

An endoscopic view of a heart valve during surgery. The image shows a circular structure with a scalloped edge, likely a valve, surrounded by various anatomical structures and surgical instruments. The background is dark, and the foreground elements are brightly lit, creating a high-contrast scene.

**AN APPRAISAL OF ADVANCED ENDOSCOPIC  
PORT ACCESS™ ATRIOVENTRICULAR VALVE SURGERY**

Hendrik J. van der Merwe

**AN APPRAISAL OF ADVANCED ENDOSCOPIC  
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**An appraisal of advanced endoscopic Port Access™  
atrioventricular valve surgery**

Hendrik J. van der Merwe

**AN APPRAISAL OF ADVANCED ENDOSCOPIC  
PORT ACCESS™  
ATRIOVENTRICULAR VALVE SURGERY**

Een evaluatie van gevorderd endoscopisch  
atrioventrikulere chirurgie door Port Access™

**Thesis**

to obtain the degree of Doctor from the  
Erasmus University Rotterdam  
by command of the  
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# CHAPTER 1

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General Introduction

## A BRIEF HISTORY OF ATRIOVENTRICULAR VALVE SURGERY

In the British Medical Journal of 1898, Daniel Samways [1] proposed that a surgical intervention may potentially be a therapeutic option for rheumatic mitral valve stenosis (MS). Sir Lauder Brunton developed and reported an animal model to perform “beating heart” transventricular mitral valve commissurotomy with a cardiovalvulotome in 1902 [2], which was clinically introduced by Elliot Carr Cutler and Samuel Levine in 1923 as the first successful atrioventricular valve (AVV) surgical procedure ever performed [3]. The 12-year-old patient survived for 4 years before passing away of pneumonia, but the poor outcomes of the subsequent 7 patients resulted in a procedural moratorium in 1929 [4].

Devastating acute left ventricle failure due to iatrogenic mitral valve regurgitation (MR) after commissurotomy resulted in Charles Bailey exploring the possibility of treating MS with an iatrogenic atrial septal defect [5]. Richard Sweet’s suggestion of performing a safe atrial diversion by an extracardiac left superior pulmonary vein to azygos vein bypass was adopted as the preferred procedure in the United States and France [6].

Improvements in the designs of closed cardiovalvulotomes by Tubbs, Brock and Dubost were paralleled by improved perioperative- and short term survival outcomes despite the persistence of significant postprocedural MR and a high rate of MS recurrence. Efforts to treat residual MR by partial extracardiac annular reduction techniques and baffle implantation were described by Bailey, Harken and Jamieson [7]. Robert Glover and Julio Davila [8] reported the use of an external circumferential annular suture to reduce MR in 1955 and between 1956 and 1958, Nichols [9] described annular plication using extracardiac transatrial sutures.

The subsequent introduction of cardiopulmonary bypass in 1956 enabled safe intracardiac AVV access with Dubost and Guiraun introducing transseptal biatrial- [10] and right atrial approaches [11] respectively. Lillehei reported the first suture mitral valve annuloplasty in 1957 [12] and in 1959, the concept of posteromedial annuloplasty was reported by Merendino [13]. Other ingenious mitral valve repair techniques were described by Kay [14,15], Wooler [16], Reed [17] and McGoon [18].

However, in the absence of reproducible and reliable mitral valve repair results, the options of prosthetic valve replacement were explored, with Nina Braunwald and Andrew Morrow implanting a polyurethane prosthesis reinforced with Dacron in the mitral position in 1960. This milestone event was followed by the successful implantation of a caged ball valve by Starr in the same year [6,10]. Significant technological advances in prosthetic valve design over the subsequent two decades resulted in reliable and safe perioperative- and long term outcomes.

Motivated by the complications associated with prosthetic valves at that time, Alain Carpentier [20, 21] and Carlos Duran [22, 23] focused their efforts on developing AVV repair techniques. In 1968, Carpentier performed the first remodelling annuloplasty with a prosthetic ring and refined the concepts of simple- and complex AVV reconstructive surgery [24, 25]. Evolution in tricuspid valve repair- and replacement techniques were largely ignored until diagnostic modalities increased the awareness of disease, with surgical principles mirroring the established techniques of mitral valve surgery.

## THE CLINICAL IMPACT OF ATRIOVENTRICULAR VALVE DISEASE

### Atrioventricular valve stenosis

Atrioventricular valve stenosis is defined as ventricular inflow obstruction at the level of the mitral- (MV) or tricuspid valve (TV) due to a variety of causes outlined in table 1. **Mitral stenosis (MS)** results in elevated left atrial- and pulmonary venous pressures, pulmonary artery hypertension, increased right ventricle end-diastolic pressure, progressive right ventricle dilatation and TV regurgitation [26, 27]. Although left ventricular diastolic pressure is usually preserved in isolated MS, dysfunction eventually occurs in 25% of patients with chronic MS. The predominant cause of MS is rheumatic fever, with rheumatic changes documented to be present in 99% of MS valves excised at the time of replacement [28]. Isolated MS occurs in 33% of patients with rheumatic heart disease, which has a long latent phase and 10-year survival greater than 80%. It is reported that 60% of patients remain asymptomatic with no clinical MS progression [26-28] due to a variable annual MV area loss ranging between 0.09-0.32cm<sup>2</sup> [29]. Once symptomatic, 10-year survival ranges between 0% to 15% [30-34] due to progressive pulmonary- and systemic congestion (60% - 70% of patients), systemic embolism (20% - 30% of patients), pulmonary embolism (10% of patients) and infection (1% - 5% of patients). Data from unoperated patients in the surgical era still reported a 5-year survival rate of only 44% in patients with symptomatic MS who refused intervention [35]. **Tricuspid valve stenosis (TS)** occurs in less than 3% of the international population, is mostly of rheumatic origin, occurs rarely in isolation and is clinically significant in 5% of patients [26, 27]. TS result in right atrial enlargement, obstructed systemic venous return, hepatic enlargement, decreased pulmonary blood flow and peripheral congestion [28].

**Table 1. Etiology of atrioventricular valve stenosis**

Inflammatory / Autoimmune diseases
Rheumatic fever
Systemic lupus erythematosus
Rheumatoid arthritis
Mucopolysaccharidoses (Hunter-Hurler phenotype)
Fabry disease
Whipple disease
Methysergide therapy
Neoplastic (malignant carcinoid disease)
Congenital stenosis
Pseudo-stenosis
Non-rheumatic annular calcification
Infective endocarditis with large obstructive vegetation
Atrial myxoma with valve obstruction
Cor triatriatum (mitral valve)

### Atrioventricular valve regurgitation

Atrioventricular valve regurgitation is defined as the retrograde ejection of blood from the ventricle into the atrium across the MV or TV during systole, which result in volume overload of the ventricle at the end of diastole. Tables 2a and 2b outline the various acute and chronic etiology. **Mitral valve regurgitation (MR)** is the second commonest cardiac valve pathology [26-28, 30], with mild MR detectable in 20% of middle-aged and older adults. *Acute MR* result in an acute increase in left ventricular end-diastolic volume and a decrease in left ventricular end-systolic volume, which leads to an acute supranormal total stroke volume with diminished forward stroke volume. This results in an acute increase in left atrial pressure, pulmonary congestion and left ventricle volume overload with clinical features of acute left ventricle failure.

**Table 2a. Etiology of acute atrioventricular valve regurgitation**

Annulus disorders
Infective endocarditis (abscess formation)
Trauma (post-valve surgery, technical problems)
Paravalvular leak (suture interruption, infective endocarditis)
Leaflet disorders
Infective endocarditis (perforation, vegetation)
Trauma (post-percutaneous balloon valvotomy, blunt- or penetrating chest trauma)
Myxomatous degeneration
Systemic lupus erythromatosus (Libman-Sacks lesion)
Rupture of chordae tendineae
Idiopathic (spontaneous)
Myxomatous degeneration (valve prolapse, Marfan syndrome, Ehlers Danlos)
Infective endocarditis, acute rheumatic fever
Trauma (percutaneous balloon valvotomy, conduction leads, chest trauma)
Papillary muscle disorders
Coronary artery disease (ventricle dysfunction, papillary muscle rupture)
Acute global ventricular dysfunction
Infiltrative disease (amyloidosis, sarcoidosis)
Trauma (percutaneous balloon valvotomy, conduction leads, chest trauma)
Primary prosthetic valve disorders
Prosthetic valve dysfunction
Biological leaflet perforation / mechanical strut-, disc or ball failure

In *chronic compensated MR*, the left atrium and left ventricle remodel to accommodate the volume overload. Progressive eccentric left ventricle hypertrophy maintains forward stroke volume and cardiac output, which eventually dilates to present as cardiac dysfunction and decompensated MR, ultimately leading to pulmonary edema and cardiogenic shock. Studies suggest that compensated severe MR have a 10-year mortality risk or need of intervention of 90% [30]. *Decompensated MR* is associated with an annual mortality risk of 6-7% and poor interventional outcomes [30]. **Tricuspid valve regurgitation (TR)** results from primary structural abnormalities or secondary left ventricle myocardial dysfunction, MV disease, pulmonary vascular disease or right ventricle dysfunction. TR causes right ventricle volume overload, increased right atrial pressure, decreased systemic venous drainage, decreased pulmonary blood flow and clinical features of right-sided congestive heart failure with hepatic congestion, peripheral edema and ascites. Mortality of rheumatic TR with treatment is less than 3% [26-28, 30]. Mortality associated with TR secondary to myocardial dysfunction or dilatation is up to 50% at 5 years [28].

**Table 2b. Etiology of chronic atrioventricular valve regurgitation**

Congenital abnormalities
Clefts, fenestrations
Ebstein anomaly (tricuspid valve)
Endocardial cushion defects
Infective / Inflammatory processes
Rheumatic heart disease
Infective endocarditis (annular, leaflets or chordal involvement)
Systemic lupus erythromatosus
Scleroderma
Degenerative / connective tissue abnormalities
Myxomatous degeneration of leaflets
Ehlers-Danlos syndrome
Marfan syndrome
Pseudoxanthoma elasticum
Structural abnormalities
Annular dilatation (ventricular dilatation, aneurysms, cardiomyopathies)
Chordal elongation / rupture (spontaneous, myocardial infarction, trauma)
Papillary muscle dysfunction (ischemia, myocardial infarction, cardiomyopathies)
Pharmacological side-effects
Ergotamine, Methysergide, Pergolide, Anorexiant
Neoplastic disease
Atrial myxoma
Carcinoid syndrome

## ATRIOVENTRICULAR VALVE SURGERY OR TRANSCATHETER INTERVENTIONS?

The introduction of new operative techniques and innovative technology to treat AVV disease require rigorous evaluation that defines its applicability compared with the current standard or accepted evidence based therapy. The results of scientifically sound randomized controlled trials (RCTs) are regarded as the highest level of clinical evidence and are used to construct contemporary therapeutic guidelines and recommendations. Boutron and colleagues reported that up to 35% of RCTs have non-significant results [36], which implies that without sound scientific verification, a significant number of patients risk exposure to new, but inferior therapeutic strategies.

The safety and efficacy of new techniques and technology should be evaluated by observational studies if RCTs are not available or possible, of which the true benefit or superiority should be verified by RCTs if the outcomes are positive [37]. Financial incentives and industry biases are unfortunately part of contemporary cardiovascular research and it is important for clinicians to be aware of important flaws in interpreting evidence and trial results [38].

The rapid advances in transcatheter AVV technology, which include the MitraClip™ (Abbott Laboratories, Illinois, USA) [39-41], percutaneous annuloplasty- [42-44] and transcatheter mitral valve replacement devices [45], resulted in the reclassification of traditional surgical patients to be eligible for both surgery and transcatheter therapeutic options and it is becoming increasingly difficult to accurately define the optimal treatment pathway. Current guidelines on the treatment of valvular heart disease reemphasise the value and need of a shared decision-making heart team [26-28]. In view of the progressive paradigm shift towards less invasive procedures, it is expected that current and future cardiac surgeons will need to expand their surgical- and transcatheter service delivery to offer alternatives to classic full sternotomy access for routine AVV procedures [46-47]. Experienced centres are expanding their patient selection criteria to include patients who were previously considered contraindicated due to difficult access- or complex repair- and replacement procedures [48-52] and it is imperative that the cardiac surgery community unite to offer evidence-based-, hybrid cardiac interventional care.

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# CHAPTER 2

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Aim and Outline



**AIM**

The aim of this thesis is to appraise the clinical application-, safety-, feasibility- and sustainability of advanced techniques in difficult access- and complex atrioventricular valve endoscopic Port Access™ surgery.

**OUTLINE**

**Part 1** of this manuscript provides an overview of modern generic minimally invasive atrioventricular valve surgery, highlights the basic principles of endoscopic Port Access™ surgery and describes a systematic outline of how to plan and establish a safe- and sustainable Port Access™ program.

The factors that contribute to adverse events associated with Port Access™ atrioventricular valve surgery are investigated in **Part 2**. The pitfalls and potential risk reduction strategies are discussed as part of an ongoing process to assist new centres with incorporating minimally invasive Port Access™ techniques into routine practice and to emphasise important aspects of knowledge and skills development.

**Part 3** aims to evaluate the safety- and sustainability of new developments in advanced Port Access™ atrioventricular valve surgery and focuses on two aspects. Firstly, the clinical- and echocardiographic outcomes of patients who were historically considered contraindicated to undergo Port Access™ surgery are described. Secondly, the perioperative- and long term outcomes of complex Port Access™ atrioventricular valve repair- and replacement techniques are evaluated for safety-, feasibility and long term durability.

Anecdotal reports on advanced techniques in Port Access™ surgery are described in **Part 4** and aim to evaluate its safety- and feasibility for pathology that are considered to be beyond the routine procedures.

# PART 1

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THE BASIC PRINCIPLES OF PORT ACCESS™ SURGERY



# CHAPTER 3

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Minimally invasive atrioventricular valve surgery –  
current status and future perspectives

Van der Merwe J, Casselman F, Van Praet F

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**ABSTRACT**

We are currently witnessing rapid evolution in minimally invasive- and catheter-based atrioventricular valve interventions as acceptable alternatives to classic sternotomy access (CSA). Collectively, minimally invasive atrioventricular valve surgery (MIAS) is associated with significant learning curves and its routine application is met with varying degrees of enthusiasm in view strict quality control, clinical governance and outcome reporting. Whether the reported potential benefits and comparable efficacy across a range of long-term outcome measures reported by experienced MIAS centres can be translated into general international surgical practice are not well defined. This paper describes the historic evolution of MIAS, the contemporary clinical outcomes of MIAS compared with CSA and the application of MIAS in “real-life” general practice.

**INTRODUCTION**

We are currently witnessing rapid evolution in the development, marketing and utilization of robotic- [1-3], endoscopic- [4-5] and transcatheter [6-9] atrioventricular valve (AVV) repair- and replacement technology as alternatives to classic sternotomy access (CSA). Collectively, minimally invasive atrioventricular valve surgery (MIAS) is associated with significant learning curves [10], which in the context of increasing patient age, operative risk profiles, expectations and strict quality control [11-13], potentially deter upcoming centres from incorporating MIAS programs that utilize videoscopic- or robotic vision, modified instruments, perfusion- and myocardial protective strategies into clinical practice.

As a result, CSA is still considered by many as the standard approach for AVV disease and subsequent reports emerged that challenge the historically documented potential benefits associated with MIAS [14]. In addition, sceptics may prefer interventionist driven transcatheter intervention (TCI) programs to avoid the transitional challenges associated with establishing MIAS programs [15]. Various experienced MIAS centres reported their routine use of MIAS for all isolated AVV pathology with excellent long term results [16-17], but whether their clinical outcomes can indeed be translated into general international surgical practice are not well defined [18-20]. This paper describes the historic evolution of MIAS, the contemporary clinical outcomes of MIAS compared with CSA and the application of MIAS in “real-life” general practice.

**REVIEW CRITERIA**

Contemporary, peer reviewed reports on minimally invasive mitral- and tricuspid valve surgery were selected and reviewed for intraoperative-, in-hospital-, postdischarge- and health economic outcomes and references.

**THE HISTORICAL EVOLUTION OF MIAS**

In the British Medical Journal of 1898, Daniel Samways became the first physician to propose that rheumatic mitral valve (MV) stenosis be treated by surgical intervention. Sir Lauder Brunton subsequently developed and reported his animal model of transventricular mitral commissurotomy in 1902 [21], which was clinically applied as the first successful AVV surgical operation by Elliot Carr Cutler and Samuel Levine in 1923 [22]. The 12-year-old patient survived for 4 years before passing away of pneumonia, but the poor outcomes of the subsequent 7 patients resulted in a procedural moratorium in 1929 [23].

The introduction of cardiopulmonary bypass in 1956 enabled safe intracardiac AVV access with Dubois and Guiraun introducing the concepts of a transseptal biatrial- [24] and right atrial approaches [25] respectively. The visionary repair concepts of MV regurgitation were proposed and refined by Davila [26], Nichols [27], Kay [28], Carpentier [29], McGoon [30] and many others [31].

Navia and Gosgrove [32] were the first to report the concept and outcomes of a non-sternotomy-, parasternal MV approach in 25 patients in 1996. There were no hospital deaths, reoperations for

bleeding, embolic complications or wound infection. Cohn and his group also described their similar findings with this approach in 43 patients [33].

The reported success of laparoscopy in general surgery resulted in the application and development of video assisted thoracic surgery, which provided Alain Carpentier and his team the opportunity to perform the first video-assisted-, right mini-thoracotomy MV-repair using ventricular fibrillation in 1996 [34], which subsequently provided the platform for various centres to refine and further develop MIAS. Port Access™ surgery (PAS), which consists of peripheral cardiopulmonary bypass (CPB), guidewire directed antegrade endoaortic balloon occlusion (EABO), venting, cardioplegia delivery and videoscopic guidance of routine AVV procedures through a 4cm right antero-lateral working, was initially developed by Heartport, Inc. (Redwood City, CA, USA) in 1994 and was introduced by Stevens and colleagues as a surgical method for performing coronary artery bypass grafting [35].

The teams of Frederick Mohr [36], Hugo Vanermen [37-38] and others [39-40] refined and incorporated PAS techniques into their routine MIAS clinical practice and reported the significant potential benefits in their extensive series. As an alternative to EABO, direct aortic clamping (DAC) was introduced by Angouras and Michler [41] and further developed by Chitwood [42-44].

Recent developments in MIAS access include the introduction of a right vertical infraaxillary thoracotomy- [45] and periareolar incision approach [46] with excellent results.

Carpentier performed the first completely robotic MV procedure using the Da Vinci Surgical System (Intuitive Surgical, Inc. Sunnyvale, California, USA) [46], with various international groups now performing robotic AVV surgery as a routine with excellent reported outcomes [47-48].

## CONTEMPORARY CLINICAL OUTCOMES OF MIAS COMPARED WITH CSA

### Cardiopulmonary bypass-, ischemic- and procedure times

The pathophysiological- and inflammatory effects of CPB and cardioplegic arrest for CSA and MIAS are well described [49]. Various reports suggest that MIAS is associated with up to 15% longer CPB-, ischemic- and procedure times compared to CSA for both simple- and complex AVV surgical procedures [50-61]. The transition to using single shaft instruments through limited working space and other technical factors are reported as possible contributing factors in the early experience [62-63].

### Success of complex repair- and replacement procedures

The group from Aalst reported their MIAS series of 2872 patients [64], of which 2183 (76.0%), 54 (1.9%) and 635 (22.1%) underwent isolated MV-, isolated TV and combined MV and TV procedures. MV-repair was achieved in 96.4% (n = 1822 of 1891) of primary annular dilatation and degenerative valves and constituted 81.7% (n = 2866) of all MIAS procedures (n = 3507). Other groups also reported excellent MIAS repair results for simple- and complex AVV procedures [17], which can also be achieved in the early learning curve [62-63]. Various reports suggest no significant difference in the success of simple- or complex AVV procedures whether performed by MIAS or CSA [57, 65].

## Vascular Complications

The majority of MIAS reports utilize peripheral retrograde CPB and obtain safe cardioplegic arrest by either EABO or DAC [46]. For PAS, the group from Aalst reported an incidence of 0.4% for aortic dissection, of which the majority occurred during the initial learning curve [64]. Compared with CSA, various conflicting reports suggest that MIAS is associated with increased central aortic- or major vascular injury risk [57, 59-61]. However, refinements in preoperative aorto-iliac-axis evaluation strategies, cardiopulmonary bypass techniques [66- 67], the acquisition of guidewire skills and the application of transesophageal echocardiographic (TEE) guided cannulation- and EABO placement techniques [68] significantly decrease the risks of vascular injuries [69]. In addition, it appears that EABO is associated with less bleeding and vascular injury risks compared with DAC [70-73].

### Conversion to classic sternotomy due to adverse MIAS events and its impact on clinical outcome

The incidence of MIAS conversion to CSA due to adverse intraoperative events ranges considerably, with experienced centres reporting an incidence of 3.0% [64] to 3.7% [17]. The group from Aalst suggested an increased mortality associated with conversion during PAS [64] and also reported their individual conversion rates in the context of complex isolated AVV endocarditis (9.1%) [74], redo-PAS after previous PAS (19.2%) [75], difficult access congenital chest wall deformities (0%) [76], extreme obesity (0%) [77], post-cardiac transplantation (0%) [78] and hypertrophic obstructive cardiomyopathy with associated AVV disease (0%).

### Neurological Events

Seeburger and his team observed postoperative neurological impairment in 3.1% of their MIAS series [17], of which 2.1% and 1.0% were classified as minor and major neurological events (NE) respectively. Various studies report no difference in NE [49, 56], transient neuropathy- [53] or permanent NE [65] incidence between MIAS and CSA, while isolated reports of a decreased NE incidence following MIAS are documented [17,44].

However, the recent Society of Thoracic Surgeons-Adult Cardiac Surgical Database (STS-ACSD) report [61], supported by the Consensus Statement of the International Society of Minimally Invasive Coronary Surgery (ISMICS) 2010 [79] and other reports [55-57, 59-60], suggest that MIAS does indeed increase NE risk by 0.9% compared to CSA. Retrograde femoral cannulation was not considered to be an independent predictor of NE.

In addition to preoperative vascular screening, refinements in de-airing techniques under TEE guidance and operative field CO2 flooding resulted in improved neurological outcomes [79]. The team from Aalst reported a NE incidence of 1.2% for their PAS series of 2872 patients [64]. MIAS strategies that utilize antegrade perfusion has low NE risk and excellent outcomes. Recent multi-institutional reports suggest no significant difference in NE between EABO and DAC [70-73].

### Cardiac complications

Various studies compared cardiac outcomes between MIAS and CSA and did not identify any significant difference in the incidence of perioperative myocardial infarction, low cardiac output syndrome, tamponade or inotropic requirements [52-53, 57]. For PAS, the group from Aalst reported their incidence of cardiac death (0.2%), acute myocardial infarction (0.7%) and low cardiac output syndrome (1.0%) in their series of 2872 patients [64].

A 10% incidence of postoperative atrial fibrillation (POAF) was reported for PAS in the PAIR registry, which is lower than CSA reports [80]. Mihos suggested that MIAS for isolated valve surgery reduces postoperative AF and resource use when compared with CSA [81]. Dogan [52] and Chitwood [44] suggested no difference in permanent postoperative pacemaker requirements between MIAS and CSA.

### Postoperative bleeding and transfusion requirements

Extensive postoperative transfusions (POT) and reexploration for bleeding (RE) are associated with increased mortality and morbidities [82]. Dogan and his colleagues reported significant decrease in chest drain output in MIAS compared to CSA [52], which was reconfirmed by Glower [56] and other comparative reports [53-55].

It is suggested that the packed red cell units transfused are less with MIAS compared with CSA [53-55], but the percentage of patient transfused are similar [52-55, 61]. Various studies also confirm a significant reduction in RE for bleeding with MIAS compared to CSA [65, 83-85], with the group from Leipzig reporting their RE rate of 5.1% [17].

### Respiratory morbidities

Comparative reports identified no significant difference between MIAS and CSA with regards to the development of postoperative pneumonia, pneumothorax, pleural effusion or other pulmonary complications [86] and it is suggested that ventilation time and subsequent intensive care stay, is significantly reduced with MIAS [55-60].

### Gastrointestinal events

Comparative reports identified no significant difference between MIAS and CSA with regards to the development of postoperative gastrointestinal events [44, 53].

### Renal dysfunction

McCreath and his colleagues [87] observed a highly significant independent association between surgical approach and renal function, indicating a greater risk of acute renal injury in CSA compared to

MIAS performed by PAS and suggested that PAS may be preferable to conventional methods for patients with high renal risk. Other comparative reports however, identified no significant difference in postoperative renal failure between MIAS and CSA [57, 61].

### Wound infection

In a comparative report by Grossi and his colleagues, wound infection occurred in 0.9% and 5.7% of MIAS and CSA patients respectively, which increased to 1.8% for MIAS and 7.7% for CSA in the elderly [88]. Felger, however, reported no significant difference [53]. Interestingly, the risk of developing mediastinitis [57] and wound dehiscence [59] is reported to be the same for MIAS and CSA. The impact and potential benefit of MIAS in immunosuppressed patients with AVV disease are not yet reported and may indicate a potential wound healing advantage compared with CSA in developing countries.

### Duration of hospital stay

It is suggested that MIAS is associated with decreased intensive care stay, total hospital duration and resource usage compared to CSA [89-92]. However, in-hospital stabilisation of anticoagulation regimes and completion of 6 weeks antibiotic course in cases of infective endocarditis, does not reflect the isolated impact on hospitalization of MIAS [74-78].

### In-hospital mortality

Contemporary reports do not suggest a significant all-cause in-hospital mortality difference between MIAS and CSA [52-63] or EBAO and DAC [70-73]. The group from Aalst reported a perioperative mortality of 2.6% for their PAS series [64].

### Postdischarge survival

Limited comparative reports on long term risk of all-cause mortality between MIAS and CSA are available and do not identify a significant 1- and 3-year survival difference [45]. The group from Aalst reported the intermediate- and long term PAS survival in the context of infective endocarditis (69.4% at 10 years) [74], extreme obesity (100% at mean follow-up 39.4±88.4 months) [76], left ventricle outflow tract resection and AVV surgery (100% at mean follow-up 49.7±30.0 months) and redo-PAS after previous PAS (95.8% at 5 years) [75].

### Freedom from readmission and reintervention

No significant difference between MIAS- and CSA readmission within 30 days, risk of endocarditis or recurrence or need for valve related reintervention are reported [44, 57, 59].



### Quality of life and patient satisfaction

Compared with CSA, small thoracic incisions are associated with less pain, discomfort, and postoperative analgesics requirements [33, 53]. The group from Aalst suggested that more than 98% of the patients were extremely pleased with the cosmetic result of PAS, with 42% reporting an invisible scar, 93% favourably assessing procedure related pain and 34% fully recovered within 4 weeks [4,16]. Faster recovery of patients undergoing MIAS compared to CSA was demonstrated by Glower and his colleagues [56] and it is also reported that patients undergoing MIAS as their second procedure all perceived a faster and less painful recovery than their original CSA [53], with a small but significant decrease in NYHA class after 1 year in favour of MIAS compared to CSA [57-65]. The impact of MIAS specific to young patients and rapid recovery are not yet defined and may offer a potential advantage in return to normal duty and productivity in both first-world- and developing countries compared to CSA.

### Healthcare economic implications of MIAS and CSA

Comprehensive cost-effectiveness analysis of the incremental costs and benefits of MIAS compared to CSA are limited. Atluri and his colleagues demonstrated no difference in total cost (operative and postoperative) between MIAS and CSA [93] and concluded that MIAS can be performed with overall equivalent cost and shorter hospital stay relative to CSA, as the greater operative cost is offset by shorter intensive care unit and hospital stays. Santana demonstrated that MIAS resulted in significant reductions in costs of cardiac imaging and laboratory tests, lower use of blood products, fewer perioperative infections, faster recovery, shorter hospital length of stay, fewer requirements for rehabilitation and lower readmission rates in the following postoperative year and concluded that MIAS is safe, effective and significantly more cost-effective than CSA [94]. Grossi suggested that MIAS provide similar mortality, less morbidity, fewer infections, shorter stay, and significant cost savings during primary admission compared to CSA, which translate into additional institutional cost savings [95]. The limited health care resources in developing countries may benefit from MIAS and further investigations are warranted.

### APPLICATION OF MIAS IN ROUTINE SURGICAL PRACTICE – OVERCOMING THE LEARNING CURVE

Holzney and his colleagues [63] assessed the individual MIAS learning process from 3895 operation performed by 17 surgeons by analysing operation time and complication rates using sequential probability cumulative sum failure analysis. They identified the typical number of operations to overcome the learning curve to range between 75 and 125 procedures and further suggested that more than 1 procedure per week is required to maintain acceptable results. In addition, they reported that the individual learning curves varied markedly, proving the need for good monitoring or mentoring in the initial phase.

De Praetere and his colleagues from Leuven [62] assessed the MIAS learning curve by using a logarithmic curve-fit regression analysis of the CPB times, procedure complexity and the number of concomitant procedures. They reported the learning curve to be 30 procedures, with a significant reduction in aortic cross-clamp time before and after the end of the learning curve. The complexity of AVV reconstruction gradually increased and the proportion of mitral valve replacement decreased by gradually expanding MIAS indications. They concluded that the transition from CSA to MIAS could safely be introduced into practice without mortality, longer intensive care- or hospitalization.

Hunter reported a systematic approach on how to initiate a MIAS program [96] and identified techniques of AVV repair, TEE-guided cannulation, incisions, instruments, visualization, aortic occlusion and CPB strategies as seven key aspects to master during the learning curve. He also emphasised the principles of systems awareness, teamwork, communication, ownership and leadership, all of which are paramount to performing safe and effective MIAS.

Murzi [97] applied control charts (CUSUM curves) to monitor individual MIAS surgeon outcomes with a predetermined acceptable failure rate, alert- and alarm lines and clear procedure failure definitions. They identified significant inter-surgeon learning curve variation and concluded that the transition towards MIAS can be performed with low morbidity and mortality.

### CONCLUSION

CSA for AVV disease is well established, but its role in contemporary clinical practice are continuously being redefined by rapid evolution in transcatheter- and MIAS technology, patient preference and industry driven marketing. However, the routine application of MIAS is met with varying degrees of enthusiasm in view of learning curves, strict quality control, clinical governance and outcome reporting. It is therefore imperative that contemporary international MIAS outcomes are meticulously evaluated for evidence of well-defined patient- and healthcare economic benefits before adopting these techniques into clinical practice. This review confirms the historically reported potential benefits of MIAS compared with CSA and comparable efficacy across a range of long-term efficacy measures such as freedom from reoperation and long-term survival. Surgeons should be encouraged to adopt and apply MIAS in an exciting era of progressive transcatheter intervention preference, whether in a first- or third-world clinical context.

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# CHAPTER 4

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The principles of Port Access™ atrioventricular valve surgery – how to start and sustain a safe and effective program

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**ABSTRACT**

The ongoing evolution in transcatheter (TC) and minimally invasive surgical technology for atrioventricular valve (AVV) disease is paralleled by an aging- and higher surgical risk patient population, increasing public expectations, quality control and clinical governance. International treatment guidelines and changes in referral patterns progressively favour less invasive procedures, which require that both current- and future cardiac surgical practices become proficient in minimally invasive atrioventricular valve surgical- (MIAS) and TC procedures. The transition from classic sternotomy access to MIAS approaches that utilizes videoscopic- or robotic vision, modified long-shafted instruments, transoesophageal echocardiographic- or fluoroscopic guidewire directed peripheral cardiopulmonary bypass and endoaortic balloon occlusion device placement (Port Access™ Surgery, PAS) or external direct aortic clamping are associated with learning curves that are challenging to master in an era of decreasing surgical volume, training opportunities and healthcare cost constraints. Excellent perioperative- and long term outcomes with the routine application of MIAS utilizing PAS technology for isolated primary- and redo-AVV procedures are reported and it is suggested that the introduction of PAS in new centres should follow a systematic approach that include careful infrastructure planning, MIAS and PAS skills development and careful initial patient selection criteria under expert guidance. This manuscript provides an overview of the historic evolution of PAS, contemporary PAS technology, PAS infrastructure planning and the operative principles of PAS with the intention of assisting upcoming centres to establish and maintain safe- and effective PAS programs.

**INTRODUCTION**

Transcatheter- (TC) and minimally invasive atrioventricular valve surgical (MIAS) technology are rapidly evolving and are paralleled by increasing patient expectations [1], quality control [2], clinical governance [3] and patient risk profiles [4]. In an era of decreasing surgical volume, training opportunities, operative exposure and constrains in healthcare cost, upcoming surgeons are required to master challenging MIAS learning curves while maintaining acceptable clinical outcomes [5-6]. It is now well recognised that both current- and future cardiac surgical practices will be expected to be proficient in MIAS and TC device implantation [7-8], but the implementation and maintenance of such programs require systematic logistical and infrastructure planning.

Port Access™ atrioventricular valve surgery (PAS) utilizes videoscopic- or robotic vision, modified instruments, transoesophageal echocardiographic- or fluoroscopic guided peripheral cardiopulmonary bypass (CPB) and endoaortic balloon technology or external aortic clamping techniques to facilitate primary- [9-10] and redo- [11-12] MIAS repair- and replacement procedures. Between February 1<sup>st</sup> 1998 and May 31<sup>st</sup> 2019, a total of 3180 patients underwent PAS procedures at our institution for isolated atrioventricular valve (AVV) pathology. This manuscript provides an overview of the historic evolution of PAS, contemporary PAS technology, PAS infrastructure planning and the operative principles of PAS to assist new centres to establish and maintain safe- and effective PAS programs.

**HISTORICAL EVOLUTION OF PORT ACCESS™ SURGERY**

The concept of PAS was originally developed in 1994 (Heartport Inc., Redwood City, CA, USA) with the intention of using any combination of central- or peripheral CPB, endoaortic balloon occlusion-, retrograde cardioplegia- and pulmonary artery venting catheter devices to facilitate minimally invasive cardiac surgical procedures. Animal studies at Stanford- and New York University [13] demonstrated PAS feasibility and safety with subsequent United States Food and Drug Administration approval in 1996 [14-17]. More than 18000 minimally invasive cardiac procedures, which included coronary artery bypass grafting, were performed using components of PAS technology between 1996 and 2000 and its ergonomic advantage of allowing MIAS through small working ports without additional external instrumentation [18-20], especially in total endoscopic- [21-23] and robotic surgery [24-25], became well recognised. Edwards Lifesciences (Irvine, California, US) subsequently took ownership of PAS and recently reported a global use of PAS technology in 12689 patients between 2014 and 2017.

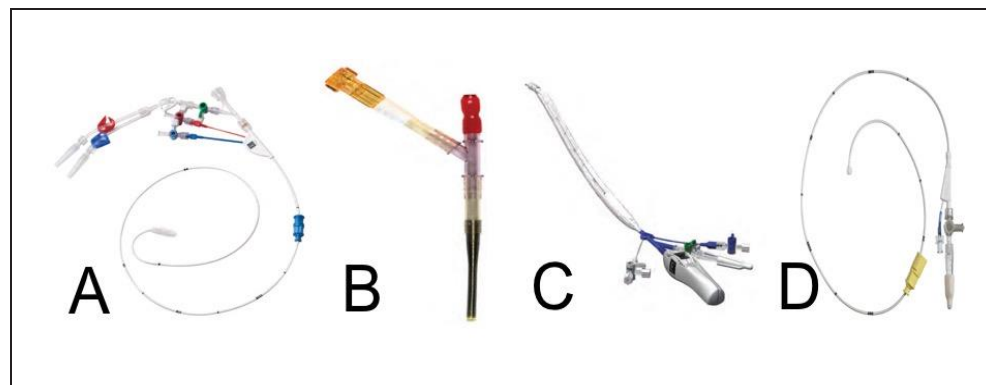
**CURRENT PORT ACCESS™ TECHNOLOGY**

IntraClude™ (Edwards Lifesciences, Irvine, California, USA) is a composite endoaortic balloon occlusion device (10.5 Fr, 100 cm length) that facilitates antegrade cardioplegia delivery, aortic root venting and pressure monitoring for ascending aorta sizes ranging 20-40 mm (Figure 1A). It is advanced to the sinotubular junction under transoesophageal echocardiographic- (TEE) or fluoroscopic guidance over a 200 cm 0.0038 J-tip guidewire through the side arm of the EndoReturn™ femoral arterial cannula



(21-23 Fr, Edwards Lifesciences, Irvine, California, USA)(Figure 1B). The QuickDraw™ femoral venous cannula (22-25 Fr, Edwards Lifesciences, Irvine, California, USA) is inserted under TEE or fluoroscopic guidance into the right atrium and is compatible with percutaneous approaches. The ProPlege™ peripheral retrograde cardioplegia device (9 Fr, 59 cm, Edwards Lifesciences, Irvine, California, USA), is a triple lumen device that is inserted through an internal jugular vein sheath into the coronary sinus under TEE guidance as an adjunct to endoaortic balloon occlusion for additional retrograde cardioplegia delivery (Figure 1C).

The EndoVent™ pulmonary catheter (8.3 Fr, Edwards Lifesciences, Irvine, California, USA) is inserted through the internal jugular- or subclavian vein as an additional pulmonary artery venting device (Figure 1D). Optisite™ (17 Fr, Edwards Lifesciences, Irvine, California, USA) is a peripheral cannula that can be utilized for additional arterial cannulation in cases of high CPB flow pressures. Special atrial retractors facilitate intracardiac access to perform robotic- or endoscopic atrioventricular valve repair and replacement procedures.



**Figure 1.** Current Port Access™ surgery technology include (A) an endoaortic balloon occlusion device (IntraClude™), (B) a peripheral arterial cannula with side arm (EndoReturn™), (C) a peripheral coronary sinus cardioplegia device (ProPlege™) and (D) a peripheral pulmonary artery vent catheter (EndoVent™). © Edwards Lifesciences Corporation. July 2019.

## INFRASTRUCTURE PLANNING

### PAS health care economics

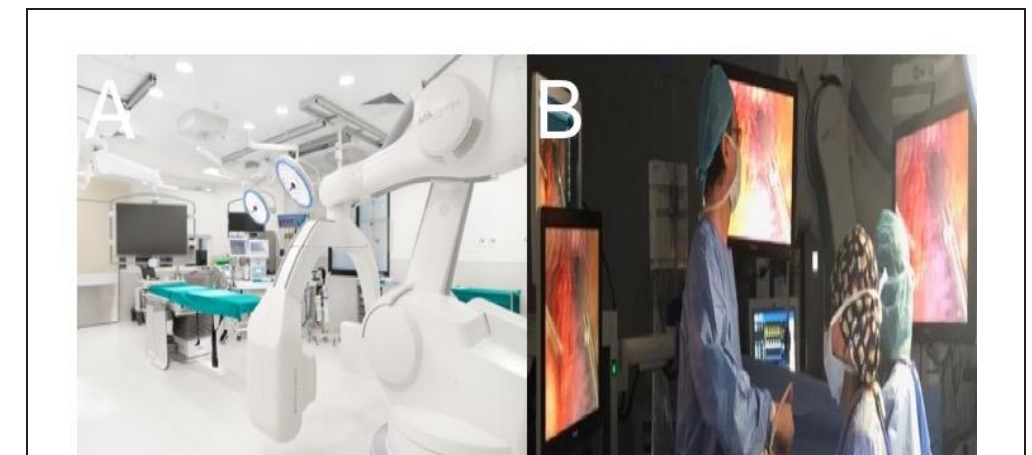
Evidence of proven efficacy, safety, feasibility and cost-effectiveness are required to obtain institutional support as a first step in initiating a PAS program. Atluri [26] and Santana [27] independently suggested that the greater operative cost associated with MIAS is offset by reduced costs of cardiac imaging, laboratory tests, lower use of blood products, fewer perioperative infections, faster recovery, shorter

hospital length of stay, fewer requirements for rehabilitation and lower readmission rates. Equipment acquisition- and operative theatre upgrades account for the majority of the initial institutional capital investment and the disposable costs can subsequently be offset against the cost savings mentioned.

