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Surgical therapy in patients with active infective endocarditis: seven-year single centre experience in a subgroup of 255 patients treated with the Shelhigh® stentless bioprosthesis

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Abstract

Objective: We investigated outcomes after surgical therapy in patients with active infective endocarditis (AIE) with regard to survival in relation to surgical urgency, valve position, number of valves implanted and abscess formation. We aimed to identify independent risk factors for early mortality. **Methods and results:** Two hundred and fifty-five patients received Shelhigh® bioprostheses between February 2000 and March 2007. A total of 74.1% had native and 25.9% prosthetic AIE. Surgery was regarded as urgent in 57.3% and as an emergency procedure in 38.4%. There was a highly significant difference in survival rate between patients who were operated on urgently versus in an emergency ($p < 0.0001$), between single and double valve replacement ($p = 0.0206$) and between patients with and without abscess formation ($p = 0.0245$). There were two cases of early reinfection (0.78%) and six of late reinfection (2.35%) leading to re-operation. **Conclusions:** The survival of patients differs significantly in dependence on their surgical urgency. Better outcome could have been achieved if patients had been referred earlier for surgery and operated upon before heart failure or septic shock developed. Long-term survival was better in patients without abscess formation. The low reinfection rate of Shelhigh® bioprostheses in AIE is promising and the early and mid-term results achieved need to be verified in the long-term course.

Keywords: Infective endocarditis; Surgery; Bioprosthesis

1. Introduction

Despite improvements in medical care, the incidence of left-sided active infective endocarditis (AIE) has remained unchanged over the past few decades. It is reported to affect a median of 3.6—5.4/100,000 persons per year, increasing in individuals over 65 years old to 15.0/100,000 persons per year, with a male:female ratio of 2:1. This unchanging incidence may be explained by changes in both the spectrum of causative organisms and in the patients affected [1]. New groups at risk of endocarditis have emerged, for example the increasingly aging population with heart valve sclerosis, patients with prosthetic valves, those exposed to nosocomial infections, haemodialysis patients and intravenous drug-abusers [2].

Clinical variability and complexity of AIE, which requires individualised, patient-tailored assessment and therapy [3], makes standardisation and comparison of patients' therapy difficult therefore the published studies are mostly not comparable with each other because of their heterogeneity [4].

In the period from January 1986 to March 2007 there were 1077 patients operated on due to AIE at the Deutsches Herzzentrum Berlin. To exclude the effects of different valve types on the outcome after an endocarditis operation, we analysed a subgroup of AIE patients ($n = 255$) in whom the same bioprosthesis (Shelhigh®) was implanted between February 2000 and March 2007. The retrospective study analysed both prospectively updated data and patients recently operated upon.

The aim of this study was to investigate the outcome after surgical therapy in these AIE patients, particularly with regard to the survival in relation to surgical urgency, valve position, the number of implanted valves and abscess formation. One other objective was to analyse the reinfection rate of the implanted prostheses in regard to our previous findings in a larger group of patients over a longer period [5,6].

Finally, goals of this study were to find clinical differences between early survivors and non-survivors (≤30 days) and to

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identify independent risk factors for early mortality by application of univariate and multivariate analysis.

2. Patients and methods

2.1. Patient population

An overview of the patient population is given in Table 1. Between February 2000 and March 2007, 255 patients with AIE (186 men, 69 women, median age 59 years) received implantation of a Shelhigh® stentless valve prosthesis. In 186 (72.9%) patients native valve endocarditis and in 69 (27.1%) prosthetic valve endocarditis was present. A large proportion of patients were referred to our department in a condition of cardiac decompensation: 59 (23.1%) patients were intubated, 51 (20.0%) had protracted septic shock and 62 (24.3%) required high doses of catecholamines. The operation was performed electively in 11 (4.3%), urgently in 146 (57.3%) and as an emergency procedure in 98 (38.4%) patients. Staphylococci (36.4%) and Streptococci (26.6%) were the most common micro-organisms found in the blood culture with a high percentage of *St. aureus* (23.5%). Follow-up was completed in all survivors by telephone contact with the patient, by analysing standardised mail questionnaires sent to the patients, by consulting the population registry and by contacting peripheral hospitals.

The median follow-up time was 0.91 years (range 0 days to 7.1 years), with 469.4 patient years.

