

Surgical treatment of aortic valve endocarditis with aortic annular involvement: a 26-years experience

Aortik anülüsü etkileyen aort kapak endokarditinin cerrahi tedavisi: 26 yıllık deneyim

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Background: In this study, we report early and late results of surgical treatment of aortic valve endocarditis with aortic annular involvement.

Methods: Between December 1985 and January 2011, 42 consecutive patients (32 males, 10 females; mean age 39.0±13.3 years; range 16 to 67 years) were retrospectively analyzed in terms of surgical findings and operative procedures. The blood cultures were positive in 25 patients (59.5%) and the most commonly identified microorganism was streptococcus (n=15, 35.7%). Fourteen patients (33.3%) had a medical history of previous cardiac surgery and 13 (31.0%) had prosthetic valve endocarditis. The mean duration of follow-up were 7.9±4.4 years (range 0.1 to 18.2 years).

Results: All patients underwent a total of 64 surgical procedures. The most commonly performed procedure was aortic valve replacement with 26 patients (61.9%), followed by aortic root replacement in 15 (35.7%) and primary repair of periprosthetic leakage in one patient (2.4%). Nine patients (21.4%) had concomitant procedures for the mitral valve. In-hospital mortality was seen in nine patients (21.4%). Postoperatively seven patients had (16.7%) low cardiac output, six had (14.3%) heart block, however, only two of them required permanent pacemaker. The actuarial survival rates at one, five and 10 years were 80.0±6.3%, 69.9±7.3% and 64.9±8.3%, respectively.

Conclusion: Although surgery for aortic valve endocarditis with annular involvement has high in-hospital mortality rate, long-term survival is satisfactory for surviving patients.

Key words: Annulus; aortic valve; endocarditis.

Amaç: Bu çalışmada aortik anülüsü etkileyen aort kapak endokarditinin cerrahi tedavisine ilişkin erken ve geç dönem sonuçlar bildirildi.

Çalışma planı: Aralık 1985 - Ocak 2011 tarihleri arasında toplam 42 ardışık hasta (32 erkek, 10 kadın; ort. yaş 39.0±13.3 yıl; dağılım 16-67 yıl) cerrahi bulgular ve uygulanan cerrahiler açısından retrospektif olarak incelendi. Hastaların 25'inde (%59.5) kan kültüründe üreme tespit edildi ve streptokok en çok (n=15, %35.7) tespit edilen mikroorganizma oldu. On dört hastanın (%33.3) tıbbi öyküsünde geçirilmiş kalp ameliyatı varken, 13 hastada (%31) protez kapak endokarditi vardı. Ortalama takip süresi 7.9±4.4 (dağılım 0.1-18.2 yıl) yıl idi.

Bulgular: Hastaların tümüne toplam 64 cerrahi işlem uygulandı. Yirmi altı (%61.9) hasta ile aort kapak replasmanı en sık uygulanan işlem iken, bunu 15 hasta ile aort kök replasmanı ve bir hasta (%2.4) ile periprostetik kaçağın primer onarımı takip etti. Dokuz hastaya (%21.4) eş zamanlı mitral kapak işlemi yapıldı. Hastane mortalitesi dokuz hastada (%21.4) görüldü. Ameliyat sonrası yedi hastada (%16.7) düşük kalp debisi, altı hastada (%14.3) ise kalp bloku gelişti, fakat yalnızca iki hastada kalıcı kalp pili kullanımı gerekti. Hastaların hesaplanan bir, beş ve 10 yıllık sağkalım oranları sırasıyla %80.0±6.3, %69.9±7.3 ve %64.9±8.3 idi.

Sonuç: Aortik anülüsü etkileyen aort kapak endokarditi cerrahisi yüksek hastane mortalitesine sahip olsa da, yaşayan hastaların uzun dönem sağkalımları tatmin edicidir.

Anahtar sözcükler: Anülüs; aort kapak; endokardit.



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Annular involvement remains a challenging problem for the treatment of both native (NVE) and prosthetic valve endocarditis (PVE). Although surgery may be unavoidable in about one third of the patients, the indication and appropriate procedure are still controversial.^[1] The success of the surgical treatment depends on the location and extent of the lesions, which may contain less virulent organisms.^[2] Several operative techniques have been proposed to completely exclude the abscess cavities from the circulation and reconstruct the affected cardiac structure after debridement.^[3] This report summarizes our experience in the surgical treatment of patients suffering from aortic valve endocarditis with annular involvement over a period of 26 years.

