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Predictive factors of short-term mortality after surgical aortic valve replacement: a 10-year tertiary care hospital experience

Czynniki predykcyjne krótkoterminowej śmiertelności po chirurgicznej wymianie zastawki aortalnej — 10 lat obserwacji w szpitalu uniwersyteckim

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Abstract

Introduction. Aortic valve replacement (AVR) is a standard surgical procedure for symptomatic severe aortic stenosis (AS). This study aimed to identify predictors of short-term mortality after AVR. The pre-surgical risk stratification in patients with symptomatic severe AS may help decide on the most adequate treatment.

Material and methods. A retrospective, observational study included 1171 patients who underwent surgical AVR in a large tertiary medical centre over 10 years (2009–2019). The early mortality defined as the mortality within one month after surgery was analysed.

Results. The mean age of the study group was 64 (± 10) years. The most common aetiology of the aortic valve disease was a degenerative process (78.9%). The postoperative complication rate was 19.1% and the short-term mortality rate was 3.4%. An increased risk of short-term mortality after AVR was related to type 2 diabetes (6.1% vs. 2.6%; $p = 0.006$), chronic kidney disease (stage 3 to 5; 25% vs. 2.8%; $p < 0.001$), history of percutaneous coronary intervention (PCI) (8.2% vs. 3.1%; $p = 0.045$), active infective endocarditis (20.5% vs. 2.9%; $p = 0.007$), significant mitral (24% vs. 2.6%; $p < 0.001$) and tricuspid regurgitation (25.7% vs. 2.9%; $p = 0.001$), periprocedural complications (15.4% vs. 0.5%; $p < 0.001$), and emergency AVR (11.3% vs. 2.7%; $p = 0.001$). The independent predictors of short-term mortality identified by multivariate analysis were active infective endocarditis (odds ratio [OR]: 4.99; $p = 0.045$), duration of the surgical procedure (OR: 1.00; $p = 0.018$) and New York Heart Association (NYHA) class III–IV (OR: 1.97; $p = 0.01$).

Conclusions. Active infective endocarditis, duration of the surgical procedure and NYHA class III-IV are the independent predictors of short-term mortality after AVR and should be considered in deciding on the most adequate treatment.

Keywords: aortic valve replacement, aortic valve stenosis, risk factors, short-term mortality, surgery

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Introduction

Aortic valve stenosis (AS), the most common acquired valvular heart disease is an emerging health problem in the ageing population of the western world [1]. About 7% of the population aged 65 and older suffer from degenerative AS [2]. Intervention is recommended for symptomatic severe, high-gradient AS (recommendation class I B) [3, 4]. Without the operation, the prognosis remains dismal, with a 50% mortality rate at 2 years [2]. After surgery, patients with severe AS show improvement in cardiovascular symptoms and survival [3, 5].

According to the guidelines, symptomatic severe AS is a class I indication for aortic valve replacement (AVR) [6]. However, approximately one-third of patients with valvular heart disease above the age of 75 are not referred for surgery [2]. Typically, it is related to a surgical risk in the elderly who demonstrate various comorbidities, are frail and suffer from severe left ventricular dysfunction [2]. At present, such patients are offered lower-risk intervention options, i.e., transcatheter aortic valve implantation (TAVI) [2, 7]. Moreover, new approaches for AVR are being implemented, employing conventional mechanical or biological prostheses as well as sutureless valves [4].

The risk of operative mortality and morbidity related to AVR is currently well-established based on patient demographic and clinical variables. Validated systems for assessing the risk of in-hospital mortality after major cardiac surgery such as EuroSCORE II (The European System for Cardiac Operative Risk Evaluation II) [8] and Society of Thoracic Surgeons (STS) [9] are available. Predictors of early post-AVR complications should also be considered in deciding on the type of operation. Several factors related to the patient's overall health status, type of surgical procedure and periprocedural complications have been identified as predictors of short-term mortality [3, 5, 10, 11].

This study aimed to identify predictors of short-term mortality after AVR defined as all-cause mortality within 30 days after surgery.

Materials and methods

A retrospective, observational study was performed that included preoperative data and follow-up data concerning 1171 patients who underwent surgical AVR at the Tertiary University Hospital from January 2009 to December 2019. Data were collected from the Outpatient Cardiology and Cardiac Surgery Clinics Database. Investigated were demographic parameters, medical history, chronic and peri-procedural medical treatment, echocardiography parameters, procedural data, and outcome measures.