The study population of 255 patients represents 23.7% of all patients operated on at our institution due to AIE over the past 20 years and 48.9% of all surgical endocarditis patients for the study period (n = 521).

Table 1
Patient population

Period	February 2000 to March 2007
Patients with AIE	n = 255
Men	n = 186 (72.9%)
Women	n = 69 (27.1%)
Age	
Median	59 years
Mean	55.7 years
Range	17–85 years
Endocarditis	
Native AIE	n = 189 (74.1%)
Prosthetic AIE	n = 66 (25.9%)
Preoperative status	
Intubation	n = 59 (23.1%)
Septic shock	n = 51 (20.0%)
High-dose catecholamines	n = 62 (24.3%)
Operation	
Elective	n = 11 (4.3%)
Urgent	n = 146 (57.3%)
Emergency	n = 98 (38.4%)
Blood micro-organisms	
Staphylococci	n = 93 (36.4%)
St. aureus	*n = 60 (23.5%)*
Streptococci	n = 68 (26.6%)
Viridans streptococci	*n = 20 (7.8%)*
Enterococcus species	n = 30 (11.7%)
Culture negative	n = 47 (18.4%)
Others	n = 17 (6.6%)
Follow-up	
Median	0.91 years
Range	0 day to 7.1 years
Patient years	469.4 years

Indication	No. of patients
Progressive heart failure	154 (60.4%)
+Recurrent septic embolisms	45 (17.6%)
+Vegetations	49 (19.2%)
+Therapy-resistant septic infections	58 (22.7%)
Abscess formation	119 (46.6%)
Aortic	84 (32.9%)
Mitral	25 (9.8%)
Aortic + mitral	10 (3.9%)
Therapy-resistant septic infection	92 (36.1%)
Recurrent septic embolism	79 (30.9%)
Large (>2 cm) obstructive vegetations	74 (29.1%)
Others	8 (3.1%)

AIE: active infective endocarditis.

2.2. Indications for surgery and operations performed

An overview of operative indications during the acute phase of AIE is given in Table 1.

In general patients had several indications for surgery during antibiotic treatment for AIE. The majority had to be operated on due to progressive heart failure in combination with recurrent septic embolisms, vegetations or therapy-resistant infections. One hundred and nineteen patients (46.6%) developed an abscess in the aortic and mitral valve.

An overview of the number of Shelhigh® bioprostheses implanted and their position is given in Table 2.

In the 255 patients 269 operations were performed with 307 Shelhigh® valve implantations. Two hundred and two (79.2%) patients received single valve and 53 (20.8%) double valve replacement. Thirty-eight patients received concomitant CABG operation.

2.3. Definition of active infective endocarditis

AIE was defined on the basis of vegetations or abscess shown in the echocardiogram and accompanied by positive blood cultures or intraoperatively harvested valve cultures, on the basis of clinical evidence of persistent sepsis or recurrent septic embolism, or on the basis of the intraoperative diagnosis.

Table 2
Numbers of Shelhigh® bioprostheses implanted and their position

Valve type	No.
Single valve implantation	212
Aortic valve	116
Aortic conduit	26
Mitral valve	64
Tricuspid valve	6
Double valve implantation	57
Aortic and mitral valve	30
Left- and right-sided implantation	8
Others	19

2.4. Statistical analysis

SPSS for Windows version 12.01 was used. Qualitative data are presented as number (n) and percent. For quantitative data means ± standard error were calculated. Analysis of survival and freedom from end-points was performed according to Kaplan–Meier estimation. Comparison of survival in different patient groups used the Gehan test.

A logistic regression model was applied to investigate possible risk factors for early mortality (<30 days). First all possible risk factors were evaluated with a univariate approach, followed by multivariate logistic regression with backward elimination procedure.

Survivors and non-survivors were compared by Pearson's χ^2-test or Student's t-test accordingly. A value of $p < 0.05$ was considered statistically significant.

3. Results

3.1. Overall survival and survival in relation to surgical urgency

The survival curves for the whole study population (n = 255) and the comparison between the patients operated on electively (n = 11, 4.3%) or urgently (n = 146, 57.3%) and those operated on in an emergency (n = 98, 38.4%) are given in Fig. 1.

