

Surgical Treatment of Infective Mitral Valve Endocarditis

Markus J. Wilhelm^{1,2}, Reza Tavakoli¹, Kathrin Schneeberger¹, Simon Hörstrupp², Oliver Reuthebuch², Burkhardt Seifert³, Marko Turina^{1,2}, Michele Genoni¹

¹Department of Cardiac Surgery, City Hospital Triemli, Zurich, ²Department of Cardiovascular Surgery, University Hospital Zurich, Zurich, ³Department of Biostatistics, Institute for Social and Preventive Medicine, University of Zurich, Zurich, Switzerland

Background and aim of the study: The approach to mitral valve endocarditis is a surgical challenge, and the optimal procedure remains a matter of debate. In this condition, mitral valve repair appears feasible, but its long-term effects - as opposed to more often practiced valve replacement - have not yet been determined. Herein, the authors' experience of surgical treatment of infective mitral valve endocarditis is presented, with reference to surgical replacement or reconstruction.

Methods: A retrospective analysis was performed of all patients with infective native mitral valve endocarditis treated surgically at the University Hospital Zurich and the City Hospital Triemli Zurich between 1980 and 1996. Of 154 patients, 97 (63%) underwent mitral valve replacement, and 57 (37%) mitral valve reconstruction.

Results: The 30-day mortality was 3.2% (5/154); 4% (4/97) after replacement and 1.7% (1/57) after reconstruction ($p = 0.67$). Survival (Kaplan-Meier) was 93%, 81% and 61% after one, five and 10 years, respectively. There was no significant difference between valve replacement and reconstruction in

terms of long-term survival ($p = 0.15$), but there was a trend towards better survival after reconstruction than replacement if only cardiac deaths were considered ($p = 0.1$). At follow up, reconstruction patients were significantly less frequently symptomatic (NYHA class III/IV) than replacement patients (0% versus 29%; $p = 0.002$), had a lower incidence of atrial fibrillation and need for pacemaker implantation (29% versus 47%; $p = 0.04$), and tended to have less dyspnea in daily life (20% versus 38%; $p = 0.07$). Reoperation in patients surviving more than 30 days was more common in replacement than in reconstruction patients.

Conclusion: The present data suggest a trend for better clinical outcome after mitral valve reconstruction than after replacement when treating mitral valve endocarditis. These results encourage mitral valve reconstruction in mitral valve endocarditis, but recommendations to clinicians undertaking surgery on mitral valve endocarditis must be made with caution.

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The incidence of infective endocarditis in the general population is approximately 20 per 100,000 (1). Prolonged antibiotic therapy remains the treatment of choice for native valve endocarditis, once the causative organism has been identified. However, despite advances in the diagnosis and antimicrobial treatment of infective endocarditis, eradication of the septic focus and abolition of the accompanying systemic manifestations frequently require surgical intervention. In

other clinical situations - for example, valve dysfunction, organ failure, development of abscesses or large mobile vegetations, peripheral or cerebral embolization, prosthetic valve endocarditis or fungal infection - expeditious surgery is often indicated while the infection remains active. Since the mid-1960s, mitral valve replacement has been proposed as a therapeutic strategy for active infective endocarditis of the mitral valve that is not responsive to antibiotic therapy alone (2,3). Carpentier suggested in 1983 that mitral valve repair, without valve replacement, might also be an effective alternative surgical treatment for a variety of disorders, including endocarditis (4). In the present retrospective study, the long-term results of surgically treated mitral valve endocarditis were analyzed, with particular emphasis on the surgical strategy employed.

Address for correspondence:
Michele Genoni MD, FECS, Division of Cardiac Surgery, Stadtspital Triemli, Birmensdorferstrasse, CH 8063 Zurich
e-mail: michele.genoni@triemli.stzh.ch

Clinical material and methods

Patients

A retrospective analysis was performed on all 154 patients with infective native mitral valve endocarditis treated surgically at the University Hospital Zurich and the City Hospital Triemli Zurich between 1980 and 1996. Patients with prosthetic mitral valve endocarditis were excluded. During the early period of the study, the clinical diagnosis of endocarditis was based primarily on factors including persistent bacteremia, new regurgitant heart murmur, vasculitis and fever, similar to the Von Reyn criteria (5). In the early 1990s, with the availability of reliable echocardiographic methods (notably transesophageal echocardiography), evidence on echocardiography such as demonstration of vegetation, abscess or new valvular regurgitation was added as a criterion for clinical diagnosis, in addition to parameters of positive blood cultures, vasculitis and fever, in accordance with the Durack criteria (6).