### PAS and hybrid operative theatre design

Modern MIAS- and hybrid cardiovascular- and thoracic operating rooms are designed to facilitate TC and MIAS procedures in conjunction with efficient workflow, safety, access, lights, imaging modalities and theatre hygiene. Building a “state of the art” hybrid operating room (Figure 2) is a considerable economic investment for every institution, but various reports from the United States and China [28], suggest that case load potentially triple based upon the hybrid theatre setup, with a complete return on investment within 2 years.

For PAS, the basic operative room layout must be able to accommodate a cardiac anaesthetic- and TEE machine, an endoscopic camera- and CO2 delivery stack, a CPB machine, various synchronised screens for neuro-cardio-respiratory-, TEE- and 2D and 3D endoscopic image projection and adequate ergonomics that can accommodate 2 anaesthetists, 2 perfusionists, 2 surgeons, a theatre nurse and a support nurse. It is imperative that all routine cardiovascular equipment, guidewires, grafts, stents and sutures are readily available if required.



**Figure 2.** (A) Hybrid Port Access™ surgery operative theatre. (B) Port Access™ atrioventricular valve surgery performed using 3-D imaging technology

### Teamwork, communication, ownership and leadership

To promote trust, communication, effective teamwork, training and education, established PAS centres advocate a patient-centred-, multidisciplinary cardiac operative team that include an experienced anaesthesiologist [29], perfusionist [30], a skilled cardiac surgeon, surgical assistant, an experienced operative nurse and cardiac nursing support. It is suggested that a dedicated theatre team visit established PAS centres for training and mentorship and that a constant team initiate the PAS program for at least 20 cases [31]. Frequent constructive postoperative team debriefing sessions that focus on continuous improvement strategies are invaluable and reinforces ownership of each team member under the surgical leadership. Intraoperative communication is essential and each team member's opinion and concerns should be respected and addressed throughout any PAS procedure. For continuation of postoperative care, the expanded team members include skilled intensive care-, ward- and outpatient nurses, physiotherapists, other allied health care professionals, the patient's family and referring physicians.

### PATIENT SELECTION

In an era where surgical volume is progressively decreasing, emerging PAS programs should practice extreme caution in the initial patient- and valve pathology selection. Even though PAS is applied as a routine in experienced centres without exclusion criteria [32-37], it is suggested that emerging programs should preferably not offer PAS to patients with high risk clinical-, anatomical- and echocardiographic characteristics, which are outlined in table 1. In addition to routine cardiac surgical preoperative investigations, evaluation of the aorta-iliac-femoral-axis by contrasted computerised tomography, magnetic resonance imaging or an additional peripheral contrast injection during coronary angiography, is mandatory. In 511 consecutive patients that underwent PAS in an experience centre over a 5-year period, lung adhesions (n = 5, 1.0%) and peripheral cannulation complications (n = 4, 0.9%) required sternotomy conversion despite detailed preoperative evaluations [38].

<b>Table 1. Relative contraindications to initial Port Access™ surgery patient selection</b>	
<b>Patient characteristics</b>	
Potential difficult access	
Morbidity obesity	
Thoracic wall deformities	
Previous right thoracotomy	
Previous right thoracic irradiation or trauma	
Contraindications to- or unsuccessful right lung isolation	
Previous right ilio-femoral peripheral vascular interventions	
High surgical risk	
Elderly and high frailty index	
Previous cardiac surgery	
Urgent / emergency status	
Multiorgan dysfunction	
Poor respiratory function	
Other comorbidities risking adverse perioperative outcomes	
Vascular disease	
Aorta-iliac-femoral-artery-axis calcification, atheroma or aneurysms	
Common femoral artery diameter smaller than 8mm	
Ascending aorta ectasia, dilatation or aneurysm larger than 40mm	
Sinotubular junction or aortic root dilatation more than 40mm	
<b>Echocardiographic characteristics</b>	
Complex valve pathology for repair or replacement	
Barlow's morphology	
Infective endocarditis	
Severe posterior annular calcification	
Aortic valve regurgitation	
Advanced cardiomyopathy	
Severe pulmonary hypertension	

### PROCEDURAL OVERVIEW

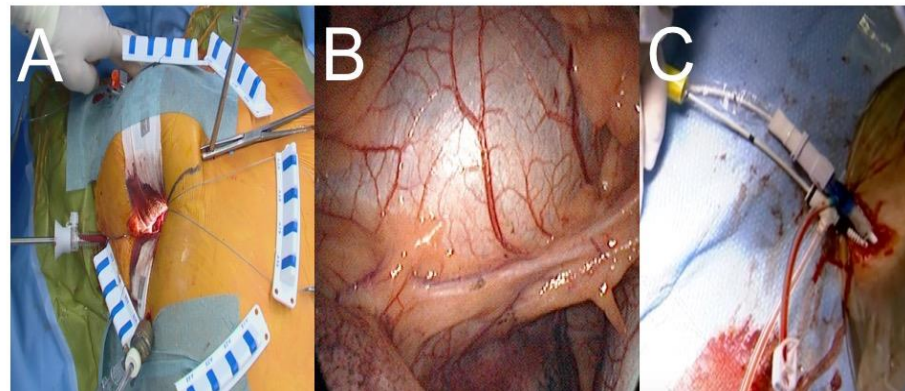
#### Patient positioning and port incisions

The patient is positioned supine with the right arm flexed and external defibrillation pads applied. An inflatable cushion is used to elevate the right hemithorax following routine cardiac anaesthesia that includes the insertion of a double lumen endotracheal tube, right internal jugular central venous- and right radial artery catheters, urinary catheter, rectal temperature monitoring and TEE probe. It is advised to utilise a right internal jugular venous cannula (16-18Fr, Optisite™, Edwards Lifesciences, Irvine,

California, USA) as additional venous drainage during the learning period. Various experienced centres however, rely only on single femoral venous cannulation augmented by vacuum assisted drainage. The use of bilateral radial artery catheter monitoring may be used during the early experience to ensure continuous hemodynamic monitoring in case of aortic dissection or endoballoon dislodgement that may occlude the innominate artery.

A 4-6 cm, non-rib spreading working port with a soft tissue retractor (SurgiSleeve™, 2.5-6 centimeters, Covidien, Massachusetts, USA) is established over the 4<sup>th</sup> intercostal, anterior axillary space, halfway between the clavicle and inferior xyphoid-costal border. The diaphragmatic dome should be palpable. A 7-mm port is inserted 2 to 3 intercostal spaces inferior to the working port for continuous CO<sub>2</sub> insufflation and left atrial vent line placement. A 5-mm endoscopic port- and a 5-mm left atrial retractor shaft are inserted latero-posteriorly- and parasternal-medially to the working port in the 4<sup>th</sup> intercostal space respectively (Figure 3A). The retractor-shaft is externally anchored to a Bookwalther™ retractor (Symmetry Surgical, Tennessee, USA) and a steel wire introduced through a needle in 2<sup>nd</sup> intercostal space, mid-clavicular line to facilitate valve exposure by retracting annuloplasty sutures anterolaterally.

Unobstructed visual- and working access are ascertained by resecting excessive pericardial fat (Figure 3B) and retracting the diaphragmatic dome infero-laterally with exteriorized traction sutures. The additional use of retrograde coronary sinus cannulation for cardioplegia delivery (ProPlege™) and pulmonary artery venting (EndoVent™) can be considered, but is not generally utilized during the initial learning curve (Figure 3C).



**Figure 3.** (A) Basic operative setup. (B) Endoscopic pericardial view. (C) EndoVent™ and ProPlege™ inserted in the right internal jugular vein.

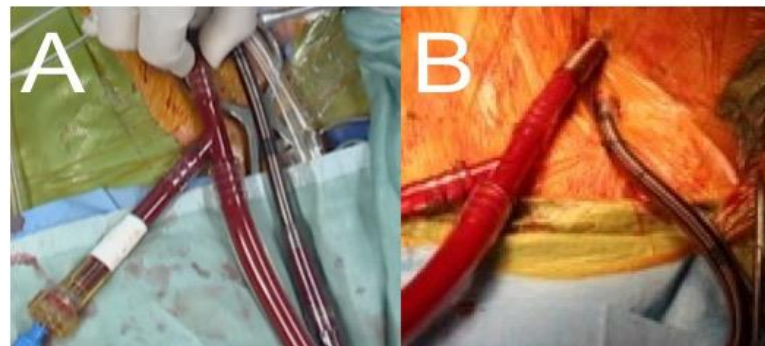
### Peripheral vascular cannulation and IntraClude™ positioning

A 4-cm right groin incision provide access to the right common femoral artery and vein during which care is taken to avoid the medial lymphatic rich regions. Following systemic heparinization and confirmation of an activated clotting time more than 400 seconds, the femoral vein is punctured first by using the Seldinger technique. A radio-opaque guidewire is inserted into the right atrium under TEE or fluoroscopic guidance, after which the QuickDraw™ venous cannula is advanced over the guidewire and secured with the cannula tip adjacent to the intraatrial septum. Vacuum assist venous drainage is a necessary adjunct for femoral venous cannulation. The common femoral artery is similarly punctured above the deep branch bifurcation followed by the TEE guided insertion of a guidewire into the descending aorta. The artery is subsequent dilated and an appropriately sized EndoReturn™ cannula inserted, de-aired, secured and observed for pulsatile waveforms. The use of peripheral limb saturation monitoring is suggested to monitor for leg ischemia during peripheral CPB, but the routine use of distal perfusion strategies, which include additional cannulation, is controversial and not generally advocated.

The IntraClude™ catheter device is inserted through the EndoReturn™ side-arm, de-aired and carefully advanced over its guidewire across the descending aorta, the aortic arch and into the ascending aorta under TEE guidance and is then locked into position (Figure 4A). Total percutaneous cannulation using vascular closure devices [39] can be performed as a favourable alternative (Figure 4B), but is not advocated if inexperienced. Peripheral vascular spasm may occur and can be identified by dampening of the arterial curve on the CPB machine, which then requires contralateral cannulation. This is achieved with the insertion of an Optisite™ cannula in the left common femoral artery, which is then connected to the EndoReturn™ tubing in a Y-configuration arterial inflow circuit. CPB- and systemic hypothermia to 32 degrees Celsius are carefully initiated. CPB pressures more than 300 mmHg require temporary flow cessation and contralateral cannulation as described.

It is reported that insufficient CPB flow occur in 0.2%-, guidewire resistance in 0.6%- and cannulation related aortic dissection in 0.2% of PAS procedures, which emphasises the importance of meticulous preoperative aorta-iliac-femoral-axis evaluation, access planning and careful guidewire manipulation techniques [40]. Central aortic cannulation by sternotomy conversion is advocated to ensure patient safety in cases of concern or persistent difficulty. Alternative cannulation access, which include right axillary artery or direct central aortic cannulation is not advised for the initial PAS learning experience. Peripheral saturation monitoring of the cannulated limb should be mandatory to detect hypoperfusion and the routine use an additional distal perfusion cannula is utilised in some centres.

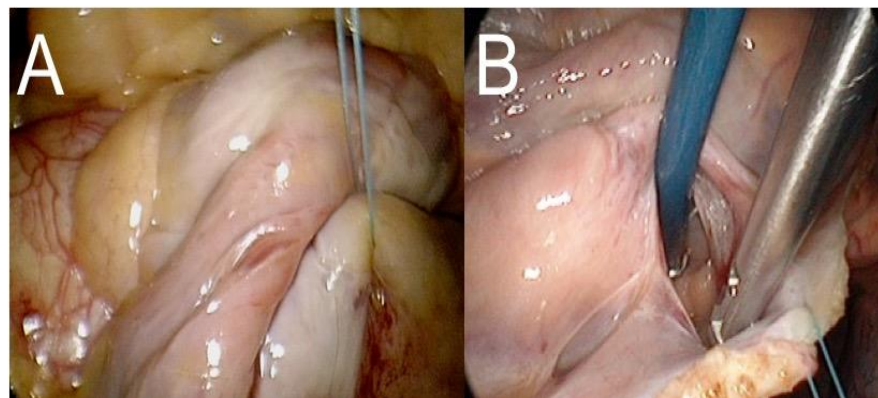




**Figure 4** (A) Peripheral cannulation through open exposure. (B) Total percutaneous cannulation

#### Atrial exposure and preparation

Once safe CPB is ascertained, a longitudinal pericardiectomy is performed above the phrenic nerve, with subsequent exteriorised retraction sutures used to provide unobstructed endoscopic views and working port access of the superior- and inferior vena cava, aorta, atria and interatrial groove (Figure 5A). An additional suspension suture on the intraatrial groove provides additional exposure for an uncomplicated left atriotomy. The oblique sinus is exposed and the intraatrial groove developed in preparation for atriotomy (Figure 5B).



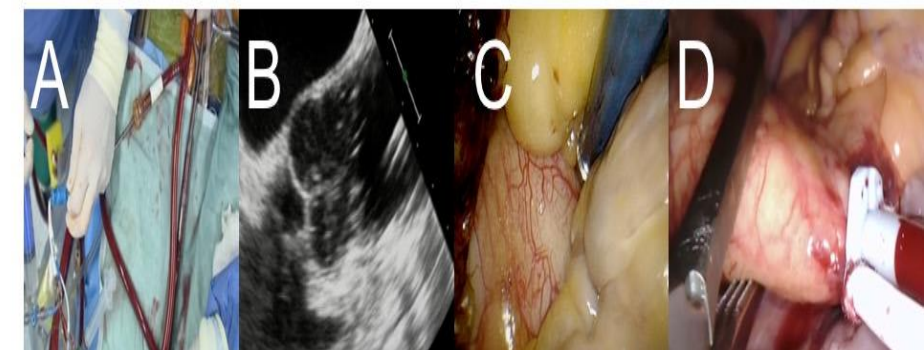
**Figure 5.** (A) Retraction of the intraatrial groove. (B) Oblique sinus exposure

#### IntraClude™ inflation, antegrade cardioplegia delivery and venting

Once all team members confirm satisfactory parameters and readiness, the assisting surgeon stabilises the EndoReturn™ cannula with his / her right hand, the IntraClude™ device position is reconfirmed by TEE, partially inflated to approximately 75% of the volume of the ascending aorta and adenosine (0.25 mg/kg) manually syringe-flushed through the device port to achieve rapid diastolic cardiac arrest (Figure 6A). The balloon is then fully inflated under TEE guidance and positioned between the sinotubular ridge and innominate artery (Figure 6B) while antegrade cardioplegia is delivered and monitored by aortic root- and cardioplegic line pressures.

The retrograde CPB inflow will push the balloon towards the aortic valve and it is important to pull the device back under TEE guidance to ensure it remains at the sinotubular junction. It is then locked in position while ensuring satisfactory right arterial line pressures. Endoscopic visualisation and palpation of the aorta with a rigid sucker confirm TEE positioning (Figure 6C). Sudden loss of radial artery trace suggests innominate artery obstruction due to dislodgement and require rapid repositioning. Even though the safety of current PAS technology compared to direct external aortic clamping strategies utilized in MIAS are well described [41-44], emerging centres should also be familiar with alternative external aortic clamping-, cardioplegia delivery and antegrade venting techniques.

Following the placement of a long antegrade venting / cardioplegia needle into the ascending aorta, the transverse sinus is carefully developed with blunt dissection and an external aortic clamp carefully introduced through a separate port to cross-clamp the aorta under endoscopic vision (Figure 6D). The clamp is applied without injuring the pulmonary artery or left atrial appendage. The infrequent application of ventricular fibrillation should also be mentioned. Conversion to sternotomy is strongly advocated if any difficulties are anticipated or occur.



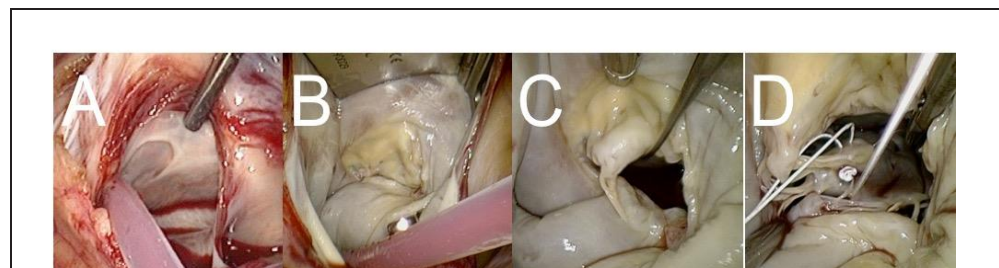
**Figure 6.** (A) IntraClude™ inflation under (B) transoesophageal echocardiographic guidance, which is followed by (C) manual confirmation of the device position. (D) External aortic clamping across the transverse sinus with antegrade cardioplegia and venting.

### Atriotomy and valve exposure

Following a generous left atriotomy (Figure 7A), a left atrial retractor with collapsing side arm (USB medical, Hartboro, USA) is inserted into the left atrium, followed by the placement of a cardiotomy vent into the left superior pulmonary vein (Figure 7B). The retractor blade angle can be manually adjusted to ensure unobstructed endoscopic visualization and single shaft instrument access to the mitral valve (MV) and it is recommended to invest adequate time and effort in establishing optimal visualization for procedural ease, especially for suture placement in the anterior MV annulus. Superior- and inferior vena cava occlusion is required for safe right atriotomy and can be achieved with clamps, tape-snares or endoballoon occlusion (Reliant™, Medtronic, Minneapolis, USA) through the internal jugular- and femoral vein respectively.

Experienced centres may only use femoral vein cannulation and by retracting the cannula into the inferior vena cava with careful vacuum assisted drainage and flow adjustments, obtain access to the tricuspid valve (TV). It is advocated that emerging centres utilise bicaval venous drainage and safe caval occlusion. Modified TV-retractors or exteriorising sutures can be utilised to obtain easy access and working angles.

For intraatrial neoplasm excision, the risk of fragmentation may prohibit the use of an atrial retractor and visualization can subsequently be established by traction sutures. In pronounced pectus excavatum deformities, the retractor may be positioned on the left parasternal border. The antero-posterior retraction distance between the right atrium and anterior chest wall may be extremely limited and additional manoeuvres are required to facilitate exposure, which include tilting the patient maximally to the left while applying low positive end-expiratory pressure to the left lung.



**Figure 7.** (A) Left atriotomy. (B) Retractor placement. (C) Valve analysis. (D) Neochord placement.

### Intraatrial and atrioventricular valve procedures

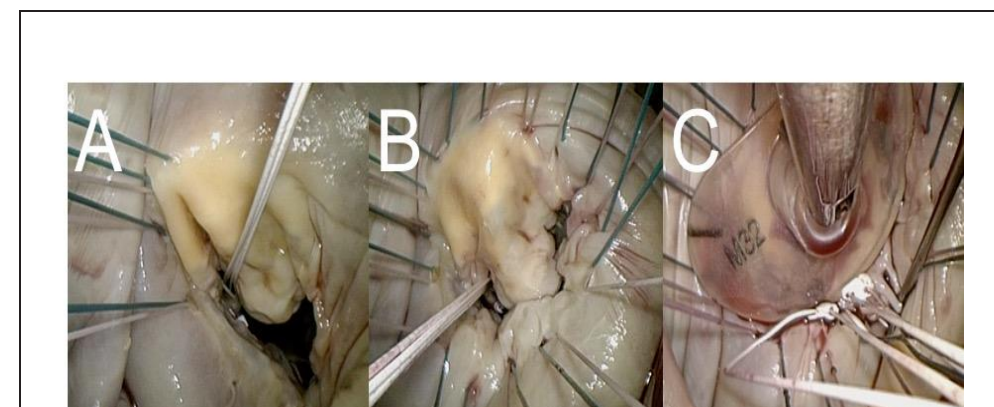
Large PAS series report the incidence of isolated MV-, isolated TV and combined MV and TV procedures to be 76.0%, 1.9% and 22.1% respectively [40]. It is advocated that simple isolated MV or

TV procedures are selected during the initial learning experience. The findings of a thorough intraoperative intraatrial inspection and systematic valve analysis should correlate with the pathology identified by preoperative TEE (Figure 7C). Routine subvalvular, valvular and annular repair- and replacement procedures can be performed using special long shafted instruments. In cases of MV repair, it is suggested that subvalvular neochords (Gore-Tex™, Gore & Associates Inc., Arizona, USA) are placed first if required (Figure 7D) and that annuloplasty suture placement start at P1 progressing up to mid-A2 segment (Figure 8A). Possible IntraClude™ rupture can occur with deep suturing in this zone and requires awareness.

Experienced centres advocate the use of additional traction maneuvers, which include a retracting steel wire, to improve MV exposure. Segments P3 to mid-A2 sutures are subsequently placed, followed by the remainder of P1 to P3 (Figure 8B). This sequence prevents distortion of the annulus and allows for perfect exposure. The valve is appropriately sized (Figure 8C) and then parachuted into position. The technique of knot tying deserves special mention (Figure 9A), as long shafted knot-tying devices require continuous suture tension provided by the surgical assistant and good coordination between the surgeon and assistant (Figure 9B). Knotting devices (e.g. Core-knot™, LSI solutions, New York, USA; other options exist) can also be utilised.

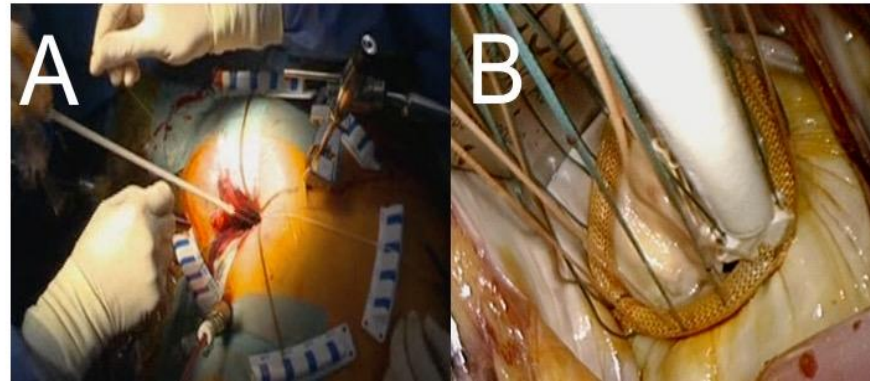
Experienced centres report a 96.4% MV repair success for primary annular dilatation and degenerative valves, with MV- (Figure 10A) and TV (Figure 10B) repair procedures constituting 82% of experienced PAS program [40]. Simple atrial septal defects can be corrected with appropriately sized patch closure (Figure 11A).

The base of intraatrial neoplasms are widely excised without manipulation and any defects reconstructed accordingly. Cryoablation for atrial fibrillation (Figure 11B) is performed with an argon-gas surgical ablation system (Medtronic, Minneapolis, USA) prior to annuloplasty suture placement and patent foramen ovale (PFO) routinely closed in 2 layers with a running 3-0 polypropylene suture.

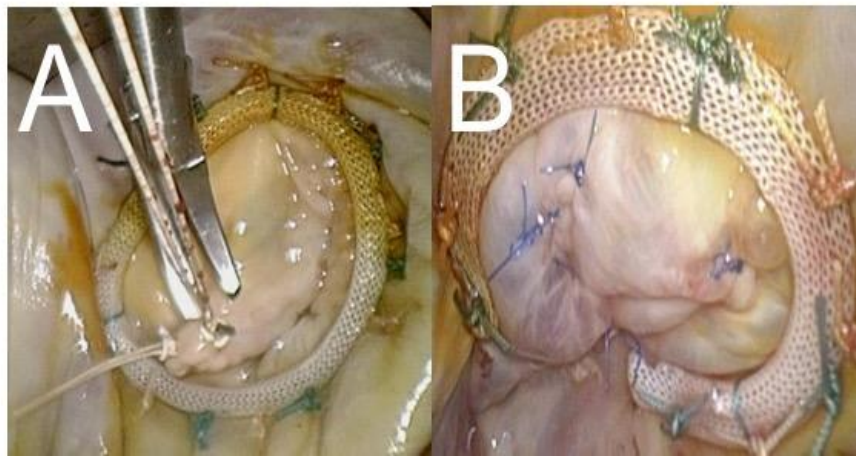


**Figure 8.** (A) Annular suture placement starting from P1 to mid-A2 segment. (B) Completed annular suture placement. (C) Annular ring sizing

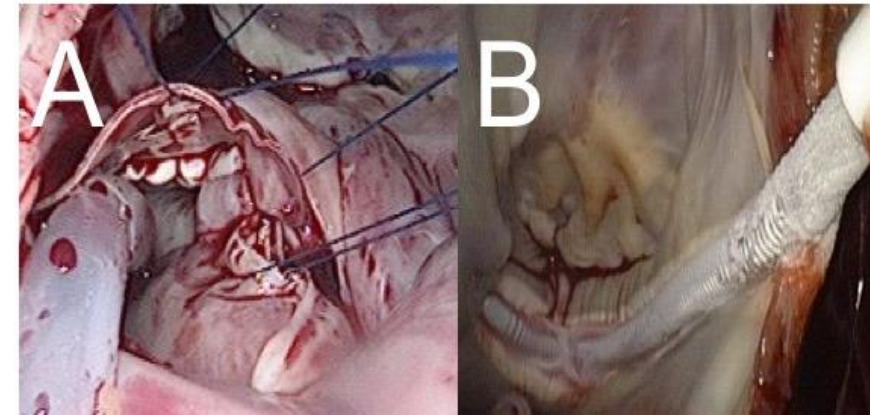




**Figure 9.** (A) Extrathoracic knotting with a surgical assistant and subsequent (B) sliding of the knot onto the annular ring.



**Figure 10.** Complex repair of (A) mitral- and (B) tricuspid valve



**Figure 11.** Non-atrioventricular valve procedures considered safe for initiating a Port Access™ program include (A) simple atrial septal defect patch closure and (B) cryoablation for atrial fibrillation.

#### De-airing and procedure conclusion

Once the intended procedure is satisfactorily completed, the left superior pulmonary venting catheter is positioned across the MV into the left ventricle and the left atrium closed with two running 3-0 polypropylene sutures from the superior- and inferior incision apex respectively, which is initially snared with the vent across the mitral valve and subsequently tied once the vent is removed. De-airing under TEE guidance is achieved by filling of all cardiac chambers, antegrade aortic root venting through the IntraClude™ device and left ventricular venting through the cardiomy suction vent in conjunction with continuous CO<sub>2</sub> insufflation of the right hemithorax. A temporary epicardial pacing wire is placed on the left ventricular diaphragmatic surface before deflating the IntraClude™ device with the patient in Trendelenburg position.

Once general intraoperative parameters are stable and systematic TEE valve- and contractility analysis confirm satisfactory results and are satisfactory, CPB is discontinued and the deflated IntraClude™ device carefully removed. Femoral venous decannulation is performed first, followed by femoral artery decannulation once volume infusions are completed. Post-decannulation femoral artery patency should be confirmed by duplex doppler or pulse palpation and any distal perfusion concerns should be immediately addressed by either contrasted angiography and/or reexploration. The cardiomy suction venting- and atrial retracting incisions are utilised for drainage tubes into the pericardium and hemithorax. The pericardium is subsequently loosely approximated and all wounds sutured in layers to prevent subcutaneous surgical emphysema or lung herniation. Postoperative cardio-respiratory support, sedation, analgesia and other appropriate medication are continued in

intensive care, with an individualised in-hospital treatment pathway supervised by a multidisciplinary team.

### OVERCOMING SPECIFIC LEARNING CURVES AND THE POTENTIAL ROLE OF SIMULATION TRAINING

Simple atrial septal defect-, intraatrial myxoma- and uncomplicated valve procedures are preferred procedures during the initial learning curve. Hunter [31] identified AVV repair techniques, TEE-guided cannulation, incision placement and setup, transition to single shaft instrument use, AVV visualization and CPB strategies as seven key aspects that contribute to a steep learning curve. The importance of a team consensus on time limit definitions where conversion is warranted is advised to ensure continuous patient safety during the learning period. Holzhey [45] identified the typical number of operations to overcome the learning curve to range between 75 and 125 procedures and further suggested that more than 1 procedure per week is required to maintain acceptable results. De Praetere [46] reported the learning curve to be 30 procedures, with a significant reduction in aortic cross-clamp time before and after the end of the learning curve. In an era of decreasing surgical volume, simulation team training is strongly advocated (Figure 12).

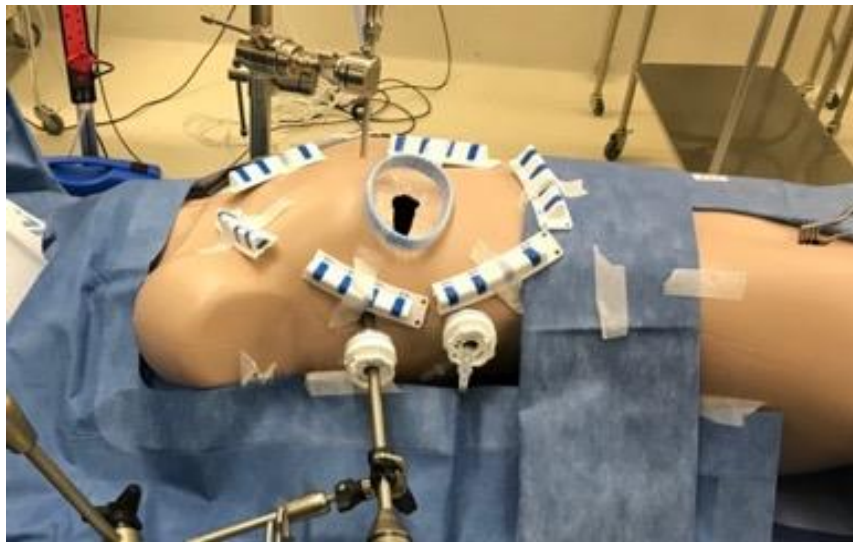


Figure 12. Port Access™ simulator

### FUTURE PERSPECTIVES AND CONCLUSION

TC and MIAS technology will continue to evolve and efforts to simplify these platforms will continue as robotic technology-, instrumentation and imaging modalities develop. PAS is proven to be safe and effective for simple and complex AVV surgery and is considered to be a reliable alternative to meet increasing patient demands for less invasive surgical procedures within the context of healthcare trends that aim limits cost-, time- and hospital resources. Experienced centres offer PAS without exclusion criteria, but careful planning and implementation of new programs should focus on risk management and excellent outcomes. Patients are the greatest advocates of a successful PAS program and every effort to reduce adverse outcome risk within a team context should be priority.

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# CHAPTER 5

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Mitral valve replacement – current and future perspectives

Van der Merwe J, Casselman F

**ABSTRACT**

The favourable outcomes achieved with modern mitral valve repair techniques redefined the role of mitral valve replacement. Various international databases report a significant decrease in replacement procedures performed compared to repairs and contemporary guidelines limit the application of surgical mitral valve replacement to pathology in which durable repair is unlikely to be achieved. The progressive paradigm shift towards endoscopic- and robotic mitral valve surgery are also paralleled by rapid developments in transcatheter devices, which is progressively expanding from experimental approaches to becoming clinical reality. This paper outlines the current role and future perspectives of contemporary surgical mitral valve replacement within the context of mitral valve repair and the dynamic evolution of exciting transcatheter alternatives.

**INTRODUCTION**

The rapid development, favourable impact and simplification of durable mitral valve repair techniques redefined the modern role of mitral valve replacement [1-5]. The significant decrease in mitral valve replacement procedures performed in developed countries parallel modern international guidelines that strongly advocate mitral valve repair whenever possible [6-9]. In addition, the increasing reports of experimental catheter-based device implantation are appealing to both clinicians and patients [10]. This paper outlines the current role and future perspectives of contemporary surgical mitral valve replacement within the context of mitral valve repair and the dynamic evolution of exciting transcatheter alternatives.

**INDICATIONS FOR MITRAL VALVE REPLACEMENT**

Current guidelines limit mitral valve replacement to irreparable valve pathology that will result in poor durability outcomes, especially in patients unlikely to tolerate future reinterventions. Factors that contribute to poor repair durability and that will require future reintervention include significant annular calcification, valvular dystrophic-, inflammatory- or infective changes, subvalvular thickening or fusion and space obliteration and progressive cardiomyopathy [11].

The persistently high incidence of rheumatic valvular disease with subsequent mitral valve stenosis in developing countries favour mitral valve replacement if primary percutaneous mitral valve balloon valvuloplasty is unavailable or clinically contraindicated. Aggressive annular decalcification and heroic repair strategies are reported with inconsistent long term outcomes [12-13]. Advanced valvular cardiomyopathy, age and debilitating comorbidities are associated with poor mitral valve surgical outcomes and it is reported that a substantial portion of severely symptomatic mitral valve patients are prohibited surgical intervention by institutional heart teams for these reasons [14-15].

The progressive clinical application of transcatheter replacement devices will most likely offer therapeutic alternatives to these patients and redesign current guidelines and recommendations for the generic approach to mitral valve disease.

**CURRENT PROSTHESIS TYPES AND SELECTION**

The surgical replacement of a stenotic or insufficient mitral valve is based on the premise that the prosthesis type chosen will have a beneficial impact on cardiac function and quality of life within the context of perioperative risks and long term prosthesis complications. In modern practice, seven mechanical [16-23], six stented biological porcine- [24-28] and one bovine pericardial prostheses [29] are available and approved for clinical use, which are classified and illustrated in table 1 and figure 1 respectively. The technical specifications and hemodynamic profiles of each device are well described and should be integrated in the prosthesis selection process. Mechanical valves are generally acquitted from structural failure [30], but require life-long anticoagulation with associated thromboembolic and bleeding risks. Biological valves are inevitably subjected to structural degeneration and may require



future reintervention. Current international recommendations for bioprosthetic implantation include informed patients that refuse mechanical valves, when safe therapeutic mechanical valve anticoagulation levels are unlikely to be achieved or contraindicated due to bleeding risks, when mechanical valve thrombosis occur despite sufficient anticoagulation, when pregnancy is contemplated in young woman, when future reinterventions can be performed at low risk, patients older than 70 years and patients with life expectancy judged to be less than the presumed durability of the bioprosthesis.

A mechanical prosthesis is recommended according to the desire of the informed patient if there are no contraindications for long-term anticoagulation, if risk factors for accelerated structural valve deterioration are absent, patients already on anticoagulation as a result of having a mechanical prosthesis in another valve position, in patients younger than 65 years, in patients with a reasonable life expectancy for whom future redo valve surgery would be at high risk and in patients already on long-term anticoagulation due to high risk of thromboembolism. The choice of prosthesis should be individualized within the context of patient expectations, values and healthcare preferences. The advent of transcatheter mitral valve devices will offer exciting alternatives to patients currently deemed unfit for surgery and will undoubtedly redefine the indications for mitral valve replacement in the future.

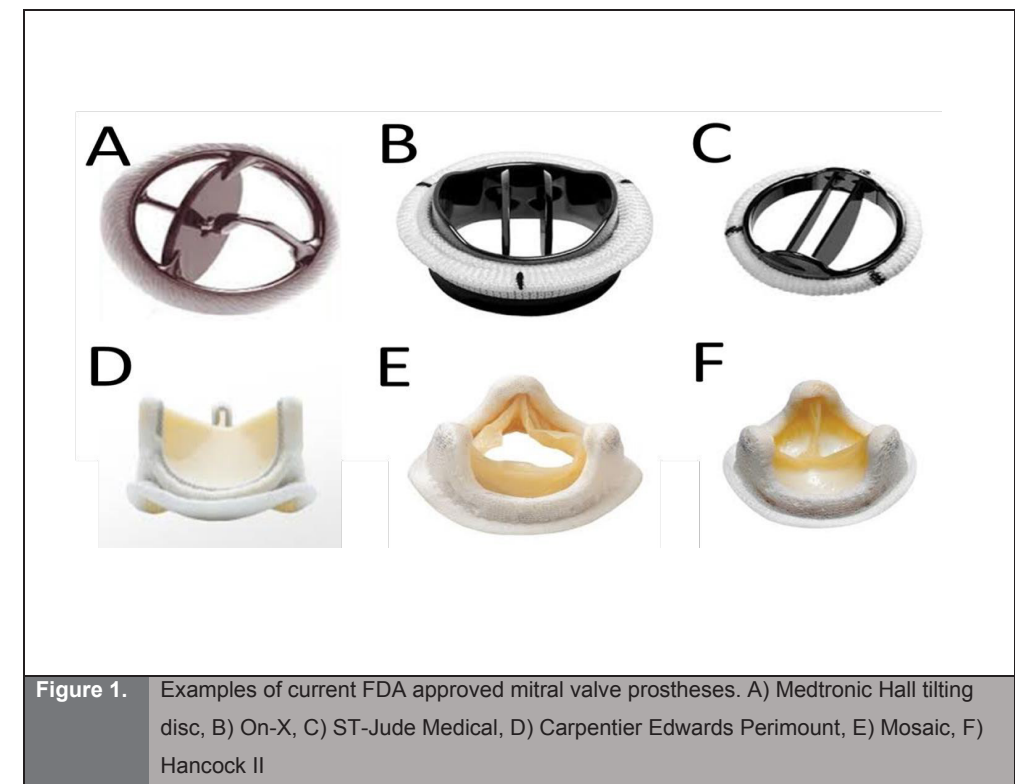
#### TECHNICAL CONSIDERATIONS AND OPERATIVE COMPLICATIONS

Median sternotomy is still the most common incision for mitral valve surgery, while various minimal access, endoscopic (Figure 2A) - and robotic approaches are becoming increasingly established as excellent alternatives [31-32].

Table 1. Current Food and Drug Administration (FDA) approved mitral valve prosthesis	
Mechanical valves	Bioprosthetic valves
Starr-Edwards	Porcine
Tilting disc	Hancock I
Medtronic hall tilting disc	Hancock II
Omnicarbon tilting disc	Carpentier Edwards Porcine
Bi-leaflet	Mosaic
St-Jude Medical	St-Jude Biocor
Carbomedix	Pericardial
ATS	Carpentier Edwards-Perimount
On-X	

The mitral valve can be accessed and exposed through either Sondergaard's groove, transeptally or by a transatrial oblique approach [33]. Native subvalvular apparatus should be preserved or reinforced to maintain left ventricular geometry and function [34-35]. Extreme calcification of the posterior annulus may require radical removal, which partially detaches the left atrium from the left ventricle. Sutures

should be placed into the annulus and it is generally advocated to use non-everting stitches for bioprosthetic valves and everting stitches for mechanical valves. Leaflet mobility should be assessed to ascertain no entrapment by subvalvular structures. It is generally recommended that mechanical prosthesis should be orientated in an anti-anatomic fashion [36] and bioprosthetic strut location orientated such that contact with the ventricular wall and impingement on the left ventricular outflow tract are avoided.



**Figure 1.** Examples of current FDA approved mitral valve prostheses. A) Medtronic Hall tilting disc, B) On-X, C) ST-Jude Medical, D) Carpentier Edwards Perimount, E) Mosaic, F) Hancock II

Left ventricular rupture occur in 1% of procedures and can occur at the level of the annulus, papillary muscles or mid-ventricular zones [37]. It is associated with aggressive decalcification and endocardial disruption that result in the intermyocardial fibre dissection of blood with subsequent reported mortality of 50%. Immediate recognition and replacement of the valve with dissection tract incorporation is required.

## POSTOPERATIVE OUTCOMES, LONG TERM FOLLOW-UP AND COMPLICATIONS

Operative mortality associated with isolated mitral valve replacement is reported to range between 4-7% and is influenced by age, premorbid valvular cardiomyopathy and other comorbidities [38-39]. Lower operative mortalities were reported with minimally invasive approaches [40]. There are no differences in 10-year survival between mechanical and biological valves when patient characteristics are taken into account, which is reported to range between 50 and 60% [41-42].