PATIENTS AND METHODS

The study was approved by the local hospital ethics committee, and the patient data was collected from the hospital records retrospectively. Between December 1985 and January 2011, 42 consecutive patients (32 males and 10 females; mean age 39.0±13.3 years; range 16-67) with aortic valve endocarditis complicated by periannular abscess (out of a total of 174 patients with aortic valve endocarditis; 24.1%) underwent surgery at our institution. We used the modified Aranki criteria to define active, healed, native, prosthetic, and culture-negative endocarditis.^[4] Diagnoses were confirmed during the operation by the presence of leaflet perforation, vegetations, or valvular and perivalvular tissue destruction, and acute or chronic inflammatory changes viewed via microscopy verified the diagnosis of endocarditis.

Twenty-nine patients (69.0%) presented with NVE and 13 (31.0%) with PVE, with early PVE cases being excluded from the analysis. No significant differences were seen in the average ages of the patients with NVE and PVE (38.8±12.7 vs. 39.5±14.9, respectively; p=0.415). Vegetations on the mitral prosthetic valve were detected in three cases while mitral valve periprosthetic leakage was present in two others. In addition, 20 patients (33.3%) had a previous history of cardiac surgery, and four had undergone two cardiac operations. Furthermore, 11 patients had been operated on for aortic valve procedures and four for double valve procedures. The remaining patient had aortic reconstruction but no replacement. The preoperative characteristics are summarized in Table 1. We did not perform coronary angiography on any of the patients in order to avoid embolic complications.

The diagnosis of infective endocarditis was made according to the Duke criteria.^[5] All of the

patients were examined by either transthoracic (TTE) or transesophageal (TEE) echocardiography, which revealed valvular vegetation, annular abscesses, aorticoatrial communication, or periprosthetic leakage. Intraoperatively, annular involvement was considered when an abscess penetrated into the valvular annulus or the adjacent myocardial structures or when the vegetations attacked the aortic annulus or adjacent structures. Gross vegetations were detected in 12 patients (28.6%) preoperatively.

Indications for surgery and valve choice

The patients were scheduled for surgery when the diagnoses were made, and 22 (52.4%) were operated on in the active phase of the infection. The indications for emergency surgery were big (>10 mm), mobile vegetations on the aortic valve, acute leaflet rupture and cardiac decompensation, a periannular extensive abscess with an intracardiac fistula, and prosthetic valve dysfunction. In 20 patients (47.6%), the operation was performed after the antibiotic treatments were completed and the patient was stabilized. The valve choice was primarily made

Table 1. Preoperative characteristics

| Preoperative characteristic | n | % | Mean±SD |
|--|----|------|-----------|
| Age | | | 39.0±13.3 |
| Gender | | | |
| Male | 32 | 76.2 | |
| Female | 10 | 23.8 | |
| Fever | 28 | 66.7 | |
| Septic emboli | | | |
| Central | 2 | 4.8 | |
| Peripheral | 6 | 14.3 | |
| NYHA Classification | | | |
| Class 1 | 3 | 7.1 | |
| Class 2 | 13 | 31.0 | |
| Class 3 | 20 | 47.6 | |
| Class 4 | 6 | 14.3 | |
| Congestive heart failure | 24 | 57.1 | |
| Renal dysfunction | 5 | 11.9 | |
| Infectious etiology | 4 | 9.5 | |
| Chronic dialysis dependent | 1 | 2.4 | |
| Periprosthetic leakage | 6 | 14.3 | |
| Emergency operation | 7 | 16.7 | |
| Left ventricular dysfunction (EF <40%) | 5 | 11.9 | |
| Electrocardiography | | | |
| Sinus rhythm | 37 | 88.1 | |
| Complete heart block | 2 | 4.8 | |
| Left bundle branch block | 2 | 4.8 | |
| Atrial fibrillation | 1 | 2.4 | |

SD: Standard deviation; NYHA: The New York Heart Association.

according to the degree of destruction in the annular area. Prosthetic materials were used when the aortic root was not extensively destroyed by the infectious process, with homografts and xenografts being used when available.

