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ORIGINAL ARTICLE

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Full sternotomy and minimal access approaches for surgical aortic valve replacement: a multicentre propensity-matched study

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Key question

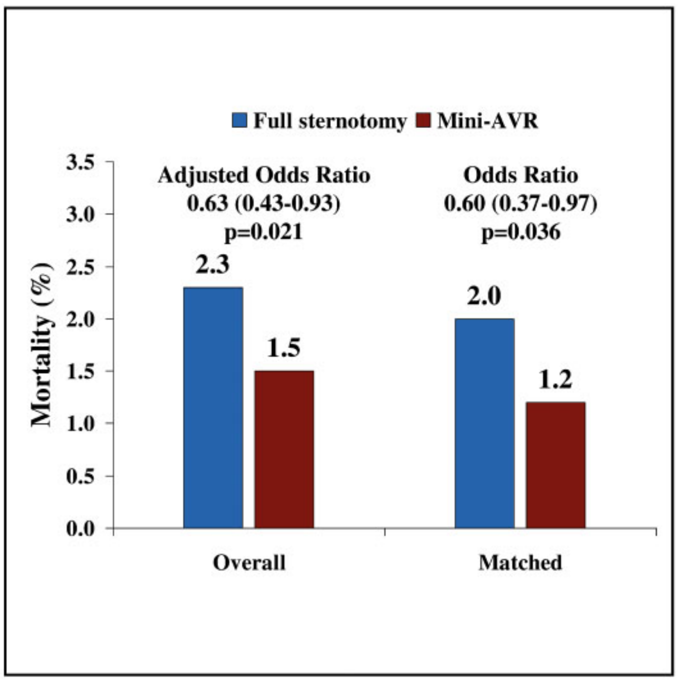
Are early outcomes different in patients undergoing surgical AVR through a full sternotomy and via minimal access approaches (mini-AVR)?

Key finding(s)

The 30-day mortality rate is lower in patients receiving mini-AVR compared to the full sternotomy approach.

Take-home message

Mini-AVR provides a survival advantage compared to the patient's risk profile.



Abstract

OBJECTIVES: Surgical aortic valve replacement (AVR) can be performed via a full sternotomy or a minimal access approach (mini-AVR). Despite long-term experience with the procedure, mini-AVR is not routinely adopted. Our goal was to compare contemporary outcomes of mini-AVR and conventional AVR in a large multi-institutional national cohort.

METHODS: A total of 5801 patients from 10 different centres who had a mini-AVR (2851) or AVR (2950) from 2011 to 2017 were evaluated retrospectively. Standard aortic prostheses were used in all cases. The use of the minimally invasive approach has increased over the

CONVENTIONAL VALVE OPERATIONS

years. The primary outcome is the incidence of 30-day deaths following mini-AVR and AVR. Secondary outcomes are the occurrence of major complications following both procedures. Propensity-matched comparisons were performed based on the multivariable logistic regression model.

RESULTS: In the overall population patients who had AVR had an increased surgical risk based on the EuroSCORE, and the 30-day mortality rate was higher (1.5% and 2.3% in mini-AVR and AVR, respectively; $P = 0.048$). Propensity scores identified 2257 patients per group with similar baseline profiles. In the matched groups, patients who had mini-AVR, despite longer cardiopulmonary bypass (81 ± 32 vs 76 ± 28 min; $P = 0.004$) and cross-clamp (64 ± 24 vs 59 ± 21 min; $P \leq 0.001$) times, had lower 30-day mortality rates (1.2% vs 2.0%; $P = 0.036$), reduced low cardiac output (0.8% vs 1.4%; $P = 0.046$) and reduced postoperative length of stay (9 ± 8 vs 10 ± 7 days; $P = 0.004$). Blood transfusions (36.4% vs 30.8%; $P \leq 0.001$) and atrial fibrillation (26.0% vs 21.5%, $P \leq 0.001$) were higher in patients who had the mini-AVR.

CONCLUSIONS: In a large multi-institutional recent cohort, minimal access approach aortic valve replacement is associated with reduced 30-day mortality rates and shorter postoperative lengths of stay compared to standard sternotomy. A prospective randomized trial is needed to overcome the possible biases of a retrospective study.

Keywords: Aortic valve • Aortic valve replacement • Cardiovascular surgery • Heart valve

ABBREVIATIONS

AUC	Area under the receiver operating characteristic curve
AVR	Aortic valve replacement
CI	Confidence intervals
Mini-AVR	Minimal access approach aortic valve replacement
OR	Odds ratios

INTRODUCTION

Treatment of aortic valve disease is rapidly evolving. Aortic valve replacement (AVR) via a full sternotomy is well tolerated and has demonstrated excellent long-term event-free survival and quality of life even in high-risk elderly patients [1]. At the same time the use of minimally invasive surgical approaches, after decades of scepticism, is increasing in the attempt to further reduce postoperative morbidity and to improve patient satisfaction. However, not all cardiac surgeons offer minimal access approach aortic valve replacement (mini-AVR) because there is uncertainty as to whether it offers advantages over conventional AVR.

