

Original Articles

Minimally Invasive Aortic Valve Replacement on Minimally Invasive Extracorporeal Circulation: Going beyond Aesthetics

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Abstract: We present our multidisciplinary and multistep strategy in patients undergoing minimally invasive aortic valve replacement (mAVR) on minimally invasive extracorporeal circulation (MiECC) compared with control groups of a single strategy and conventional techniques. This cohort study included high-risk patients (Society of Thoracic Surgeons [STS] risk score >8%) undergoing aortic valve surgery under different strategies during the period from January 2017 until March 2019. Patients were matched for age, gender, body mass index, and STS score: group 1 (MiAVR) based on a minimally invasive technique with J-mini-sternotomy, rapid deployment valve (RDV), and type IV customized MiECC; group 2 (control-mAVR) consisted of minimally invasive technique with only J mini-sternotomy and RDV on a conventional extracorporeal system; group 3 (control-MiECC): full sternotomy and type IV customized MiECC; and group 4 (control): full sternotomy on a conventional extracorporeal system. The MiAVR group had

significantly less duration of x-clamp time (35.4 ± 11 minutes), postoperative respiratory support (4.1 ± 1 hour), postoperative hemorrhage (250 ± 50 mL), and intensive care unit stay ($1 \pm .5$ days) than the control-conventional (group 4) group. Seventy-six percent of patients did not receive any blood products in MiAVR ($p = .025$ vs. group 4). Incidence of atrial fibrillation (8%) and low cardiac output (14%) in MiAVR were significantly better than control. Critics of minimally invasive techniques sustain that potential advantages are offset by a longer cross-clamp and cardiopulmonary bypass duration, which may translate into inferior clinical outcomes. We advocate that our multidisciplinary approach supported by multiple technologies may be associated with faster recovery and superior outcomes than conventional minimally/conventional techniques. **Key-words:** aortic valve, replacement, minimally invasive surgery, cardiopulmonary bypass, aorta. *J Extra Corpor Technol. 2020; 52:90–5*

Since Cosgrove and Sabik first described minimally invasive aortic valve replacement (mAVR) in 1996, there has been a significant expansion in popularity, experience, and techniques (1). There is a growing understanding of the outcomes compared with traditional aortic valve replacement (AVR) with median sternotomy, including survival, perioperative times, and complications. However, much of the early literature on minimally invasive cardiac surgery (MICS) focused on technical reports or small case series.

The safety and feasibility have been demonstrated, yet questions remain regarding the relative efficacy over traditional sternotomy approaches. Recently, there has been a growth in the body of published literature on long-term outcomes, with most reports suggesting that significant cardiac operations that have traditionally been performed through a median sternotomy can be performed through a variety of minimally invasive approaches with equivalent safety and durability (2).

The concept of minimally invasive extracorporeal circulation (MiECC) was introduced to create a system that integrates all the advances in technology (centrifugal pump, short surface-coated tubing with inert surfaces, bubble trap-removing devices, left ventricle venting systems, soft-shell reservoir, and—if required—modular hard-shell reservoir for blood management) in one closed

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cardiopulmonary bypass (CPB) circuit. This system, which implicates a pooled strategy including surgical, anesthesiologic, and perfusion management techniques, allows for more physiological perfusion and minimizes the side effects of extracorporeal circulation. Therefore, MiECC technology is now suitable for valvular and more complicated surgery. However, although MiECC demonstrated improved clinical outcomes in coronary surgery compared with conventional extracorporeal circulation, such robust evidence is still lacking in valvular patients (3).

Integration of MiECC to mAVR could transform it from limited access surgery on to a more “physiological” surgery; this could maximize clinical benefits and further improve patient outcomes, especially in high-risk populations needing additional support.

The current evidence suggests that rapid deployment/sutureless prosthetic valve substitutes (rapid deployment valve [RDV]) may have the potential to become the new gold standard treatment for mAVR by facilitating minimally invasive approaches, providing superior hemodynamic results, and allowing for shorter operative times (4,5).

