Research Square

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Surgical treatment of valve endocarditis in high-risk patients: predictors of long term outcome

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Abstract

Background

- Infective endocarditis represents a surgical challenge associated with perioperative mortality. The aim of this study is to identify risk factors that are associated with higher mortality and to determine if there are any patient subsets that should be defined as "inoperable".

Methods

- We retrospectively analyzed 123 patients operated on for infective endocardi-tis from January 2011 to December 2020. Of these, 18 patients had prosthetic valve endocarditis. We collected perioperative characteristics and performed an analysis for the identification of preoperative risk factors associated with postoperative mortality.

Results

- Preoperative renal failure, an elevation of all types of EuroSCORE (EuroSCORE I, II and logistic) and prior aortic valve re-replacement were found to be preoperative risk factors significantly associated with mortality. In-hospital mortality was 27% in patients who had previously undergone aortic valve replacement (n = 4 out of 15 operated, p = 0.01). Patients who were operated on during the active phase of infective endocarditis showed a higher mortality rate than those operated on after the acute phase (16% versus 0%; p = 0.02). The type of prosthesis used (biological or mechanical) was not associated with mortality, whereas cross-clamp time significantly correlated with mortality (mean cross-clamp time 135 ± 65 min in dead patients versus 76 ± 32 min in surviving patients; p = 0.0005).

Conclusions

- Our study demonstrates that an early and fast surgical approach may rep-resent a valuable treatment option for high-risk patients with infective endocarditis, also in case of prosthetic valve endocarditis. Although several risk factors are associated with higher mortal-ity, no patient subset is inoperable. These findings can be helpful to inform decision-making in heart team discussion.

Background

Infective endocarditis, particularly on a heart valve prosthesis, represents a surgical challenge mostly for two reasons. First, prosthetic valve endocarditis (PVE) is a life-threating complication of valve replacement that accounts for 20–30% of all cases of infective endocarditis (1, 2). Second, patients with PVE are increasingly of advanced age and at high risk. In addition, many patients considered at

intermediate-to-high risk or inoperable that have undergone transcatheter aortic valve replacement are also suscep-tible to infective endocarditis on these prostheses (1, 2).

There are well-known patient subsets that are at higher risk of mortality if under-going cardiac surgery, due to anatomical features of valve heart disease and coexistent comorbidities (3), with more than 10% of patients considered to be at too high risk for surgery (1). Although surgical techniques, prosthetic models and anesthetic management have constantly improved over the last years (3), the increasing number of patients at higher risk for surgery may affect operative success, particularly in terms of higher mortality.

The aims of this study are (i) to determine if in patients undergoing reoperation for PVE there is a threshold of risk for defining them as inoperable, and (ii) to describe our surgical strategy in the presence of PVE and annular destruction.

Methods

Patients

We retrospectively analyzed all patients operated on for acute infective endocarditis unresponsive to antibiotic therapy from January 2011 to December 2020 at our De-partment of Cardiac Surgery. Complete data collection was available for 123 patients. Of these, 18 patients had previously undergone valve replacement surgery (mitral or aortic) and developed endocarditis on the previously implanted prosthesis. PVE patients were contacted for follow-up and checked with regular clinical and echocardiographic visits. At the time of surgery, all study patients provided their consent to the use of their data and for telephone contact for follow-up.

The diagnosis of infective endocarditis was made according to the Duke criteria (4) and all PVE patients underwent early intervention within 7 days of admission, according to the ESC and AHA/ACC recommendations (4). The decision of an early approach was based on patients' hemodynamic instability, septic shock, not being responsive to vas-oconstrictors, or the anatomical risk considered too high (e.g. detachment of the valve prosthesis with annular abscess and severe perivalvular leakage). Of the 18 patients with PVE, one patient was excluded because of acute cerebrovascular events requiring a vigilant wait for at least 4 weeks. The remaining 17 patients constituted our study pop-ulation (see graphical Abstract). Of these, at first operation, 15 underwent valve replacement with a bioprosthesis and 2 with a mechanical prosthesis.

The decision for an "early" approach has always been shared within a team including a cardiac surgeon, a cardiologist and an anesthesiologist, in consultation with other professionals (infectious disease specialist, neurologist in case of concomitant brain injury, general surgeon in case of embolic damage to the abdominal organs, vascular surgeon in case of peripheral embolism with limb ischemia to be evaluated concomitantly).

Surgery

All interventions were performed under general anesthesia and complete median sternotomy or re-sternotomy. By institutional protocol, surgical preparation and femoral vein or arterial cannulation for extracorporeal circulation were performed prior to median sternotomy. After external aortic cross-clamping, cardioplegia was infused into the aortic root, except for patients with severe aortic insufficiency in whom cardioplegia was infused directly into the coronary ostia.

In PVE patients, the prosthetic valve was entirely removed and sent to the laboratory for culture examination. The (aortic or mitral) annulus and the mitro-aortic continuity were cleaned, the abscesses were emptied and washed with disinfectant solution, and pledgets were removed. In case of abscesses involving the aortic annulus, the new prosthetic model was positioned inside the aortic root, far from the destroyed annulus. Special attention was paid to the patency of the coronary ostia in the vicinity of the new prosthesis. The choice of the prosthetic model to be implanted (mechanical, biological, stentless, sutureless) was based on the patient's clinical and anatomical conditions, life expectancy and, if possible, will.