Microbiological studies

In addition, the blood cultures were positive in 25 patients (59.5%), and the most commonly identified microorganisms were various strains of streptococcus (35.7%). The results of the microbiological studies can be seen in Table 2.

Operative technique

All patients underwent moderate (28 °C) hypothermic cardiopulmonary bypass (CPB) via bicaval cannulation of either the ascending aorta (n=39) or the femoral artery (n=3). Isothermic blood cardioplegic solution was also administered by the retrograde route during aortic cross-clamping.

The most commonly performed procedure was aortic valve replacement in 26 patients (61.9%) followed by aortic root replacement in 15 (35.7%) and primary repair of periprosthetic leakage in one (2.4%). For eradication of aortic valve endocarditis, aortic annular skeletonization was performed. All infected and necrotic tissue around the annulus, and when present, within the abscess and fistula between the ventriculoarterial junction and the sinotubular junction, were resected. In addition, all vegetations were also removed. When necessary, a resected annular area was covered with a glutaraldehyde-treated autologous pericardial patch sutured to firm, fibrous tissue for a secure anastomosis or valve implantation. The approaches to the patients with fistulas have been previously reported.^{16,71} The list of procedures can be seen in Table 3.

The mitral valve was explored in all cases, with appropriate procedures being performed in nine of the patients. In addition, 15 had aortic root replacements, one underwent replacement of the prosthesis with aortic root enlargement, and another underwent concomitant subaortic discrete membrane resection (Table 3). The

Table 2. Microbiological study results

| Isolated organism | n | % |
|--|----|------|
| Negative culture | 17 | 40.5 |
| Streptococcus | 15 | 35.7 |
| Staphylococcus | 7 | 16.7 |
| Brucella | 2 | 4.8 |
| Methicillin resistant <i>Staphylococcus aureus</i> | 1 | 2.4 |

average aortic cross-clamp and total perfusion times were 111.0±30.8 (range 46-188) and 146.0±63.7 (range 65-411) minutes, respectively.

Follow-up

All patients received at least four weeks of postoperative antibiotic therapy. Broad -range antibiotics (vancomycine and aminoglycosides) were preferred for the culture- negative cases while the other patients were treated according to their antibiograms. The patients were followed up in the outpatient clinic of our hospital for a mean duration of 7.9±4.4 years (0.1-18.2), for a total of 244.2 patient-years.

Statistical analysis

All statistical analyses were performed using the SPSS version 16.0 statistical software package (SPSS Inc., Chicago, IL, USA). The continuous variables were expressed as mean ± standard deviation (SD), and the ranges were also calculated. Furthermore, the discrete variables were expressed as frequencies and percentages. Comparisons of the discrete variables were made via a chi-square test, and the survival, freedom from recurrence, and freedom from reoperation analyses were conducted using the Kaplan-Meier estimate. The survival comparisons were made

Table 3. Procedures

| Procedures | n | % |
|--|----|------|
| Mechanical aortic valve replacement | 26 | 61.9 |
| Redo aortic valve replacement | 5 | 11.9 |
| Aortic root replacement | 15 | 35.7 |
| Bentall de Bono | 6 | 14.3 |
| Xenograft implantation | 5 | 11.9 |
| Homograft implantation | 3 | 7.1 |
| Cabrol procedure | 1 | 2.4 |
| Aortic root enlargement | 1 | 2.4 |
| Fistula repair | 5 | 11.9 |
| Drainage of a subaortic abscess and patch repair | 2 | 4.8 |
| Resection of a subaortic discrete membrane | 2 | 4.8 |
| Primary repair of a periprosthetic leak at the aortic prosthesis | 1 | 2.4 |
| Patch repair of an aneurysm in the sinus of valsalva | 1 | 2.4 |
| Patch repair of an ascending aortic pseudoaneurysm | 1 | 2.4 |
| Patch repair of a ventricular septal defect | 1 | 2.4 |
| Mitral valve procedures | 9 | 21.4 |
| Mitral valve replacement | 6 | 14.3 |
| Mitral reconstruction | 2 | 4.8 |
| Primary repair of a periprosthetic leak at the mitral prosthesis | 1 | 2.4 |

with a log-rank test, and *p* values of less than 0.05 were accepted as statistically significant differences.

