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Full Sternotomy, Hemisternotomy, and Minithoracotomy for Aortic Valve Surgery: Is There a Difference?

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Elisa Mikus, MD, Simone Calvi, MD, Gianluca Campo, MD, Rita Pavasini, MD, Marco Paris, MD, Eliana Raviola, MD, Marco Panzavolta, MD, Alberto Tripodi, MD, Roberto Ferrari, MD, PhD, and Mauro Del Giglio, MD, PhD

Cardiothoracic and Vascular Department, Maria Cecilia Hospital, GVM Care & Research, Cotignola (RA); Cardiovascular Institute, Azienda Ospedaliero-Universitaria di Ferrara, Cona (FE); and Cardiovascular Department, Istituto Clinico San Rocco, Ome (BS), Italy

Background. **This study compared perioperative results and mortality rates of different approaches to perform aortic valve replacement (AVR), describing predictors favoring one approach over the others.**

Methods. **All patients who underwent AVR were enrolled. The choice of the approach was left to surgeon's preference. Data were retrospectively collected, and the major baseline characteristics (including age, sex, body mass index, creatinine clearance, preoperative condition, cardiovascular risk factors, functional status, and left ventricular ejection fraction, etc.) and intraoperative variables were recorded. To adjust for differences in baseline characteristics between the study groups, a propensity score matching was performed. Linear and logistic regression analyses were performed.**

Results. **Partial upper hemisternotomy was performed in 820 patients (43%), right anterior minithoracotomy in 488 (26%), and median sternotomy in 599 (31%). After propensity score matching, three groups of 377 patients were obtained. Cardiopulmonary bypass and cross-clamp times were shorter in the right anterior minithoracotomy group than in the median sternotomy and partial upper hemisternotomy groups ($p < 0.001$). No significant differences in in-hospital mortality were observed ($p = 0.9$). Renal failure (odds ratio, 5.4; 95% confidence interval, 2.3 to 11.4; $p < 0.0001$), extracardiac arteriopathy (odds ratio, 2.9; 95% confidence interval, 1.1 to 6.7; $p = 0.017$), and left ventricular ejection fraction (odds ratio, 0.96; 95% confidence interval, 0.93 to 0.99; $p = 0.009$) emerged as independent predictors of in-hospital mortality.**

Conclusions. **Minimal-access isolated aortic valve surgery is a reproducible, safe, and effective procedure with similar outcomes and operating times compared with conventional sternotomy.**

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In the last decades, the number of patients affected by aortic valve disease (AVD) requiring invasive treatment has greatly increased, mainly because of the aging of the population and the steady spread of new medical technologies [1–3]. Despite the increased use of new percutaneous transcatheter aortic valve implantation techniques, surgical aortic valve replacement (AVR) remains the gold standard for the treatment of AVD and is routinely performed through median sternotomy. With the aim to simplify the AVR procedure and to reduce patients' surgical trauma, alternatives for minimally invasive surgical accesses have been proposed since 1996, when Cosgrove and Sabik [4] reported the first parasternal approach for minimally invasive AVR (MIAVR). Since then, new possible approaches for MIAVR have been described, resulting in the most popular partial upper hemisternotomy (PUH) and right anterior minithoracotomy (RAT) approaches.

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On one hand, several studies clearly showed that MIAVR could be considered an effective alternative to standard full median sternotomy (MS) besides being related to a reduction in postoperative pain, days of hospitalization, ventilation times, occurrence of renal failure, and need for blood transfusion [5–12]. On the

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Address correspondence to Dr Mikus, Cardiothoracic and Vascular Department, Maria Cecilia Hospital, GVM Care & Research, Via Corriera 1, 48010 Cotignola (RA), Italy; email: elisamikus@yahoo.it.

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other hand, data on the clinical benefits comparing different minimally invasive techniques are lacking. Therefore, the aim of this study was to compare perioperative results and mortality rates of different approaches to perform AVR.

Material and Methods

The Comitato Etico Area Vasta Romagna "Comitato Etico IRST IRCCS-AVR" approved the study protocol (No. 1189), and each patient signed an informed consent. All patients who underwent AVR were enrolled. Data were prospectively collected, and the major baseline characteristics (including age, sex, body mass index, creatinine clearance, preoperative condition, cardiovascular risk factors, functional status, and left ventricular ejection fraction, etc) and intraoperative variables were recorded in a database. The study was conducted following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (Supplemental Table 1).