The 30-day, 1-, 3- and 5-year survival for the whole study population was 76.5% ± 2.7%, 59.9% ± 3.2%, 52.9 ± 3.4% and 46.8% ± 4.0%, respectively.

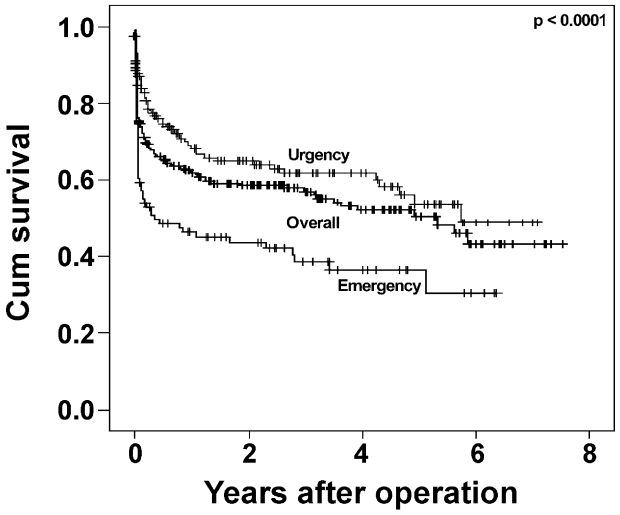
There was a non-significant difference between the survival of native endocarditis patients compared to those with prosthetic endocarditis. The 30-day, 1-, 3- and 5-year survival for the native endocarditis population was 77.8% ± 3.0%, 63.4% ± 3.6%, 54.8 ± 4.0% and 51.7% ± 4.3% compared to 72.7% ± 5.5%, 49.7% ± 6.4%, 47.6 ± 6.4% and 36.9% ± 7.4% for the prosthetic group, respectively (p = 0.1371).

We found a highly significant difference between the survival rates of patients with elective and urgent surgery versus those operated on in an emergency: the 30-day, 1-, 3- and 5-year survival rate after elective and urgent operation was 87.3% ± 2.7%, 68.3% ± 4.0%, 61.8% ± 4.2% and 53.7% ± 5.3% respectively, in comparison to 59.2% ± 5.0%, 46.4% ± 5.1%, 38.8% ± 5.3% and 36.5% ± 5.5% after emergency operation ($p < 0.0001$). Analysis of the survival curve shows a particularly clear difference between the two groups in the first 30 days.

There were six (2.3%) intraoperative deaths, five due to septic multiorgan failure and one due to myocardial failure. Main causes of the 60 (23.5%) early deaths (≤30 days) were septic multiorgan failure in 46 (76.6%), myocardial failure in 6 (10.0%), cerebral bleeding in 5 (8.3%), haemorrhagic shock in 2 (3.3%) cases and pulmonary emboli in 1 (1.6%) case.

3.2. Survival in relation to valve position and comparison of single versus double valve replacement

The survival curves showing the relationship with valve position and the comparison of single and double valve replacement in patients with left-sided AIE are given in Fig. 2.



Urgency

	Survival (%)	pts. at risk	No. of events
30 days	87.3 ± 2.7	134	20
1 year	68.3 ± 4.0	85	47
3 years	61.8 ± 4.2	48	54
5 years	53.7 ± 5.3	21	58

Overall

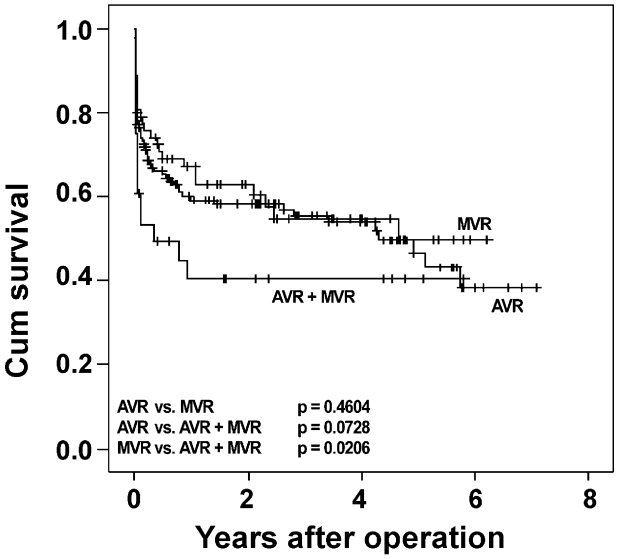
	Survival (%)	pts. at risk	No. of events
30 days	76.5 ± 2.7	191	60
1 year	59.9 ± 3.2	124	99
3 years	52.9 ± 3.4	69	111
5 years	46.8 ± 4.0	27	116

