ORIGINAL ARTICLE

More for less — long-term survival modeling for surgical aortic valve replacement follow-up: The division between a ministernotomy and a full sternotomy approach

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ABSTRACT

Background: This study aimed to assess long-term results after surgical AVR (sAVR) depending on the used surgical technique (ministernotomy vs. full sternotomy) and to determine which patient- and treatment-related attributes were most associated with shorter time to the main endpoint.

Methods: Out of 2147 patients, who underwent sAVR from January 2006 to December 2017, 615 patients were treated minimally invasively (MIAVR) and 1532 patients received conventional full sternotomy aortic valve replacement (FSAVR). Multiple Cox regressive models corresponding to the four major endpoints were developed. Long-term survival and a time to re-hospitalization for acute coronary syndrome, stroke, and heart failure (HF) were analyzed independently. Kaplan-Meier actuarial analysis was performed for univariate comparison.

Results: The median follow-up time was 71.9 months. No significant difference in terms of long-term survival was found between MIAVR and FSAVR (hazard ratio [HR], 0.99; $P = 0.91$). Novel advantages of MIAVR in preventing re-hospitalization for late cerebrovascular events and the progression of HF were observed (HR, 0.53; $P = 0.03$; HR, 0.64, $P = 0.005$; respectively). Importantly, for the late mortality risk, early in-hospital complications dominated. However, the baseline atrial fibrillation (AF), diabetes, pulmonary disease, and impaired mobility showed the strongest patient-specific prediction for the other three long-run models.

Conclusions: MIAVR through ministernotomy provides at least as good long-term survival as FSAVR. Nevertheless, it should be recommended for diabetic, poor-mobility patients with pre-existing AF to reduce their high cerebrovascular risk and to limit the progression of HF. MIAVR also needs to be considered in patients with chronic lung diseases to improve their extremely poor survival prognosis.

Key words: minimally invasive aortic valve replacement, ministernotomy, mini-invasive cardiac surgery, long-term outcomes, independent predictors

INTRODUCTION

Surgical aortic valve replacement (sAVR) remains the first-line intervention for the management of severe aortic valve pathologies in the Western world, and it has been well documented to provide acceptable short- and long-term outcomes [1, 2]. For the majority of symptomatic and asymptomatic patients with indications for aortic valve intervention, who are younger than 75 years and at low risk of surgery, sAVR represents a class I recommendation with a level of evidence B (the European Society of Cardiology/European Association for Cardio-Thoracic Surgery [ESC/EACTS]), exceptionally with a level A according to the American Heart Association/American College of Cardiology (AHA/ACC) guidelines for patients younger than 80 years with acceptable

WHAT'S NEW?

The key message of this study is minimal invasiveness and its favorable clinical aspects with regard to long-term outcomes following surgical treatment of aortic valve diseases. This study evaluated long-term outcomes after surgical aortic valve replacement (sAVR) depending on the techniques used (ministernotomy vs. full sternotomy). The authors found that ministernotomy positively affects the cerebrovascular risk profile and the progression of heart failure, reducing time to re-hospitalization for such diagnoses. In addition, the reliability of the data and the study methodology allow the identification of the strongest predictors of poor long-term prognosis, providing a reliable source of information for comparison with other non-surgical treatment methods.

life expectancy [3, 4]. From its inception, full sternotomy (FSAVR) has been routinely considered as a reference approach. However, since the introduction of minimally invasive aortic valve replacement (MIAVR) by Cosgrove [5], a large variety of less invasive surgical techniques have been increasingly developed, with ministernotomy being most commonly performed.

Although MIAVR ensures that 30-day mortality and morbidity are comparable with FSAVR [6, 7], its impact on long-term results has not yet been definitively determined. In addition, the ever-changing risk profiles of patients eligible for sAVR, combined with globally evolving trends aiming to minimize any procedural invasiveness and with the wide implementation of TAVI procedures, could have a modulating effect on the reception of methodological advancements. From this perspective, well-grounded outcomes may have changed over the past two decades. Hence, there is a need to fill in the existing evidence gaps and to re-evaluate long-term results following sAVR.

This analysis aims to evaluate long-term outcomes after sAVR depending on the used surgical technique and to determine which patient- and treatment-related attributes are most associated with shorter time to the main endpoint.

METHODS

This observational research was approved by our institutional review board and complies with the International Committee of Medical Journal Editors' recommendations for reporting about patients.

Inclusion and exclusion criteria

Consecutively collected data of patients who underwent isolated sAVR at our institution from January 2006 to December 2017 were analyzed. Patients who required simultaneous treatment of another heart valve, coronary artery disease, or ascending aortic aneurysm were not included in the study. Previous cardiac surgery, salvage procedure, and active endocarditis were also considered as exclusion criteria. Finally, 2147 patients were included in the analysis, in whom either of the two surgical approaches was applied: 615 patients underwent minimally invasive through J-shaped ministernotomy (MIAVR) and 1532 a conventional full sternotomy (FSAVR).

Surgical techniques

FSAVR

Transesophageal echocardiography (TEE) was routinely applied before the procedure to confirm indications and to set the operative strategy. The sternum was cut midline from the sternoclavicular junction to the xiphoid appendage. Total pericardiotomy was made and extracorporeal circulation (ECC) was set up centrally. A venting line was inserted through the right superior pulmonary vein. Moderate hypothermia (32°C) was used. Repeated, cold, bloody cardioplegia was administered antegradely to the aortic bulb or directly to the coronary ostia in the presence of significant aortic insufficiency. Additional retrograde perfusion *via* the coronary sinus has been utilized in 68% of cases. A new prosthesis was implanted in a continuous manner using 2.0 monofilament sutures. After weaning cardiopulmonary by-pass (CPB), ventricular pacing wires and chest drains were placed. TEE examination was used to evaluate procedural results.