All patients had documented bacterial endocarditis of the mitral valve and acute infection confirmed by positive blood cultures (72%), operative findings of acute inflammation, or positive cultures of excised tissue. The most common infecting organisms were *Streptococcus* sp. in 72 patients (47%) and *Staphylococcus aureus* in 17 patients (11%). Confirmed *Staph. aureus* endocarditis was seen in almost twice as many patients in the replacement group (13%) as in the reconstruction group (7%). *Enterococcus* was detected in five patients (5%) of the replacement group, and in two (3%) of the reconstruction group. The results of cultures were unknown in 43 patients (28%) (Table I).

Preoperatively, 60% of the patients were in NYHA functional class III/IV (74% in the mitral valve replacement group versus 37% in the reconstruction group; $p = 0.01$) (Fig. 1). Overall, 26% of patients had atrial fibrillation (31% versus 18%; $p = 0.059$), and 13% had septic embolism (14% versus 11%; $p = \text{NS}$) (Table II). Surgery in acute endocarditis was performed in 114 patients (74%), while 40 patients (26%) underwent elective surgery. In the mitral valve replacement group, 76 patients (78%) were operated on in the acute phase, and 21 (22%) electively in the chronic period; in the mitral valve reconstruction group, 38 patients (67%) underwent surgery in acute endocarditis, and 19 (33%) in the chronic phase. Acute endocarditis was defined as the period within six weeks from onset of symptoms while antibiotic therapy was still ongoing. Elective surgery meant operation in the chronic phase of endocarditis after completion of a six-week course of antibiotic treatment. In patients with *Staph. aureus* endocarditis, the time from onset of symptoms to surgery was significantly shorter than in patients with other pathogens ($p = 0.039$).

Surgery in the acute phase was indicated in the presence of vegetations ≥ 8 mm or vegetations with increasing size on repeat echocardiography, in patients with thromboembolic complications, persistent septicemia, acute valvular regurgitation or hemodynamic compromise despite antibiotic and inotropic therapy. In the chronic phase, a hemodynamically relevant mitral insufficiency (grade $\geq \text{III}$ on a scale of I to IV on echocardiography) was the indication for surgery. Mitral valve replacement was performed in 97 patients (63%), and mitral valve reconstruction in 57 (37%).

Table I: Spectrum of pathogens.

Pathogen	Total	Mitral valve replacement	Mitral valve reconstruction
<i>Staphylococcus aureus</i>	17 (11)	13 (76)	4 (24)
All <i>Streptococcus</i> sp.	72 (47)	41 (57)	31 (43)
<i>Strep. viridans</i>	32 (21)	22 (69)	10 (31)
<i>Strep. sanguis</i>	10 (6)	8 (80)	2 (20)
<i>Strep. mitis</i>	6 (4)	1 (17)	5 (83)
<i>Strep. bovis</i>	5 (3)	4 (80)	1 (20)
<i>Streptococcus</i> (others)	19 (12)	6 (32)	13 (68)
<i>Haemophilus</i>	5 (3)	2 (40)	3 (60)
<i>Enterococcus</i>	7 (5)	5 (72)	2 (28)
Other pathogens*	10 (6)	4 (40)	6 (60)
Unknown [†]	43 (28)	31 (72)	12 (28)

Values in parentheses are percentages.

*Other pathogens included: *Cardiobacter hominis* (n = 2), *Actinobacillus* (n = 2), Q-fever (n = 2), *Erysipelothrix rhusiopathiae* (n = 1), *Listeria monocytogenes* (n = 1), *Staphylococcus epidermidis* (n = 1), *Staphylococcus lugdunensis* (n = 1 patient).

[†]Microbiological data unavailable for these patients.