In 1993, the first mini-AVR was performed through a right thoracotomy [2]. Subsequently, a variety of incisions, including partial lower and transverse sternotomy as well as a parasternal approach, have been adopted. Nowadays, the right anterior thoracotomy and upper hemisternotomy are the predominant approaches for the mini-AVR [3].

At present, there are no guidelines to either recommend or discourage surgeons from using minimally invasive approaches in aortic valve surgery because of the lack of definitive prospective randomized studies. Knowledge is based on retrospective single-centre studies and small randomized controlled trials. In fact, a recent Cochrane meta-analysis could be performed on only 7 small randomized controlled trials and did not show any outcome differences in patients who had AVR via a full sternotomy or an upper hemisternotomy [4].

In order to contribute to the determination of the best surgical strategy for patients undergoing AVR, the aim of the present study was to review early outcomes in a large multicentre cohort of patients who had aortic valve surgery either with full sternotomy (AVR) or mini-AVR.

MATERIALS AND METHODS

Data from 10 Italian cardiac centres were analysed from January 2011 through December 2017. All patients who received first-time isolated AVR through a standard sternotomy or a minimal access approach (partial hemisternotomy or right anterior mini-thoracotomy) were considered for the analysis.

Clinical and administrative databases are prospectively utilized in all of the centres. All patients signed an informed consent form to allow clinical and administrative data storage and utilization for scientific purposes according to the General Data Protection Regulation (GDPR). Because of the retrospective nature of this study, the local ethics committees waived the need for patient consent.

The primary outcome of the study is the comparison of the incidence of 30-day deaths following AVR and mini-AVR. For discharged patients, the follow-up was performed at internal outpatient clinics or at referral centres. Secondary outcomes included the occurrence of major complications following both procedures: stroke, worsening kidney function, permanent pacemaker insertion, reopening for bleeding, postoperative atrial fibrillation and low cardiac output. All major outcomes were reported according to Valve Academic Research Consortium-2 definitions [5].

The choice of performing a minimal access approach and the type of minimal access approach were based on the preference of the surgeon. The following technique has been described previously [6]. For the ministernotomy approach, a 6- to 7-cm skin incision was performed and the sternum partially opened in a J-shaped fashion, up to the 3rd/4th intercostal space. Arterial and venous cannulations were usually accomplished through the main surgical site (ascending aorta and right atrium with a double-stage cannula). If the right atrium was difficult to expose, then venous drainage was achieved with a percutaneous venous cannula, advanced through the right femoral vein into the right atrium using the Seldinger technique under transoesophageal echocardiographic guidance. The right anterior minithoracotomy was performed through a 5- to 7-cm incision at the 2nd or 3rd intercostal space without rib resection. The ascending aorta or the femoral artery was used for cannulation, depending on the patient's anatomy and the surgeon's preference. Venous drainage was achieved in the fashion described for a ministernotomy. A preoperative computed tomography scan without contrast enhancement was sometime performed to evaluate the anatomical relationship between the intercostal spaces, sternum, ascending aorta and aortic valve. Vacuum-assisted cardiopulmonary bypass was established; a left ventricular vent was placed through the right superior pulmonary vein or the pulmonary artery; and the patient was cooled to 34°C. The ascending aorta was clamped with the external cross-clamp, and anterograde cardioplegic solution was administered into the aortic root or selectively into the coronary ostia using warm blood cardioplegia. In all cases, the surgical field was flooded with carbon dioxide at a flow of 0.5 l/min. Only standard stented aortic valve prostheses were implanted (mechanical prostheses: Carbomedics and Bicarbon families of aortic valves, Carbomedics/LivaNova, London, UK; biological prostheses: porcine Hancock II and Mosaic^{TM}, Medtronic, Minneapolis, MN, USA; pericardial: Carpentier-Edwards, Edwards Lifesciences, Irvine, CA, USA; Mitroflow and Crown PRT LivaNova/Sorin, London, UK); no sutureless or rapid deployment valves have been utilized [6].

