atrium. At this point, the endoaortic balloon system is deployed to cross-clamp the aorta and to deliver antegrade cardioplegia. Once cardiac arrest is confirmed, the robotic system is used to perform the coronary arteriotomy and the LIMA to LAD anastomosis. The endoaortic balloon clamp is removed, with external defibrillation if necessary. The robotic system is removed, the patient is weaned from cardiopulmonary bypass, and after protamine administration, the femoral vessels decannulated and closed. Chest tubes and pacing wires are placed, and all wounds are closed. A schematic representation of the flow of the TECAB operation is provided in Figure 1.

Intraoperative Exclusion Versus Conversion

Once enrolled patients were taken to the operating room, an additional set of intraoperative criteria were utilized to exclude patients from robotic TECAB for technical or anatomic reasons that were not identifiable preoperatively. Examples of these exclusionary criteria include dense pleural adhesions, hemodynamic intolerance of CO₂ insufflation, or intramyocardial coronary target. A complete listing of intraoperative exclusion criteria are listed in Table 3. In contrast, intraoperative conversions were defined as cases in which a TECAB procedure in progress had to be abandoned and converted to an alternative approach because the surgeon could not proceed endoscopically, for reasons such as patient instability, LIMA injury, unsatisfactory anastomosis, excessive bleeding, or robotic system malfunction.

Study Endpoints

The primary efficacy endpoint of the study was the composite endpoint of LIMA-LAD graft patency and

Table 2. Preoperative Exclusion Criteria

1. Body mass index > 35.0 kg/m ²
2. Left ventricular ejection fraction < 0.30
3. Decompensated congestive heart failure (NYHA class III or IV)
4. Acute pulmonary edema
5. Severe uncontrolled hypertension
6. Severe peripheral vascular disease limiting vascular access (eg, femoral, iliac, or aortic aneurysm, dissection or occlusive disease)
7. Acute stroke
8. Aortic valve endocarditis
9. Severe coagulopathy (bleeding diathesis)
10. Digitalis intoxication
11. Severe anemia
12. Severe symptomatic electrolyte imbalance
13. Documented anaphylactic reaction to angiographic contrast media
14. Acute renal failure
15. Chronic renal failure secondary to diabetes
16. Active gastrointestinal bleeding
17. Unexplained fever, which may be due to infection
18. Untreated active infection
19. Severe lack of cooperation by patient due to psychologic or severe systemic illness
20. Severe concomitant illness that drastically shortens life expectancy or increases risk of therapeutic interventions
21. Acute myocardial infarction requiring emergent CABG or postinfarction angina or early angina after non-Q wave infarction
22. History of acute myocardial infarction in preceding 30 days prior to proposed coronary artery surgery
23. Moderate to severe aortic and mitral valve disease
24. Hemodynamic instability (cardiogenic shock: systolic blood pressure <90 mm Hg, LVEDP >20 mm Hg, cardiac index <2.5 L/min/m ²)
25. Severe ascending and/or aortic arch calcification as determined by radiographic or echocardiographic studies
26. Severe cerebrovascular disease including a history of prior stroke (within 1 month) and/or stenosis (>70%) of either internal carotid artery
27. Connective tissue disease
28. Anatomy unsuitable for endoscopic visualization of the thorax (eg, morbid obesity with remarkable axillary adiposity or physical deformities of or affecting the thorax; eg, scoliosis, kyphosis)
29. History of median sternotomy, left thoracotomy, or radical mastectomy
30. Undergone previous radiation therapy of the mediastinum or thorax
31. History of severe asthma, emphysema, chronic obstructive pulmonary disease, or pulmonary fibrosis
32. Pleural adhesions or symphysis visible on the chest x-ray
33. Uncontrolled diabetes mellitus (>2 serum glucose concentrations of >350 mg/dL within 7 days)
34. Pregnancy
35. Participating in another competing investigational protocol
36. Patient unwilling or unable to comply with any protocol requirements (including return for follow-up visit)
37. Use of gastroepiploic artery bypass grafts

CABG = coronary artery bypass grafting; LVEDP = left ventricular end-diastolic pressure; NYHA = New York Heart Association.

freedom from target vessel reintervention during the period of observation. For the purposes of this evaluation, a patent graft was defined as a graft with 50% or less stenosis of the distal anastomosis as determined by 3-month postoperative follow-up coronary angiography [9]. The primary safety endpoints of the study were freedom from major adverse cardiac events, including mortality, target vessel reintervention, and myocardial infarction.

These and other clinical endpoints, including intraoperative conversion rates and other adverse events, were compared with a historical cohort of patients who under-

went conventional single-vessel, arrested heart coronary artery bypass grafting (CABG) surgery. This comparison was based on data obtained from a specific query of the Society of Thoracic Surgeons (STS) National Database for the years 2000–2002 [STS Adult Cardiac National Database; Core Data Elements Summary, Custom Query version 2.41, Adult Coronary Artery Bypass Procedures 2000–2002].

Follow-up and Data Collection

PREOPERATIVE ASSESSMENT. Patients referred for coronary artery bypass surgery had a preoperative visit consisting of a medical history, physical examination, and

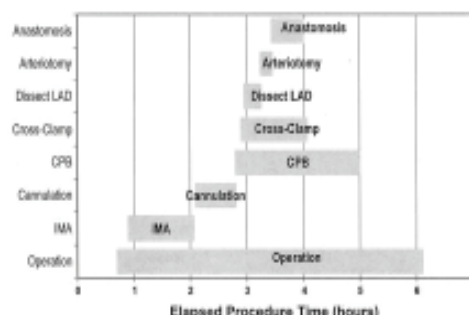


Fig 1. Typical flow of totally endoscopic coronary artery bypass (TECAB) procedure. (CFB = cardiopulmonary bypass; IMA = internal mammary artery; LAD = left anterior descending.)

diagnostic tests, including but not limited to coronary angiography, transthoracic echocardiography, stress electrocardiogram (ECG), resting 12-lead ECG and chest x-ray. Based on this information and the established inclusion-exclusion criteria, the investigator determined the need for surgical revascularization and the appropriateness of the patient for robotically assisted TECAB.

INTRAOPERATIVE AND INTENSIVE CARE UNIT (ICU) ASSESSMENT. For each case, intraoperative times were determined based on perfusion, anesthesia, and operative records or were explicitly recorded during the operation. The details of the surgical procedure, including revascularization scheme, steps of the surgical procedure that were completed robotically, conversion to alternate techniques, time to conversion and reason for conversion, were documented in the operative case report forms.

IMMEDIATE POSTOPERATIVE ASSESSMENT. Immediate postsurgical clinical information was recorded per standard hospital practice and as indicated by the investigator as a part of routine postoperative cardiac care. A postoperative resting 12-lead ECG, chest x-ray, and cardiac enzymes were obtained per standard of care at that institution.

FOLLOW-UP POSTOPERATIVE ASSESSMENT. Patients had a follow-up visit approximately 3 months postoperatively, at which point angiograms were obtained. Supplemental postoperative studies, such as a stress ECG, transthoracic

echo, resting 12-lead ECG, and physical exam were obtained in order to complete the clinical assessment of the patient.

Core Laboratory Review of Angiographic Studies

A primary core laboratory at the Hoag Heart Institute reviewed all preoperative and postoperative angiographic studies. The core laboratory reviewer was masked to the individual institution's assessment of graft patency.

Data Collection, Entry, and Verification

Clinical information for patients enrolled in the study was collected at all participating institutions and verified against the patients' medical records by qualified personnel designated by the study sponsor. All applicable information from the medical charts was recorded onto standardized case report forms and entered into a database.

Statistical Methods

All continuous variables were analyzed using a nonparametric, Wilcoxon rank sum test for two group comparisons. Categorical data were analyzed using χ^2 tests for association with or without continuity correction. In the case of small cell comparisons a Fisher's exact test was used. In all cases 2-tailed *p* values of less than 0.05 are considered significant. The binomial distribution was used for the assessment of binary outcomes (ie, patency) with Agresti's formula used for the computation of one-sided 95% confidence intervals. Conversion rate comparisons were made with those seen in a literature survey of published conversion rates based on similar cardiac operations of comparable complexity. Comparisons of the incidence of significant adverse events were made between da Vinci TECAB and coronary artery bypass as reported in a customized query from the STS National Database (2000-2002) for single-vessel arrested heart sternotomy CABG. For these comparisons, a normal approximation to the da Vinci arrested heart TECAB summary statistic was used. Generalized estimating equations were used for analyzing the learning curve effects associated with times to complete various tasks associated with CABGs. This method takes into consideration the underlying correlation structure of repeated

Table 3. Intraoperative Exclusion Criteria

1. Blood pressure drop of greater than 20% of baseline or less than 80 mm Hg (systolic) for greater than 15 minutes at insufflation pressure of <10 mm Hg
2. Adhesions between pericardium and chest wall severely limiting visibility (≤ 3 cm between anterior surface of pericardium and chest wall after insufflation [max. 10 mm Hg pressure])
3. Working space 3 cm between anterior surface of pericardium and chest wall
4. Intraoperative complications pertaining to cardiopulmonary bypass (catheter positioning, excessive bleeding at cannulation site, defective cannulation equipment, complications associated with aortic occlusion or cardioplegia delivery)
5. Intramyocardial LAD previously not identified on coronary angiogram or target LAD diameter less than 1.5 mm

LAD = left anterior descending (coronary artery).

Table 4. Patient Demographics

No.	85
Age (yrs)	
Mean	58.4
SD	9.6
Range	34.3-77.1
BMI (kg/m ²)	
Mean	27.6
SD	3.7
Range	19.5-39.1
Gender n (%)	
Female	16 (18.8)
Male	69 (81.2)

BMI = body mass index.

measurements (ie, a given surgeon's case experience over time).

Data Safety Monitoring Board Review of Clinical Trial Safety

Data from the study were reviewed by a cardiac surgeon who was not an investigator in the study. All adverse events, including all conversions and reinterventions in this study were reviewed. The reviewer was blinded to the institution at which each case was performed and to the surgeon who performed each case.