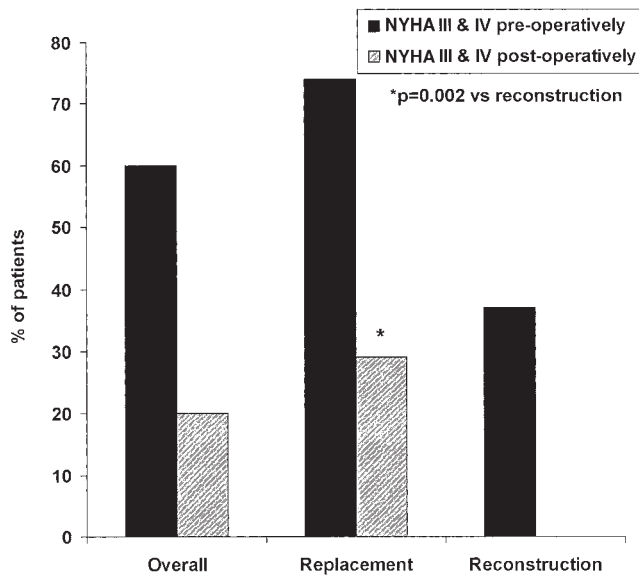


Figure 1: Preoperative and postoperative symptom status of mitral valve replacement and reconstruction patients (NYHA classes III and IV).

Among the 154 patients (53 women, 101 men), the mean age was 52 ± 11.8 years (range: 14 to 76 years). The mean follow up period was 7.0 ± 4.7 years (median 6.7 years). At the end of the follow up period, 57 patients (37%) had died. With respect to mortality, follow up was 100% complete. With regard to morbidity, some patients living outside the country could not be contacted to complete a questionnaire; hence, the routine questionnaire from the previous year was used in the analysis.

Surgical procedures

In all patients, surgery was performed using cardiopulmonary bypass (CPB) with either crystalloid or blood cardioplegia at moderate hypothermia. The mean CPB time was 88 ± 33 min (replacement 88 ± 17 min; reconstruction 89 ± 37 min; $p = \text{NS}$), and the mean aortic cross-clamp time was 53 ± 26 min (replacement 54 ± 23 min; reconstruction 50 ± 35 min; $p = \text{NS}$). Intraoperative findings as described by the surgeons during mitral valve replacement and reconstruction are listed in Table III.

The percentage of mitral valve reconstructions increased throughout the study period from 0% in 1980 to 63% in 1996. Mitral valve replacement was performed with a CarboMedics Standard mechanical mitral heart valve (CarboMedics Inc., Austin, TX, USA) in 18 patients, a St. Jude Medical mechanical heart valve (St. Jude Medical, Inc., St. Paul, MN, USA) in 32 patients, an Omnicarbon mitral prosthesis (MedicalCV, Inc., Inver Grove Heights, MN, USA) in five patients, a Björk-Shiley mitral prosthesis (Shiley,

Table II: Patient preoperative condition.

Preoperative parameter	Mitral valve replacement	Mitral valve reconstruction
NYHA class III/IV	74	37*
Atrial fibrillation	31	18#
Septic embolism	14	11§

Values are percentages of patients in each group.
* $p = 0.01$; # $p = 0.059$; § $p = \text{not significant}$.

Inc., Irvine, CA, USA) in nine patients, a Carpentier-Edwards Porcine Bioprosthesis (Edwards Lifesciences Corporation, Irvine, CA, USA) in 25 patients, and a Hancock Mitral Bioprosthesis (Medtronic Foundation, Minneapolis, MN, USA) in eight patients. Mitral valve reconstruction was performed according to the Carpentier ($n = 30$) or Whooley ($n = 27$) techniques. In case of leaflet perforation, all surrounding infected tissue was resected, and the defect covered with autologous pericardium pretreated with glutaraldehyde. Autologous pericardium was also used to restore defects of the mitral valve annulus.

Additional cardiac interventions were required in 56 patients (36%). These included aortic valve replacement in 36 patients (23%) (25 replacement patients (26%) and 11 reconstruction patients (19%)), reconstruction of the tricuspid valve in 11 patients (7%) (11 replacement patients (11%) and no reconstruction patients), coronary artery bypass surgery in eight patients (5%) (four replacement patients (4%) and four reconstruction patients (7%)), and closure of an atrial septal defect in one patient of the replacement group. Patients undergoing mechanical valve replacement and those with chronic atrial fibrillation were placed on lifelong warfarin therapy. Patients receiving bioprostheses and those who underwent mitral valve

Table III: Intraoperative findings.