The minimally invasive concept should be broader than incisions targeting high-risk patients via additional technology to reduce trauma, operative time, inflammation, and transfusion, aiming better outcomes. We present our multidisciplinary and multistep strategy in patients undergoing mAVR on MiECC compared with single strategy and control groups.

PATIENTS AND METHODS

This study was approved by the Institutional Ethics Committee (2306/2017). Patient informed consent forms for treatment, data collection, and analysis for scientific purposes were collected in all cases.

Study Population, Data Collection, and Analytic Plan

During the period from January 2017 until March 2019, data of 112 patients who underwent AVR with minimally invasive technique, J-mini-sternotomy, RDV, and type IV MiECC in our institution were prospectively collected (group 1: MiAVR). Data of control groups within the same period were collected retrospectively. Control groups consisted of minimally invasive technique with J mini-sternotomy and RDV on a conventional extracorporeal system (group 2: mAVR), full sternotomy and type IV customized MiECC (group 3: control-MiECC), and full sternotomy on a conventional extracorporeal system (group 4: control). All patients underwent coronary angiography, and significant coronary lesion needing intervention was excluded.

The use of propensity score matching addressed treatment selection bias. Patients were matched by propensity score for age, gender, body mass index, and the Society of Thoracic Surgeons (STS) risk score to have 50 patients in each group. Exclusion criteria were severe hemodynamic instability requiring high doses of inotropic drugs, severe heart failure (the New York Heart Association IV), ejection fraction <30%, severe renal failure/dialysis or severe hepatic disease, previous cardiac surgery, emergency surgery, severe pulmonary hypertension, and a history of stroke or significant neurological dysfunction.

Surgery

Anesthesia was induced with fentanyl (35 $\mu\text{g}/\text{kg}$), and muscle relaxation was established with pancuronium bromide (.1 mg/kg). Patients were intubated endotracheally. All patients were administered 3 mg/kg heparin sodium (Liquemine; Roche, Istanbul, Turkey). Systemic full-dose heparinization was achieved according to the individual patient’s response to heparin in all groups. Activated clotting time was measured using a Hemochron 801 (International Technidyne Corporation, Edison, NJ) and maintained >480 seconds. A cell saver system (Xtra, Sorin Group, Sorin, Mirandola, Italy) is used to preserve the red cell mass for all groups. Vacuum-assisted venous drainage was used routinely for all cases. Moderate hypothermia was induced at 30°C. Retrograde autologous priming was performed. Control groups (groups 3 and 4) received Sorin mechanical valve (LivaNova, London, United Kingdom). The outcome measures such as blood transfusion, extubation, and intensive care unit (ICU)/hospital stay were all evaluated by a specific protocol, similar for all groups.

In minimally invasive groups, before skin incision, the jugular notch, the sternal midline, and the xiphoid were marked to facilitate surgical incision and accelerate conversion to full sternotomy in case of unexpected complications.

Following a 4- to 5-cm skin incision, an upper J-mini-sternotomy extended to the 3rd or 4th right intercostal space was performed. Peripheral cannulation (femoral artery/vein) was the first choice for CPB inflow and venous drainage. When it is not feasible, ascending aorta and right atrium were used. The right superior pulmonary vein was cannulated for left ventricle venting. After normothermic CPB institution, with an empty heart, a subxiphoid spiral drain is placed, to continuously infuse carbon dioxide into the pericardial cavity. The ascending aorta was gently clamped using a specially designed clamp for minimally invasive interventions. A transverse aortotomy was performed, and the aortic valve is exposed. Following aortotomy, the aortic cusps were removed and the annulus accurately decalcified. After proper sizing, a RDV (Perceval, LivaNova) was implanted. The aortotomy was closed using a standard technique. Before releasing the aortic

