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Clinical Research

Redo surgical aortic valve replacement: An outdated technique in the era of valve-in-valve procedures?

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ABSTRACT

Background: The treatment of degenerative prosthetic aortic valves is increasingly important. However, redo surgical aortic valve replacement (Re-SAVR) carries higher perioperative risks than primary surgical aortic valve replacement.
Aim: This study aims to identify predictors of early morbidity and death after Re-SAVR.
Methods: A retrospective analysis of 220 patients scheduled for elective Re-SAVR between 2009 and 2017 was conducted. Patients were divided into isolated ($n = 87$) and combined ($n = 133$) redo procedures. The primary endpoint was in-hospital death, and secondary endpoints were postoperative complications, such as stroke, dialysis and pacemaker implantation. Regression analysis identified independent predictors of death.
Results: Among the patients undergoing Re-SAVR (mean age, 62.6 ± 13.2 years; 71% male; mean EuroSCORE II, 12.6 ± 11.1%), 86.4% received biological prostheses and 13.6% received mechanical prostheses. The in-hospital death rate was 5.7% for isolated Re-SAVR and 18.0% for combined procedures ($P = 0.003$). Excluding patients with endocarditis, the in-hospital death rate was 0% for isolated Re-SAVR and 19.7% for combined procedures ($P = 0.002$). The incidence of postoperative complications after an isolated procedure was similar to that after a combined procedure. Independent predictors of 30-day death were previous coronary artery bypass grafting (odds ratio: 14.12, 95% confidence interval: 4.40–51.35; $P < 0.001$), a combined procedure (odds ratio: 7.01, 95% confidence interval: 2.09–31.54; $P = 0.004$) and New York Heart Association functional class III/IV (odds ratio: 3.73, 95% confidence interval: 1.31–12.58; $P = 0.020$).
Conclusions: The perioperative risk of death after isolated Re-SAVR in patients without endocarditis was 0%. Independent predictors of in-hospital death included previous coronary artery bypass grafting, combined procedures and New York Heart Association class III/IV. These findings may inform the decision-making process of the heart team regarding the optimal approach (surgical or transcatheter) for redo aortic valve replacement.

1. Abbreviations

CABG	coronary artery bypass grafting
CI	confidence interval
NYHA	New York Heart Association
OR	odds ratio
Re-SAVR	redo surgical aortic valve replacement
SAVR	surgical aortic valve replacement
TAVI	transcatheter aortic valve implantation
ViV-TAVI	valve-in-valve transcatheter aortic implantation

2. Background

Surgical aortic valve replacement (SAVR) and transcatheter aortic valve implantation (TAVI) are the current treatment options of choice for severe aortic dysfunction, as outlined in the relevant clin-

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ical guidelines [1]. Despite the favourable long-term outcomes of surgical aortic bioprostheses [2,3], structural valve deterioration remains a significant concern, and is the most common indication for redo surgical aortic valve replacement (Re-SAVR) [4]. The reasons for valve dysfunction are either stenosis or regurgitation, caused by pannus formation, thrombus deposition and subsequent calcification of the valve [5].

Over the past two decades, the number of implanted bioprosthetic valves has increased, especially in younger patients [6,7]. This trend has been accelerated by the implementation of valve-in-valve transcatheter aortic implantation (ViV-TAVI) [8]. ViV-TAVI is considered less invasive, and offers a good alternative to Re-SAVR in older and high-risk surgical patients [9]. However, leaflet thrombosis and reduced leaflet motion remain a cause for concern regarding the long-term outcome for patients undergoing TAVI [10]. Younger patients more often choose a bioprosthetic aortic valve to improve their quality of life and avoid the need for lifetime systemic anticoagulation required with mechanical prostheses [6]. Additionally, new tissue bioprostheses have excellent haemodynamics and are already designed for ViV-TAVI procedures with a stent expansion zone [11]. However, as a result of increased life expectancy, most patients outlive their bioprosthesis, necessitating mandatory reintervention. Re-SAVR is still the contemporary gold standard of care [1]. However, it is associated with higher morbidity and death rates than the initial SAVR. An analysis of the Society of Thoracic Surgeons Adult Cardiac Surgery Database revealed that Re-SAVR had a death rate of 4.7%, compared with 2.2% for primary SAVR [12]. Therefore, identifying risk factors for an inferior outcome after Re-SAVR is crucial in guiding the heart team's decision regarding appropriate treatment of degenerated aortic valve prostheses.