Emergency

	Survival (%)	pts. at risk	No. of events
30 days	59.2 ± 5.0	57	40
1 year	46.4 ± 5.1	39	52
3 years	38.8 ± 5.3	21	57
5 years	36.5 ± 5.5	6	58

Fig. 1. Overall survival and survival in relation to surgical urgency in patients with active, infective endocarditis after Shelhigh® implantation.

There was no significant difference between the survival rates of patients after aortic valve (AVR) or mitral valve replacement (MVR): the 30-day, 1-, 3- and 5-year survival rate after AVR was 76.3% ± 3.7%, 59.1% ± 4.4%, 55.6% ± 4.6% and 46.4% ± 5.8%, respectively, in comparison to 80.7% ± 5.0%, 67.9% ± 6.1%, 54.8% ± 7.1% and 49.8% ± 8.0% after MVR (p = 0.46). Compared to all study patients with single valve replacement, patients with double valve replacement (AVR and MVR) had a significantly worse survival rate: the 30-day survival rate after AVR and MVR was 60.7% ± 9.2% and for 1-, 3- and 5-year it remained at 40.4% ± 9.7% (p = 0.0336). Comparison of the survival curves of single versus double valve replacement showed a non-significant trend toward better survival after AVR alone (p = 0.0728) and a highly significant better survival after MVR alone (p = 0.0206)



AVR

	Survival (%)	pts. at risk	No. of events
30 days	76.3 ± 3.7	100	32
1 year	59.1 ± 4.4	65	53
3 years	55.6 ± 4.6	39	56
5 years	46.4 ± 5.8	14	60

MVR

	Survival (%)	pts. at risk	No. of events
30 days	80.7 ± 5.0	50	12
1 year	67.9 ± 6.1	33	20
3 years	54.8 ± 7.1	17	25
5 years	49.8 ± 8.0	6	26

AVR + MVR

	Survival (%)	pts. at risk	No. of events
30 days	60.7 ± 9.2	16	11
1 year	40.4 ± 9.7	9	16
3 years	40.4 ± 9.7	5	16
5 years	40.4 ± 9.7	2	16

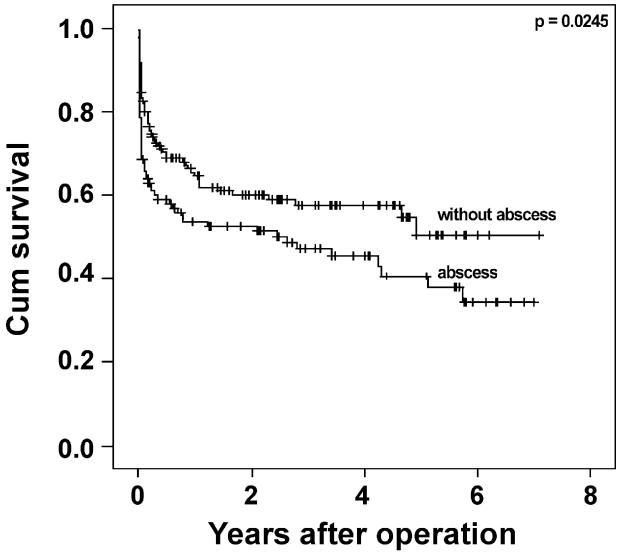
Fig. 2. Survival in relation to valve position and comparison of single versus double valve replacement in patients with active, infective endocarditis after Shelhigh® implantation.

(Fig. 2), but the patients at low risk for the double valve replacement group has to be taken into consideration. A particularly clear difference is seen between the two groups in the first 30 days and in the period of between 1 month and 1 year.

3.3. Survival in relation to abscess formation

The survival curves in relation to abscess formation are shown in Fig. 3.