**Figure 2.** Endoscopic mitral valve surgery using long shaft instruments and peripheral cannulation

Thromboembolism is the most common postoperative complication of both bioprosthetic and mechanical valves and occurs at a rate of 1.5-2.0% per patient year and is significantly increased in chronic atrial fibrillation and large left atrial size [43-44]. All mitral valve prostheses require postoperative anticoagulation, with lifelong Vitamin K antagonists recommended for all patients with a mechanical prosthesis or bioprostheses who have other indications for anticoagulation [45]. Current guidelines suggest target INR levels according to prosthesis thrombogenic risk. Carbomedics, Medtronic Hall, St

Jude Medical and ON-X are regarded as low risk and require mean INR levels above 2.5, whereas all other bileaflet valves are considered medium risk for which INR levels above 3 are suggested. Lillehei-Kaster, Omniscience, Starr-Edwards, Bjork-Shiley and other tilting-disc valves are classified as high risk and require mean INR levels above 3.5. Patient-related risk factors are also considered and include mitral or tricuspid valve replacement, previous thromboembolism, atrial fibrillation; mitral stenosis of any degree and left ventricular ejection fraction less than 35%.

The presence of one or more patient risk factors requires a target INR level increase by 0.5. Current guidelines [8-9] recommend the use of vitamin K antagonists for the first three months after implantation of a bioprosthesis. Bleeding rates related to the use of Vitamin K antagonists are more frequent with mechanical valves, which are reported to be 2-4% per patient year of which the majority occur within the first year following surgery. The addition of low-dose aspirin should be considered in patients with concomitant atherosclerotic disease and in patients with a mechanical prosthesis after thromboembolism despite adequate INR [8]. New oral anticoagulants (NOAC), including factor 10 inhibitors, are currently not recommended as substitutes for Vitamin K antagonists [8-9]. In case of valve thrombosis, thrombolytics may be used to treat mitral prosthetic thrombosis in the absence of cardiogenic shock. If thrombolysis fails, or if there is hemodynamic compromise, valve replacement is required [46].

Prosthetic valve endocarditis risks are similar for both types and are reported to be 1.5- 3% for the 1st year and 3-6% within 5 years. Long term endocarditis risk is 0.2-0.35% per patient year thereafter and appears to be slightly higher with mechanical valves. Endocarditis prophylaxis and management of prosthetic valve endocarditis are extensively described in specialized guidelines [47].

Prosthetic valve degeneration is the most significant complication of bioprosthetic valves. The 10 year freedom from clinically significant structural valve degeneration associated with biological valves are reported to be 78%, 89% and 100% when implanted in patients younger than 60-, between 60-70- and older than 70 years respectively [48-49]. Annual echocardiographic follow-up is recommended after the first 5 years following implantation to detect early signs of structural valve degeneration, regurgitation or features of progressive stenosis, which include calcification, leaflet stiffening and reduced effective orifice area.

Reoperation is warranted in symptomatic patients with severe regurgitation or significant transprosthetic gradient increase and should be considered in asymptomatic patients with significant prosthetic dysfunction, provided that they are at low risk of perioperative complications. Prophylactic replacement of a bioprosthesis that is older than 10 years and without structural deterioration, may be considered if an operative intervention is required on another valve or on the coronary arteries.

Percutaneous balloon interventions should be avoided in the treatment of stenotic left-sided bioprostheses. Treating bioprosthetic failure by transcatheter valve-in-valve implantation is feasible in patients considered to be inoperable or high-risk [50], but is not an established alternative to surgery. Patient prosthesis mismatch can occur when the indexed geometric orifice area is less than 1.5cm<sup>2</sup>/m<sup>2</sup> and may warrant replacement if high gradients and symptoms persist despite optimal medical therapy [51].

Paravalvular leak is reported to occur in 1.5% of patients [52-53]. It can be avoided by selecting a prosthesis with a large sewing ring in heavily calcified or poor quality annular tissue. The use of pledgeted, non-everting mattress sutures and reinforcing the annulus with Teflon strips are reported [54-55]. Reoperation is recommended if diagnosed early postoperatively, if related to endocarditis, or if associated with hemolysis requiring repeated blood transfusions or symptoms. Transcatheter closure is feasible, but reports that confirm consistent efficiency are limited at present [56]. It may however, be considered in heart team determined high risk or inoperable patients.

### FUTURE PERSPECTIVES

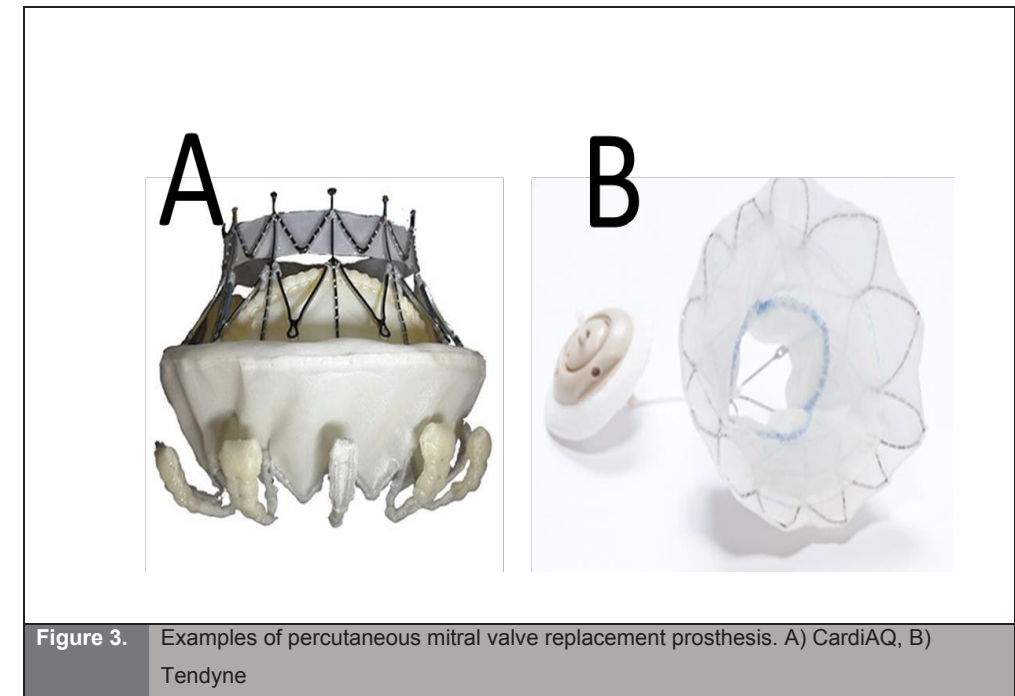
The rapid development of catheter-based replacement devices and the continuous changes in patient expectations provide exciting prospects for the future treatment of mitral valve disease. The feasibility of transcatheter mitral valve replacement was demonstrated on June 12th, 2012, when Lars Sondergaard implanted the first generation CardiAQ valve system (CardiAQ Valve Technologies, Inc., Irvine, CA, USA), through transfemoral-transseptal access in an inoperable 86-year-old patient [57].

Four transcatheter mitral valve systems [58-60] that have subsequently been implanted in humans (Figure 3) and are in current clinical use include the second generation CardiAQ valve system (Edwards Lifesciences, Irvine, California, USA), Tiara™ valve (Neovasc Inc., Richmond, Canada), Tendyne™ valve (Tendyne Inc., Roseville, MN, USA) and Twelve valve (Medtronic, Minneapolis, USA).

These valves consist of nitinol self-expanding frames, bovine pericardial leaflets (Tendyne, however is porcine), a fabric sealing skirt (CardiAQ consists of a pericardial skirt) and are delivered through direct transapical access. CardiAQ can also be delivered by transfemoral-transseptal access. Other devices, such as HighLife (HighLife SAS, Paris, France), Caisson (Caisson Interventional, LLC, Maple Grove, USA) and M-Valve (Boston Scientific, Massachusetts, USA) are in preclinical development and will attempt to further offer innovative design solutions to overcome the challenges of catheter-based mitral valve replacement [61].

### CONCLUSION

The role of mitral valve replacement is under continuous reevaluation and is at present limited to irreparable valves or patients at high risk for future reinterventions. Successful outcomes are determined by meticulous perioperative risk assessment, prosthesis selection, anticoagulation management and long term clinical surveillance in well informed and compliant patients. Endoscopic and robotic surgical approaches introduced attractive alternatives to conventional sternotomy access and are progressively becoming favored as the preferred surgical approaches by heart teams worldwide. Transcatheter mitral valve implantations are now a clinical reality and will undoubtedly redefine the role of mitral valve replacement in the near future.



**Figure 3.** Examples of percutaneous mitral valve replacement prosthesis. A) CardiAQ, B) Tendyne

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# PART 2

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RISK REDUCTION STRATEGIES IN PORT ACCESS™ SURGERY



# CHAPTER 6

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Reasons for conversion and adverse intraoperative events in endoscopic Port Access™ atrioventricular valve surgery and minimally invasive aortic valve surgery

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## ABSTRACT

### Objective

This study reports the factors that contribute to sternotomy conversions (SC) and adverse intraoperative events in minimally invasive aortic- (MI-AVS) and endoscopic Port Access™ atrioventricular valve surgery (MI-PAS).

### Methods

In total, 3780 consecutive patients with either aortic- or atrioventricular valve disease underwent minimally invasive valve surgery (MIVS) at our institution between February 1st 1997 and March 31st 2016. MI-AVS was performed in 908- (mean age 69.2±11.3 years, 45.2% female, 6.2% redo-cardiac surgery) and MI-PAS in 2872 patients (mean age 64.1±13.3 years, 46.7% female, 12.2% redo-cardiac surgery).

### Results

A cumulative total of 4415 MIVS procedures (MI-AVS = 908, MI-PAS = 3507) included 1537 valve replacements (MI-AVS = 896, MI-PAS = 641) and 2878 valve repairs (MI-AVS = 12, MI-PAS = 2866) in isolation or combination. SC was required in 3.0% (n = 114 of 3780) of MIVS patients, which occurred in 3.1% (n = 28 of 908) of MI-AVS- and 3.0% (n = 86 of 2872) of MI-PAS patients respectively. Reasons for SC in MI-AVS included inadequate visualization (n = 4, 0.4%) and arterial cannulation difficulty (n = 7, 0.8%). For MI-PAS, SC was required in 54 (2.5%) of isolated mitral valve procedures (n = 2183). Factors that contributed to SC in MI-PAS included lung adhesions (n = 35, 1.2%), inadequate visualization (n = 2, 0.1%), ventricular bleeding (n = 3, 0.1%) and atrioventricular dehiscence (n = 5, 0.2%). Neurological deficit occurred in 1 (0.1%) and 3 (3.5%) of MI-AVS and MI-PAS conversions respectively. No operative- or 30 day mortalities were observed in MI-AVS conversions (n = 28). The 30-day mortality associated with SC in MI-PAS (n = 86) was 10.5% (n = 9).

### Conclusion

MIVS is increasingly being recognized as the “gold-standard” for surgical valve interventions in the context of rapidly expanding catheter-based technology and increasing patient expectations. Surgeons need to be aware of factors that contribute to SC and adverse intraoperative outcomes to ensure that patients enjoy the maximum potential benefit of MIVS and to apply effective risk reduction strategies that encourage safer- and sustainable MIVS programs.

## INTRODUCTION

We are currently witnessing an evolution in catheter-based aortic- [1-2] and atrioventricular valve repair [3-4] and replacement technology [5], which is paralleled by increasing patient expectations [6] and extensive industry driven marketing that potentially favour percutaneous approaches above surgical options [7-8]. The potential benefits associated with minimally invasive valve surgery (MIVS) are now well established [9-10] and the contemporary role of conventional sternotomy (or even minimally invasive approaches) for aortic- and atrioventricular valve surgery is continuously being redefined.

It is now generally accepted that current- and future cardiac surgeons need to acquire minimally invasive valve intervention- and surgical skills to strengthen our positions in the future treatment of valvular heart disease [11]. MIVS is associated with learning curves and often deter surgeons from incorporating MIVS techniques into clinical practice in a current era of strict quality control and accountability [12], clinical governance [13-14] and an increasing patient risk profile [15]. The intention of this study is to provide an in-depth overview of factors that contribute to sternotomy conversion- and adverse intraoperative outcomes during MIVS as part of an ongoing effort to equip surgeons with safe and efficient MIVS risk reduction strategies.

## METHODS

This is a retrospective study of a single-centre MIVS database, in which the reasons for sternotomy conversions, the incidence of intraoperative major adverse cardiac- and cerebrovascular events (MACCE) and the impact of sternotomy conversion on 30-day mortality were defined as primary outcomes.

In total, 3780 consecutive patients that required aortic- or atrioventricular valve interventions underwent MIVS without exclusion criteria at our institution between February 1st 1997 and March 31st 2016. MI-AVS was performed in 908 (24.0%) patients and MI-PAS in 2872 (76.0%) patients. The relevant preoperative patient characteristics, valve pathology and surgical indications, that includes detailed valve analysis for aortic-, mitral- and tricuspid valve pathology according to Carpentier (n = 3780) are outlined in Table 1.

The mean body mass index (BMI) for MI-AVS- and MI-PAS patients were 26.5 ± 4.4 m<sup>2</sup> / kg and 25.1 ± 4.5 m<sup>2</sup> / kg respectively. The mean logistic EuroSCORE was utilised from January 1st 2007, included 534 MI-AVS- (mean 6.1±6.5) and 1713 MI-PAS patients (mean 8.6±12.4) up to date and is outlined in table 2. The median logistic EuroSCORE for MI-PAS was 4.5 (range 1.2 - 98.0).

Table 1.	Preoperative patient characteristics, valve pathology and surgical indications (n = 3780)			
	MI-AVS (n = 908)		MI-PAS (n = 2872)	
Patient characteristics	n	% of 908	n	% of 2872
Mean age (years)		69.2±11.3		64.1±13.3
Age above 80 years	152	16.7	222	7.7
Female	410	45.2	1341	46.7
Mean body mass index above 30 m <sup>2</sup> / kg	173	19.1	316	11.0
Previous cardiac surgery	56	6.2	365	12.7
Previous MI-AVS	15	1.7	-	-
Previous MI-PAS	-	-	60	2.1
Preoperative state				
Elective	867	95.5	2719	94.7
Urgent	41	4.5	153	5.3
Active endocarditis	4	0.4	62	2.2
Left ventricle ejection fraction <30%	10	1.1	83	2.9
<b>Valve pathology</b>				
Native Valve	898	98.9	2711	71.1
Degenerative/Sclerotic disease	643	70.8	2041	71.1
Rheumatic	125	13.7	231	13.7
Congenital	111	12.2	328	11.4
Endocarditis	15	1.7	102	3.4
Neoplasm	4	0.4	9	0.3
Prosthetic Valve / Ring	15	1.7	161	5.6
Structural dysfunction / Repair failure	14	1.5	159	5.5
Thrombosis	1	0.1	2	0.1
<b>Surgical indications**</b>				
Type 1	69	7.6	1064	37.0
Type 2	42	4.6	1508	52.5
Type 3	797	87.8	300	10.4

MI-AVS: minimally invasive aortic valve surgery, MI-PAS: minimally invasive Port Access™ surgery  
 \*\* Carpentier A, Adams D, Filsoufi F. Carpentier's Reconstructive Valve Surgery. Saunders Elsevier. 2010: 5-10, 217-220.

Table 2.	Preoperative mean logistic EuroSCORE*** outline as of January 1 <sup>st</sup> 2007.			
	MI-AVS (n = 534)		MI-PAS (n = 1713)	
Patient characteristics	n	% of 534	n	% of 1713
Mean logistic EuroSCORE		6.1±6.5		8.6±12.4
Chronic obstructive pulmonary disease	28	5.2	102	6.0
Extracardiac arteriopathy	38	7.1	205	12.0
Neurological dysfunction	6	1.1	52	3.0
Renal dysfunction	6	1.1	36	2.1
Active endocarditis	1	0.2	41	2.4
Critical preoperative status	3	0.6	44	2.6
Left ventricular ejection fraction <30%	5	0.9	64	3.7

\*\*\*Roques F, Michel P, Goldstone AR, Nashef SA. The logistic EuroSCORE. *Eur Heart J.* 2003; 24(9):882-3

### Surgical techniques – endoscopic Port Access™ atrioventricular valve surgery

Our techniques primary [16-17]- and redo-Endoscopic Port Access™ atrioventricular valve surgery peripheral cardiopulmonary bypass (CPB)-[20] and endoaortic balloon occlusion [21] include routine preoperative aorta-iliac-femoral-axis evaluation by an additional iliac artery contrast injection during cardiac catheterization or by magnetic resonance angiography, venous drainage through the right internal jugular- (16-18 Fr, Optisite™, Edwards Lifesciences, Irvine, California, USA) and femoral vein (22-25 Fr, QuickDraw™, Edwards Lifesciences, Irvine, California, USA). Arterial inflow is established by a femoral artery cannula with Y-arm (21 Fr or 23 Fr, EndoReturn™, Edwards Lifesciences, Irvine, California, USA) through which an endoaortic balloon (IntraClude™, Edwards Lifesciences, Irvine, California, USA) is advanced to establish aortic occlusion and delivery of cold antegrade crystalloid cardioplegia. All guidewires and cannulae are advanced and positioned under transesophageal echocardiography (TEE) guidance, with venous cannulation established first using standard inferior vena cava and bicaval TEE views. Femoral artery cannulation and subsequent endoballoon advancement are guided by standard TEE images of the descending aorta, aortic arch, ascending aorta, sinotubular junction and aortic root.

A 4cm non-rib-spreading working port incision is established over the 4th anterior-axillary intercostal space and special endoscopic long shafted instruments utilized to perform standard mitral- (MV) and tricuspid valve (TV) procedures. Argon-gas cryoablation (Medtronic, Minneapolis, USA) and left atrial appendage closure are performed in patients with atrial fibrillation or previous stroke.

Patent foramen ovale are routinely closed and post-procedural de-airing accomplished by left atrial- and aortic balloon venting catheters, continuous flooding of the operative field with CO<sub>2</sub> and TEE evaluation for residual air in the left ventricle. Temporary epicardial- or transjugular ventricular pacing wires are routinely placed. Preoperative imaging to evaluate lung adhesions are not routinely performed.

### Surgical techniques – minimally invasive aortic valve surgery

Our surgical technique for MI-AVS [22-24] includes a 4- to 8-cm midline skin incision starting at the manubrium-sternal joint and partial upper J-shape mini-sternotomy with an oscillating saw down to either the 3rd or 4th right intercostal space. Percutaneous femoral- and internal jugular veins are utilized for venous drainage and direct antegrade ascending aorta cannulation for arterial inflow. Femoral artery and vein cannulation through a 3- to 4-cm oblique groin incision may be used in selected patients with short aortas or impaired working space.

Cold crystalloid cardioplegia is used in addition to mild systemic cooling (32 degrees) and delivered through the aortic root for induction and directly in the ostia to maintain arrest. Left ventricle distention is prevented by intermittent antegrade aortic root venting in cases of severe aortic valve incompetence.

Incision and closure of the aorta, valve excision, debridement, suture-placement and prosthetic implantation are all performed using standard instrumentation. Extensive decalcification is facilitated by table angle manipulation, careful resection to avoid fragment loss and meticulous saline flushing. De-airing is achieved by continuous CO2 flooding of the operative field and aortic root vent under TEE surveillance.

### Data analysis

All intraoperative data were collected from a prospective database. The continuous- and categorical outcomes were assessed by the incidence of adverse events (mean ± standard deviation) and the calculated intraoperative- and 30-day mortality. The study was approved by the institutional ethics review committee, the authors agreed to the manuscript as written and take responsibility for data integrity.

## RESULTS

### Intraoperative outcomes

In total, 4415 MIVS procedures (MI-AVS = 908, MI-PAS = 3507) were performed in 3780 consecutive patients as isolated- or combined valvular procedures per patient and included 1537 valve replacements (MI-AVS = 896, MI-PAS = 641) and 2878 valve repairs (MI-AVS = 12, MI-PAS = 2866). The procedures performed are outlined in table 3. The mean cardiopulmonary bypass- and ischemic times are described in table 4.

MI-PAS consisted of 2183 (76.0%), 54 (1.9%) and 635 (22.1%) isolated MV-, isolated TV and combined MV and TV procedures respectively. MV-repair was achieved in 96.4% (n = 1822 of 1891) of primary annular dilatation and degenerative valves and constituted 81.7% (n = 2866) of all MI-PAS procedures (n = 3507). Sternotomy conversion (SC) was required in 114 of 3780 (3.0%) patients that underwent MIVS, of which MI-AVS and MI-PAS constituted 28 (0.7%) and 86 (2.3%) respectively. SC rates during the initial 4-year learning curves were 3.7% (n = 7 of 188) and 3.3% (n = 14 of 421) for MI-

AVS and MI-PAS respectively. The reasons for SC are outlined in table 5. Conversions that occurred prior to cross-clamping or endoballoon inflation are considered as a “risk aversion strategy change” or early conversions, whereas late conversions are defined as conversions during / after cross-clamping.

For MI-PAS, SC was required in 54 (2.5%), 2 (4.6%) and 30 (4.7%) of isolated MV- (n = 2183), TV- (n = 54) and combined MV-TV (n = 635) procedures respectively. Reasons for SC in isolated MV surgery (n = 54) included poor visualization (n = 2, 3.7%), bleeding (n = 4, 7.4%), lung adhesions (n = 23, 42.6%), cannulation difficulty (n = 15, 27.8%), aorta dissection (n = 8, 14.8%) and atrioventricular dehiscence (n = 2, 3.7%). Intraoperative major adverse cardiac- and cerebrovascular events (MACCE) for the series (n = 3780) and SC (n = 114) are outlined in table 6. Significant intraoperative neurological deficit occurred in 1 (0.1%) and 3 (3.5%) of MI-AVS and MI-PAS conversions respectively.

Procedures performed	MI-AVS (n = 908)		MI-PAS (n = 3507)	
	n	% of 908	n	% of 3507
Valve replacement	896	98.7	641	18.3
Mechanical prosthesis	160	17.6	274	7.8
Biological prosthesis	736	81.1	367	10.5
Stented prosthesis	722	79.5	367	10.5
Stentless prosthesis	2	0.2	-	-
Sutureless prosthesis	12	1.3	-	-
Valve repair	12	1.3	2866	81.8
Concomitant cardiac procedures	20	2.2	1128	32.2
Left ventricle outflow tract resection	16	1.8	50	1.4
Patent foramen ovale closure	2	0.2	280	8.0
Ventricle septum defect closure	1	0.1	3	0.1
Atrial fibrillation ablation	1	0.1	819	23.4
Hybrid percutaneous coronary intervention	17	1.9	88	2.5
Concomitant non-cardiac procedures	22	2.4	-	-
Carotid surgery	4	0.4	-	-
Thymectomy	1	0.1	-	-

Table 4. Mean cardiopulmonary bypass- (CPBt) and ischemic times (It) in minutes		
Procedure	CPBt**	It***
MI-AVS (n = 908)	108.5 ± 30.0 (50 - 325)	76.8 ± 20.2 (26 - 220)
Aortic valve repair	87.8 ± 22.9 (50 - 128)	55.6 ± 15.1 (31 - 83)
Aortic valve replacement	109.8 ± 31.9 (50 - 325)	77.0 ± 20.4 (26 - 220)
MI-PAS (n = 2872)	140.7 ± 43.0 (54 - 440)	97.0 ± 31.0 (28 - 256)
Isolated MV-surgery	132.7 ± 41.3 (54 - 440)	90.9 ± 29.3 (28 - 242)
Isolated TV-surgery	140.9 ± 36.0 (76 - 242)	92.6 ± 24.1 (45 - 162)
Combined MV-TV surgery	167.7 ± 42.3 (82 - 402)	117.7 ± 30.6 (32 - 302)
MI-AVS sternotomy conversions	140.0 ± 61.5 (58-282)	75.9 ± 29.2 (39-142)
MI-PAS sternotomy conversions	149.5 ± 72.0 (63 - 402)	93.6 ± 45.9 (34 - 302)

MI-AVS: minimally invasive aortic valve surgery; MI-PAS: minimally invasive Port Access™ surgery; MV: mitral valve; TV: tricuspid valve; \*\* The mean CPBt reported in minutes (range); \*\*\* The mean It reported in minutes (range)

Table 5. Reasons for sternotomy conversion (n = 3780)				
Reasons for conversion	MI-AVS (n = 908)		MI-PAS (n = 2872)	
	n	% of 908	n	% of 2872
Early conversions	13	1.4	73	2.5
Lung adhesions	-	-	35	1.2
Poor visualization	4	0.4	2	0.1
Cannulation difficulty	7	0.8	36	1.3
Iliac vein rupture	2	0.2	-	-
Iliac artery rupture	-	-	2	0.1
Guidewire resistance	5	0.6	17	0.6
Insufficient flow	-	-	6	0.2
Aortic dissection	-	-	11	0.4
Porcelain aorta	2	0.2	-	-
Late conversions	15	1.7	13	0.5
Bleeding	9	1.0	7	0.2
Aorta bleeding	9	1.0	-	-
Ventricle perforation	-	-	3	0.1
Atrial bleeding	-	-	4	0.1
Endoaortic balloon rupture	-	-	1	0.03
Resistant arrhythmia	3	0.3	-	-
Prosthesis dysfunction	1	0.1	-	-
Increased procedure complexity	2	0.2	5	0.2

Table 6. Intraoperative major adverse cardiac- and cerebrovascular events (MACCE)				
Intraoperative MACCE for total series (n = 3780)	MI-AVS (n = 908)		MI-PAS (n = 2872)	
	n	% of 908	n	% of 2872
Cardiac death	2	0.2	7	0.2
Acute myocardial infarction	-	-	19	0.7
Congestive cardiac failure	9	1.0	29	1.0
Stroke	17	1.9	34	1.2
Intraoperative MACCE for conversions (n = 114)	n	% of 28	n	% of 86
Cardiac death	-	-	5	5.8
Acute myocardial infarction	-	-	3	3.5
Congestive cardiac failure	1	0.1	1	1.2
Stroke	1	0.1	3	3.5

#### The impact of conversion on intraoperative- and 30 mortality

The operative mortalities for the total MI-AVS- (n = 908) and MI-PAS (n = 2872) series were 2.0% (n = 18) and 2.6% (n = 74) respectively. No operative- or 30 day mortalities were observed in patients that required MI-AVS conversions (n = 28). The 30 day- and total in-hospital mortality associated with SC in MI-PAS (n = 86) were 10.5% (n = 9) and 15.1% (n = 13) respectively, of which 5 (5.8%) patients were intraoperative- and 8 (9.3%) postoperative mortalities. Intraoperative mortalities occurred secondary to atrioventricular dehiscence (n = 2, 2.3%), ventricle rupture (n = 1, 1.2%) and aortic dissection (n = 2, 2.3%). Late postoperative mortalities occurred in SC for aortic dissection (n = 2, 2.3%, day 1 and 38) and low cardiac output syndrome (n = 6, 7.0%, day 1, 2, 4, 8, 43, 59).

#### DISCUSSION

The potential benefits associated with MIVS are now well established [9-10] and the future relevance of conventional sternotomy access for valve surgery is continuously being redefined. It is generally accepted that cardiac surgeons need to expand their skills in catheter-based- and minimally invasive- approaches to remain relevant in the treatment of valvular heart disease in the current era [11]. However, strict quality control [12], clinical governance, increasing patient expectations, an aging population with increased comorbidities and extensive industry driven marketing that favour "no surgeon required" technology, are not conducive to acquiring MIVS skills [13-15].

Our MI-AVS program was initiated in October 1997 and constitutes 24.0% (n = 908) of our MIVS program (n = 3780) at present. We established the partial upper j-mini-sternotomy approach as our preferred technique irrespective of body habitus, anatomical variation, presentation or patient risk profile, which is not the case for other MI-AVS approaches [25]. It offers circumferential access to the aorta and right atrium, even in obese patients (n = 173, 19.1%) and allows for easy conversion to full sternotomy if required, which occurred in 28 (3.1%) of patients. Poor visualization accounted for 4



(0.4%) sternotomy conversions, which we limit by elevating the upper body, strategically placed retraction sutures and theatre table angle adjustments. Placement of annular U-sutures follows the same rules as in standard procedures, with the insertion of three initial commissural sutures often optimizing exposition. Cannulation related SC occurred in 7 (0.8%) patients, which emphasizes the importance of advancing all guidewires and cannula under skilled TEE surveillance, careful tactile manipulation and refraining from forcing wires through areas of resistance.

Porcelain aorta, which can be predicted by routine chest radiography [26], required deep hypothermic arrest by SC in 2 (0.2%) patients. MI-AVS is in our opinion, not recommended in cases where an aortic cross-clamp cannot be safely applied. Aortotomy bleeding required SC in 9 (1.0%) of patients and can be minimized by using two running sutures and by ensuring hemostasis and control before discontinuing cardiopulmonary bypass.

Resistant arrhythmias resulted in 3 (0.3%) conversions, which can be reduced by appropriate pharmacological interventions, the application of external defibrillation paddles and the use of paediatric internal shock paddles. We also routinely place temporary pacemaker wires on the right ventricle prior to de-clamping. Even though SC was required for prosthetic dysfunction (n = 1, 0.1%), root enlargement (n = 1, 0.1%) and for an aortic interposition graft (n = 1, 0.1%), the feasibility of MI-AVS in these contexts are well described [23]. Conversion rates improved rapidly following the initial 4-year learning curve of 3.7% (n = 7 of 188). MI-AVS sternotomy conversion had no impact on 30-day mortality.

Our MI-PAS program was initiated in February 1997 and constitutes 76.0% (n = 2872) of our MIVS program at present. It allows focused endoscopic access to the atrioventricular valves with perioperative- and long term results equal to- or better than conventional sternotomy outcomes [27]. It is considered by many to pose the most extensive MIVS learning curve and requires dedication, commitment and technical development of the whole operating team. Systematic valve evaluation, guidewire advancement and peripheral cannula placement under TEE surveillance are invaluable and considered to be a prerequisite in ensuring safe and sustainable programs.

Adverse early- and late intraoperative events that required SC, occurred in 86 (3.0%) of patients. The initial 4-year learning curve conversion rate was 3.3% (n = 14 of 421). Lung adhesions accounted for 35 (1.2%) of SC, which occurred in the context of primary- (n = 2507, 87.3%), redo-cardiac- (n = 365, 12.7%) and redo-PAS (60, 2.1%) procedures. Previous right hemithorax interventions are not considered contraindications and we do not routinely perform any special imaging investigations to identify lung adhesions. Targeted access to the valves are obtained by careful release of anterior-, mediastinal- and diaphragm adhesions without causing pulmonary tears or bleeding. Poor visualization resulted in SC in 2 (0.1%) patients and can be avoided by ensuring the correct placement of camera-, working- and retractor ports, with strategic placement of retraction sutures and appropriate table positioning, as valuable adjuncts. Obesity (n = 316, 11%) is not considered a contraindication, but not recommended in the early learning experience.

Cannulation challenges required SC in 36 (1.3%) patients and included the early identification of guidewire advancement resistance (n = 17, 0.6%) and insufficient CPB flow (n = 6, 0.2%), with aortic dissection occurring in 11 (0.3%) patients during the initial learning curve and which also accounted for 2 (0.1%) intraoperative mortalities associated with SC in our series. A low threshold to convert single-

to bilateral femoral artery cannulation ensures safe CPB and perfusion pressures in cases of insufficient CPB flow. The importance of TEE was already emphasised and controlled guidewire advancement techniques are of utmost importance [28-29]. Bleeding accounted for 7 (0.2%) of SC, which included pacemaker placement related right ventricle perforation (n = 3, 0.1%) and aortotomy bleeding (n = 4, 0.1%). We recommend temporary pacemaker placement on the diaphragmatic aspect of the muscular left ventricle, which limits the risk of right ventricle bleeding. The right atrium is closed by 2 running sutures and the left atrium by single layer.

A single event of endoaortic balloon rupture by suture puncture (0.03%) due to non-coronary sinus displacement, required SC. It can be avoided by careful initial TEE guided placement at the sinotubular junction, inflation under TEE guidance, confirmation of position prior to left aortotomy and careful annular suture placement between the antero-lateral commissure and the A2-segment. Atrioventricular dehiscence occurred in 5 (0.2%) patients, which were repaired by valve reimplantation following SC. Severe posterior annular calcification can be identified by routine preoperative imaging and should be resected with extreme caution [30].

## STUDY LIMITATIONS

This series reflects the outcomes of a single centre with extensive MI-AVS and MI-PAS experience. The use of sternotomy access was abandoned since the introduction of our respective MI-AVS and MI-PAS programs, which are routine for isolated aortic- and atrioventricular valve disease at our institution. All patients were offered these interventions with the intention to treat, which resulted in the absence of a control group or propensity matching.

The mean logistic EuroSCORE, which is standardized for sternotomy access, was utilized as control group for operative outcomes. The initial 4-year learning curves reported in this series are descriptive and were not subjected to CUSUM analysis or other statistical methodology. It is our intention to provide a platform for current and future current surgeons to adapt and adopt MIVS into their routine surgical practice.

## CONCLUSION

MIVS is evolving and increasingly being recognized as the “gold-standard” for surgical valve interventions in the context of rapidly expanding catheter-based technology and increasing patient expectations. Surgeons need to be aware of factors that contribute to SC and adverse intraoperative outcomes to ensure that patients enjoy the maximum potential benefit of MIVS by applying effective risk reduction strategies that encourage safer- and sustainable MIVS programs as part of an ongoing effort to strengthen our positions as surgeons in the future of valvular heart disease interventions.

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# CHAPTER 7

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Complications and pitfalls in minimally invasive atrioventricular valve surgery utilizing endoaortic balloon occlusion technology

Van der Merwe J, Van Praet F, Casselman F.

## ABSTRACT

### Background

This study reports the intraoperative complications, reasons for sternotomy conversion (SC) and the important pitfalls associated with minimally invasive atrioventricular valve surgery by endoaortic balloon occlusion (MIAS) that may assist emerging centres in developing safe-, efficient- and sustainable programs.

### Methods

Perioperative data for patients operated over the last 5 years was obtained from a prospective database. In total, 511 consecutive patients with isolated atrioventricular valve disease (AVV) disease underwent MIAS (mean age  $65.6 \pm 13.7$  years, 46.8% female, 21.7% redo-cardiac surgery, 5.7% previous MIAS, 2.9% isolated AVV endocarditis, 13.9% body mass index above  $30 \text{ m}^2 / \text{kg}$ ) at our institution between May 1st 2013 and April 30th 2018. The mean EuroSCORE II was  $5.9 \pm 9.4\%$  and rheumatic AVV disease was diagnosed in 32 (6.3%) patients. Other surgical indications included chronic atrial fibrillation ( $n = 142$ , 27.8%) and left ventricle outflow tract (LVOT) obstruction in conjunction with mitral- (MV) or tricuspid valve (TV) disease ( $n = 7$ , 1.4%).

### Results

Procedures performed included 122 AVV replacements (MV = 105, TV = 17) and 478 AVV repairs (MV = 383, TV = 95) in isolation or combination. Concomitant procedures included cryoablation ( $n = 142$ , 27.8%) and LVOT resection ( $n = 7$ , 1.4%). Intraoperative complications that required SC occurred in 16 (3.1%) patients and in 13 of 399 (3.3%) isolated MV procedures. Reasons for SC included lung adhesions ( $n = 5$ , 1.0%), cannulation difficulty ( $n = 3$ , 0.6%), atrioventricular dehiscence ( $n = 1$ , 0.2%) and bleeding ( $n = 4$ , 0.8%). Other perioperative complications included neurological deficit ( $n = 2$ , 0.4%) and myocardial infarction ( $n = 1$ , 0.2%). The intraoperative- and 30-day mortality for the 5-year MIAS series ( $n = 511$ ) was 0.4% ( $n = 2$ ) and 4.5% ( $n = 23$ ) respectively. Complications that resulted in SC ( $n = 16$ ) were associated with a 25% ( $n = 4$ ) 30-day mortality.

### Conclusion

Minimally invasive surgical approaches for AVV disease are increasingly being recognized as the “gold-standard” in the context of rapidly expanding transcatheter technology and increasing patient expectations. In an era of strict quality control and clinical governance, emerging MIAS centres need to be aware of the possible intraoperative complications and potential pitfalls to apply effective risk reduction strategies that encourage safe- and sustainable programs.

## INTRODUCTION

The current evolution in transcatheter atrioventricular valve (AVV) repair- and replacement technology [1-3] is paralleled by extensive industry driven marketing [4] and increasing patient expectations [5] that potentially favour catheter-based approaches above surgical options [6]. Subsequently, the contemporary role of conventional sternotomy- (CSA) and even minimally invasive AVV surgery approaches are continuously being redefined. It is now generally accepted that current- and future cardiac surgeons need to acquire minimally invasive- and interventional skills to strengthen our positions in the future treatment of AVV disease [7-9].

Minimally invasive AVV surgery that utilizes endoaortic balloon occlusion technology (MIAS, also known as Port Access™ Surgery), is associated with extensive learning curves, which in a current era of strict quality control and accountability [10], clinical governance [11- 12] and an increasing patient risk profile [13], may deter emerging centres from incorporating MIAS into their clinical practice.

The intention of this manuscript is to provide an in-depth overview of intraoperative complications and the reasons for sternotomy conversion (SC) associated with MIAS and to outline the potential pitfalls that may assist in the development of safe-, efficient- and sustainable programs.

## METHODS

We performed a retrospective study of a single-centre prospective MIAS database, in which the complication, reasons for sternotomy conversions and the incidence of intraoperative major adverse cardiac- and cerebrovascular events (MACCE) that occurred over the last 5 years were evaluated. The impact of SC on 30-day mortality were also evaluated.

In total, 511 consecutive patients that required AVV interventions between May 1st 2013 and April 30th 2018, underwent MIAS without exclusion criteria at our institution by our current surgical team. The study was approved by the institutional ethics review committee and all authors accept responsibility for data integrity and the manuscript as written.

### Patient selection and work-up

The indication for MIAS has expanded in experience centres to include isolated AVV disease in primary- [14-16] and redo-cardiac surgery [17, 18], cryoablation for atrial fibrillation [19] and intracardiac neoplastic resection [20]. The relevant preoperative patient characteristics, AVV pathology and surgical indications are outlined in Table 1. The mean body mass index (BMI), mean- and median logistic EuroSCORE were  $25.7 \pm 4.5 \text{ m}^2 / \text{kg}$  ( $15.2 - 45.0$ ),  $10.0 \pm 13.4\%$  ( $1.2 - 98.0$ ) and 5.2% respectively. In total, 600 surgically correctable AVV abnormalities were diagnosed in the 511 consecutive patients.

<b>Table 1. Preoperative patient characteristics and valve pathology (n = 511)</b>		
<b>Patient characteristics</b>	<b>n</b>	<b>% of 511</b>
Mean age (years, range)	65.6 ± 13.7 (17.5 – 92.7)	
Age above 80 years	61	11.9
Female	239	46.8
Mean body mass index (m <sup>2</sup> / kg)(range)	25.7 ± 4.5 (15.2 – 45.0)	
above 30 m <sup>2</sup> / kg	71	13.9
Previous cardiac surgery	111	21.7
Previous Port Access™ surgery	29	5.7
<b>Preoperative state</b>		
Elective	459	89.9
Urgent / emergency	52	10.2
Mean Logistical EuroSCORE (range)	10.0 ± 13.4 (1.02 - 98.0)	
Mean EuroSCORE II (range)	5.9 ± 9.4 (0.5 – 76.8)	
Active endocarditis	15	2.9
Left ventricle ejection fraction <30%	17	3.3
Neurological dysfunction	20	3.9
Poor mobility	24	4.7
Renal dysfunction	332	65.0
Chronic obstructive pulmonary disease	38	7.4
Extracardiac arteriopathy	94	18.4
<b>Valve Pathology</b>	<b>n</b>	<b>% of 600</b>
Annular dilatation	198	33.0
Degenerative/Sclerotic disease	285	47.5
Rheumatic disease	33	5.5
Congenital abnormalities	5	0.8
Endocarditis (acute / chronic)	20	3.3
Native valve	17	2.8
Prosthetic valve	3	0.5
Ischemic valvulopathy	4	0.7
Prosthetic valve thrombosis	1	0.2
Prosthetic valve paravalvular leak	5	0.8
Prosthetic valve dysfunction	1	0.2
Trauma	6	1.0
Other	42	7.0

### Preoperative preparation

We routinely perform preoperative aorta-iliac-femoral-axis (AIFA) evaluation in all patients either during coronary catheterization or by magnetic resonance angiography. Computerized tomography is not routinely utilized in redo-surgery and no special investigations are performed to evaluate the presence of lung adhesions in patients with previous right hemithorax interventions. All patients are offered the option of MIAS with the intention to treat. Routine cardiac surgical workup is followed by an elaborate informed consent process, which also include the possibility of SC, after which the patient selects a preferred treatment pathway.

