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ORIGINAL ARTICLE

Repair versus replacement of the aortic valve in active infective endocarditis

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Abstract

OBJECTIVES: Aortic valve repair has advantages over replacement in stable aortic regurgitation. It is unclear whether this is similar in active endocarditis.

METHODS: From January 2000 to July 2009, 100 patients (age 54.9 ± 15.1 years) underwent surgery for aortic valve endocarditis. Thirty-three patients were treated by valve repair (I) and 67 underwent valve replacement (II: 51 biologic, 10 mechanical valves, 6 Ross operations). In Group I, cusp and root lesions were treated by autologous pericardial patches. A root abscess was present in 32 cases (I: 27%, II 34%; $P = 0.82$). Concomitant procedures ($n = 49$) were mitral repair (I: 10, II: 11; $P = 0.12$) and coronary bypass (I: 4, II: 11; $P = 0.77$). All patients were followed. Cumulative follow-up was 268 patient-years (mean 2.7 ± 3.0 years). In a retrospective analysis, we analysed the outcome.

RESULTS: Hospital mortality was 15% (I: 9%, II: 18%; $P = 0.37$). Survival at 5 years was significantly better after repair (I: 88%, II 65%; $P = 0.047$). Ten patients were reoperated (I: 35%, II: 10%; $P = 0.021$) between 1 month and 5 years postoperatively. Actuarial freedom from aortic regurgitation of grade II or higher was 80% at 5 years (I: 66%, II: 87%; $P = 0.066$). In Group I, this was influenced by aorto-ventricular (AV) morphology (tricuspid 80%, bicuspid 50%; $P = 0.0045$). Freedom from reoperation in reconstructed tricuspid valves ($n = 20$) was 87% at 5 years, which was identical to Group II ($P = 0.40$). At 5 years, freedom from thromboembolic events was 93% (I: 100%, II: 90%; $P = 0.087$) and that from bleeding complications was 100%.

CONCLUSIONS: AV repair for active endocarditis seems to lead to better survival compared with replacement. The use of large patches in combination with bicuspid anatomy results in increased risk of late failure.

Keywords: Aortic regurgitation • Active endocarditis • Aortic valve repair • Aortic valve replacement

INTRODUCTION

In the past 15 years, aortic valve repair has emerged as a new alternative to aortic valve replacement in the treatment of stable aortic regurgitation (AR) [1]. Aortic valve reconstruction has not only been shown to avoid disadvantages of anticoagulation, but the incidence of valve-related complications has also been lower than that previously reported for aortic valve replacement [2].

Active infective endocarditis (AIE) is one of the diseases leading to AR. Complicated AIE requires surgical treatment in order to improve the prognosis, which is otherwise poor [3]. For decades, surgical treatment of complicated AIE almost exclusively consisted of valve replacement, thus confining the patients to the typical prosthesis-related complications with possible recurrence of AIE on the implanted prosthesis [4]. In the past decade, there has been increasing evidence in the treatment of mitral valve AIE that valve reconstruction may improve postoperative survival, even though with the possible disadvantage of a higher risk of reoperation [3].

Based on our experience with elective repair in stable AR [1], we have expanded the reconstructive approach also to patients with AR due to AIE. In a retrospective study, we analysed the short- and mid-term results and compared them to them to contemporary results of valve replacement for AIE.

MATERIAL AND METHODS

Between January 2000 and July 2009, 100 patients were treated surgically for complicated AIE involving the native aortic valve. Their mean age was 55 ± 15 years, and 77 patients were males. The aortic valve was tricuspid in 74, bicuspid in 23 and unicuspid in 3 patients. Thirty-one patients required intensive care treatment including mechanical ventilation ($n = 13$) for treatment of severe heart failure. AR was mild to moderate in 16 and severe in 84 instances. Pure regurgitation was present in 89, and mixed disease in 11 cases. A jet lesion was not observed on the mitral or aortic valve.