RESULTS

Mortality

Nine patients (21.4%) had in-hospital mortality, and five of these had PVE. However, when we compared the mortality rates in the PVE and NVE cases, no statistical significance was found (38.5% vs. 13.8%, respectively; *p*=0.107). The reason for the mortality was low cardiac output in seven patients and sepsis in two others. One of the septic patients also had low cardiac output syndrome (LCOS) postoperatively and the homograft failed due to a recurrence of the infectious process. The patients who died of sepsis did not have septic emboli preoperatively, and only one of them had a fever before the operation.

Morbidity

Postoperative fever was seen in 14 patients (33.3%), and three of these had no fever prior to the surgery. Complete heart block was present in six patients (14.3%) postoperatively, but only two of them (4.8%) required the implantation of a permanent pacemaker. In addition, two of these patients had PVE and four had aortic root procedures. Moreover, only one of the patients with postoperative heart block who had undergone a redo aortic valve replacement (AVR) and aortic root enlargement died in the early postoperative period. Furthermore, no mortality occurred in the patients who required a permanent pacemaker. Renal dysfunction was present in 12 patients (28.6%), with four (9.5%) requiring dialysis. Pulmonary morbidity was seen in six patients (14.3%), and two others (4.8%) had postoperative cerebrovascular events. However, these two patients did not have any septic emboli preoperatively. One of them had a recurrence and a reoperation during the hospitalization period, and he died on the 45th postoperative day. The patients with PVE and NVE were compared regarding postoperative morbidity, and although the absolute frequencies varied, they were not statistically significant (61.5% vs. 31.0%, respectively; *p*=0.063).

Follow-up

Of the 33 patients who survived, 31 completed the follow-up process. Two patients were lost to follow-up, and one of these had been operated on 26 years earlier. Additionally, four patients (12.9%) had mortality after discharge, and one of them died suddenly one month after leaving the hospital because of congestive heart failure. He had been categorized as New York Heart Association (NYHA) Class 4 preoperatively,

but his left ventricular function was normal. His preoperative cultures were also negative. One other patient had prosthetic valve endocarditis along with streptococcal growth in his cultures. He had previously undergone two operations before having infective endocarditis, with prosthetic aortic valve implantation being initially performed followed later by aortic root replacement. His cardiac functions had also been normal. Unfortunately, he had a recurrence of infective endocarditis and failed to respond to therapy. He died six months after being discharged. In addition, one of the long-term survivors died from a stroke in his ninth year of follow-up, and another had prosthetic valve endocarditis along with postoperative renal dysfunction with a need for dialysis. He died in the fourth year of follow-up because of chronic renal failure. The actuarial survival for one, five, and 10 years was 80.0±6.3%, 69.9±7.3%, and 64.9±8.3%, respectively. When the patients with PVE and NVE were compared, the difference was statistically significant (*p*=0.046). The actuarial survival for patients with PVE at one, five, and 10 years was 61.5±13.5%, 46.2±13.8%, and 46.2±13.8%, respectively, whereas it was 81.5±7.5%, 81.5±7.5% and 73.3±10.2% for patients with NVE at the same intervals.

A recurrence of infection occurred in three cases, and one of these was summarized earlier in the article. The other two cases had relapses of infection before being discharged and were taken for reoperations. One was a second redo case who had undergone aortic valve replacement, and he had his prosthesis replaced with aortic root enlargement. Primary repair of the periprosthetic leak attributable to the infective endocarditis was also performed on this patient. After recurrence, this patient underwent a reoperation in which the prosthesis was replaced, but he died of sepsis on the 12th postoperative day. The other patient had a native valve disease. He underwent a homograft replacement, but there was a functional failure that resulted in low cardiac output. A reoperation was performed in the first postoperative month, but during the postoperative course, sepsis developed, causing mortality on the 45th postoperative day. No other patients required reoperations apart from these three cases. Although none of the patients who received biological grafts had recurrences, the difference was not statistically significant (0% vs. 10.7%, respectively; *p*=1.000). Furthermore, the freedom from recurrence from infection at the first year was 91.8±4.6%, and this remained stable throughout the follow-up period. Moreover, the freedom from reoperation was 95.0±3.4% in the first year, and this also remained stable.