### Equipment preference card

The IntraClude™ device (Edwards Lifesciences, Irvine, California, USA) is a composite endoaortic balloon occlusion device (10.5 Fr, 100 cm length) that facilitates antegrade cardioplegia delivery, aortic root venting and aortic root pressure monitoring (Figure 1).

It is inserted over a guidewire through a Y-arm of the EndoReturn™ (21-23 Fr, Edwards Lifesciences, Irvine, California, USA) femoral arterial cannula and advanced to the aortic sinotubular junction. The safety- and efficiency of current PAS technology compared to other clamping strategies are well described [33-36].

The QuickDraw™ femoral venous cannula (22-25 Fr, Edwards Lifesciences, Irvine, California, USA) is used for venous drainage and is also compatible with percutaneous approaches. Right internal jugular cannulation (16-18 Fr, Optisite™, Edwards Lifesciences, Irvine, California, USA) augments venous drainage. Single-, long shafted instruments facilitate routine and advanced AVV procedures through endoscopic working ports.

### Procedure outline

Our routine techniques are well described [14-20] and a total of 3072 patients underwent MIAS at our institution up to date. All guidewire advancement and cannulation are established under transoesophageal echocardiography (TEE) guidance, with venous cannulation performed first using standard inferior vena cava and bicaval TEE views. Femoral artery cannulation and subsequent endoballoon advancement are guided by standard TEE images of the descending aorta, aortic arch, ascending aorta, sinotubular junction and aortic root.

A 4-cm non-rib-spreading working port incision is established over the 4th anterior-axillary intercostal space. In extreme obese patients [21], we utilize an endoscopic non-rib-spreading access site soft tissue retractor (SurgiSleeve™, 2.5-6 centimetres, Covidien, Massachusetts, USA) for additional wound protection, long (53- or 100 millimetre) endoscopic camera trocars (Vectec SA, Hauterive, France) and establish all intercostal ports by blunt dissection (Figure 2). Unobstructed visual- and working access are ascertained by resecting excessive pericardial fat and retracting the diaphragmatic dome infero-laterally with exteriorized traction sutures.



For difficult access congenital chest wall deformities [22], an adequate working angle and adequate atrioventricular valve access are the most demanding technical challenges. We routinely position our atrial retractor in the right parasternal zone, lateral to the 4th intercostal space internal mammary bundle, but in cases of pronounced pectus excavatum deformities, the retractor may be positioned on the left parasternal border. The limited antero-posterior retraction distance between the right atrium and anterior chest wall may require tilting the patient maximally to the left while applying low positive end-expiratory pressure (PEEP) to the left lung. Exteriorized stay sutures are utilized to obtain tricuspid valve (TV) exposure, instrument access and adequate working angles in cases of unsuccessful right atrial retraction.

Argon-gas cryoablation (Medtronic, Minneapolis, USA) and left atrial appendage closure are performed in patients with atrial fibrillation or previous stroke (Figure 3). Patent foramen ovale are routinely closed and post-procedural de-airing performed by left atrial- and aortic balloon venting catheters, continuous flooding of the operative field with CO<sub>2</sub> and TEE evaluation for residual air in the left ventricle.

For access to the left ventricle outflow tract [23], segment A1-A3 of the MV are detached from the annulus. Following careful septal myomectomy by sharp resection, the MV is augmented with an oversized bovine pericardial patch. Temporary epicardial- or transjugular ventricular pacing wires are routinely placed.

The atrioventricular valve- (n = 600) and concomitant procedures (n = 253) performed by MIAS in 511 consecutive patients between May 1st 2013 and April 30th 2018, are outlined in table 2 and consisted of 399 (78.1%), 23 (4.5%) and 89 (17.4%) isolated MV-, isolated TV and combined MV and TV procedures respectively. MV-repair was achieved in 97.0 % (n = 324 of 334) of primary annular dilatation and degenerative valves. The mean cardiopulmonary bypass- and ischemic times are also described in table 2.



Figure 1 IntraClude™ endoaortic balloon occlusion device



Figure 2. Port Access™ surgery in extreme obesity

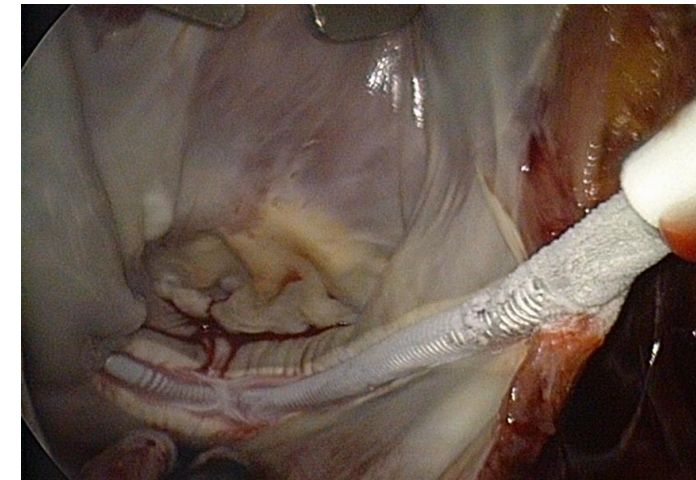


Figure 3. Endoscopic Port Access™ cryoablation

For access to the left ventricle outflow tract [23], segment A1-A3 of the MV are detached from the annulus. Following careful septal myomectomy by sharp resection, the MV is augmented with an oversized bovine pericardial patch. Temporary epicardial- or transjugular ventricular pacing wires are routinely placed.

#### Role of team members

We advocate a patient-centred-, multidisciplinary team approach that include cardiologists, experienced anaesthesiologists [24], perfusionists [25], theatre-, intensive care-, ward- and outpatient nurses, physiotherapists, other allied health care professionals, the patient family and referring physicians. Intraoperative communication is essential and each expert opinion should be respected and considered during the procedure. Postoperative intensive care is coordinated by a team of full-time on-site cardiac intensivists, which is followed by a structured and individualized in-hospital multidisciplinary rehabilitation program. Continuation of care is ascertained by the referring physician as part of patient centred service delivery.

#### Postoperative management

Cardio-respiratory support, sedation and analgesia are administered as indicated in intensive care and a structured in-hospital rehabilitation program initiated as soon as possible. All patients undergo pre-discharge transthoracic echocardiographic evaluation for satisfactory operative result confirmation.

Infective endocarditis is treated with appropriate antibiotics for 6 weeks under the supervision of an infective endocarditis team and long term anticoagulation regimes initiated and stabilized in-hospital in cases of mechanical prosthetic implantation or chronic atrial fibrillation. All patients are reviewed within 6 weeks postdischarge, after which continuation of care is ascertained by the referring cardiologist and family physician.

<b>Table 2. Procedures performed, cardiopulmonary bypass- and ischemic times.</b>		
<b>Valve procedures performed (n = 600)</b>	<b>n</b>	<b>% of 600</b>
Mitral valve procedures	488	81.3
Replacement	105	17.5
Mechanical prosthesis	30	5.2
Biological prosthesis	75	12.5
Repair	383	63.8
Tricuspid valve procedures	112	18.7
Replacement (biological prosthesis)	17	3.8
Repair	95	15.8
Isolated mitral valve procedures	399	66.5
Isolated tricuspid valve procedures	23	3.8
Combined mitral- and tricuspid valve procedures	89	14.8
<b>Concomitant cardiac procedures (n = 253, 49.5%)</b>	<b>n</b>	<b>% of 511</b>
Left ventricle outflow tract resection	7	13.7
Patent foramen ovale closure	84	16.4
Atrial fibrillation ablation	142	27.8
Hybrid percutaneous coronary intervention	20	39.1
<b>Cardiopulmonary bypass time (minutes)</b>		
Isolated mitral valve surgery	142 ± 40 (46 – 314)	
Isolated tricuspid valve surgery	138 ± 34 (76 – 242)	
Combined mitral- and tricuspid valve surgery	193 ± 44 (118 – 360)	
Sternotomy conversions (all included)	207 ± 102 (98 - 387)	
<b>Ischemic time (minutes)</b>		
Isolated mitral valve surgery	96 ± 30 (28 - 220)	
Isolated tricuspid valve surgery	91 ± 25 (45 - 162)	
Combined mitral- and tricuspid valve surgery	38 ± 27 (89 - 214)	
Sternotomy conversions (all included)	126 ± 59 (55 - 242)	

## RESULTS AND OUTCOMES

Adverse early- and late intraoperative events that required sternotomy conversion (SC) occurred in 16 (3.1%) patients. SC that occurred prior to EABO device inflation are considered “risk aversion strategy changes” or early conversions, whereas late conversions are defined as conversions during or after EABO inflation.

The reasons for SC are outlined in table 3 and included lung adhesions (n = 5, 1.0%) and cannulation difficulty (n = 4, 0.8%). Perioperative neurological deficit occurred in 2 (0.4%) patients. Other perioperative major adverse cardiac- and cerebrovascular events (MACCE) are outlined in table 4.

The intraoperative- and 30-day mortality for the total series (n = 511) was 0.4% (n = 2) and 4.5% (n = 23) respectively. The 30 day- and total in-hospital mortality associated with SC for perioperative complications (n = 16) was 25.0 % (n = 4).

<b>Table 3. Intraoperative complications and reasons for sternotomy conversion (n = 16)</b>		
<b>Complications and conversions</b>	<b>n</b>	<b>% of 511</b>
Early complications and conversions	9	1.7
Lung adhesions	5	1.0
Cannulation difficulty	4	0.8
Guidewire resistance	3	0.6
Aortic dissection	1	0.2
Late complications and conversions	7	1.4
Bleeding	4	0.8
Ventricle perforation	1	0.2
Atrial bleeding	3	0.6
Endoaortic balloon rupture	1	0.2
Atrioventricular dehiscence	1	0.2
Aortic valve injury	1	0.2
Total conversion rates	16	3.1

<b>Table 4. Perioperative major adverse cardiac- and cerebrovascular events (MACCE)</b>		
<b>Intraoperative MACCE for total series (n = 511)</b>	<b>n</b>	<b>% of 511</b>
Cardiac death	2	0.4
Acute myocardial infarction	1	0.2
Congestive cardiac failure	7	1.4
Stroke	6	1.2
<b>Intraoperative MACCE for complications and conversions</b>		
Cardiac death	1	6.3
Acute myocardial infarction	0	0
Congestive cardiac failure	1	6.3
Stroke	0	0

### TIPS, TRICKS AND PITFALLS

MIAS is associated with extensive learning curves and in an era where surgical volume is progressively decreasing, emerging centres should be cautious of offering MIAS as a routine to patients with difficult right hemithorax- or AVV access (previous right thoracotomy, lung adhesions, radiation therapy, obesity

or chest wall deformities), high risk- and frail patients, peripheral vascular disease, severely calcified AVV annuli and AVV pathology that require complex repair or replacement techniques. With experience, patient selection may expand to include difficult access extreme obese patients [21], congenital chest wall deformities [22], redo-cardiac surgery [17], redo-MIAS after previous MIAS [18], MIAS in the context of previous orthotopic cardiac transplant [26], complex isolated AVV endocarditis [27], left ventricle outflow tract obstruction with associated AVV disease [23], giant atrial myxoma resection [28] and other complex MIAS procedures [29].

Lung adhesions accounted for 5 (31.3%) of SC (n = 16), which occurred in the context of primary- (n = 400, 78.3%), redo-cardiac- (n = 111, 21.7%) and redo-MIAS (n = 29, 5.7%) procedures. Previous right hemithorax interventions are not considered contraindications in experienced centres and we do not routinely perform any special imaging investigations to identify lung adhesions. Computerized tomography is considered to be of value in redo-cardiac surgery where patent coronary artery bypass grafts are documented and the graft positions are of interest. Targeted access to the valves are obtained by careful release of anterior-, mediastinal- and diaphragm adhesions by combination of blunt and sharp dissection without causing pulmonary tears or bleeding. In the unlikely event of pulmonary injury, we advocate suture repair prior to initiating systemic anticoagulation.

We prefer a 4-cm right groin incision over the skin-line that facilitates the exposure of the anterior surfaces of the right common femoral artery and vein while avoiding the medial lymphatic regions. Total percutaneous cannulation using vascular closure devices can be performed as a favourable alternative. A low threshold to convert single- to bilateral femoral artery cannulation in cases of high CPB and perfusion pressures should be respected. Routine preoperative aorta-iliac-femoral-axis (AIFA) evaluation is mandatory in all patients either during coronary catheterization or by magnetic resonance angiography. Peripheral vascular diameters less than 7 mm, extensive common femoral artery anterior surface- or diffuse AIFA calcification, previous common femoral artery interposition grafts, severe central- and peripheral vascular tortuosity and ascending aorta diameter more than 40.0mm should be approached with extreme caution.

TEE surveillance of controlled and smooth guidewire advancements and peripheral device placements is a prerequisite for safe and sustainable MIAS [31-32]. The identification of any resistance or abnormal tactile feedback while advancing guidewires are warnings of potential complications and attempts to force any guidewire or device is strongly discouraged. Cannulation challenges that required SC occurred in 4 (0.8%) patients and included the early identification of guidewire advancement resistance (n = 3, 0.6%), with aortic dissection occurring in 1 (0.2%) patient.

It is suggested that a preselected team under surgical leadership undergo training at an established MIAS centre and practice their operative steps in a simulation or “dry-lab” setting before performing the first 20 cases [30]. It is imperative that all team members are comfortable with the procedure and aware of the potential pitfalls. Frequent postoperative team de-briefing sessions is advised to identify improvement strategies and to reinforce ownership of each team member under the surgical leadership.

All MIAS procedures are prepared, cleaned- and draped according to routine sternotomy access principles and a sternotomy saw should always be immediately available to ensure rapid sternotomy



conversion if required. The adjustment of the procedure from MIAS to sternotomy should be conducted in a systematic- and organised manner.

Aortic valve injury (n = 1, 0.2%) and EABO device rupture by suture puncture (n = 1, 0.2%) occurred due to post-inflation migration of the device into the non-coronary sinus. The device positioning is subjected to retrograde CPB flow pressures and intrinsic device tension and should therefore be locked against the arterial Y-connecting inflow cannula. It can be avoided by careful initial TEE guided placement at the sinotubular junction, TEE confirmation of its position prior to left atriotomy and careful annular suture placement between the antero-lateral commissure and the A2-segment. We advocate only partial inflation to approximately 75% of the volume of the ascending aorta in conjunction with the administration of adenosine (0.25 mg/kg) as a syringe-flush to achieve rapid diastolic cardiac arrest before full inflation and positioning under TEE guidance. Loss of right radial artery pressure indicates cranial EABO migration that obstructs the innominate artery and should be corrected immediately.

Bleeding accounted for 4 (0.8%) of SC, which included pacemaker placement related left ventricle perforation (n = 1, 0.2%) and atriotomy bleeding (n = 3, 0.6%). The right atrium is closed by 2 running sutures and the left atrium by single layer. We recommend temporary pacemaker placement on the diaphragmatic aspect of the muscular left ventricle, which is considered to be of lower bleeding risk compared to the right ventricle. All working ports and incisions should be endoscopically controlled for bleeding prior to closure.

Atrioventricular dehiscence occurred in 1 (0.2%) patient, which was controlled by valve reimplantation following an uneventful SC. Severe posterior annular calcification can be identified by routine preoperative imaging and should be resected with extreme caution [34].

## CONCLUSION

The application of MIAS are continuously evolving in the context of rapidly expanding catheter-based technology and increasing patient expectations. Awareness of pitfalls, reasons for SC and other adverse intraoperative events are imperative to applying effective risk reduction strategies that potentially assist in developing safe- and sustainable programs.

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# PART 3

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DEVELOPMENTS IN ADVANCED ENDOSCOPIC PORT ACCESS™  
ATRIOVENTRICULAR VALVE SURGERY

# CHAPTER 8

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Endoscopic atrioventricular valve surgery in extreme obesity

Van der Merwe J, Casselman F, Stockman B, Vermeulen Y, Degrieck I, Van Praet F



## ABSTRACT

Obesity is one of the greatest public health challenges of the 21st century and the world-wide incidence of extreme obese patients is increasing. Sternal dehiscence and wound infections are amongst the devastating morbidities associated with classic sternotomy in these patients. The perceived technical challenges, in-hospital morbidity- and increased mortality risks often deter surgeons from offering these patients the option and benefits of minimally invasive approaches. This case series presents our perioperative- and long term clinical- and echocardiographic outcomes of endoscopic Port Access™ atrioventricular valve surgery in 7 consecutive patients with body mass index above 40, operated by our current surgical team.

## INTRODUCTION

Obesity is a significant public health challenge [1] and recent reports suggest that the incidence of extreme obese patients (EOP) with body mass index (BMI) greater than 40 and 50 increased four- and five times respectively over the last 20 years [2]. Sternal dehiscence, wound infection and respiratory complications are amongst the devastating morbidities associated with conventional sternotomy approaches in EOP [3,4].

The reported exclusion of EOP from minimally invasive (MI) outcome data reports due to the perceived technical challenges and risks of adverse outcomes [5], undermines the potential beneficial role of MI approaches in these patients.

This retrospective, observational, single-centre case series presents the perioperative and long term clinical and echocardiographic outcomes of endoscopic Port Access™ surgery (EPAS) for atrioventricular valve disease in 7 consecutive extreme obese patients operated by our current surgical team between November 1st 2008 and September 30th 2015.

## CASE SERIES

The relevant preoperative EOP characteristics and surgical indications, which may be multiple per patient, are outlined in Table 1 and Table 2 respectively. Our routine EPAS technique [6] is modified in the context of EOP (Figure 1A). The skin folds and excessive subcutaneous tissues are retracted away from incision areas during draping. We establish our working port over the 4th intercostal, anterior axillary space and utilise an endoscopic non-rib-spreading access site soft tissue retractor (SurgiSleeve™, 2.5-6 centimeters, Covidien, Massachusetts, USA) for additional wound protection.

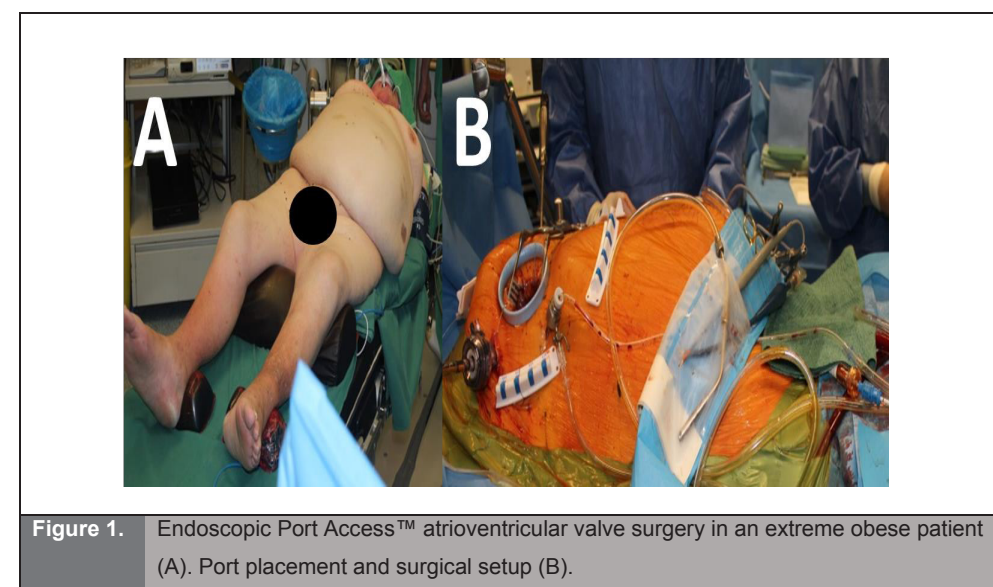
We use extra-long (53- or 100 mm) endoscopic camera trocars (Vectec SA, Hauterive, France) and establish all intercostal ports by blunt dissection (Figure 1B). Unobstructed visual- and working access are ascertained by resecting excessive pericardial fat and retracting the diaphragmatic dome infero-laterally with exteriorized traction sutures.

Preoperative aorta-iliac-femoral-axis (AIFA) evaluation is routinely performed in all patients either during coronary catheterization or by magnetic resonance angiography. Classic open femoral vascular exposure or total percutaneous peripheral cannulation is performed with the use of vascular closure devices (Figure 2A) according to surgical preference. Lymphatic regions in the groin are avoided to minimize devastating postoperative lympho-infective (LI) wound complications.

Peripheral cardiopulmonary bypass (CPB) is established by transesophageal echocardiography (TEE) guided cannulation of the right internal jugular vein- (16-18 Fr, Optisite™, Edwards Lifesciences, Irvine, California, USA), right femoral vein- (22-25 Fr, QuickDraw™, Edwards Lifesciences, Irvine, California, USA) and right femoral artery cannulation (21 or 23 Fr, EndoReturn™, Edwards Lifesciences, Irvine, California, USA). An endoaortic balloon (IntraClude™, Edwards Lifesciences, Irvine, California, USA) is utilized for aortic occlusion and delivery of cold antegrade crystalloid cardioplegia.

<b>Table 1. Preoperative patient characteristics (n = 7)</b>			
<b>Patient characteristics</b>		<b>n</b>	<b>% of 7</b>
Mean age (years, range)		65.8±10.6(46.4-76.8)	
Age above 70 years		3	42.9
Female		1	14.3
Mean body mass index (m <sup>2</sup> / kg)(range)		43.3±3.8 (40.2-52.1)	
Mean length (cm)		162.6±9.8 (150-178)	
Mean weight (kg)		114.0±12.4 (96-138)	
<b>Comorbidities present</b>			
Hypertension		7	100.0
Hypercholesterolemia		3	42.9
Type I diabetes mellitus		3	42.9
Previous DVT and PE		2	28.6
Obstructive sleep apnea syndrome		4	57.1
Abnormal lung function		5	71.4
FEV1 < 90%		5	71.4
DLCO < 80%		5	71.4
Hypertrophic obstructive cardiomyopathy		1	14.3
Atrial fibrillation		6	85.7
Renal dysfunction		3	42.9
Pulmonary hypertension		7	100.0
Mean pulmonary artery pressure (mmHg)		61.1±15.0 (45-84)	
Mean EuroSCORE II (range)		5.2±1.5 (3.1-7.3)	
Mean left ventricular function (range)		51.6±9.5 (38 -63)	
Impaired (< 50%)		1	14.3
<b>New York Heart Association functional status</b>			
III		5	71.4
IV		2	28.6
FEV1 = forced expiratory volume in 1 second; DLCO = diffusing capacity for carbon monoxide; DVT = deep venous thrombosis; PE = pulmonary embolism			

<b>Table 2. Surgical indications (n = 7)</b>			
<b>Surgical indications</b>		<b>n</b>	<b>% of 7</b>
Mitral valve dysfunction		7	100.0
Annular dilatation		2	28.6
Myxomatous degenerative disease		2	28.6
Rheumatic valve disease		2	28.6
Systolic anterior motion		1	14.3
<b>Carpentier-Edwards classification</b>			
Type I		2	28.6
Type II		3	42.9
Type IIIa		2	28.6
Tricuspid valve dysfunction		3	42.9
Carpentier-Edwards classification (Type I)		3	42.9
Patent foramen ovale		1	14.3
Atrial fibrillation		3	42.9
Left ventricle outflow tract obstruction (gradient 80mmHg)		1	14.3



**Figure 1.** Endoscopic Port Access™ atrioventricular valve surgery in an extreme obese patient (A). Port placement and surgical setup (B).

Routine atrioventricular valve surgery, as outlined in Table 3, is performed with long shafted instruments. Endoscopic transatrial left ventricular outflow tract (LVOT) resection is performed by detaching the anterior MV-leaflet segments A1-A2-A3 from the MV-annulus with subsequent

myomectomy from the aortic valve to the papillary muscle base. The anterior MV-leaflet is reattached to the annulus with the incorporation of an oversized bovine pericardial patch.

Tricuspid valve (TV) surgery is performed by bicaval snaring, argon-gas surgical cryoablation (Medtronic, Minneapolis, USA) and left atrial appendage closure for chronic atrial fibrillation and closure of patent foramen ovale (PFO) routinely performed.

Post-procedural TEE guided de-airing is ensured by left atrial- and aortic balloon venting catheters and continuous flooding of the operative field with CO<sub>2</sub>. Temporary ventricular pacing wires are placed on the ventricular aspect.

Table 3. Procedures performed, cardiopulmonary bypass- and ischemic times (n = 7)		
Procedures performed	n	% of 7
Mitral valve repair	5	71.4
Ring implantation	5	71.4
Leaflet resection	1	14.3
Leaflet patch reconstruction	1	14.3
Cleft closure	3	42.9
Papillary muscle transfer	1	14.3
Secondary chordae release	1	14.3
Neochordal implantation	2	28.6
Mitral valve replacement	2	28.6
Left ventricle septal myomectomy	1	14.3
Tricuspid valve repair	1	14.3
Ring implantation	1	14.3
Foramen ovale closure	1	14.3
Cryoablation	3	42.9
Left atrial appendage exclusion	6	85.7

Cardio-respiratory support, pulmonary hypertension protocols, sedation, analgesia, glycaemic control, wound reviews (Figure 2B and C) and anticoagulation stabilisation are applied as indicated in intensive care and general ward.

There were no 30-day mortalities. One patient (14.3%) required revision for bleeding, which was performed through the same incision without further complications. Prolonged intensive care admission (more than 6 days), incision wound infection, dialysis, hospital acquired pneumonia and eventual permanent pacemaker insertion all occurred in 1 patient (14.3%), who sustained a perioperative stroke and subsequent mechanical valve thrombosis on day 10 postoperatively. This was treated medically and eventual home discharge achieved on day 72.

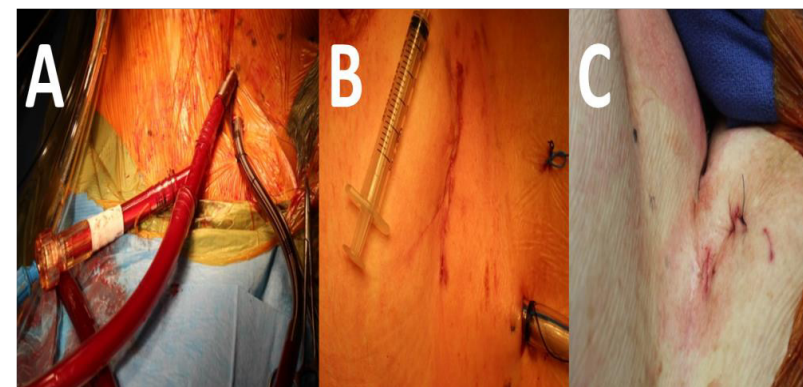


Figure 2. Percutaneous cardiopulmonary bypass facilitated by vascular closure devices (A). Postoperative working port- (B) and groin incision (C).

The mean length of hospitalization was  $22.6 \pm 22.7$  days (range 7-72). Analyses of a total of 276.0 patient months (100% complete, range 2.2 - 84.5 months, mean  $39.4 \pm 88.4$  months, 85.7% longer than 2 years) revealed no late mortalities, no reinterventions, no residual MV-regurgitation more than grade I following MV-repair and no paravalvular leaks post-MV-replacement.

Residual TV-regurgitation more than grade II was present in 1 patient (14.3%), the mean systolic pulmonary artery pressure was  $38.7 \pm 15.6$  mmHg and 6 patients (85.7%) had residual BMI greater than 40. New York Heart Association (NYHA) class I or II was achieved in 6 patients (85.7%).

## DISCUSSION

The devastating morbidities associated with conventional sternotomy access in extreme obese patients are well described and no reports currently describe the outcomes of minimally invasive approaches for atrioventricular valve disease in this population.

Our single-centre series of 7 patients confirmed the benefits of our strategy despite the presence of significant high risk comorbidities. There were no 30 day- or long term follow-up mortalities, no late atrioventricular valve reinterventions, no residual mitral valve regurgitation more than grade I, paravalvular leaks or residual tricuspid valve regurgitation more than grade II. Preoperative atrial fibrillation (AF) was present in 6 patients (85.7%), of which 5 patients (71.4%) maintained sinus rhythm at recent review.

## CONCLUSION

Endoscopic Port Access™ surgery for atrioventricular valve disease in extreme obese patients can safely be performed in experienced centres with favourable perioperative- and long term procedural-, clinical- and echocardiographic outcomes. Extreme obesity should not be perceived as a contraindication to endoscopic approaches and should not deter surgeons and referring physicians from offering these patients the full range of benefits associated with minimally invasive cardiac surgery.

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# CHAPTER 9

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Endoscopic atrioventricular valve surgery in adults with difficult-to-access uncorrected congenital chest wall deformities

Van der Merwe J, Casselman F, Stockman B, Vermeulen Y, Degrieck I, Van Praet F.

**ABSTRACT****Objective**

This study presents the first report on in-hospital- and long term outcomes of endoscopic Port Access™ atrioventricular valve surgery (EPAAVVS) in adult patients with uncorrected congenital chest wall deformities (CCWDs).

**Methods**

Our current surgical team performed EPAAVVS in 7 consecutive adult patients (mean age 51.3±16.4 years, 14.3% female, 50% older than 60 years, mean EuroSCORE II 0.8±0.1%) with uncorrected CCWDs between November 1st 2009 and November 30th 2015. Mean left ventricular ejection fraction was 66.0±8.5%. Surgical indications included isolated- or combined symptomatic mitral valve (MV) regurgitation (n = 7, 100%), left ventricular outflow tract (LVOT) obstruction (n = 1, 14.3%) and patent foramen ovale (n = 3, 42.9%). Fibroelastic deficiency accounted for 57.1% of MV-pathology and 5 patients (74.1%) presented with New York Heart Association (NYHA) class III symptoms. CCWDs included isolated pectus excavatum (n = 5, 71.4%) and mixed pectus excavatum and carinatum (n = 2, 28.6%). The mean Haller- and Correction Index were 2.7±0.5 and 21.4±10.2% respectively.

**Results**

Procedures performed included MV-repair (n = 7, 100%), TV-repair (n = 1, 14.3%) and left ventricular septal myomectomy (n = 1, 14.3%). There were no sternotomy conversions or complications with chest wall entry or atrioventricular valve exposure. The mean cardiopulmonary bypass- and cross-clamp times were 162.1±48.1- and 113.7±33.5 minutes respectively. No patients required mechanical ventilation- or intensive care treatment longer than 24 hours. There were no surgical revisions, in-hospital respiratory- or chest wall morbidities. The mean length of hospital stay was 7.4±1.0 days. A total of 208.0 patient months (mean 29.7±26.5) were available for long term clinical- and echocardiographic analysis. There were no 30 day- or long term mortalities and no patient required reintervention for residual atrioventricular valve pathology. All patients were classified as NYHA I during recent consultations and echocardiographic follow-up confirmed no residual MV-regurgitation greater than grade I in any patient.

**Conclusion**

EPAAVVS in adults with uncorrected CCWD is safe, feasible and durable and can successfully be performed by experienced teams in HI and CI of up to 3.3 and 38.3% respectively with favourable long term clinical- and echocardiographic outcomes. The mere presence of uncorrected CCWD should not deter surgeons from offering these patients the full benefits of minimally invasive cardiac surgery.

**INTRODUCTION**

We are currently witnessing a progressive paradigm shift from conventional sternotomy approaches to innovative minimally invasive (MI) strategies in the surgical treatment of atrioventricular valve disease (AVVD) [1]. We have previously reported our experience in endoscopic Port Access™ atrioventricular valve surgery (EPAAVVS) for primary- [2-4] and redo-atrioventricular valve- [5, 6], selected cardiac oncology- [7] and arrhythmia surgery [8].

The anatomical- and physiological characteristics of congenital chest wall deformities (CCWDs), that includes the spectrum of isolated and mixed pectus deformities, are well described [9]. Adult patients with uncorrected CCWDs and surgically correctable AVVD present unique challenges in MI approaches, especially in obtaining adequate valve exposure and acquiring unobstructed endoscopic instrument working angles.

Reports on MI atrioventricular valve surgery in the context of CCWDs do not exist and is regarded by many as a contraindication to MI surgery. We report the first in-depth in-hospital-and long term outcome report of 7 consecutive uncorrected adult CCWDs patients with symptomatic AVVD that underwent EPAAVVS by our current surgical team.

**METHODS**

This is a retrospective observational study of a single-centre EPAAVVS database. In-hospital data are collected prospectively. Our current surgical team performed a total of 652 EPAAVVS procedures for new- or recurrent AVVD between November 1st 2009 and November 30th 2015, of which 7 patients presented with CCWDs that included isolated- or mixed pectus deformities. The preoperative patient characteristics and surgical indications, which may be multiple per patient, are outlined in Table 1 and 2 respectively.

**Operative techniques and postoperative treatment pathway**

Our cardiopulmonary bypass (CPB)-, endoaortic balloon occlusion- and endoscopic operative techniques for routine primary- and redo-EPAAVVS have been extensively described [2-8] and require individualized modifications in the context of CCWDs.

The chest wall characteristics of all patients with isolated- or mixed pectus deformities are preoperatively evaluated by either combined anterior- and lateral chest x-ray- or computerized tomographic imaging. These investigations do not influence our EPAAVVS strategy decision making, but assists in planning endoscopic instrument selection- and atrial retractor port positioning.

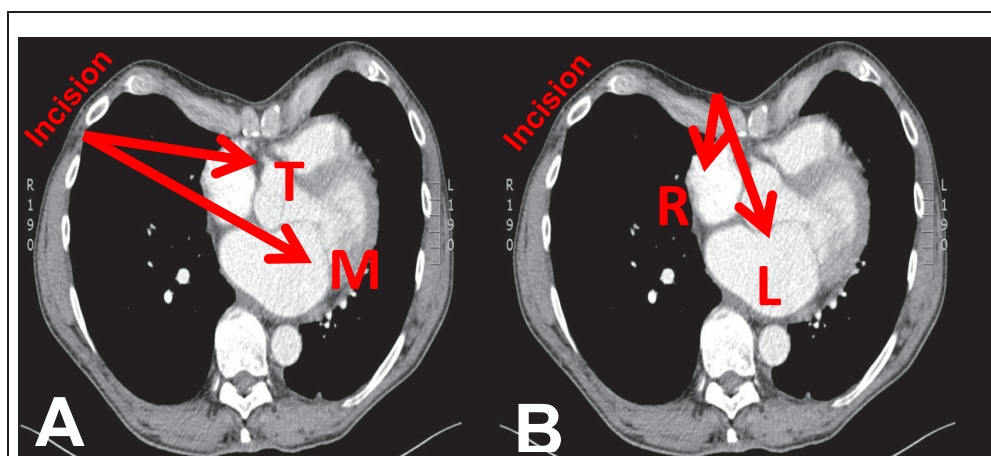
<b>Table 1. Preoperative patient characteristics (n = 7)</b>		
<b>Patient characteristics</b>	<b>n</b>	<b>% of 7</b>
Mean age (years)	51.3±16.4 years	
Age above 60 years	3	42.9
Female	1	14.3
Mean body mass index (m <sup>2</sup> / kg)	22.9±3.1	
<b>Comorbidities present</b>		
Hypertension	1	14.3
Hypercholesterolemia	1	14.3
Atrial fibrillation	2	28.6
Permanent pacemaker	1	14.3
Pulmonary hypertension	1	14.3
Mean systolic pulmonary artery pressure (mmHg)	26.0±5.5	
Mean EuroSCORE II (range)	0.8±0.1 (0.6 to 1.0)	
Mean left ventricular function (range)	66.0±8.5 (55 -82)	
<b>New York Heart Association classification</b>		
II	2	28.6
III	5	71.4
<b>Pectus deformity characteristics</b>		
Isolated pectus excavatum	5	71.4
Mixed pectus excavatum and carinatum	2	28.6
Mean Haller Index (Range)	2.7± 0.5 (2.0 to 3.3)	
2.0 to 2.5	3	42.9
2.5 to 3.0	2	28.6
3.0 to 3.5	2	28.6
Mean Correction Index (Range)	21.4±10.2 (13.0 to 38.2)	
10-20%	5	71.4
20-30%	0	0
>30%	2	28.6
Mean sternal indentation depth (cm)	3.2± 1.7 (2.1 to 6.3)	
Mean sternal indentation length (cm)	10.9± 4.8 (6.6 to 18.6)	
Mean sterno-vertebral diameter (cm)	11.2± 2.2 (8.6 to 14.4)	
Mean thoracic cross diameter (cm)	29.6± 2.7 (25.9 to 33.5)	

<b>Table 2. Isolated- and combined surgical Indications (n = 7)</b>		
<b>Surgical indications</b>	<b>n</b>	<b>% of 7</b>
Mitral valve dysfunction	4	57.1
Chordal rupture	2	28.6
Leaflet prolapse	1	14.3
Systolic anterior motion	1	14.3
<b>Pathology</b>		
Fibroelastic deficiency	4	57.1
Barlow's morphology	2	28.6
Hypertrophic obstructive cardiomyopathy	1	14.3
<b>Carpentier-Edwards classification</b>		
Type II	7	100.0
Tricuspid valve dysfunction	1	14.3
<b>Carpentier-Edwards classification</b>		
Type I	1	14.3
Patent foramen ovale	3	42.6
Atrial fibrillation	2	28.6

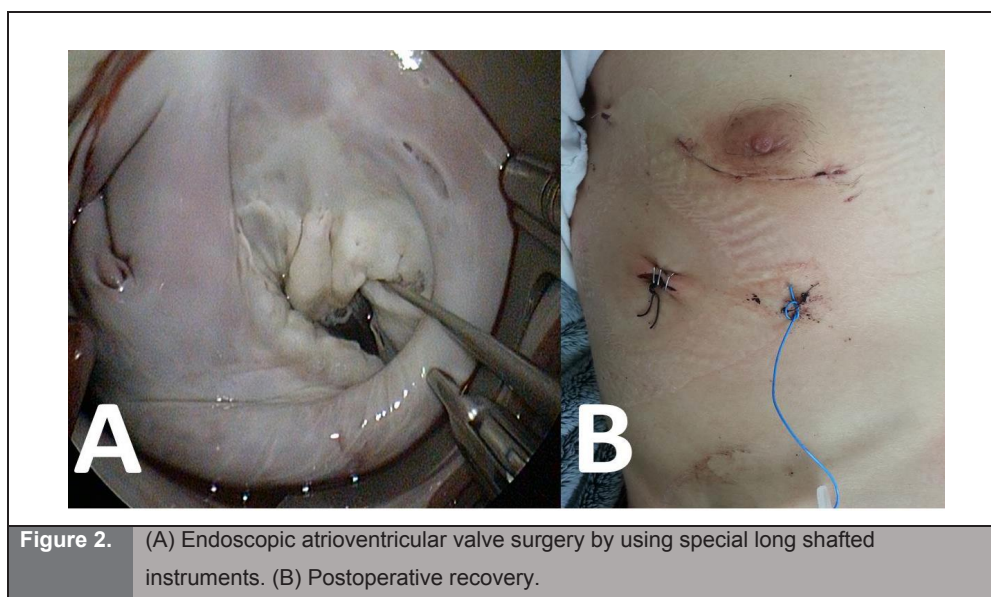
We routinely perform our antero-lateral EPAAVVS incision over the 4th intercostal space. Establishing an adequate working angle (Figure 1A) and adequate atrioventricular valve access (Figure 1B) are the most demanding technical challenges.