Hence, the objective of our study was to analyse in-hospital death after Re-SAVR, and to identify predictors of in-hospital death.

3. Methods

3.1. Ethical statement

Data acquisition was performed anonymized and retrospectively. Therefore, in accordance with German law, no ethical approval is needed, and informed patient consent was waived.

3.2. Patient selection and data collection

The study was a single-centre retrospective observational trial. Data acquisition was completed in accordance with the Declaration of Helsinki. Between January 2009 and December 2017, 220 consecutive patients underwent Re-SAVR at our institution because of severe symptomatic aortic stenosis or regurgitation. Re-SAVR was the only inclusion criterion. No exclusion criteria were introduced to reflect daily clinical practice. The indication for Re-SAVR was determined after thorough discussion within the institutional heart team and in accordance with the current guidelines of the European Society of Cardiology and the European Association of Cardiothoracic Surgery [1]. Reoperation of the aortic valve was performed according to institutional standards; this involved a median full sternotomy with cardiopulmonary bypass and cannulation of the ascending aorta, moderate hypothermia and cardioplegia-induced cardiac arrest. Patients with isolated Re-SAVR ($n = 87$) were compared with combined redo procedures ($n = 133$). Pre-, intra- and postoperative variables were obtained from the in-hospital medical records. The following clinical variables were recorded: age at the time of surgery; sex; cardiovascular risk factors (e.g. positive family history, diabetes, dyslipidaemia, arterial hypertension); history of stroke; atrial fibrillation; coronary heart disease; pulmonary hypertension (defined as systolic pulmonary arterial pressure > 60 mmHg measured during preoperative transthoracic echocardiography); chronic obstructive pulmonary disease; and dialysis. In addition, operative times, such as cardiopulmonary bypass time or cross-clamp time, were recorded. Complications during the inpatient stay were also recorded, such as intraoperative complications (e.g. extracorporeal membrane oxygenation or intra-aortic balloon pump support) or postoperative complications (e.g. rethoracotomy for bleeding, pacemaker implantation, wound healing disorder, sepsis or stroke). The primary endpoint was in-hospital death, and secondary endpoints included postoperative complications, such as extracorporeal support, myocardial infarction, stroke, dialysis and pacemaker implantation.

3.3. Statistical analysis

Categorical variables are presented as absolute numbers (percentages), and continuous variables as means ± standard deviations. The primary endpoint of 30-day death was analysed in a multiple logistic regression model. Potential risk factors were included in the model simultaneously. In a stepwise procedure, non-significant terms were removed based on a likelihood ratio test. In each step, the term with the smallest change in likelihood is removed if this change is still insignificant. Otherwise, this backward selection is finished. The initial and final model were expressed in terms of adjusted odds ratios (ORs), 95% confidence intervals (CIs) and *P*-values. The area under the receiver operating characteristic curve was used to represent the discriminatory ability of the regression models and competing models were compared using DeLongs test. A *P*-value < 0.05 was considered statistically significant. Statistical analyses were performed using the statistical software R, version 3.3.3 (R Core Team [2017]. R Foundation for Statistical Computing, Vienna, Austria).

4. Results

4.1. Clinical baseline characteristics

Baseline characteristics are outlined in Table 1. The mean age at reoperation was 62.6 ± 13.2 years, and 29.1% of the patients were female. The mean EuroSCORE II was 12.6 ± 11.1, and 52.7% of the patients presented with New York Heart Association (NYHA) class ≥ III. Cardiovascular risk factors were present in most of the patients: dyslipidaemia, 71.4%; arterial hypertension, 85.9%; diabetes, 15.0%. A history of coronary artery disease was present in 32.7%, and a history of stroke in 14.5%. In the entire study cohort, 10.5% had undergone more than one previous heart surgery, whereas 69.1% had had an isolated SAVR as a previous procedure. The reason for redo surgery was structural valve degeneration in

Table 1
Preoperative baseline characteristics ($n = 220$).

