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Surgery for Bentall endocarditis: short- and midterm outcomes from a multicentre registry

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Abstract

OBJECTIVES: Endocarditis after the Bentall procedure is a severe disease often complicated by a pseudoaneurysm or mediastinitis. Reoperation is challenging but conservative therapy is not effective. The aim of this study was to assess short- and midterm outcomes of patients reoperated on for Bentall-related endocarditis.

METHODS: Seventy-three patients with Bentall procedure-related endocarditis were recorded in the Italian registry. The mean age was 57 ± 14 years and 92% were men; preoperative comorbidities included hypertension (45%), diabetes (12%) and renal failure (11%). The logistic EuroSCORE was 25%; the EuroSCORE II was 8%.

RESULTS: Preoperatively, 12% of the patients were in septic shock; left ventricular-aortic discontinuity was present in 63% and mitral valve involvement occurred in 12%. The most common pathogens were *Staphylococcus aureus* (22%) and *Streptococci* (14%). Reoperations after a median interval of 30 months (1–221 months) included a repeat Bentall with a bioconduit (41%), a composite mechanical (33%) or biological valved conduit (19%) and a homograft (6%). In 1 patient, a heart transplant was required (1%); in 12%, a mitral valve procedure was needed. The hospital mortality rate was 15%. The postoperative course was complicated by renal failure (19%), major bleeding (14%), pulmonary failure (14%), sepsis (11%) and multiorgan failure (8%). At multivariate analysis, urgent surgery

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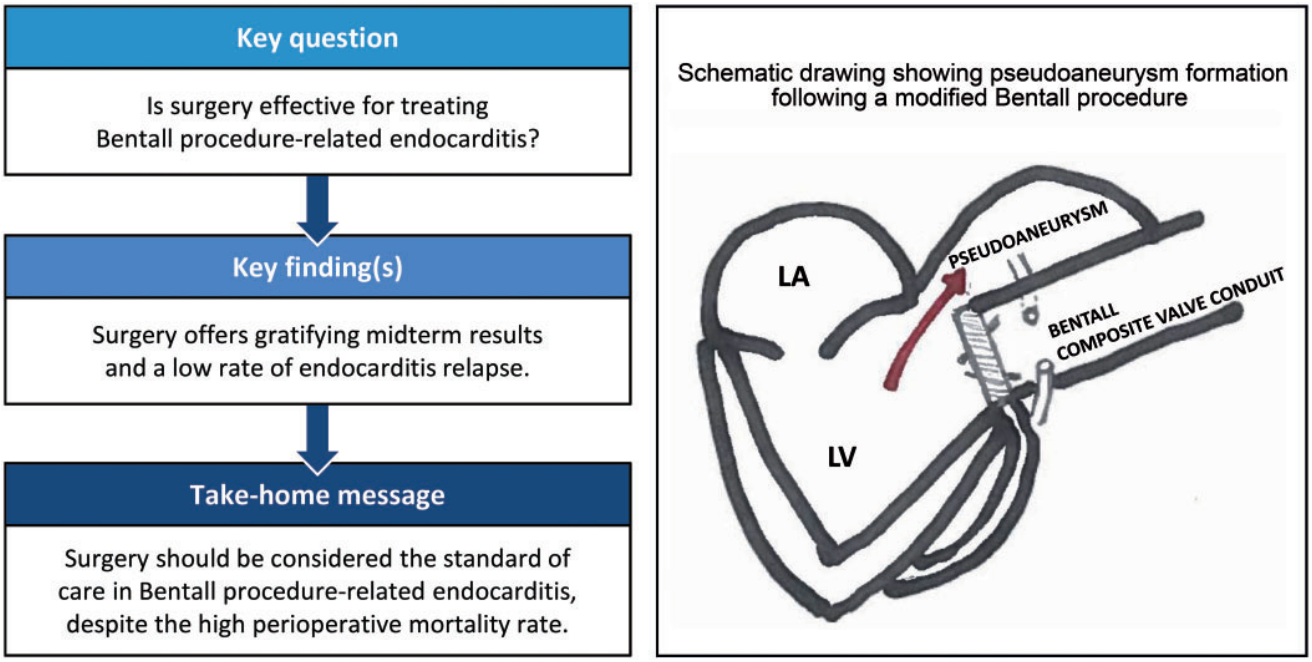
was a risk factor for early death [hazard ratio 20.5 (1.9–219)]. Survival at 5 and 8 years was 75 ± 6% and 71 ± 7%, with 3 cases of endocarditis relapse.