Statistical analyses

Data are reported as mean ± standard deviation, median (interquartile range) or percentage for categorical variables. We used the Student's *t*-test to compare continuous variables. Associations between categorical variables were evaluated using the χ^2 test. Because many preoperative variables were different between groups, we evaluated a propensity score matched cohort using an automated procedure to pair patients 1:1 from the 2 surgical approaches. The propensity score was based on the multivariable logistic regression model for mini-AVR surgery including gender, age, arterial hypertension, diabetes mellitus, hypercholesterolaemia, renal dysfunction, respiratory or lung disease, previous disabling stroke, history of cancer, atrial fibrillation, peripheral vascular disease, coronary artery disease, ejection fraction category (31–50% and ≤30% vs >50%) and EuroSCORE. Matching was performed in a 1:1 ratio by selecting from the 2 groups patients of the same gender and age (within ±1 year of difference). All possible pairs were ordered by the absolute difference in propensity score, selecting those with the lowest value within a maximum caliper width of 0.25 of the standard deviation of the linear predictor of the propensity score [7]. For the 579 patients (273 full sternotomy and 306 minimally invasive approach) for whom preoperative risk factors were not available, the matching procedure was based on gender, age and EuroSCORE. The success of matching was evaluated by computing absolute standardized differences in the distribution of patient characteristics in the matched cohort before and after matching. Post-matching standardized differences <10% indicated successful balance. To account for the dependence of the matched pairs, between-group differences after matching were tested with univariate conditional logistic regression models on an indicator variable denoting the surgical approach. A logistic regression model was used to evaluate multivariate predictors of death in the overall population. Odds ratios (OR) with 95% confidence intervals (95% CI) were estimated. Model calibration was verified by the Hosmer–Lemeshow test. A *P*-value <0.05 was considered statistically significant without adjustment for multiple comparisons among secondary outcomes. Discrimination evaluation was based on the area under the receiver operating characteristic curve (AUC). All analyses were conducted using STATA software, version 14 (StataCorp LP, College Station, TX, USA).

RESULTS

During the study period, 5801 patients underwent AVR in 10 hospitals: in 2950 cases a full sternotomy (AVR) was performed whereas in 2851 a mini-AVR was the chosen approach. The use of the mini-AVR has increased over the years; it has become the most practiced approach (Fig. 1A). Patients in the mini-AVR group were older and had higher rates of cardiovascular risk, respiratory dysfunction and history of cancer. Atrial fibrillation was more frequent in the full sternotomy group, which had worse left ventricular function and a slightly higher EuroSCORE (Table 1). By using a matching procedure, 2257 patients per group were paired to select 2 similar subsamples of procedures. The model used to generate the propensity score had good discrimination and calibration for predicting the surgical approach (AUC = 0.629 and Hosmer–Lemeshow test, *P* = 0.337). No differences in demographic and preoperative data were observed between the 2 matched groups (Table 1). Figure 2 shows the absolute standardized differences of preoperative data before and after matching: all differences between the AVR and the mini-AVR were present in the overall population were eliminated in the matched subsample. A total of 111 (1.9%) deaths were observed: 69 (2.3%) in the AVR group and 42 (1.5%) in the mini-AVR (*P* = 0.016) with a temporal trend towards reduction in the number of deaths in the latter group (Fig. 1B). The EuroSCORE discriminated well between patients with and without events (AUC 0.736 and 0.719, respectively, for the additive version and the EuroSCORE II). In comparison to a full sternotomy, a mini-AVR was associated with fewer deaths (OR 0.63, 95% CI 0.43–0.93; *P* = 0.021), adjusting for EuroSCORE II. Similarly, the mini-AVR remained associated with fewer deaths (OR 0.60, 95% CI 0.38–0.93; *P* = 0.023) when we adjusted for preoperative data. In this full model, predictors of death were also age (OR 1.05 per year, 95% CI 1.02–1.08; *P* = 0.002), renal dysfunction (OR 3.49, 95% CI 1.89–6.46; *P* < 0.001), lung disease (OR 4.46, 95% CI 2.88–6.89; *P* < 0.001), ejection fraction ≤30% (OR 1.42, 95% CI 1.62–13.04; *P* = 0.004) whereas arterial hypertension, diabetes mellitus, hypercholesterolaemia, previous disabling stroke, history of cancer, atrial fibrillation, peripheral vascular disease and coronary artery disease did not reach statistical significance. The model had a high level of discrimination (AUC = 0.782) without deviations in calibration (Hosmer–Lemeshow test; *P* = 0.365).

Table 2 shows intraoperative and postoperative data by procedure in the overall population and in the subgroups of subjects paired by propensity score. Patients who had the mini-AVR had longer cardiopulmonary bypass and cross-clamping times, larger valve sizes, shorter postoperative lengths of stay, a less frequent postoperative low cardiac output but higher need of blood transfusions and incidence of postoperative atrial fibrillation (Table 2). These significant differences were observed also in propensity-matched groups that showed fewer deaths with the mini-AVR than with the full sternotomy approach. The mini-AVR group had a lower 30-day mortality rate both in the overall population and in the propensity score matched patients (1.2% vs 2.0%; *P* = 0.036). No difference was detected in worsening renal function, permanent pacemaker insertion, wound infection,