Results

Training Phase

A total of 18 institutions entered the training program with the intention of participating in the multicenter TECAB trial. All 18 sites completed stages 1 and 2 of the training program, and 12 of these completed all 5 stages and were allowed to proceed to enrollment of TECAB patients. At the twelve sites completing stage 5 of the protocol, 21 training cases (stage 5) were performed, with anastomosis times averaging 24 ± 9 minutes (range, 14-49 minutes).

Demographics

A total of 98 patients were enrolled in the trial (not including stage 5 training cases) at 12 centers (see Appendix). Of these, 13 were excluded intraoperatively and did not undergo TECAB. The reasons for these exclusions will be discussed in the next section. Demographics and baseline characteristics of the remaining cohort of 85 patients undergoing TECAB are summarized in Tables 4 and 5.

Intraoperative Exclusions and Conversions

Thirteen of 98 enrolled patients (13%) were excluded from the trial intraoperatively. Ten patients were excluded for inability to establish effective peripheral cannulation (6 patients with prohibitive peripheral vascular disease, 2 with poor venous cannula position and inadequate drainage, and 2 with endoaortic balloon migra-

tion). Two others were excluded for deeply intramyocardial coronary targets that could not be visualized epicardially, and one was excluded for dense pleuropericardial adhesions. Of the 13 excluded patients, 10 underwent coronary bypass surgery by left minithoracotomy (arrested or beating heart minimally invasive direct coronary artery bypass [MIDCAB]), and 3 underwent sternotomy. Five of the remaining 85 patients (5.9%) undergoing TECAB required intraoperative conversion to another approach. In these cases, conversion was prompted by damage of the LIMA graft (2 patients) or inadequacy of the coronary anastomosis (bleeding in 1 case, poor graft flow in 2 cases), and these patients were converted to sternotomy.

Operative and ICU Data

In the 85 patients undergoing TECAB, total operative time was 353 ± 89 minutes (mean \pm SD), with a range of 200 to 600 minutes. Notable subcomponents of this operative time included internal mammary artery harvest time (60 ± 24 minutes; range, 26-187 minutes), cardiopulmonary bypass time (117 ± 44 minutes; range, 41-254 minutes), aortic cross-clamp time (71 ± 26 minutes; range, 30-140 minutes), and coronary anastomosis time (28 ± 11 minutes; range, 14-82 minutes). Postoperative ventilation time was 14 ± 28 hours (range, 0-217 hours), ICU length of stay was 35 ± 37 hours (range, 4-288 hours), and hospital length of stay was 5.1 ± 3.4 days (range, 1.2-25.5 days). Twenty-six of 85 patients (31%) received blood products perioperatively.

Completeness of Follow-Up

Of the 85 patients undergoing TECAB, all were followed through to study completion. One patient underwent

Table 5. Preoperative Characteristics

Characteristics	No. (%)
	85
Smoking	57 (67.1)
Hypertension	47 (57.3)
Diabetes	18 (21.9)
Family history of CAD	41 (50.3)
Dyslipidemia	68 (80.9)
Myocardial infarction	32 (37.6)
Arrhythmia	9 (11.9)
Cerebrovascular disease	3 (3.5)
Peripheral vascular disease	2 (2.5)
Chronic renal failure	1 (1.1)
Angina	67 (79.7)
Dyspnea	18 (21.7)
Average preoperative LVEF	
Mean	56.2
SD	10.2
Range	(30-85)

CAD = coronary artery disease; LVEF = left ventricular ejection fraction.

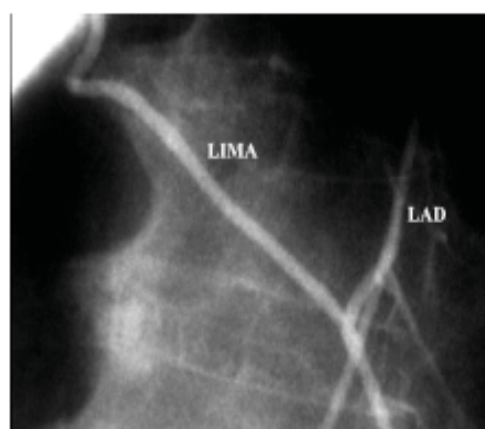


Fig 2. Postoperative angiogram 3 months after totally endoscopic coronary artery bypass. (LAD = left anterior descending; LIMA = left internal mammary artery.)

target vessel reintervention for graft occlusion. Three-month postoperative angiography was performed in 76 of the 85 patients (89%), echocardiography in 72 (85%), and stress testing in 58 (68%). A frame from a representative 3-month angiogram is shown in Figure 2.

Efficacy Endpoints

Of the 85 patients undergoing TECAB, 5 (6%) were converted to other techniques. One patient (1%) required reintervention of the target vessel on the first postoperative day, for graft occlusion. Three-month angiography was performed in 76 patients, and revealed anastomotic

occlusion in 2 cases and significant anastomotic stenosis ($\geq 50\%$) in 4 others. Of these 6 patients, only one (who was symptomatic) underwent reintervention after the three-month angiogram. Thus, a total of 7 of 80 patients having TECAB had either target vessel reintervention or angiographic documentation of graft failure. Because 5 patients had neither a reintervention nor an angiogram, this corresponds to a freedom from graft failure or a reintervention rate of 68/75, or 91%.

Safety Endpoints

Major adverse cardiac events (MACE) were defined as all-cause mortality, myocardial infarction, or target vessel reintervention. There were no deaths from any cause in the cohort during the study period. There was one perioperative myocardial infarction, and 4 target vessel reinterventions (as described above), corresponding to 5 MACE events in 85 patients (5.9%). The incidence of these and other adverse events in the study group is listed in Table 6, along with corresponding incidences from a query of the STS database for similar patients undergoing single-vessel coronary bypass on the arrested heart by sternotomy in 2000–2002. The comparison indicates that our study cohort compared favorably with the STS database cohort. There were 5 groin infections, which did not result in major morbidity but were a TECAB-specific complication not usually associated with conventional approaches, which only infrequently utilize femoral cannulation. Finally, the transfusion rate of 31% was higher than expected, and may reflect the effects of longer cardiopulmonary bypass times in some patients.

Table 6. Adverse Events

Description of Event	TECAB Trial	STS Database (2000–2002)	p Value ^a
No. (%)	85	11,382	
Mortality - all causes	0	(2.5)	0.03
Myocardial infarction	1 (1.1)	(8.2)	<0.05
Target vessel reintervention	4 (4.7)	(2.6)	NS
Cardiac arrest	1 (1.2)	(1.2)	NS
Heart failure	1 (1.2)	52 (8.6)	<0.05
Postop AFB (new onset)	1 (1.2)	1,909 (16.8)	<0.05
Ventricular tachycardia	1 (1.2)	-	-
Iliac/femoral artery dissection	0 (0)	14 (0.12)	NS
Pleural effusions requiring thoracentesis	3 (3.5)	-	-
Reop for bleeding	3 (3.5)	197 (1.7)	NS
Postcardiotomy syndrome	2 (3.1)	-	-
Respiratory failure (>48 hours)	2 (3.1)	542 (4.8)	NS
Postop renal failure	1 (1.2)	235 (2.0)	NS
Gastrointestinal complications	2 (3.1)	187 (1.6)	NS
Pulmonary embolus	1 (1.2)	189 (1.7)	NS
Groin infection	5 (5.9)	-	-

^a STS database point estimates were compared against study group estimates based on second-order approximation to the 95% confidence interval of each rate.

AFB = atrial fibrillation; STS = Society of Thoracic Surgeons.

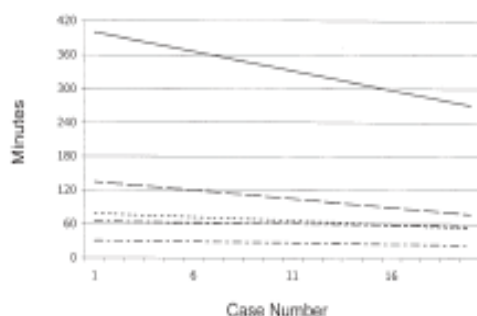


Fig 3. Operative time learning curves. (— = total operating room; -- = cardiopulmonary bypass; . . . = cross-clamp; - · - = internal mammary artery; - - - = anastomosis.)

Learning Curve Analysis

The "learning curve" refers to the phenomenon of improved performance with increasing experience. By plotting each surgeon's individual operative time data against his level of experience (ie, case number), scatter plots were generated, from which best-fit equations were generated. The results of this analysis are depicted graphically in Figure 3. The mean reduction of time with increasing experience was statistically significant for total operative time, cardiopulmonary bypass time, cross-clamp time, and anastomosis time, but not for IMA harvest time.

Comment

Enthusiasm for minimally invasive cardiac surgery has recently been bolstered by the introduction of a new category of technologic achievement: the computerized telemanipulator. In 1997 the first intracardiac procedures (mitral valve repairs) were performed using a prototype of the current da Vinci system [10]. These operations were performed through small thoracotomy incisions, since the "micro-wrists" allowed the surgeons to complete complex maneuvers without placing their hands within the chest. Over subsequent years, the da Vinci system was tested in FDA IDE trials of robotically assisted mitral valve repair [2] and atrial septal defect repair [3].

The technical dexterity and three-dimensional visualization afforded by robotic technology has also been applied to CABG. In 1999, Loumet and colleagues reported the first use of the da Vinci system for coronary bypass surgery [4]. According to this pioneering report, the robotic system was used to harvest internal mammary artery grafts in four patients, and to complete the remainder of the CABG operation in two of these patients by a totally endoscopic approach (TECAB). A year later, Falk and colleagues [5] reported a much larger experience of robotically assisted CABG surgery, which included 22 patients undergoing TECAB. Subsequent reports of similar experiences by Kappert and colleagues [11] and Dogan and colleagues [8] have supported the feasibility of robotically assisted TECAB. Notwithstand-

ing the achievements of these and other pioneering surgeons, early outcome data were available only in the form of anecdotal single-center reports, and selection criteria for TECAB, as well as technical details of the procedures (on-pump versus off-pump, arrested versus beating heart, target vessel and conduit selection, etc), were not standardized. Therefore, prior to granting approval of TECAB as an indication for use of the da Vinci system, the Food and Drug Administration required the evaluation of this new operation in a controlled clinical safety and efficacy trial.