From the study population of 255 patients, 119 (46.6%) showed abscess formation. Of these, 84 patients developed isolated abscess of the aortic valve, 25 patients of the mitral valve and 10 patients abscess formation on both valves (Table 1). Comparing the groups with and without abscess, the figures for better survival in patients without abscess were highly significant: the 30-day, 1-, 3- and 5-year survival for patients without abscess formation was 82.6% ± 3.2%, 64.6% ± 4.1%, 57.5% ± 4.5% and 50.4% ± 6.2%, respectively, in comparison to 68.5% ± 4.4%, 53.7% ± 4.8%, 47.1% ± 5.1% and 40.6% ± 5.6% in patients with abscess formation ($p = 0.0245$).



Without abscess

	Survival (%)	pts. at risk	No. of events
30 days	82.6 ± 3.2	118	25
1 year	64.6 ± 4.1	75	49
3 years	57.5 ± 4.5	40	56
5 years	50.4 ± 6.2	11	58

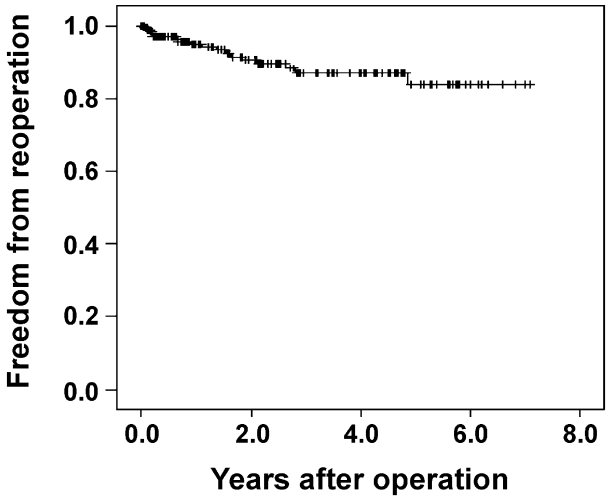
Abscess

	Survival (%)	pts. at risk	No. of events
30 days	68.5 ± 4.4	74	35
1 year	53.7 ± 4.8	49	50
3 years	47.1 ± 5.1	29	55
5 years	40.6 ± 5.6	16	58

Fig. 3. Survival in relation to abscess formation in patients with active, infective endocarditis after Shelhigh® implantation.

3.4. Reinfection after Shelhigh® implantation

A total of 22 out of 255 patients (8.6%) developed reinfection following Shelhigh® implantation. Of these, 17 (6.6%) had to be re-operated upon and 5 (2.0%) were treated conservatively. In the conservatively treated group there was one case of early (39 days) and four of late reinfection (76—330 days, mean 139 days) with four of these patients being i.v. drug-abusers. In this high risk group three patients, all drug addicts, died due to septic multiorgan failure; the other two patients could be discharged home.



	Freedom from reop.	pts. at risk	No. of events
30 days	100	189	0
1 year	94.4 ± 1.8	121	8
3 years	87.0 ± 3.2	65	16
5 years	83.8 ± 4.4	24	17

Fig. 4. Freedom from re-operation due to reinfection in patients with active, infective endocarditis after Shelhigh® implantation.

In the 17 patients with re-operation there were two early reinfections (<60 days) at the 41st and 59th postoperative day (0.78%) with the same micro-organism and six late reinfections (2.35%) up to 1 year postoperatively (73 — 329 days, mean 191 days).

Fig. 4 shows the freedom from re-operation due to reinfection: the 30-day, 1-, 3- and 5-year rates were 100%, 94.4% ± 1.8%, 87.0% ± 3.2% and 83.8% ± 4.4% for the whole population.

In the comparison between the native ($n = 19$) and prosthetic endocarditis ($n = 3$) patients there was a non-significant difference between the freedom from reinfection rate of both groups. The 30-day, 1-, 3- and 5-year freedom from reinfection for the native endocarditis population was 100%, 95.9% ± 1.8%, 85.3 ± 4.0% and 80.3% ± 6.1% compared to 100%, 91.4% ± 4.8%, 91.4 ± 4.8% and 91.4% ± 4.8% for the prosthetic group, respectively ($p = 0.8356$).

3.5. Clinical differences between early survivors and non-survivors (≤30 days)

Clinical differences between early survivors and non-survivors (≤30 days) after Shelhigh® implantation calculated using Pearsons χ^2-test are given in Table 3.