CONCLUSIONS: Surgery is effective in treating endocarditis following the Bentall procedure although it is associated with high perioperative mortality and morbidity rates. Endocarditis relapse seems to be uncommon.



Keywords: Endocarditis • Bentall procedure • Aortic valve • Aortic surgery • Aortic root

ABBREVIATIONS

CABG	Coronary artery bypass grafting
CI	Confidence interval
CT	Computed tomography
HR	Hazard ratio
IE	Infective endocarditis
MBP	Modified Bentall procedure
MOF	Multiorgan failure
MV	Mitral valve

INTRODUCTION

Infective endocarditis (IE) is becoming a prevalent issue among cardiovascular diseases [1–3]. Prosthetic graft infection has been reported in up to 3% of patients following aortic surgery [4]. Infection of composite aortic valve conduits used to replace the aortic valve and the ascending aorta in the modified Bentall procedure (MBP) [5, 6] represents a medical and surgical challenge due to the extensive involvement of the periprosthetic space and possibly of the coronary artery buttons. In such cases, conservative treatment with antibiotics alone is generally associated with a poor outcome [7, 8]. Surgical treatment is always advisable, but the few studies available on reoperation for IE after a previous MBP generally report high mortality (up to 75%) and morbidity rates [5, 6, 9]. Furthermore, the surgical timing, technical strategies and associated medical treatments are still being debated [5, 6, 9].

The aim of this study was to review data from the multicentre Italian Registry for Surgical Treatment of Native or Prosthetic Valve Infective Endocarditis [2], to analyse patients affected by IE following MBP and to assess their outcomes during early and midterm follow-up.

METHODS

Study population

A series of 73 patients who had an MBP from 1983 to 2018 and who were reoperated on from 2001 to 2019 because of IE were identified in the Italian registry and were included in this analysis. This retrospective study was approved by each institutional review board without the need for patient informed consent.

Definitions

The diagnosis of IE was based on the Duke University criteria [1]; although mediastinal infection could not be excluded in the absence of visible signs of an inflammatory process, we considered

mediastinitis only the presence of purulent material in the mediastinum requiring specific treatment. All the variables collected in the data set were defined according to the EuroSCORE parameters, whereas treatment and outcomes were reported following specific recommendations for endocarditis [10, 11]. The primary end point was hospital death, defined as death occurring within 30 days or any time during the first hospitalization. Secondary end points were late survival and incidence of major postoperative complications other than death, including endocarditis relapse, kidney injury, respiratory failure, multiorgan failure (MOF), sepsis, major bleeding, stroke, complete atrioventricular block, acute myocardial infarction, malignant ventricular arrhythmias and advanced cardiac failure.

Demographics

Main patient characteristics are summarized in Table 1. The mean age was 57 ± 14 years (range 23–85) and 67 patients were men (92%); 33 (45%) had hypertension, 16 (22%) had heart failure, 9 (12%) had diabetes, 8 (11%) had previous neurological thromboembolic lesions, 8 (11%) had chronic renal failure, 6 (8%) had chronic obstructive pulmonary disease, 4 (5%) had obesity, 2 (3%) had extracardiac arteriopathy and 2 (3%) had liver cirrhosis. The mean left ventricular ejection fraction was 56 ± 8%, and 2 (3%) had systolic pulmonary artery pressure >50 mmHg.