The present study demonstrated that TECAB can be performed with acceptable safety. In 85 patients, there were no deaths, and only one postoperative myocardial infarction. Other adverse events, such as target vessel reintervention, renal failure, and reoperation for bleeding occurred with equal or lesser frequency than in patients undergoing similar coronary bypass procedures by conventional approaches.

Efficacy in this study was defined as freedom from the composite endpoint of target vessel reintervention or angiographic graft failure after three months. By this definition, after excluding 5 intraoperative conversions and 5 patients without angiographic follow-up data, 68 of 75 evaluable patients, or 91%, had effective procedures. Three of the intraoperative conversions were due to mammary artery damage or anastomotic bleeding, while two were from poor graft flow as assessed by intraoperative angiography.

These results compare reasonably with available data from studies of coronary bypass surgery by minimally invasive and conventional approaches. In a study by Diegeler and colleagues [12], in which a cohort of 271 patients underwent LIMA-LAD bypass by a minithoracotomy, beating heart approach (MIDCAB), angiography revealed a graft patency rate of 88.2% at hospital discharge and of 91.5% at 6 months. In a similar study by Mack and colleagues [13], the graft patency rate after MIDCAB was 91%. Jatene and colleagues [14] reported the angiographic follow-up of 120 patients who had off-pump coronary artery bypass (OPCAB) by sternotomy or minithoracotomy (MIDCAB). In cases performed without a cardiac stabilization device, early (pre-discharge) graft patency was only 79%; when a stabilizer was used, the patency rate improved to 90%. In a sub-study of the International Multicenter Aprotinin Graft Experience (IMAGE) trial [15], in which all patients underwent on-pump CABG by sternotomy, Berger and colleagues found that early angiographic LIMA-LAD patency was 90.9%. Finally, in a recent randomized study by Khan and colleagues [16] published in the New England Journal of Medicine in 2004, off-pump CABG resulted in an observed 3-month angiographic patency rate of 92% for IMA grafts and for grafts to the left anterior descending artery. Although these grafts in patients undergoing conventional, on-pump CABG had a patency rate of 100%, the authors concede that "our rate ... in the on-pump group is at the high end of the reported range," citing the paper by Nathoe and colleagues [17], published a year earlier in the same journal,

in which the angiographic graft patency rate after on-pump CABG was 93%.

There were five conversions in the trial, corresponding to a rate of 6%. These were cases in which intraoperative difficulties prompted the choice of an alternative approach in order to complete the coronary bypass operation. All converted patients had three-month angiography documenting graft patency, and none underwent reintervention of the target vessel postoperatively. This conversion rate compares favorably with studies of other novel minimal access operations, such as MIDCAB [18, 19], minimally invasive aortic valve replacement [20], and thoracoscopic IMA harvest [21], in which conversion rates ranged from 3.9% to 8.3%.

A unique component of our trial was the mandatory, stepwise training program that required prospective investigators to achieve minimum standards of proficiency in specific tasks in order to "graduate" to the full TECAB operation. The enforcement of this program achieved several goals. First, surgeons unable or unwilling to master basic but important components of the TECAB operation, such as robotic IMA harvesting and peripheral perfusion with endoaortic balloon clamping, never entered the trial, minimizing technical failures. Second, the learning curves for certain tasks were established prior to trial entry; as an example, our analysis confirms that IMA harvest times for surgeons in the trial had reached a plateau before the first TECAB was ever performed. Finally, in the face of the recent FDA approval of robotically assisted CABG (which was attained on the basis of data from this study), our stepwise training plan will serve as a prototype in the development of a larger scale training program.

Our study has its limitations. Patients were not randomized to different minimally invasive techniques, such as OPCAB and MIDCAB, so that comparative evaluation of TECAB safety and efficacy data is dependent on intrinsically imperfect historical data. Furthermore, although TECAB is often proposed as a less invasive alternative to OPCAB and MIDCAB, two "off-pump" procedures, safety concerns led to the decision that the trial would study TECAB in the "on-pump," arrested heart setting. This fact somewhat limits the extrapolation of our results to other "more desirable" descendants of arrested heart single-vessel TECAB, such as beating heart TECAB and multivessel TECAB. This is unfortunate, since it is difficult to support the concept of an "on-pump" operation for single-vessel coronary disease as anything more than a steppingstone to beating heart or multivessel TECAB. Finally, although complication rates in our trial compare favorably with those reported to the STS database for patients undergoing single-vessel CABG, we must be cautious in deriving strong conclusions from this comparison, as the two patient cohorts were not prospectively randomized or retrospectively matched. Notwithstanding these limitations, the experience obtained in this trial is certain to further the development of other TECAB variants. Early proof of this is the fact

that several of our trial investigators have already accumulated a significant experience in multivessel and beating heart TECAB since the trial's end.

In conclusion, our multicenter, prospective evaluation of robotically assisted, totally endoscopic coronary bypass surgery demonstrated that this operation can be performed with acceptable safety and efficacy by surgeons who undertake a structured and rigorous training program. Although TECAB will make its greatest impact when applied in an off-pump setting and/or for multivessel disease, this trial confirms the feasibility of coronary bypass surgery by robotic means and suggests a continued role for robotic technology in the pursuit of ideal procedures that will deliver maximal efficacy and safety in the treatment of cardiovascular disease with minimal invasiveness.

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Appendix

Participating Centers

Onze Lieve Vrouw Clinic
Aalst, Belgium
Leopold Franzen Hospital
Innsbruck, Austria
Odessa Regional Hospital
Odessa, Texas
Henrico Doctors Hospital
Richmond, Virginia
Saint Agnes Medical Center
Fresno, California
Lenox Hill Hospital
New York, New York
Columbia University Medical Center
New York, New York
St. Joseph's Hospital of Atlanta
Atlanta, Georgia
Carilion Roanoke Memorial Hospital
Roanoke, Virginia
St. Lukes Medical Center
Milwaukee, Wisconsin
Sacred Heart Medical Center
Spokane, Washington
Hospital University of Pennsylvania
Philadelphia, Pennsylvania

DISCUSSION

DR FRANK SELLKE (Boston, MA): You take young patients with good LV (left ventricular) function and give them an 88% graft patency at six months, all in six hours of operating. Do you think this has a future?

DR ARGENZIANO: That is a very good question. There really is a two-part answer. The first question is do we think that a six-hour operation which requires cardiopulmonary bypass and femoral cannulation has a future for single vessel disease, and I think the answer is no, because in fact there are very few people who have had to do that after the trial. The stipulation was that we had to prove that this was safe in a more comfortable on-pump setting. There is no question that this is really a steppingstone in that the MIDCAB (minimally invasive direct coronary artery bypass) or the mini ThoraCAB, whatever you want to call it, the endo-ACAB, certainly achieves similar goals without the cardiopulmonary bypass.

With respect to your question about the success rate or the efficacy end point, again, if you ask any cardiac surgeon, well, what is your LIMA (left internal mammary artery) to LAD (left anterior descending) patency rate, they will say, oh, it is 100% or 99%. There was Mrs. Nussbaum. The problem is we don't know what mammary patency rates are, and if you look at the literature, if you look at every study, including the large aprotinin study, which looked at angiographic patency rates, and some of the MIDCAB trials and some of the OPCAB (off-pump coronary artery bypass) trials, any study that has ever looked at vein or mammary patency rates has found the patency rates, in reality, to be much less than people think. So do I think that 88% is a good success rate? I don't, but I suspect that if we took our patients in our practices and did routine three-month angiograms we might be surprised at what would be found.

DR SUDHIR P. SRIVASTAVA (Odessa, TX): I have a comment on your earlier question, and I think it is a very relevant question. Of course the trial, as Mike has pointed out, was really a springboard to get to the next stage, and I think since then the beating heart and da Vinci coronary revascularization is being done, and in fact in many centers those timings have really come down. We have done about 50 cases since July since the FDA (Food and Drug Administration) cleared the coronary anastomosis, and our single vessel timings are down to around two to two and a half hours, and these patients, many of them go home the next day, and we have 100% graft patency. So I think it was an evolutionary step for a later purpose.

DR ARGENZIANO: Sudair should be really congratulated. Dr Srivastava was one of the investigators in our study, and he and a few others have really kind of taken the lead that of course was established by our European colleagues, some of whom were in the trial, some of whom weren't, in moving to the next step, and of course, beating heart TECAB is being performed in Europe and at several centers here in the United States. And frankly, there are learning curves associated with all these procedures. Of the 12 centers that were involved, eight of the surgeons in the center did at least five cases, but there were some who did less. So obviously learning curve is important.

DR OMAR M. LATTOUF (Atlanta, GA): Dr. Argenziano, I have a couple of comments for you. Six patients in your group were converted out of the planned TECAB because of peripheral vascular disease. Did you perform femoral ultrasound in advance, preoperatively, for those patients and would you do that now based on your experience? The second point, you had a 10% stenosis or occlusion rate. Did you use a shunt in the LAD, or

would you use a shunt in the LAD to keep that patent and give you a better chance of graft patency?

DR ARGENZIANO: With respect to the femoral cannulation, all patients did not receive ultrasounds but in fact there was a peripheral vascular exam involving pulses and Dopplers and history. As you know, patients with coronary disease do have some incidence of significant peripheral vascular disease of the iliofemoral system. There was no specific criterion for that, and I think that was something that we did learn. There was significant incidence of this. This is really a problem that doesn't need too much of a solution because, of course, the goal is to do this without cannulation.

You were talking about intracoronary shunts. We didn't because this was an arrested heart trial, and so it was cardioplegic arrest and it was a still heart. Certainly, for the surgeons that are performing beating heart TECAB, the shunt has been helpful, as it is in other forms of OPCAB.

DRINDERJIT S. GILL (Cleveland, OH): The angiograms that you had in the study, were they analyzed in a single core lab or were they done in individual hospitals?