Age at reoperation (years)	62.6 ± 13.2
Female sex	64 (29.1)
EuroSCORE II	12.6 ± 11.1
NYHA class ≥ III	116 (52.7)
Reduced LVEF (≤ 45%)	50 (22.7)
Diabetes	33 (15.0)
Dyslipidaemia	157 (71.4)
Arterial hypertension	189 (85.9)
Coronary artery disease	72 (32.7)
Systolic pulmonary arterial pressure ≥ 60 mmHg	28 (12.7)
Atrial fibrillation	47 (21.4)
COPD	26 (11.8)
Dialysis	7 (2.3)
History of stroke	32 (14.5)

Data are expressed as mean ± standard deviation or number (%). COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association.

Table 2
Intraoperative data ($n = 220$).

Reason for redo surgery	
Active endocarditis	93 (42.2)
Structural valve degeneration	123 (56.0)
Paravalvular leakage	2 (0.9)
Valve thrombosis	2 (0.9)
Isolated aortic valve replacement	87 (39.5)
Combined surgery	133 (60.5)
Aortic surgery	77 (35.0)
Valve surgery	57 (25.9)
CABG	26 (11.8)

Data are expressed as number (%). CABG: coronary artery bypass grafting.

56.0%, active endocarditis in 42.2%, paravalvular leakage in 0.9% and valve thrombosis in 0.9% (Table 2). The mean size of the implanted prostheses was 24.1 ± 2.3 mm at the previous procedure compared with 23.9 ± 2.0 mm at the index procedure ($P = 0.47$). At previous surgery, biological prostheses were used in 74.5% of the cases and mechanical prostheses in 14.5%; in 10% of cases, the type of prosthesis used was not identifiable. At the time of Re-SAVR, 86.4% of the patients received a biological prosthesis and 13.6% received a mechanical prosthesis.

4.2. Postoperative outcome: Isolated versus combined Re-SAVR

A total of 133 patients underwent a concomitant procedure (60.5%) compared with 87 patients who had isolated Re-SAVR (39.5%). Concomitant surgeries included additional aortic surgery in 35.0%, mitral and/or tricuspid valve surgery in 25.9% and coronary artery bypass grafting (CABG) in 11.8%. Cardiopulmonary bypass and aortic cross-clamp times were significantly shorter in isolated compared with combined Re-SAVR (Table 3). The in-hospital death rate for the entire study cohort was 13.2% after Re-SAVR. In the present study, the patients who had undergone more than one previous surgical procedure had either a unicuspid or a bicuspid aortic valve at the index procedure. Among such patients with more than one previous surgery, one patient died, resulting in an in-hospital death rate of 4.35%. When comparing isolated Re-SAVR ($n = 87$) with combined Re-SAVR ($n = 133$), there were no significant differences in ventilation time ($P = 0.13$), length of intensive care unit stay ($P = 0.36$) and length of hospital stay ($P = 0.09$) (Table 3). The in-hospital death rate was significantly lower for isolated Re-SAVR (5.7%) compared with combined Re-SAVR (18.0%; $P = 0.003$). In patients without endocarditis ($n = 119$), the in-hospital death rate was 0% (0/53) for isolated Re-SAVR compared with 19.7% (13/66) for combined Re-SAVR ($P = 0.002$). Postoperative complications are highlighted in Table 4. In summary, no significant differences were found between the two groups besides the increased in-hospital death rate after combined procedures.

4.3. Postoperative outcome: survival versus death

Univariate analysis of in-hospital deaths indicated that a higher EuroSCORE II (20.64 ± 13.90 vs. 11.44 ± 10.14; $P < 0.001$), NYHA class III/IV (79.3% vs. 48.7%; $P < 0.001$) and a higher incidence of previous CABG (37.9% vs. 6.8%; $P < 0.001$) resulted in a significantly higher death rate (Table 5). Accordingly, aortic cross-clamp time ($P = 0.028$) and cardiopulmonary bypass time ($P < 0.001$) were significantly longer in the group who died. Postoperative complications were also more frequent, including postoperative extracorporeal membrane oxygenation support as a result of low cardiac output (17.2% vs. 2.1%; $P = 0.002$), dialysis (27.6% vs. 5.8%; $P < 0.001$), sepsis (10.3% vs. 1.6%; $P = 0.032$) and stroke (13.8% vs. 3.7%; $P = 0.042$).