The initial operation consisted of MBP for an ascending aorta and/or root aneurysm with concomitant aortic stenosis or incompetence; in 2 patients (3%), the MBP was performed for aortic valve endocarditis. In 63 patients, the prior MBP was the first cardiac procedure, whereas 10 (14%) had already undergone a previous cardiac operation. Combined or single associated surgical procedures had been performed in 5 patients (7%): coronary artery bypass grafting (CABG) in 3, mitral valve (MV) replacement in 3 or MV repair in 1.

Table 1: Preoperative patient characteristics and diagnostic criteria

Preoperative data	
Patients	73
Age (years), mean ± SD	57 ± 14
Men gender, *n* (%)	67 (92)
Arterial hypertension, *n* (%)	33 (45)
Diabetes, *n* (%)	9 (12)
Atrioventricular block, *n* (%)	4 (5)
Obesity, *n* (%)	4 (5)
COPD, *n* (%)	6 (8)
Chronic heart failure, *n* (%)	16 (22)
Cirrhosis, *n* (%)	2 (3)
Chronic renal failure, *n* (%)	8 (11)
LV ejection fraction (%), mean ± SD	56 ± 8
Pulmonary artery pressure >50 mmHg, *n* (%)	2 (3)
Shock, *n* (%)	9 (12)
C-reactive protein (mg/l), mean ± SD	39 ± 78
White blood cells ($\times 10^3/\mu l$), mean ± SD	9 ± 6
Urgent, *n* (%)	31 (42)
Emergency, *n* (%)	4 (5)
Initial procedure	
Mechanical composite conduit, *n* (%)	58 (79)
Biological composite conduit, *n* (%)	15 (21)
Logistic EuroSCORE, mean ± SD	25 ± 20
EuroSCORE II, mean ± SD	8 ± 9
Diagnostic criteria, *n* (%)	
2-Dimensional echocardiography	72 (99)
CT	46 (63)
PET CT	18 (25)
SPECT	3 (4)
NMR angiography	3 (4)

COPD: chronic obstructive pulmonary disease; CT: computed tomography; LV: left ventricular; NMR: nuclear magnetic resonance; PET: positron emission tomography; SD: standard deviation; SPECT: single-photon emission computed tomography.

Surgical technique

All patients were reoperated on through a repeat median sternotomy. The type of technique was generally based on patient age, pathological findings and surgeon preference. In most cases, after accurate debridement of all necrotic tissues and foreign material, the infected field was irrigated with saline and diluted iodine solution and at times with antibiotics. In patients with extensive infection and evident signs of aggressive conduit involvement, conduit excision was always performed followed by a new MBP. In the presence of annular abscesses, left ventricular outflow or annular reconstruction was obtained with the liberal use of glutaraldehyde-fixed bovine pericardium. In cases complicated by mediastinitis, the procedure was completed by additional omentum transposition via a minilaparotomy incision. Associated CABG or MV procedures were usually performed prior to composite conduit replacement.

Follow-up

Follow-up of all patients was conducted in each participating centre through phone interviews; information was also gathered by reviewing charts and individual databases. Missing data were obtained by contacting the referring physicians or cardiologists. To obtain uniformity of data from each centre, efforts were made to elicit any prosthesis- and procedure-related complications occurring during the follow-up examination by adherence to the more recent guidelines [9]. Follow-up ended in March 2018 and was 100% complete; median follow-up was 56 months (range 1–178 months).