MIAVR

All procedural aspects were similar to the conventional method, but some significant modifications need mentioning. External defibrillating pads were always applied before the procedure. After a 5–7 cm skin incision, the upper J-shaped hemi-sternotomy from the sternoclavicular junction to the level of third or fourth intercostal space was performed with right internal mammary artery (RIMA) preservation. Partial upper pericardiotomy was done and direct central cannulation was performed for ECC. A venting line was inserted into the pulmonary trunk. Only antegrade administration of the cardioplegic solution was utilized. Safe placement of epicardium pacing wires needed the heart to stay unfilled. It was done before aortic de-clamping. Continuous insufflation of carbon dioxide and TEE guidance facilitated the air removal process. Before weaning CPB, a flexible mediastinal Blake's drain was inserted into the pericardium through previously tunneled retrosternal space.

Predictor variable selection

For the study, three types of covariates were specified. All data were retrieved from the institutional archive elec-

Table 1. Preoperative factors considered predictors for Cox proportional hazards models with the split between MIAVR and FSAVR (n = 1696)

Patient-related variables — PR-VARS			
	MIAVR	FSAVR	*P*-value
Female sex, n (%)	239 (51.4)	486 (39.5)	<0.001
Urgent procedure, n (%)	226 (48.6)	503 (40.9)	0.004
Obesity, n (%)	196 (42.2)	499 (40.5)	0.58
Diabetes mellitus, n (%)	151 (32.5)	380 (30.9)	0.56
COPD, n (%)	102 (21.9)	257 (20.9)	0.64
CKD, n (%)	69 (14.8)	228 (18.5)	0.08
Coronary artery disease, n (%)	129 (27.7)	426 (34.6)	0.01
History of myocardial infarction, n (%)	29 (6.2)	144 (11.7)	0.001
Previous PCI, n (%)	40 (8.6)	156 (12.7)	0.02
Atrial fibrillation, n (%)	101 (21.7)	254 (20.6)	0.64
Carotid artery stenosis >70%, n (%)	76 (16.3)	219 (17.8)	0.52
PAOD, n (%)	68 (14.6)	191 (15.5)	0.65
Stroke within 6 months, n (%)	23 (4.9)	67 (5.4)	0.72
Impaired mobility, n (%)	136 (29.2)	213 (17.3)	<0.001
Age, years, mean (SD)	64.3 (13.9)	63.2 (12.9)	0.12
LVEDD, mm, mean (SD)	50.7 (7.8)	52.6 (9.0)	0.001
LVEF, %, mean (SD)	53.3 (8.2)	50.9 (10.7)	0.001
NYHA classification, median (IQR)	2 (2–3)	2 (2–3)	0.41
EuroSCORE scale, median (IQR)	5 (4–7)	6 (3–7)	0.39
Aortic valve defect (stenosis, combined), n (%)	423 (91.0)	1053 (85.5)	0.003
LVEF ≤35%, n (%)	20 (4.3)	134 (10.9)	<0.001
LVEDD ≥60 mm, n (%)	76 (16.3)	243 (19.7)	0.09

Abbreviations: CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; FSAVR, full sternotomy aortic valve replacement; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MIAVR, minimally invasive aortic valve replacement; NYHA, New York Heart Association; PAOD, peripheral arterial occlusive disease; PCI, percutaneous coronary intervention

tronic database. No missing values were observed (Tables 1 and 2):

- P-R VARS — included the patient demographics and comorbidity characteristics;
- T-R VARS — consisted of intraoperative measures and in-hospital outcomes;
- S-I VAR — surgical technique indicator = MINI: (MIAVR=1; FSAVR=0).

Long-term outcome variable specification

Prime endpoints were particularized by four major late adverse events, the occurrence of which was prospectively monitored. The death records were obtained from the Civil Status Death Registry supported by the Mortality Rate Index of the National Health Fund, covering 100% of sAVR population with attainable information (n = 2147). Supplementary medical data, cataloged in an encoded form according to the ICD-10 nomenclature, was formally made available by the Silesian Department of National Health Fund and is exclusively applicable only to residents of the Silesian Region, who comprised 79% of sAVR patients (475 MIAVR and 1221 FSAVR). The main endpoints represented quantitative "time-to-event" data. Notably, the death event was used to censor the cases in models 2–4, thus ensuring further correct calculation of the median follow-up time.

- Late survival — an event defined by all-cause death;
- Myocardium — an event detailed by hospitalization for troponin (+) acute coronary syndromes;
- Stroke — an event specified by hospitalization for ischemic or hemorrhagic stroke;
- Failure — an event denoted by hospitalization for the symptoms of heart failure (HF).