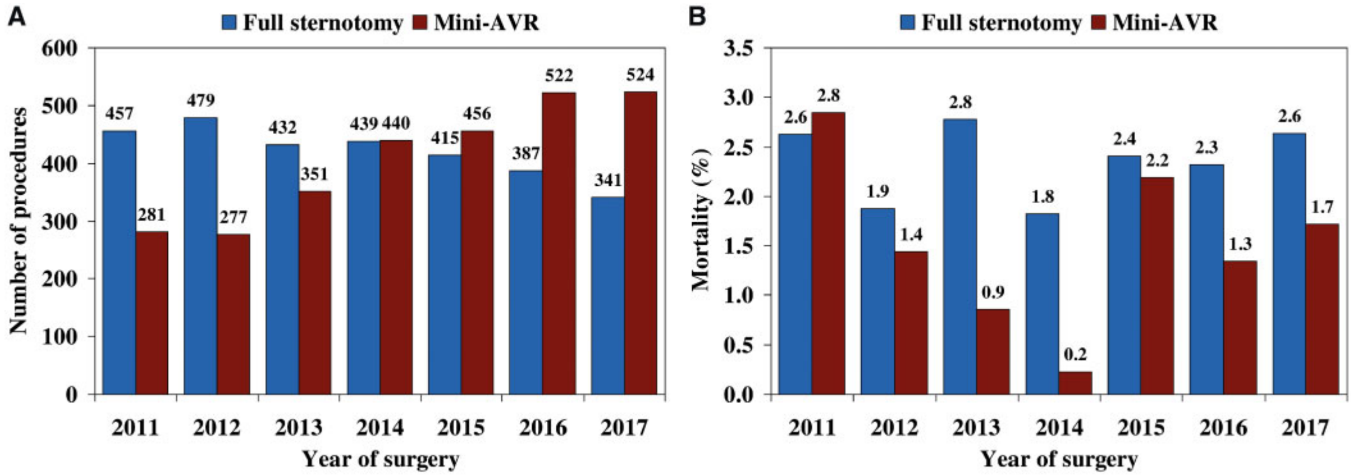


Figure 1: Trends of surgical approaches during the years of the study (**A**); 30-day mortality rate over the years of the study based on the surgical approach (**B**). Mini-AVR: minimal access approach-aortic valve replacement.

Table 1: Characteristics of patients by procedure in the overall population and in the subgroups paired by propensity score

	Overall				Propensity score matching		
	All (n = 5801)	AVR (n = 2950)	Mini-SAVR (n = 2851)	P-value	AVR (n = 2257)	Mini-SAVR (n = 2257)	P-value
Male gender	3072 (53.0)	1570 (53.2)	1502 (52.7)	0.682	1186 (52.5)	1186 (52.5)	
Age (years)	71.9 ± 11.5	71.6 ± 11.7	72.3 ± 11.3	0.026	73 ± 10	73 ± 10	
Body mass index (kg/m^2)	27.5 ± 4.6	27.5 ± 4.5	27.4 ± 4.6	0.732	27.6 ± 4.5	27.4 ± 4.6	0.470
Arterial hypertension	3919 (75.0)	2062 (77.0)	1857 (73.0)	0.001	1529 (75.8)	1558 (77.3)	0.218
Diabetes mellitus	990 (19.0)	470 (17.6)	520 (20.4)	0.008	367 (18.2)	389 (19.3)	0.347
Hypercholesterolaemia	2682 (51.4)	1299 (48.5)	1383 (54.3)	<0.001	1011 (50.1)	1050 (52.1)	0.130
Renal dysfunction	193 (3.7)	101 (3.8)	92 (3.6)	0.762	65 (3.2)	73 (3.6)	0.480
Respiratory or lung disease	1036 (19.8)	458 (17.1)	578 (22.7)	<0.001	377 (18.7)	357 (17.7)	0.368
Previous disabling stroke	99 (1.9)	55 (2.1)	44 (1.7)	0.388	37 (1.8)	39 (1.9)	0.816
History of cancer	345 (6.6)	138 (5.2)	207 (8.1)	<0.001	120 (6.0)	111 (5.5)	0.484
Atrial fibrillation	520 (10.0)	291 (10.9)	229 (9.0)	0.024	209 (10.4)	198 (9.8)	0.544
Peripheral vascular disease	376 (7.2)	187 (7.0)	189 (7.4)	0.538	145 (7.2)	138 (6.8)	0.665
Coronary artery disease	627 (12.0)	252 (9.4)	375 (14.7)	<0.001	217 (10.8)	219 (10.9)	0.907
Ejection fraction (%)				<0.001			0.978
>50	3849 (73.7)	1818 (67.9)	2031 (79.8)		1554 (77.1)	1555 (77.1)	
31–50	1304 (25.0)	807 (30.1)	497 (19.5)		447 (22.2)	445 (22.1)	
≤30	69 (1.3)	52 (1.9)	17 (0.7)		15 (0.7)	16 (0.8)	
EuroSCORE additive (points)	6.3 ± 2.5	6.5 ± 2.6	6.1 ± 2.3	<0.001	6.3 ± 2.3	6.2 ± 2.3	
EuroSCORE II (%)	3.0 ± 5.0	3.1 ± 5.2	2.9 ± 4.7	0.130	2.9 ± 4.7	3.0 ± 4.9	