4.4. Independent predictors of in-hospital death

Multivariable regression analysis was conducted to identify predictors of in-hospital death (Table 6). The results showed that NYHA class III/IV (OR: 3.73; 95% CI: 1.31–12.58; $P = 0.020$), a combined procedure at the time of Re-SAVR (OR: 7.01, 95% CI: 2.09–31.54; $P = 0.004$) and previous CABG (OR: 14.12, 95% CI: 4.40–51.35; $P < 0.001$) were independent predictors of in-hospital death after Re-SAVR. Age ($P = 0.52$), female sex ($P = 0.82$), severely reduced left ventricular function ($P = 0.36$), EuroSCORE II ($P = 0.17$) and active endocarditis ($P = 0.55$) were not significant predictors. The area

Table 3
Perioperative data: isolated versus combined redo surgical aortic valve replacement.

	Isolated ($n = 87$)	Combined ($n = 133$)	P
Cardiopulmonary bypass time (minutes)	174.0 ± 87.1	262.0 ± 103.2	< 0.001
Aortic cross-clamp time (minutes)	103.2 ± 46.0	157.6 ± 68.9	< 0.001
Ventilation time (hours)	13.8 ± 26.1	20.9 ± 31.3	0.13
Length of stay in ICU (days)	5.1 ± 12.1	5.9 ± 11.8	0.36
Length of stay in hospital (days)	10.8 ±12.9	12.6 ± 15.5	0.09

Data are expressed as mean ± standard deviation. ICU: intensive care unit.

Table 4
Postoperative complications: isolated versus combined redo surgical aortic valve replacement.

Complications	Isolated ($n = 87$)	Combined ($n = 133$)	P
In-hospital death	5 (5.7)	24 (18.0)	0.003
In-hospital death (patients without endocarditis)	0/53 (0.0)	13/66 (19.7)	0.002
ECMO	3 (3.5)	6 (4.5)	> 1.00
IABP	3 (3.5)	9 (6.8)	0.37
Myocardial infarction	2 (2.3)	2 (1.5)	0.65
Dialysis	5 (5.8)	14 (10.5)	0.33
Pericardial tamponade	4 (4.6)	6 (4.5)	> 1.00
Re-exploration for bleeding	10 (11.5)	25 (18.8)	0.19
Pacemaker implantation	13 (14.9)	34 (25.6)	0.07
Sepsis	2 (3.0)	4 (3.0)	> 1.00
Stroke	2 (2.3)	9 (6.8)	0.21
Tracheotomy	5 (5.8)	8 (6.0)	> 1.00
Impaired wound healing	2 (2.3)	3 (2.3)	> 1.00

Data are expressed as number (%). ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic balloon pump.

Table 5
Perioperative data: alive at discharge versus in-hospital death.

	Alive (n = 191; 86.8%)	Deceased (n = 29; 13.2%)	P
EuroSCORE II	11.44 ± 10.14	20.64 ± 13.90	< 0.001
NYHA class			< 0.001
I/II	98 (51.3)	6 (20.7)	
III/IV	93 (48.7)	23 (79.3)	
Previous CABG	13 (6.8)	11 (37.9)	< 0.001
Aortic cross-clamp time (minutes)	133.38 ± 65.34	160.96 ± 70.80	0.028
Cardiopulmonary bypass time (minutes)	214.83 ± 94.80	316.93 ± 129.36	< 0.001
Concomitant procedure	109 (57.1)	24 (82.8)	0.008
Postoperative complications			
ECMO	4 (2.1)	5 (17.2)	0.002
IABP	7 (3.7)	5 (17.2)	0.012
Dialysis	11 (5.8)	8 (27.6)	< 0.001
Re-exploration for bleeding	24 (12.6)	11 (37.9)	0.002
Sepsis	3 (1.6)	3 (10.3)	0.032
Stroke	7 (3.7)	4 (13.8)	0.042

Data are expressed as mean ± standard deviation or number (%). CABG: coronary artery bypass grafting; ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic balloon pump; NYHA: New York Heart Association.