Data were expressed as mean ± standard deviation for continuous variables and as counts and percentage for categorical variables. An analysis for the identification of preoperative risk factors associated with postoperative mortality was carried out. A logistic regression analysis was performed. Variables with a p-value of < 0.2 in univariable analysis were entered into multivariable analysis with stepwise selection.

Results

The preoperative characteristics of the study patients are reported in Table 1. Among preoperative risk factors, preoperative renal failure, all types of EuroSCORE (EuroSCORE I, II and logistic) and prior aortic valve re-replacement were found to be significantly associated with mortality. In-hospital mortality was 27% in patients who had previously undergone aortic valve replacement ($n = 4$ out of 15 operated, $p = 0.01$).

Table 1
Preoperative characteristics.

							p-Value Univariate
Variables	**Total**	**%/±**	**Dead**	**% Dead**	**Alive**	**% Alive**	**Log Regression**
Male sex	73	59.35	4	5%	69	95%	0.2
Female sex	50	40.65	6	12%	44	88%	0.2
Tricuspid valve disease	8	6.5	1	13%	7	88%	0.64
Aortic valve disease	89	72.36	9	10%	80	90%	0.22
Mitral valve disease	51	41.46	6	12%	45	88%	0.22
Diabetes	18	14.63	2	11%	16	89%	0.62
NIDDM	14	11.38	2	14%	12	86%	0.38
Diabetes diet	3	2.44	0	0%	3	100%	1
IDDM	1	0.81	0	0%	1	100%	1
Hypercholesterolemia	62	50.41	5	8%	57	92%	0.98
Hypertension	99	80.49	7	7%	92	93%	0.39
Ex smoker	19	15.45	2	11%	17	89%	0.68
Current smoker	17	13.82	1	6%	16	94%	0.72
Gastrointestinal disease	10	8.13	0	0%	10	100%	1
Renal dysfunction	10	8.13	3	30%	7	70%	0.02
Dialysis	2	1.63	0	0%	2	100%	1
Respiratory disease	10	8.13	0	0%	10	100%	1
Cerebro-vascular disease	7	5.69	0	0%	7	100%	1
Liver disease	53	43.09	0	0%	53	100%	1
Cancer	2	1.63	1	50%	1	50%	0.08
Neurologic dysfunction	3	2.44	1	33%	2	67%	0.15
Peripheral artery disease	2	1.63	0	0%	2	100%	1
Atrial fibrillation/flutter	23	18.7	2	9%	21	91%	0.91
Pacemaker	3	2.44	1	33%	2	67%	0.15

							p-Value Univariate
REDO (re-AVR)	15	12.2	4	27%	11	73%	0.01
REDO (re-MVR)	3	2.44	0	0%	3	100%	1
Age, years	63.78	13.46	68.8	9.8	63.34	13.68	0.2267
EuroSCORE	8.86	4.23	14.1	3.35	8.4	3.99	0.0006
Log EuroSCORE	0.18	0.2	0.45	0.23	0.15	0.17	0,0049
EuroSCORE II	14.42	19.09	47.39	22.91	11.08	15.21	0.0007

Patients who were operated on during the active phase of infective endocarditis showed a higher mortality rate than those operated on after the acute phase (16% versus 0%; p = 0.02). The type of prosthesis used (biological or mechanical) was not associated with mortality, whereas cross-clamp time significantly correlated with mortality (mean cross-clamp time 135 ± 65 min in dead patients versus 76 ± 32 min in surviving patients; p = 0.0005) (Table 2).

Table 2
Operative characteristics.

							p-Value Univariate
Variables	**Total**	**%/±**	**Dead**	**% Dead**	**Alive**	**% Alive**	**Log Regression**
Active endocarditis	58	47.15	9	16%	49	84%	0.02
No active endocarditis	53	43.09	0	0%	53	100%	1
Aortic cross-clamp time	81.25	39.4	135.6	65.18	76.05	32.01	0.0005
Biological prosthesis	54	43.9	7	13%	47	87%	0.1
Mechanical prosthesis	69	56.1	3	4%	66	96%	0.1

After adjusting for confounders, logistic EuroSCORE (p = 0.022, odds ratio [OR] 1.047, 95% confidence interval [CI] 1.007–1.090) and cross clamping time (p < 0.001, OR 1.031, 95% CI 1.012–1.049) were found to be independent predictors of 30-day mortality.

Discussion

Our study described the experience of our center with the surgical treatment of patients with endocarditis. However, our discussion will be focused on the results obtained in patients with PVE undergoing early surgery. These patients are the most "delicate" and at risk and are often considered inoperable due to their

comorbidities and clinical status. Although PVE patients are at higher risk than patients with native valve endocarditis, our study demonstrates that an early surgical approach may represent a valuable treatment option for this high-risk population. In other words, our study aims to demonstrate that early surgery in patients with PVE, albeit at very high risk, is associated with a good outcome in most cases.