Comparing the two groups the following statistically significant clinical differences were found: early non-survivors more often underwent emergency operation ($p = 0.001$) and showed greater abscess formation intra-operatively ($p = 0.029$). Preoperatively more non-survivors were on artificial ventilation ($p \leq 0.001$) showed more pulmonary oedema ($p \leq 0.002$), developed more septic shock ($p \leq 0.001$), were more often on high-dose catecholamines ($p \leq 0.001$) and had more renal insufficiency ($p = 0.016$) and diabetes mellitus ($p = 0.022$). Early non-survivors showed more infection with *Staphylococcus* species ($p = 0.004$), a non-significant trend towards *St. aureus* infection ($p = 0.092$) and less infection with *Streptococcus* species ($p = 0.048$) compared to survivors.

Table 3
Differences between early survivors and non-survivors (≤30 days) after Shelhigh® implantation calculated by using Pearsons χ^2-test

Variables	Survivors	Non-survivors	*p* value
Gender			
Male	97 (52.2%)	89 (47.8%)	0.408
Female	40 (58.0%)	29 (42.0%)	
Endocarditis			
Native endocarditis	107 (56.6%)	82 (43.4%)	0.118
Prosthetic endocarditis	20 (45.5%)	36 (54.5%)	
Priority of operation			
Urgent operation	89 (61.0%)	57 (39.0%)	**0.001**
Emergency operation	39 (39.8%)	59 (60.2%)	
Number of valves implanted			
One	113 (55.9%)	89 (44.1%)	0.166
Two	24 (45.3%)	29 (54.7%)	
Abscess formation			
No	86 (59.7%)	58 (40.3%)	**0.029**
Yes	51 (45.9%)	60 (54.1%)	
Preop. ventilation			
No	120 (60.9%)	77 (39.1%)	<**0.0001**
Yes	17 (29.3%)	41 (70.7%)	
Preop. septic shock			
No	125 (61.3%)	79 (38.7%)	<**0.0001**
Yes	12 (23.5%)	39 (76.5%)	
Preop. catecholamines			
No	121 (63.0%)	71 (37.0%)	<**0.0001**
Yes	16 (25.4%)	47 (74.6%)	
Preop. renal insufficiency			
No	89 (60.1%)	59 (39.9%)	**0.016**
Yes	48 (44.9%)	59 (55.1%)	
Preop. diabetes mellitus			
No	114 (57.6%)	84 (42.4%)	**0.022**
Yes	23 (40.4%)	34 (59.6%)	
Preop. pulmonary oedema			
No	120 (58.5%)	85 (41.5%)	**0.002**
Yes	17 (34.0%)	33 (66.0%)	
Preop. cerebral embolisation			
No	110 (55.0%)	90 (45.0)	0.436
Yes	27 (49.1%)	28 (50.9%)	
Preop. spleen embolisation			
No	113 (51.6%)	106 (48.4%)	0.093
Yes	24 (66.7%)	12 (33.3%)	
Reinfection			
No	126 (53.8%)	108 (46.2%)	0.586
Yes	9 (47.4%)	10 (52.6%)	
Staphylococcus species infection			
No	131(80.9%)	31 (19.1%)	**0.004**
Yes	60 (64.5%)	33 (35.5%)	
Staphylococcus aureus infection			
No	151 (77.4%)	44 (22.6%)	0.092
Yes	40 (66.7%)	20 (33.3%)	
Streptococcus species infection			
No	134 (71.7%)	53 (28.3%)	**0.048**
Yes	57 (83.8%)	11 (16.2%)	

Table 4
Risk factors for early mortality (≤30 days) in the univariate logistic regression analysis after Shelhigh® implantation