Table 1: Patient characteristics

	All patients (n = 100)	I (n = 33)	II (n = 67)	P-value
Male sex (n)	77	28	49	0.22
Age (years)	54.9 ± 15.1 (18–86)	50.2 ± 13.8 (24–71)	57.2 ± 15.1 (18–86)	0.029
Body surface area (m^2/kg)	2.0 ± 0.2 (1.5–2.7)	2.0 ± 0.3 (1.6–2.7)	1.9 ± 0.2 (1.5–2.5)	0.051
EuroSCORE	22 ± 18% (4–82%)	12 ± 9% (4–36%)	26 ± 20% (4–82%)	0.044
Cardiovascular morbidity				
Atrioventricular block	16	3	13	0.25
Previous pacemaker	9	0	9	0.028
Coronary artery disease	20	5	15	0.44
Hypertension	13	4	9	1.0
Peripheral arterial disease	6	0	6	0.17
Liver disease	9	3	6	1.0
Liver cirrhosis CHILD A	7	3	4	0.68
Other	2	0	2	1.0
Renal failure	23	3	20	0.023
Creatinine > 2 mg/dl	13	2	11	0.21
Acute failure	6	0	6	0.17
Chronic dialysis	4	1	3	1.0
Previous malignancy	17	3	14	0.17
Relevant obstructive lung disease (FEV1 < 60% predicted)	5	1	4	1.0
Diabetes mellitus	13	4	9	1.0
Drug abuse	11	2	9	0.33

The reasons for surgery were AR with heart failure (n = 84), the echocardiographic demonstration of perivalvular abscess (n = 20), the presence of large and mobile vegetations (n = 65) alone or in combination. Thirty-seven individuals had experienced embolism into the brain (n = 24), kidneys (n = 4), spleen (n = 10) or peripheral organs (n = 16).

Sixteen preoperative patients had an aorto-ventricular (AV) block (AV I°: n = 8; AV II°: n = 2; AV III°: n = 6). All nine patients in Group II had previously undergone pacemaker implantation.

Blood cultures were positive in 67 instances, and intraoperative cultures in 36 cases [40 *Staphylococcus* (24 *Staphylococcus aureus*), 27 *Streptococcus*, 12 *Enterococcus*, 1 *Acinetobacter*]. In 21 instances, no pathogen could be identified.

Comorbidity was present in 83% of patients. Cardiac disease included endocarditic involvement of the mitral valve (n = 10), structural or functional mitral regurgitation without endocarditis (n = 17) and coronary artery disease (n = 20). Renal failure (creatinine > 2.0 mg/dl) was present in 13 patients, of which 4 were dialysis-dependent and 6 patients needed acute dialysis (Table 1). Drug abuse was present in 11 individuals.

Preoperatively, all patients or legal guardians were carefully informed about the different options in aortic valve surgery. The option of a mechanical valve was given to all patients <70 years, and a biological prosthesis was recommended as treatment for patients >60 years. For individuals <40 years, valve replacement with a pulmonary autograft was considered a principal option. Reconstruction was considered as a possibility if the valve did not exhibit calcification on echocardiography. For the ultimate decision, contraindications against anticoagulation, age of the patient and the informed patient's wish were primarily considered.

Anaesthesia and operative technique

All patients received general anaesthesia using standard continuous intravenous administration of Propofol and Sufentanyl. In all patients, the chest was opened by a median sternotomy. Aortic and right atrial cannulation was used for extracorporeal circulation; bicaval venous drainage was employed if the mitral valve was also involved in the endocarditic process. After cross-clamping, the aorta was opened by a transverse incision 5–10 mm above the sinutubular junction, and cold blood cardioplegia was given directly into the coronary ostia. All vegetations were removed and aortic valve and root carefully assessed.

The valve was replaced if preexisting cusp calcification was present. A decision in favour of repair was made (1) if endocarditic destruction predominantly affected the body of the cusps, sparing the free margin, (2) did not involve all cusps and (3) affected <50% of the tissues of each cusp. The presence of perivalvular abscess had no influence on the decision of repair versus replacement. In addition, patients' age and the informed opinion regarding long-term anticoagulation were taken into consideration. In the absence of perivalvular abscess, the operation was limited to the valve only.

If a decision in favour of reconstruction was made, autologous pericardium was harvested and pretreated in 1.5% glutaraldehyde solution for 3 min, followed further by rinsing in normal saline for 3 min. All destructed tissue was excised. Pericardial patches were created intentionally 10–20% larger than the cusp defect to be closed in order to minimize the chance of inadvertent cusp restriction. The pericardium was then sutured into the cusp defect using a 6-0 monofilament polypropylene suture. One cusp was reconstructed in 20 instances, two cusps in 8 and three cusps in 2 patients. Care was taken to normalize cusp configuration by achieving an effective height of at least 9 mm [5, 6].