Finding	Mitral valve replacement (n = 97)	Mitral valve reconstruction (n = 57)
Vegetation	33	28
Chordal rupture	20	39
Valve rupture	9	18
Valve perforation	15	11
Calcification	13	4
Valve thickening	16	0
Prolapse	9	18
Annulus destruction	6	4
Annulus dilatation	4	19

Values are percentages of patients in each group.

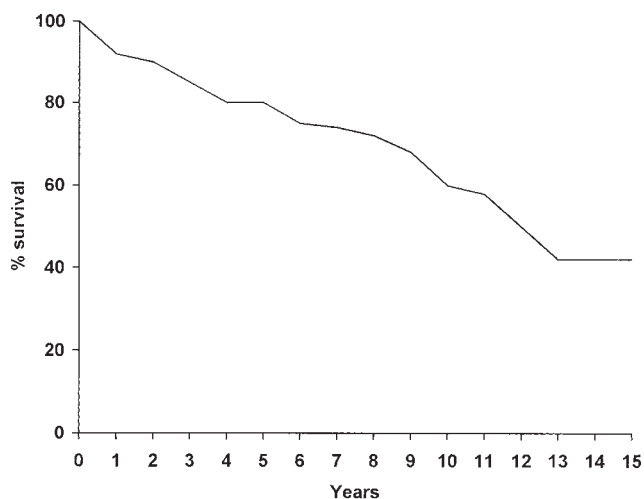


Figure 2: Overall actuarial survival after surgical treatment of mitral valve endocarditis.

reconstruction were administered anticoagulation therapy for three months postoperatively.

Statistical analyses

Comparisons between groups were performed using Fisher's exact test. Survival analysis was performed using the Kaplan-Meier method, and comparison of survival between groups using the log rank test. Dependence of survival from continuous variables was analyzed using Cox-regression. SPSS 11.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analyses. A p -value ≤ 0.05 was considered to be statistically significant, while a p -value > 0.05 and ≤ 0.1 was considered to be a statistical trend.

Results

The overall 30-day mortality was 3.2% (5/154); 4% (4/97) in the replacement group and 1.7% (1/57) in the reconstruction group ($p = 0.67$). In the replacement group, one patient died after a cerebral embolism, one due to multi-organ failure, and two as a result of heart failure. The one patient in the reconstruction group died in septic shock. Overall perioperative morbidity (<30 days after surgery) was 41% (63/154 patients), with 62% (60/97) after valve replacement and 5% (3/57) after reconstruction ($p < 0.001$). The most frequent complications were arrhythmias ($\geq 80\%$ atrial fibrillation), infection (pneumonia, urinary tract) and hemorrhage requiring re-exploration, which was necessary in 11/97 patients (11%) after replacement and in 2/57 patients (4%) after reconstruction.

Overall survival (Kaplan-Meier) was 93% after one year, 81% after five years, and 61% after 10 years (Fig. 2). Among 52 patient deaths in the long term, 20 were

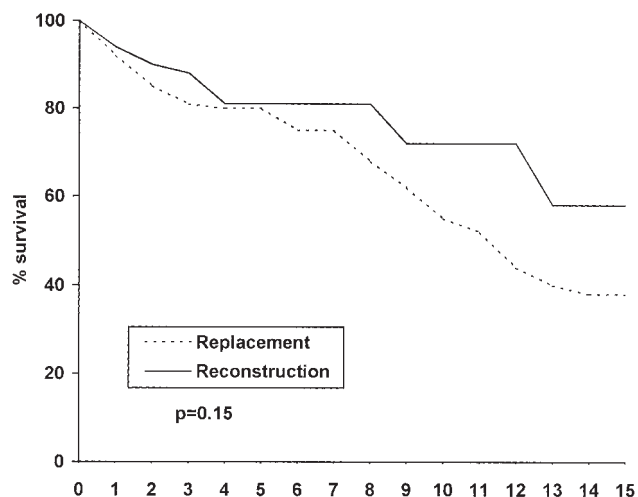


Figure 3: Actuarial survival after mitral valve replacement and mitral valve reconstruction in patients with mitral valve endocarditis.