Statistical analysis

Continuous variables are presented with their mean (±standard deviation) or median (min–max) values, whereas the absolute frequency and percentages are reported for categorical variables. A parsimonious logistic binary regression model was built to identify risk factors for early death and major complications. All the preoperative and operative variables were tested at univariate analysis, and those with a *P*-value <0.2 were initially included in the model. Then a backwards selection approach was used. Results were reported as odds ratios with 95% confidence intervals (CIs). Actuarial curves for survival and freedom from major complications were constructed using the Kaplan–Meier method. The multivariate proportional hazard Cox regression model was used to estimate the risk factors for late deaths. Results were reported as hazard ratios (HRs) with 95% CI. The final models were internally validated using bootstrapping with the analysis of distortion of C-statistics. Analyses were performed with IBM SPSS Statistics 22 for Microsoft Windows (IBM Corp., Armonk, NY, USA).

RESULTS

Clinical presentation and diagnosis of infective endocarditis

Nine patients (12%) were in septic shock preoperatively; 7 (10%) required preoperative intubation; and 1 (1%) had intra-aortic balloon implantation; 31 patients (42%) underwent urgent and 4 (5%), emergency reoperations. Four patients (5%) presented with a complete atrioventricular block. Clinical diagnosis of IE was made according to recent guidelines [10] and confirmed by means of 2-dimensional echocardiography in 99% of patients, by computed tomography (CT) in 63% and by positron emission CT in 25%, as a single or a combined test. Single-photon emission CT or nuclear magnetic resonance angiography was used in only 3 cases.

Staphylococcus aureus was identified as the infective agent in 16 patients (22%), *Streptococci* in 11 (15%), *Staphylococcus* other than *aureus* in 8 (11%), *Enterococcus faecalis* in 3 (4%), *Pseudomonas aeruginosa* in 2 (3%), fungi in 1 (1%) and other pathogens in 14 (19%). Figure 1 summarizes the results of blood cultures, showing that 23% of the blood cultures had negative results.

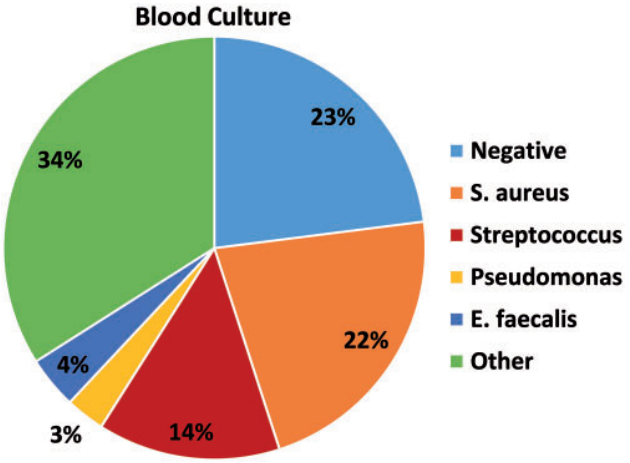


Figure 1: Results of blood cultures.

Operative data

Reoperation for IE was performed after a median interval of 30 months (range 1–221 months) from the original MBP; only one patient underwent a redo operation within the first postoperative month. The main operative data are presented in Table 2. The median aortic cross-clamp time was 138 min (range 70–297 min), and the median cardiopulmonary bypass duration was 183 min (range 110–523 min).

Intraoperative findings revealed the severe involvement of cardiac structures in most cases, generally with a combination of lesions: left ventricular-aortic discontinuity was present in the majority of cases (46 patients, 63%), periaortic abscesses in 43 patients (59%) (Fig. 2), pseudoaneurysms in 26 (36%), vegetations in 16 (22%), cusp perforations or fistulas in 5 (7%), whereas mediastinitis, with the presence of purulent material, occurred in 3 patients (4%).