In a matched retrospective cohort study of 139 dialysis patients, Farrington et al. reported that the risk of PVE and death after valve replacement was significantly higher in dialysis patients than in patients without dialysis (5). However, the mortality rate was less than 20% and the timing of intervention was unknown. This finding is consistent with our results, suggesting that operation should be taken into consideration also in patients at higher risk, even if burdened by a high mortality rate. Likewise, we also recorded a correlation between preoperative renal insufficiency and mortality. In this population, any delay to intervention or medical treatment alone can result in higher mortality (6). Although we did not include a control group on medical therapy, the mortality rate we recorded in operated patients was lower than in previous studies with a control group (6). Additionally, it is well-known that PVE is associated with high mortality particularly when urgent surgery is needed (7). In the analysis by Revilla et al (7), the main indication for urgent surgery was heart failure. This could also be ascribed to the waiting time until surgery leading to worsening of heart failure and hemodynamic instability in emer-gency. In our opinion, a “wait-and-see” approach may have resulted in critical clinical conditions and extensive anatomical injury (8, 9).

Also the surgical technique plays a role, especially if a complex procedure for en-docarditis with annular or root destruction should be performed, though associated with higher mortality (10). In case of aortic root involvement, several prosthetic models seem helpful in facilitating the radicality of the procedure or favoring resistance to recurrence (11, 12). In our population of high-risk patients, we chose to adopt the simplest technique by minimizing ischemic time, and priority was given to the removal of the infected tissue and implantation of the new prosthesis in an area distant from the previous one (13). In other words, radicality is key but a fast procedure is very important because prolonged cross-clamp time is correlated with postoperative mortality.

Age is another factor to be taken into consideration when evaluating operability. In patients undergoing surgery for infective endocarditis, regardless of whether native valve endocarditis or PVE, available evidence shows that advanced age is associated with higher mortality rates up to 20% in patients above 75 years (14). Of the 4 patients aged > 75 years included in our PVE population, only one died, supporting surgical indication also in this high-risk patient subset undergoing re-operation. Advanced age is a risk factor common to all interventions in cardiac surgery and not only for endocarditis per se.

We believe there may be a “bias” towards some patients who are considered to be at too high risk for surgery. For instance, patients undergoing transcatheter aortic valve implantation (TAVI) have been found to have a risk for developing infective endocarditis similar to those undergoing surgical aortic valve replacement, and no differences have been reported between these two patient subsets when undergoing surgery/re-surgery (15–17). These findings should prompt us to evaluate operability and the risk of

mortality at the time of first intervention. Patients undergoing TAVI and re-operated for endocarditis, given the historical period and the chronological sequence, are at least at intermediate risk if not considered inoperable (2). It is also likely that, in some specific conditions related to endocarditis, the risk scores we commonly use are not helpful in correctly assessing the patient's predicted risk (18). Also in our study, some patients had a EuroSCORE II > 60/70%, which would have represented an absolute contraindication for intervention. In contrast, the surgical procedure in these patients was performed with good efficacy, indirectly suggesting the incomplete appropriateness of these scores in some cases of endocarditis.

In our opinion, a surgical and early approach should be adopted in these high-risk patients, as this strategy performs better than a “wait-and-see” or non-surgical approach, regardless of the predicted risk score. This opinion is shared by other colleagues who also addressed the issue of hospital costs, concluding that these patients should receive a rapid diagnosis and treatment in order to improve morbidity, mortality and reduce postoperative hospital costs (19). The delay to surgery is not merely due to a “wait-and-see” approach but can also be related to diagnostic delays. In this regard, we fully agree with our colleagues who, by developing institutional protocols, have managed to reduce diagnostic times and, consequently, improve survival (20). The take home message of our study therefore is that all PVE patients should be operated early, though larger studies are necessary to confirm our findings.

Conclusions

The question „which came first, the chicken or the egg” is still open. Our study demonstrates that an early and fast surgical approach might represent a valuable treatment option for high-risk redo patients with PVE. These findings can be helpful to inform decision-making in heart team discussion.

Abbreviations

ACC: American college of Cardiology

AHA: American Heart Association

CI: Confidence interval

ESC: European society of Cardiology

OR: Odds ratio

PVE: Prosthetic valve endocarditis

TAVI: transcatheter aortic valve implantation

Declarations

Ethics approval and consent to participate: The study was evaluated and approved by the institutional board for clinical trials, Anthea Hospital GVM Care&Research (internal protocol; decision 2021 Feb) **And** Informed consent was obtained from all subjects involved in the study.

Consent for publication: All authors have read and agreed to the published version of the manuscript.

Availability of data and materials: The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: None.

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Authors' contributions: GN participated in manuscript writing, revision and conception. GS writing the manuscript. MM gives support in conception. NB: participated in conception and manuscript vision. AA gives support in statistical analysis. MG participated in support and supervision. FF participated in support and conception. PM participated in support and supervision. IC participated in support, re-writing and revision. GS participated in supervision. All authors read and approved the final manuscript.

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