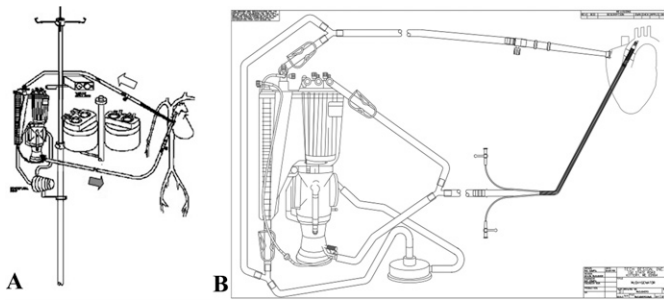


Figure 1. Schematic setup of conventional (A) and pinnacle MiECC systems (B).

clamp, two pacing wire electrodes were sutured to the right ventricle. The operation was then completed as usual. In MiECC and conventional groups, the ascending aorta was cannulated for arterial inflow and the right atrium for venous return.

Circuit

MiECC: We continue our practice with our U.S. patented designed condensed extracorporeal circuit, the Pinnacle system, where the oxygenator and the pumps are brought closer to the operating table (within 30 inches) with the help of a series of telescopic swivel steel poles to which they are attached (Figure 1) (6). The control console is retained at the usual remote location of 2 ft behind the Pinnacle system.

This is a condensed, dual-function, open/closed configuration circuit that uses components that are surface-coated, with a shortened tubing priming volume under 800 mL. It includes a centrifugal pump and a venous air removal device with an incorporated shunt which bypasses the reservoir for closed configuration. CPB was instituted on either open configuration, with a hard-shell venous reservoir and cardiotomy, or closed configuration, with a flexible venous reservoir. A condensed cardioplegia circuit infused fluid into the blood pulled from the oxygenator. Pinnacle system is a concept/design rather than a specific

product in the market. This design can be constructed by any product available. The system is classified as type IV with respect to the position paper published by the International Society of Minimally Invasive Extracorporeal Circulation (MiECTIS) (3) (Table 1).

It consists of the following materials: arterial/venous cannulas (DLP, Minneapolis, MN) attached to 30 inches of $3/16 \times 3/8$ -inch coated tubing, a hollow fiber oxygenator with integrated arterial filter (Inspire 6[®] Phisio-coated, LivaNova), integrated open reservoir centrifugal pump (Revolution[®], LivaNova), 30 inches of $3/16 \times 1/2$ -inch coated tubing, and an S5 heart–lung machine (LivaNova).

Blood cardioplegia is administered using $3/16 \times 1/4$ -inch coated tubing with the cardioplegia heat exchanger (CSC 14, LivaNova PLC, Mirandola, Italy). The length of this line is also 30 inches. The circuit that we use for cardioplegia delivery is straightforward. Blood is taken directly from the oxygenator with $1/4$ -inch tubing and, using a pediatric roller pump, injected directly into the aortic root or coronary sinus. A U.S. patented delivery system with an incorporated syringe pump delivers potassium to the system. The temperature of the cardioplegia is delivered at 4°C.

Conventional: CPB was instituted via arterial/venous cannulas (DLP) attached to coated tubing and a hollow fiber oxygenator with integrated arterial afilter (Inspire 6[®] Phisio-coated, LivaNova). Venous blood was drained by gravity into a hard-shell venous reservoir (Inspire, LivaNova) and reinfused into the patient using a centrifugal pump (Revolution[®], LivaNova). The circuit was primed with 1,200 mL (with a 200 mL safety margin in the reservoir) of Plasma-Lyte[®] A. Control groups with conventional techniques received 4:1 blood cardioplegia every 20 minutes. Moderate hypothermia was induced at 30°C. The need for conversion to full sternotomy and/or conventional extracorporeal circulation and any complication or technical discomfort for both surgeons/perfusionists regarding the use of MiECC during the cases were reported.

Table 1. Definition of different types of MiECC.