After completion of repair, the configuration of all cusps was checked carefully. Residual prolapse was corrected by central plication of the free margin along the nodulus Arantii using a single 5-0 or 6-0 polypropylene suture (Prolene™; Ethicon, Inc., Hamburg, Germany) to achieve an effective height of up to 9–10 mm according to the body size [5].

Table 2: Concomitant cardiac/aortic operations

	n	I (n = 33)	II (n = 67)	P-value
Mitral valve repair	21	10	11	0.12
Mitral valve replacement	6	0	6	0.17
Tricuspid valve repair	5	0	5	0.17
Aorto-coronary bypass	15	4	11	0.77
Ascending aortic replacement	2	1	1	1.0

Localized perivalvular abscess cavities were debrided and closed with an autologous pericardial patch. Extensive abscess formation, i.e. partial or complete atrioventricular dehiscence, was treated by root replacement, using a stentless bioprosthesis or a pulmonary autograft. Replacement was performed with a mechanical prosthesis in 10, a biological prosthesis in 51 (stented 36, stentless 15) and a pulmonary autograft in 6 patients.

Concomitant procedures were commonly performed before the operation on the aortic valve (Table 2).

Management cusps (repair)

In Group I, 42 pericardial patches were used for repair of the aortic cups in 30 patients. In 20 patients, one patch was inserted, 8 were treated two patches and three patches were required in 2 instances. In three cases, there was no need for a pericardial patch after debridement of the cups. The size of the pericardial patches was <1 cm in 12 instances, ~1 cm in 9 and >1 cm in 9 cases. Different sizes were used for subsequent analysis. The patients were classified for subsequent analysis according to the largest patch.

Management root

In 32 patients, an abscess of the aortic root was found intraoperatively (I: 30%, II: 34%; P = 0.65). When a root abscess was present and the aortic valve was repaired (n = 8), a pericardial patch was used to close the abscess cavity and to reconstruct the root. In one patient with concomitant root dilatation, replacement of the aortic root was performed with a Dacron graft.

In patients with aortic valve replacement and root abscess, the cavity was closed with a pericardial patch in five cases, and root replacement was required in the remaining nine cases (only stentless biological valves).

All patients underwent transesophageal echocardiography intraoperatively (Sequoia 256™, Acuson, Mountain View, CA, USA). The presence of regurgitation was documented by colour Doppler and quantified according to standard criteria [7]. Postoperative echocardiography was performed by transthoracic means. The presence of regurgitation as perivalvular leak or valvular regurgitation after repair was documented and quantified. In addition, systolic peak and mean gradients were determined by continuous wave Doppler.

All patients with a mechanical valve replacement or atrial fibrillation were treated with phenocourmarin and patients with coronary disease were treated with acetylsalicylic acid. One patient with aortic valve repair had atrial fibrillation and was treated with phenocourmarin after the surgery.

All patients were treated with specific antibiosis intravenously for 6 weeks postoperatively. All patients were followed with a mean follow-up time of 2.7 ± 3.0 years (4 days to 8.6 years).

Statistical analysis

Survival, late AR ≥ grade II and need for reoperation on the aortic valve for recurrence of AR or AIE were analysed using Kaplan–Meier analysis. The patients were analysed in two groups according to the type of treatment, i.e. repair versus replacement. Univariate tests were performed using Mann–Whitney test and Fisher's exact test. All values are expressed as mean ± standard deviation, whereas the Kaplan–Meier curve expressed as mean ± standard error.

Statistical analysis was performed using GraphPad Prism 5.0. Long-term survival and freedom from recurrent AR or reoperation were compared between the groups using the log-rank test. A P-value of <0.05 was considered statistically significant.

RESULTS

Of the 100 patients, 33 (33%) underwent aortic valve reconstruction and 67 patients (67%) aortic valve replacement. Concomitant cardiac/aortic operations were necessary in 48 patients (Table 2). There was a significant difference in preoperative EuroSCORE between Groups I and II (P = 0.0002).

Mean cardiopulmonary bypass time time was 101 ± 39 min (I: 97 ± 35 min, II: 103 ± 41 min; P = 0.55) and aortic cross-clamping time was 68 ± 24 min (I: 68 ± 22 min, II: 68 ± 25 min; P = 1.0). Mean ventilation time was 1.6 ± 3.2 days (I: 0.9 ± 1.9 days, II: 2.0 ± 3.6 days; P = 0.26). The patients with the repaired aortic valves had a shorter intensive care unit stay (I: 2.1 ± 2.0 days, II: 4.1 ± 4.0 days; P = 0.0087).