Patient Selection

The study included all 1,907 consecutive patients hospitalized at the Maria Cecilia Hospital (Cotignola, RA, Italy) between January 2010 and March 2017, undergoing isolated AVR, through PUH, RAT, or MS. The choice of the approach was left to surgeon's preference; the only exclusion criterion for RAT was a previous left pneumectomy. Patients who needed an emergency AVR because of endocarditis were excluded if they had a periannular abscess requiring annulus implantation and reconstruction with pericardium.

Surgical Team

The surgical team consisted of 8 cardiac surgeons, of whom only 4 performed RAT, but all of them performed PUH or MS.

Surgical Technique

The intubation during RAT was performed with a double-lumen endotracheal tube. Transesophageal echocardiography was performed in all patients for monitoring heart and valve function during the operation. The MS was performed in a standard fashion. The PUH differed only for a J incision through a 5-cm to 6-cm skin incision at the fourth intercostal space. RAT was performed with a pillow was positioned under the right shoulder. A 4- to 6-cm skin incision at the third right intercostal space was performed, and a soft tissue retractor (CV MICS [Sorin Group, Milan, Italy], the ThruPort Systems [Edwards Lifesciences, Irvine, CA], or the SurgiSleeve [Covidien, Mansfield, MA) was used for spreading the chest wall. Three deep pericardium stay sutures were pulled toward the operator to obtain the best surgical exposure using the Endo Close trocar site closure device (Covidien) outside the chest wall, as previously described [13].

A total central arterial and venous cannulation was preferred for most of the patients. The best location for cannulation and clamp was decided after a tactual assessment of the ascending aorta. Peripheral cannulation during RAT was used in 42 patients to provide a better operating field overview at the beginning of our experience [14].

Prosthetic valves were mainly implanted using 3 running 2-0 polypropylene sutures starting from the annulus below the right coronary ostium and moving to the annulus below the left and the noncoronary sinuses, in a standard fashion independently from the surgical approach.

For pain management, all patients were treated with morphine (0.25 to 0.30 mg/kg intravenous infusion) for 24 hours after the operation and paracetamol (1 g thrice daily).

Outcomes

All patients were prospectively monitored for the occurrence of adverse events during their hospitalization. The primary outcome of the study was in-hospital mortality. Secondary outcomes were postoperative variables, including intubation time, surgical revision caused by postoperative bleeding, the need of red blood cell transfusion, intensive care unit length of stay, pneumonia (diagnosed by roentgenogram/computed tomography scan or positive bacterial culture), hemodialysis, intraoperative or postoperative implantation of an intraaortic balloon or extra corporal membrane oxygenation, pacemaker implantation, sternal dehiscence, and stroke.

Statistical Analysis

Demographics and other baseline characteristics are summarized for the overall population and according to the type of surgical approach. For continuous variables, the Shapiro-Wilk test was performed to investigate the normality of the distribution. Continuous variables with normal distribution are presented as mean and SD and otherwise as median and interquartile range (IQR). Categorical variables are summarized as number and percentages. Renal failure was defined as chronic increased creatinine level exceeding 1.5 mg/dL. Extracardiac arteriopathy was defined as the presence of significant narrowing of arteries most often due to atherosclerosis with a vessel stenosis exceeding 70%, or a history of percutaneous angioplasty or operation for vessel disease.

The exploratory comparison between the three cardiac surgical approaches was done using a χ^2 test or Kruskal-Wallis test, as appropriate. Propensity score matching was performed to account for differences in baseline clinical characteristics between patients treated with the different surgical approaches (MS vs PUH vs RAT). A propensity score was generated for each patient in a standard fashion by performing a logistic regression, with surgical approach as the dependent variable. All baseline clinical variables with p of less than 0.1, which were expected to influence in-hospital mortality, are summarized in Table 1.