MiECC	Aim	Components
Type I	Standard	This closed circuit comprises an afferent tube which drains blood from the right atrium to the pump, and, then, to the oxygenator, and returns it to the arterial circulation with the efferent tube
Type II	Air handling	A venous bubble trap/air removing device is added to the standard MiECC circuit to facilitate air-handling and avoid air capture in the venous line
Type III	Volume management	A soft-shell reservoir is added to the circuit to collect volume from the patient and return during the perfusion in case of any need
Type IV	Modular configuration	A hard-shell reservoir is added as an extra component integrated to the venous line to convert the system to an open circuit that could facilitate blood management and/or any other intraoperative issues

Table 2. Baseline characteristics of groups.

	Group 1, MiAVR	Group 2, Control-mAVR	Group 3, Control-MiECC	Group 4, Control-Conventional
Age (years)	71 ± 8	68 ± 10	73 ± 10	67 ± 10
Female (n)	35	33	31	39
BSA (m ²)	1.8 ± 0.4	1.76 ± 0.4	1.83 ± 0.4	1.81 ± 0.4
Diagnosis (AS/AS + AR)	33/17	29/21	37/13	30/20
Mean gradient (mmHg)	65.4 ± 15	60.7 ± 15	69.2 ± 15	59.6 ± 15
STS risk score (%)	10.1 ± 1	9.4 ± 1	10.1 ± 1	10.5 ± 1
Ejection fraction (%)	45.6 ± 10	42.9 ± 10	49.1 ± 10	44.4 ± 10
Associated disorders (HT/DM/COPD)	39/32/24	40/31/28	42/30/31	36/39/30

AS, aortic stenosis; AR, aortic regurgitation; HT, hypertension; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease.

Cerebral Oxygen Saturation (rSO₂)

Near-infrared monitoring used the INVOS 4100 cerebral oximeter (Somanetics Corp., Troy, MI). This measure is a weighted average of both mixed arterial and venous oxygen saturations in the cerebral cortex, and rSO₂ values were automatically collected every 30 seconds on an internal clock and stored as a Microsoft Excel file. Data were then retrospectively collected, averaged, and synchronized with pump records.

as well as two groin wound seromas, were reported. The postoperative mean gradient of aortic valve was 8.8 ± 3 mmHg in group 1, 10.5 ± 3 mmHg in group 2, 11.5 ± 3 mmHg in group 3, and 11.1 ± 5 mmHg in the control group. Overall, perioperative data are summarized in Table 3. rSO₂ measurements were significantly better in the group 1 vs. group 4 (68.95 ± 5% and 60.3 ± 5%; *p* = .0034) following CPB including postoperative first day.

STATISTICAL ANALYSIS

Statistical analysis was performed using IBM SPSS Statistics, version 22.0 for Windows (SPSS Inc, Chicago, IL). The data were reported as mean ± SD. The results were considered significant for *p* ≤ .05. To test for differences between the groups at particular time points, we first constructed a QQ plot (probability plot) to test for normal distribution of the investigated data. Subsequently, either the *t* test or the Wilcoxon or Mann–Whitney *U* test was used for quantitative values. If the conditions for the *t* test were met, then it was used before the Wilcoxon or Mann–Whitney *U* test. To calculate differences between groups over time, multiple analyses were performed, i.e., repeated-measure (RM analysis of variance) analysis.

DISCUSSION

MICS continues to evolve and expand with growth in technology and surgeon experience. Reducing surgical trauma by minimizing skin incisions has transformed abdominal surgery, resulting in significant improvements in outcome. In cardiac surgery, such efforts have also been made, but similar benefits could not be demonstrated. In addition, any potential benefit comes at the cost of increased CPB and cross-clamp times, leading to questions regarding the safety of MICS.

RESULTS

Baseline characteristics of the patients are summarized in Table 2. We have not reported any complication or technical discomfort regarding the use of MiECC during the cases. In none of the cases, there was a need for conversion to full sternotomy and/or conventional extracorporeal circulation.