Statistical analysis

Univariate comparison and multivariable survival data modeling were applied to assess long-term outcomes after sAVR. The model-building process occurred in two blocks. In the first, a forward stepwise method was employed to identify the best-fitted predictors from the set of P-R VARS and T-R VARS. Next, S-I VAR was entered in the second block to guarantee that it would be in the final model. All main interaction terms were checked for significance. The omnibus tests were used to select the variables at every step. The χ^2 change was the difference between the –2 log-likelihood of the adjacent models. If the significance of the difference was less than 0.05, the variable was added to the model. The variable was excluded if the significance of the difference was greater than 0.1. Finally, the most appropriate Cox regressive (CPH) models were synthesized for each event. All independent covariates passed the testing for proportional hazard assumption. The log-likelihood score, Concordance index, and Log-likelihood ratio test were conducted to measure goodness of fit. The effects of the individual regression coefficients were presented as hazard ratios (HR) with their 95% confidence intervals (CI) and plotted at baseline mean survival function of all fitted predictors. For univariate analysis, the Kaplan-Meier

Table 2. Early in-hospital outcomes and intra-operative measures considered predictors for *Cox* proportional hazards models with the split between MIAVR and full sternotomy aortic valve replacement (FSAVR) (n = 1696)

Treatment-related variables — TR-VARS			
Postoperative	**MIAVR**	**FSAVR**	***P*-value**
Re-exploration for bleeding, n (%)	22 (4.7)	69 (5.6)	0.55
Re-exploration for tamponade, n (%)	13 (2.8)	39 (3.2)	0.76
Cardiac complications, n (%)	8 (1.7)	44 (3.6)	0.06
LOS, n (%)	20 (4.3)	122 (9.9)	0.001
IABP, n (%)	5 (1.1)	26 (2.1)	0.22
Inotropic support, n (%)	71 (15.3)	227 (18.4)	0.13
Postoperative atrial fibrillation, n (%)	133 (28.6)	314 (25.5)	0.22
PPI, n (%)	9 (1.9)	45 (3.7)	0.09
Neurological complications, n (%)	47 (10.1)	163 (13.2)	0.08
Postoperative stroke, n (%)	8 (1.7)	27 (2.2)	0.57
Psychotic disorders, n (%)	38 (8.2)	129 (10.5)	0.07
Postoperative renal injury, n (%)	30 (6.5)	114 (9.3)	0.08
Hemodiafiltration, n (%)	10 (2.2)	35 (2.8)	0.5
Hemothorax, n (%)	27 (5.8)	57 (4.6)	0.38
Pneumothorax, n (%)	9 (1.9)	14 (1.1)	0.24
SWI, n (%)	4 (0.9)	48 (3.9)	0.001
PWI, n (%)	2 (0.5)	6 (0.5)	1.0
PCS, n (%)	17 (3.7)	47 (3.8)	0.89
RBC, median (IQR)	2 (0–3)	0 (0–2)	0.001
ICU ≥100 hours, n (%)	24 (5.2)	103 (8.4)	<0.001
Mechanical ventilation ≥24 hours, n (%)	13 (2.8)	88 (7.1)	0.04
24h blood loss ≥1000 ml, n (%)	27 (5.8)	110 (8.9)	0.03
Hospital stay ≥14 days, n (%)	28 (6.0)	72 (5.8)	0.91
Intraoperative			
Prosthesis size, mm, median (IQR)	23 (23–25)	23 (23–25)	0.84
Bioprosthesis, n (%)	303 (65.2)	698 (56.7)	0.002
Bicuspid valve, n (%)	119 (25.6)	175 (14.2)	<0.001
Rheumatic pathology, n (%)	80 (17.2)	293 (23.8)	0.004
Degenerative pathology, n (%)	249 (53.5)	613 (49.8)	0.17
MINI, n (%)	465 (27.4)	1231 (72.6)	
CPB time ≥120 min, n (%)	101 (21.7)	189 (15.4)	0.002
Aortic cross-clamp time ≥90 min, n (%)	58 (12.5)	118 (9.6)	0.09

Abbreviations: CPB, cardiopulmonary by-pass; IABP, intra-aortic balloon pump; ICU, intensive care unit; MINI, ministernotomy approach; LOS, low cardiac output syndrome; PPI, permanent pacemaker implantation due to total A-V block; PCS, post-pericardiotomy syndrome; PWI, profound wound infection; RI, renal injury (creatinine >200 µmol/l); RBC, red blood cells units transfused; SWI, superficial wound infection

estimation was done with the log-rank test, log(-log) transformation at a fixed point in time test, and restricted mean survival time (RMST) function.

Categorical variables were expressed as numbers (percent) and compared with Pearson's χ^2 test. Continuous variables were expressed as means (standard deviation [SD]), when non-parametric as medians (interquartile range [IQR]) and compared with the t-test or the Mann-Whitney U test, as appropriate. Two-sided *P*-values were used at a significance cut-off of 0.05. All statistical analyses were done in Python version 3.8.3 using Lifelines Application release 0.25.1.

RESULTS

The median follow-up times were: 71.9 (41.3–102.9) months for the 'LS' model, 58.9 (31.1–90.4) months for the 'M' model, 59 (31.4–90.6) months for the 'S' model, and 61.3 (32.0–93.3) months for the 'F' model.

Univariate

Overall comparison between MIAVR and FSAVR revealed no statistical differences in terms of long-term survival and the time to myocardial infarction (Figure 1). Late stroke-free survival was significantly higher in the MIAVR group ($P = 0.03$) (Figure 2A, B). When compared to MIAVR, FSAVR had a shorter time to re-hospitalization for HF ($P = 0.06$) (Figure 2C, D).

Multivariable

Ministernotomy was not a risk factor in the 'LS' and 'M' models (Table 3). However, the 'S' model showed that ministernotomy independently prevented the occurrence of late stroke, giving a 34% risk reduction compared to full sternotomy. In addition, the 'F' model demonstrated that ministernotomy slowed down the progression of HF. MIAVR patients had a 39% lower risk of re-admission (Table 4).