Early mortality

Fifteen patients died within 30 days after surgery for an early mortality of 15% (I: 3, II: 12; P = 0.37), and an additional 7 patients never left the hospital (I: 1, II: 6; P = 0.42). They died between the second and the ninth months for a hospital mortality of 22%. The causes of early death were septic multi-organ failure (n = 19), myocardial failure related to preoperative coronary embolism (n = 1), left ventricular (LV) dysfunction (n = 1) or intracerebral bleeding (n = 1). There was no significant effect of age on hospital mortality (mean age survivors 53.7 ± 14.5 years versus deceased 58.3 ± 16.6 years; P = 0.22).

Early morbidity

Reexploration for postoperative haemorrhage was necessary in 14 patients (I: 2, II: 12; P = 0.13). Postoperative atrioventricular block required implantation of a pacemaker in four instances (I: 1, II: 3; P = 1.0). A perivalvular leak was observed in 13 patients after valve replacement. Valvular regurgitation was seen in 18 individuals after repair and graded as I (n = 13), II (n = 5) or more (n = 0).

Seizures were observed in two patients within the first few days postoperatively in Group II and could be stopped with anti-epileptic treatment within 5 days.

Late mortality

Five patients died late (between 3 and 6 years) from myocardial failure ($n = 4$), or LV dysfunction following secondary mitral valve replacement ($n = 1$). Survival at 4 years was 72% (Fig. 1) and it was higher after repair (88%) compared with replacement (65%). This difference was significant ($P = 0.047$).

In patients with tricuspid aortic valves, survival at 4 years was 97% (I: 100%, II: 93%; $P = 0.36$), and 5-year survival in individuals with biscuspid valves was 73% (I: 100%, II: 52%; $P = 0.088$). There was no significant effect of age on late mortality, and late mortality was only slightly higher in patients >70 years ($P = 0.26$).

Late morbidity

During follow-up, new AR was found in one patient each after replacement and after repair (Figs 2 and 3). Eight patients developed a progressive increase of AR from mild to severe, of which six were reoperated. Actuarial freedom from AR ≥ II at 5 years was 80%. AR recurred more frequently after repair (66%) versus replacement (87%) with borderline significance ($P = 0.066$).

Recurrence of endocarditis occurred in eight individuals, all within the first postoperative 60 days. Two had undergone repair, and six aortic valve replacement (incidence 6 vs. 9%; $P = 1.0$). Recurrence was more frequent in bicuspid morphology (5 of 23) than in tricuspid aortic valves (3 of 72; $P = 0.019$). Three of these patients died shortly after the diagnosis was established, and the other five underwent successful reoperation.

Eleven patients required reoperation on the aortic valve due to recurrent AR ($n = 6$) or infective endocarditis ($n = 5$). The cause of AR in the replacement group was due to perivalvular leak. All patients survived the reoperation and were discharged in good condition. The need for reoperation was more frequent after repair than after replacement (I: 7, II: 4; $P = 0.043$). Actuarial freedom from reoperation on the aortic valve at 5 years was 82% (I: 65% versus II: 90%; Figs 4 and 5). Valve stability in patients with tricuspid valves (I: 86%, II: 85%) was unaffected by the choice of treatment, i.e. repair versus replacement.

Freedom from reoperation in patients with bicuspid valves was 60% in Group I and 90% in Group II ($P = 0.077$) at 5 years. The size of pericardium inserted for cusp reconstruction was found to be an additional predictor of failure. The need for reoperation only occurred in patches >1 cm. Freedom from reoperation was 22% at 5 years in these patients.

Bleeding complications were not observed. Neurological complications—most likely related to thromboembolic events—

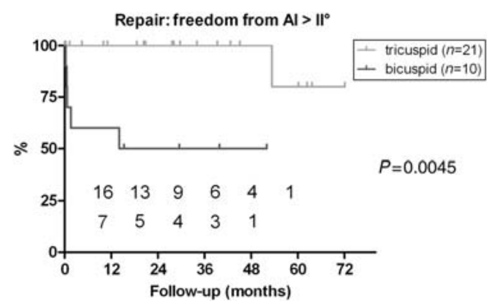

Figure 3: Group I: freedom from AR > II° after aortic valve repair, stratified by aortic valve morphology.