Statistical analysis

Quantitative variables were characterized with basic descriptive statistics: means and standard deviations. The normality of the distributions was verified with the Shapiro-Wilk's test for normality. Discrete variables (nominal, ordinal, dichotomous) were characterized by giving the number of observations for each category and percentage. The chi-square test was used to compare patient groups for dichotomous (survival/death) and nominal variables. Multivariate analysis for selected variables was performed using logistic regression models. Results were considered statistically significant for $p < 0.05$.

Results

During 10 years, 1171 patients aged 18-88 years underwent AVR and were included in the study. The detailed demographic and clinical characteristics of the study group are presented in Table 1.

Table 1. Clinical characteristics of the study group*

Variable	Total study group (n = 1171)
Age (years) mean ± SD	64.03 ± 10.7
Arterial hypertension	72.0%
History of myocardial infarction and/or percutaneous coronary intervention	28.6%
Hyperlipidaemia	62.0%
Atrial fibrillation	11.1%
NYHA class	I 4.3%
	II 41.8%
	III 7.8%
	IV 0.5%
Infective endocarditis	
Active	7.4%
In the past	1.9%
Chronic kidney disease	G1 47.8%
	G2 36.0%
	G3a 10.9%
	G3b 3.3%
	G4 1.5%
	G5 0.5%
Diabetes type 2	22.4%
Oral antihyperglycaemic drugs	13.0%
Insulin	5.9%
Ejection fraction	54%

*Data are presented as n (%) unless otherwise specified; NYHA — New York Heart Association; SD — standard deviation

Table 2. Complications after surgical aortic valve replacement

Complications	n	%
Respiratory	142	12.55
Bleeding/tamponade	60	5.29
Myocardial infarction	40	3.42
Neurological	40	3.42
Local infection	20	1.71
Temporary pacemaker implantation	17	1.45
Acute kidney injury	32	2.73
Death	40	3.42

The history of heart surgery was noted in 4.3 % of patients: 2.7% had undergone valvular surgery, 0.7% coronary artery bypass graft (CABG), 0.6% aortic surgery, 0.2% combined CABG and valvular surgery, and 0.1% combined valvular and aortic surgery. A degenerative process (78.9%) was the most common aetiology of AS, while in the other patients, infectious (9.3%), rheumatic (1.6%), functional (4.4%), and congenital (3.9%) aetiology was noted. Almost 97% of the study population underwent surgery on the native valve.

The AVR procedure lasted on average 207 minutes (100 minutes of the extracorporeal circulation time). The average diameter of the implanted valve was 22.53 mm. Mechanical valves were implanted in 23.4% of patients and biological valves in 76.6% of patients.

The complication rate was 19.1% and included death, respiratory and neurological complications, myocardial infarction, haemorrhage requiring blood transfusion, pericardial effusion, local infection, a need for temporary pacemaker implantation and acute kidney injury (Table 2).

During hospitalization and within one month since the discharge from hospital 40 patients died (3.4%). The variables that differed significantly between the patients with the fatal short-term follow-up and the rest of the study group were: diabetes (6.1% vs. 2.6%; p = 0.006), chronic kidney disease (stage 3 to 5, according to Kidney Disease Improving Global Outcomes [KDIGO] [12]; 25% vs. 2.8%; p < 0.001), significant mitral regurgitation (24% vs. 2.6%; p < 0.001), significant tricuspid regurgitation (25.7% vs. 2.9%; p = 0.001) and urgent indications for AVR (11.3% vs. 2.7%; p = 0.001). The short-term mortality rate was 3-fold higher in the group of patients with a history of PCI (8.2% vs. 3.1%; p = 0.045), 7-fold higher in patients with active infective endocarditis (20.5% vs. 2.9%; p = 0.007), 30-fold higher in patients with periprocedural complications (15.4% vs. 0.5%; p < 0.001) and almost 40-fold higher in patients who developed multi-organ complications (65.6% vs. 1.7%; p < 0.001).

Table 3 shows the results of the univariate and multivariate analysis for predicting short-term mortality after AVR. Independent predictors of short-term mortality were active infective endocarditis (OR: 4.99; CI: 1.03–24.12; p = 0.045), duration of the surgical procedure (OR: 1.00; CI: 1.00–1.01; p = 0.018) and New York Heart Association (NYHA) class III–IV (OR: 1.97; CI: 1.77–3.31; p = 0.01).