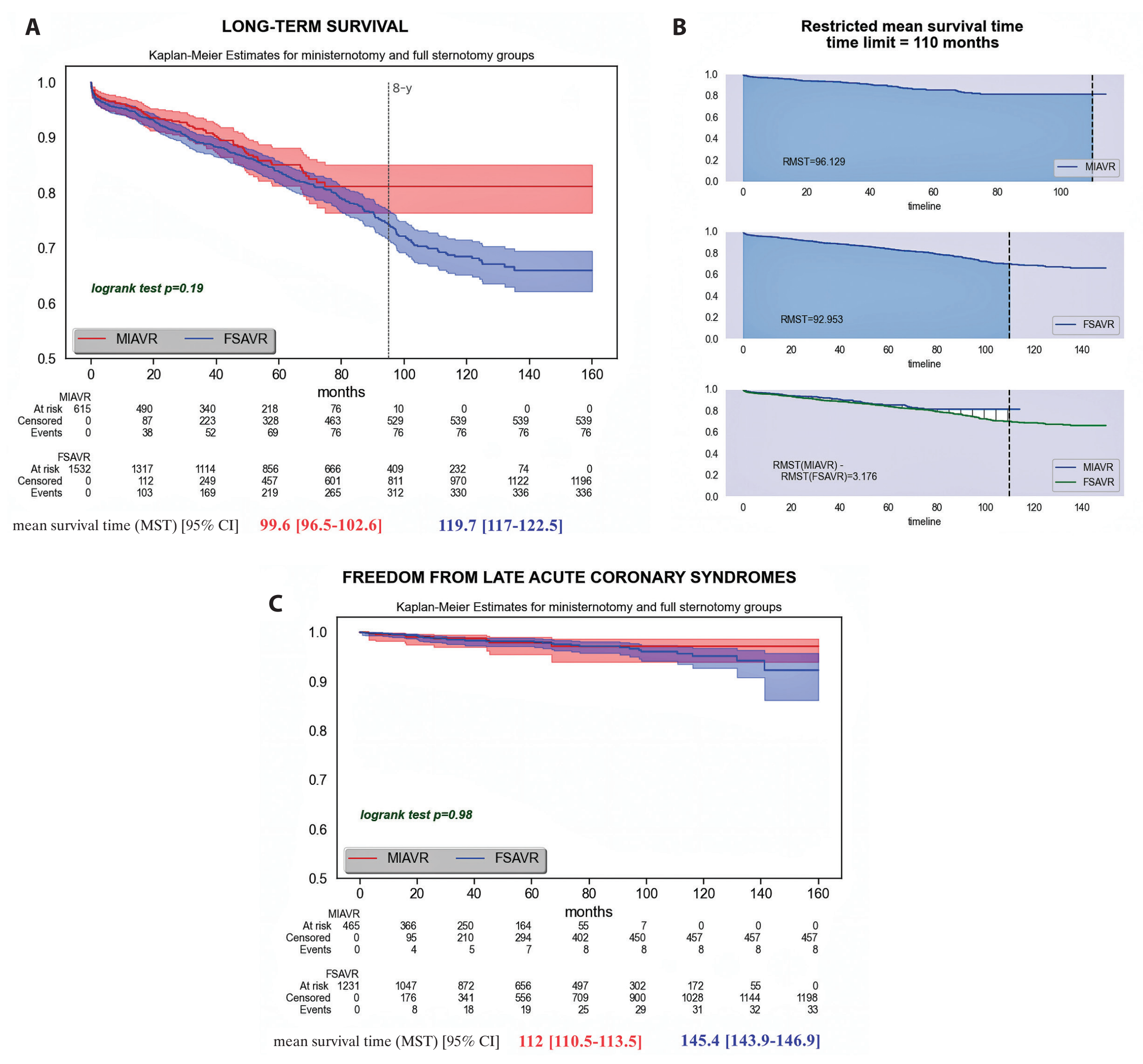

Figure 1. Univariate comparison between "MINI" groups — models: 'LS' and 'M'. **A.** Long-term survival. Kaplan-Meier survival curves (solid lines) with their 95% CI (shaded areas). The vertical grey dashed line indicates the point (8-y) when the difference becomes significant ($P = 0.002$); **B.** Restricted mean survival time test shows a 3.2-month loss for full sternotomy aortic valve replacement (FSAVR); **C.** Incidence of late myocardial infarction

The strongest predictors of shorter survival after surgical AVR included postoperative HDF, early cardiac complications, and prolonged mechanical ventilation beyond 24 hours. Baseline pulmonary disease and peripheral arterial occlusive disease prevailed as the most dramatic patient-specific risk factors.

When analyzing the effect of factors on other major long-term outcomes after sAVR, preoperative atrial fibrillation, type 2 diabetes mellitus, history of myocardial infarction, left ventricular ejection fraction (LVEF) less than 35%, and impaired mobility had the worst predictive value (Tables 3 and 4, Figure 3).

DISCUSSION

The current 'LSMSF' analysis introduces an innovative "modus operandi" for the assessment of late outcomes after sAVR. The outstanding feature of this study is provision of credible, updated estimates for further comparative analyzes and its focus on factors that (negatively or positively) impact the end long-term treatment effects in a statistically significant fashion.