Table 6
Multivariable regression analysis for in-hospital death.

	Initial model			Reduced model		
	OR	95% CI	P	OR	95% CI	P
Age at reoperation	1.02	0.97–1.08	0.52			
Female sex	0.87	0.26–2.70	0.82			
NYHA class III/IV	3.05	0.94–11.52	0.08	3.73	1.31–12.58	0.020
Severely reduced LV function	0.37	0.03–2.52	0.36			
Combined procedure at re-SAVR	5.73	1.56–27.92	0.016	7.01	2.09–31.54	0.004
EuroSCORE II	1.03	0.99–1.08	0.17			
Previous CABG	11.77	3.52–45.05	< 0.001	14.12	4.40–51.35	< 0.001
Active endocarditis	1.39	0.46–4.17	0.55			

CABG: coronary artery bypass grafting; LV: left ventricular; NYHA: New York Heart Association; Re-SAVR: redo surgical aortic valve replacement.

under the receiver operating characteristic curve for the regression model was 0.806 (95% CI: 0.713–0.900).

5. Discussion

Over the past decade, there has been an increase in the implantation of bioprosthetic valves, resulting in a substantial rise in the rate of redo aortic valve surgery. There are various treatment options when addressing a dysfunctional aortic valve prosthesis. The preferred treatment option remains the surgical replacement of the prosthetic valve using a median sternotomy approach. With advances in technology and the established use of TAVI, the ViV-TAVI method is emerging as a promising alternative for individuals at high risk from surgical procedures. Especially with the help of novel machine learning tools, patients undergoing TAVI can now be optimally treated and discharged [13]. Nowadays, TAVI can be a feasible option even for high-risk patients with predominant aortic regurgitation [14]. Our study has highlighted that the perioperative risk for isolated Re-SAVR is very low, and is similar to that for primary SAVR, according to the literature (e.g. 2.2% after isolated primary aortic valve surgery) [12]. However, combined procedures at reoperation, previous CABG and NYHA class ≥ III were significant independent risk predictors for in-hospital death.

Previous studies have reported an in-hospital death rate of 4.6–7.5% following Re-SAVR [12,15,16]. In Leipzig, Leontyev et al. highlighted that Re-SAVR for aortic prosthetic valve endocarditis was associated with a high perioperative death rate compared with non-endocarditis (24.3% vs. 6.8%) [17]. Several studies have shown a higher risk of death in patients with a previous mechanical prosthesis compared with a biological valve. However, a study from the 1980s concluded that the type of previous prosthesis did not influence the postoperative outcome [18]. In the present study, 42% of Re-SAVR procedures were for endocarditis, thus indicating that prosthetic valve replacement is frequently attributable to endocarditis. This emphasizes the elevated risk of endocarditis associated with prosthetic valves. Consequently, alternative native solutions should be given due consideration, particularly in non-elderly adults (e.g. aortic valve repair or the Ross procedure). Recently, Jones et al. reported a 26.1% operative death rate for malfunctioning mechanical valves compared with 8.1% for bioprosthetic valves. Furthermore, replacement of a mechanical valve was identified as an independent predictor of operative death, resulting in a 2.25-fold increase in deaths [19]. In our study group, 74.5% of the patients had a biological prosthesis and 14.5% had a mechanical prosthesis at previous surgery. The type of prosthesis was not a significant predictor of in-hospital death.

At present, SAVR is still the benchmark for low-risk and/or younger patients because of its superior performance in postoperative haemodynamics and reduced operative death rates [1,20,21], whereas ViV-TAVI is emerging as the preferred choice for patients deemed inoperable or at high risk [9]. Our investigation aimed to further highlight the prerequisites for a redo procedure, thereby providing guidance for selecting either a surgical or interventional approach. In our study cohort, combined procedures at reoperation, previous CABG procedure and symptomatic patients (e.g. NYHA class ≥ III) emerged as independent significant predictors of in-hospital death. A study by Leontyev et al. further identified emergency surgery, preoperative shock, aortic root abscess and peripheral vascular disease as risk factors for in-hospital death after Re-SAVR [22]. Other authors have also highlighted additional predictors of in-hospital death, such as reduced left ventricular ejection fraction, preoperative neurological dysfunction, endocarditis, urgency of reoperation and age [18,22–24]. In contrast, age and reduced left ventricular ejection fraction were not independent risk factors for death after Re-SAVR in our study.