Data are reported as mean ± standard deviation or n (%). Renal dysfunction: dialysis or creatinine level >2 mg/dl. Body mass index available for 4236 patients and 3276 paired by propensity score. Risk factors from arterial hypertension to ejection fraction available in 5222 patients and 4032 paired by propensity score. The 2257 pairs were selected by the matching procedure on the basis of age, gender and propensity score (2016 pairs with complete preoperative risk factors) or EuroSCORE (241 pairs missing preoperative risk factors).
AVR: aortic valve replacement; mini: minimal access approach; SAVR: surgical aortic valve replacement.

reopening for bleeding, reintubation, confusion/delirium, stroke and intensive care unit length of stay.

Mortality rates by hospitals and surgeons

Figure 3 shows mortality rates within institutions (Fig. 3A and B) and within operators (Fig. 3C and D) by cases volume and by EuroSCORE II predicted risk. For both approaches, the observed mortality rate was lower than that expected with EuroSCORE II. The mortality rates associated with specific providers and surgeons had greater variability with the full sternotomy than with the mini-AVR (Fig. 3A and C); with the mini-AVR, the mortality rate was more homogeneously low for providers and operators (Fig. 3B and D).

Upper hemisternotomy versus a right anterior thoracotomy

The majority of the operations were upper hemisternotomies (1770 vs 1081). Patients in this group were slightly younger with less renal dysfunction but had a higher incidence of preoperative stroke and worse ejection fractions. However, no differences in the EuroSCORE were evident (3.0 ± 5.3 vs 2.9 ± 4.3 with a right minithoracotomy and an upper ministernotomy,

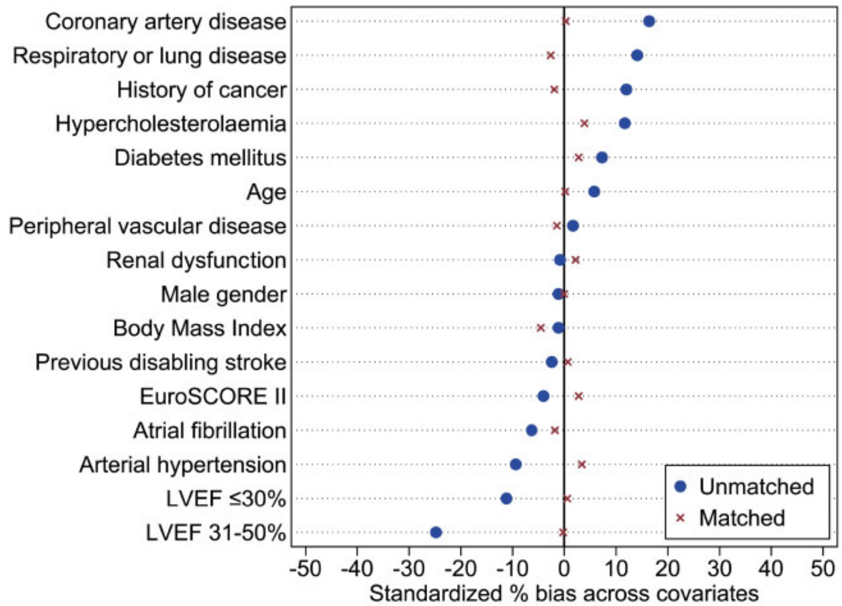


Figure 2: Absolute standardized differences before and after matching. LVEF: left ventricular ejection fraction.

Table 2: Intraoperative and postoperative data by procedure in the overall population and in the subgroups paired by propensity score