Long-term mortality risk

The "LS" model disclosed that ministernotomy is not a risk factor for long-term survival. This estimation dramatically contradicts the findings of other researchers who claimed that ministernotomy correlated with a 2.5-fold higher hazard of shorter survival [8]. Conversely, there is no sufficient evidence to consider specific properties of MIAVR in prolonging survival after surgery, which has also been reported [9]. Analogously to several well-documented studies [10–12], our analysis confirms MIAVR to be a safe

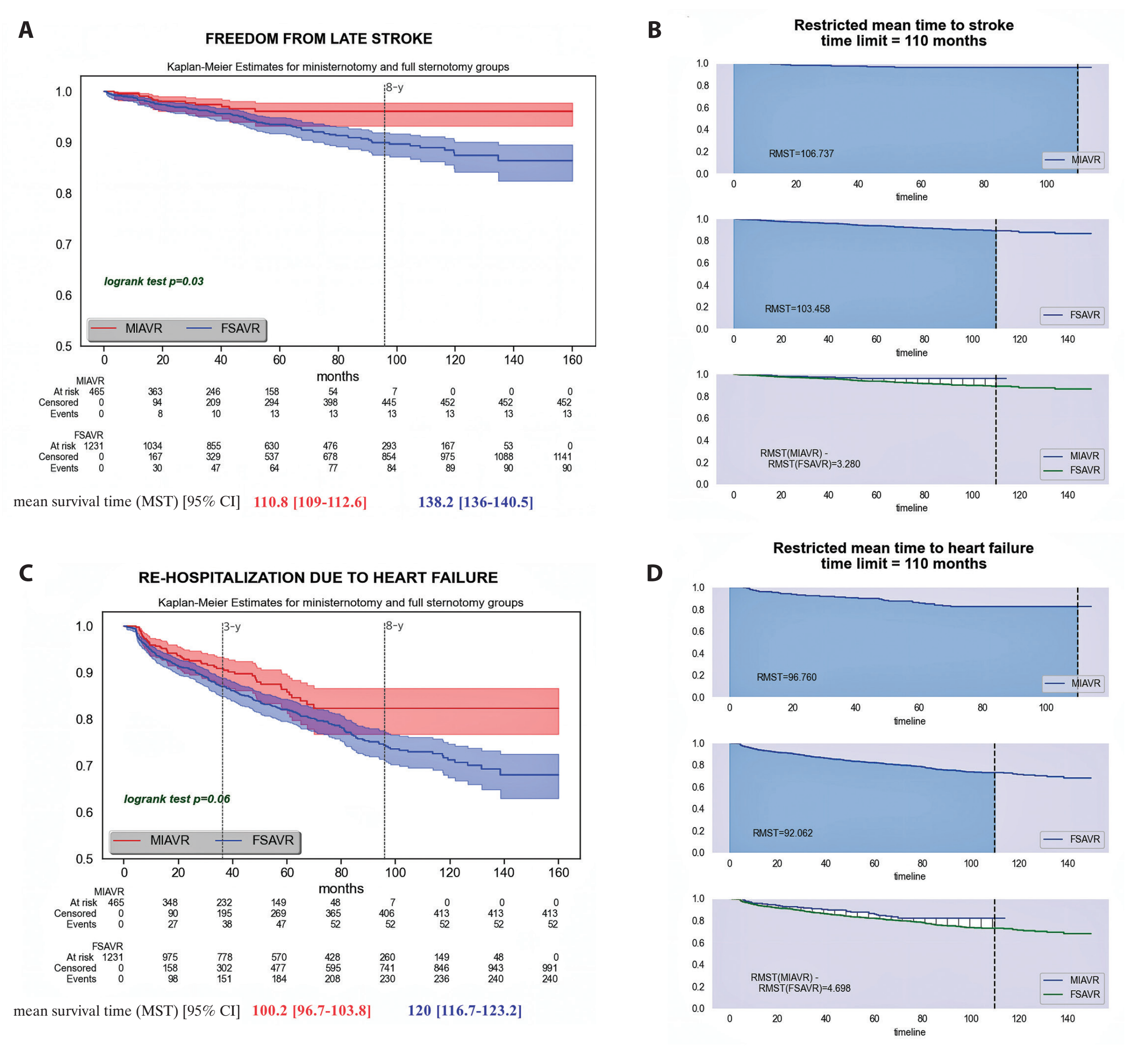

Figure 2. Univariate comparison between "MINI" groups — models: 'S' and 'F'. **A.** The occurrence of late stroke. Kaplan-Meier survival curves (solid lines) with their 95% CI (shaded areas). The vertical grey dashed line indicates the point (8-y) when the difference becomes significant ($P = 0.002$); **B.** Restricted mean survival time test shows a 3.3-month loss in stroke-free survival for full sternotomy aortic valve replacement (FSAVR); **C.** Freedom from re-hospitalization due to the progression of heart failure. Vertical grey dashed lines indicate the points (3-y, 8-y) when the difference becomes significant ($P = 0.05$, $P = 0.01$, respectively); **D.** Restricted mean survival time test shows a 4.7-month loss in time to re-admission for FSAVR

method and essentially validates this less invasive approach for universal consideration in every patient eligible for aortic valve surgery.

It must be emphasized, first and foremost, that T-R VARS showed a very poor prognosis of survival after sAVR (Table 3A), unlike chronic kidney disease, dialysis, reduced LVEF <30%, and history of myocardial infarction (MI) reported by other investigators [13]. It is worthwhile noting that these comorbidities were also proven to be hazardous in our sAVR population. However, when applied to the model with intra- and postoperative measures simultaneously, their significance was lost.

Secondly, the size of implanted aortic valve prosthesis had a significant impact on life expectancy, while the type of prosthesis did not. The hazard for patients with aortic ring equal to 29 mm was 0.7 times the baseline risk, which corresponded to a 41% risk reduction in relation to the subjects sized 19 mm (Figure 3B).