cardiac-related, and 32 were non-cardiac. Of the 20 cardiac deaths, 17 were in the replacement group (18% of 93 patients surviving >30 days), and three after reconstruction (5% of 56 patients surviving >30 days). If only cardiac deaths were considered, Kaplan-Meier curves indicated a trend towards better survival after valve reconstruction than after replacement. Thus, the one-, five- and 10-year survivals after valve replacement were 96.5, 92.5 and 79%, respectively, and after reconstruction were 98, 95.4 and 95.4%, respectively ($p = 0.1$). Two of the cardiac deaths were related to recurrent endocarditis, both in the replacement group. Thus, overall mortality due to reinfection was 1.3%. Mortality was higher in patients with *Staph. aureus* endocarditis (10/17; 59%) than in those with endocarditis caused by all other pathogens (30/94; 32%). Accordingly, the one-, five- and 10-year Kaplan-Meier survivals in patients with *Staph. aureus* endocarditis were 76.5, 65 and 44%, respectively, and in those with endocarditis caused by all other pathogens were 98.9, 84.9 and 67%, respectively ($p = 0.008$).

Survival was significantly negatively affected by patient age. Cox-regression univariate analysis revealed a relative risk of 1.047, which indicates a 5% increase in risk per year ($p < 0.001$). In a multivariate Cox-regression, the result did not change when adjusted for the type of operation (replacement versus reconstruction) ($p = 0.23$). Survival was also significantly negatively affected by prolonged duration of surgery as measured by CPB and aortic cross-clamp times. For CPB time, Cox-regression univariate analysis revealed per minute a relative risk of 1.011, which indicates a 1% increase in risk per minute, and per hour a relative risk of 1.93, indicating an almost 100% increase in risk per hour ($p = 0.01$). In a multivariate Cox-regression, the

result did not change when adjusted for the type of operation (replacement versus reconstruction) ($p = 0.32$). For aortic cross-clamp time, Cox-regression univariate analysis revealed per minute a relative risk of 1.013, which indicates a 1% increase in risk per minute, and per hour a relative risk of 2.17, indicating a more than 100% increase in risk per hour ($p = 0.037$). In a multivariate Cox-regression, the result did not change when adjusted for the type of operation (replacement versus reconstruction) ($p = 0.87$). There was a trend towards poorer survival in patients who were highly symptomatic (NYHA class I/II versus class III/IV) ($p = 0.1$).

As seen with early mortality ($p = 0.67$), there was no statistically significant difference between mitral valve replacement and reconstruction with respect to long-term survival ($p = 0.15$) (Fig. 3). In the long term, patients undergoing valve reconstruction were significantly less frequently symptomatic (NYHA class III/IV) than patients after replacement (0% versus 29%; $p = 0.002$) (see Fig. 1), had a lower incidence of atrial fibrillation and requirement for pacemaker implantation (29% versus 47%; $p = 0.04$), and also tended to have less dyspnea in daily life (20% versus 38%; $p = 0.07$). Reoperation in patients surviving for more than 30 days was more common in the valve replacement group (6/93 patients; 6.5%) than in the reconstruction group (1/56 patients; 1.8%). The time interval between original surgery and reoperation was 5.7 ± 3.9 years (range: 1 to 13 years) in the replacement group, and one year in single reconstruction patient. The main reason for reintervention was recurrent endocarditis ($n = 5$). One patient in the replacement group died soon after reoperation, from septic multi-organ failure.

Discussion

Although the results of the present study did not reveal any statistically significant differences with regard to survival, there was a trend towards less mortality after valve reconstruction than after replacement for mitral valve endocarditis. Furthermore, valve reconstruction was associated with less perioperative and long-term morbidity as compared to replacement. These results provide encouragement to retain a preference for mitral valve reconstruction in mitral valve endocarditis. It is difficult however to transfer these data to different clinical settings, and so recommendations to others treating mitral valve endocarditis by surgery must be made with caution.