In line with the results of our study, the perioperative risk in patients who had isolated Re-SAVR was significantly lower compared with those who had combined procedures during Re-SAVR. This finding was also observed in previous studies, where the risk escalates with the complexity of the Re-SAVR procedure [17,25,26]. Multiple studies have highlighted that concomitant valve procedures increase the risk of death [26,27].

Currently, the ViV-TAVI procedure has emerged as a valuable alternative to Re-SAVR in inoperable or high-risk patients, particularly those with degenerated bioprosthesis. Especially in high-risk groups, ViV-TAVI is preferred because of its minimally invasive nature, shorter intensive care unit and hospital stays and reduced bleeding events [9,20]. However, Dvir et al. highlighted that ViV-TAVI is associated with a higher risk of valve malpositioning and ostial obstruction complications [8]. In addition, Re-SAVR seems to be associated with superior postoperative outcomes compared with ViV-TAVI in terms of haemodynamic variables (e.g. lower mean aortic gradient and less paravalvular leak) [4,15,20,28]. Nevertheless, a meta-analysis by Godzek et al. found no significant differences in the rates of cardiovascular death, myocardial infarction, stroke, acute kidney injury or 30-day death [20]. Another meta-analysis by Nalluri et al. showed similar results, with no significant differences in procedural, 30-day and 1-year death rates between ViV-TAVI and Re-SAVR [29]. Other studies have reached the same conclusion, reporting similar 30-day death rates (approximately 4–5%) for both ViV-TAVI and Re-SAVR [15,28,30]. Whereas those studies highlighted ViV-TAVI as a good alternative to Re-SAVR, in terms of high-risk patients, Re-SAVR remains the only option for the treatment of infectious endocarditis or additional cardiac disease [31].

However, if no endocarditis is present, the perioperative risk of Re-SAVR is similar to that of primary SAVR. Our findings are in line with Potter at al., who showed that Re-SAVR in patients without endocarditis results in a similar early operative death rate to the first SAVR [24]. In case of an isolated Re-SAVR, the procedure can be carried out with a low risk of in-hospital death, considering the Re-SAVR as a procedure of choice for such a patient cohort. Therefore, younger patients can be offered a Re-SAVR with no increased risk of death, but with superior haemodynamics and a reduced risk of structural valve deterioration [20]. However, in patients without endocarditis, but with risk factors such as previous CABG or high NYHA class (≥ III), ViV-TAVI should be discussed within an interdisciplinary heart team. For these cases, even the necessity of a combined procedure should be evaluated by a dedicated heart team if interventional treatment of all pathologies is possible, considering a four-fold increased risk compared with a combined Re-SAVR.