Although many attempts have been initiated to define a prosthesis-patient size mismatch (PPM) and to determine the threshold for its clinically relevant form, the conclusions varied among studies, sometimes quite substantially. Blackstone et al. [14] showed that an indexed effective orifice area (iEOA) reduced to 1.1 cm^2/m^2 did not decrease intermediate- nor long-term survival of 1109 patients with aortic valve sizes ≤19 mm (mean follow-up, 5.3 years). On the contrary, recently published meta-analyses have revealed that moderate PPM (iEOA <0.85 cm^2/m^2) was associated with increased long-term all-cause mortality in younger patients, females, and patients with LV dysfunction, but

Table 3. Multivariate Cox analysis of long-term outcomes after surgical aortic valve replacement — 'LS' and 'M'. **A.** Long-term survival; **B.** Development of late acute coronary syndromes

Independent predictive factors for late mortality and long-term cardiovascular risk

A. Model LS
Event: 412 Censored: 1735 Total: 2147

Predictor	HR exp(β)	*P*-value	95% CI	
			Low	Up
Age	1.02	0.003	1.01	1.03
Female	0.66	<0.001	0.52	0.85
NYHA	1.35	0.002	1.17	1.56
PD	1.37	0.01	1.09	1.71
PAOD	1.31	0.03	1.02	1.68
ES	1.1	0.004	1.03	1.17
Cardiac complications	2.18	<0.001	1.46	3.25
Neurological complications	1.41	0.01	1.1	1.8
Hemodiafiltration	3.47	<0.001	2.2	5.47
Renal injury	1.6	0.002	1.15	2.21
PCS	0.52	0.03	0.29	0.93
Prosthesis size	0.93	0.02	0.88	1.28
Inotropic support	1.38	0.01	1.08	1.75
Mechanical ventilation ≥24 hours	2.68	<0.001	1.96	3.66
MINI	0.99	0.91	0.76	1.28

p-LL = –2754.5; Concordance 0.73
LL-ratio test = 370.7 on 15 df

B. Model M
Event: 41 Censored: 1655 Total: 1696

Predictor	HR exp(β)	*P*-value	95% CI	
			Low	Up
History of MI	2.74	0.01	1.34	5.61
LVEF ≥35%	2.05	0.07	0.93	4.52
Diabetes mellitus	2.12	0.02	1.13	3.99
CPB time ≥120 min	2.3	0.01	1.19	4.47
MINI	0.99	0.98	0.44	2.21

p-LL = –264.5; Concordance 0.68
LL-ratio test: 24.6 on 5 df

Abbreviations: CI, confidence interval; CPB, cardio-pulmonary by-pass; ES, EuroSCORE scale; HR, hazard ratio; MI, myocardial infarction; MINI, ministernotomy approach; NYHA, New York Heart Association classification; LL, log-likelihood; LVEF, left ventricular ejection fraction; PAOD, peripheral arterial occlusive disease; PCS, post-pericardiotomy syndrome; PD, pulmonary disease

Table 4. Multivariate Cox analysis of long-term outcomes after surgical aortic valve replacement — 'S' and 'F'. **A.** Late occurrence of stroke; **B.** Re-hospitalization for the progression of heart failure

Independent predictors for long-term cerebrovascular risk and development of late heart failure

A. Model S
Event: 103 Censored: 1593 Total: 1696

Predictor	HR exp(β)	*P*-value	95% CI	
			Low	Up
Atrial fibrillation	1.67	0.02	1.08	2.57
Diabetes mellitus	1.53	0.04	1.02	2.28
Psychotic disorders	2.06	0.001	1.26	3.36
MINI	0.53	0.03	0.29	0.95

p-LL = –697.6; Concordance 0.63
LL-ratio test = 23.7 on 4 df

B. Model F
Event: 292 Censored: 1404 Total: 1696

Predictor	HR exp(β)	*P*-value	95% CI	
			Low	Up
NYHA	1.36	<0.001	1.15	1.61
Atrial fibrillation	1.83	<0.001	1.41	2.36
PD	1.36	0.02	1.05	1.76
Diabetes mellitus	1.42	0.001	1.12	1.81
Impaired mobility	1.58	0.002	1.21	2.05
Aortic valve defect (S, C)	1.57	0.03	1.04	2.38
LVEDD ≥60 mm	1.44	0.02	1.07	1.94
Inotropic support	1.43	0.01	1.08	1.91
PPI	0.24	0.01	0.08	0.76
Pneumothorax	2.2	0.03	1.07	4.53
Hospital stay ≥14 days	1.55	0.03	1.04	2.33
MINI	0.64	0.005	0.47	0.87