	Overall				Propensity score matching		
	All (*n* = 5801)	AVR (*n* = 2950)	Mini-SAVR (*n* = 2851)	*P*-value	AVR (*n* = 2257)	Mini-SAVR (*n* = 2257)	*P*-value
Intraoperative variables							
Cardiopulmonary bypass time (min)	78 ± 32	76 ± 30	81 ± 34	<0.001	76 ± 28	81 ± 32	0.004
Cross-clamp time (min)	61 ± 23	59 ± 22	64 ± 24	<0.001	59 ± 21	64 ± 24	<0.001
Valve size (mm)	22.9 ± 1.9	22.8 ± 1.9	23.0 ± 1.8	<0.001	22.7 ± 1.9	23.0 ± 1.8	<0.001
Postoperative variables							
Blood transfusions	1796 (33.6)	875 (31.4)	921 (35.9)	<0.001	656 (31.0)	742 (36.4)	<0.001
Renal function worsening	354 (6.6)	179 (6.4)	175 (6.8)	0.561	125 (5.9)	141 (6.9)	0.090
Atrial fibrillation	1334 (23.0)	610 (20.7)	724 (25.4)	<0.001	486 (21.6)	589 (26.1)	<0.001
Permanent pacemaker insertion	156 (2.7)	75 (2.5)	81 (2.8)	0.487	53 (2.4)	62 (2.7)	0.393
Wound infection	58 (1.0)	34 (1.2)	24 (0.8)	0.233	25 (1.1)	18 (0.8)	0.288
Reopening for bleeding/complications	159 (2.9)	79 (2.8)	80 (2.9)	0.739	60 (2.8)	52 (2.4)	0.288
Reintubation	93 (1.7)	48 (1.7)	45 (1.8)	0.932	41 (1.9)	31 (1.5)	0.319
Confusion/delirium	96 (1.8)	55 (2.0)	41 (1.6)	0.299	40 (1.9)	32 (1.6)	0.542
Non-disabling stroke	21 (0.4)	14 (0.5)	7 (0.3)	0.179	12 (0.6)	6 (0.3)	0.232
Disabling stroke	17 (0.3)	9 (0.3)	8 (0.3)	0.941	6 (0.3)	7 (0.3)	0.763
Low cardiac output	72 (1.3)	49 (1.8)	23 (0.9)	0.006	30 (1.4)	16 (0.8)	0.046
30-Day deaths	111 (1.9)	69 (2.3)	42 (1.5)	0.016	46 (2.0)	28 (1.2)	0.036
ICU length of stay (days)	1.8 (1.0–2.0)	1.7 (0.9–2.0)	1.9 (1.2–2.0)	0.326	1.7 (0.9–2.0)	1.9 (1.5–2.0)	0.071
Postoperative days	9 ± 7	10 ± 7	9 ± 7	0.030	10 ± 7	9 ± 8	0.004

Data are reported as mean ± standard deviation, median (interquartile range) or *n* (%). Low cardiac output: intra-aortic balloon pump and/or inotropic use for more than 2 days. Postoperative data were available, respectively, in the overall population and in those matched by propensity; in 5345 and 4152 for blood transfusions; in 5348 and 4153 for renal function worsening; in 5797 and 4510 for atrial fibrillation or permanent pacemaker insertion; in 5799 and 4512 for wound infection; in 5574 and 4330 for reopening for bleeding/complications; in 5347 and 4153 for reintubation or confusion/delirium or stroke; in 5349 and 4155 for low cardiac output.

AVR: aortic valve replacement; ICU: intensive care unit; mini: minimal access approach; SAVR: surgical aortic valve replacement.

respectively; $P = 0.396$). An upper hemisternotomy required longer cross-clamp times (75 ± 33 vs 84 ± 34 min; $P < 0.001$) and cardiopulmonary bypass times (59 ± 26 vs 66 ± 23 min, $P < 0.001$) as well as a need for more blood transfusions [274 (29.1%) vs 647 (40.0%); $P < 0.001$] compared to a right anterior thoracotomy. No other significant differences in clinical outcomes were observed.

Reopening for bleeding and blood transfusions

We analysed the trends of reopening for bleeding and blood transfusions during the study period in the overall population. In the patients who had the AVR during the years 2011–2014, reopening for bleeding occurred in 2.8% of the patients; in the years 2015–2017, in 2.7% (0.95, 0.60–1.52; $P = 0.841$). In the