In cases of mitral valve (MV) surgery, we routinely position our left atrial retractor in the 4th intercostal space, right parasternal zone, lateral to the internal mammary bundle. In more pronounced pectus excavatum deformities, the retractor may be positioned on the left parasternal border. The antero-posterior retraction distance between the right atrium and anterior chest wall may be extremely limited and additional maneuvers are required to facilitate exposure. These include tilting the patient maximally to the left while applying low positive end-expiratory pressure (PEEP) to the left lung. In cases of unsuccessful right atrial retraction, exteriorized stay sutures are utilized to obtain tricuspid valve (TV) exposure, instrument access and adequate working angles.

Routine atrioventricular valve surgery is performed by using special endoscopic long shafted instruments (Figure 2A). Left ventricle septal myomectomy is performed by detaching the anterior MV-segments A1-A2-A3 from the annulus and subsequent careful sharp myocardial resection that extend from the aortic valve to the base of the papillary muscles. Reconstruction of the anterior MV-leaflet to the annulus is facilitated by the incorporation of an oversized bovine pericardial patch.



**Figure 1.** Endoscopic atrioventricular valve access difficulties in uncorrected congenital chest wall deformities: A) Establishing an adequate long shaft instrument working angle to the mitral- (MV) and tricuspid valve (TV). B) Obtaining adequate antero-posterior retraction of the right (RA) and left atrium (LA) for valve exposure.



**Figure 2.** (A) Endoscopic atrioventricular valve surgery by using special long shafted instruments. (B) Postoperative recovery.

For TV surgery, we establish total CPB by snaring the superior- and inferior vena cava. Cryoablation for atrial fibrillation (AF) is performed with an argon-gas surgical ablation system (Medtronic, Minneapolis, USA) and patent foramen ovale (PFO) routinely closed. We exclude the left atrial appendage in patients with AF or previous stroke.

Intensive care admission includes cardio-respiratory support, sedation and analgesia as indicated. Postoperative chest tubes are removed after 48 hours and a structured multidisciplinary in-hospital- and postdischarge rehabilitation program initiated as soon as possible (Figure 2B).

#### **Postdischarge follow-up**

All patients are reviewed within 6 weeks following surgery and continuation of care ascertained by the referring cardiologist and physician. Postdischarge echocardiographic- and clinical data were obtained by reviewing the most recent patient consultations (n = 7, 100%).

#### **Data analysis**

All in-hospital data and outcomes were collected from a prospective EPAAVVS database and assessed by the incidence of adverse events. Postdischarge data was collected retrospectively for survival-, freedom from reoperation-, clinical- and echocardiographic outcomes (n = 7) and are expressed as the mean  $\pm$  standard deviation (SD).

The study was approved by the institutional ethics review committee and individual consent waived. All authors had full access to the data, take responsibility for its integrity and have read and agree to the manuscript as written.

## **RESULTS**

#### **Intraoperative outcome**

A total of 7 consecutive adult patients with uncorrected CCWD and surgically correctable AVVD underwent EPAAVVS over a 69.0 months period. The procedures performed and associated cardiopulmonary bypass- and cross-clamp times are outlined in Table 3. There were no sternotomy conversions or complications in establishing vascular access, chest entry or atrioventricular valve exposure.

#### **Postoperative- and in-hospital outcomes**

Mechanical ventilation was successfully weaned on the same day of surgery in all patients. Intensive care discharge within 24 hours was achieved in all patients. Apart from new onset postoperative AF in 2 patients (28.6%), no other in-hospital morbidities, including surgical revisions for any cause, low cardiac output syndrome, stroke, acute renal dysfunction requiring dialysis, respiratory- or chest wall complications, wound infections or lymphoceles occurred. There were no 30-day mortalities and the mean length of hospitalization was  $7.4 \pm 1.0$  days.



<b>Table 3. Procedures performed, cardiopulmonary bypass- and endoballoon occlusion times (n = 7)</b>		
<b>Procedures performed</b>	<b>n</b>	<b>% of 7</b>
Mitral valve repair	7	100.0
Ring implantation	6	85.7
Cleft closure	1	14.3
Papillary muscle transfer	1	14.3
Secondary chordae release	1	14.3
Left ventricle septum myectomy	1	14.3
Leaflet patch augmentation	1	14.3
Neochordae implantation	7	100.0
Tricuspid valve repair	1	14.3
Ring implantation	1	14.3
Patent foramen ovale closure	3	42.9
Cryoablation	2	28.6
Left atrial appendage exclusion	2	28.6
Mean cardiopulmonary bypass time (minutes)	162.1±48.1 (108-221)	
Mean endoballoon occlusion time (minutes)	113.7±33.5 (78-165)	

### **Survival-, freedom from reoperation-, clinical- and echocardiographic outcomes**

A total of 208.0 patient months (mean 29.7±26.5, range 0.2-72.2) were available for recent long term survival-, freedom from atrioventricular valve reintervention-, current clinical status- and echocardiographic analysis. Follow-up data longer than 6 months were present in 6 patients (85.7%). There were no late deaths or reinterventions.

Latest clinical- and echocardiographic reviews confirmed a mean left ventricle ejection fraction of 59.2±5.3% and the absence of residual- or recurrent mitral valve regurgitation greater than grade I in all patients (n = 7, 100%). Tricuspid valve regurgitation more than grade II was present in 2 patients (28.6%). NYHA class I clinical status was achieved in all patients (n = 7, 100%).

### **DISCUSSION**

Posterior depression of the sternum and lower costal cartilages produce the characteristic appearance of isolated or mixed pectus excavatum (IMPE), which is reported to develop in 0.3% of the general population with an undefined primary aetiology [9]. Adult patients with uncorrected CCWD that include the IMPE spectrum, may present with surgically treatable atrioventricular valve disease [10-11] and can render significant minimally invasive (MI) technical challenges as a result of the decreased central anterior-posterior thoracic diameter, cardiac displacement to the left hemithorax and right ventricle- and mitral valve annulus compression. These perceived difficult access patients often deter surgeons from

offering a MI surgical option and deny these patients the full range of benefits associated with MI cardiac surgery.

Our current surgical team performed 652 EPAAVVS procedures between November 1st 2009 and November 30th 2015 and modified our standard technique to safely perform endoscopic atrioventricular valve surgery in the presence of decreased antero-posterior- or sternal-vertebral diameters.

We utilized both the Haller Index (HI) and Correction Index (CI) as IMPE severity markers in our study [12-14]. The HI, which is defined as the ratio of the transverse thoracic- and minimum sterno-vertebral diameter, was until recently considered to be the benchmark IMPE severity marker. Reports have demonstrated a 47.8% overlap between patients with IMPE and controls when only HI is employed, rendering HI potentially an inaccurate diagnostic measurement. The Correction Index (CI), which represents the indentation depth as a percentage of the maximum sterno-vertebral diameter, is considered to be more accurate in severity assessment. Other standardized protocols have also been proposed in an effort to increase the reliability of diagnosis and correct assessment of severity [15, 16]. HI greater than 3.25 and CI above 30%, which are generally accepted to indicate severe IMPE deformities, were present in 2 patients (28.6%). EPAAVVS was successfully performed in separate patients with maximum HI and CI of up to 3.3 (CI = 34.1) and 38.3% (HI = 2.9), which also reflect the discrepancy between the HI and CI as severity markers. The mean HI (2.7±0.5) and CI (21.4±10.2%) suggest a mild-to-moderate mean IMPE deformity profile in our series. There were no sternotomy conversions or complications in establishing atrial-, atrioventricular valve- or vascular access in any patient. We acknowledge, however, that right minithoracotomy working angle and atrioventricular valve exposure may be technically impossible in extreme IMPE presentations. Single-stage cardiac- and pectus correction procedures have recently been reported [17, 18] and future studies in which MI pectus correction precedes MI cardiac intervention to address these access challenges are certainly warranted.

We plan our MI atrial retractor blade insertion port and blade depth according to preoperative chest imaging, which include routine anterior- and lateral x-rays or supplemental computerized tomography [19]. Adequate exposure to successfully perform the planned procedure was obtained in all patients.

Concomitant elongated anterior mitral valve (MV) disease with left ventricular outflow tract obstruction was present in 1 patient (14.3%) with hypertrophic obstructive cardiomyopathy, which we previously reported to be treatable by EPAAVVS [20]. We were able to perform a successful left ventricular septal myectomy and MV reconstruction without complication.

There were no revisions, stroke, renal dysfunction, wound complications or postoperative air leaks in any patient, nor were any secondary pulmonary interventions required. New onset postoperative AF occurred in 2 patients (28.6%), which were successfully converted prior to hospital discharge. We initiate and stabilize anticoagulation- and rehabilitation programs in-hospital, which accounts for our mean length of hospitalization of 7.4±1.0 days. We prefer endoaortic occlusion over transaortic clamping [21, 22] and recently reported our own multi-institutional experience on its safety and efficacy [23].

There were no 30 day- or long term mortalities and no patient required reintervention for residual- or recurrent atrioventricular valve disease. All patients presented satisfactory functional



improvements at recent reviews. Echocardiographic data confirmed the absence of significant recurrent atrioventricular valve disease. We believe that referring physicians and surgeons should be made aware of high-quality alternatives to conventional sternotomy for atrioventricular valve procedures in this difficult access patient group.

#### **STUDY LIMITATIONS**

This small series reflects the outcomes of the current surgical team of a single centre with extensive primary- and redo-EPAAVVS experience. Sternotomy is no longer performed for primary- or redo-atrioventricular valve procedures at our institution.

We have no defined control group in this series and have therefore utilized the EuroSCORE II, which is standardized for sternotomy access, as a comparative control group. The enrolment period of this study was 63 months and its impact on our conclusions was not subjected to sensitivity analyses.

#### **CONCLUSION**

EPAAVVS in perceived difficult access adults with uncorrected CCWDs that include the pectus spectrum with HI and CI up to 3.3 and 38.3% respectively, is safe, feasible and durable with favourable long term clinical- and echocardiographic outcomes when performed in experience centres. The mere presence of uncorrected CCWDs should not deter surgeons from offering these patients the full benefits of minimally invasive cardiac surgery.

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An endoscopic view of a heart valve during surgery. The image shows a complex, fibrous structure with a central opening. A surgical instrument is visible at the top, and a circular structure is highlighted in the lower-left quadrant. The background is dark, with some lighter, branching structures.

# CHAPTER 10

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Endoscopic Port Access™ surgery for late orthotopic cardiac transplantation atrioventricular valve disease

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J Heart Valve Dis. 2017;26(2):124-129.

## ABSTRACT

### Background

This study presents the perioperative- and long term outcomes of redo-endoscopic Port Access™ surgery (REPAS) for late atrioventricular valve disease (AVVD) in orthotopic cardiac transplant (OCT) patients.

### Methods

Our current surgical team performed REPAS for late AVVD in 7 consecutive OCT patients (mean age 57.9±17.2 years, EuroSCORE II 21.2±14.7%) between February 1st 2004 and October 31st 2015. The mean OCT-REPAS time interval was 7.8±4.6 years (range 1.3-13.8). New York Heart Association (NYHA) class III or IV symptoms were present in 4 (57.1%) patients. The mean left ventricle ejection fraction was 52.9 ± 3.9%. Surgical indications included severe mitral valve (MV)- and tricuspid valve (TV) regurgitation in 3 (43.9%) and 6 (85.7%) patients respectively. Etiological factors included endomyocardial biopsy trauma (n = 6, 85.7%), degenerative disease (n = 2, 28.6%) and fungal endocarditis (n = 1, 14.3%).

### Results

Procedures performed included MV-repair (n = 3, 42.9%) and TV-replacement (n = 3, 42.9%). There were no sternotomy conversions or revisions for any cause. The mean cardiopulmonary bypass- and ischemic times were 178.4±48.6 and 118.3±39.5 minutes respectively. In-hospital morbidities included hospital acquired pneumonia (n = 2, 28.6%). There were no wound infections or 30-day mortalities. The mean length of hospitalization was 18.3±11.0 days. A total of 204.3 (mean 29.2 ± 45.6) patient months were available for long term clinical-and echocardiographic analysis (n = 7, 100% complete). No MV- or TV reinterventions were required. NYHA class II or less was achieved in 5 (71.2%) patients. No patient presented with residual MV-regurgitation greater than grade I.

### Conclusion

REPAS for late AVVD in OCT patients is safe and durable with favourable procedure related mortality, in-hospital morbidities and long term cardiac specific outcomes in experienced centres. Our technique provides an attractive benchmark against which emerging percutaneous interventions may be measured and earlier referral should be considered

## BACKGROUND

Advances in orthotopic cardiac transplantation (OCT)- and organ preservation techniques, immunosuppression regimes, infection control, prophylaxis and specialized multidisciplinary team approaches resulted in improved short- and long term survival and quality of life [1]. These improved long term outcomes are paralleled by an increased incidence of disabling late acute- or progressive post-transplantation atrioventricular valve disease (AVVD) [2-4] secondary to endomyocardial biopsy trauma, progressive donor heart degenerative valve disease and coronary arteriopathy related ischemic valvulopathy [5]. Surgery for symptomatic post-PCT AVVD is usually performed by classical redo-sternotomy or right thoracotomy [6-12] and reports of percutaneous interventions are progressively emerging [13].

We initiated our endoscopic Port Access™ surgery program in February 1997 [14-18] and reported our experience in previous cardiac- [19] and Port Access™ surgery [20]. This study provides an in-depth overview of our redo-endoscopic Port Access™ surgery (REPAS) experience in 7 consecutive OCT patients that underwent late AVVD correction by our current surgical team.

## METHODS

This is a retrospective study of a single-centre prospective REPAS database. A total of 345 REPAS procedures were performed between February 1st 2004 and October 31st 2015, of which 7 were in the context of late acute- and progressive AVVD post-OCT. The relevant preoperative patient characteristics and surgical indications, which may be multiple per patient, are outlined in Table 1 and 2 respectively.

### *Surgical techniques and in-hospital treatment pathway*

Our routine REPAS techniques were extensively described [19-20]. Our working port incision is established over the 4th intercostal, anterior axillary space. Lung adhesions are carefully released from the chest wall, diaphragmatic surface and pericardium. The potential presence of lung adhesions do not influence our access decision making and is not investigated preoperatively.

The aorta-iliac-femoral-axis (AIFA) is routinely evaluated in all patients either during coronary catheterization or by magnetic resonance angiography. Peripheral cardiopulmonary bypass (CPB) is established under transesophageal echocardiographic guided cannulation of the right internal jugular vein (18 Fr, Optisite™, Edwards Lifesciences, Irvine, California, USA), right femoral vein (22 Fr or 25 Fr, QuickDraw™, Edwards Lifesciences, Irvine, California, USA) and right femoral artery (21 Fr or 23 Fr, EndoReturn™, Edwards Lifesciences, Irvine, California, USA). An endoaortic balloon (IntraClude™, Edwards Lifesciences, Irvine, California, USA) is utilized for aortic occlusion and cold antegrade crystalloid cardioplegia delivery.

Table 1. Preoperative patient characteristics (n = 7)		
Patient characteristics	n	% of 7
Mean age (years)	57.9±17.2	
Age above 70 years	2	28.6
Female	1	14.3
Mean body mass index (m <sup>2</sup> / kg)	25.2±3.0	
Comorbidities present		
Hypertension	5	71.4
Hypercholesterolemia	5	71.4
Type I diabetes mellitus	2	28.6
Multiple previous sternotomy	1	14.3
Atrial fibrillation	1	14.3
Positive chronic infective serology	4	57.1
Cytomegalovirus	3	42.9
Toxoplasmosis	1	14.3
Ebstein-Barr virus	1	14.3
Varicella Zoster virus	1	14.3
Permanent pacemaker	3	42.9
Peripheral vascular disease	2	28.6
Renal dysfunction	3	42.9
Pulmonary hypertension	6	85.7
Mean pulmonary artery pressure (mmHg)	40.9±11.0	
Critical preoperative state	2	28.6
Underlying malignancy	1	14.3
Mean EuroSCORE II (range)	21.2±14.7 (5.5-43.6)	
Mean left ventricular function (range)	52.9±3.9 (45 -55)	
Impaired (< 50%)	1	14.3
New York Heart Association Classification		
II	3	42.9
III	3	42.9
IV	1	14.3

Table 2. Surgical Indications (n = 7)		
Surgical indications	n	% of 7
Mitral valve dysfunction	3	42.3
Endocarditic leaflet destruction	1	14.3
Myxomatous degenerative disease	2	28.6
Carpentier-Edwards classification		
Type I	1	14.3
Type II	2	28.6
Tricuspid valve dysfunction	6	85.7
Leaflet rupture / traumatic injury	6	85.7
Sick sinus syndrome	2	28.6
Patent foramen ovale	2	28.6
Atrial fibrillation	1	14.3

For TV-access, an occlusive endovascular balloon (Reliant™, Medtronic, Minneapolis, USA) is advanced through the right internal jugular cannula to occlude the superior vena cava, which avoids potentially hazardous pericaval dissection. Careful flow- and drainage control allow for perfect valve visualization without an additional inferior vena cava occlusion balloon. Routine atrioventricular valve surgery is performed with long shafted instruments (Figure 1).

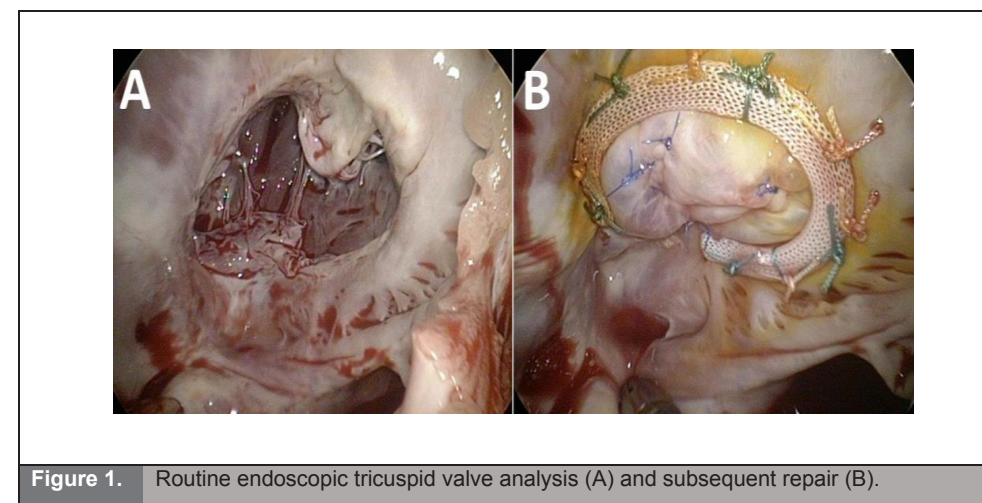


Figure 1. Routine endoscopic tricuspid valve analysis (A) and subsequent repair (B).



Cryoablation is performed with an argon-gas surgical ablation system (Medtronic, Minneapolis, USA) and patent foramen ovale (PFO) routinely closed. De-airing is ensured by a left atrial- and aortic balloon venting catheters, continuous flooding of the operative field with CO<sub>2</sub> and TEE surveillance for residual air in the left ventricle. Temporary ventricular pacing wires are placed either percutaneously through the right internal jugular vein or transvalvular under direct endoscopic visualization.

Cardio-respiratory support, sedation, analgesia and patient specific immunosuppressive regimes are administered as indicated in intensive care. A structured in-hospital- and postdischarge rehabilitation program is supervised by a multidisciplinary cardiac transplant team (MDCTT). Anticoagulation therapy with fenprocoumon (3M Health Care Ltd) is initiated and stabilized in-hospital with conversion to acetyl salicylic acid after 3 months in the absence of persistent postoperative atrial fibrillation or mechanical valve implantation.

#### Follow-up

Surgical review routinely occurs at 6 weeks and continuation of care ascertained under MDCTT guidance. Postdischarge echocardiographic- and clinical data were obtained from latest follow-up consultation records

#### Data analysis

All in-hospital data were collected from a prospective database. Post-discharge data were collected retrospectively. In-hospital outcomes were assessed by the incidence of adverse events and data are expressed as the mean  $\pm$  standard deviation (SD). The study was approved by the institutional ethics review committee. All authors agreed to the manuscript as written and take responsibility for data integrity.

## RESULTS

#### Intraoperative outcome

A total of 7 OT-patients underwent REPAS for late acute- or progressive post-OCT-AVVD. There were no intraoperative mortalities, sternotomy conversions, access site- or CPB complications. The performed procedures, CPB- and occlusion times are described in Table 3.

#### Postoperative course and in-hospital outcome

Mechanical ventilation was weaned within 48 hours of surgery in 6 patients (85.7%). There were no postoperative strokes or 30 day mortalities. Irreversible multiorgan failure from fungal endocarditis (EuroSCORE II = 40.3) accounted for 1 in-hospital mortality on the 38th postoperative day.

Procedures performed	n	% of 7
Mitral valve repair	3	42.9
Ring implantation	3	42.9
Leaflet repair	1	14.3
Leaflet resection	1	14.3
Cleft closure	1	14.3
Papillary muscle transfer- or shortening	1	14.3
Secondary chordae release	1	14.3
Neochordae implantation	1	14.3
Tricuspid valve repair	3	42.9
Ring implantation	3	42.9
Leaflet repair / patch reconstruction	3	42.9
Cleft closure	3	42.9
Neochordae implantation	2	28.6
Tricuspid valve replacement	3	42.9
Permanent pacemaker implantation	2	28.6
Patent foramen ovale closure	2	28.6
Cryoablation	1	14.3
Mean cardiopulmonary bypass times (minutes)	178.4 $\pm$ 48.6 (122-224)	
Mean endoballoon occlusion time (minutes)	118.3 $\pm$ 39.5 (63-162)	

In hospital complications and morbidities are outlined in Table 4. The mean length of hospitalization was 18.3 $\pm$ 11.0 days (range 8-38). There were no revisions for any cause, low cardiac output syndrome, persistent postoperative air leak longer than 72 hours or residual pleural collections that required drainage or wound infections.

	n	% of 7
Mechanical ventilation > 72 hours	1	14.3
Acute renal dysfunction requiring dialysis	3	42.9
Respiratory morbidity		
Hospital acquired pneumonia	2	28.6
Post-surgery rhythm abnormalities		
Permanent pacemaker implantation	1	14.3
New onset atrial fibrillation	1	14.3
Groin lymphocele	2	28.6

### **Survival-, freedom from reoperation-, clinical- and echocardiographic follow-up**

A total of 204.3 (mean 29.2±45.6) patient months post-REPAS, and 862.4 (mean 123.2±90.8) patient months post-OCT were available for analysis. Late deaths occurred in 4 patients due to neutropenic sepsis (2.4 months), fatal arrhythmia (4.2 months), malignancy (56.0 months) and respiratory failure (122.5 months) respectively. There were no REPAS-, MV- or TV reinterventions required. Latest clinical- and echocardiographic review of post-discharge patients (n = 6) confirmed NYHA functional class I, II, and III in 4 (66.7%), 1 (16.7%) and 1 (16.7%) patients respectively.

There were no recurrent- or new episodes of AF. No patient required the implantation of a new pacemaker or internal cardiac defibrillator. The mean left ventricle ejection fraction- and pulmonary artery pressure were 54.9±8.4 % and 28.3±9.1 mmHg respectively. There were no new- or recurrent MV-regurgitation more than grade I, TV-regurgitation more than grade II or paravalvular leaks.

### **DISCUSSION**

Advances in orthotopic cardiac transplant (OCT) patient management resulted in improved short- and long term survival [1], which are paralleled by an increased incidence of late acute-or progressive post-transplantation atrioventricular valve disease (AVVD). It is reported that significant mitral (MV) -, tricuspid (TV) - and pulmonary (PV) valve regurgitation are present in 32%, 19-84% and 42% of OCT patients respectively [2-4]. Surgery for AVVD is conventionally performed by classical redo-sternotomy or conventional right thoracotomy and is considered to be the most effective treatment strategy for intractable right- [5-9] and left heart failure [10- 12]. In addition to the progressive paradigm shift towards less invasive cardiac interventions, reports of percutaneous technology for post-OCT AVVD treatment are progressively emerging [13].

We developed extensive experience in REPAS [19-20], which avoids the risks associated with redo-sternotomy entry and redo-cardiac exposure. REPAS provides direct- and targeted atrial access with excellent valve visualization for standard surgical procedures.

All patients in our series had lung adhesions of varying severity. There were no sternotomy conversions or post-REPAS respiratory morbidities that required surgical intervention.

There were no complications in establishing peripheral vascular access or total cardiopulmonary bypass. We preferentially utilize an endoaortic balloon for occlusion [21-22]. There were no post-procedural targeted valve dysfunction, any neurological events or low cardiac output syndrome. Postoperative dialysis was required in 3 patients (42.6%), 2 of whom had severe renal impairment preoperatively. The 3rd patient was subjected to a cardiopulmonary perfusion time of 212 minutes. New onset postoperative atrial fibrillation (AF) occurred in 1 patient (14.3%), which was successfully reconverted prior to hospital discharge. No patient developed recurrent- or new post-discharge AF.

Emergency surgery was performed in 1 patient (14.3%) with fungal MV-endocarditis, severe TV-regurgitation and multiorgan failure (EuroSCORE II 40.3) and 1 patient (14.3%) with endomyocardial biopsy related TV-rupture and cardiac arrest (EuroSCORE II of 43.6). The first patient underwent MV-repair by ring implantation, papillary muscle repositioning, neo-chordal implantation and TV-replacement

with cardiopulmonary bypass- and ischemic times of 224- and 162 minutes respectively. He passed away on the 38th postoperative day. The second patient underwent urgent TV-replacement and was discharged after 14 days. She passed away after 4.3 months due to a fatal arrhythmia. Her clinical- and echocardiographic follow-up confirmed the absence of residual AVVD prior to her event.

We initiate and stabilize anticoagulation-, immunosuppressive- and rehabilitation regimens in-hospital, which accounts for our mean length of hospitalization of 18.3 (range 8-38) days.

There were no 30-day mortalities in our series despite a EuroSCORE II of 20.2±14.7% (range 5.5-43.6%). Late postdischarge cardiovascular interventions included percutaneous coronary intervention (n = 2, 28.6%), superficial femoral angioplasty (n = 1, 14.3%) and arteriovenous fistula surgery for dialysis (n = 1, 14.3%) after 4.0-, 2.0- and 8.0 years respectively.

The long-term freedom from cardiac reintervention, clinical- and echocardiographic follow-up suggest favourable REPAS related mortality, periprocedural morbidity and long term procedural durability.

### **STUDY LIMITATIONS**

This small series reflects the outcomes of the current surgical team of a single centre with extensive REPAS experience. Sternotomy is no longer performed for isolated AVVD. The EuroSCORE II was therefore utilized as comparative sternotomy control group. The enrolment period of this study was 11.0 years and the impact on our conclusions was not subjected to sensitivity analyses

### **CONCLUSION**

REPAS for late AVVD in OCT patients is safe and durable with favourable procedure related mortality, in-hospital morbidities and long term cardiac specific outcomes in experienced centres. It avoids the reentry risks posed by conventional sternotomy, offers direct targeted access to the atrioventricular valves and provides an attractive benchmark against which emerging percutaneous interventions may be measured. Earlier referral should be considered to avoid adverse outcomes related to progressive post-OCT AVVD

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# CHAPTER 11

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Late redo-Port Access™ surgery after Port Access™ surgery

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## ABSTRACT

### Objective

This study presents the first report on short- and long term outcomes in redo-Port-Access™ surgery after previous Port Access™ surgery (redo-PAS-PAS) for new- or recurrent mitral valve- (MV) and tricuspid valve (TV) disease.

### Methods

Our current surgical team performed redo-PAP-PAS in 26 consecutive patients who had previous Port Access™ surgery (mean age  $65.8 \pm 13.3$  years, 46.2% female, 42.3% older than 70 years, mean logistical EuroSCORE  $22.5 \pm 21.6\%$ ) between February 1st 1997 and June 30th 2014. Surgical indications included amongst others MV prosthesis dysfunction ( $n = 8$ , 30.8%), endocarditis ( $n = 10$ , 38.5%) and TV dysfunction ( $n = 3$ , 11.5%). The mean time interval between primary- and redo-PAS-PAS was  $70.32 \pm 57.4$  months.

### Results

Redo-PAS-PAS procedures included MV-replacement ( $n = 19$ , 73.1%), MV-repair ( $n = 5$ , 19.2%), and TV-repair ( $n = 2$ , 7.7%). Sternotomy conversion was required in 5 patients (19.2%), of which 4 (15.4%) were early conversions due to lung adhesion and 1 (3.8%) due to a late intraoperative complication. The mean cardiopulmonary bypass- and cross-clamp times were  $163.3 \pm 57.9$  minutes and  $101.2 \pm 43.8$  minutes respectively. Postoperative mechanical ventilation longer than 72 hours was required in 4 patients (15.4%). In-hospital morbidities included hospital acquired pneumonia ( $n = 3$ , 11.5%), postoperative air leaks ( $n = 2$ , 7.7%) and revision for bleeding ( $n = 1$ , 3.8%). The mean length of hospital stay was 16.1 days. Long term clinical- and echocardiographic follow-up were  $48.3 \pm 39.2$  months and  $44.6 \pm 32.9$  months respectively. The Kaplan-Meier analyses for survival and freedom from MV or TV reintervention ( $n = 26$ ) at 5 years were 83.9% and 95.8% respectively with 91.3% of surviving patients classified as being NYHA II or less. Echocardiographic follow-up showed no residual MV regurgitation more than grade I in all redo-MV repairs and no paravalvular leaks post-valve replacement.

### Conclusion

Redo-PAS-PAS is our routine approach and we apply this strategy in the majority of patients who had previous Port Access™ surgery. The predicted procedure related mortality, morbidities, patient satisfaction and long term outcomes are favourable.

## INTRODUCTION

We are witnessing a gradual increase in the number and age of patients undergoing reoperations for valvular heart disease paralleled by increased comorbidity, operative risks and quality of life expectations [1]. Reasons include ongoing degeneration of older bioprosthetic valves, valve repair failure and progressive native valve dysfunction in the context of previous non-valve cardiac surgery. At the same time, smaller incision and non-sternotomy approaches are becoming progressively established as excellent alternatives to conventional cardiac surgery [2].

We initiated our total endoscopic Port Access™ program in February 1997, Shortly after the first description of minimally invasive valve surgery (MI-VS) by Cosgrove [3] and the first report of mitral valve repair through minithoracotomy by Carpentier [4]. We established this technique as our routine approach for all isolated mitral- and tricuspid valve surgery [5- 7], arrhythmia- [8] and selected cardiac oncology surgery [9]. We subsequently extended the application of our technique to redo-surgery as an excellent alternative to conventional surgery [10].

This study provides an in-depth overview of our total endoscopic redo-Port Access™ surgery experience in 26 consecutive patients that underwent redo-atrioventricular valve surgery by our current surgical team in the context of previous Port Access™ surgery (redo- PAS-PAS).

## METHODS

This is a retrospective review of a single-centre prospective database. Our current surgical team performed a total of 177 redo-cardiac surgery procedures for new- or recurrent atrioventricular valve disease by Port Access™ between February 1st 1997 and June 30th 2014, of which 26 were in the context of previous Port Access™ Surgery (redo-PAS-PAS).

The relevant preoperative patient characteristics and clinical data are outlined in Table 1. The indications for reoperation, which may be multiple at presentation, are described in table 2.

### *Surgical techniques and in-hospital treatment pathway*

Our techniques for primary- and redo-PAS have been extensively described [5-7]. We perform the redo-minithoracotomy through the initial primary-PAS incision (Figure 1) and carefully release lung adhesions from the incision site, diaphragmatic surface and pericardium for adequate access. Preoperative imaging studies to determine the severity of pleural- or lung adhesions are not included in our patient evaluation and does not influence our access decision making.

Preoperative vascular access evaluation is routinely performed in all redo-patients either by an additional contrast injection in the iliac arteries during cardiac catheterization or by magnetic resonant angiography.



<b>Table 1. Preoperative patient characteristics (n = 26)</b>		
<b>Patient characteristics</b>	<b>n</b>	<b>% of 26</b>
Mean age (years)	65.8±13.3	
Age above 70 years	11	42.3
Female	12	46.2
<b>Comorbidities present</b>		
Previous sternotomy	4	
Prior to primary-PAS	2	71.4
Between primary-PAS and redo-PAS-PAS	2	71.4
Atrial fibrillation	8	28.6
Chronic obstructive pulmonary disease	3	14.3
Permanent pacemaker	3	14.3
Peripheral vascular disease	5	57.1
Neurological dysfunction	1	42.9
Renal dysfunction	2	14.3
Pulmonary hypertension	2	14.3
Emergency surgery / Critical preoperative state	3	14.3
<b>EuroSCORE I</b>		
Mean (range)	10.0±3.8 (6 to 19)	
Logistical (range)	22.5 ±21.6%(4.0 to 85.4)	
Mean EuroSCORE II (range)	14.2% (1.7 to 84.1)	
<b>Left ventricular function</b>		
Impaired (EF < 50%)	5	15.4
Mean ejection fraction (%)	61.2±13.3	

<b>Table 2. Surgical indications (n = 26)</b>		
<b>Surgical indications</b>	<b>n</b>	<b>% of 26</b>
Mitral valve dysfunction	25	96.3
Prosthesis dysfunction	8	30.8
Mechanical	7	26.9
Endocarditis	4	15.4
Thrombosis	1	3.8
Paravalvular leak	2	7.7
Biological	1	3.8
Endocarditis	0	0
Degeneration	1	3.8
Paravalvular leak	0	0
Post repair endocarditis	6	23.1
Repair Failure	10	38.5
Fibro-elastic disorder / myxomatous	7	26.9
Barlow morphology	2	7.7
Congenital abnormality	1	3.8
Type I recurrence	1	3.8
Type II recurrence	8	30.8
Type III recurrence	1	3.8
Progressive native valve dysfunction in the context of previous non-valve PAS	2	7.7
Previous cryoablation for atrial fibrillation	1	3.8
Previous atrial septal defect closure	1	3.8
Tricuspid valve dysfunction	3	11.5
Functional	2	7.7
Organic	1	3.8



**Figure 1.** Preoperative- (left) and postoperative redo-PAS-PAS (right) incision

We establish venous drainage through the right internal jugular- (16 Fr to 18 Fr, Optisite™, Edwards Lifesciences, Irvine, California, USA) and femoral vein (22 Fr or 25 Fr, QuickDraw™, Edwards Lifesciences, Irvine, California, USA) respectively. A femoral artery cannula with Y-arm (21 Fr or 23 Fr, EndoReturn™, Edwards Lifesciences, Irvine, California, USA) is utilized for arterial flow and an endoaortic balloon (IntraClude™, Edwards Lifesciences, Irvine, California, USA) for aortic occlusion and cold antegrade crystalloid cardioplegia delivery.

All guidewires and cannulae are positioned under transesophageal (TEE) guidance. We position an occlusive endoballoon (Reliant, Medtronic, Minneapolis, USA) through the right internal jugular vein into the superior vena cava and snare the inferior vena cava to obtain total cardiopulmonary bypass for primary- or redo-tricuspid valve surgery.

We use an argon-gas surgical ablation system (Medtronic, Minneapolis, USA) for cryoablation. Long-shafted instruments, standard valve surgery techniques and left atrial appendage exclusion by endoraphy in patients with a history of cerebrovascular disease or peripheral emboli are routinely used and performed.

Temporary ventricular pacing wires are either placed percutaneous through the right internal jugular vein or under endoscopic vision on the diaphragmatic ventricular epicardium if accessible. De-airing is ensured by a venting catheter in the left atrium, continuous flooding of the operative field with CO<sub>2</sub>, antegrade balloon catheter venting and TEE surveillance for residual air in the left ventricle.

Cardio-respiratory support, sedation and analgesia are administered as indicated in intensive care. Postoperative chest tubes are routinely removed 48 hours postoperatively and all patients receive structured in-hospital- and post-discharge rehabilitation. Anticoagulated therapy with fenprocoumon (3M Health Care Ltd) is initiated and stabilized in-hospital and continued for 3 months, with conversion to acetyl salicylic acid in the absence of persistent postoperative atrial fibrillation (AF) or mechanical valve implantation.

### **Follow-up**

All patients attend an outpatient clinic 6-8 weeks postoperatively in addition to the continuation of care by their cardiologist and general practitioner. Postdischarge echocardiographic- and clinical data were obtained by treating physician communication.

### **Data analysis**

All in-hospital data were collected prospectively. However, this study design was retrospective as the post-discharge data was collected retrospectively. In-hospital outcomes were assessed by the incidence of adverse events. Postdischarge survival- and freedom from reoperation estimates were determined by Kaplan-Meier analysis and are expressed as a proportion  $\pm$  SE based on the intention to treat principle of the total population (n = 26).

Data are expressed as the mean  $\pm$  standard deviation and analysed with SPSS Statistics 20.0 (IBM, USA). The study was approved by the institutional ethics review committee. The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

## **RESULTS**

### **Intraoperative outcome**

A total of 26 patients underwent redo-PAS-PAS. The procedures performed are outlined in Table 3. Sternotomy conversion occurred in 5 patients (19.2%), of which 4 (15.4%) were early conversions due to extensive lung adhesions and 1 (3.8%) late conversion due to atrioventricular dehiscence during mitral valve replacement. Mitral valve redo-repairs were performed in 5 of the 10 patients (50%) who underwent previous PAS-mitral valve repair.

There were no complications in establishing vascular access or cardiopulmonary bypass. However, an iliac vein rupture occurred in 1 patient (3.8%) during post-procedure decannulation. The cardiopulmonary bypass- and cross-clamp times are depicted in Table 4. Combined procedures included additional tricuspid valve repair or cryoablation.

Table 3. Redo-PAS-PAS procedures performed (n = 26)		
Procedures performed	n	% of 26
Mitral valve replacement	19	73.1
Mechanical prosthesis	11	42.3
Bioprosthesis	8	30.8
Tricuspid valve replacement	1	3.8
Bioprosthesis	1	3.8
Mitral valve repair	5	19.2
Annuloplasty ring explantation / reimplantation	3	11.5
Cleft closure	3	11.5
Leaflet resection	1	3.8
Neochordae implantation	3	11.5
Tricuspid valve repair	2	7.7
Additional procedures performed	6	23.1
Cryoablation	5	19.2
Patent foramen ovale closure	1	3.8

Table 4. Cardiopulmonary bypass- (CPBt) and cross-clamp time (CCt) (n = 26)		
	Mean CPBt (range)	Mean CCt (range)
Overall (n = 26)	163.3±57.9	101.2±43.8
Redo-PAS-PAS (n = 21)	166.0 (66-360)	101.4 (40-229)
Mitral valve replacement (n = 16)		
Isolated procedure (n = 13)	154.4 (91 – 245)	100.6 (60-141)
Combined procedure (n = 3)	190.0 (152-271)	109.7 (95-200)
Mitral valve repair (n = 4)		
Isolated procedure (n = 1)	360.0	229.0
Combined procedure (n = 3)	133.7 (122-141)	48.9 (78-95)
Isolated tricuspid valve replacement (n = 1)	149.0	96.0
Sternotomy conversions (n = 5)	151.8 (103-282)	100.0 (55-128)
Mitral valve replacement (n = 3)		
Isolated procedure (n = 2)	105.0 (103-282)	69.0(64-128)
Combined procedure (n = 1)	271.0	200.0
Mitral valve repair (n = 1)		
Isolated procedure (n = 1)	122.0	55.0

### Postoperative course and in-hospital outcome

Mechanical ventilation was weaned on the day of surgery in 18 patients (69.2%). Intensive care discharge within 72 hours occurred in 15 patients (57.7%). Total in-hospital- and 30-day mortality were 7.7% (n = 2) due to endocarditis related multiorgan failure (EuroSCORE II = 68.2) and low cardiac output syndrome (EuroSCORE II = 84.1) respectively.