DR ARGENZIANO: All angiograms were sent to a primary core laboratory which rendered an independent blinded assessment, but they were also evaluated by the individual cath labs in the member hospitals, and if there was a disagreement between the primary core lab and the institutional lab, then those studies were referred to a secondary core lab for adjudication.

DR GILL: And a second question. How many of these patients had hybrid diseases?

DR ARGENZIANO: Approximately 30% to 40% of the patients in the study were participants in some form of hybrid scheme.

DR DIMITRI NOVITZKY (Tampa, FL): I have concerns about the study because of such a long ischemic and bypass time. My first question, is it ethical to continue with the study? If you yourself will require coronary bypass surgery, which way would you prefer? For myself, I would choose a standard midline sternotomy. I know that we need to be innovative and introduce changes in surgical procedures. The driving force for the patient care should be the surgeon and not the industry. You should not allow yourself to be pushed and therefore compromise the patient outcome.

DR ARGENZIANO: Thank you for your comments. Your questions are all questions that run through our minds any time we engage in innovative work. Without question, from the first use of the cardiopulmonary bypass machine to what we are doing today, there is a certain amount of trepidation that is involved in the changing of a standard. However, without that sort of thinking, innovation certainly has no chance. But I would have to agree with you that from an ethical standpoint we were very careful. We had a data safety monitoring board, which was chaired by a very experienced, minimally invasive surgeon from Europe who was not involved in the trial, and every adverse event was reviewed, and there was specific criteria for halting the trial or modifying the numbers, and those were not achieved.

With respect to whether I would have this operation done, again, as I say, the healthy patient with a good ventricle certainly has a low risk of complications, but this trial was a steppingstone trial, and based on what we have learned, we have already moved ahead to the next step. So the answer to your question, if I had a single vessel that needed to be revascularized, I would not have trouble having a beating heart TECAB performed by a surgeon with experience in that area. But again, the trick is getting the experience.

State-of-the-art - Cardiac general Robot-assisted cardiac surgery

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Summary

Recognition of the significant advantages of minimizing surgical trauma has resulted in a substantial increase in the number of minimally invasive (MI) cardiac surgical procedures being performed. Synchronously, technological advances in optics, instrumentation and perfusion technology have facilitated routine totally endoscopic robotic cardiac surgery using the da Vinci® telemanipulation system (Intuitive Surgical Inc.). This technology has been applied to many cardiac surgical procedures, in particular, mitral valve repair (MVP) and totally endoscopic coronary artery bypass grafting (TECAB), allowing the surgeon to operate through 5 mm port sites rather than a traditional median sternotomy. In this rapidly evolving field, we review the clinical results of robotic cardiac surgery.

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Keywords: Surgical procedures; Minimally invasive; Thoracic surgery; Video-assisted; Robotics; Telemedicine/instrumentation

1. Introduction

During the past decade, recognition of the significant advantages of minimizing surgical trauma by reducing incision size and eliminating rib-spreading have resulted in a substantial increase in the number of minimally invasive (MI) cardiac surgical procedures being performed. These benefits have included less pain, shorter hospital stays, faster return to normal activities and improved cosmesis [1]. At the same time, improvements in surgical instrumentation, perfusion technology and visioning platforms have facilitated these advances such that MI approaches have now become the standard of care at certain institutions worldwide due to excellent results. Endoscopic instrumentation, with only four degrees of freedom, significantly reduces the dexterity needed for delicate cardiac surgical procedures, and the loss of depth perception by using two-dimensional video monitors further increases operative difficulty. Robotic surgery provides a solution to these problems and represents a paradigm shift in the delivery of healthcare for both the patient and the surgeon.

Robotic systems consist of telemanipulators where end-effectors, or micro-instruments, are controlled remotely from a console. The da Vinci® S system (Intuitive Surgical, Mountain View, CA, USA) is the most widely used and is comprised of a surgeon console, an instrument cart and a visioning platform. The operative console allows the surgeon to immerse himself into the operative field through high-definition three-dimensional imaging. Finger and wrist movements are registered through sensors and translated into motion-scaled tremor-free movements avoiding the

fulcrum effect and instrument shaft shear forces common to long-shafted endoscopic instruments. Wrist-like articulations at the ends of micro-instruments bring the pivoting action of the instrument to the plane of the operative field improving dexterity in tight spaces and allowing truly ambidextrous suture placement.

The greatest growth in robotic procedures has been in the field of urology with rapid dissemination of robot-assisted radical prostatectomy worldwide. Currently, over 1700 robotic cardiac operations are performed in the USA per year but with a yearly increase of about 400 cases, or about 25% growth per year [2]. The most common applications in cardiac surgery are for mitral valve repair (MVP) and endoscopic coronary artery bypass grafting (CABG). The last 15 months have, however, seen two critical editorials in the Journal of Thoracic and Cardiovascular Surgery questioning the clinical value of robotics in cardiac surgery [2, 3]. This article will review the published evidence, assess the limitations of robotic technology and look at likely future directions.

2. Mitral valve repair

The first robotic MVP was performed in May 1998 by Carpentier using an early prototype of the da Vinci® articulated intracardiac 'wrist' robotic device [4]. A week later, Mohr performed the first coronary anastomosis and repaired five mitral valves (MVs) with the device [5]. Grossi et al. of New York University partially repaired a MV using the Zeus™ system (Computer Motion Inc, Goleta, CA, USA) but no annuloplasty ring was inserted. Four days later, in May 2000, Chitwood performed the first complete da Vinci® mitral repair in North America. Two Food and Drug Administration (FDA) trials subsequently led to approval in Novem-

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ber 2002 of the da Vinci® system for MV surgery [6, 7]. Although a small (3–4 cm) utility incision is still necessary for the patient-side surgeon to pass sutures and needles in and out of the chest, advances in 3D visualization and instrumentation, particularly the development of the robotic left atrial EndoWrist® retractor, have progressed to a point where totally endoscopic mitral procedures using the full spectrum of Carpentier's repair techniques are routinely practiced.

There are no randomized studies comparing robotic to either video-assisted or sternotomy MV surgery. However, in a non-randomized study, Woo et al. demonstrated that robotic surgery patients had a significant reduction in blood transfusion and length of stay compared to sternotomy patients [8], whereas the only difference that Folliquet et al. noted was a shorter hospital stay (7 days vs. 9 days, $P=0.05$) [9]. The largest reported single center experience is 300 cases with 0.7% and 2.0% 30-day and late mortalities, respectively [10]. No sternotomy conversions or MV replacements were required. Immediate post-repair echocardiograms showed 98% had either no or trivial residual mitral regurgitation (MR). Complications included 2 (0.7%) strokes, 2 (0.7%) transient Ischemic attacks, 3 (1.0%) myocardial infarctions and 7 (2.3%) re-operations for bleeding. The mean hospital stay was 5.2 ± 4.2 (S.D.) days and 16 (5.3%) patients required a re-operation at a mean of 319 ± 327 days from the original operation. Mean postoperative echocardiographic follow-up at 815 ± 459 (S.D.) days demonstrated that 7.6% had moderate or severe recurrent MR. Five-year Kaplan–Meier survival was equivalent to conventional surgery at $96.6 \pm 1.5\%$ with $93.8 \pm 1.6\%$ freedom from re-operation.

Murphy et al. reported their experience in 127 patients of which five were converted to median sternotomy [11]. Seven patients underwent mitral valve replacement (MVR) and 114 had MVPs. Complications included one in-hospital and one late mortality as well as a 1.6% incidence of stroke and 17% new onset of atrial fibrillation (AF). Post-discharge echocardiogram results were available in 98 patients with a mean follow-up of 8.4 months. There was no more than 1+ residual MR in 96.2%. These two series demonstrate that robotic MV surgery is safe with excellent short-term results and is associated with good mid-term durability. As more experience has been gained with the use of robotic techniques, surgeons are tackling more complex MV disease such as anterior and bileaflet repairs with results comparable to published national data using conventional techniques [12]. Nevertheless, long-term follow-up is needed to determine whether these results will be comparable to the 10- and 20-year data reported by others. As technology continues to improve, these procedures will become easier and more reproducible and better results will likely follow. Comparative data on pain, speed of recovery, quality of life and return to work are necessary to assess the benefits that have been demonstrated for other MI and robotic cardiac procedures [13].

3. Coronary revascularization

The range of robotic coronary operations ranges from internal mammary artery (IMA) harvest with a hand-sewn

anastomosis, performed either on- or off-pump through a mini-thoracotomy or median sternotomy, to totally endoscopic coronary artery bypass grafting (TECAB). Anastomoses in all coronary territories have been successfully performed even in sequential configuration and using anastomotic couplers [14]. Early reports demonstrated the feasibility and safety of harvesting the IMA with the da Vinci® system with harvest times <30 min achievable once the learning curve had been negotiated [15].

In 1998, Loumet demonstrated the feasibility of TECAB on an arrested heart by using da Vinci® to harvest the left IMA (LIMA) and to perform a LIMA to left anterior descending (LAD) coronary anastomosis in two patients [16]. In 2000, Falk reported TECAB on 22 patients of which four were converted to mini-thoracotomy for anastomotic bleeding or graft issues [17]. In the remaining 18 patients, grafts were widely patent at three months with no major complications. The same group subsequently reported the first off-pump TECAB using an endoscopic stabilizing device [18]. Dogan reported 45 arrested heart TECAB procedures in 2002, of which eight patients underwent double-vessel revascularization with both IMAs [19]. The initial conversion rate of 22% dropped to 5% in the last 20 patients, a trend which is mirrored in other studies [20]. The procedural time for single-vessel TECAB was 4.2 ± 0.4 h, cardiopulmonary bypass (CPB) time was 136 ± 11 min and aortic cross-clamp (XC) time was 61 ± 5 min.

Subramanian achieved multi-vessel revascularization (mean number of grafts, 2.6) in 30 patients using robotically-harvested IMAs [21]. Depending on the specific target, either a mini-thoracotomy or transabdominal approach was employed. Twenty-nine (97%) patients were extubated on the operating table, 77% were discharged within 48 h and only two patients needed readmission. In addition, only one patient needed conversion to sternotomy and there was no mortality. However, the largest single institution series comes from Srivastava with 150 patients undergoing robotic-assisted bilateral IMA harvesting and off-pump CABG via a mini-thoracotomy [22]. Two patients presented with chest pain after discharge secondary to graft occlusion; in both cases, treatment using percutaneous intervention was successful. In 55 patients undergoing computed tomography angiography at 3 months, all 136 grafts were patent.