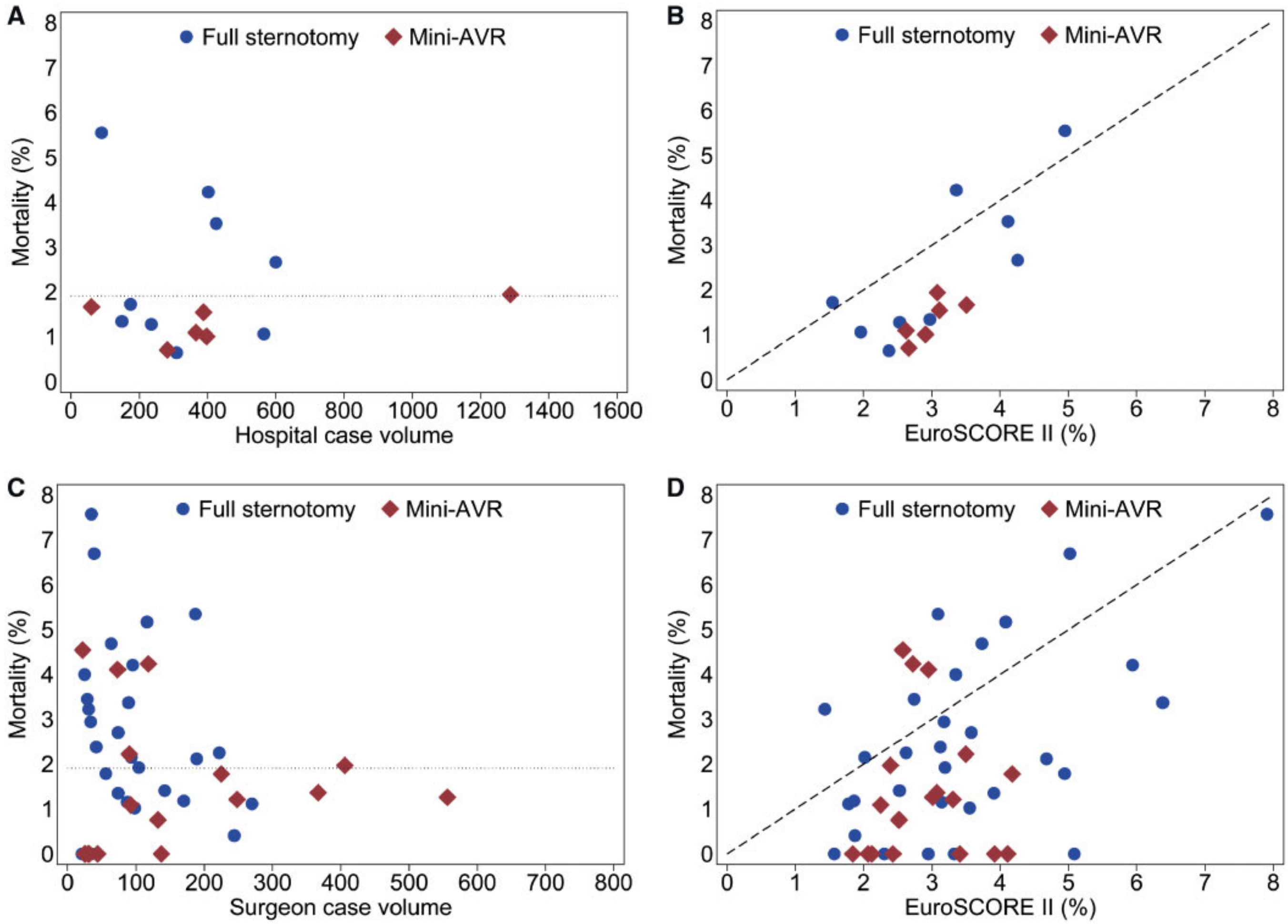


Figure 3: Hospital mortality rates within institutions by case volume and by EuroSCORE II predicted risk (**A** and **B**, respectively) for cardiac surgery centres with more than 50 procedures per approach. Mortality rates for surgeons with more than 20 cases per approach by case volume and by EuroSCORE II predicted risk (**C** and **D**, respectively). The dotted lines in (**A**) and (**C**) refer to the overall mortality rate. Mini-AVR: minimal access approach-aortic valve replacement.

patients who had the mini-AVR, reopening for bleeding occurred in 3.9% in the period 2011–2014 and in 2.0% in the period 2015–2017 (0.52, 0.33–0.82; $P = 0.005$). Similarly, in patients who had the AVR in the years 2011–2014, blood transfusions were necessary in 31.4% of the patients whereas in the years 2015–2017, they were necessary in 31.5% (1.0, 0.85–1.18; $P = 0.98$). In the mini-AVR group, blood transfusions were administered in 39.6% in the period 2011–2014 and in 32.0% in the period 2015–2017 (0.71, 0.61–0.84; $P = 0.001$).

DISCUSSION

The treatment of aortic valve disease is changing. Since the introduction of transcatheter aortic valve implantation, high- and intermediate-risk patients with aortic stenosis have been increasingly treated with this technique. A recent comparison of surgical treatment with the transcatheter approach in low-risk patients [8] suggests that more patients with aortic stenosis receive a transcatheter valve implant than a surgical replacement. It is therefore of paramount importance to define the best strategy to offer patients undergoing surgical treatment. After decades of scepticism, surgeons are becoming more familiar with the minimal access approaches. Studies have shown that results obtained by reducing surgical exposure and trauma are at least equal to those obtained with a full sternotomy [9].

We investigated a large multicentre cohort of patients who had surgical AVR relatively recently. The minimal access approach was associated with a significant reduction of the 30-day mortality rate. This result was evident after adjustment for the EuroSCORE II, after adjustment for preoperative risk factors and also in propensity score matched groups. This finding is important for several reasons: First, it was obtained recently in a large multicentre cohort. Second, most of the centres and surgeons involved used both operative techniques. Finally, the overall mortality rate was low (1.9%), not only in the patients who had the mini-AVR (1.5%) but also in the AVR group (2.3%), lower than the rate expected from the EuroSCORE II. The observed/expected mortality ratio based on EuroSCORE II was 0.74 in patients who had AVR and 0.52 in those who had the mini-AVR. This finding is in line with the observed/expected mortality ratio after transcatheter aortic valve implantation [10], suggesting that future comparisons between these techniques should be performed with the minimal access approach in the surgical arm [6].