In hospital complications and morbidities, which were multiple in 5 patients (19.2%), are outlined in Table 5. Surgical revisions were required in 2 patients (7.7%) and were performed via Port Access™ through the same incision. The mean length of hospitalization was 16.1 days (range 6 to 74).

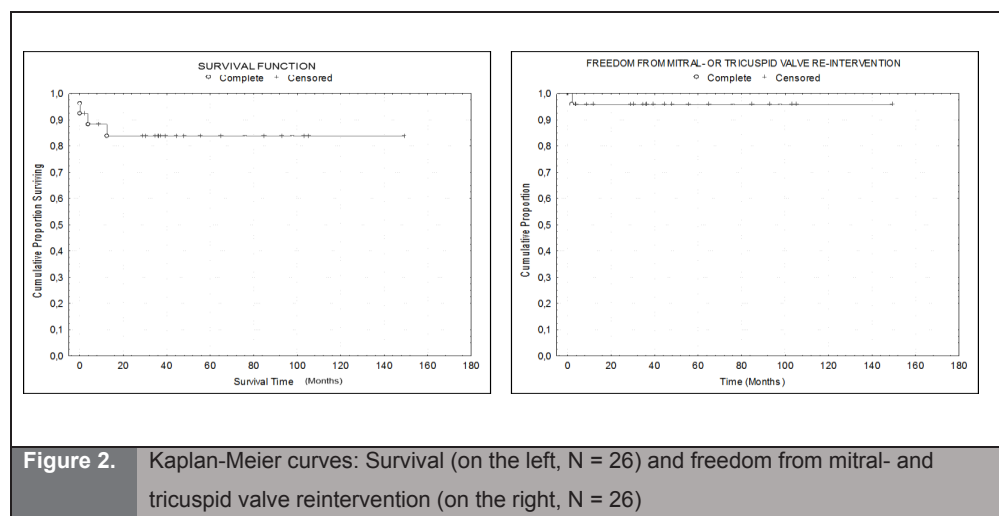
### Survival-, freedom from reoperation-, clinical- and echocardiographic follow-up

Updated long term survival-, freedom from mitral- and tricuspid valve reintervention and clinical follow-up data were available for all patients (n =26, 100%) over a mean of 48.3±39.2 months postoperatively. No echocardiographic data was older than 8 months.

Table 5. In-hospital morbidity other than death (n = 26)		
Morbidity	n	% of 26
Intensive care admission > 72 hours	11	42.3
Mechanical ventilation > 72 hours	4	15.4
Revision	2	7.7
Bleeding	1	3.8
Repair / Replacement failure	1	3.8
Low cardiac output syndrome	3	11.5
Cerebrovascular event / stroke	1	3.8
Acute renal dysfunction requiring dialysis	3	11.5
Respiratory morbidity		
Residual pleural collections requiring drainage	7	26.9
Hospital acquired pneumonia	3	11.5
Postoperative air leak > 72 hours	2	7.7
Post-surgery rhythm abnormalities		
Permanent pacemaker implantation	3	11.5
New onset atrial fibrillation	4	15.4
Age above 70 years	3	11.5
Redo-groin incision morbidity		
Wound infection (groin)	1	3.8
Lymphocele	2	7.7

The Kaplan-Meier Curves for survival and freedom from mitral- and tricuspid valve reintervention than include all patients (n = 26) are presented in Figure 2. Late deaths occurred in 2 patients due pneumonia (3.8 months) and progressive heart failure (12.5 months). Survival for the total patient group (n = 26) at 1- and 5 years was 88.3% and 83.9% respectively. One patient (3.8%) required reoperation for residual mitral valve regurgitation at 1.4 months. He underwent subsequent mitral valve replacement via Port Access™.

Freedom from mitral- or tricuspid valve reintervention at 5 years was 95.8%. The long term echocardiographic- and clinical outcomes are outlined in Table 6. The mean echocardiographic follow-up time was  $44.6 \pm 32.9$  months and a cumulative total of 980.8 postoperative echocardiographic months were available for analysis. In total, 21 of the 23 surviving patients (91.3%) were classified as NYHA I or II.



<b>Table 6. Long term echocardiographic- and clinical outcomes (n = 23)</b>		
<b>Echocardiographic outcomes (n = 23, 44.6±32.9 months)</b>	<b>n</b>	<b>% of 26</b>
<b>Mitral valve repair (n = 5)</b>		
Mean left ventricle ejection fraction (%)	58.0±4.5	
Mean gradient (mmHg)	6.8±4.1	
Recurrent / residual mitral regurgitation		
None	1	3.8
Grade I	4	15.4
Grade II or more	0	0
<b>Mitral valve replacement (n = 16)</b>		
Mean left ventricle ejection fraction (%)	53.2±12.0	
Mean gradient (mmHg)	4.8±2.1	
Paravalvular leak	0	0
<b>Tricuspid valve repair (n = 3)</b>		
Recurrent / residual tricuspid regurgitation		
None	2	7.7
Grade II or more	1	3.8
<b>Tricuspid valve replacement (n = 1)</b>		
Mean gradient (mmHg)	3.0	
<b>Clinical outcomes (n = 23, 48.3±39.2 months)</b>		
<b>New York Heart Association functional status</b>		
Class I	14	53.8
Class II	8	30.8
Class III	1	3.8
Class IV	0	0
New onset atrial fibrillation	1	3.8
New pacemaker / internal cardiac defibrillator	3	11.5

## DISCUSSION

The incidence of redo-cardiac procedures is increasing as an aging population present with degeneration of bioprosthetic valve implantations, valve repair failure and native valve disease progression in the context of previous cardiac surgery [1].

Various centres now perform minimally invasive mitral- and tricuspid valve surgery as an alternative to conventional mitral valve surgery and new technologies that allow percutaneous- and transapical valve implantation are emerging [2]. We initiated our endoscopic Port Access™ program in 1997 and established this approach as our preferred technique for mitral- and tricuspid valve surgery [5-9], also after previous cardiac surgery [10] including previous Port Access™ surgery (redo-PAS-PAS). All 26

patients reported in this series underwent redo-PAS-PAS in the context of previous primary PAS by mini-thoracotomy.

Early sternotomy conversion as a risk aversion strategy change due to extensive lung adhesions occurred in 4 patients (15.4%). This limited extensive lung injury and facilitated conventional atrioventricular valve exposure. None of these patients developed subsequent respiratory morbidities. Late sternotomy conversion due to an intraoperative adverse event occurred in 1 patient (3.8%). The majority of patients in this series (n = 21, 80.8%) retained the clinical- and cosmetic benefits of minimally invasive surgery. Postoperative air leaks occurred in 2 patients (7.7%), which resolved within 7 days without requiring secondary surgery.

There were no complications in establishing redo-vascular access or cardiopulmonary bypass, which was either through the primary-PAS incision or contralateral groin depending on preoperative imaging and clinical judgment. An iliac vein rupture occurred during decannulation in 1 patient (3.8%) and was the only adverse cardiopulmonary bypass- and vascular event. The primary incision and vasculature were utilized in this case. Moments after decannulation we noticed rapid abdominal distention with associated hemodynamic compromise. Immediate laparotomy confirmed an iliac vein rupture, which was subsequently repaired with home discharge achieved on day 13 postoperatively.

Postoperative low cardiac output syndrome (LCOS) was present in 3 patients (11.5%) with preoperative left ventricular ejection fractions of 65%, 50% and 15% and EuroSCORE II of 19.2%, 68.2% and 84.1% respectively. All 3 patients required mitral valve replacement in the context of either endocarditis (n = 2, 7.7%) or ischemic cardiomyopathy (n = 1, 3.8%). The mean ischemic time was 88.7 minutes. These were high risk patients with mortalities (n = 2, 7.7%) on day 2 and 6 postoperatively and one hospital discharge (3.8%) on day 14. We consider myocardial protection adequate and attribute these findings to premorbid risks.

The three patients (11.5%) who required postoperative dialysis had perfusion times of 279, 239 and 103 minutes respectively. Atrioventricular dehiscence occurred during redo-mitral valve replacement in the first patient and required sternotomy conversion. She was discharged after 31 days.

Permanent stroke (subarachnoid hemorrhage on the second post-operative day) occurred in 1 patient (3.8%) and was unlikely procedure related.

Reexploration for postoperative bleeding occurred in 1 patient (3.8%). Reoperation for unexpected tissue confirmation of endocarditis post-tricuspid valve repair resulted in reoperation and subsequent valve replacement (n = 1, 3.8%). Both reoperations were performed using the same incision.

We routinely advocate redo-valve repair if anatomically feasible, especially in women of child-bearing age to avoid the teratogenic-risks associated with vitamin K-antagonist. We performed a complex redo-repair that consisted of a redo-annular ring placement, additional posterior leaflet resection, neochordal insertions and cleft closure in a 38 year old female with a Barlow-type mitral valve who presented with recurrent mitral valve incompetence 6 months after her primary mitral valve repair. She was discharged after 7 days despite a cardiopulmonary bypass- and ischemic time of 360 and 229 minutes respectively. Her clinical follow-up confirmed an ejection fraction of 55%, no residual mitral valve regurgitation and NYHA II clinical status at 30 months.

New onset atrial fibrillation (AF) occurred in 4 patients (15.4%), of which 3 (75%) were older than 70 years. Age is an established risk factor for postoperative AF and cardioplegia type has little influence. [13-15].

In total, 10 patients (38.5%) were reoperated in the context of endocarditis. Infection was successfully controlled in all surviving patients (n = 9, 90%) with no subsequent infection recurrence or need for reintervention. Aggressive annular debridement and pericardial patch reconstructions can be performed by PAS in experienced centres. We initiate and stabilize anticoagulation- and rehabilitation regimens in-hospital, which accounts for our mean length of hospitalization of 16.1 days.

The 30-day mortality (n = 2, 7.7%, EuroSCORE II of 84.1% and 68.2%) in our series is well below the predicted EuroSCORE I and II (22.5 and 14.2) estimates. We used both the EuroSCORE I and EuroSCORE II as predictor for operative outcome as the calibration and predictability improvements of the latter are still to be confirmed [16]. Whether minimally invasive- and conventional redo-cardiac surgery contribute equally to the risk scoring are not yet established.

The long-term survival-, freedom from reoperation, echocardiographic- and clinical follow-up suggest an acceptable long term durability and patient outcome.

### Study Limitations

This relatively small series reflects the outcomes of the current surgical team of a single centre with extensive primary- and redo-Port Access™ surgery experience. We have no institutional control group as sternotomy is not performed anymore for primary- or redo-mitral- and tricuspid valve procedures.

We therefor utilized the EuroSCORE, which is standardized for sternotomy access, as a comparative control group. The enrolment period of this study was 17 years and its impact on our conclusions was not subjected to any sensitivity analyses.

### CONCLUSION

We now routinely perform redo-PAS-PAS in view of its various technical advantages and good clinical outcomes. We believe that this series provides additional evidence that redo-PAS-PAS is an acceptable and very attractive redo-modality in the context of previous Port Access™ surgery in centres with PAS experience. The majority of patients retain the benefits of minimally invasive surgery.



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An endoscopic view of a surgical procedure. The image shows a large, circular, perforated surgical instrument, likely a stapler or grasper, positioned within a body cavity. The surrounding tissue is dark and appears to be part of the heart or a major vessel. The lighting is focused on the instrument, highlighting its metallic texture and the perforations. The overall scene is complex and technical, typical of a minimally invasive surgical approach.

# CHAPTER 12

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Endoscopic Port Access™ left ventricle outflow tract resection and atrioventricular valve surgery

Van der Merwe J, Casselman F, Van Praet F

## ABSTRACT

The continuous evolution in robotic-, endoscopic- and transcatheter cardiac interventions resulted in innovative techniques that simultaneously address left ventricular outflow tract obstruction (LVOTO) and concomitant atrioventricular valve (AVV)-pathology in the context of hypertrophic obstructive cardiomyopathy (HOCM). We present our brief report of 13 consecutive HOCM patients with concomitant AVV-disease, who underwent endoscopic left ventricular septal myectomy (LVSM) and AVV-surgery by Port Access™ (EPAS) between March 1st 2010 and October 31st 2015.

Our EPAS technique in the context of HOCM utilizes peripheral cardiopulmonary bypass, endoaortic balloon occlusion and a 4cm right antero-lateral thoracic working port. Access to the LVOTO is obtained by detaching the anterior mitral valve (MV) leaflet from the annulus. Controlled sharp LVSM is then performed from the aortic leaflet base to the papillary muscles. Subsequent routine AVV surgery is performed using long shafted instruments.

There were no sternotomy conversions, LVSM complications or 30-day mortalities. The mean length of hospitalization was  $17.7 \pm 18.1$  days. Long term clinical- and echocardiographic analysis of 645.7 patient months (n = 13, 100% complete) identified 2 late mortalities, which were not procedure-, HOCM- or AVV-related. All patients (n = 13, 100%), including the late mortalities, had significant improvement in their quality of life, a 100% long term freedom from reintervention and no residual peak instantaneous LVOTO gradients more than 15 mmHg.

This brief report emphasises that simultaneous LVSM and concomitant AVV-surgery by EPAS can safely be performed in experienced centres with favourable long term outcomes.

## INTRODUCTION

Adult hypertrophic obstructive cardiomyopathy (HOCM) is as an autosomal dominant cardiac sarcomere protein gene abnormality associated with an annual 1-2% sudden cardiac death risk [1] and is defined as unexplained left ventricular (LV) thickness greater than 15 mm in 1 or more LV segments resulting in LV outflow tract obstruction (LVOTO), LV-diastolic dysfunction and conduction abnormalities.

Systolic anterior motion (SAM) and regurgitation of the mitral valve (MV) may occur due to concomitant anterior MV-leaflet elongation and anterior papillary muscle displacement towards the LVOT. Degenerative-, infective- and rheumatic atrioventricular valve (AVV)-disease may also be present as independent pathology in the context of HOCM and LVOTO.

Left ventricle septal myectomy (LVSM) with or without concomitant AVV-surgery is conventionally performed either by isolated transaortic valve-, transatrial-, transventricular- or combined transaortic valve and left atrial access [2-8] through midline sternotomy. The progressive paradigm shift towards endoscopic- [9], robotic- [10] and transcatheter cardiac interventions [11-12] resulted in innovative techniques to simultaneously address LVOTO and AVV-pathology.

This brief report of 13 consecutive HOCM patients with concomitant AVV-pathology, presents the perioperative- and long term clinical- and echocardiographic outcomes of LVSM and AVV-surgery by endoscopic Port Access™ surgery (EPAS), operated by our current surgical team between March 1st 2010 and October 31st 2015.

## PATIENT SELECTION AND WORK-UP

EPAS is the routine procedure for isolated AVV-disease at our institution [13] and no preoperative contraindications prohibit our endoscopic approach. We reported our experience in difficult access extreme obese patients [14], congenital chest wall deformities [15], redo-cardiac surgery [16] and redo-EPAS after previous EPAS [17].

The relevant preoperative HOCM patient characteristics and surgical indications are outlined in Table 1 and Table 2 respectively. Presenting symptoms included angina, syncope and dyspnoea in 6 (46.2%), 4 (30.7%) and 9 (69.2%) patients respectively. The preoperative peak LVOT gradient of 173 mmHg measured in one patient was confirmed by transesophageal echocardiography (TEE) and catheterization. Two patients (15.4%) had previous cardiac operations, which included a minimally invasive direct coronary artery bypass grafting (104.3 months prior to current HOCM presentation) and conventional sternotomy aortic valve replacement with Morrow-procedure (1.3 months prior current HOCM presentation) at another institution.

## PREOPERATIVE PREPARATION

Preoperative aorta-iliac-femoral-axis (AIFA) evaluation is routinely performed in all patients either during coronary catheterization or by magnetic resonance angiography.

We do not routinely perform computerized tomography in redo-surgery and perform no special investigation to evaluate the presence of lung adhesions. Routine cardiac surgical workup is followed by an elaborate informed consent process in which the various options are discussed and a final treatment strategy elected.

Patient characteristics	n	% of 13
Mean age (years)	57.3±14.5	
Female	5	38.5
Mean body mass index (range)	27.6±5.1 (22.5-42.2)	
Comorbidities present		
Hypertension	9	69.2
Hypercholesterolemia	5	38.5
Type I diabetes mellitus	1	7.7
Previous cardiac surgery	2	15.4
Chronic obstructive pulmonary disease	2	15.4
Atrial fibrillation	7	53.8
Renal dysfunction	2	15.4
Pulmonary hypertension	8	61.5
Mean sPAP** (mmHg)	36.5.9±14.4 (25-80)	
Critical preoperative state	1	7.7
Mean EuroSCORE II (range)	4.2±5.4 (1.0-17.8)	
Mean left ventricular function % (range)	62.1±7.8 (55-77)	
Mean left ventricular outflow tract gradient (mmHg)	74.8±42.5 (15-173)	
Mean interventricular septum diameter (millimetres)	19.5±4.5 (15-28)	
Mitral valve regurgitation	13	100
Grade II	2	15.4
Grade III	5	38.5
Grade IV	6	46.2
Tricuspid valve regurgitation	9	69.2
Grade I	6	46.2
Grade II	1	7.7
Grade III	2	15.4
New York Heart Association Functional Status		
II	4	30.8
III	9	69.2

\*\* sPAP: mean systolic pulmonary artery pressure

Surgical indications	n	% of 13
Mitral valve dysfunction	13	100
Systolic anterior motion (SAM)	12	92.3
Endocarditis	1	7.7
Myxomatous degenerative disease	2	15.4
Rheumatic valve disease	1	7.7
Tricuspid valve dysfunction	3	23.1
Patent foramen ovale	3	23.1
Atrial fibrillation	2	15.4

#### EQUIPMENT PREFERENCE CARD

All LVSM and isolated AVV-procedures in the context of HOCM are performed by EPAS using special long shafted instruments without additional special equipment. A bovine pericardial patch is used to augment the anterior MV leaflet if required.

#### PROCEDURE

Our routine EPAS technique [18] is modified in the context of HOCM and concomitant AVV-pathology. However, the standard EPAS operative setup remains unchanged (Figure 1A). Peripheral cardiopulmonary bypass (CPB) is established by transesophageal echocardiography (TEE) guided cannulation of the right internal jugular vein- (16-18 Fr, Optisite™, Edwards Lifesciences, Irvine, California, USA), right femoral vein- (22-25 Fr, QuickDraw™, Edwards Lifesciences, Irvine, California, USA) and right femoral artery cannulation (21 Fr or 23 Fr, EndoReturn™, Edwards Lifesciences, Irvine, California, USA). An endoaortic balloon (IntraClude™, Edwards Lifesciences, Irvine, California, USA) is utilized for aortic occlusion and delivery of cold antegrade crystalloid cardioplegia.

Routine- and complex MV and tricuspid valve (TV)-surgery, as outlined in Table 3, are performed with long shafted instruments through a 4th intercostal, antero-lateral thoracic working port. Access to the left ventricular outflow tract (LVOT) is obtained by detaching the anterior MV-leaflet from the annulus (Figure 1B), which is followed by routine plication of both papillary muscles away from the LVOT (Figure 1B). Controlled sharp LV-septal muscle resection is performed from the base of the aortic valve to the papillary muscles (Figure 1D), of which the excision depth is guided by preoperative LV-septal diameter by TEE measurements. LV-septum perforation and extensive resection in conduction regions are avoided.

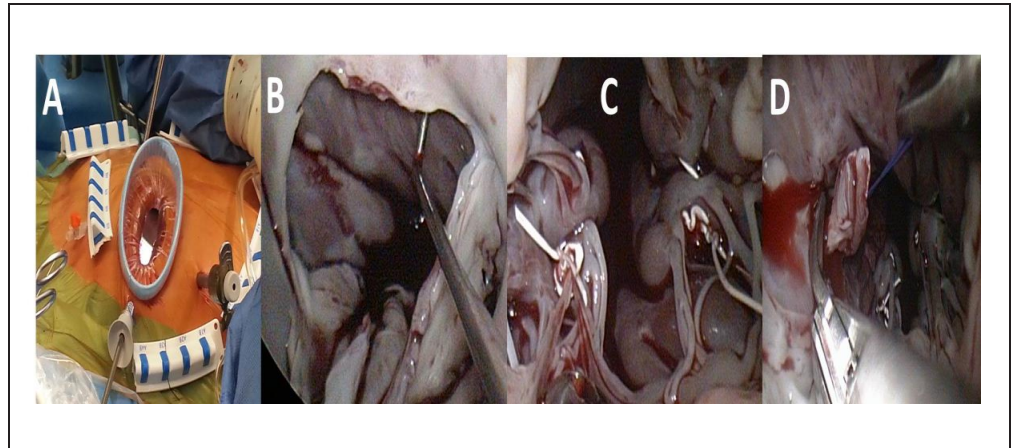
In cases of MV-repair, an oversized bovine pericardium patch is incorporated into the annular reattachment (Figure 2A and 2B). Significant SAM was present in 12 patients (92.3%), of which successful MV repair was achieved in 7 (53.8%). MV-replacements were reserved for rheumatic-, advanced myxomatous- or high risk valves for short term repair failure. For TV surgery through a right



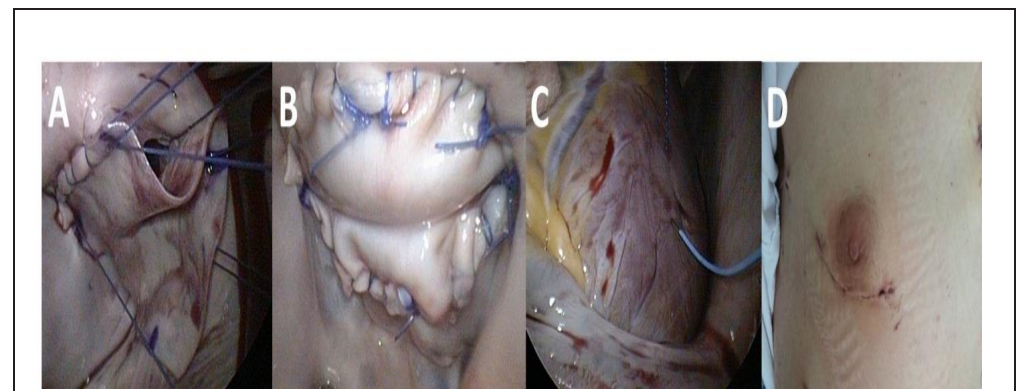
atriotomy, the superior- and inferior vena cava are snared. Cryoablation is performed with an argon-gas surgical ablation system (Medtronic, Minneapolis, USA), the base of the left atrial appendage oversewn in patients with atrial fibrillation or previous stroke and patent foramen ovale are also routinely closed.

Post-procedural de-airing is ensured by left atrial- and aortic balloon venting catheters, continuous flooding of the operative field with CO<sub>2</sub> and TEE surveillance for residual air in the left ventricle. Temporary epicardial- (Figure 2C) or transjugular ventricular pacing wires are routinely placed.

<b>Table 3. Procedures performed, cardiopulmonary bypass- and endoballoon occlusion times (n = 13)</b>			
<b>Procedures performed</b>	<b>n</b>	<b>% of 13</b>	
Mitral valve repair	7	53.8	
Ring implantation	7	53.8	
Leaflet patch reconstruction (anterior +/- posterior)	7	53.8	
Leaflet resection	2	15.4	
Cleft closure	2	15.4	
Papillary muscle plication +/- transfer	7	53.8	
Secondary chordae release	1	7.7	
Neochordae implantation	6	46.2	
Edge-to-Edge repair	1	7.7	
Mitral valve replacement	6	46.2	
Tricuspid valve repair	1	7.7	
Ring implantation	1	7.7	
Permanent pacemaker implantation	1	7.7	
Patent foramen ovale closure	3	23.1	
Left atrial appendage exclusion	3	23.1	
Cryoablation	2	15.4	
Elective hybrid percutaneous coronary intervention	1	7.7	
Mean cardiopulmonary bypass time (minutes)(range)	202.2 ± 65.5	(133-314)	
Mean endoballoon occlusion time (minutes)(range)	140.2 ± 49.3	(76-220)	



**Figure 1.** Routine EPAS setup (A) is followed by left ventricular outflow tract (LVOT) access. The anterior mitral valve (MV)-leaflet segments A1-A3 are detached from its anterior annular attachment (B). Both papillary muscles are plicated away from the LVOT (C). Left ventricle septal myomectomy is subsequently performed by controlled sharp muscle resection that extend from the aortic valve towards the left ventricle apex up to the base of the papillary muscles (D).



**Figure 2.** Reattachment of the anterior MV-leaflet to the annulus is performed with the incorporation of an oversized pericardial patch (A) and the concluded mitral valve repair reviewed (B). A temporary pacemaker wire is attached to the diaphragmatic surface of the left ventricle (C) and routine postoperative recovery initiated (D).



## TEAM MEMBERS

All patients are presented at a specialised multidisciplinary team meeting, which consist of cardiac surgical-, cardiology-, anaesthetic-, radiology-, allied medical-, trainee- and administrative staff members. Operative procedures are conducted within a specialised team context that consist of a TEE trained anaesthetist [19], 2 minimally invasive cardiac surgeons and a trainee, operative nurses and a perfusionist experienced in EPAS perfusion [20] procedures.

Postoperative intensive care is coordinated by a team of full-time onsite cardiac intensivists, which is followed by a structured and individualised in-hospital multidisciplinary rehabilitation program. Finally, continuation of care ascertained by the referring physician as part of patient centred service delivery.

## POSTOPERATIVE MANAGEMENT

Cardio-respiratory support, sedation and analgesia are administered as indicated in intensive care and a structured in-hospital rehabilitation program (Figure 2D) initiated as soon as possible. All patients undergo pre-discharge transthoracic echocardiographic evaluation for satisfactory operative result confirmation.

Infective endocarditis is treated with appropriate antibiotics for 6 weeks under the supervision of an infective endocarditis team and long term anticoagulation regimes initiated and stabilized in-hospital in cases of mechanical prosthetic implantation or chronic atrial fibrillation. All patients are reviewed within 6 weeks postdischarge, after which continuation of care is ascertained by the referring cardiologist and family physician.

## OUTCOMES

There were no sternotomy conversions, complications in establishing vascular- or LV-outflow tract access, LV-septum perforations or 30 day mortalities. One patient (7.7%) presented with active staphylococcal MV-endocarditis, a peak instantaneous LVOT gradient of 88.0 mmHg and IVSD of 22.0 mm. The patient underwent extensive anterior- and posterior MV-leaflet resection, debridement, autologous annular patch- and leaflet xenograph pericardial patch reconstruction in addition to LV-outflow tract resection.

Revisions for bleeding (n = 1, 7.7%) and residual MV-dysfunction post-repair (n = 1, 7.7%) were performed through the same incisions without residual complications. One patient (7.7%) developed an ischemic stroke on the 10th postoperative day due to a MV-mechanical prosthesis thrombosis that resolved with conservative therapy. The patient was eventually discharged after 72 days in hospital.

There were no wound infections or persistent air leaks and the mean length of hospitalization was  $17.7 \pm 18.1$  days (range 7-72). Other in-hospital morbidities are outlined in table 4. Postoperative dialysis was required in 2 patients (15.4%), of whom 1 (7.7%) had severe renal impairment preoperatively. Both patients were subjected to cardiopulmonary perfusion times of 133.0 minutes.

Morbidity	n	% of 13
Revisions	2	15.4
Residual valve dysfunction	1	7.7
Bleeding	1	7.7
Stroke	1	7.7
Acute renal dysfunction requiring dialysis	2	15.4
Respiratory morbidity		
Residual pleural collections requiring drainage	1	7.7
Hospital acquired pneumonia	1	7.7
Rhythm Abnormalities		
Postoperative permanent pacemaker implantation	2	15.4
New onset atrial fibrillation	2	15.4

Postdischarge echocardiographic- and clinical data (645.7 patient months) are described in table 5 and were obtained by reviewing the latest consultation records (n = 13, 100% complete), of which 12 (92.3%) patients had follow-up periods longer than 2 years. Clinical follow-up (mean  $49.7 \pm 30.0$  months) for survival identified 2 late mortalities at 40.1- (fatal stroke, age 82.6 years) and 85.0 postoperative months (ischemic colitis, age 76.5 years) respectively.

There were no procedure-, HOCM-, AVV-related late mortalities or reinterventions. All patients (n = 13, 100%), including the late mortalities, were classified as NYHA I or II during their latest clinical review. Echocardiographic follow-up (mean  $36.6 \pm 30.1$  months) identified no residual- or recurrent peak instantaneous LV-outflow tract gradients more than 15 mmHg. Asymptomatic chordal SAM was diagnosed in one patient (7.7%) with a mean gradient of 11 mmHg (40.1 months postoperative).

Echocardiographic follow-up (mean $36.6 \pm 30.1$ months)	n	% of 13
Mean left ventricle ejection fraction (%)	54.9 $\pm$ 8.4	
Residual mitral valve regurgitation equal to or less than grade I	11	
Residual tricuspid valve regurgitation more than grade II	2	
Peak left ventricle outflow tract gradient < 15 mmHg	13	
Mean interventricular septal diameter (mm)	14.2 $\pm$ 4.9	
Mean systolic pulmonary artery pressure (mmHg)	34.5 $\pm$ 13.0	
Clinical follow-up (mean $49.7 \pm 30.0$ months)	n	% of 13
New York Heart Association functional status		
Class I	9	69.2
Class II	4	30.8
New onset atrial fibrillation	1	7.7

### TIPS, TRICKS AND PITFALLS

LV-outflow tract resection with or without AVV-surgery is most commonly performed through conventional midline sternotomy and is not recommended as part of the initial EPAS skills acquisition in upcoming centres. For experienced EPAS operators, this approach provides direct- and targeted access to the LV-outflow tract, the majority of the interventricular septum, the MV and TV. Plication of the papillary muscles away from the LVOT reduces the risk of residual valvular- and chordal SAM and is considered an essential step for a successful LVOT gradient reduction outcome.

Annular detachment of the anterior MV should be wide and extend from segment A1 to A3. Careful suture retraction of the detached anterior MV-leaflet facilitates unobstructed endoscopic access to the LVOT. LVSM depth is determined by preoperative TEE diameter measurements and perforation avoided by careful en-bloc sharp resection from the base of the aortic valve to the papillary muscles. The incorporation of an oversized bovine pericardial patch into the anterior MV-leaflet ensures that the coaptation line is pushed posteriorly, which decreases the risk of residual valvular SAM. TEE should confirm an adequate and uncomplicated LVSM and AVV-procedure.

### CONCLUSION

This small series of a very limited patient population reflects the outcomes of the current surgical team of a single centre with extensive EPAS experience. Simultaneous LVSM and AVV-surgery by EPAS is safe, effective and allow for durable LV-outflow tract gradient reduction-, SAM- and AVV-surgery outcomes. Our series achieved a 100% long term freedom from reintervention and improved quality of life in all patients with no significant new- or recurrent echocardiographic AVV- pathology. EPAS offers the potential benefits associated with minimally invasive cardiac surgery and is an attractive alternative to conventional approaches for HOCM and concomitant AVV-disease.

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# CHAPTER 13

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Endoscopic Port Access™ surgery for isolated  
atrioventricular valve endocarditis

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Vermeulen Y, Degrieck I, Van Praet F

## ABSTRACT

### Objective

This study reports the clinical- and echocardiographic outcomes of endoscopic Port Access™ surgery (EPAS) for isolated active- and convalescent atrioventricular valve endocarditis (AVVE).

### Methods

Our current surgical team performed EPAS in 66 consecutive patients with isolated AVVE (mean age  $65.5 \pm 12.7$  years, 37.9% female, mean EuroSCORE II =  $31.2 \pm 24.9\%$ , 45.5% prosthetic AVVE, Staphylococcus Aureus 22.2%), between May 1st 2004 and July 31st 2015. Isolated mitral valve (MV) endocarditis was present in 53 (80.4%) patients, which included 11 (16.7%) periannular abscesses.

### Results

Procedures performed included MV-repair ( $n = 15$ , 22.7%) and left ventricle septal myomectomy ( $n = 1$ , 1.5%). Reasons for sternotomy conversion ( $n = 6$ , 9.1%) included lung adhesions ( $n = 3$ , 4.5%). The mean cardiopulmonary bypass- and ischemic times were  $167.2 \pm 48.7$ - and  $112.6 \pm 33.3$  minutes respectively. In-hospital morbidities included revision for bleeding ( $n = 6$ , 9.1%). 30-day survival was 87.9%. Causes of in-hospital mortalities ( $n = 12$ ) included low cardiac output syndrome ( $n = 3$ , 4.5%). Age, critical preoperative status and EuroSCORE II score predicted mortality individually at the 5% level of significance. The Kaplan-Meier analyses (mean  $63.2 \pm 42.5$  months) for survival- and freedom from AVVE reintervention at 10 years were 69.4% and 98.4% respectively. Of mid-term survivors ( $n = 50$ , 93.9% complete), 94.0% ( $n = 47$ ) were classified as NYHA II or less with no MV-regurgitation greater than grade I.

### Conclusion

Complex atrioventricular valve surgery in the context of AVVE can be endoscopically performed in experienced centres and should not deter surgeons from offering AVVE patients the potential benefits of minimally invasive cardiac surgery.

## INTRODUCTION

We are witnessing progressive evolution in the clinical approach to infective endocarditis, which include specialised guidelines within a multidisciplinary team context [1-2]. The indications for surgical intervention are well described [3] and is currently performed through sternotomy or right thoracotomy access [4] to allow aggressive debridement, infection control and restoration of valve morphology, either by reconstructive- [5-7] or replacement procedures [8-9].

The dismal survival- and quality of life outcomes are well reported [10]. The role of minimally invasive- and catheter based therapies for isolated atrioventricular valve endocarditis (AVVE) remains undefined in an era of ongoing technological advances and increasing patient expectations.

We initiated our minimally invasive atrioventricular valve program by Port Access™ (EPAS) in February 1997 and provide an in-depth overview of our experience in 66 consecutive patients that underwent surgery for isolated acute- and convalescent AVVE.

## MATERIAL AND METHODS

This is a retrospective observational study of a single-centre database. Our current surgical team performed EPAS in 66 consecutive patients with isolated AVVE between May 1st 2004 and July 31st 2015, with the relevant preoperative patient characteristics outlined in Table 1.

No patient selection or exclusion criteria were applied as sternotomy access for MV- and TV pathology was abandoned with the introduction of our EPAS program in 1997. The mean and median EuroSCORE II were  $31.2 \pm 24.9\%$  and 23.2% respectively. The surgical indications, which may be multiple per patient, are described in Table 2. The microbiological profiles are outlined in Table 3.

### *Surgical techniques and in-hospital treatment pathway*

Our EPAS techniques, that include peripheral cardiopulmonary bypass (CPB) - and endoaortic balloon occlusion are well described [11-17]. Preoperative thoracic imaging studies are not routinely performed specific for minimally invasive incision or thoracic access planning. We prefer endoaortic occlusion over transaortic clamping [18] and routinely perform aorta-iliac-femoral-axis angiography during preoperative coronary catheterization in stable patients and utilize computerised tomography (CT) imaging in cases of emergencies.

Whenever possible, the primary AVVE infection source is identified and appropriately treated before cardiac surgical consideration. EPAS for AVVE is only considered once comprehensive transesophageal echocardiographic (TEE) examination excluded the involvement on non-atrioventricular valves and structures [19].

We perform AVVE surgery without delay in patients with prosthetic AVVE, congestive cardiac failure, uncontrolled sepsis, abscesses or risk for persistent systemic emboli, provided that cerebral haemorrhage is excluded by cranial computerised tomography [20-21]. We attempt to postpone surgery



for 4 weeks in cases of intracranial haemorrhage and do not consider clinically silent cerebral embolism or transient ischemic attacks as surgical contraindications [22-24].

Once CPB, cardioplegic arrest and intracardiac exposure are established, radical excision of all macroscopically infected valvular-, subvalvular-, annular- and periannular tissue are performed using long shafted instruments.

Patient characteristics	n	% of 66
Mean age (range)	65.5±12.7 (29.5-85.3)	
Age above 70 years	26	39.4
Female	25	37.9
Mean body mass index (range)	27.6±5.1 (22.5-42.2)	
Active endocarditis	41	62.1
Convalescent- or blood culture negative endocarditis	25	37.9
Comorbidities present		
Previous cardiac surgery	34	51.5
Chronic obstructive pulmonary disease	7	10.6
Permanent pacemaker / internal defibrillator	12	18.2
Peripheral vascular disease	17	25.8
Renal dysfunction	13	19.7
Dialysis	5	7.6
Pulmonary hypertension	6	9.1
Hypertrophic obstructive cardiomyopathy	1	1.5
Marfan syndrome	1	1.5
Congestive cardiac failure	52	78.8
Cerebrovascular embolization / stroke	12	18.2
Critical preoperative state	9	13.6
EuroSCORE II		
Mean (range)	31.2±24.9 (1.7 to 97.8)	
0 – 10	13	19.7
11 – 40	31	47.0
41 – 70	13	19.7
71 – 100	9	13.6
Impaired left ventricle function (<50%)	5	7.6

Subsequent valve repair or replacement is determined by the quality of the remaining valvular structures. Annular patch reconstruction is performed according to routine principles [25], as are the valve leaflets by using either bovine- or native pericardial patches according to surgical preference. The

subvalvular apparatus are reattached with sutures (Gore-Tex™, Arizona, USA) to the free edges of the atrioventricular valves as indicated.

Surgical indications	n	% of 66
Isolated mitral valve endocarditis	53	80.3
Native valve endocarditis	28	42.4
Prosthetic valve endocarditis	25	37.9
Previous repair	12	18.2
Previous replacement	13	19.7
Mechanical prosthesis	10	15.2
Biological prosthesis	3	4.5
Periannular abscess or fistulous tract	11	16.7
Isolated tricuspid valve endocarditis	6	9.1
Native valve endocarditis	6	9.1
Combined mitral- and tricuspid valve endocarditis	7	10.6
Native valve endocarditis	2	3.0
Mitral- or tricuspid valve prosthetic endocarditis	5	7.6
Device related endocarditis	11	16.7
Atrial fibrillation	4	6.1
Left ventricle outflow tract obstruction	1	1.5
Patent foramen ovale	1	1.5
<b>Time interval between previous cardiac surgery and infective endocarditis presentation</b>		
<b>Previous Cardiac Procedure</b>	<b>Years (range)</b>	
Mitral valve repair (n = 14, 21.2%)	5.7±6.4 (0.1-21.2)	
Mitral valve replacement (n = 16, 24.2%)	11.7±8.3 (0.2-27.5)	
Tricuspid valve surgery (repair: n = 3, 4.5%, replacement: n = 1, 1.5%)	10.8±10.7 (0.3-21.6)	
Pacemaker or internal defibrillator implantation (n = 11, 16.7%)	5.2±6.8 (0.2-21.8)	
Isolated cryoablation (n = 1, 1.5%)	0.2	

Access to the left ventricle outflow tract is obtained by annular detachment of anterior MV segments A1 to A3 in cases of outflow obstruction. The septal myomectomy is performed by sharp dissection that extends from the aortic valve to the base of the left ventricle [26]. In cases of atrial fibrillation, cryoablation is performed with an argon-gas surgical ablation system (Medtronic, Minneapolis, USA) and the left atrial appendage oversewn. Patent foramen ovale (PFO) are routinely closed. Previously implanted intracardiac devices (pacemakers, defibrillators, cardiac resynchronization therapy devices) are removed with excision of all contact lesions at the level of the tricuspid valve (TV), right atrium, free

wall of the right ventricle and distal superior vena cava [27]. Temporary epicardial pacing wires are routinely placed on the left ventricular aspect and in cases of permanent pacemaker dependency, staged percutaneous transvenous- or permanent epicardial electrode reimplantation are performed once patient recovery excludes residual infection or as indicated.