To define the pairwise groups, a first propensity score between the two smaller groups was created. The resulting group was used to calculate the third pairwise group with a second propensity score [15]. Matching was

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Table 1. Demographics and Clinical Characteristics by Type of Operation of the Unmatched Cohorts

Variable[a]	Upper Hemisternotomy (n = 820)	Right Minithoracotomy (n = 488)	Full Sternotomy (n = 599)	*p* Value
Age, years	72.9 ± 10.2	71.8 ± 11.9	73.7 ± 9.7	0.084
Age >80 years	26.1	24.6	28.0	0.429
Male sex	54.1	55.9	48.9	0.046
BMI, kg/m^2	27.5 ± 4.2	27.3 ± 4.6	27.0 ± 4.2	0.181
Obesity (BMI >30 kg/m^2)	24.5	24.6	24.7	0.996
BMI ≤24 kg/m^2	19.9	23.8	24.4	0.087
Urgent indication	5.4	3.9	14.4	<0.001
Etiology				<0.001
Stenosis	9.5	10.7	10.0	
Regurgitation	8.3	8.6	9.3	
Mixed	2.0	0.2	7.5	
Other	0.7	0.2	3.5	
Family history	25.7	34.6	23.5	<0.001
Hypertension	72.3	68.6	72.5	0.290
Diabetes mellitus	17.9	19.5	25.0	0.004
Smoker	32.2	33.1	26.7	0.095
COPD	13.2	8.6	11.5	0.043
Renal failure	6.6	4.7	8.8	0.025
Creatinine, mg/dL	1.1 ± 3.0	1.0 ± 0.5	1.2 ± 3.6	0.016
Cerebrovascular accident	4.5	2.7	4.5	0.202
Extracardiac arteriopathy	7.1	6.6	10.0	0.058
Cardiac rhythm				0.033
Paroxysmal AF	3.2	2.9	3.0	
Permanent AF	6.7	2.5	7.0	
NYHA III to IV	40.2	31.6	46.4	<0.001
Ejection fraction	0.597 ± 0.098	0.616 ± 0.097	0.591 ± 0.112	<0.001
Ejection fraction <0.30	1.3	0.8	2.5	0.067
EuroSCORE				
Additive	6.6 ± 2.3	6.1 ± 2.1	7.7 ± 2.7	<0.001
Logistic	8.0 ± 6.9	6.3 ± 4.3	11.4 ± 12.4	<0.001

[a] Continuous data are shown as the mean ± SD and categorical data as the percentage of patients.

AF = atrial fibrillation; BMI = body mass index; COPD = chronic obstructive pulmonary disease; EuroSCORE = European System for Cardiac Operative Risk Evaluation; NYHA = New York Heart Association Functional Classification.

performed by randomly selecting a patient included in one group and looking for the patient included in the other groups with the nearest logit-transformed propensity score, as described elsewhere [16]. The group with the smaller sample size was considered as a control and was compared with the other two treatment groups. For the propensity score calculation, reducing bias, the greedy matching algorithm with MatchIt packages was used [17]. Of note, differences in the adverse events were tested with the logistic regression in the unmatched cohorts and with the χ^2 test in the matched cohorts.

According to the analysis performed, the regression coefficients or the odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each potential predictor. Linear and logistic models were both developed, including surgical procedures, age, and body mass index as the fixed effect. The other independent variables have been selected from the baseline variables collected in the database using a stepwise selection procedure. Statistical tests were based on a two-sided significance level of 0.05. Statistical analyses were performed with R software (The R Foundation for Statistical Computing, Vienna, Austria).

Results

The overall study population included 1,907 patients who underwent AVR for symptomatic severe aortic stenosis. PUH was performed in 820 patients (43%), RAT in 488 (26%), and MS in 599 (31%).

Baseline Characteristics in Unmatched Cohorts

Main data are reported in Table 1. Briefly, patients undergoing MS had more frequently an urgent indication for the operation (14.4%) than patients undergoing PUH (5.4%) and RAT (3.9%; $p < 0.001$). Cardiovascular risk factors, comorbidities, and functional status were not homogeneously represented in the three groups

Table 2. Demographics and Clinical Characteristics by Surgery Type of the Propensity-Matched Cohorts