Nevertheless, outcomes have been equivalent to matched sternotomy cases, and there is no doubt that the number of patients undergoing minimally invasive mitral or aortic procedures is slowly increasing. To date, almost half of all isolated mitral cases in Germany and roughly one-fourth in the United States are performed through minimized access. These numbers were less than half 10 years ago. So how can this development be justified if the evidence for it seems to be questionable or even missing? (7,8).

No statistically significant differences were obtained in any of the conventional laboratory evaluation testing among groups. There was one cerebrovascular accident in group 2 and no aortic dissection in any group. Two femoral arterial pseudoaneurysms in group 1 and three in group 2,

There is enough evidence today supporting the primary use of MICS in specialized reference centers. Although the information from prospective randomized trials is limited, the bulk of data may serve as a surrogate for a “non-inferiority” endpoint. The conduction of large prospective randomized trials in the future is unlikely (9,10).

We have a more 4-year experience of MICS in our clinic and performing about all AVRs in minimally invasive fashion. Addition of RDV is also important. We believe we can overcome the prolonged cross-clamp duration even in experienced centers via sutureless technology. In our study,

Table 3. Perioperative clinical outcome.

	Group 1, MiAVR	Group 2, Control- mAVR	Group 3, Control- MiECC	Group 4, Control- Conventional	<i>p</i> vs. Group 4	<i>p</i> -Matched (Only Significant Differences Displayed)
Duration of x-clamp (minutes)	40.4 ± 11*,†	44 ± 12*,†	58 ± 12	61 ± 14	= .038	1 vs. 3 <i>p</i> = .042 2 vs. 3 <i>p</i> = .048
Respiratory support (hour)	4.1 ± 1*	5.5 ± 3*	7.2 ± 5	11.4 ± 5	= .0022	–
Postop hemorrhage (mL)	250 ± 50*	350 ± 50	420 ± 50	550 ± 50	= .034	–
Patients with no transfusion (%)	76 *	60	54	48	= .025	–
Red blood cell transfusion (Unit)	.5 ± .5*	2 ± 0.5	1.8 ± 0.5	2.6 ± 0.5	= .014	–
Incidence of atrial fib (%)	10	12	8	8	>.05	–
Incidence of AV block (%)	4	6	2	2	>.05	–
Low cardiac output (%)	14*	20	18	24	= .025	–
ICU stay (days)	1 ± .5*	1.5 ± 0.5	2.1 ± 0.5	2.8 ± 0.5	= .04	–
Hospital stay (days)	4.1 ± 2*	5.2 ± 3	5.8 ± 3	6.1 ± 3	= .045	–
Mortality (%)	2	2	0	4	>.05	–

**p* vs. control-conventional.

†*p* vs. control-MiECC.

cross-clamp times were significantly better than controls confirming the impact on RDV.

The perceived benefits of MICS are well established and include cosmesis, reduced surgical trauma, blood loss, the incidence of atrial fibrillation and pain, preserved lung function, and shorter hospital length of stay, consequently involving less use of hospital resources and reduced costs. These results come from extensive cohort studies and meta-analyses from centers dedicated to this technique. The price to be paid for that smaller incision, in almost every study, comes as increased total CPB, cross-clamp, and operative times (when excluding off-pump coronary surgery that avoids CPB). The imminent question that arises is straightforward: Should MICS be defined exclusively based on “minimal access” surgery without aiming toward a more “physiologic” CPB? Is it rational to perform complex surgery through a tunnel, such as in mini-thoracotomy AVR or minimally invasive mitral surgery, aiming to reduce the systemic inflammatory response while, at the same time, the patient is hemodiluted by excessive crystalloid prime with a conventional CPB circuit that runs for more than 120 minutes? We consider that the implementation of an MiECC strategy should become a fundamental component of MICS (11–13).