A multicenter Investigational Device Exemption trial was reported by Argenziano in 2006 [23]. Ninety-eight patients requiring single-vessel LAD revascularization were enrolled at 12 centers; 13 patients (13%) were excluded intraoperatively (e.g. failed femoral cannulation, inadequate working space). In the remaining 85 patients who underwent TECAB, CPB time was 117 ± 44 min, XC time was 71 ± 26 min and hospital length of stay was 5.1 ± 3.4 days. There were 5 (6%) conversions to open techniques. There were no deaths or strokes, one early reintervention and one myocardial infarction. Three-month angiography was performed in 76 patients, revealing significant anastomotic stenoses (>50%) or occlusions in six patients (7.1%). Overall freedom from reintervention or angiographic failure was 91% at three months. US FDA approval of use of da Vinci® for coronary revascularization was largely based on this study.

The largest multicenter experience was reported by de Cannière et al. in 2007 and involved five European institu-

tions with 228 patients undergoing TECAB (on-pump, $n=117$; off-pump, $n=111$) [20]. The overall mortality was 2.1% and the conversion rate of 28% decreased with time and did not adversely affect outcome. The overall procedural efficacy, as defined by angiographic patency or lack of ischemic signs on stress electrocardiography, was 97% at six months. The incidence of major adverse cardiac events within six months was 5%. The rate of target vessel reintervention was slightly higher for both on- and off-pump procedures compared to that reported for open procedures in the Society of Thoracic Surgeons national database.

In summary, these reports of robotically-assisted coronary surgery have mostly involved highly-selected patient populations requiring limited revascularization usually of the anterior wall. In these circumstances, surgeons have been able to achieve totally endoscopic LIMA-LAD grafting with high success rates albeit after the initial learning curve. It is still not clear whether TECAB or robotically-enhanced MI direct CABG provides superior outcomes. Hybrid or integrated revascularization effectively combines the survival benefits of LIMA-LAD grafting as a MI procedure with PCI of a second or third coronary target. Integrating these two procedures into one therapeutic modality aims to provide the patient with the beneficial aspects of each successive technique in the least invasive way possible. It is likely to become utilized more frequently particularly with advances in robotic instrumentation. Recent work by Katz has demonstrated that this approach can be accomplished with no mortality, low peri-operative morbidity and excellent 3-month angiographic LIMA patency (96.3%) [24]. Klati et al. recently reported 91% LIMA-LAD patency at 9 months for simultaneous integrated coronary revascularization using a robotically-enhanced technique [25]. Five-year freedom from reintervention of the LAD after robotic TECAB is 87.2% which leaves room for improvement but is reflective of the early experience typically associated with new techniques [26]. Refinements in anastomotic technology, endoscopic stabilization and target vessel identification systems will all facilitate routine TECAB.

4. AF surgery

The Cox-Maze III procedure is an effective surgical treatment for AF. However, it is not widely applied due to its complexity, increased operative times, and the risk of bleeding. Various energy sources have been introduced to simplify the traditional 'cut and sew' approach and also to allow the development of less invasive therapies. There have been a few case reports of patients undergoing combined robotic MV and AF (MV/AF) surgery demonstrating that these procedures are safe [27–29]. One small ($n=16$) series of patients undergoing robotic MV/AF surgery using the Flex-10 microwave catheter (Gildant, Indianapolis, IN) from our own institution has been reported [30]. The ablative procedure added 42 ± 16 min to the MV repair and 1.3 days to hospitalization. At six months follow-up, 73% were in sinus rhythm, 20% were paced and 7% were in AF. In our overall robotic experience, about 18% of patients undergoing MV surgery have a concomitant procedure for AF, usually a cryomaze [10].

Robotically-assisted surgery for lone AF is in its infancy being first reported in an animal model in 2002 [31] and later in humans in 2004 [28, 32, 33] to achieve pulmonary vein isolation. An on-pump endocardial approach has been reported by ourselves and others [34] using cryoablation to replicate the Cox-Maze III lesion set and further results are awaited.

5. Left ventricular lead placement

Numerous prospective studies have demonstrated that cardiac resynchronization therapy with or without implantable cardioverter-defibrillator capability improves ventricular function, exercise capacity and quality of life, as well as reducing mortality and heart failure hospitalizations in patients with symptomatic heart failure and delayed intra-ventricular conduction despite optimal medical therapy [35]. Left ventricular lead placement is usually accomplished percutaneously through coronary sinus cannulation, advancing the lead into a major cardiac vein. This technique is associated with long fluoroscopy times and is not applicable to all patients because of anatomical limitations in coronary venous anatomy. Early and late failures occur in ~12% and 10% of procedures, respectively [36]. Surgical epicardial lead placement is often a rescue therapy for these patients.

Early reports by Derosé et al. demonstrated the efficacy of robot-assisted LV lead implantation [37]. They reported results for 13 patients, six of whom had previous CABG, with no complications or technical failures. Navia's series of mini-thoracotomy or robotic/endoscopic LV lead placement included 41 patients without mortality, intra-operative complications or implantation failures [38]. A MI surgical approach is very attractive as it allows surgeons to determine the best epicardial site for implantation by mapped stimulation and may, therefore, entail greater success rates than transvenous implantation. A randomized study comparing both techniques is in progress.

6. Intra-cardiac tumor resection

Cardiac tumors, although relatively uncommon and mostly benign, should almost always be resected to prevent thromboembolic complications. Murphy et al. recently reported robotic excision of three left atrial myxomas using either a left atriotomy or right atriotomy with trans-septal approach. Autologous pericardial patches were used to repair septal defects following excision [39]. The mean CPB and XC times were 103 ± 40 min and 64 ± 2 min, respectively. Impressive results were reported with all patients being discharged on day 4 and resuming normal activity three weeks after surgery. Similarly, Woo et al. used robotic techniques to excise an aortic valve papillary fibroelastoma with the patient being discharged on the 3rd postoperative day and back to work within one month [40].

7. Congenital surgery

A few congenital cardiac conditions in both children and adults lend themselves to a MI approach. Torracca et al. and Wimmer-Greinecker et al. were the first to report small series of patients undergoing robotic atrial septal

defect (ASD) repair in Europe [41, 42]. In a US FDA Investigational Device Exemption trial, Argenziano et al. demonstrated that ASDs in adults can be closed safely and effectively using totally endoscopic robotic approaches with a median XC time of 32 min [43]. One of 17 patients had a residual shunt across the atrial septum which was repaired via mini-thoracotomy on postoperative day 5. The reoperative finding was that the atrial septal primary suture line was intact but there was a tear medial to it. This failure was therefore likely related to use of a direct closure technique rather than using a patch repair and therefore not a failure of the robotic technique per se. Bonaros et al. showed that the learning curve is steep and associated with a rapid decrease in operative times [44]. Morgan subsequently demonstrated that robotic ASD closure hastens postoperative recovery and improves quality of life compared to either a mini-thoracotomy or median sternotomy approach [13].

Del Nido's group from the Boston Children's Hospital published their 2-year experience with 15 patients undergoing patent ductus arteriosus (PDA) closure ($n=9$) or vascular ring repair ($n=6$) utilizing the da Vinci® system [45]. The patients were aged 3–18 years and only one was converted to a thoracotomy because of pleural adhesions. The total operative times were a little prolonged at 170 ± 46 min (PDA) and 167 ± 48 min (vascular ring). Nevertheless, all were extubated in the operating room and were discharged after a median of 1.5 days. Le Bret et al. compared operative times for robotically-assisted PDA closure using the Zeus System (Computer Motion, Inc, Goleta, CA) vs. videothoracoscopic surgery and noted similar operative times to Del Nido's group (162 min) for the robotic cohort but much shorter durations for the videothoracoscopic cohort (83.5 min), with equivalent clinical outcomes [46].

8. Limitations

Limitations specifically related to the use of robotic techniques in cardiac surgery include:

1. *Incomplete and delayed motion tracking* – while tele-manipulation systems may eventually enhance endoscopic surgical performance by eliminating some human deficits such as tremor, such systems not only add a second information processing system but also cause inertia by additional electronic and mechanical parts. This was elegantly demonstrated by Jacobs et al. in 20 subjects using an endoscopic trainer designed to simulate beating-heart conditions [47]. The subjects were asked to touch targets manually or robotically with the da Vinci® system with different patterns of increasing index of difficulty (resting model and moving at frequencies of 35, 60 and 90 bpm). Robotic assistance slowed task completion by 2.9 times and increased the error rate. At a frequency of 90 bpm, robotic tracking became much more difficult. However, these data must be interpreted in the context that the subjects had no prior robotic experience and, as we have seen, there is a clear learning curve. These limitations might negatively affect dexterity and the quality of an anastomosis in beating-heart surgery. Therefore, future progress must

be directed to ensuring better quality stabilization, development of algorithms for virtual immobilization, increased bandwidth and different hardware design that will allow for a faster response.

2. *Lack of tactile feedback* – In our experience, visual clues such as tissue deformation provide adequate information. Reiley et al. demonstrated that visual force feedback primarily benefits novice robot-assisted surgeons with diminishing benefits among experienced surgeons [48].
3. *Cost* – Initial capital outlay, instruments and maintenance. These will come down with time and may be justified by a reduction in hospital stay, patient morbidity, invasiveness and speed of recovery. Morgan et al. specifically addressed this issue and found an increase in hospital costs of \$3444 for robotic MVP compared to a sternotomy approach when factoring in the initial capital investment of the system [49].
4. *Learning curve* due to the inherent complexity of the system. Training programs are conducted in formal training centers and consist of didactics, familiarization with the system and then practice on inanimate objects, cadavers and live animals [50].
5. *Additional operative time* to position the robotic system and for instrument changes.