p-LL = –1950.5; Concordance 0.69
LL-ratio test: 137.0 on 12 df

Abbreviations: see Table 3

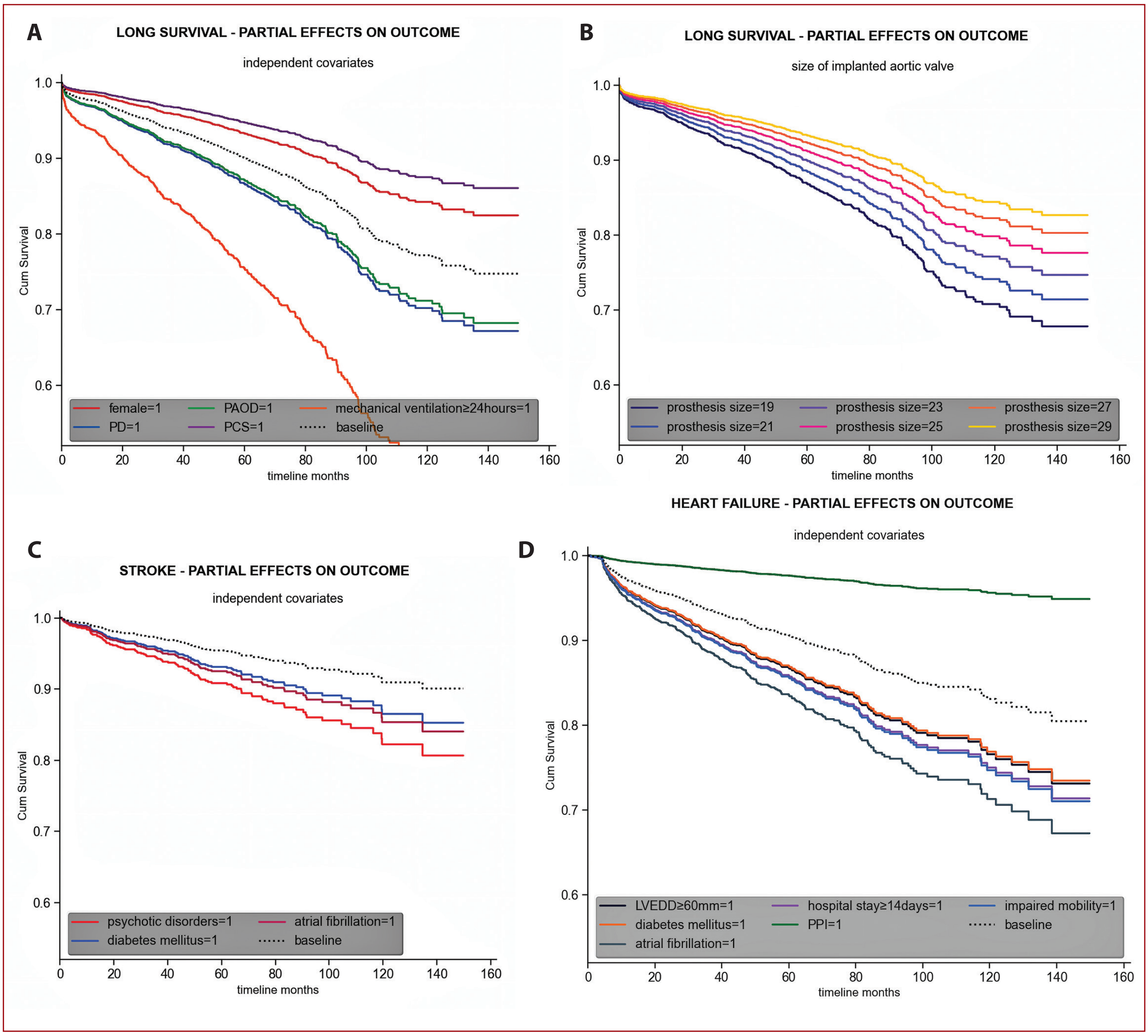

Figure 3. Partial effects of various independent predictors on main long-term outcomes plotted at the baseline risk. **A.** Long-term survival; **B.** Effect of aortic prosthesis diameter on late mortality; **C.** Late stroke-free survival; **D.** Progression of heart failure

Abbreviations: see Table 1

severe PPM (iEOA <0.65 cm^2/m^2) was a significant predictor in all populations undergoing sAVR and TAVI procedures [15, 16]. Similarly, this study postulates the hemodynamics of aortic prosthesis to pose the principal risk since it was observed that a significant number of deaths occurred in the presence of one specific kind of implanted prosthesis, correlated with a relatively smaller iEOA and a higher transvalvular gradient than other valves labeled at the same size.

Notwithstanding, peripheral arterial occlusive disease (PAOD) was singled out as one of the worst prognostic factors limiting the length of life. The latest report describing the final 5-year outcomes in the PARTNER-1 trial has shown that PAOD impaired survival in the TAVI group, favoring a surgical method instead [17]. Surprisingly, chronic pulmonary disease is more important to aortic valve surgery than PAOD. Similar results have been presented in a recent 5-year follow-up analysis of patients with Eurolog ≥15% which showed that chronic obstructive pulmonary disease was an independent strong factor increasing the hazard of death more than twice (HR, 2.1) [18]. Herein, we share the opinion of Cleveland Clinic clinicians that respiratory impairment measured as diminished forced expiratory volume in one second (FEV_1), especially below 50% of the norm, drastically reduces long-term survival and accelerates the progression of HF in patients who underwent sAVR. In such patients, a ministernotomy approach is suggested; with more preserved respiratory function, an improved long-term prognosis can be expected [19]. Although there have been reports on significant deterioration of respiratory function (FEV_1) 7 days after surgery in the minimally invasive group (–34% vs. –17%; $P = 0.003$), despite the randomized design of the study, the small size of the included groups and their considerable heterogeneity do not allow reliable conclusions to be drawn [20].

Unpredictably, patients who were correctly diagnosed and properly treated for moderate to severe post-pericardiotomy syndrome (PCS) during initial hospitalization experienced a protective effect against premature death, with a 34% risk decrease in contrast to other patients. Admittedly, this finding contradicts new research However, in our sAVR population, a noticeable 30-day prevalence of PCS was observed relatively rarely and was at 3.7%, unlike the reported 11.2% [21]. Above all, the 'LS' model captures the unrecognized latent or subacute chronic forms of this pathological immune response to surgery that appear symptomatic within several weeks after discharge and may limit long-term survival to a greater extent than clinically apparent acute characteristics.

Long-term coronary risk

Since the prevalence of acute coronary syndromes has been reported to be low at around 1% after 18 months [22], it has similarly reached approximately 2% after 63 months in our analysis, which somewhat restricts the predictive performance of the 'M' model. Nevertheless, for a coronary risk profile, the patient-specific factors dominate, where the critically determinable comorbidities are previous MI and LVEF ≤35%. Despite the fact, that prolonged CPB time >120 minutes tops a large negative score, the surgical approach seems not to be predictive (Table 3B). However, such a noticeable drawback emphasizes the rationale behind referring the sclerotic octogenarians with LVEF ≤35% and a history of MI for minimally invasive surgery, especially when a longer CPB time would be expected.