So far only 1 single-centre retrospective study demonstrated a survival advantage of mini-AVR over standard sternotomy. Merk *et al.* [11], analysing 477 propensity-matched patients in each group, showed that the mini-AVR was associated with a lower incidence of intra-aortic balloon pump usage and of in-hospital deaths. Moreover, in the other retrospective study and meta-analyses, mini-AVR was never associated with an increased number of deaths; in fact, it was often associated with decreased morbidity rates. Ghanta *et al.* [12] reported on 1341 patients operated on in 17 hospitals; of the 289 propensity-matched patients who had conventional or mini-AVR, those who had mini-AVR needed fewer blood transfusions, had less time on the ventilator and faster discharge; the operative mortality rate was also lower (0.3% vs 2.1%) although not significantly so due to the small sample size. Similarly, Bowdish *et al.* [13] reported their single-centre experience comparing a right anterior thoracotomy with a conventional sternotomy showing advantages in terms of less blood product usage, lower wound infection rates and decreased hospital stay.

The reason behind the reduced mortality rate observed in our mini-AVR patients is difficult to determine because the causes of death are unfortunately not reported in the database. It is interesting to note, however, that patients who had the mini-AVR had a significantly lower incidence of low cardiac output syndrome. Interestingly, this finding was also reported in the large meta-analysis by Shehada *et al.* [9] and in the Leipzig experience [11].

We previously demonstrated that minimal access heart valve surgery, including mini-AVR, is associated with a reduced inflammatory reaction and coagulopathy [14]: IL-6, C-reactive protein, prothrombin factor 1.2 and cardiac troponin I levels were lower than in patients who had a full sternotomy. This result is another possible factor supporting the improved clinical outcomes observed in the patients who had the mini-AVR.

Contrary to expectations driven by previous studies, we observed an increased risk of reopening for bleeding and blood transfusions in the mini-AVR group. Minimizing the opening of the sternum and reducing surgical trauma should decrease blood oozing and the risk of coagulopathy. However, we have noted a significant impact of the study period on reopening for bleeding and blood transfusions, indicating a possible learning-curve effect on this important clinical outcome.

In this study, valve replacements were all performed with standard mechanical or biological prostheses. Sutureless and rapid deployment aortic bioprostheses are producing promising clinical and haemodynamic results by reducing cross-clamp and cardiopulmonary bypass times [15, 16]. It is possible to hypothesize further improvement in the clinical outcome by using these prostheses with the minimally invasive approach. Both upper hemisternotomy and right anterior thoracotomy have been widely used in our population having minimally invasive procedures; no differences in outcomes were apparent between these techniques, although no meaningful adjustments were used. In a previous well-balanced report from our group, no differences in outcomes could be observed between these minimal access approaches [17].

Limitations

Our study has some important limitations. First, the retrospective design contains the bias of the choice of a treatment based on the patient's clinical state and the physician's preference. This preference, however, has been predominantly driven by the learning curve: At the beginning of each surgeon's experience, there is a natural and understandable reluctance to treat all cases using a minimal access approach. Second, follow-up information is unavailable at this time. Third, the choice of the minimal access approach (ministernotomy or right minithoracotomy) was biased by the surgeons' preferences and might be associated with different perfusion strategies.

CONCLUSION

In conclusion, in a large retrospective multicentre evaluation of patients who underwent AVR between 2011 and 2017, mini-AVR was associated with a significantly lower 30-day mortality rate compared to the full sternotomy approach. The observed/expected mortality ratio based on the EuroSCORE II demonstrated a survival advantage compared to the patient's risk profile. Patients who had mini-AVR experienced higher rates of postoperative atrial fibrillation and blood transfusions, particularly in the initial observation period. To overcome the possible biases of patients' and surgeons' selection of our retrospective study, a large multicentre prospective randomized trial should be performed by experienced surgeons to support our results conclusively; however, such a trial will be difficult to perform and there are enough data in the literature to state that mini-AVR techniques are potential tools to improve patient care.

Conflict of interest: none declared.

Author contributions

Domenico Paparella: Conceptualization; Data curation; Investigation; Methodology; Validation; Writing - Original Draft. **Pietro Giorgio Malvindi:** Conceptualization; Data curation; Investigation; Validation; Writing - Review & Editing. **Giuseppe Santarpino:** Investigation; Supervision; Validation; Visualization. **Marco Moscarelli:** Conceptualization; Investigation; Methodology. **Piero Guida:** Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Writing - Original Draft. **Khalil Fattouch:** Conceptualization; Supervision; Validation; Visualization. **Vito Margari:** Conceptualization; Data curation; Writing - Review & Editing. **Luigi Martinelli:** Conceptualization; Supervision; Validation. **Alberto Albertini:** Investigation; Supervision. **Giuseppe Speziale:** Conceptualization; Supervision; Validation.

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