At reoperation, a repeat MBP was performed using a composite conduit with a mechanical prosthesis in 24 patients (33%) and with a bioprosthesis in 14 (19%). The following mechanical conduits were used: St. Jude Medical (Abbott Laboratories, Abbott Park, IL, USA) in 11 patients, Carbomedics Carboseal (LivaNova, Saluggia, Italy) in 12 and Sorin Bicarbon (LivaNova) in 1. The following composite conduits incorporating a stented biological valve were used: Mitroflow (LivaNova) in 8 cases, Perimount (Edwards Lifesciences, Irvine, CA, USA) in 5 and Abbott Trifecta (Edwards Lifesciences) in 1. In addition, 30 patients (41%) received a bioconduit: 29 patients a BioIntegral pericardial (BioIntegral Surgical, Inc., Mississauga, ON, Canada) and 1 an Edwards Prima Plus stentless porcine root (Edwards Lifesciences). Furthermore, in 4 patients (5%) an aortic homograft was used whereas a heart transplant was performed in 1 (1%) after 5 previous unsuccessful MBPs. A combined procedure was performed in 19 cases (26%): 11 patients had in addition CABG; 6 had MV replacement and 3 had MV repair. Mean prosthesis size in composite conduits was 24 ± 5 mm. Furthermore, in the 3 patients with overt mediastinitis, an omental flap was used.

Table 2: Operative data and intraoperative findings

Operative data	
Cardiopulmonary bypass time (min), median	187
Aortic cross-clamp time (min), median	138
Type of composite graft, *n* (%)	
Mechanical valve conduit	24 (33)
Bioconduit	30 (41)
Biological conduit with stented prosthesis	14 (19)
Homograft	4 (5)
Heart transplant	1 (1)
Mitral valve replacement	6 (8)
Mitral valve repair	3 (4)
Operative findings, *n* (%)	
Left ventricle–aortic discontinuity	46 (63)
Abscess	43 (59)
Pseudoaneurysm	26 (36)
Vegetations	16 (22)
Cusp perforation	5 (7)
Fistula	5 (7)
Mediastinitis	3 (4)

Early outcome

There were 11 early deaths (15%) (Table 3) with an expected mortality rate according to logistic EuroSCORE of 25%, to EuroSCORE II of 8% and to EndoSCORE of 14%, with an observed/expected ratio of 1.1 [2, 11]. Causes of early deaths were MOF in 4 cases, surgical bleeding in 3, sepsis in 2 and sudden cardiac death in 1; in 1, the cause of early death could not be ascertained. The median postoperative stay was 17 days (6–147 days); during this interval, 28 patients (38%) experienced 1 or more major complication: renal failure in 14 (19%), need for dialysis in 12, major bleeding in 10 (14%), need for surgical revision in 7, respiratory insufficiency in 10 (14%), sepsis in 8 (11%) and MOF in 6 (8%) (Table 4).

At multivariate analysis, urgent or emergency surgery was found to be a risk factor for early death [HR 12 (1.4–104) and HR 39.1 (2.25–679.3), respectively].

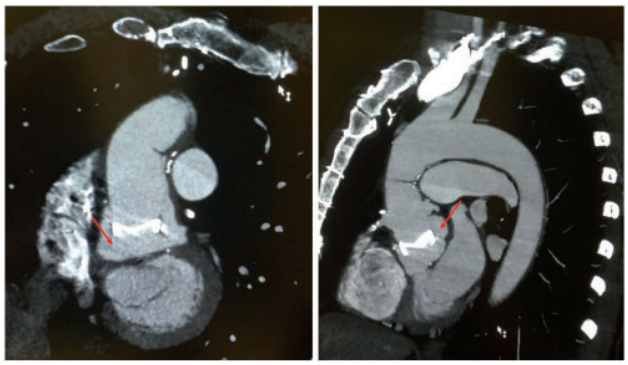


Figure 2: Computed tomography scans showing pseudoaneurysm formation at the proximal suture line.