Long-term cerebrovascular risk

Ministernotomy has proven to be a meaningful protective factor against a late occurrence of stroke, as evidenced by its positive contribution to the 'S' model (Table 4A). Beyond some reports showing beneficial 1-month neurological outcomes in MIAVR patients [6, 12], a huge gap in evidence on distant results still exists. Surgical AVR seems to outperform transcatheter aortic valve implantation (TAVI) in stroke prevalence at a 16.5-month follow-up with the rate of 2.83% vs. 3.45% [22]. This finding, however, was contested in a recent meta-analysis involving 16544 patients that showed the pooled estimates for stroke to be comparable over a one-year period (4.6% vs. 5.0%, respectively) [23]. A multicenter review by Foroutan et al. [24] has demonstrated that a 10-year cardiovascular (CV) risk reached almost 3%, irrespective of the surgical approach. Incidentally, this value appears to have been underestimated, as the reliable CV risk in the present analysis was 6% after 5 years. Importantly, the 'LSMSF' study explicitly demonstrates a 47% lower CV risk for MIAVR. Our experience has suggested excluding the diversity of prosthesis types and new postoperative atrial fibrillation (AF) from known causes. Conversely, non-surgical AF was rather predominant in predicting stroke, as expected. A plausible supposition remains that less surgical invasiveness, reduced activation of the kinin pathway products following less pain, retained respiratory function, and favorable management of blood products may jointly reduce a surgery-specific inflammatory response. If combined with faster postoperative mobilization and recovery, MIAVR could optimize the patient's thromboembolic profile, thus preventing further major CV events.

Development of heart failure

Not only has MIAVR been applied to a larger number of diabetic patients with impaired mobility, but it also tends to restrain the progression of HF independently, given a lower 39% risk of re-admission for such a diagnosis. This encouraging finding suggests the importance of faster mobilization and recovery in a better circulatory condition than suspected, but multifactorial causality precludes a full clarification.

It is important to note that the New York Heart Association (NYHA) functional class and preexisting AF appear as the most powerful predictors of HF, as shown in the Cox multivariate study by Ruel et al. [25], which reported the hazard ratio of HF for sAVR patients to be 3.74 and 1.74 in the presence of chronic AF and LV dysfunction. In our analysis, LV enlargement >60 mm, rather than LVEF ≤30%, seems to be a more serious risk factor for HF prediction (Table 4B).

Finally, the development of conduction abnormalities should be thoroughly discussed because they are inseparable from any invasive procedure performed on the aortic valve. Among TAVI devices, the 30-day incidence of complete atrioventricular block (CAVB) depended on the deployment mechanisms, such as the balloon-expandable (6%–10%) and self-expanding valves (17%–30%) [26]. Our experience shows a 3.2% prevalence of CAVB for sAVR. The latest Bayesian meta-analysis of 16432 patients, who have undergone sAVR or TAVI, has highlighted the superiority of sAVR over the transcatheter method by showing a 67% reduction in permanent pacemaker implantation [27]. Notably, the multidimensional pathophysiology of new-onset bradyarrhythmias imbues them with a dynamic nature, enabling a smooth transition from the initial latent forms, through left bundle branch block (LBBB)-induced LV dyssynchrony, to the symptomatic higher degree conductive disturbances that can occur after hospital discharge. In the light of the current literature, the 'LSMSF' analysis uncovers an additional benefit for the permanent cardiac pacing specific to sAVR. A recently published study by Mehaffey et al. [28] have revealed a significant independent correlation of the necessity for long pacing with increased 7.5-year mortality and morbidity. In our follow-up, patients requiring a stimulator device to be inserted because of postoperative CAVB had a much lower 19% risk of recurrent HF. Therefore, it becomes a paramount issue to identify those sAVR recipients likely to develop late total heart blocks, in particular presenting with a baseline right bundle branch block (RBBB), RBBB, pre-existing left anterior hemiblock, and a new-onset LBBB, to facilitate individual decision-making and the optimal timing of pacemaker implantation.

Limitations

Due to the retrospective nature, the current research has inherent constraints. Based on a regional approximation, in addition to survival analysis, the study includes non-fatal adverse events affecting residents of the Silesian Voivodeship, which may restrict its general relevance for the entire Polish population. Despite the many patient- and treatment-specific factors that were used for survival model syntheses, this analysis may have been unable to account for the influence of residual unmeasured and unknown confounders that could impact the time to the primary event. Although the newly acquired logistic ES II is a more efficient scoring system than the ES I, it could not be applied to each sAVR participant. The present study has also lacked the assessment of other patient outcomes including quality-of-life scores and the time to return to daily life activities. Late valve-specific adverse events have not been analyzed either but will be the subject of our further exploration.

CONCLUSIONS

The presented 'LSMSF' study provides reliable evidence of the safety of MIAVR in terms of late mortality risk and reveals further meaningful advantages of ministernotomy in preventing stroke and HF during long-term follow-up. Consequently, MIAVR should be recommended for diabetic, poor-mobility patients with pre-existing AF to reduce their high cerebrovascular risk and to limit the progression of HF requiring re-hospitalization. MIAVR also needs to be considered in patients with chronic lung diseases to improve their extremely poor survival prognosis.

Since early postoperative complications lead to catastrophic predictions in our survival analysis, tailoring of invasive strategy to the patient risk characteristics and close post-surgery monitoring for late-onset adverse events are pivotal in ameliorating surgical AVR outcomes.

Article information

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