9. Conclusion

Robotic cardiac surgery is an evolutionary process and we are simply at one point on a continuum. If 'time were told' on robotic cardiac surgery as Dr Robicsek's editorial in the February 2008 issue of the Journal of Thoracic and Cardiovascular Surgery would have us believe, then why is there a 25% yearly increase in the number of robotic operations being performed in the US? Statistics he presents such as '65% of US cardiac surgical institutions that own a da Vinci® do not use it' are not surprising when the uptake of robotic technology has grown to 25% of all US cardiac surgical programs. Clearly many centers have hopped on the 'robotic bandwagon' only to be disappointed. It is unlikely that this growth in robotic technology is being mirrored in Europe. This expensive technology is now becoming concentrated in a few reference centers where the cost of robotic technology can be offset against a high institutional volume and where the necessary surgical expertise and experience exist. This is also necessary from a research and development perspective if we are to overcome some of the current limitations of this approach.

Although the surgical robot allows unprecedented closed chest surgical access to the heart, it is only one of many new tools that are prerequisite for successful MI cardiac surgery. Further development of new adjunctive technologies such as retraction and stabilization systems, sutureless anastomotic devices and image guidance systems is vital. Miniaturization of technology will enable us to progress to routine totally endoscopic cardiac surgery through incisions of only a few millimeters in diameter. This will require a combined effort of physicians with our industry partners to fill in the technological gaps that are present in our current armamentarium of MI tools.

It is vital to ensure success that formal training in these MI and robotic techniques is obtained. It is likely that in the future surgical vision and training systems will be able to model most surgical procedures through immersive technology, much like a 'flight simulator', where one may be able to simulate, practice and perform the operation without a patient. Surgical scientists must continue to critically evaluate this technology. Despite enthusiasm, caution cannot be overemphasized as traditional cardiac operations still enjoy proven long-term success and ever-decreasing morbidity and mortality and remain our measure for comparison.

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Multivessel beating heart robotic myocardial revascularization increases morbidity and mortality

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Objective: The vast majority of reports describing beating heart robotic myocardial revascularization (total endoscopic coronary artery bypass) contain very small numbers of patients undergoing single-vessel bypass. We present a large series of patients undergoing multivessel total endoscopic coronary artery bypass.

Methods: We performed a retrospective clinical review of 106 patients undergoing total endoscopic coronary artery bypass (72% multivessel) at 1 institution by 1 experienced cardiac surgeon/physician assistant team. These results were compared with the expected clinical outcomes from conventional coronary artery bypass grafting calculated using the Society of Thoracic Surgeons risk calculator.

Results: Of the 106 patients, 1% underwent quadruple total endoscopic coronary artery bypass, 8% triple, 63% double, and 28% single. The emergent conversion rate for hemodynamic instability was 6.6%. The postoperative renal failure rate (doubling of baseline serum creatinine or dialysis required) was 7.5%. Overall, 23 patients (21.7%) exhibited at least 1 major morbidity/mortality (4 deaths). The number of vessels bypassed (single/double/triple/quadruple) correlated positively with the surgical/operating room time, the lung separation time, vasoactive medication use, blood use, a postoperative ventilation time longer than 24 hours, intensive care unit length of stay, and hospital length of stay. An increased surgical time was significantly associated with major morbidity ($P = .011$) and mortality ($P = .043$). A comparison with the Society for Thoracic Surgeons expected outcomes revealed a similar hospital length of stay but an increased incidence of prolonged ventilation ($P = .003$), renal failure ($P < .001$), morbidity ($P = .045$), and mortality ($P = .049$).

Conclusions: Our results suggest that addressing multivessel coronary artery disease using total endoscopic coronary artery bypass offers no obvious clinical benefits and might increase the morbidity and mortality. (*J Thorac Cardiovasc Surg* 2012;143:1056-61)

Minimally invasive surgery has potential benefits (facilitated rehabilitation/discharge) but also has potential risks (increased complexity).¹ Total endoscopic coronary artery bypass (TECAB) is performed using a robotic system that allows the surgeon to operate through a series of small thoracic incisions. Such surgery was first performed in humans in 1998,² ushering in a new era in cardiothoracic surgery.^{3,4}

Most reports using robotic technology during cardiac surgery have done so with some form of minithoracotomy and/or cardiopulmonary bypass (CPB), with or without myocardial arrest.⁵⁻¹⁰ The few reports describing TECAB (without minithoracotomy/CPB) have contained small numbers of patients undergoing single-vessel coronary artery bypass

grafting (CABG).¹¹⁻¹⁶ We report our experience with multivessel TECAB and compared the outcomes with the expected outcomes from conventional CABG calculated using the Society of Thoracic Surgeons (STS) risk calculator. The use of robotic assistance in cardiac surgery remains controversial.¹⁷⁻²⁰ Our analysis has helped to clarify the potential benefits and risks associated with this technology.

METHODS

The University of Chicago institutional review board approved the present study and informed consent was waived. We retrospectively reviewed the records of all 106 patients who had undergone TECAB from July 2007 to February 2009 at our institution. One cardiac surgeon/physician assistant (CS/PA) team performed every TECAB, with 1 of 6 experienced cardiac anesthesiologists. All were scheduled for off-pump beating heart 1- to 4-vessel TECAB using the da Vinci robotic system (Intuitive Surgical, Sunnyvale, Calif). Clinically important right coronary artery disease thought amenable to percutaneous coronary intervention was scheduled for stent placement after TECAB (before hospital discharge).

After application of standard monitors, anesthesia was induced with intravenous midazolam, fentanyl, propofol, and vecuronium, and the patient was intubated with a left-sided double-lumen endotracheal tube. A radial arterial line and a right internal jugular vein introducer were inserted. A pulmonary artery catheter and transesophageal echocardiographic probe were used in all patients. External defibrillation patches were appropriately placed. Surgery was performed with single-lung ventilation (when

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CPB	= cardiopulmonary bypass
CS/PA	= cardiac surgeon/physician assistant
euroSCORE	= European System for Cardiac Operative Risk Evaluation
HLOS	= hospital length of stay
ICU	= intensive care unit
LAD	= left anterior descending
LIMA	= left internal mammary artery
pRBCs	= packed red blood cells
RIMA	= right internal mammary artery
STS	= Society of Thoracic Surgeons
TECAB	= total endoscopic coronary artery bypass

requested by the surgeon for exposure), and the patient was positioned supine. Intravenous nitroglycerin (5 µg/min) and lidocaine (1 mg/min) were administered to attenuate coronary artery spasm and prevent reperfusion arrhythmias.

Surgery was performed as previously described by Srivastava and colleagues.¹⁷ After single-lung ventilation was achieved, intercostal incisions were made (variations determined from revascularization schemes). Carbon dioxide was used to insufflate the chest (usually 10–15 mm Hg), and the robotic arms were placed. With the CS at the console and the PA scrubbed and in the field controlling the robotic instrumentation, the left internal mammary artery (LIMA) and, if needed, the right internal mammary artery (RIMA) were harvested. Pericardiotomy was performed, the target sites were identified, and a cannula was inserted through a subcostal port. Systemic intravenous heparinization (100 U/kg) was achieved (target activated clotting time, 250 seconds). A myocardial stabilizer was used to minimize movement of the target vessels. When all anastomotic sites appeared satisfactory, intravenous protamine (10 mg/kg) was administered. A Doppler probe was used to assess the flow measurements. A chest tube drain was inserted behind the left lung, followed by gentle re-inflation of the left lung. The thoracic incisions were then surgically closed.

The patients were transported to the intensive care unit (ICU), usually with a single-lumen endotracheal tube or spontaneously ventilating after extubation in the operating room (OR). The goal was extubation 2 to 4 hours after ICU arrival. Mobilization by physical therapists occurred on the second postoperative day (POD), and the lines were removed. The patients were transferred to the rehabilitation floor when clinically appropriate.

The preoperative records (anesthesia, surgery) were reviewed for demographic data, comorbid conditions, number of diseased vessels, and severity of ventricular dysfunction. The OR records (surgery, nursing, perfusion) revealed the number of grafts performed, surgical time, and OR time. The anesthesia records provided the total lung separation time, use/nonuse of vasopressors (continuous infusion of dobutamine, epinephrine, norepinephrine, norepinephrine, and/or vasopressin), urine output, and any clinical problems. The postoperative records (ICU, floor notes) were reviewed for the interval to extubation, ICU length of stay (HLOS), hospital length of stay (HLOS), morbidity, and mortality.

The logistic version of the European System for Cardiac Operative Risk Evaluation (euroSCORE) was used to calculate the predicted perioperative mortality for each patient.²¹ Postoperative renal failure was defined as the doubling of the preoperative serum creatinine or new requirement for

postoperative dialysis. Bleeding was considered "excessive" if transfusion of 6 or more units of packed red blood cells (pRBCs) occurred within 24 hours after the surgical incision. Major morbidity was defined as ventricular trauma, emergent conversion, excessive bleeding, renal failure, acute graft failure, incomplete revascularization (inability to perform surgical bypass, inability to insert a coronary stent, or unaddressed disease found by postoperative angiography), or gross stroke.

The demographic, disease, and surgical characteristics and outcomes are summarized using the mean, standard deviation, and range or frequency counts and percentages. Comparisons across the groups were made using the Wilcoxon rank-sum test for continuous variables or chi-square tests (or Fisher's exact tests, as appropriate) for categorical variables. When comparing the 2 series of patients, 2-sample *t* tests were used for continuous variables because the raw data from Srivastava and colleagues¹⁷ were unavailable. The correlations between the continuous or ordinal (eg, number of vessels bypassed) were assessed using Spearman rank correlation coefficients. The Cochran-Armitage trend test was used to examine whether the proportion of patients with morbidity, mortality, pRBC use, vasoactive medication use, or prolonged ventilation increased with an increasing number of vessels bypassed. Logistic regression models were fit to assess the likelihood of certain outcomes (eg, pRBCs or vasoactive medication use) stratified by the surgical time. In addition, 1 degree of freedom goodness of fit chi-square tests were performed to compare the number of patients with a particular outcome in the present series with that expected according to the STS risk calculator. A 2-sided *P* < .05 was considered statistically significant. No adjustments for multiple comparisons were made. All analyses were performed using Stata, version 11 (StataCorp, College Station, Tex).