Table 3: Early outcomes

Early outcomes	
Number of patients	73
30-Day deaths, *n* (%)	11 (15)
Intensive care unit stay (days), median (range)	7 (1–60)
Hospital stay (days), median (range)	17 (6–147)
Major complications, *n* (%)	28 (38)
Major bleeding, *n* (%)	10 (14)
Surgical revision, *n* (%)	7 (10)
Sepsis, *n* (%)	8 (11)
Multiorgan failure, *n* (%)	6 (8)
Pulmonary failure, *n* (%)	10 (14)
Haemorrhagic stroke, *n* (%)	2 (3)
Thromboembolism, *n* (%)	3 (4)
Renal failure, *n* (%)	14 (19)
Dialysis, *n* (%)	12 (16)

Late outcome

There were 6 late deaths caused by MOF in 3 (50%), cardiac failure in 1 (17%), sepsis in 1 (17%) and unknown cause in 1 (17%). Actuarial survival at 5 and 8 years was 75 ± 6% and 71 ± 7%, respectively (Fig. 3). At multivariate analysis, combined surgery [HR 5.6 (1.4–30.3)] and a C-reactive protein level of 1.01 (1–1.02) were risk factors for late death. Three patients developed recurrent IE after 16, 26 and 126 months, respectively. Two were reoperated on with implantation of a bioconduit; 1 died of sepsis.

DISCUSSION

MBP represents the gold standard treatment in patients with aneurysms of the ascending aorta and aortic valve stenosis or regurgitation not amenable to repair [12]. Long-term follow-up data indicate excellent survival and freedom from major complications following the MBP using either a mechanical or biological composite conduit [7, 8].

IE following graft replacement of the ascending aorta is an uncommon but challenging complication because it can lead to pseudoaneurysm or abscess formation with the possible occurrence of mediastinitis and devastating consequences [7, 8, 13–16]. Also after MBP, composite valve conduit infection is substantially uncommon with no cases of IE observed at long-term

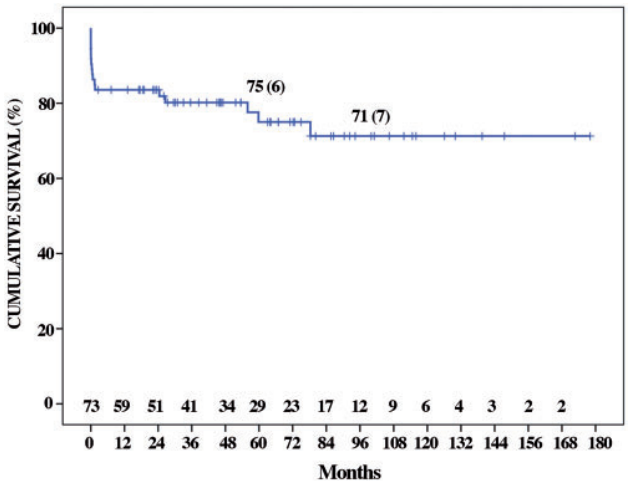


Figure 3: Actuarial survival. Numbers on the horizontal axis indicate patients at risk at each postoperative interval.

follow-up in a large series using mechanical valve conduits [12]. In the present report, which analysed data from a national multicentre registry, diagnosis of IE after MBP was made in only 2% out of >4000 patients with prosthetic endocarditis [1, 2]. In most cases, severe involvement of cardiac structures was present, mainly characterized by disconnection of the mitro-aortic continuity with periaortic abscesses, as observed in 63% of patients. These lesions can further evolve into an aortic pseudoaneurysm, which may lead to compression and erosion of mediastinal structures and eventual rupture with massive bleeding. An early operation is usually advocated to prevent these complications [17]. However, concern exists regarding the preoperative clinical conditions of these patients, presenting usually in heart failure and sepsis. Furthermore, surgical repair poses technical challenges due to the difficulty of handling infected frail tissues while reimplanting the coronary ostia and securing the new valved graft into the left ventricular outflow tract or the risks associated with a redo sternotomy in the presence of extensive cardiac and vascular tissue disruption. Some series indicated a short interval between the initial operation and IE; in other experiences the risk of aortic graft infection has been demonstrated to occur even many years after surgery [7, 8, 13–16]. Our findings indicate a large range of time intervals between MBP and onset of IE with a median range of 30 months from the initial procedure; only one patient required a second MBP within the first 4 postoperative weeks whereas another was reoperated on >18 years later. These data confirm a persistent risk of IE, justifying continuous patient monitoring following an MBP.