Variable[a]	Upper Hemisternotomy (n = 377)	Right Minithoracotomy (n = 377)	Full Sternotomy (n = 377)	*p* Value
Age, years	74.1 ± 9.2	74.2 ± 9.9	73.2 ± 9.3	0.108
Age >80 years	27.9	28.9	24.7	0.395
Male sex	49.9	49.1	49.1	0.969
BMI, kg/m^2	27.2 ± 4.1	27.0 ± 4.3	27.2 ± 4.3	0.65
Obesity (BMI >30 kg/m^2)	21	23.9	26.8	0.171
BMI ≤24 kg/m^2	21	25.5	24.4	0.313
Urgent indication	5.8	5	4.5	0.708
Etiology				0.935
Stenosis	82.2	81.7	82	
Regurgitation	6.9	8.5	8	
Mixed	10.6	9.3	9.8	
Other	0.3	0.6	0.3	
Family history	30	28.6	26.8	0.623
Hypertension	72.1	70.8	72.1	0.897
Diabetes mellitus	23.1	21.5	20.7	0.721
Smoker	28.3	31.1	26.8	0.33
COPD	9.5	10.1	9.5	0.961
Renal insufficiency	5.3	5.6	7.4	0.415
Creatinine, mg/dL	1.0 ± 0.5	1.0 ± 0.5	1.0 ± 0.3	0.655
Cerebrovascular accident	3.7	3.2	2.4	0.571
Extracardiac arteriopathy	7.7	8	6.9	0.848
Cardiac rhythm				
Paroxysmal AF	3.7	3.2	3.7	0.995
Permanent AF	2.9	3.2	2.9	
NYHA III to IV	38.7	36.9	39.5	0.744
Ejection fraction	0.607 ± 0.091	0.608 ± 0.098	0.605 ± 0.109	0.752
Ejection fraction <0.30	0.5	0.8	1.9	0.171
EuroSCORE				
Additive	6.6 ± 2.1	6.6 ± 1.8	6.7 ± 1.9	0.973
Logistic	7.9 ± 6.2	6.3 ± 4.3	11.4 ± 12.4	0.671

[a] Continuous data are shown as the mean ± SD and categorical data as the percentage of patients.

AF = atrial fibrillation; BMI = body mass index; COPD = chronic obstructive pulmonary disease; EuroSCORE = European System for Cardiac Operative Risk Evaluation; NYHA = New York Heart Association Functional Classification.

(Table 1). The additive and logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) values were statistically higher in the MS group. Outcomes in the unmatched cohort are summarized in Supplemental Table 2.

Baseline Characteristics in Matched Cohorts

After propensity score matching, we obtained three homogeneous groups (Table 2). Each group consisted of 377 patients with good balance in the main cardiovascular risk factors and comorbidities.

Intraoperative Data in Matched Cohorts

Intraoperative variables differed significantly between groups. Skin-to-skin time was significantly longer in the RAT group (193 ± 54 minutes) compared with the PUH (168 ± 34 minutes, $p = 0.001$) and MS (169 ± 52 minutes; $p = 0.001$) groups (Fig 1). However, cardiopulmonary bypass and cross-clamp times were shorter in the RAT group (cardiopulmonary bypass: 57 ± 20 minutes vs 69 ± 21 minutes in PUH [$p = 0.009$] and 67 ± 28 minutes in MS, $p = 0.01$; cross-clamp: 45 ± 16 minutes vs 58 ± 19 minutes in PUH [$p = 0.01$] and 54 ± 22 minutes in MS, $p = 0.03$; Fig 1). The analysis over time showed that there was a significant reduction of cross-clamping time and of cardiopulmonary bypass time over the years in the RAT group ($p < 0.0001$ for both; Supplemental Table 3).

Outcomes in Matched Cohorts

In-hospital mortality did not differ significantly between the groups ($p = 0.9$), occurring in 1.9% in the RAT, 2.1% in the PUH, and 2.1% in the MS groups. As reported in Table 3, we did not observe any significant difference in secondary outcomes. The only exception was the occurrence of wound infection, which was significantly higher in the MS group ($p = 0.01$; Table 3). The need of surgical revision for bleeding was slightly but not significantly higher in the RAT group ($p = 0.054$), and the analysis over

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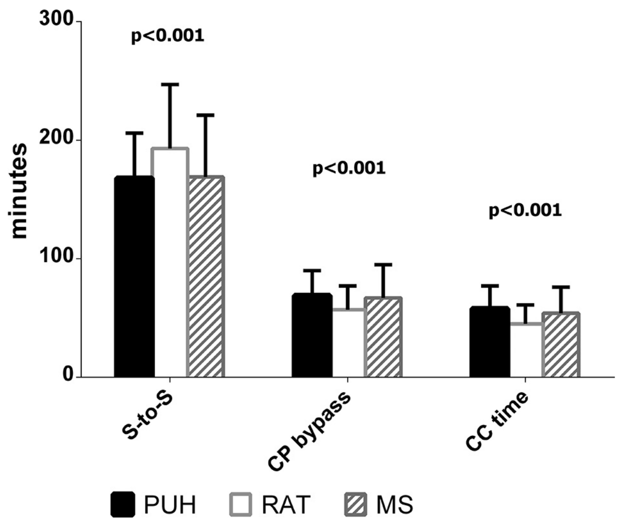

Fig 1. Intraoperative variables in matched cohorts. Data are presented as the mean (height of the bars) and the SD (range bars). (CC = cross-clamp; CP = cardiopulmonary; MS = median sternotomy; PUH = partial upper hemisternotomy; RAT = right anterior minithoracotomy; S-to-S = skin-to-skin.)

time showed a significant reduction of the need of surgical revision for bleeding over the years ($p = 0.018$; Supplemental Table 3, Supplemental Fig 1).