Discussion

Several factors should be considered in predicting short-term mortality after AVR. Edwards et al. in their study identified factors strongly associated with an adverse outcome. They included: a need for reoperation, emergency or salvage procedures, recent infarction and renal failure [13]. Yamauchi et al. [14] identified 11 factors for hospital mortality after AVR: age, preoperative dialysis, chronic lung disease, non-cardiac vascular disease, congestive heart failure, atrial fibrillation, NYHA class ≥ III, history of stroke/transient ischaemic attack, concomitant CABG, cardiogenic shock and concomitant mitral regurgitation [14].

As stated by Tjang et al. [3], the risk of short-term mortality after AVR was strongly increased by emergency surgery and moderately increased by older age, aortic insufficiency, coronary artery disease, longer cardiopulmonary bypass time, reduced left ventricular ejection fraction, infective endocarditis, hypertension, implantation of mechanical valves, preoperative pacing, dialysis-dependent renal failure [3]. Kvidal et al. [5] mentioned the following independent factors that influence early mortality: advanced NYHA functional class (III or IV), preoperative atrial fibrillation and older age (over 70 years) [5]. In a single-centre study conducted by Chen et al. [10], preoperative NYHA IV, smoking, low ejection fraction, previous cardiac

Table 3. Univariate and multivariate analysis in predicting short-term mortality in patients undergoing surgical aortic valve replacement

Variable	Univariate			Multivariate		
	OR	CI	p-value	OR	CI	p-value
Infective endocarditis (active)	2.99	1.39–6.46	0.005	4.99	1.03–24.12	0.045
NYHA class III–IV	3.10	1.90–5.05	< 0.001	1.97	1.77–3.31	0.01
Duration of the surgical procedure	1.01	1.01–1.02	< 0.001	1.00	1.00–1.01	0.018

CI — confidence interval; NYHA — New York Heart Association; OR — odds ratio surgery, tricuspid regurgitation, and concomitant coronary artery bypass grafting were independent risk factors for short-term mortality after valve surgery [10]. However, this model was rather suitable for patients in China because of the demographic characteristics of the study population [10]. In the Jordanian population Ibrahim et al. identified older age, emergency/salvage surgery, use of beta-blockers for less than 1 month preoperatively and use of a biological valve in the aortic position as significant and independent predictors of 30-day mortality after valvular surgery [11].

Toumpoulis et al. [15] reported outcomes observed in 1376 consecutive patients who underwent isolated or combined heart valve surgery. The authors revealed six independent predictors for in-hospital mortality identified before, during or after operation: preoperative dialysis, preoperative endocarditis, intraoperative stroke, bleeding requiring reoperation, postoperative sepsis, endocarditis, renal and respiratory failure [15]. In the present study, the short mortality rate was also significantly higher in the group of patients with periprocedural complications.

A higher occurrence of diabetes was observed in patients who died shortly after AVR. Type 2 diabetes is a significant risk factor for the development of AS, left ventricular remodelling and dysfunction [16, 17]. Khan et al. have recently found that diabetes was associated with an increased risk of in-hospital mortality in patients undergoing AVR but not TAVI [16]. In a study carried out by Ram et al. [17] type 2 diabetes was an independent predictor for long-term mortality after isolated AVR surgery but had no significant impact on short-term outcomes [17]. In contrast to data published by Ram et al. [17], the present results showed that the mortality rate was affected by the diabetic treatment strategy with worse outcomes in patients treated with oral antidiabetic drugs in comparison to patients treated with insulin. Interestingly, early mortality was reported to be lower in type 2 diabetic patients than in non-diabetic patients who underwent bioprosthetic AVR [18].

Similarly to other authors [3, 11, 19], this study showed that emergency surgery significantly increases the risk of early mortality after AVR. Other predictors of poor prognosis reported by several authors [3, 5, 10, 19, 20] and confirmed in the study group of patients are chronic kidney disease, active infective endocarditis and NYHA class III–IV. The following results showed that significant mitral regurgitation and tricuspid regurgitation have a negative impact on short-term prognosis after valve surgery, which corresponds to results obtained by Chen et al. [10] and Ruel et al. [21]. Valvular surgery performed in patients with a definite left-sided infective endocarditis was associated with a negative short-term outcome but was markedly associated with reduced mortality in long-term follow-up [22].