Diagnosis of IE following MBP is not always simple and straightforward. Nevertheless, a precise definition of the lesions and demonstration of involvement of specific intracardiac structures are mandatory before surgery for correct timing and surgical planning and to stratify each individual surgical risk. Generally, it is suggested that a multimodality diagnostic pathway should be followed, consisting of a mutually advantageous combination of various imaging techniques [9]. Among these, multislice CT angiography remains the best single and most specific tool for accurate assessment of the prosthetic aorta, the anastomotic sites and abscess detection; however, in the early postoperative period, CT angiography might be non-specific with the need to switch to other imaging modalities such as single-photon emission CT or nuclear magnetic resonance.

Table 4: Results of multivariated analysis of eraly mortality and major complications

Logistic regression	OR	Lower 95% CI	Upper 95% CI	*P*-value
Early deaths				
Negative blood or specimen culture	3.274	1.002	14.568	0.049
Elective surgery (reference)				
Urgent surgery	11.98	1.381	104.259	0.024
Emergency surgery	39.13	2.254	679.269	0.012
Early major complications				
Urgent/emergency surgery	2.372	1.011	5.987	0.048
Staphylococcus aureus or *Enterococcus faecalis*	2.704	1.047	8.625	0.041
Abscess	2.306	1.013	7.158	0.048

CI: confidence interval; OR: odds ratio.

The role of echocardiography in this setting has often been debated; it is a readily available technique that can be performed at the bedside, particularly in severely ill patients, to evaluate valve function, but its effectiveness in analysing accurately the perigraft area has been questioned [9]. However, the present experience clearly showed how echocardiography was the preferred diagnostic technique. CT scans were reported in only 63% of patients, and more advanced multimodality images, in only 25% of them.

The treatment of an infected valved conduit is still a matter of debate. Coselli *et al.* [5] obtained successful results with prosthetic graft replacement. Gott *et al.* [18] reported a series of 7 patients treated conservatively with only a 29% survival rate, whereas later they successfully treated 5 patients with Marfan syndrome with early IE using antibiotics alone. Others have used a conservative, graft-sparing surgical strategy comprising open surgical disinfection followed by omentum flap coverage of the ascending aorta and arch graft with good immediate outcomes but limited long-term follow-up [14–16]. In the present series, none of the patients were managed with antibiotics alone or with a graft-sparing approach. Indeed, all subjects were treated with composite graft excision and repeat MBP because the common policy of all centres in the registry was to eliminate all infected material to obtain compete eradication of the infection. From the registry data it appears that a CABG was required in 5 patients due to the complexity of coronary ostia mobilization whereas no Cabrol procedures have been reported.

Infected Bentall grafts have often been replaced with new synthetic grafts containing a mechanical prosthesis with generally good results with low rates of IE recurrence [4–6]. Ralph-Edwards *et al.* [19] reported a 91% early survival rate despite the need for complex left ventricular outflow tract reconstruction with glutaraldehyde-fixed bovine pericardium, albeit with a 25% incidence of recurrent prosthetic valve IE. Good results were reported also by Hagl *et al.* [17] in 23 patients with only one case of IE relapse. Other procedures to reduce the risk of IE recurrence have been proposed such as the use of mediastinal irrigation with an antibacterial solution and coverage of the graft with viable omentum and muscular flap reconstruction [16].

In our series, the re-MBP was the preferred technique, using a mechanical conduit in 33% and a biological conduit in 19% of cases, the latter being usually constructed by suturing a stented bioprosthesis inside a synthetic graft. It has been shown that cryopreserved homografts are associated with improved outcomes, including lower relapse rates, fewer postoperative complications and better survival rates despite a limited number of patients reported [1, 20]. Indeed, homografts are more resistant to infection, perhaps because of better antibiotic penetration and the inherent attraction of immune cells; furthermore, they are more pliable and enable the graft to conform better to the debrided annulus. However, limited availability, early calcific degeneration and limited length in case of the need of a combined arch replacement represent major disadvantages.