RESULTS

From July 2007 to February 2009, 106 patients underwent TECAB. The preoperative demographic and intraoperative data are listed in Table 1.

A total of 39 patients (36.8%) experienced morbidity or mortality (Table 2). Some patients were counted more than once in Table 2 (eg, emergent conversion with postoperative pneumothorax). One intraoperative RIMA-obtuse marginal tear resulted in cardiac arrest and emergent thoracotomy (with CPB) for revision. The patient then returned to the OR the next day for additional revision (median sternotomy). A patient with right ventricular trauma returned to the OR for repair of bleeding from the LIMA-left anterior descending (LAD) anastomosis and right ventricular tear site. Left ventricular trauma in 1 patient was caused by the myocardial stabilizer and required emergent sternotomy. Four patients underwent elective intraoperative conversion by way of a thoracotomy (not considered a morbidity). All required elective conversion because of surgical technical difficulty. Seven patients underwent emergent perioperative conversion because of hemodynamic instability. Five required sternotomy (2 intraoperative, 3 requiring a return to the OR) and 2 required thoracotomy (both intraoperative). Of the 3 intraoperative CPB initiations, 2 were emergent. The 1 elective CPB initiation (closed chest) was required for hemodynamic instability (the patient also experienced postoperative stroke). Eight patients developed postoperative renal failure, of whom, 3 required dialysis. Seven patients had incomplete

TABLE 1. Preoperative demographics/intraoperative data (n = 106)

Variable	Value
Age (y)	
Mean \pm SD	63.6 \pm 11.5
Range	38–87
Female gender (n)	27 (25.5)
Body mass index (kg/m ²)	
Mean \pm SD	30.4 \pm 6.2
Range	17.6–58.0
Hypertension (n)	78 (73.6)
Hypercholesterolemia (n)	98 (92.5)
Diabetes mellitus (n)	36 (34.0)
History of smoking (n)	29 (27.4)
Peripheral vascular disease (n)	5 (4.7)
Central vascular disease (n)	10 (9.4)
Preoperative creatinine >2.0 mg/dL (n)	2 (2.2)
Ejection fraction $<50\%$ (n)	24 (23.8)
Previous myocardial infarction (n)	30 (28.3)
Triple-vessel coronary artery disease (n)	76 (71.7)
Left ventricular ejection fraction (%)	
Mean \pm SD	53.9 \pm 13.0
Range	16–76
Repeat coronary artery bypass grafting (n)	2 (1.9)
euroSCORE	
Mean \pm SD	3.2 \pm 3.5
Range	0.9–24.4
“Low-risk” euroSCORE (<3) (n)	69 (65.1)
“Moderate-risk” euroSCORE (3–5) (n)	24 (22.6)
“High-risk” euroSCORE (≥ 6) (n)	13 (12.3)
Four-vessel TECAB (n)	1 (0.9)
Three-vessel TECAB (n)	8 (7.5)
Two-vessel TECAB (n)	67 (63.2)
One-vessel TECAB (n)	30 (28.3)
LIMA/RIMA (n)	55 (51.9)
Total surgical time (min)	
Mean \pm SD	326 \pm 139
Range	125–876
Total lung separation time (min)	
Mean \pm SD	269 \pm 123
Range	0–660
Total operating room time (min)	
Mean \pm SD	451 \pm 142
Range	240–1007
Total urine output (mL/kg/hr)	
Mean \pm SD	0.7 \pm 0.4
Range	0.1–2.0
Vasopressor infusion required (n)	55 (51.9)

Data in parentheses are percentages. euroSCOREs calculated as described by Nahel et al.²¹ SD, Standard deviation; euroSCORE, European System for Cardiac Operative Risk Evaluation; TECAB, total endovascular coronary artery bypass; LIMA/RIMA, left internal mammary artery/right internal mammary artery (dissection).

revascularization, and 3 experienced graft failure during the postoperative period (one 80% RIMA graft stenosis assessed through angiography; 2 required LIMA-LAD stent). Four returned to the OR for excessive bleeding (3 sternotomies and 1 thoracotomy).

TABLE 2. Morbidity/mortality

Period	Patients (n)
Intraoperative	
RIMA trauma	1
Ventricular trauma	2
Cardiac arrest	1
Emergent conversion	4
CPB initiation	3
Death	1
Postoperative	
New-onset atrial fibrillation	17
Pneumothorax	2
Renal failure	8
New-onset dialysis	3
Incomplete revascularization	7
Acute graft failure	3
IABP insertion	3
Cardiac arrest	1
Reintubation	2
Stroke	2
Excessive bleeding	7
Return to operating room	4
Death	3

RIMA, Right internal mammary artery; CPB, cardiopulmonary bypass; IABP, intra-aortic balloon pump.

Seven patients were extubated in the OR. Of the remaining 99, 86 were extubated within 24 hours of ICU arrival, and 13 were extubated more than 24 hours after ICU arrival. The mean ILLOS was 2.3 days (range, 0–22), and the mean HLOS was 5.2 days (range, 2–24).

Of the 106 patients, 23 (21.7%) exhibited major morbidity. The surgical time for the patients with major morbidity was significantly longer than that for the patients without major morbidity (414 ± 191 minutes vs 302 ± 111 minutes, respectively, $P = .011$). The decrease in the major morbidity/mortality rates over time (ie, with more experience) was not statistically significant. The rate was 35% among the first 26 patients, 19% among the next 27 patients, 22% among the next 27 patients, and 12% among the last 26 patients (Cochran-Armitage trend test, $P = .071$).

Four patients died. The first was a 69-year-old woman (ejection fraction, 51%; euroSCORE, 3.79) scheduled for 2-vessel TECAB. Elective conversion (thoracotomy) was required. A LIMA-LAD graft was performed; however, the right coronary artery was not revascularized. Postoperative infarction (right coronary artery territory) required intra-aortic balloon pump insertion, and renal failure (dialysis) preceded death on POD 4. The second was a 58-year-old woman (ejection fraction, 40%; euroSCORE, 1.85) scheduled for 2-vessel TECAB. LIMA-obtuse marginal and RIMA-LAD grafts were performed. Ventricular fibrillation immediately after surgery led to emergent sternotomy/initiation of CPB. Additional revascularization was performed; however, this patient was unable to be weaned

TABLE 3. Comparison of revascularization groups (n = 106)

Variable	One-vessel TECAB	Two-vessel TECAB	Three/four-vessel TECAB	P value
Total patients (n)	30 (28)	67 (63)	9 (9)	
euroSCORE	3.3 ± 2.6	3.3 ± 3.9	1.7 ± 1.4	.144
Lung separation time (min)	174 ± 73*	283 ± 99	464 ± 136	<.001
Surgical time (min)	220 ± 102*	342 ± 100	564 ± 150	<.001
Operating room time (min)	346 ± 107*	466 ± 101	695 ± 160	<.001
Vasoactive medications (n)	11 (36.7)*	37 (55.2)	7 (77.8)	.019
pRBC use (n)	1 (3.3)	3 (4.5)	3 (33.3)	.021
Renal failure (n)	3 (10.0)	5 (7.5)	0 (0.0)	.364
Postoperative ventilation >24 h (n)	1 (3.3)	9 (13.4)	3 (33.3)	.018
ILOS (d)	1.7 ± 1.3	2.4 ± 3.0	3.6 ± 1.5	.002
HLOS (d)	4.2 ± 1.7*	5.3 ± 3.4	7.2 ± 3.3	.004
Major morbidity (n)	7 (23.3)	12 (17.9)	4 (44.4)	.522
Mortality (n)	1 (3.3)	2 (3.0)	1 (11.1)	.481

Data presented as numbers of patients, with percentages in parentheses, or mean ± SD. P values from Spearman rank correlation analysis for continuous variables and Cochran-Armitage trend tests for dichotomous variables. TECAB, Total endoscopic coronary artery bypass; SD, standard deviation; pRBC, packed red blood cells; ILOS, intensive care unit length of stay; HLOS, hospital length of stay. *P < .05 compared with patients undergoing multivessel TECAB using Wilcoxon rank-sum tests for continuous variables and chi-square tests (or Fisher's exact test, as appropriate) for dichotomous variables.

from CPB secondary to myocardial dysfunction. The third patient was an 85-year-old man (ejection fraction, 62%; euroSCORE, 4.79) scheduled for 2-vessel TECAB. Elective conversion (thoracotomy) allowed surgery to be performed uneventfully (LIMA-LAD, vein graft-diagonal). However, postoperative myocardial failure (postoperative ejection fraction 10%), and renal failure (dialysis) preceded death on POD 6. The fourth was a 71-year-old female (ejection fraction, 55%; euroSCORE, 2.68) scheduled for 4-vessel TECAB, which was performed uneventfully (LIMA-obtuse marginal/ramus, RIMA-LAD, vein graft-diagonal). However, the patient returned to the OR because of excessive bleeding (emergent sternotomy) after cardiac arrest in the ICU. Subsequent stroke preceded death on POD 8. The surgical time in patients with mortality was significantly longer than in patients without mortality (506 ± 190 minutes vs 319 ± 132 minutes, respectively, $P = .043$).

The comparison of the revascularization groups is given in Table 3. An increasing number of vessels bypassed was significantly associated with increased vasoactive medication use ($P = .019$), pRBC use ($P = .021$), the occurrence of postoperative ventilation times longer than 24 hours ($P = .018$), and ILOS ($P = .002$). The number of vessels bypassed also correlated positively with lung separation time ($r = 0.615$; $P < .001$), surgical time ($r = 0.686$; $P < .001$), OR time ($r = 0.669$; $P < .001$), and HLOS ($r = 0.279$; $P = .004$). Compared with patients undergoing 1-vessel TECAB, patients undergoing multivessel TECAB had significantly prolonged surgical and OR times ($P < .001$ for both) and HLOS ($P = .027$). An increased surgical time was significantly associated with increased lung separation time ($r = 0.782$; $P < .001$), HLOS ($r = 0.332$; $P < .001$), an increased likelihood of vasoactive medication use (odds ratio, 1.80 per standard deviation increase in surgical time; 95%

confidence interval, 1.14–2.84; $P = .011$), pRBC use (odds ratio, 2.68 per standard deviation increase in surgical time; 95% confidence interval, 1.34–5.35; $P = .005$), and prolonged postoperative ventilation time (odds ratio, 1.80 per standard deviation increase in surgical time; 95% confidence interval, 1.07–3.04; $P = .028$).