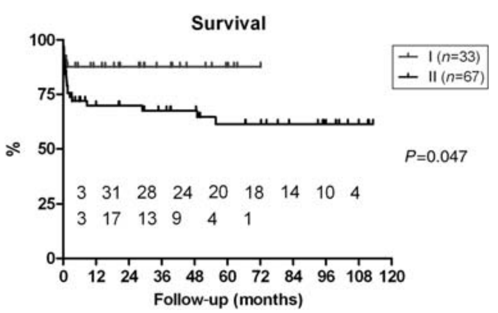

Figure 1: Survival following aortic valve repair (I) or aortic valve replacement (II) for AIE.

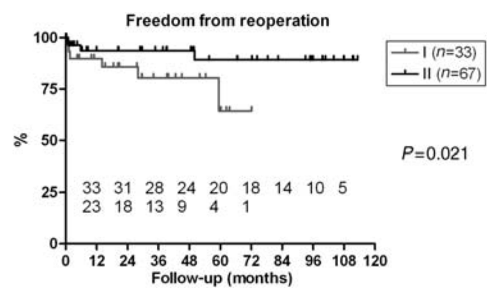

Figure 4: Freedom from reoperation after aortic valve repair (I) or aortic valve replacement (II) for AIE.

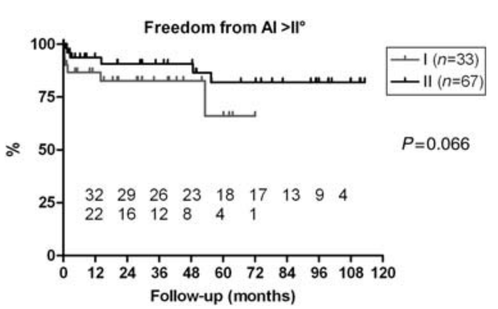

Figure 2: Freedom from AR > II° after aortic valve repair (I) or aortic valve replacement (II) for AIE.

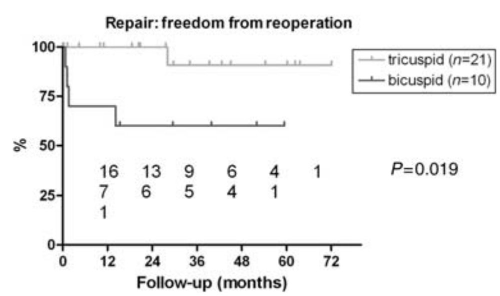

Figure 5: Group I: freedom from reoperation after aortic valve repair, stratified by aortic valve morphology.

were noticed in Group II. One patient developed generalized seizures and one had a stroke. Freedom from neurological complication was 93% (I: 100%, II: 90%; $P = 0.087$) at 5 years.

At 4 years, freedom from endocarditis was 90% (I: 97%, II: 87%; $P = 0.51$). Five patients (I: 2, II: 3) required reoperation because of re-endocarditis at the aortic valve (two *Staphylococcus*; three culture negative). The remaining three individuals had endocarditis at the mitral valve (II: 3).

DISCUSSION

Despite advances in diagnosis and medical treatment, active infectious endocarditis remains a diagnostic and therapeutic challenge. Surgical treatment of complicated AIE, i.e. valve replacement, has markedly improved the mid-term prognosis.

The long-term results of aortic and mitral valve replacement for AIE are less than optimal. Elective replacement of the aortic valve in patients under the age of 70 is associated with a 10-year survival of 66–79% [8], whereas 10-year survival after aortic valve replacement for AIE is only $54.0 \pm 7.5\%$ [9]. The reasons for this increased mortality are not clear, even though there is some evidence that the severity of AIE-related complications may not only affect short, but also long-term survival.

In addition, the ideal surgical procedure in AIE is still the subject of controversial discussion. As yet there is no randomized study looking into this question, and the heterogeneity of the AIE patients will make such a study difficult, if not impossible. A number of case series have found somewhat better long-term prognosis with mechanical valve replacement [10, 11], whereas several other similar analyses have found identical results with biological and mechanical prostheses [3, 4]. Others have propagated the use of the pulmonary autograft in AIE [12, 13], particularly in young patients. The absence of anticoagulation makes this approach theoretically attractive, particularly in those patients who have experienced cerebral embolism and are at risk of developing cerebral haemorrhage. On the other hand, it may be argued that such an aggressive operation intended to provide a long durability is difficult to justify if long-term survival is poor.