Variable	n	% of 66
Streptococcus species	19	28.8
Viridans	9	13.6
Sanguinus	1	1.5
Mitis	1	1.5
Agalactiae	2	3.0
Faecalis	5	7.6
Bovis	1	1.5
Staphylococcus species	20	30.3
Aureus	14	21.2
Lugdunens	1	1.5
Epidermidis	2	3.0
Schleiferi	1	1.5
Indifference	2	3.0
Fungal	1	1.5
Candida albicans	1	1.5
Other	1	1.5
Clostridium perfringens	1	1.5
Culture negative endocarditis	25	37.8

Postoperative cardio-respiratory support, sedation, analgesia and appropriate microbiology guided antibiotic therapy (ABT) are administered in intensive care. Continuation of care is supervised by a specialist multidisciplinary endocarditis team for the duration of 6 weeks, either as an in-, or in selected cases [1], as an outpatient.

Unfractionated heparin precedes the introduction of fenprocoumon (3M Health Care Ltd, Minnesota, US) until infection control is confirmed for 2 consecutive weeks, with conversion to acetyl salicylic acid after 3 months in the absence of atrial fibrillation or mechanical valve implantation.

### Follow-up

Postdischarge continuation of care is ascertained by the referring cardiologist and family physician with surgical review after 6 weeks. Postdischarge clinical- and echocardiographic data were obtained by reviewing the latest available consultation records.

### Data analysis

All in-hospital data were collected from a prospective database. The continuous- and categorical outcomes were assessed by the incidence of adverse events (mean ± standard deviation) and the calculated intraoperative- and 30-day mortality.

Univariate- and multivariate analysis by logistic regression, which is appropriate for binary dependent variables, were used to identify independent predictors of mortality. Variables that were possibly associated with in-hospital mortality in univariate analysis were included in the multivariable logistic regression analysis to identify independent factors for in-hospital mortality. The significance level used in univariate- and multivariable analysis was  $p < 0.05$  and all the reported  $p$  values were two-sided.

The postdischarge data was collected retrospectively. Postdischarge survival- and freedom from reoperation estimates were determined by Kaplan-Meier analysis and are expressed as a proportion ± standard error (SE) based on the intention to treat principle of the total population ( $n = 66$ ). Statistical analysis was performed with the Statistica 64 software (Dell Inc., Texas, US).

The study was approved by the institutional ethics review committee, the authors agreed to the manuscript as written and take responsibility for data integrity.

## RESULTS

### Intraoperative outcome

A total of 66 consecutive patients underwent EPAS for isolated AVVE. The procedures performed, which may be multiple per patient, CPB and endoaortic occlusion times are outlined in Table 4. Twenty-five patients presented with isolated endocarditis in the context of previous mitral valve repair, of which 15 patients (60%) underwent successful redo-repair [5-7]. No intraoperative mortalities were observed.

### Postoperative course and in-hospital outcome

The in-hospital mortality profile is outlined in table 5. All mortalities underwent mitral valve replacement in isolation ( $n = 10$ ) or combined with tricuspid valve repair ( $n = 2$ ), of which 3 were attempted repairs prior to replacement with ischemic times of 78-, 79- and 91 minutes respectively. In-hospital complications and morbidities are outlined in Table 6.

Postoperative low cardiac output syndrome occurred in 3 (n = 3, 4.5%), of which all were classified as critical clinical status preoperatively. Redo-mitral valve repair failure (n = 1, 1.5%) required revision and subsequent replacement through the same incision without further complications.

<b>Table 4. Procedures performed, cardiopulmonary bypass- and endoaortic balloon occlusion times (n = 66)</b>		
<b>Procedures performed</b>	<b>n</b>	<b>% of 66</b>
Mitral valve repair	15	22.7
Ring implantation	10	15.2
Annular pericardial patch reconstruction	3	4.5
Leaflet patch reconstruction	3	4.5
Leaflet resection	7	10.6
Cleft closure	3	4.5
Commisuroplasty	3	4.5
Papillary muscle transfer	1	1.5
Neochordae implantation	4	6.1
Mitral valve replacement	45	68.2
Mechanical prosthesis	17	25.8
Bioprosthesis	28	42.4
Tricuspid valve repair	8	12.1
Ring implantation	3	4.5
Tricuspid valve replacement	5	7.6
Mechanical prosthesis	1	1.5
Bioprosthesis	4	6.1
Patent foramen ovale closure	1	1.5
Cryoablation	4	6.1
Left ventricle outflow tract septectomy	1	1.5
Sternotomy conversions	6	9.1
Lung adhesions	3	4.5
Cannulation problems	2	3.0
Aorta dissection	1	1.5
Intraaortic balloon pump support	2	3.0
<b>Cardiopulmonary bypass- and endoaortic balloon occlusion times (minutes)</b>		
Mean cardiopulmonary bypass time	167 ± 49 (91 - 315)	
Mean endoaortic balloon occlusion time	113 ± 33 (46 - 213)	

<b>Table 5. In-hospital mortality (n = 12)</b>			
<b>Mortality</b>	<b>n</b>	<b>% of 12</b>	<b>% of 66</b>
Mean EuroSCORE II (range)	33.9±28.5 (2.7-82.9)		
Mean age in years (range)	73.0±7.7 (59.4-85.2)		
Female	7	58.3	10.6
Active endocarditis	12	100.0	18.2
Previous cardiac surgery	7	58.3	10.6
Critical preoperative status	3	25	4.5
Organism			
Staphylococcus aureus	6	50.0	9.1
Streptococcus Indifference	1	8.3	1.5
Streptococcus bovis	1	8.3	1.5
Enterococcus faecalis	1	8.3	1.5
Culture negative	3	25.0	4.5
Procedure			
Isolated mitral valve surgery	10	83.3	15.2
Combined mitral- + tricuspid valve surgery	2	16.7	3.0
Mean mortality interval (days)	19.5±18.2(1.0-59.0)		
Mortality after 15 days postoperatively	7	58.3	10.6
Sternotomy conversion	2	16.7	3.0
Mean cardiopulmonary bypass time (minutes)	145.8±33.7(98.0-209.0)		
Mean endoaortic balloon occlusion time (minutes)	99.7±27.2(55.0-145.0)		
<b>UA of in-hospital mortality (n = 66)</b>	<b>Univariate OR*(95% CI)</b>	<b>P-value</b>	
Age above 70 years	1.1 (1.003 - 1.156)	0.041	
Female	2.8 (0.760 - 10.317)	0.120	
EuroSCORE II	1.0 (1.000 - 1.051)	0.049	
Previous cardiac surgery	1.4 (0.385 - 5.085)	0.604	
Active endocarditis	1.5 (0.388 - 5.674)	0.559	
Critical clinical status	8.9 (1.869 - 42.658)	0.007	
Cardiopulmonary bypass time	1.0 (0.967 - 1.003)	0.144	
Endoaortic balloon occlusion time	1.0 (0.957 - 1.006)	0.102	
Sternotomy conversion	2.5 (0.388 - 16.113)	0.330	
Valve replacement after attempted repair	3.3 (0.641 - 16.655)	0.151	
<b>UA: univariate analysis, *OR: Odds Ratio</b>			

Morbidities	n	% of 66
Revisions	7	10.6
Residual valve dysfunction	1	1.5
Bleeding	6	9.1
Low cardiac output syndrome	3	4.5
Multiorgan failure	9	13.6
Stroke	1	1.5
Acute renal dysfunction requiring dialysis	6	9.1
Respiratory morbidity		
Residual pleural collections requiring drainage	7	10.6
Hospital acquired pneumonia	8	12.1
Tracheostomy	5	7.6
Rhythm abnormalities	14	21.2
New postoperative permanent pacemaker implantation	5	7.6
New onset atrial fibrillation	9	13.6
Lymphocele	1	1.5

The 30-day- and in-hospital survival were 87.9% (n = 58) and 80.3% (n = 54) respectively. Causes of in-hospital mortalities (n = 12) included low cardiac output syndrome (n = 3, 4.5%) and sepsis related multiorgan failure (n = 9, 13.6%). The mean length of hospitalisation for in-hospital survivors (n = 54) was 28.3 ± 14.1 days (range 7 - 72) and is outlined in Figure 1A.

Age above 70 years (OR = 1.08, CI = 1.00-1.16, p = 0.04), critical preoperative status (OR = 8.93, CI = 1.87-42.66, p = 0.005) and EuroSCORE II (OR = 1.03, CI = 1.00 - 1.15, p = 0.049) were the only univariate mortality predictors identified at the 5% level of significance. Combinations of age above 70 years (OR = 1.66, CI = 1.02 - 2.71, p = 0.041), critical preoperative status (OR = 23.16, CI 2.57 - 209.02, p = 0.006) and CPB time (OR = 0.97, CI = 0.94 - 0.99, p = 0.033) were the only multivariate mortality predictors proven to be more accurate than the univariate analysis.

#### **Mid-term survival-, freedom from reoperation-, clinical- and echocardiographic follow-up**

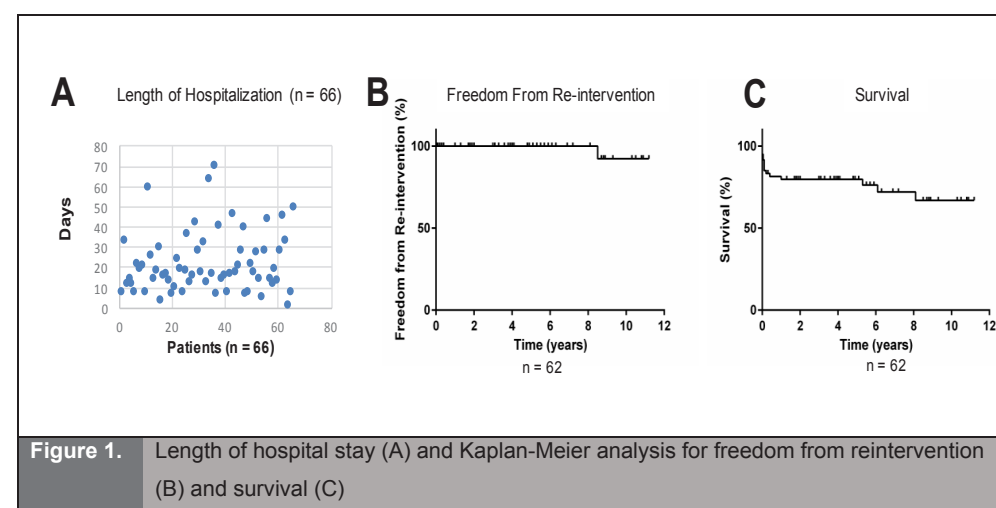
A total of 3167.7 patient months (mean 63.2 ± 42.5, median 46.5) were available for recent mid-term survival-, freedom from atrioventricular valve reintervention- and clinical status analysis. Up to date clinical- and echocardiographic data of post-discharge patients (n = 50, 93.9% complete at 12 months) are outlined in table 7. Incomplete follow-up data of 4 international patients (6.1%) were not incorporated into the mid-term outcome results. Thirty-eight of the subsequent 50 post-discharge patients analysed (76.0%) had follow-up periods longer than 3 years.

Late postoperative deaths occurred in 6 patients due to hepatic carcinoma (63.8 months), stroke (73.5 months), sarcoma (97.3 months), post-transplantation (12.5 months), cardiac failure (4.6 months) and unknown cause (23.5 months) respectively.

Clinical outcomes (mean 63.2 ± 42.5 months)	n	% of 50
<b>New York Heart Association Functional Status</b>		
Class I	37	74.0
Class II	10	20.0
Class III	3	6.0
<b>Late cardiovascular events</b>		
Stroke	2	4.0
Recurrent endocarditis	3	6.0
New onset atrial fibrillation	11	22.0
Other cardiac surgery	1	2.0
Peripheral vascular intervention	2	4.0
<b>Echocardiographic outcomes (mean 56.3 ± 40.8 months)</b>		
<b>Mitral valve function</b>		
Regurgitation less than Grade I	50	100.0
Mean gradient (mmHg)	2.7±2.7	
Paravalvular leak	1	2.0
Systolic anterior motion	1	2.0
<b>Tricuspid valve function</b>		
Regurgitation less than Grade II	50	100.0
Mean left ventricle ejection fraction (%)	57.8±10.8	
<b>Kaplan-Meier analysis for survival and freedom from reintervention (n = 62)***</b>		
<b>Years</b>	<b>Survival (%)</b>	<b>Freedom from reintervention (%)</b>
1	77.4	100.0
3	75.8	100.0
5	72.6	98.4
7	71.0	98.4
10	69.4	98.4
<b>*** Excluding lost international follow-up (n = 4, 6.1%)</b>		

AVVE recurrence was observed in 3 patients (6.0%), of which 1 patient (2.0%) required surgical reintervention after 102.4 postoperative months. The Kaplan-Meier analyses for postdischarge freedom from AVVE reintervention at 10 years was 98.4% (Figure 1B).

The Kaplan-Meier analyses for survival- (Figure 1C) at 5- and 10 years were 72.6% and 69.4% respectively. New York Heart Association class I or II status was observed in 47 (94.0%) of the 50 mid-term survivors, with residual MV-regurgitation less than grade I confirmed in all patients (n = 50, 100%).



## DISCUSSION

The role of minimally invasive surgery for acute- or convalescent atrioventricular valve endocarditis (AVVE) is not defined. We established endoscopic atrioventricular valve surgery by Port Access™ (EPAS) as our routine approach for all isolated mitral- and / or tricuspid valve pathology since February 1997 and investigated the clinical- and echocardiographic outcomes of 66 consecutive patients with isolated AVVE.

The incidence of acute AVVE (n = 41, 61.1%), septic- / pending septic shock (n = 9, 13.6%), congestive cardiac failure presentation (n = 58, 78.8%) and microbiological profile in our series correlates well with the patient characteristics described contemporary reports [3-10]. The empiric administration of antibiotics by referring physicians and the cost-related limitation of antinuclear antibody- and anti-porcine bioprosthesis allergic assays, may contribute to a higher incidence of blood culture negative endocarditis (n = 25, 37.9%) in our series [28].

A variety of simple and complex EPAS infection control- and valve reconstruction procedures were performed without compromising on the well-defined principles of infective endocarditis surgery. [4]. EPAS provides direct- and focused access to the target valves, with CPB- and endoaortic inflation times comparable with contemporary sternotomy approach reports [5]. The survival benefit of valve repair is well described [6-7] and we elect to attempt redo-repair as first line therapy in a redo-setting. Valve

replacement is only considered if the post-debridement morphology prohibits a durable repair outcome. Homografts were not utilised in our series.

One new neurological event (1.5%), which was not EPAS-AVVE related, occurred on the 10th postoperative day in a critically ill patient secondary to MV-mechanical prosthesis thrombosis. The patient was eventually discharged home after 72 days in hospital. All revisions (n = 7, 10.1%) were performed through the same incisions without residual bleeding, difficulty in achieving hemostasis or valve related complications. Postoperative dialysis was required in 6 patients (9.1%), of which 5 (7.6%) were dialysed preoperatively.

The observed 30-day mortality, within the context of a mean EuroSCORE II of  $31.2 \pm 24.9\%$  and which includes operative mortality (n = 8, 12.1%), compares well with contemporary AVVE series [4-10]. In-hospital survival was 80.3% (n = 54). In addition to the well described independent risk factors for mortality [4-7, 22], which include prosthetic AVVE, Staphylococci AVVE, septic shock, congestive heart failure, stroke and intracardiac abscess, univariate-and multivariate logistical regression analysis identified age, EuroSCORE II and critical preoperative clinical status as significant additional contributors to in-hospital mortality in our series.

Clinical- and echocardiographic follow-up of postdischarge survivors (n = 50, 93.9% complete) confirmed favourable outcomes comparable with current sternotomy access reports [4-10, 22]. No postdischarge mortality was AVVE or EPAS related. Survival and freedom from reintervention at 10 years were 69.4% and 98.4% respectively. Recurrent AVVE occurred in 3 surviving patients (6.0%), of which one patient required reoperation (102.4 months) for unsuccessfully medical therapy.

Despite EPAS-AVVE being the routine approach at our institution, we do however, caution against undertaking EPAS-AVVE during the initial learning curve of minimally invasive atrioventricular valve surgery and encourage experienced centres to offer patients the potential benefits of a minimally invasive approach.

## STUDY LIMITATIONS

This series reflects the outcomes of the current surgical team of a single centre with extensive EPAS experience. The enrolment period of this study was 11.2 years and its impact on our conclusions was not subjected to sensitivity analyses.

The use of sternotomy access was abandoned since the introduction of our MI-PAS program, which is routine for isolated atrioventricular valve disease at our institution.

All patients were offered MI-PAS with the intention to the treat, which resulted in the absence of a control group or propensity matching. The EuroSCORE II, which is standardized for sternotomy access, was utilized as control group for operative outcomes.

## CONCLUSION

Complex atrioventricular valve surgery in the context of AVVE can be performed endoscopically in experienced centres with favourable perioperative survival- and mid-term clinical- and



echocardiographic outcomes. The presence of isolated AVVE should not deter experienced surgeons from offering patients the full range of potential benefits associated with minimally invasive cardiac surgery

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# PART 4

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ANNECDOTAL REPORTS OF "BEYOND THE ROUTINE"  
PORT ACCESS™ PROCEDURES



# CHAPTER 14

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Total percutaneous cardiopulmonary bypass  
for robotic- and endoscopic atrioventricular  
valve surgery

Van der Merwe J, Casselman F, Beelen R, Van Praet F



## SUMMARY

Continuous technological advances in endoscopic-, robotic- and catheter-based cardiac interventions are paralleled by rapid evolution in cannulation strategies for circulatory support. The recent introduction of suture based percutaneous vascular closure devices (PVCD) resulted in innovative strategies to deliver peripheral endovascular therapeutic devices through the iliac- and femoral arteries. Percutaneous access allows rapid postoperative mobilization and potentially avoids the devastating neuro-lympho-vascular- and wound infection (NLVWI) morbidities associated with conventional open surgical exposure. We routinely perform endoscopic Port Access™ surgery (EPAS) for all isolated atrioventricular valve pathology and extended the application of suture based PVCD to establish total percutaneous peripheral cardiopulmonary bypass (TPCPB) in disabled-, immunosuppressed- and morbidly obese patients at risk NLVWI. In this report, we provide a stepwise description of our TPCPB technique.

## INTRODUCTION

We are currently witnessing rapid evolution in endoscopic-, robotic- and catheter-based cardiovascular technology and interventions. The recent introduction of suture based percutaneous vascular closure devices (PVCD) facilitated the percutaneous delivery of transcatheter aortic valve implantation (TAVI)- and endovascular aorta stent graft devices through the iliac- and femoral artery [1-3].

Percutaneous access allows rapid postoperative mobilization and potentially avoids the devastating neuro-lympho-vascular- and wound infection (NLVWI) morbidities (Figure 1A) associated with conventional vascular exposure [4].

We performed more than 200 percutaneous transcatheter aortic valve- (TAVI) and endovascular aortic stent implantations using suture based PVCD since the initiation of our percutaneous program in June 2012.

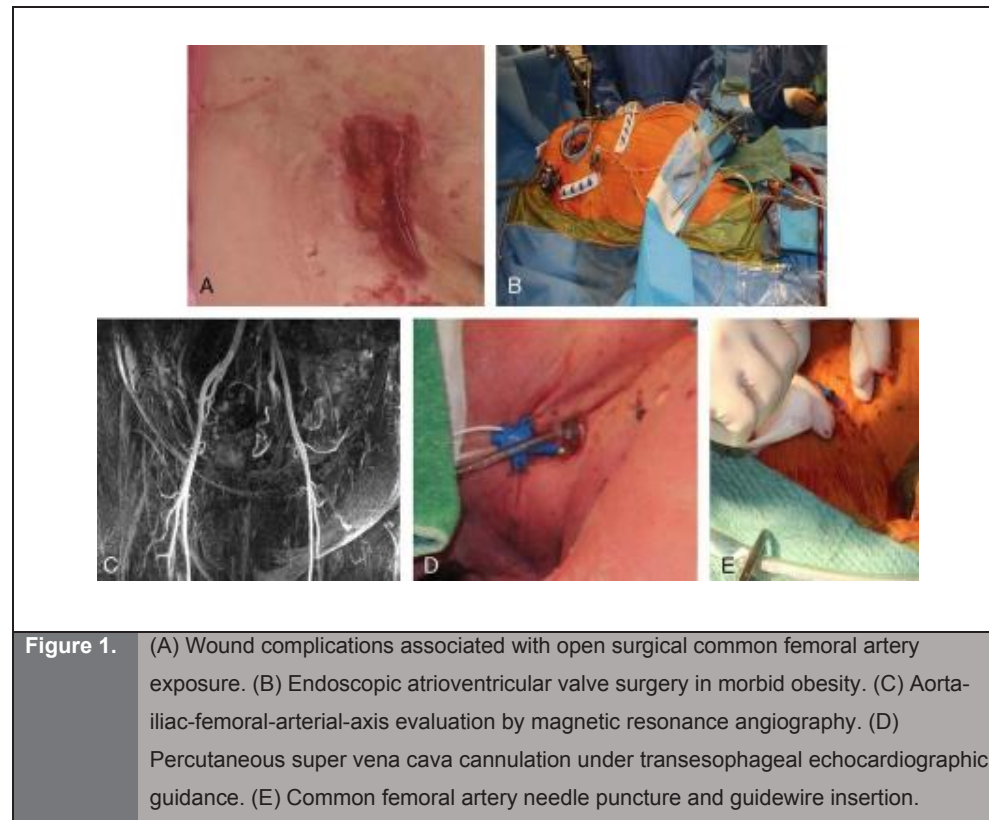
We subsequently extended the application of PVCD to establish total percutaneous peripheral cardiopulmonary bypass (TPCPB) in our endoscopic Port Access™ surgery (EPAS) program and routinely utilize this approach in disabled-, immunosuppressed- and morbidly obese patients (Figure 1B) at risk of NLVWI. In this report, we provide a stepwise description of our suture based PVCD-TPCPB technique.

## SURGICAL TECHNIQUE

We routinely evaluate the aorta-iliac-femoral arterial axis preoperatively in all patients either by an additional contrast injection in the iliac arteries during cardiac catheterization or by magnetic resonance angiography (Figure 1C). Contraindications to proceed with TPCPB by suture based PVCD include common femoral artery diameter less than 5 mm, severe calcification, lumen stenosis more than 50% and the presence of previous femoral vascular grafts.

Following routine general anaesthesia and double lumen intubation, percutaneous superior vena cava drainage (Figure 1D) is established through the right internal jugular vein (16F to 18F, Optisite™, Edwards Lifesciences, Irvine, California, USA) by transesophageal echocardiographic (TEE) guided Seldinger technique [5].

Percutaneous common femoral artery access follows systemic heparin administration and is established by careful needle puncture of the anterior arterial surface (Figure 1E), which may be guided by ultrasound in hostile groins.



**Figure 1.** (A) Wound complications associated with open surgical common femoral artery exposure. (B) Endoscopic atrioventricular valve surgery in morbid obesity. (C) Aorta-iliac-femoral-arterial-axis evaluation by magnetic resonance angiography. (D) Percutaneous superior vena cava cannulation under transesophageal echocardiographic guidance. (E) Common femoral artery needle puncture and guidewire insertion.

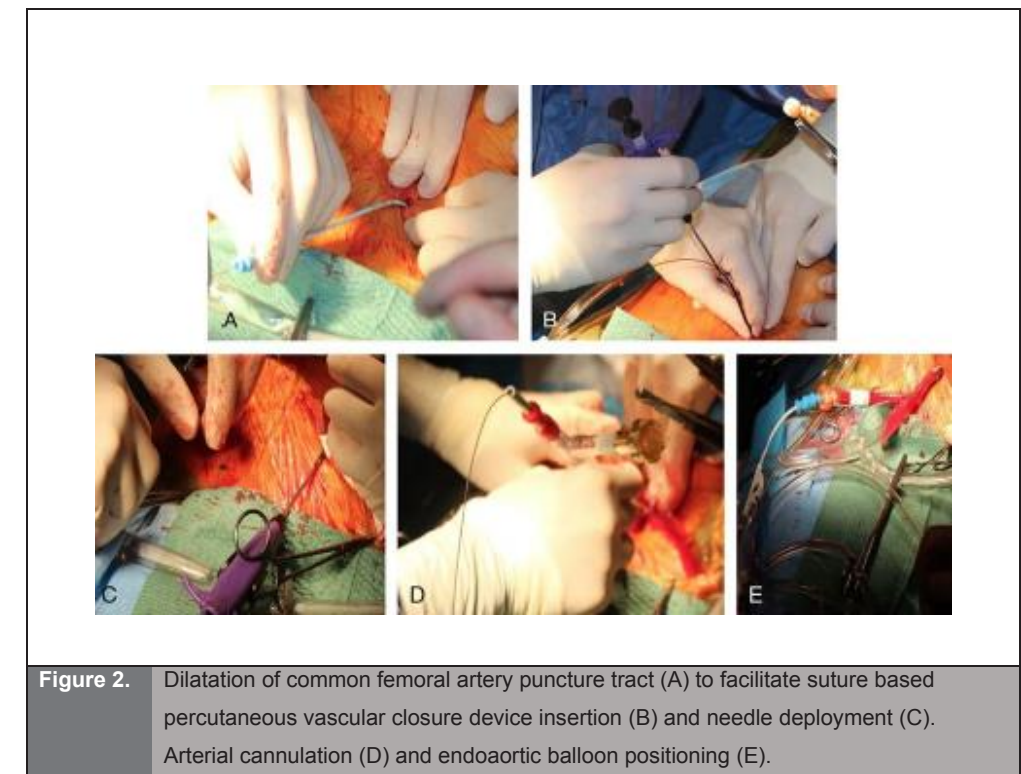
The puncture tract is dilated (Figure 2A) with a 10 Fr dilator (Avanti®, Cordis, California, USA) over a guidewire (0.035, Radifocus®, Terumo Interventional Systems, Leuven, Belgium) and either a 6 branch suture based PVCD composed of two stainless needles and one polyester suture (8-21 Fr, Perclose ProGlide™, Abbott Vascular, Santa Clara, California, USA) or a PVCD composed of four nitinol needles and two braided polyester sutures (8.5-10 Fr, Prostar XL™, Abbott Vascular, Santa Clara, California, USA) inserted according to surgical preference (Figure 2B).

The PVCD guidewire is removed once the exit port is at the skin line and pulsatile flow visualized from the marker lumen. The anchoring feet and needles are then deployed (Figure 2C) and the process repeated for a second device if the Perclose ProGlide™ is used. The corresponding suture-ends are marked to facilitate easy identification during knotting. Vascular access is maintained by reinserting the guidewire and PVCD delivery system is then removed.

A femoral artery cannula with Y-arm (21-23 Fr, EndoReturn™, Edwards Lifesciences, Irvine, California, USA) is introduced over the guidewire for arterial inflow (Figure 2D) and connected to the cardiopulmonary bypass circuit. Pulsatile backflow should be documented to confirm unobstructed intraluminal positioning. A prepared endoaortic balloon (IntraClude™, Edwards Lifesciences, Irvine, California, USA) is used for aortic occlusion and is carefully advanced over its guidewire (Figure 2E) to

the level of the sinotubular junction under TEE guidance. No resistance should be encountered and forceful maneuvers are best avoided to prevent potential life threatening vessel rupture or dissection.

Ipsilateral percutaneous femoral vein cannulation (22-25 Fr, QuickDraw™, Edwards Lifesciences, Irvine, California, USA) is then established by percutaneous needle puncture and Seldinger technique (Figure 3A). TEE guides the advancement of the guidewire and the venous cannula into the right atrium. The superior- and inferior vena cava cannulas are connected to the cardiopulmonary bypass circuit in a Y-configuration.

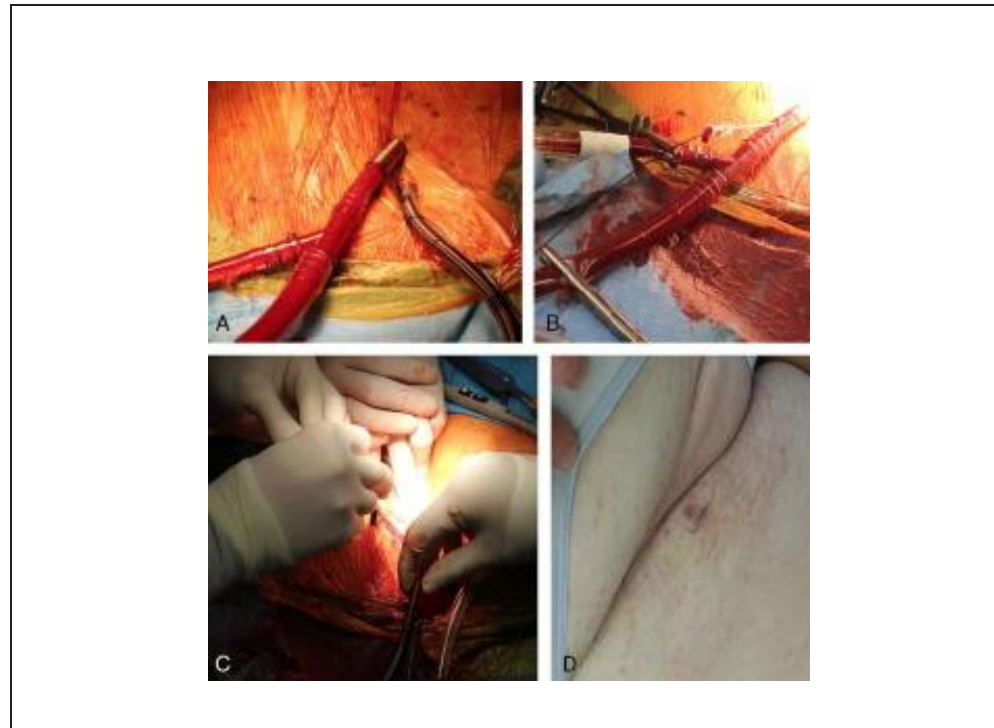


**Figure 2.** Dilatation of common femoral artery puncture tract (A) to facilitate suture based percutaneous vascular closure device insertion (B) and needle deployment (C). Arterial cannulation (D) and endoaortic balloon positioning (E).

TPCPB is initiated and the intracardiac procedure performed according to routine endoscopic principles [6]. Following TEE confirmation of successful procedural results, TPCPB is discontinued, heparin reversed and the femoral venous cannula carefully removed first. A deep horizontal mattress suture ensures venous tract hemostasis.

In preparation for arterial decannulation, a guidewire is reintroduced into the femoral artery through a separate external needle (Figure 3B) to ascertain continuation of endovascular access after careful decannulation. The PVCD sutures are securely knotted down to the arteriotomy over the guidewire (Figure 3C), which is used to insert an additional PVCD if hemostasis is not readily achieved. The

knotted sutures are then cut below the skin line and a compressive bandage routinely applied for 12 hours. Early mobilization is encouraged (Figure 3D) and supervised.



**Figure 3.** (A) Total percutaneous peripheral cardiopulmonary bypass cannulation setup. (B) Guidewire reinserterion through the arterial cannula. (C) Knotting of vascular device sutures following decannulation. (D) Postoperative cannulation wound result.

#### COMMENTS

Various suture based PVCDs are currently under investigation as part of the rapid evolution in percutaneous endovascular-, peripheral perfusion- and transcatheter cardiovascular devices and technology. The PVCD described in this report are approved to deliver endovascular devices up to 21F (Perclose ProGlide™) and 10F (Prostar XL™) respectively and are well established for facilitating endovascular procedures through femoral artery access [1-3].

We routine apply 2 single suture Perclose ProGlide™ or 1 double suture, Prostar XL™ device in TPCPB according to surgical preference. The Perclose ProGlide™ system allows the insertion of multiple devices, which not the case with the Prostar XL™ device at present. We successfully utilized the Perclose ProGlide™ and Prostar XL™ devices in 135 and 61 percutaneous aortic stent graft, TAVI and EPAS procedures respectively and do not routinely perform post-procedure on-table iliac- or

femoral artery angiography unless clinically indicated. Any suspected complications are addressed immediately by endovascular repair or surgical conversion.

Important principles to successfully apply suture based PVCD-TPCPB in patients at risk of NLVWI complications include meticulous preoperative aorta-iliac-femoral-arterial axis evaluation for contraindications, accurate target vessel needle puncturing, extremely cautious guidewire advancement, meticulous cannulation techniques and early conversion to open surgical access if unsuccessful.

TPCPB offers patients at risk of NVLWI complications the full range of benefits associated with minimally invasive cardiac interventions. In combination with suture based PVCD, the application of TPCPB may expand beyond current indications and become the routine circulatory support strategy for future robotic- and catheter-based device implantation.

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An endoscopic view of a massive atrial myxoma, a large, gelatinous, lobulated mass within the heart's atrium. The mass is dark and has a complex, branching structure. A circular surgical instrument is visible in the lower-left quadrant, and another instrument is at the top. The background is dark, highlighting the mass.

# CHAPTER 15

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Endoscopic Port Access™ resection of a massive atrial myxoma

Van der Merwe J, Casselman F, Van Praet F



## ABSTRACT

We are currently witnessing a rapid international paradigm shift from conventional sternotomy access to minimally invasive cardiac surgical approaches, also in South Africa. Endoscopic Port Access™ surgery (EPAS) is well established for the safe and durable resection of atrial myxoma (AM) and considered to be ideal pathology to master the initial EPAS learning curves. We report the successful EPAS resection of an 8.5 centimetre obstructive left AM in an 81-year old patient, which is to our knowledge, the largest AM ever resected by robotic- or endoscopic cardiac surgery. Postoperative recovery was uneventful and the patient was discharged home on the 5th postoperative day. Clinical- and echocardiographic follow-up at 12 months confirmed an excellent functional recovery and the absence of residual- or recurrent tumour.

## INTRODUCTION

Atrial myxoma (AM) is the commonest benign cardiac neoplasm, originates from multipotent mesenchymal cells and commonly presents in women between the third- and sixth decades of life [1]. Large AM may result in ventricular inflow obstruction [2-3] and the safety of conventional sternotomy resection by single- or biatrial access, is well described [4-6]. We are currently witnessing a rapid paradigm shift towards minimally invasive cardiac surgery (MICS) and specialized centres are soon to become established in South Africa.

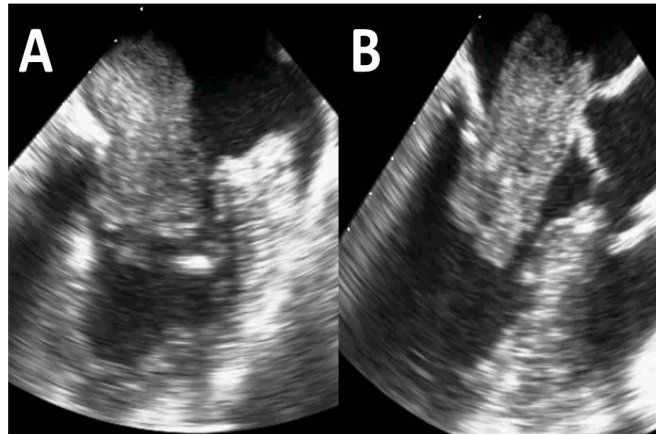
AM is considered by many minimally invasive surgeons to be ideal pathology for skill development during the initial endoscopic Port Access™ surgery (EPAS) learning curve. We have performed more than 3000 EPAS procedures at our institution since February 1997 and previously reported our experience with intracardiac oncological surgery [7]. In this report, we describe the successful resection of a massive obstructive AM in an 81-year patient, which is the largest in our series and also to our knowledge, the largest documented AM ever resected by either robotic- or endoscopic cardiac surgery.

## CASE REPORT

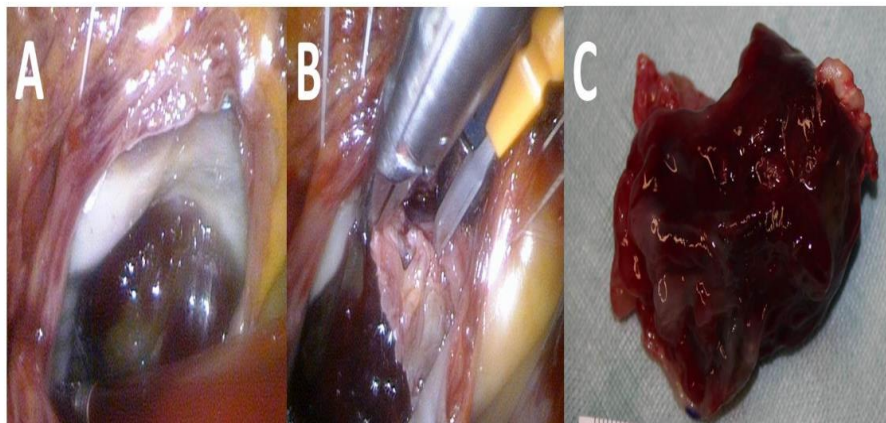
Clinical- and transthoracic echocardiographic (TTE) imaging review of an 81-year old female identified a massive left atrial mass that originated from the intraatrial septum and partially obstructed mitral valve and left ventricular inflow (Figure 1). She presented with progressive New York Heart Association (NYHA) Class III symptoms and systolic pulmonary artery pressure (sPAP) of 65 millimetres of mercury (mmHg). Additional investigations were uneventful and included coronary artery catheterization, thoracic- and aorta-iliac axis computerized tomography and pulmonary function tests. Surgical excision was proposed by our multidisciplinary team and the patient elected the option of EPAS with a predicted EuroSCORE II of 3.4%.

We routinely utilize double lumen endotracheal intubation and established a 3-4 centimetre antero-lateral working port over the 4th intercostal space. Peripheral cardiopulmonary bypass (CPB) was established over transesophageal echocardiographic (TEE) guided guidewires through the right internal jugular vein (16 Fr, Optisite™, Edwards Lifesciences, Irvine, California, USA), right femoral vein (25 Fr, QuickDraw™, Edwards Lifesciences, Irvine, California, USA) and right femoral artery (23 Fr, EndoReturn™, Edwards Lifesciences, Irvine, California, USA). An endoaortic balloon (IntraClude™, Edwards Lifesciences, Irvine, California, USA) was used for aortic occlusion and the delivery of cold antegrade crystalloid cardioplegia. Cardioplegic arrest was uneventfully achieved and subsequent left atriotomy revealed the massive obstructive septal neoplasm.

The risk of fragmentation prohibited the use of our usual endoscopic left atrial retractor (Figure 2A) and visualization was ascertained with traction sutures. A broad septal resection around the tumour base was performed with long shafted instruments without tumour manipulation or intraatrial septum perforation (Figure 2B).



**Figure 1.** Transesophageal echocardiographic (TEE) images of a massive left atrial mass (A) that obstructed left ventricle inflow (B).



**Figure 2.** Targeted endoscopic visualization of the massive atrial myxoma (A). Broad excision of the tumour base with long shafted instruments (B). Pathological examination of an intact 8.5 x 4.2 x 2.5 centimetre atrial myxoma (E).

The endocardial defect was sutured and subsequent systematic mitral valve analysis uneventful. Further endoscopic inspection of the ventricular cavity confirmed no distal fragmentation. De-airing was ensured by flooding the operative field with CO<sub>2</sub> and antegrade endoaortic balloon venting under TEE guidance. CPB- and ischemic times were 115- and 76 minutes respectively.

Discontinuation of mechanical respiratory support was achieved within 6 hours postoperatively and discharge from intensive care occurred after 12 hours. In-hospital TTE confirmed normal atrioventricular valve-, chamber- and ventricular function with no septal defect. Rapid clinical recovery warranted home discharge on the 5th postoperative day.

NYHA class I clinical status was achieved after 6 weeks and remained unchanged at 12-month follow-up. Histological examination of the intact tumour confirmed the typical findings of an AM and resection margins free of neoplastic tissue (Figure 2C). Echocardiographic review at 12-month follow-up confirmed the absence of residual- or recurrent atrial septal tumour and sPAP of 30 mmHg.

## DISCUSSION

The oncological principles and resection techniques of AM by conventional single- or biatrial sternotomy approaches are well described [4-6]. We initiated our EPAS program in 1997 and reported the safety and durability of our approach in cardiac oncological surgery [7].