Surgery is required in patients with active infective endocarditis who respond poorly to antibiotics, experience septic emboli, have evidence of annular abscess and/or show hemodynamic instability, as well as for

those who are bacteriologically cured but in whom mitral insufficiency has developed as a result of valve destruction during infection. Operating during an inactive phase of the disease process, in a sterile field after completion of antibiotic treatment, is highly desirable, but was feasible in only about 25% of patients in the present study. In the vast majority, surgery was required during the acute phase of the infection.

In this study, the 30-day mortality was low (3.2%), and similar to that reported previously (7,8). In order to compare different reports of operative mortality in acute mitral valve endocarditis, however, the extent of the infection and the nature of the underlying disease must also be borne in mind. Despite the low mortality, the early outcome was characterized by a relatively high perioperative morbidity (41%). Similar findings were reported by Alexiou et al. (9). The survival of 61% for all patients at 10 years was also similar to 10-year survival rates reported by others (7,10,11). The presence of a staphylococcal pathogen, advanced age, and extended extracorporeal and aortic cross-clamp times all negatively influenced long-term survival. Neither the preoperative hemodynamic condition, nor the surgical technique, had any statistically significant effect on survival, although poor hemodynamic condition and mitral valve replacement were both associated with a trend towards reduced long-term survival.

Apart from acute infective mitral pathology in general, hospital mortality and morbidity have been broadly demonstrated to be lower after mitral valve repair than after valve replacement. This is due mainly to an improved ventricular function associated with preservation of the subvalvular apparatus, and a lack of requirement for anticoagulant therapy and consequently fewer hemorrhagic complications (12). On the other hand, a linear rate of postoperative events such as structural valvular deterioration, thromboembolism and hemorrhage occurred in 5% of patients per year after valve replacement (13). If the condition is characterized by uncontrolled infection despite antibiotic treatment, by embolic events, or by the hemodynamic situation, Carpentier and others have recommended aggressive surgical intervention in infective valve disease (14,15) - that is, debridement of the infected valve at an early stage while the infection is limited to the heart valve tissue and before ventricular dysfunction increases. The preservation of ventricular function is of particular importance, and may be an adjunct in reducing operative mortality and morbidity by preventing poor functional results. This was reflected by the postoperative functional outcome in the present study. While postoperatively, all of the reconstruction patients had a good cardiac functional status, 29% of the replacement patients remained symptomatic.

In view of the apparent disadvantages associated with mitral valve replacement, including the implantation of foreign material into an infected area, a need for anticoagulation with its related morbidity, prosthesis-related events and deterioration of ventricular function, the present authors prefer to repair infected mitral valves, provided that adequate clearance of all infected tissue is feasible. For this reason, mitral valve repair is less common in patients suffering from staphylococcal endocarditis. Indeed, almost twice as many patients in the replacement group had confirmed endocarditis with *Staph. aureus* as patients in the reconstruction group (13% versus 7%). These patients are more likely to have mitral valve incompetence by virtue of leaflet perforation or erosion of the leaflet free edge, resulting in serious clinical consequences such as annular abscess formation and consecutive destruction (16). Overall, 11% of the present patients had confirmed infection with *Staph. aureus*, and comprised 78% of the cases of annular abscess formation and destruction. In this situation, patients do not qualify for mitral valve reconstruction due to the various types of mitral valve destruction.

In the present study, patients with valve replacement required reoperation more frequently than valve reconstruction patients, the most common reason for reintervention being recurrent endocarditis of the implanted prosthesis. Thus, the implantation of foreign synthetic material into an infected site of acute endocarditis carries a substantial risk of prosthesis reinfection. This was unequivocally reflected by the clinical findings of other investigators, who reported prosthetic valve endocarditis in 15-20% of patients despite full courses of perioperative antibiotics (15,17). Mitral valve reconstruction preserves viable native tissue that is more resistant to infection than prosthetic material, and this was reflected in the current study by the substantially lower rate of recurrent endocarditis in the reconstruction patients. However, the higher rate of extensive infections in the replacement group, particularly with *Staph. aureus*, might also have contributed to the higher frequency of reinfection. As native valve endocarditis begins on the valve leaflet, and remains there for some time before extending to the surrounding tissue, the decision to operate must not be delayed (18).

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