Xenograft roots have emerged as another option for patients with infected MBP. In our series, a bioconduit was generally preferred to a homograft (41% vs 5%). Even if xenograft roots are not recommended in cases of extensive annular debridement because of possible distortion of the valve, we did not observe any case of neoaortic valve regurgitation [21]. Moreover, reports on the Shelhigh BioConduit revealed a relatively high rate of deaths and reoperations due to endocarditis, pseudoaneurysms and structural valve failure, thus indicating the need for careful echocardiographic follow-up in these patients [22–24]. Czerny *et al.* [25] proposed an alternative orthotopic vascular reconstruction using self-made xenopericardial tube grafts that provided excellent results with regard to durability and freedom from reinfection and reoperation.

Interestingly, in 1 young patient who was reoperated on 5 times using different conduits, a heart transplant was eventually required and successfully performed because a further MBP was considered unfeasible.

Regardless of the type of technique used, IE after MBP remains challenging and high-risk from a surgical standpoint. The frequently compromised clinical status of the patient at presentation and the prolonged ischaemic times required during repair increase the myocardial damage related to the septic shock, resulting in early postoperative depression of biventricular contractility, and represent additional important risk factors for early death [26]. Surgical timing in patients with IE following MBP is a still debated issue [5, 6, 9]. From this multicentre study, we were unable to provide further meaningful information because the decision was mostly based on patient clinical presentation and the policies of each centre. However, because almost 50% of patients were operated on urgently or as emergencies, an aggressive attitude in this peculiar patient subset appears justified, especially in the presence of uncontrolled infection, septic shock, cardiac failure or critical anatomical or functional lesions. Indeed, in the present series, the operative mortality rate of 15% was accurately predicted by the EndoSCORE [2, 27], the most important risk factor for early death being an urgent or emergency operation in patients mostly with heart failure and uncontrolled IE. Negative results from blood or specimen cultures were also a risk factor for early death, a finding that does not have a clear clinical

explanation, particularly since specific data on the type and duration of antibiotic treatment prior to reoperation were not available from the registry. Survival analysis indicated that the risk of death was significant within the first month after the operation. Thereafter, the survival curve remained stable with 5- and 8-year survival rates of 75 ± 6% and 71 ± 7%, respectively.

Reoperation for MBP IE was associated with some expected complications such as major bleeding and acute kidney and pulmonary failure. Systemic inflammation, with pro-inflammatory cytokine activation, is largely recognized to compromise multiorgan function, particularly the coagulation cascade and respiratory and renal functions [5, 6, 25].

Limitations

This study has evident limitations because it is a multicentre, retrospective, non-randomized analysis. The data reported belong to a large registry comprising many Italian centres, with over 4000 patients included, of whom those with IE following an MBP represent only 2% of the total. Results obtained from such registries may be difficult to analyse because surgical techniques and indications varied among groups during the study period—an interval of more than 2 decades. Nevertheless, a uniform database has been adopted by all participants with an effort to collect the most pertinent information to obtain meaningful data on this specific issue.

CONCLUSION

In conclusion, the results from this multi-institutional registry indicated that IE represents a complex problem, especially in cases of aggressive infection and destruction of the aortic annular and periannular structures. The best treatment is still being debated, but it seems that removal of the composite conduit and repeat MBP appear to be the most effective options to allow IE eradication. The results of reoperation, despite a high early mortality rate, are gratifying in the midterm with 75 ± 6% and 71 ± 7% survival rates at 5 and 8 years postoperatively, with a low incidence of IE recurrence, and they are not influenced by the type of conduit used at a repeat MBP.

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Author contributions

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