The observed outcomes in our patients compared with the expected outcomes from conventional CABG using the STS risk calculator (available from www.sts.org) are listed in Table 4. Our patients had a significantly greater incidence

TABLE 4. Observed versus expected outcomes

Outcome	Observed (n)	Expected (n)*	P value†
Prolonged ventilation	13	5.94	.003
Short length of stay	71	63.36	.130
Long length of stay	2	3.57	.398
Renal failure	8	2.55	<.001
Stroke	2	0.85	.209
Reoperation	4	3.85	.939
Morbidity	16	9.96	.045
Mortality	4	1.56	.049

*Expected outcomes calculated from Society of Thoracic Surgeons risk calculator (available from: www.sts.org), which allows a user to calculate a patient's risk of morbidity and mortality. The risk calculator incorporates the Society of Thoracic Surgeons risk models, which are designed to serve as statistical tools to account for the effect of patient risk factors on operative morbidity and mortality. STS outcomes definitions include prolonged ventilation (tracheal extubation >24 hours), short length of stay (hospital discharge <6 days), long length of stay (hospital discharge >14 days), renal failure (serum creatinine increase to >2.0 mg/dL, doubling of preoperative creatinine, or new requirement for dialysis), stroke (confirmed neurologic deficit of abrupt onset that does not resolve within 24 hours), reoperation (for bleeding/hemorrhage, valvular dysfunction, graft occlusion, other cardiac or noncardiac reasons), morbidity (composite endpoint of operative mortality, permanent stroke, renal failure, prolonged ventilation >24 hours, deep sternal wound infection, and reoperation), mortality (death during hospitalization, even if after 30 days or death after hospital discharge but within 30 days of procedure unless the cause of death was clearly unrelated to the operation). †From 1 degree of freedom chi-square goodness of fit test.

of prolonged ventilation, renal failure, morbidity, and mortality.

DISCUSSION

TECAB for multivessel disease has been described as “uncharted territory.”¹⁸ Our series represents the largest reported pool of patients undergoing multivessel TECAB. We found that increasing the number of vessels bypassed significantly increased the surgical/OR time, lung separation time, vasoactive medication use, PRBC use, postoperative ventilation time, LOS, and HLOS. Furthermore, the increased surgical time was significantly associated with major morbidity and mortality. Finally, a comparison with the STS expected outcomes revealed a similar LOS but a significantly increased incidence of prolonged ventilation, renal failure, morbidity, and mortality. Our results suggest that addressing multivessel disease by way of TECAB offers no obvious clinical benefits and might increase the morbidity and mortality.

The vast majority of reports using robotic technology during cardiac surgery have done so with some form of minithoracotomy and/or CPB (with/without myocardial arrest) and usually describe single-vessel revascularization (LIMA-LAD).⁵⁻¹⁰ All have reported prolonged surgical/OR times—perhaps the “payoff” necessary to avoid sternotomy or thoracotomy.¹⁸ However, elective conversion rates (to sternotomy/full thoracotomy) hover around 20%.^{5,6,8} Potential benefits include enhanced postoperative recovery⁷ and decreased postoperative atrial fibrillation.⁹ Perioperative blood use might be decreased⁹ or increased.⁵ Unresolved issues include increased costs⁷ and increased technical difficulty.^{5,6} All have described a substantial learning curve.^{6,10}

The few reports describing TECAB (without minithoracotomy/CPB) involve small numbers of patients undergoing single-vessel revascularization.¹¹⁻¹⁶ We also found many of the same concerns listed previously. Falk and colleagues¹⁶ described 12 patients (all with single LIMA-LAD) and the “substantial learning curve.” Katz and colleagues¹⁵ and Gao and colleagues¹² reported on 27 patients and 4 patients (all with single LIMA-LAD), respectively, undergoing combined TECAB and percutaneous coronary intervention for multivessel disease. Gao and colleagues¹² reported that TECAB “is very demanding.” All reported long operation times and a substantial learning curve and believed this technology should be reserved for single-vessel revascularization in healthy patients.¹¹ de Canniere and colleagues¹⁴ in a multicenter report (5 centers, 74 patients, 90% single-vessel disease), found that target vessel reintervention was greater than that reported for conventional CABG and stated that TECAB had “difficulties that must not be underestimated.” Others have questioned the issue of graft patency. Bonatti and colleagues²⁰ detailed 40 patients undergoing single-

TABLE 5. Comparison of studies by Srivastava et al¹⁷ and present study

Variable	Srivastava et al ¹⁷	Present study
Total patients reported (n)	93	106
Study period	Jul 2004–Dec 2005	Jul 2007–Feb 2009
Mean age (y)	67.4 ± 12.3	63.6 ± 11.5*
Number of vessels†		
One-vessel TECAB (n)	54 (58)	30 (28)
Two-vessel TECAB (n)	35 (38)	67 (63)
Three-vessel TECAB (n)	4 (4)	8 (8)
Four-vessel TECAB (n)	0 (0)	1 (1)
Multivessel TECAB (n)	39 (42)	76 (72)†
LIMA/RIMA (n)	38 (41)	55 (52)
Perioperative sternotomy (n)	0 (0)	5 (5)
Emergent conversion (n)	0 (0)	7 (7)*
CPB required (n)	0 (0)	3 (3)
Mean operating room time (min)	272 ± 128	451 ± 142†
Stroke (n)	0 (0)	2 (2)
Return to operating room (n)	0 (0)	4 (4)
In-hospital mortality (n)	0 (0)	4 (4)
Mean hospital length of stay (d)	3.4 ± 2.0	5.2 ± 3.1†

Data presented as mean ± standard deviation; data in parentheses are percentages. TECAB, total endoscopic coronary artery bypass; LIMA/RIMA, left internal mammary artery/right internal mammary artery dissection; CPB, cardiopulmonary bypass. * $P < .05$. † $P < .001$.

vessel (LIMA-LAD) robotic revascularization (CPB, arrested heart), of whom 50% experienced “undesirable technical events” and 20% experienced “anastomotic problems.” Kappert and colleagues¹³ described 5-year follow-up data for 33 patients who underwent TECAB (95%, single; 5%, double) and found an unacceptably high (13%) LAD reintervention rate. They concluded that “clinical outcomes and need for reintervention of the target vessel leave room for improvement.”¹³

Two editorials have summed up the controversy surrounding TECAB.^{3,4} One is fairly optimistic: “The reality is, at present, no one can predict whether robotic technology is or is not going to play a major role in the future of cardiac surgery.”⁴ The other is not: “It is time to recognize that robotics are no longer a promising new technology but instead a technology that has been tried and has failed to demonstrate any clinical value, outside of its questionable use for marketing.”³

A comparison of our results with those of Srivastava and colleagues¹⁷ provides additional unique insight. These 2 series (Table 5) represent the largest reported number of patients undergoing multivessel TECAB and the same experienced CS/PA team performed all the surgeries (at 2 different institutions). This previous experience likely led to our inability to find strong evidence of a learning curve. Our patient population was quite different from that of Srivastava and colleagues¹⁷ (72% multivessel vs 42% multivessel TECAB, $P < .001$). Furthermore, Srivastava and colleagues¹⁷ reported a 13.8% exclusion/conversion rate

(all elective thoracotomy), no episodes of emergent conversion or a need for sternotomy and/or CPB, and 18 patients (19.4%) underwent planned hybrid revascularization (no failures reported).¹⁷ A comparison of these 2 series supports the notion that addressing multivessel coronary artery disease using TECAB might increase the morbidity and mortality. However, for a wide variety of reasons (different periods, different institutions, different perioperative personnel, and so forth), a comparison of these 2 studies might be inappropriate.

Intraoperative hemodynamic instability is a challenging clinical reality of TECAB.^{11,14,17,18,22} Carbon dioxide insufflation (essentially a pneumothorax) leads to cardiac displacement and decreased venous return, when coupled with potential hypoxemia/hypercarbia (prolonged single-lung ventilation), might lead to increased central venous pressure, increased pulmonary artery pressure, decreased cardiac output, and hypotension.^{11,14,17} Right ventricular dysfunction (single-lung ventilation-initiated atelectasis, hypoxic vasoconstriction) and/or left ventricular dysfunction (compliance changes) might also contribute.¹⁸ Such hemodynamic instability necessitates preload augmentation and/or the use of inotropes/vasoconstrictors. We hypothesized that increasing the number of vessels bypassed (thus increasing the single-lung ventilation time/surgical time) promotes greater hemodynamic instability (increasing vasoactive medication use) and might be the underlying etiology of the increased morbidity and mortality observed. Because of this procedure-induced hemodynamic instability, many have recommended TECAB only for single-vessel disease in patients with reasonable cardiopulmonary reserve.^{11,14,18}

Our study had all the inherent limitations associated with a retrospective analysis. Furthermore, one must remember that the predicted outcomes using the STS risk calculator are only an estimate. However, we specifically defined all major morbidities assessed. Additionally, the morbidities we believed were more along the lines of "clinical challenges" (elective conversion, new-onset atrial fibrillation) were not considered major morbidities. Also, to best compare the outcomes from TECAB versus conventional CABG, a randomized controlled trial would be ideal.

In conclusion, we have reported the largest series to date of patients undergoing multivessel TECAB by 1 CS/PA team at a single institution and compared the findings with expected outcomes from conventional CABG and with the same CS/PA team's experience at another institution. Our analysis supported the concerns voiced by others, that addressing multivessel coronary artery disease with TECAB offers no obvious clinical benefits and might increase the morbidity and mortality. At present, until efficacy is proven through proper clinical trials, TECAB myocardial revascularization should be reserved for relatively healthy

patients (reasonable cardiopulmonary reserve) undergoing single-vessel revascularization.

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