Risk factors	Odds ratio	95% CI	*p* value
Preop. septic shock	6.36	3.28–12.35	**≤0.001**
Preop. catecholamines	5.16	2.76–9.62	**≤0.001**
Emergency operation	4.19	2.30–7.61	**≤0.001**
Preop. ventilation	3.76	2.01–7.05	**≤0.001**
Preop. pulmonary oedema	3.40	1.77–6.54	**≤0.001**
Staphylococcus species	2.32	1.30–4.14	**0.004**
Abscess formation	2.16	1.21–3.85	**0.008**
Staphylococcus aureus	1.71	0.91–3.23	0.095
Number of implanted valves (one or two)	1.55	0.80–3.02	0.190
Preop. diabetes mellitus	1.52	0.79–2.91	0.202
Preop. renal insufficiency	1.30	0.73–2.30	0.358
Preop. cerebral embolisation	1.29	0.66–2.52	0.441
Preop. spleen embolisation	0.83	0.35–1.93	0.668
Native vs prosthetic endocarditis	0.77	0.41–1.45	0.423
Gender	0.77	0.40–1.50	0.452
Streptococcus species	0.48	0.23–1.00	0.051

CI: confidence interval; vs: versus; preop.: preoperative; intraop.: intraoperative.

Gender ($p = 0.408$), native or prosthetic endocarditis ($p = 0.118$), number of implanted valves ($p = 0.166$), preoperative cerebral ($p = 0.436$) or spleen embolisation ($p = 0.093$) and reinfection ($p = 0.586$) were non-significant variables in the comparison.

3.6. Risk factors for early mortality in univariate and multivariate analysis

The risk factors for early mortality in the univariate logistic regression analysis with odds ratio (OR), 95% confidence interval (CI) and *p* values are given in Table 4.

On statistical analysis the following six statistically significant risk factors for early mortality were found: preoperative development of septic shock (OR 6.36), preoperative high doses of catecholamines (OR 5.16), surgery performed in an emergency (OR 4.19), preoperative necessity of ventilation (OR 3.76) or development of pulmonary oedema (OR 3.4) and abscess formation (OR 2.16). Infection with *St. aureus* showed a non-significant trend towards early mortality (OR 1.71, $p = 0.095$) compared to infection with *Streptococcus* species, with a low OR (0.48) for early mortality.

On multivariate analysis septic shock (OR 3.75, CI 1.79–7.88, $p < 0.0001$), emergency operation (OR 2.51, CI 1.27–4.95, $p < 0.008$) and infection with *Staphylococcus* species (OR 1.98, CI 1.06–3.72, $p < 0.032$) were found to be independent risk factors for early mortality.

4. Discussion

Our study shows that the survival of patients differs significantly in dependence on the surgical urgency. The difference in survival found between the patients operated on urgently but in stable condition and those in whom the operation was an emergency procedure due to unstable haemodynamics or septic shock reflects the aggressive nature of the disease but also shows that a large number of patients with endocarditis are referred too late for operation. This is shown in the survival curve, where after the first 30 days the lines for urgent and emergency operation run parallel. Additionally, survival in patients after double valve replacement (aortic and mitral) was significantly worse than with single valve replacement. Better outcome could have been achieved if patients had been referred earlier for surgery. This view is also supported by the analysis of the 30-day mortality.

In our study early non-survivors (<30 days) as compared to early survivors were not only more often operated on in an emergency but preoperatively they showed clinical signs of cardiac decompensation: preoperatively non-survivors were significantly more often on ventilation, developed more pulmonary oedema, were on more high-dose catecholamines and had more renal insufficiency. Additionally, early non-survivors developed more septic shock and intraoperatively showed significantly more abscess formation as a sign of deterioration of the endocarditis. These results suggest that early outcome can be improved if patients are operated upon before heart failure or septic shock develops. For the risk stratification and survival in our study it has to be taken into consideration that our hospital is a referral surgical centre receiving patients who have already been treated medically elsewhere and sometimes coming for an operation as ultima ratio therapy. Our results accord with those of two published studies in which Alexiou et al. found the haemodynamic status of the patient at the time of valve replacement to be one of the most important predictors for operative mortality [7], while Reinhartz et al. showed the optimal time for operation to be before haemodynamic instability or infiltration of the paravalvular tissue by the infection occurs [8].

