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ORIGINAL ARTICLE

Risks and Challenges of Surgery for Aortic Prosthetic Valve Endocarditis

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Background	Prosthetic valve endocarditis is the most severe form of infective endocarditis. This study assessed the risks and challenges of surgery for aortic prosthetic valve endocarditis.
Methods	In total, 116 consecutive patients (98 males, age 65.2 ± 12.7 years), who underwent redo-surgery for active aortic prosthetic valve endocarditis between 2000 and 2014, were reviewed. Cox regression analysis was used to identify factors for aortic root destructions as well as for morbidity and mortality. Median follow-up was 3.8 years (0–13.9 years).
Results	Aortic root destructions (42 limited and 29 multiple lesions) were associated with early prosthetic valve endocarditis and delayed diagnosis (\geq 14 d), but not with mortality. There were 16 (13.8%) early (\leq 30 d) and 32 (27.6%) late ($>$ 30 days) deaths. Survival at 1, 5, and 10 years was 72 ± 4.3%, 56 ± 5.4%, and 46 ± 6.4%, respectively. The cumulative incidence of death, reinfection, and reoperation was 19.0% at 30 days and 36.2% at 1 year. Delayed diagnosis, concomitant procedures, and EuroSCORE II >20% were predictors for early mortality and need for mechanical circulatory support, age >70 years, and critical preoperative state were predictors for late mortality. In their absence, survival at 10 years was 70 ± 8.4%. Reinfections and reoperations occurred more frequently if \geq 1 risk factor for endocarditis and aortic root destructions were present. At 10 years, freedom from reinfection and reoperation was 89 ± 4.2% and 91 ± 4.0%.
Conclusions	The risks of death, reinfection, and reoperation are significant within the first year after surgery for aortic prosthetic valve endocarditis. Early diagnosis and aortic root destructions are the most important challenges, but advanced age, critical preoperative state, and the need for mechanical circulatory support determine long-term survival.
Keywords	Aortic prosthetic valve endocarditis • Aortic root destruction • Mortality • Morbidity

Introduction

Prosthetic valve endocarditis (PVE) is the most severe form of infective endocarditis (IE) and affects 1–6% of patients with valve prostheses necessitating surgical treatment foremost in complicated cases [1–7]. Obviously, various factors influence outcomes regarding mortality, morbidity, reinfection, and reoperation. Thus, we could recently demonstrate that cardiac and renal function, need for double valve replacement, and a prolonged preoperative interval in which patients were 20 left untreated while being symptomatic, predicted outcomes 21 in PVE patients including 92 aortic, 42 mitral, and 15 double 22 valve substitutes [7]. Aortic PVE is not only more prevalent, 23 but also frequently accompanied by aortic root destructions 24 and usually requires complex and challenging procedures 25 [8–10]. Therefore, we exclusively reviewed our experience 26 with surgery for aortic PVE during the most recent 15 years. 27 The objectives of this study were to identify predictors for 28

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patients' risk, and determine challenges of surgical **Q2** treatment.

31 Materials and Methods

32 **Patients**

A retrospective review of all patients undergoing surgery for PVE at the Department of Cardiovascular Surgery at Charité, Berlin, between January 2000 and December 2014 was performed (Institutional Ethics Committee approval EA1/032/13). We identified 116 consecutive patients (98 males, mean age 65.2 ± 12.7 years, range 28–82 years) who had redo-surgery for active aortic PVE (study cohort).

40 Surgical Treatment

All operations were performed as previously described [7]. 41 Infected prostheses were removed in total followed by metic-42 ulous debridement of abscesses and fistulas. The remaining 43 tissue was disinfected using povidone-iodine solution. 44 45 Pericardial (autologous, bovine or equine) patch repair was used for large abscess cavities, fistulas or tissue defects. 46 47 Free standing aortic root replacement as well as implantation of stentless valves in inclusion-cylinder or subcoronary 48 49 technique using two suture lines and patch repair of the aortic root were summarised as aortic root reconstruction. 50 Concomitant procedures were performed according to 51 standard techniques. Infected intravascular catheters were 52 53 removed before surgery.

54 Medical Treatment

Based on microbiological findings and guidelines, antibiotic/antimycotic treatment was continued for at least six weeks postoperatively. In cases of culture-negative PVE, the combination of vancomycin, rifampicin, and gentamicin was used. Patients presenting with recurrent PVE were treated accordingly. No patient received life-long antibiotic treatment.

61 Follow-up

Follow-up was obtained by registry office data, mail questionnaire and/or telephone interview. Complications were
confirmed by contact with the patient's cardiologist or family
physician. In case of re-hospitalisations, copies of the medical
reports were obtained.

Definitions

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As previously described, diagnosis of PVE was based on 68 clinical findings (fever, inflammatory syndromes), laboratory 69 testing (blood cultures, leukocytosis, levels of C-reactive 70 71 protein and procalcitonin), results of echocardiography as 72 well as intraoperative findings [3,7,11]. Prosthetic valve 03 endocarditis occurring within one year of surgery was clas-73 74 sified as early and beyond one year as late [3]. Endocarditis was culture-negative, if no microorganism could be identi-75 76 fied, neither in serial blood cultures nor in cultures from the 77 explanted material, despite characteristic signs of IE

(vegetations, periprosthetic destructions or pus). Perioperative risk was assessed by EuroSCORE II [12]. When IE exceeded the prosthetic valve causing dehiscence or aortic root destruction (i.e. purulent deformation and/or destruction of adjacent tissue, abscesses, and fistulas) it was considered locally uncontrolled. Extracardiac infections (pneumonia, skin and wound infections) and compromised host defense conditions (immune suppressive therapy, diabetes, dialysed chronic renal failure, alcoholism, and toxicomania) were classified as predispositions for IE [13]. Shock, acute renal failure, and the need for pharmacological circulatory support (catecholamines) or mechanical ventilation characterised the preoperative state as critical, following the definition of the EuroSCORE risk prediction model [12]. Early morbidity and mortality were defined by complications and death occurring within 30 days after surgery and late mortality by death occurring thereafter.

Statistical Analysis

Multiple imputation methodology of the statistical software package was used to impute missing data. Continuous data are presented as means and standard deviations or medians and range, respectively. Categorical variables are given as absolute and relative frequencies. The significance of the association between categorical data was examined by Fisher's exact test. Because of the explorative nature of the study, a correction for multiple testing was not performed. Survival as well as freedom from reinfection and reoperation were analysed using the Kaplan-Meier estimator and subgroups were compared by the Log-Rank-test. A stepwise logistic regression analysis (backward elimination, likelihood ratio) was used to determine independent risk factors for aortic root destruction as well as early (<30 d) morbidity and mortality. All variables from Table 1 (aortic root destruction) and Tables 1 and 2 (morbidity and mortality) with $p \le 0.25$ in the univariate analysis were included and results are presented as odds ratio (OR) with 95% confidence intervals (95%CI). A stepwise multivariable Cox regression analysis (backward elimination, likelihood ratio) including all variables from Tables 1 and 2 with $p \le 0.25$ in the univariate analysis was used to identify independent predictors of late (>30) mortality. Results are presented as hazard ratio (HR) with 95%CI. The assumption of proportional hazard was checked. The predictive performance of the risk models were assessed by determining the area under the receiver-operating characteristic curve and their calibration was evaluated by the Hosmer-Lemeshow goodness-of-fit test. All the statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA).

Results

Preoperative State

Baseline characteristics are listed in Table 1. Prosthetic valve129endocarditis affected 30 (25.9%) mechanical and 86 (74.1%)130

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