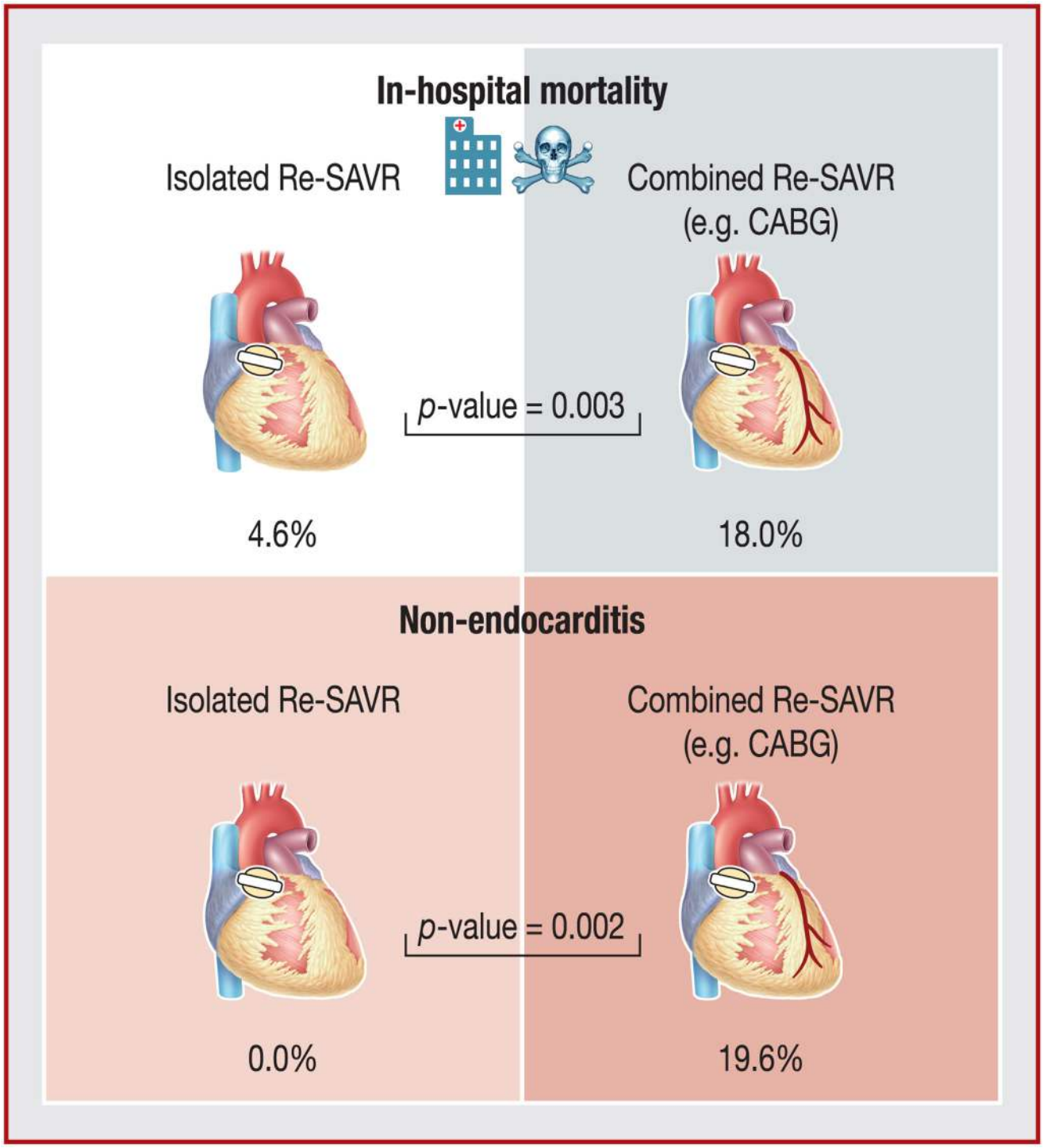
Our findings underscore the critical nature of the correct timing of the Re-SAVR, and may serve as a guide for making an informed decision for the patient with regard to the best treatment option – either a surgical or an interventional redo procedure.

5.1. Study limitations

There are some important limitations to our study. This is a retrospective analysis with all the known limitations associated with such a study design. Therefore, 10% of the valve types were unknown, which may have had an impact on the outcome. It has been reported that Re-SAVR of mechanical valves is associated with a higher operative risk of death, resulting in a 2.25-fold increase in deaths. Another important limitation is that the study was designed without a follow-up, and in-hospital death was defined as death during the hospital stay after surgery. If a patient was discharged and subsequently died, this was not recorded. However, our results highlight that Re-SAVR can be safely performed with a low risk of in-hospital death. Nevertheless, a prospective randomized study between Re-SAVR and ViV-TAVI should be carried out to confirm our excellent retrospective findings.

6. Conclusions

The perioperative risk of Re-SAVR in isolated non-endocarditis is very low. Significant independent risk predictors for in-hospital death were combined procedures at reoperation, previous CABG procedure and severe symptoms (NYHA class ≥ III). These results could potentially guide heart team decision-making regarding appropriate therapeutic allocation (Central Illustration).



Central Illustration. In-hospital death was significantly lower in patients with isolated Re-SAVR, especially in patients with non-endocarditis; CABG: coronary artery bypass grafting; Re-SAVR: redo surgical aortic valve replacement.

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Disclosure of interest

The authors declare that they have no competing interest.

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