Predictors of In-Hospital Mortality in the Matched Cohort

Overall, only renal failure (OR, 5.4; 95% CI, 2.3 to 11.4; $p < 0.0001$), extracardiac arteriopathy (OR, 2.9; 95% CI, 1.1 to 6.7; $p = 0.017$), and left ventricular ejection fraction (OR, 0.96; 95% CI, 0.93 to 0.99; $p = 0.009$) emerged as independent predictors of in-hospital mortality. Of note, the surgical approach was not related to in-hospital mortality. Similarly, after multivariate analysis for estimating variables influencing ventilation time and intensive care unit stay, the only significant factors were renal failure and urgent operation. The surgical approach seemed to have no influence. No preoperative characteristics were related to the choice of a specific surgical approach.

Comment

Our short-term data suggest that RAT is as safe as MS or PUH. To the best of our knowledge, this is the largest study database to use a propensity score analysis to compare different standardized and reproducible surgical approaches for AVR.

Contrary to previous reports, our data show that RAT required a longer skin-to-skin time but shorter cardiopulmonary bypass and cross-clamp times than MS, suggesting that a careful planning and preparation for the operation significantly reduces the length of the most critical phases of the procedure (Fig 1). Of course, as shown in Supplemental Figure 1, the trend over time of surgical approaches used has changed, mainly with a progressive increase in RAT use and a decrease in MS.

The analysis over time showed that with an increase in the number of RAT procedures performed (Supplemental Fig 2), cardiopulmonary and cross-clamp times significantly decreased, confirming the paramount importance of the learning curve. Thus, we cannot exclude that potential bias related to the experience of the single operator might justify the results, even if all of the team involved in AVR has obtained the same training and no operations have been performed by trainees. At the same

Table 3. Outcome in the Matched Cohorts

Variable[a]	Upper Hemisternotomy (n = 377)	Right Minithoracotomy (n = 377)	Full Sternotomy (n = 377)	p Value
Primary outcome				
In-hospital death	2.1	1.9	2.1	0.957
Secondary outcomes				
Intubation time, minutes	7 (5–10)	7 (5–12)	7 (5–12)	0.469
Surgical revision for bleeding	1.9	4.5	2.1	0.054
Red blood cell transfusion	53	49	51	0.546
ICU length of stay, hours	45 (38–49)	45 (39–64)	45 (38–48)	0.104
Pneumonia	1.3	1.1	0.8	0.777
Hemodialysis	0.5	1.6	1.3	0.364
Wound infection	0.8	0.3	2.4	0.017
Stroke	0.8	1.3	0.8	0.693
Delirium	3.2	0.8	2.1	0.067
Tamponade	2.9	1.9	2.7	0.621
Endocarditis	0.3	0	0.3	0.606
ARDS	0.8	0.3	0	0.173
Postoperative AF	27	33	26	0.081

[a] Categorical data are shown as the percentage of patients and continuous data as the median (interquartile range).

AF = atrial fibrillation; ARDS = acute respiratory distress syndrome; IABP = intraaortic balloon pump; ICU = intensive care unit.

time, this demonstrates that the high standardization of a procedure in expert hands could make RAT as feasible and fast as MS.

Our findings are in agreement with previous studies and meta-analyses that demonstrated similar operative safety and quality of hemisternotomy for AVR compared with full sternotomy [5, 6, 10, 11]. Lamelas and colleagues [18] suggest that elderly patients (aged ≥75 years) receiving MIAVR have a lower morbidity and mortality rate than those receiving MS, suggesting that MIAVR should be considered the first approach for this subset of patients. A more recent study by Nguyen and colleagues [19] showed that MIAVR is associated with a slightly but statistically significant improvement in outcomes compared with MS in patients with preserved left ventricular function (ejection fraction >0.40), where short-term outcomes in patients with an ejection fraction of less than 0.40 were equivalent [19]. Thus, MIAVR is a reasonable and safer modality for this high-risk cohort.