DISCUSSION

Aortic valve endocarditis has mainly been managed surgically since the report of Wallace et al.^[8] in 1965. The disease is highly fatal because of the infectious process that can lead to sepsis and the destructive process that can have significant consequences with regard to cardiac function. Recent reports on cryopreserved homografts are promising,^[9-12] but there is no substitute for radical debridement in these cases.^[13]

The use of biological materials for patients with aortic PVE is recommended due to the low reinfection rates caused by the increased penetration of antibiotics in these tissues and the presence of viable cells.^[14] Hagl et al.^[15] reported their experience regarding the use of a mechanical prosthesis in patients with PVE of the aortic valve and identified a mortality rate of 11% in 28 patients. They only had one recurrent case (4%) that died during the reoperation, and this happened at the postoperative third month. In addition, they reported a five-year survival rate of approximately 80%. In another study by David et al.^[16] they reported a 60% survival rate after five years. Our results are compatible with these reports. Although not statistically significant, none of the patients with biological grafts experienced a recurrence. This may be because of the low number of biological grafts available, and the increased use of biological grafts may decrease the recurrence rate. Knosella et al.^[12] also reported significant differences between the allograft and prosthetic groups in their study for both in-hospital and long-term mortality.

Although the total survival rate in our study was compatible with the findings in the study by Hagl et al.,^[15] the PVE results and the number of cases with NVE were lower in our series than theirs. Two possible explanations may account for this contradiction. One reason may be the lower number of cases in our series. We think this is important because the difference in morbidity rates was not significant even though the absolute frequency was about two times higher in the NVE cases. The statistical power could also have been lower. In addition, the high rate of morbidity in our series could also be responsible. As previously pointed out, the morbidity rates were higher with PVE, which may be significant. To verify this, a regression analysis could be performed on a larger number of patients. David et al.^[16] reported that a preoperative state of shock and the involvement of both the aortic and mitral annuli were associated with mortality, and our findings related to long-term survival were compatible with that study,^[16] with the differences between NVE and PVE being strikingly similar. Knosalla et al.^[12] also reported

that preoperative shock and sepsis were predictors of mortality.

The David et al.^[16] study also reported that about a third of their patients with active infective endocarditis had a paravalvular abscess, and our rates (24%) were compatible with theirs. They also determined that only 60% of their cases were diagnosed preoperatively. In our series, most of the cases were diagnosed intraoperatively as an annular involvement.

Secondary involvement of the mitral valve is important in patients with an aortic root abscess. Siniawski et al.^[17] found that approximately 25% of their cases had secondary mitral valve disease. In our report, we determined that 23.8% of the patients underwent a mitral valve procedure because of the infectious process. The same authors also reported an in-hospital mortality rate of 26.4% in the patients for whom double valve surgery was performed. Our series found nine patients who had concomitant mitral valve surgery (Table 3), and three of those (33.3%) suffered in-hospital mortality.

One significant difference between our report and others that have been published^[12,15,16] was the presence of the growth of microorganisms in the blood cultures. As shown in Table 2, around 40% of the cases were culture-negative, and the most frequently isolated bacteria was streptococcus, which contrasted with the staphylococcal predominance in the other reports. The differences between these studies and ours may be due to two reasons. One is the high rate of culture-negative cases in our study, possibly caused by the inappropriate handling of the blood cultures and the incorrect timing of the blood sampling. In most cases, blood samples are drawn when the patients are on antibiotics. The second reason may be the improper treatment of patients who are infected with streptococci, which could have led to more serious consequences.^[16]

Our study had several drawbacks. First, we had a very high rate of culture-negative cases, and this was discussed in detail in a previous analysis.^[18] Thus, our findings regarding the microorganisms must be viewed with caution. In addition, we had a low number of patients which did not allow us to perform a multivariable analysis. Some also might argue that the low rates of biological materials used in our study could also be a negative. Finally, one of the major limitations of this study was that the operations took place over a 15-year period, and the operative and medical therapies evolved markedly over this time. Although conducting a retrospective study over this length of time was not ideal, it was necessary in order

to make inferences regarding survival and follow-up. In spite of these drawbacks, we believe that our report is relevant because it consisted of patients who were operated on at a single center over an extended period of time and because there was a significant postoperative follow-up period.

Conclusion

The surgical results related to infective endocarditis of the aortic valve with annular involvement are acceptable considering the fatal state of the patients. Although the early mortality was high for our patients, the long-term survival rates were satisfactory. We also determined that successful surgery involving radical debridement resulted in a low rate of recurrence.

Declaration of conflicting interests

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