Although rapid surgical treatment in patients with extensive endocarditic infection greatly influences their morbidity and mortality rate, the optimal time point for the operation is still controversially discussed in the literature [9,10]. Because no randomised controlled trials have been conducted to clarify the role of surgery in the treatment of AIE patients and its optimal timing to improve outcomes, current practice guidelines for the surgical management of complex left-sided IE are largely based on results of observational studies and expert opinion [2,3,10]. Our results are consistent with those of published studies showing the benefit of surgical therapy. In a large, longitudinal, prospective cohort study to examine the impact of surgery Aksoy et al. determined that surgical therapy in patients with left-sided AIE is a strong independent predictor of long-term survival. In this recently published study the authors demonstrate that the use of surgery was independently predicted by age, the presence of heart failure, and intracardiac abscess, concluding that these high-risk patients may reap the most benefit from early surgery and should be considered for early, aggressive surgical therapy [11]. Vikram et al. found, in a large retrospective, observational cohort study of seven hospitals, that valve surgery for patients with complex, left-sided native valve endocarditis was independently associated with reduced 6-month mortality, particularly evident among patients with moderate to severe congestive heart failure [12].

In contrast to these findings Tleyjeh et al. recently published the results of medically and surgically treated

endocarditis patients of their non-randomised retrospective study using a propensity score analysis, suggesting that valve surgery in left-sided AIE has no survival benefit and might be associated with increased 6-month mortality, running counter to conventional clinical thinking on the presumed benefit of surgery in AIE [13]. This finding may have a number of possible explanations, mainly that surgically treated AIE patients are fundamentally different from those treated with medical therapy. These differences include increased rates of heart failure and abscess formation and a higher frequency of prosthetic valves. Each of these factors could increase the potential complexity of surgical repair and may have contributed to the high rate of in-hospital mortality seen in the surgical group [12,14].

Our study confirms previous reports that documented the association of periannular abscess complications with increased mortality and the need of surgery in almost all patients [15,16]. In our study abscess formation, which was found in 46% of the patients, was not only associated with significantly decreased survival but also showed an association with early mortality in the univariate analysis (OR 2.16, 95% CI 1.21—3.85). These results accord with data published by the investigators of the International Collaboration on Endocarditis Merged Database, a cohort from seven sites in five countries. They showed that, among 311 patients who had definite aortic valve AIE, 67 (22%) patients had periannular abscess. These patients were more likely to undergo surgery (84% vs 36%, $p < 0.001$), and their in-hospital mortality rate was higher (19% vs 11%, $p < 0.09$). In this study periannular abscess formation showed a non-significant trend towards an increased risk of death (OR 1.9, 95% CI 0.9—3.8) but failed to be an independent risk factor in multivariate analysis, in which *St. aureus* infection was independently associated with increased risk of death [17]. These results are confirmed by recently published studies in which *St. aureus* infective endocarditis is associated with high morbidity and mortality and a more severe prognosis compared with AIE caused by other pathogens [15,18]. In our study early non-survivors showed more infection with *Staphylococcus* species and a non-significant trend towards *St. aureus* infection.

Our data show that Shelhigh® bioprostheses offer very good early and mid-term clinical results in patients with AIE. The low reinfection rate found with these valves is comparable to the results achieved at our institution in the treatment of endocarditis with cryopreserved homografts [19] although with a follow-up of 469 patient years the number of Shelhigh® patients having reached mid-term follow-up is still small and the results will need to be verified in the long-term course.

In June 2007 the FDA seized all finished devices at Shelhigh's manufacturing facility due to concerns of a potential risk of nonsterility (see press release FDA June 2007, homepage; http://www.fda.gov) but did not mandate a recall of the devices. In Germany there was no government seizure but a voluntary distribution stop by Shelhigh® company. In our study no de novo infection due to possible nonsterility was found.

4.1. Study limitations

The present study is retrospective and non-randomised, using prospectively updated data. Clinical end-points such as exercise capacity and functional tests could not be assessed. There is a natural bias in the clinical assessment of the patient groups. Despite these limitations the present study represents a unique attempt to collect and analyse a single-centre experience in the surgical treatment of AIE with the use of the Shelhigh® stentless bioprosthesis over a period of 7 years in a large group of patients.

5. Conclusions

The survival of patients differs significantly in dependence on the urgency of their operations. Better outcome could have been achieved if patients had been referred earlier for surgery. Compared to early survivors, non-survivors (<30 days) showed clinical signs of cardiac decompensation and deterioration of the endocarditis suggesting that early outcome could be improved if patients are operated upon before heart failure or septic shock develops.

The low reinfection rate of Shelhigh® bioprostheses in AIE is promising and the satisfactory early and mid-term results achieved in patients with native and prosthetic endocarditis need to be verified in the long-term course.

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