Few data comparing RAT versus PUH are available. Semsroth and colleagues [16] recently published a propensity score analysis of RAT versus PUH versus MS approaches for AVR that included 118 patients per group after matching. The study showed significantly more perioperative complications in the RAT group, mainly because of (1) the need for conversion to MS, which was related with higher mortality and sternal dehiscence; (2) reexploration for bleeding and tamponade, (3) groin complications due to peripheral cannulation; and (4) hemodialysis [16]. However, Miceli and colleagues [20] demonstrated the opposite: outcomes with RAT were better compared with MS in reduction of hospitalization, ventilation time, and occurrence of postoperative atrial fibrillation, with no difference in in-hospital mortality and major postoperative complications, ventilation time, and hospital postoperative length of stay.

Thus, our study confirms that different surgical approaches are not related to in-hospital mortality and, as a consequence, the safety profile of minimally invasive AVR. Interestingly, the need of surgical revision for bleeding was slightly higher in RAT group. Of note, the rate of reoperation for bleeding was high at the beginning of our experience with MIAVR, mainly in relation to bleeding at the thoracic chest wall level and then significantly reduced, probably because of the learning curve of the procedure. Indeed, as indicated in Supplemental Figure 1, the rate of reoperation for bleeding significantly reduced after 2013, settling at approximately 3%, in line with data in the literature [21]. Hence, an accurate closure of the chest wall might explain the reduction in the need for blood transfusion.

In the three surgical approaches, the same surgical technique for extracorporeal circulation, total central cannulation, and cardioplegia was used, with the exception for the double-lumen intubation used for RAT.

Our policy is to follow a standard protocol for the management of patients independently of the surgical technique used; thus, our results are fully comparable. Furthermore, this is probably the reason we did not find (as others did) differences in ventilation times and in intensive care unit and hospital lengths of stay between the groups. Moreover, RAT might be better accepted from a psychologic point of view and also because of the decreased pain in the postsurgical period, providing similar safety and clinical results than full sternotomy [22]. However, a reliable variable does not exist to check postoperative pain independently from anesthetic technologies and individual variability. It is logical to suppose that a correct RAT performed without rib fracture is less painful.

At the state of the art, several studies and a meta-analysis [23, 24] compared invasive with minimally invasive approaches for AVR. The added value of our report is related to the description of a real-life scenario, the enrollment of a large number of consecutive patients, and the comparison among three different approaches showing that RAT had a longer skin-to-skin time but reduced cross-clamp and cardiopulmonary bypass times.

Data obtained by our study confirm the safety of the minimally invasive surgical approaches for AVR in equivalent data on in-hospital mortality, reduced cardiopulmonary bypass and cross-clamp times, and above all, with a lower occurrence of wound infection. Other authors have reported a reduced prevalence of wound dehiscence with minimally invasive approaches [9, 16, 24] but without a statistically significant difference. New studies are needed to confirm this hypothesis, and mainly valuing the risk of wound dehiscence in MIAVR in obese or diabetic high-risk patients.

Moreover, the absence of an association between ventilation time and intensive care unit stay with the type of surgical approach should be a stimulus for the maximum use of both RAT and PUH for AVR, surgical approaches that are even more preferred by patients, resulting in a viable alternative in the age of percutaneous aortic valve implantation. Therefore, considering the absence of statistically significant differences of minimally invasive approaches for AVR versus MS in in-hospital mortality and postoperative complications, MIAVR might represent an alternative for patients needing AVR.

Limitations

This study has several limitations. First, due to the limited variables prospectively collected in the database, we cannot exclude bias or other unknown potential confounding factors.

Second, this was not a randomized controlled trial, and the choice of the surgical approach was not defined on the basis of some specific criteria but was left to surgeon choice.

Third, as shown in Supplemental Figure 1, the use of the three surgical approaches differed over years. These trends in the choice of the surgical approach describe our daily clinical practice.

Fourth, this study represents the experience of 1 surgical center without a formal sample size calculation.

Finally, we have only data regarding in-hospital mortality, which is an important safety measure, but we do not have data regarding long-term follow-up.

Conclusion

Minimal access isolated aortic valve surgery is a reproducible, safe, and effective procedure with similar outcomes and no longer operating times compared with conventional sternotomy.

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