The targeted endoscopic left atrial- and tumour visualization eliminates any unintentional cardiac manipulation, tumour fragmentation and risk of embolization. Patient recovery was swift and resulted in complete resolution of preoperative symptomatology.

We believe that AM provide a good learning platform for initial EPAS programs and the diagnosis of massive AM, as in this case, should not deter referring physicians and surgeons from offering patient the full range of benefits associated with minimally invasive cardiac surgery.

## CONCLUSION

Atrial myxomas offer good learning platforms to establish MICS skills during the initial EPAS learning curves. The perceived complexity of massive AM should not deter referring physicians or surgeons from offering patients the full benefits associated with minimally invasive cardiac surgery.

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# CHAPTER 16

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Single-stage minimally invasive surgery for synchronous primary pulmonary adenocarcinoma and left atrial myxoma

Van der Merwe J, Beelen R, Martens S, Van Praet F

## ABSTRACT

We report the first successful short term outcome of single stage combined video-assisted thoracic surgery (VATS) lobectomy and Port Access™ surgery (PAS) in a patient with operable primary right lower lobe adenocarcinoma and a synchronous cardiac myxoma. The VATS right lower lobectomy with systematic lymph node dissection was performed first, followed by myxoma excision by PAS through the same working port incision. The histopathological analysis confirmed a pT2aN0M0R0 (TNM 7th edition) primary poorly differentiated pulmonary adenocarcinoma and a completely excised cardiac myxoma. Postoperative recovery was uneventful and follow-up at 6 weeks confirmed an excellent surgical- and oncological outcome

## INTRODUCTION

The clinical application of video-assisted thoracic surgery (VATS) for pulmonary oncological resection and Port Access™ surgery (PAS) for intracardiac tumour excisions is well established in experienced centres [1, 2]. Synchronous primary pulmonary- and intracardiac neoplasms are rare and traditionally surgically approached by staged- or simultaneous open strategies that present significant morbidities and surgical risks [3].

We performed 2851 PAS procedures since the initiation of our program in 1997, which includes 58 intracardiac oncological resections. Our VATS program was established in 2012. We report the first successful short term outcome of single stage VATS lobectomy, systematic nodal dissection (SND) and PAS in a patient with a synchronously occurring pulmonary adenocarcinoma and cardiac myxoma.

## CASE REPORT

Oncological surveillance of a 70-year old male identified an enlarging heterogeneous mass in the apical segment of his right lower lobe, 3 years after he underwent a left open thoraco-phreno-laparotomy and partial esophagectomy for stage 1 distal esophageal adenocarcinoma (pT1N0M0, TNM 7th). Computed tomography- (CT), positron emission tomography- (PET) and bone skeletal scintigraphy scans clearly defined the pulmonary malignancy (25 millimetre maximum diameter) and excluded distal metastases (Figure 1A and 1B).

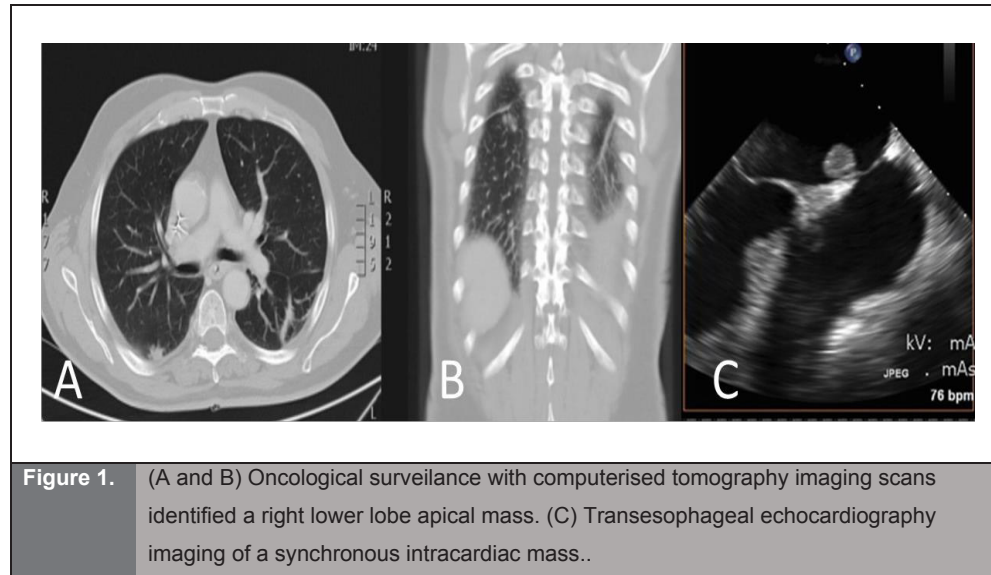
A left atrial mass (18 millimetre maximum diameter) of non-homogenic echogenicity that originated from the atrial septum was incidentally diagnosed and further investigated by transesophageal echocardiography (Figure 1C). The working diagnosis of synchronous cardiac myxoma and primary- or metastatic pulmonary malignancy was proposed. Lung functions tests and coronary catheterization were unremarkable.

The patient elected the option of a single stage ipsilateral VATS- and PAS-approach as definitive diagnostic- and therapeutic procedures. Following general anaesthesia, double lumen tube intubation and insertion of routine monitoring catheters, the patient was first positioned in left decubitus position. Anterior axillary ports were inserted in the 3rd, 5th and 8th intercostal space with an additional posterior axillary line port in the 5th intercostal space (Figure 2A).

Routine dissection of adhesions, the inferior pulmonary ligament and interlobar fissure was followed by division of the inferior pulmonary vein (Endo GIA™ 30mm, Covidien, Mansfield, Massachusetts, USA), pulmonary arterial branches (Endo GIA™ 30mm, Covidien, Mansfield, Massachusetts, USA) and bronchus (Endo GIA™ 60mm, Covidien, Mansfield, Massachusetts, USA). The right lower lobe was carefully maneuvered into an endobag (Endo Catch™, Covidien, Mansfield, Massachusetts, USA), after which systematic nodal dissection of stations R2 to R10 were performed (Figure 2B).

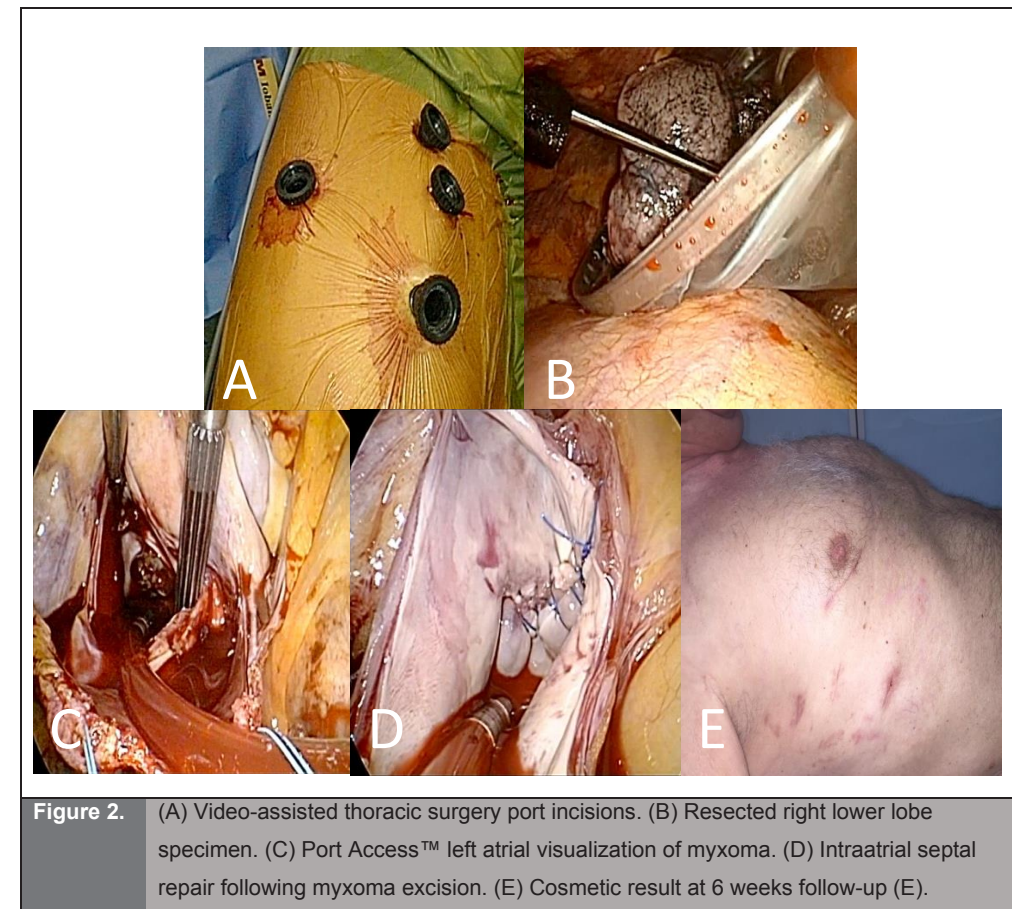
The patient was then positioned supine for PAS with venous drainage through the right internal jugular- (16 Fr to 18 Fr, Optisite™, Edwards Lifesciences, Irvine, California, USA) and femoral vein (22 Fr or 25 Fr, QuickDraw™, Edwards Lifesciences, Irvine, California, USA) respectively.





A femoral artery cannula with Y-arm (21 Fr or 23 Fr, EndoReturn™, Edwards Lifesciences, Irvine, California, USA) was utilized for arterial flow and an endoaortic balloon (IntraClude™, Edwards Lifesciences, Irvine, California, USA) for aortic occlusion and cold antegrade crystalloid cardioplegia delivery. The 3rd intercostal space VATS port was extended anteriorly as a 4 cm working port, through which the endobag and resected lung were extracted. The endoscope and CO<sub>2</sub> were introduced through the 3rd and 5th intercostal VATS ports respectively.

An 18x18 mm localized left atrial mass was excised from the intraatrial septum with 2-3 mm margins and the resulting defect primarily closed (Figure 2C and 2D). De-airing was ensured by a venting catheter in the left atrium, antegrade balloon catheter venting and TEE surveillance for residual air in the left ventricle. Cardiopulmonary bypass (CPB)- and ischemic time was 64 minutes and 34 minutes respectively.



Histopathological- and epidermal growth factor receptor (EGFR) analysis of the malignant pulmonary mass and lymphnodes confirmed the diagnosis of a pT2a, N0, R0, PI1 (TNM 7th edition) primary pulmonary adenocarcinoma with resistance to tyrosine kinase inhibitors. The histopathological evaluation of the cardiac mass confirmed a completely excised cardiac myxoma.

Patient recovery was swift, uneventful and suitable for further home base care 7 days postoperatively. Clinical follow-up at 6 weeks revealed excellent physical-, cosmetic- and oncological recovery (Figure 2E).

## DISCUSSION

Single stage ipsilateral minimally invasive surgery avoids the morbidity, cost, progressive tumour growth and potential tumour dissemination associated with time delays in the traditional two stage open procedures for specifically right sided hemithorax pathology [3]. We acknowledge that certain rare metastatic lung carcinomas may arise on the cardiac septum and that some authors perform cardiac

surgery first to exclude cardiac metastases [4]. We prefer to perform VATS before PAS to minimize the debatable risk of tumour dissemination and well-established coagulopathy effects related to CPB [5].

Our successful- and potentially curative concomitant single stage VATS and PAS oncological resection resulted in a good clinical- and cosmetic outcome, rapid patient recover and overall patient satisfaction

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# PART 5

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DISCUSSION AND CONCLUSIONS

SUMMARY

SAMENVATTING

EPILOGUE



# CHAPTER 17

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Discussion and conclusions



## THE BASIC PRINCIPLES OF PORT ACCESS™ SURGERY

Classic sternotomy access (CSA) for atrioventricular valve disease (AVV) disease is well established, but its role in contemporary clinical practice are continuously being redefined by rapid evolution in transcatheter technology, patient preferences and industry driven marketing.

The routine application of minimally invasive atrioventricular valve surgery (MIAS) is met with varying degrees of enthusiasm in view of steep learning curves, strict quality control, increasing clinical governance and progressive emphasis on transparent outcome reporting. The historically reported comparable efficacy of MIAS and CSA across a range of efficacy measures such as perioperative mortality, the success of the intended procedure, the incidence of vascular complications, neurological events, postoperative bleeding, respiratory morbidities, freedom from reoperation and long-term survival are confirmed (Chapter 3) and it is suggested that the surgical community should be encouraged to adopt and apply MIAS techniques into clinical their practices.

Port Access™ surgery (PAS) utilizes endovascular technology to perform safe- and efficient MIAS. The incorporation of PAS into routine practice is associated with a significant learning period that requires a stepwise implementation strategy under the guidance of experienced centres (Chapter 4). Infrastructure expansion, technical skills acquisition, teamwork, careful patient selection criteria and ongoing collaboration with expert centres are contributing factors that enhance the safety and efficacy during the initial transition period from CSA to PAS. Patients are regarded as the greatest advocates of a successful PAS program and every effort should be undertaken to reduce the risks of adverse outcome within the context of teamwork and patient centred service delivery.

The rapid advances in mitral valve repair techniques currently limit the indications of mitral valve replacement to valve pathology considered to be irreparable or at high risk of repair failure and patients considered to be unsuitable for future reinterventions. The role of endoscopic- and robotic surgical approaches will continue to evolve within the context of rapidly expanding transcatheter technology (Chapter 5). Successful mitral valve replacement outcomes are determined by meticulous perioperative risk assessment, prosthesis selection, anticoagulation management and long-term clinical surveillance in well informed and compliant patients.

## RISK REDUCTION STRATEGIES IN PORT ACCESS™ SURGERY

It is important for emerging MIAS centres to be aware of factors that contribute to sternotomy conversion and adverse intraoperative events. Meticulous preoperative patient evaluation for potential complications (especially peripheral vascular status), careful procedure planning, skilful technical execution under imaging guidance and effective teamwork are amongst the various factors that may reduce the incidence of adverse perioperative events (Chapter 6). The ability to recognize and successfully manage adverse intraoperative events are equally important to ensure patient safety and sustainable PAS programs (Chapter 7). Risk reduction strategies should be part of all expanding MIAS programs.

## NEW DEVELOPMENTS IN ADVANCED ENDOSCOPIC PORT ACCESS™ ATRIOVENTRICULAR VALVE SURGERY

Chest wall abnormalities and previous right hemithorax interventions that prohibited safe endoscopic atrioventricular valve access and complex valve pathology that require advanced repair- and replacement techniques for durable long-term outcomes were traditionally regarded as PAS contraindications.

Extreme obese patients are at risk of adverse perioperative events, which include wound- and respiratory complications. PAS for isolated AVV disease can safely be performed in experienced centres with favourable perioperative- and long-term procedural-, clinical- and echocardiographic outcomes (Chapter 8) and should not deter experienced surgeons and referring physicians from offering these patients the full range of potential benefits associated with MIAS.

Adults with perceived difficult access, uncorrected congenital chest wall deformities (CCWD) present extensive PAS challenges. By adjusting retractor positions and modifying existing techniques, safe and durable clinical and echocardiographic outcomes are achievable (Chapter 9).

Redo-atrioventricular valve surgery is associated with challenging technical AVV access and potential perioperative adverse events. PAS provides focused and targeted atrioventricular valve access without the need of extensive multistructural adhesiolysis. Late AVV disease invariably occurs in orthotopic cardiac transplant patients and excellent perioperative- and long-term clinical and echocardiographic outcomes are achievable with PAS (Chapter 10). Experienced centres regard PAS as a benchmark against which emerging percutaneous devices can be measured and may warrant earlier referral to avoid adverse outcomes related to progressive AVV disease.

Previous surgical procedures through right thoracotomy access is associated with lung adhesions and potential reentry difficulty for safe endoscopic AVV access. Redo-PAS after previous PAS, using the same skin incisions and peripheral vascular access as the primary procedure, is safe with favourable perioperative- and long-term clinical- and echocardiographic outcomes (Chapter 11) and is used as a routine approach in experienced centres.

The surgical treatment of hypertrophic obstructive cardiomyopathy with associated atrioventricular valve disease is extremely complex and requires a combination of left ventricle septal myectomy and atrioventricular valve correction procedures through various access possibilities. The perioperative- and long-term clinical and echocardiographic outcomes of single stage correction of left ventricle outflow tract obstruction and AVV-disease by PAS is safe, effective and durable (Chapter 12). Left ventricle outflow tract gradient reduction-, correction of systolic anterior motion of the mitral valve- and other AVV-surgical outcomes are favourable, with a 100% long-term freedom from reintervention and improved quality of life achievable in experienced centres without new- or recurrent echocardiographic AVV- pathology.

Isolated AVV endocarditis is associated with dismal perioperative- and long-term outcomes and present extensive technical challenges to achieve thorough debridement and complex AVV reconstructions. The perioperative safety and long-term durability of PAS in the context of isolated AVV

endocarditis can be performed with favourable perioperative survival- and mid-term clinical- and echocardiographic outcomes in experienced centres (Chapter 13).

#### **ANNECDOTAL REPORTS OF “BEYOND ROUTINE” PORT ACCESS™ PROCEDURES**

As an invaluable alternative to conventional open peripheral vascular access, a total percutaneous cardiopulmonary bypass technique for robotic- and endoscopic PAS avoids the devastating neurological-, lymphatic-, vascular- and wound infection morbidities associated with conventional vascular exposure in high risk patients for wound complications (Chapter 14).

Atrial myxomas offer good learning platforms to establish PAS skills during the initial learning curves and can also be utilized in the successful resection of perceived complex massive atrial myxomas with a satisfactory perioperative- and long-term clinical and echocardiographic outcome (Chapter 15).

Synchronous right pulmonary- and intracardiac neoplastic disease are traditionally resected by staged thoracic and sternotomy access.

Single stage ipsilateral video-assisted pulmonary resection and PAS resection of a myxoma using the same incisions avoid the morbidity, cost, progressive tumour growth and potential tumour dissemination associated with time delays in the traditional two stage open procedures for right hemithorax pathology (Chapter 16). The successful- and potentially curative concomitant single stage oncological resections resulted in a good clinical- and cosmetic outcome, rapid patient recover and overall patient satisfaction.

#### **CONCLUSION**

This thesis evaluated the safety and feasibility of advanced endoscopic PAS techniques for the surgical treatment of difficult-to-access and complex atrioventricular valve pathology, which were traditionally regarded as minimally invasive procedure contraindications. It was also the intention of this thesis to identify risk reduction strategies that may assist upcoming centres to safely initiate and sustain effective PAS programs.

The favourable observational study outcomes achieved by experienced PAS centres should ideally be subjected to randomized controlled trials. However, the routine application of PAS with the intention to treat resulted in limited classic sternotomy access control groups, which complicate the design of scientifically acceptable randomized control trials.

Hopefully, emerging centres will embrace the challenges of incorporating PAS into their practices and utilize safe and effective risk reduction strategies to gradually expand their service delivery to treat difficult-to-access and complex atrioventricular valve disease by PAS as a routine.



# CHAPTER 18

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Summary



## THE BASIC PRINCIPLES OF PORT ACCESS™ SURGERY

We are currently witnessing an exciting paradigm shift towards minimally invasive atrioventricular valve surgery. Whether the clinical outcomes reported by experienced centres can be translated in routine surgical practice, are addressed in **chapter 3**. A detailed literature overview comparing contemporary conventional sternotomy access- and minimally invasive atrioventricular surgery outcomes confirms the potential benefits historically described for minimally invasive approaches.

**Chapter 4** focuses on the principles of Port Access™ surgery and describes a step-by-step strategy of how to incorporate Port Access™ surgery into routine surgical practice. The current and future perspectives of conventional-, endoscopic Port Access™ surgery and transcatheter mitral valve interventions are described in **chapter 5**.

## RISK REDUCTION STRATEGIES IN PORT ACCESS™ SURGERY

The current professional environment of strict quality control, clinical governance, an aging population and industry driven marketing that favour transcatheter interventions, are not conducive to incorporating new techniques into clinical practice.

**Chapter 6** outlines the reasons for conversion and adverse intraoperative events in endoscopic Port Access™ atrioventricular valve surgery and minimally invasive aortic valve surgery. In **chapter 7**, the complications and pitfalls specific to Port Access™ surgery are described in detail and strategies outlined to ensure a safe- and sustainable Port Access™ program.

## NEW DEVELOPMENTS IN ADVANCED ENDOSCOPIC PORT ACCESS™ ATRIOVENTRICULAR VALVE SURGERY

The role of Port Access™ surgery in routine atrioventricular valve surgery is well described. The indications are evolving to include patient profiles, pathology and complex procedures historically considered to be contraindications to minimally invasive approaches.

In **chapter 8**, the clinical- and echocardiographic outcomes of endoscopic Port Access™ atrioventricular valve surgery in extreme obesity are evaluated. **Chapter 9** describes the perioperative and long term outcomes of endoscopic atrioventricular valve surgery by Port Access™ in adults with difficult-to-access uncorrected congenital chest wall deformities. The potential role of endoscopic Port Access™ surgery in late orthotopic cardiac transplantation atrioventricular valve disease is outlined in **chapter 10**. In **chapter 11**, the clinical- and echocardiographic outcomes of late redo-Port Access™ surgery after previous Port Access™ surgery are described.

The perioperative- and long term outcome of advanced endoscopic Port Access™ left ventricle outflow tract resection and atrioventricular valve surgery are discussed in **chapter 12**. Complex reconstructive endoscopic Port Access™ surgery for isolated atrioventricular valve endocarditis is evaluated in **chapter 13**.

## ANNECDOTAL REPORTS OF BYEOND ROUTINE PORT ACCESS™ PROCEDURES

An advanced total percutaneous cardiopulmonary bypass strategy for robotic- and endoscopic atrioventricular valve surgery is described in **chapter 14**. The endoscopic resection of a massive atrial myxoma by Port Access™ is discussed in **chapter 15** and in conclusion, the single-stage resection of a synchronous primary pulmonary adenocarcinoma and left atrial myxoma by video-assisted thoracic surgery and Port Access™ surgery using the same incisions is outlined in **Chapter 16**.



# CHAPTER 19

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Samenvatting



## DE BASIS PRINCIPES VAN PORT ACCESS™ CHIRURGIE

We zijn momenteel getuige van een opwindende paradigmaverschuiving naar minimaal invasieve atrioventriculaire klepchirurgie. Of de klinische resultaten gerapporteerd door ervaren centra kunnen worden vertaald in routinematige chirurgische praktijk, wordt behandeld in **hoofdstuk 3**. Een gedetailleerd literatuuroverzicht waarin de hedendaagse conventionele toegang via sternotomie wordt vergeleken met minimaal invasieve atrioventriculaire chirurgie bevestigt de potentiële voordelen die historisch zijn beschreven voor minimaal invasieve ingrepen.

**Hoofdstuk 4** is gericht op de principes van Port Access™ chirurgie en beschrijft stapsgewijs de strategie om poorttoegangschirurgie op te nemen in de routinematige chirurgische praktijk. De huidige en toekomstperspectieven van conventionele, endoscopische Port Access™ chirurgie en transkatheter mitraalklep interventies worden beschreven in **hoofdstuk 5**.

## RISICO REDUCERENDE STRATEGIE IN PORT ACCESS™ CHIRURGIE

Het huidige professionele klimaat van strikte kwaliteitscontrole, klinische governance, een vergrijzende bevolkingen en een door de industrie gestuurde marketing die trans-katheter interventies ten goede komt, zijn niet bevorderlijk om nieuwe technieken in de klinische praktijk op te nemen. **Hoofdstuk 6** schetst de redenen voor conversie en intra-operatieve complicaties gerelateerd aan Port Access™ voor atrioventriculaire klepchirurgie en minimaal invasieve aortaklepchirurgie.

In **hoofdstuk 7** worden de complicaties en valkuilen, specifiek voor Port Access™ chirurgie in detail beschreven en strategieën geschetst om een veilig en duurzaam Port Access™ programma te kunnen waarborgen.

## NIEUWE ONTWIKKELINGEN IN GEAVANCEERDE ENDOSCOPISCHE PORT ACCESS™ ATRIOVENTRICULAIRE KLEPCHIRURGIE

De rol van Port Access™ chirurgie bij routinematige atrioventriculaire klepchirurgie is goed beschreven. De indicatiestelling is dynamisch en evolueert om ook die patiënten profielen, pathologie en complexe procedures die in het verleden beschouwd worden als contra-indicaties voor minimaal invasieve benaderingen te overwegen. In **hoofdstuk 8** worden de klinische en echocardiografische uitkomsten van endoscopische atrioventriculaire klepchirurgie bij extreme obesitas geëvalueerd.

**Hoofdstuk 9** beschrijft de perioperatieve en langetermijn resultaten van endoscopische atrioventriculaire klepchirurgie bij volwassenen met moeilijk toegankelijke niet-gecorrigeerde congenitale thoraxwand misvormingen.

De mogelijke rol van endoscopische Port Access™ chirurgie bij lange termijn atrioventriculaire klepaandoeningen na orthotopische cardiale transplantatie wordt uiteengezet in **hoofdstuk 10**.

In **hoofdstuk 11** worden de klinische en echocardiografische resultaten van late redo-Port Access™ chirurgie na voorgaande Port Access™ chirurgie beschreven.

De korte en lange termijn resultaten van geavanceerde endoscopische Port Access™ linker ventrikel outflow tract resectie en atrioventriculaire klepchirurgie worden besproken in **hoofdstuk 12**. Complexe reconstructieve endoscopische Port Access™ chirurgie voor geïsoleerde atrioventriculaire klep-endocarditis wordt in **hoofdstuk 13** geëvalueerd.

## ANECDOTISCHE VERSLAGEN VAN DE PROCEDURES OVER DE GRENZEN VAN ROUTINE PORT ACCESS™ HEEN

Een geavanceerde totale percutane cardiopulmonale bypass strategie voor robot- en endoscopische atrioventriculaire klepchirurgie wordt beschreven in **hoofdstuk 14**. De endoscopische Port Access™ chirurgische resectie van een massief atriaal myxoma wordt besproken in **hoofdstuk 15**. In **hoofdstuk 16** wordt een geavanceerde strategie geschetst voor single stage minimaal invasieve chirurgie voor een synchroon primaire pulmonale adenocarcinoom en linker atriaal myxoma.



# CHAPTER 20

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PhD Portfolio

**PhD PORTFOLIO (including European Fellowships)**

Erasmus MC Department: Cardiothoracic Surgery  
 PhD Period: 2015-2019  
 Promotors: Prof. Dr. A.P Kappetein  
 Prof. Dr. A.J.J.C. Bogers

<b>Conferences attended specific to cardiothoracic surgery</b>	
Society for Cardiothoracic Surgery	2011
Society for Cardiothoracic Surgery	2012
Belgian Association of Cardiothoracic Surgery	2013
The future of surgery in Belgium, EUMS, Brussels, Belgium	2013
Belgian Association of Cardiothoracic Surgery	2014
South African Heart Association	2014
Belgian Association of Cardiothoracic Surgery	2015
European Association of Cardiothoracic Surgery	2015
South African Heart Association	2016
Belgian Association of Cardiothoracic Surgery	2016
World Society of Cardiothoracic Surgery	2016
European Association of Cardiothoracic Surgery	2016
European Association of Cardiothoracic Surgery	2017
European Association of Cardiothoracic Surgery	2018
International Society of Minimally Invasive Cardiothoracic Surgery	2019
<b>Oral presentations</b>	
Society for Cardiothoracic Surgery	2012
Belgian Association of Cardiothoracic Surgery	2013
The future of surgery in Belgium, EUMS, Brussels, Belgium	2013
Belgian Association of Cardiothoracic Surgery	2014
South African Heart Association	2014
Belgian Association of Cardiothoracic Surgery	2015
European Association of Cardiothoracic Surgery	2015
South African Heart Association	2016
Belgian Association of Cardiothoracic Surgery	2016
World Society of Cardiothoracic Surgery	2016
European Association of Cardiothoracic Surgery	2016
European Association of Cardiothoracic Surgery	2017
European Association of Cardiothoracic Surgery	2018
International Society of Minimally Invasive Cardiothoracic Surgery	2019

<b>Courses attended specific to cardiothoracic surgery</b>	
Coronary Artery Surgery, Gloucester, United Kingdom	2012
Advanced Minimally Invasive Thoracic Surgery, Elancourt, Paris, France	2012
London Core Curriculum Review, London, United Kingdom	2012
Aortic Dissection Master Class, London, United Kingdom	2013
Mitral valve repair, Gloucester, United Kingdom	2013
Total Arterial Revascularization Master class, Oxford, United Kingdom	2013
Advanced Diagnostic Bronchoscopy, NHLI, London, United Kingdom	2013
VATS lobectomy (Rob McKenna), Wimat Centre, Cardiff, United Kingdom	2013
The 8 <sup>th</sup> annual conference on mechanical circulatory support, Germany	2014
Extra-Corporeal Life Support, Leuven, Belgium	2014
3-D minimally invasive cardiothoracic surgery, OLV-Clinic, Aalst, Belgium	2015
Minimally Invasive Cardiac Surgery, Maastricht, Netherlands	2016
Local scientific meetings	2011-2017
<b>Courses attended specific to clinical governance</b>	
Equality and Diversity, Royal Brompton Hospital, London, United Kingdom	2012
Good Clinical Practice, Royal Brompton Hospital, London, United Kingdom	2012
Information Governance, Royal Brompton Hospital, London, United Kingdom	2012
Patient Safety Workshop, Royal Brompton Hospital, London, United Kingdom	2012
Mastering your risks, Medical Protection Society, London, United Kingdom	2012
Mastering adverse outcomes, Medical Protection Society, London, United Kingdom	2012
Mastering professional interaction, London, United Kingdom	2012
<b>Courses attended specific to management</b>	
Project management, Royal Brompton Hospital, London, United Kingdom	2012
Budget management, Royal Brompton Hospital, London, United Kingdom	2012
Royal Brompton Leadership Course, Royal Brompton Hospital, London, United Kingdom	2012
Recruitment, selection and interviewing, London, United Kingdom	2012
Resolving workplace conflict, Royal Brompton Hospital, London, United Kingdom	2012
Leading from the front: Operative Theatre, London, United Kingdom	2012
Communication and assertiveness, Royal Brompton Hospital, London, United Kingdom	2012
Appraisal training, Royal Brompton Hospital, London, United Kingdom	2012

<b>Courses attended specific to junior staff training</b>	
Setting learning objectives, London deanery, United Kingdom	2012
Assessing educational needs, London deanery, United Kingdom	2012
How to give feedback, London deanery, United Kingdom	2012
Supervision, London deanery, United Kingdom	2012
Career support, London deanery, United Kingdom	2012
Workplace based assessment, London deanery, United Kingdom	2012
Small group teaching, London deanery, United Kingdom	2012
Teaching clinical skills, London deanery, United Kingdom	2012
Facilitating learning in the workplace, London deanery, United Kingdom	2012
Diversity, equal opportunities and human rights, London deanery, United Kingdom	2012
Introduction to educational research, London deanery, United Kingdom	2012
Improve your lecturing skills, London deanery, United Kingdom	2012
Appraisals London deanery, United Kingdom	2012
Involving patients in clinical teaching, London deanery, United Kingdom	2012
Interprofessional teaching London deanery, United Kingdom	2012
Managing the trainee in difficulty, London deanery, United Kingdom	2012
Ensuring and maintaining quality in educational training, London, United Kingdom	2012
Structured assessment of clinical competence, London deanery, United Kingdom	2012
<b>Course coordinator</b>	
National Course Director: Cardiac Surgical Unit Advanced Life Support (RSA)	2017
National Course Director: Perioperative Cardiac Surgical Care (RSA)	2017

<b>Professional memberships</b>	
European Society of Intensive Care Medicine	2016
European Society of Cardiothoracic Surgeons	2009
European Society of Thoracic Surgeons	2010
Belgian Association of Cardiothoracic Surgeons	2014
South African Society for Cardiothoracic Surgery	2010
South African Trauma Association	2009
South African Critical Care Society	2009
Faculty of Medical Leadership and Management, United Kingdom	2012
Medical Protection Society, United Kingdom and South Africa	2010
<b>Council registrations</b>	
General Medical Council, United Kingdom	2002
Health Professions Council of South Africa	2002
Orde der Geneesheren, Belgium	2014





# CHAPTER 21

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List of publications

## LIST OF PUBLICATIONS

1. **Van der Merwe J**, Casselman F, Beelen R, Van Praet F. Total percutaneous cardiopulmonary bypass for robotic- and endoscopic atrioventricular valve surgery. *Innovations* 2017;12(4):296-299
2. **Van der Merwe J**, Casselman F. Mitral valve replacement – current and future perspectives. *Open J Cardiovasc Surg.* 2017; 13(9) :1179065217719023.
3. **Van der Merwe J**, Van Praet F, Stockman B, Degrieck I, Vermeulen Y, Casselman F. Reasons for conversion and adverse intraoperative events in endoscopic Port Access™ atrioventricular valve surgery and minimally invasive aortic valve surgery. *Eur J Cardiothorac Surg.* 2018 Aug 1;54(2):288-293
4. **Van der Merwe J**, Casselman F, Stockman B, Vermeulen Y, Degrieck I, Van Praet F. Endoscopic atrioventricular valve surgery in extreme obesity. *Türk Göğüs Kalp Damar Cerrahisi Dergisi.* 2017;25(4):654-658
5. **Van der Merwe J**, Casselman F, Stockman B, Vermeulen Y, Degrieck I, Van Praet F. Endoscopic atrioventricular valve surgery in adults with difficult-to-access uncorrected congenital chest wall deformities. *Interact Cardiovasc Thorac Surg.* 2016;23(6):851-855.
6. **Van der Merwe J**, Casselman F, Stockman B, Vermeulen Y, Degrieck I, Van Praet F. Endoscopic Port Access™ surgery for late orthotopic cardiac transplantation atrioventricular valve disease. *J Heart Valve Dis.* 2017;26(2):124-129.
7. **Van der Merwe J**, Casselman F, Stockman B, Vermeulen Y, Degrieck I, Van Praet F. Late redo-Port Access™ surgery after Port Access™ surgery. *Interact Cardiovasc Thorac Surg.* 2016 Jan;22(1):13-8
8. **Van der Merwe J**, Casselman F, Van Praet F. Endoscopic Port Access™ left ventricle outflow tract resection and atrioventricular valve surgery. *J Vis Surg.* 2018; 4: 100
9. **Van der Merwe J**, Casselman F, Stockman B, Roubelakis A, Vermeulen Y, Degrieck I, Van Praet F. Endoscopic Port Access™ surgery for isolated atrioventricular valve endocarditis. *Interact Cardiovasc Thorac Surg.* 2018;27(4):487-493
10. **Van der Merwe J**, Casselman F, Van Praet F. Endoscopic Port Access™ resection of a massive atrial myxoma. *SA Heart.* 2016; 13: 4: 302 – 303
11. **Van der Merwe J**, Beelen R, Martens S, Van Praet F. Single-Stage minimally invasive surgery for synchronous primary pulmonary adenocarcinoma and left atrial myxoma. *Ann Thorac Surg.* 2015; 100(6):2352-4
12. **Van der Merwe J**, Coddens J, Casselman F. Acute single leaflet dysfunction and spontaneous recovery of a previously implanted bi-leaflet mechanical mitral prosthesis during unrelated isolated minimally invasive aortic valve replacement: a surgical decision making dilemma in a high risk patient. *J Cardiovasc Surg* 2017;58(1):131-132
13. Roubelakis A, Casselman F, **Van der Merwe J**, Stockman B, Degrieck I, Van Praet. Robotic-enhanced coronary surgery in octogenarians. *Interact Cardiovasc Thorac Surg.* 2017; 24(3):384-387.
14. Casselman F, **Van der Merwe J**, Ferrara A, Barbato E. The present day potential role of fractional flow reserve-guided coronary artery bypass graft surgery. *J Thorac Cardiovasc Surg.* 2016; 151(4):926-32
15. **Van der Merwe J**, Casselman F, Stockman B, Van Praet F, Beelen R, Maene L, Vermeulen Y, Degrieck I. Minimally invasive primary aortic valve surgery: the OLV Aalst experience. *Ann Cardiothorac Surg.* 2015 Mar;4(2):154-9
16. **Van der Merwe J**, Casselman F, Verstreken S, Stockman B. Acute ascending aorta dissection in a bicuspid aortic valve cardiac allograft 11 years after orthotopic cardiac transplantation. *Eur J Cardiothorac Surg.* 2017; 51(1):191
17. **Van der Merwe J**, Casselman F, Van Praet F. Minimally invasive atrioventricular valve surgery – current status and future perspectives. Under review: *South African Heart Journal*
18. **Van der Merwe J**, Casselman F, Van Praet F. The principles of Port Access™ surgery – How to start and sustain a safe and effective program. *Accepted: Journal of Visual Surgery*
19. **Van der Merwe J**, Casselman F, Van Praet F. Complications and pitfalls in Port Access™ atrioventricular valve surgery. *J Vis Surg* 2018; 4:248
20. **Van der Merwe J**, Casselman F. Fractional flow reserve guided coronary artery bypass grafting - new developments and future perspectives. *Vessel Plus* 2019;3:24
21. **Van der Merwe J**, Casselman F, Stockman B, Vermeulen Y, Degrieck I, Van Praet F. Reasons for conversion and adverse intraoperative events in robotically enhanced minimally invasive coronary artery revascularization. *Accepted: Innovations*



# CHAPTER 22

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About the Author

Hendrik Johannes (Johan) van der Merwe was born on 27th August 1978 in Durban (South Africa) and obtained his basic medical degree (MBChB) from the University of Pretoria (South Africa) in 2002. He completed his compulsory Internship- (2003) and senior house officer training (2004) at Baragwanath Hospital (South Africa, the largest hospital in the southern hemisphere) and Sebokeng Hospital (South Africa) respectively, with special interest in general- and trauma surgery, cardiology, pulmonology and intensive care.

He joined the department of cardiothoracic surgery at the University of Pretoria (South Africa) in 2005 as specialist registrar for 6 years, serving an adult- and paediatric population of more than 6 million people.

He qualified as specialist cardiothoracic surgeon and intensivist in 2010 at the age of 32 years and completed certified fellowships at the Royal Brompton Hospital (London, United Kingdom, 2011-2012), University Hospital Leuven (Leuven, Belgium, 2013) and Onze Lieve Vrouw Clinic (Aalst, Belgium, 2014-2016) with subspecialization in advanced endoscopic thoracic oncological interventions and surgery, cardiac assist device implantation, cardiac transplantation, off-pump- and total arterial coronary artery revascularization and robotic-, endoscopic-, hybrid- and transcatheter cardiovascular- and thoracic surgery. During this period, he enrolled at Erasmus Medical Centre (Rotterdam, Netherlands) as a doctorate candidate and is currently continuing his role as voluntary departmental research fellow at Onze Lieve Vrouw Clinic.

In 2016, he became the first South African to be admitted as a Fellow to the European Board of Cardiothoracic Surgeons (EBCTS) following the successful participation in the pan-European examination (FETCS). In close collaboration with his mentors, he founded the *Atlantic Cardiovascular- and Thoracic Institute* ([www.acvti.co.za](http://www.acvti.co.za)) on January 1st 2017 and heads *The Keyhole Heart Centre* ([www.thekeyholeheartcentre.co.za](http://www.thekeyholeheartcentre.co.za)) in Cape Town, South Africa. He is currently an active member of various international cardiothoracic-, intensive care-, trauma- and leadership societies and continues to focus on developing himself as an endoscopic and transcatheter surgeon, researcher, leader, trainer and active community member.



**Hendrik J. Van der Merwe**  
**MBChB (Pret), MMED (Thorax)(Pret), FETCS (EBCTS)**



# CHAPTER 23

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I wish to thank a number of prominent colleagues, whose guidance and assistance were invaluable in the development of my research portfolio and in particular, for the development of this thesis at the present time.

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