In contrast to results presented by other authors [3, 5, 23], hypertension and atrial fibrillation were not identified as significant predictors of negative postoperative outcomes in the present study. According to Wang et al. [23], atrial fibrillation was associated with several cardiovascular and cardiac surgery risk factors but stayed independently associated with short-term mortality after AVR procedure [23].

Along with some already indicated predictors of short-term mortality in patients undergoing surgical AVR [3, 5, 10], the risk analysis clearly showed a negative impact of periprocedural complications and duration of the surgical procedure. To the authors' knowledge, the history of PCI is a predictor of short-term mortality revealed in the present study but the only unmentioned in literature.

Conclusions

Along with well-known comorbidities that affect the outcome after AVR, i.e., type 2 diabetes, renal dysfunction, significant mitral and tricuspid regurgitation, the history of PCI appears to be another important factor that should be considered in AVR risk stratification. Independent predictors of short-term mortality after AVR are active infective endocarditis, duration of the surgical procedure, and NYHA class III–IV.

Additional information

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics statement

Not applicable due to retrospective design of this study

Author contributions

MMT — 33%; RZ — 15%; DT — 10%; EO — 10%; JD — 10%; KP — 22%.

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Conflict of interest

The authors report no competing interests.

Supplementary material

None.

Streszczenie

Wstęp. Wymiana zastawki aortalnej (AVR, *aortic valve replacement*) jest rutynowym postępowaniem w przypadku ciężkiej, objawowej stenozy aortalnej. Celem badania była identyfikacja czynników predykcyjnych śmiertelności krótkoterminowej po AVR. Przedoperacyjna stratyfikacja ryzyka u tych pacjentów może być pomocna w podejmowaniu decyzji o najbardziej odpowiedniej metodzie leczenia.

Materiał i metody. Retrospektywne badanie obserwacyjne, obejmujące 1171 pacjentów poddanych zabiegowi AVR, przeprowadzono w dużym ośrodku medycznym trzeciego stopnia referencyjności na przestrzeni 10 lat (2009–2019). Śmiertelność krótkoterminową zdefiniowano jako zgon w ciągu miesiąca od AVR.

Wyniki. Średni wiek osób badanych wynosił 64 (± 10) lata. Najczęstszą przyczyną wady aortalnej były zmiany zwyrodnieniowe (78,9%). Odsetek powikłań pooperacyjnych wyniósł 19,1%, a śmiertelność krótkoterminowa 3,4%. Zwiększone ryzyko śmiertelności krótkoterminowej po zabiegu AVR było związane z cukrzycą typu 2 (6,1% *vs.* 2,6%; p = 0,006), przewlekłą chorobą nerek (stadium 3 do 5; 25% *vs.* 2,8%; p < 0,001), przezskórną interwencją wieńcową w wywiadzie (8,2% *vs.* 3,1%; p = 0,045), aktywnym infekcyjnym zapaleniem wsierdzia (20,5% *vs.* 2,9%; p = 0,007), istotną niedomykalnością zastawki mitralnej (24% *vs.* 2,6%; p < 0,001) i zastawki trójdzielnej (25,7% *vs.* 2,9%; p = 0,001), powikłaniami okołozabiegowymi (15,4% *vs.* 0,5%; p < 0,001) oraz koniecznością wykonania AVR w trybie nagłym (11,3% *vs.* 2,7%; p = 0,001). Za pomocą analizy wieloczynnikowej zidentyfikowano niezależne predyktory śmiertelności wczesnej: aktywne infekcyjne zapalenie wsierdzia (iloraz szans [OR, *odds ratio*]: 4,99; p = 0,045), czas trwania zabiegu chirurgicznego (OR: 1,00; p = 0,018) oraz klasę czynnościową według *New York Heart Association* (NYHA) III–IV (OR: 1,97; p = 0,01).

Wnioski. Aktywne infekcyjne zapalenie wsierdzia, czas trwania zabiegu chirurgicznego oraz klasa czynnościowa NYHA III–IV są niezależnymi wskaźnikami śmiertelności krótkoterminowej po AVR i powinny być uwzględniane w podejmowaniu decyzji o najbardziej odpowiedniej metodzie leczenia.

Słowa kluczowe: wymiana zastawki aortalnej, zwężenie zastawki aortalnej, czynniki ryzyka, śmiertelność krótkoterminowa, operacja chirurgiczna

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