We have been using MiECC for more than 10 years in our clinic. We believe the positive impact on, especially, protection from the CPB-related inflammatory response. In this study, matched comparison did not show any significant benefit for the MiECC-only group. Probably, the impact of MiECC on early outcomes could not be demonstrated because of low patient population. But, when combined with mAVR, significant better clinical outcomes could be reached.

We believe that the concept of MICS can evolve even further by going beyond a simple reduction of the surgical incision: by increasing the technical and technological

content of the intervention according to a multidisciplinary approach, clinical outcomes after MICS can be enhanced, and postoperative recovery may be fastened with an increased patient and family satisfaction. MiECC system represents an essential tool in the field of MICS, and the implementation of an MiECC strategy should be considered a fundamental component of the modern AVR approaches. However, despite promising results, the penetration of MiECC remains low, and the impact of this technology on the clinical outcomes of patients undergoing mAVR has still to be defined (14–16).

MICS expands the operative portfolio, allowing the treatment of patients that may have been considered too complex for surgery before. We suggest that modern cardiac surgery may have difficulties to prevail in its full width if MICS is not embraced. We also suggest that MICS is associated with substantial improvements in patient outcomes, however, in areas that are unlikely to be tested with randomized controlled trials. Last, we need to be honest and just with our patients and offer them the procedure that based on the current evidence for all techniques (conventional surgery, MICS, or interventional) provides them with the best short-/long-term outcomes, even at the expense of the use of CPB. The problem is that trials for both MICS and/or MiECC are performed in experienced centers. We believe we have come to a safety level of the dissemination of both techniques in any center. Clinical trials composed of centers without any exclusion would give more reliable and motivating results.

Even in meta-analyses, MICS has found to be equivalent and/or noninferior to conventional techniques; our aim is to use every tool possible to reach significantly better results. We—to some degree—showed significant benefits in this study, but we certainly need new studies with higher patient population.

Minimally invasive surgery with the implementation of novel procedures could prove to be a significant competitor of transcatheter aortic valve implantation (TAVI), particularly in high-risk patients. In a recent multicenter propensity-matched study comparing outcomes of 214 patients matched to either RDV-AVR or TAVI, there was no difference in 30-day or 1-year mortality, stroke, bleeding, or myocardial infarction. However, the RDV-AVR patients had a higher procedural success rate and less incidence of paravalvular leaks at the cost of higher incidence of pacemaker insertion than the TAVI cohort. Conversely, the TAVI cohort had a significantly shorter ICU stay and hospitalization duration and significantly lower peak and mean aortic gradients. The main advantage of RDV-AVR is the resection of the native valve and the annular decalcification that could translate into better hemodynamic profiles and possibly better long-term outcomes, which would be pertinent in younger patients. In low-risk patients, minimally invasive aortic valve replacement results in similar mortality, stroke, reoperation rates for bleeding, and midterm survival (after adjusting for confounders), but shorter hospital length of stay and a trend ($p = .075$) toward shorter ICU stay, than full sternotomy AVR. Therefore, minimally invasive aortic valve replacement should stand as a benchmark against TAVI in these patients (17,18).

MICS continues to evolve and expand with growth in technology and surgeon experience. Now that a significant amount of data has emerged on the safety and efficacy of MICS across a range of surgical operations, there is evidence to support the widespread adaptation of such techniques. In the future, there will likely be a higher request for MICS approaches by patients seeking cardiac surgical options with reduced surgical trauma that allows for a faster return to normal activities and improved quality of life. In addition, MICS itself will continue to evolve in the future through the growing use of percutaneous technology, hybrid operating rooms, and ongoing collaborations with interventional cardiologists. We believe expanding MICS with the implementation of novel extracorporeal techniques and RDV may have enormous potential in competition.

LIMITATIONS

The present study has certain limitations. It is a retrospective analysis of prospectively collected data with a relatively small cohort of patients, and, therefore, conclusions are necessarily limited in their application. Propensity analysis is a powerful statistical technique, but it is

limited by the number and accuracy of the assessed variables.

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