The experience in AIE of the mitral valve was initially characterized by similar controversy regarding replacement device [14]. Based on the positive results of mitral repair in degenerative mitral disease, repair was also introduced for AIE of the mitral valve [15]. With increasing experience, it was found that patient survival following repair of mitral AIE was improved over replacement, even though the risk of reoperation was increased [3]. In particular, repair resulted in a lower incidence of valve-related complications compared with replacement [16, 17].

Over the past 15 years, reconstruction has also been extended to stable aortic valve regurgitation. Surgical techniques have been defined for different valve pathologies [2, 18], and the probability of valve-related complications has been lower than what has been reported for aortic valve replacement [19]. Based on our positive experience in elective aortic valve repair, we decided to explore the role of reconstructive techniques also for AIE of the aortic valve. The current results seem to mirror the findings that have previously been made in mitral AIE.

Survival was significantly improved after repair compared with replacement as the most important finding. The heterogenous patient population and limited number did not allow us to distinguish completely between improved survival based on patient risk factors versus better survival due to repair-associated advantages. Interestingly, however, we did not observe significant differences in valve-related complications between cohorts. While this finding is not statistically relevant because of limited numbers, some valve-related complications may be hidden in the instances of late mortality after aortic valve replacement.

The benefit of improved survival came at the price of an increased risk of reoperation, a finding that is similar to the experience in mitral repair for AIE [20]. The similarity appears plausible at first sight, even though a closer look revealed that morphology of the aortic valve had a strong influence on repair durability. Freedom from reoperation was excellent (90% at 5 years) in tricuspid valves, whereas durability was significantly inferior in bicuspid aortic valve anatomy. This observation is similar to findings in elective repair of bicuspid aortic valves (BAVs) which were published recently [21]. Similar to the results of elective repair, we found a larger aortoventricular junction (AVJ) in failed bicuspid valves. In addition, there is the theoretic but plausible argument that the BAV is exposed to more stress throughout the cardiac cycle than the tricuspid aortic valve. At this time, it is unclear whether reduction in the AVJ will stabilize the repair and also the functional results, or whether BAV patients should better undergo replacement as first choice.

The effect of valve morphology may have been exaggerated or caused by the size of the pericardial patch. All reoperations occurred in the presence of a large patch (>1 cm).

A smaller patch size lead to a 5-year stability of 100%, freedom from reoperation in patients with bicuspid valves and a large patch ($n = 5$) was 0% at 5 years.

Limitation of the study

The consequence of the current analysis should be carefully interpreted. This was not a randomized study but a retrospective study of consecutive patients. We have consistently taken same approach to aortic valve repair with participation of the same surgeon (H.J.S.).

Replaced patients were sicker with respect to preoperative intensive care treatment and mechanical ventilation for severe heart failure. This may have had a separate influence on long-term survival.

CONCLUSION

In conclusion, repair is an attractive option for AIE of the aortic valve. In the presence of large cusp defects (>1 cm), in particular in bicuspid valves, replacement appears the better option.

Conflict of interest: none declared.

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EDITORIAL COMMENT

Aortic valve repair for active infective endocarditis

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Aortic valve replacement is the standard treatment when surgery is needed for active infective endocarditis of the aortic valve. Although there have been a few isolated case reports on aortic valve repair for the treatment of active infective endocarditis [1–2], the largest series ever published is in this issue of the Journal [3]. Mayer *et al.* [3] have an article titled 'Repair versus replacement of the aortic valve in active infective endocarditis' where the authors compared the outcomes of aortic valve repair in 33 patients with those of aortic valve replacement in 67 patients. The title suggests that aortic valve repair is an alternative to valve replacement to treat active endocarditis when in reality it is not; it is only possible in selected patients as the authors defined in their manuscript and the reader may redefine based on the results. Be as it may, the fact that they repaired the aortic valve in 33% of the cases with active infective endocartitis, including one in four with aortic root abscess, is a formidable task, and I congratulate them for trying to expand the indications of aortic valve repair to this very sick group of patients. This would be possible only in the hands of the senior surgeon of the University Cardiac Unit of Homburg, Germany, who probably has performed more aortic valve repairs than anyone in the world.

In this series of aortic valve repairs for active infective endocarditis, 30 patients required partial resection of one or more cusps and reconstruction with glutaraldehyde fixed autologous pericardium whereas 3 patients had only debridement of the