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Original Article / Özgün Makale

Prosthetic valve endocarditis: A challenging complication of prosthetic valves

Protez kapak endokarditi: Protez kapakların zorlayıcı bir komplikasyonu

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ABSTRACT

Background: This study aims to evaluate the surgical outcomes of prosthetic valve endocarditis.

Methods: A total of 21 patients (6 males, 15 females; mean age 58.9±12.6 years; range, 33 to 79 years) who were surgically treated for prosthetic valve endocarditis between January 2013 and January 2018 were retrospectively analyzed. Surgical indications included persistent fever for more than seven days after antibiotherapy, congestive heart failure refractory to medical treatment, vegetations larger than 1 cm on echocardiography, the presence of fungal endocarditis, severe valvular leak and valvular dysfunction, and staphylococcal prosthetic valve endocarditis.

Results: Five patients had previous aortic valve replacement and three of the aortic prostheses were re-replaced. Two patients had coexisting native mitral valve endocarditis and double valve replacement was done. Thirteen patients had previous mitral valve replacement and 12 of the mitral prostheses were re-replaced. One patient had coexisting native aortic valve endocarditis and double valve re-replacement was done. Three patients had previous aortic valve replacement + mitral valve replacement. Mitral valve endocarditis was diagnosed in two patients and these patients had only mitral valve re-replacement. The other patient had double valve endocarditis, and double valve replacement was done. The mean time from the first operation to the development of endocarditis was 7.3±5.7 years. Of five lost patients, two died from multiple organ failure, one from low cardiac output, one from pneumonia, and one from respiratory failure.

Conclusion: Radical resection of the infected tissues is critical to achieve favorable surgical outcomes. Single valve replacement of the infected valve may be preferred in patients having previous double valve replacement. Mechanical valves or bioprostheses can be used for re-replacement procedures.

Keywords: Infective endocarditis, prosthetic heart valve, surgical treatment.

ÖZ

Amaç: Bu çalışmada protez kapak endokarditinin cerrahi sonuçları değerlendirildi.

Çalışma planı: Ocak 2013 - Ocak 2018 tarihleri arasında protez kapak endokarditi nedeniyle cerrahi olarak tedavi edilen toplam 21 hasta (6 erkek, 15 kadın; ort. yaş 58.9±12.6 yıl; dağılım, 33-79 yıl) retrospektif olarak incelendi. Cerrahi endikasyonlar antibiyotik tedavisinden sonra yedi günden uzun süren inatçı ateş, medikal tedaviye dirençli konjestif kalp yetmezliği, ekokardiyografide 1 cm'den büyük vejetasyon, fungal endokardit, ciddi valvüler kaçak ve valvüler disfonksiyon varlığı ve stafilokok protez kapak endokarditi idi.

Bulgular: Beş hastaya daha önce aort kapak replasmanı yapılmıştı ve aort protezlerinin üçü yeniden değiştirilmişti. İki hastada beraberinde nativ mitral kapak endokarditi olup, çift kapak replasmanı yapıldı. On üç hastaya daha önce mitral kapak replasmanı yapılmıştı ve mitral protezlerin 12'si yeniden değiştirilmişti. Bir hastada beraberinde nativ aort kapak endokarditi olup, çift kapak replasmanı yapıldı. Üç hastaya daha önce aort kapak replasmanı + mitral kapak replasmanı yapılmıştı. İki hastaya mitral kapak endokarditi tanısı kondu ve bu hastalarda yalnızca mitral kapak yeniden değiştirildi. Diğer hastada iki kapakta da endokardit vardı ve çift kapak replasmanı yapıldı. İlk ameliyattan endokardit gelişimine kadar geçen ortalama süre 7.3±5.7 yıl idi. Kaybedilen beş hastanın ikisi çoklu organ yetmezliğine, biri düşük kalp debisine, biri pnömoniye ve biri de solunum yetmezliğine bağlı olarak kaybedildi.

Sonuç: Olumlu cerrahi sonuç elde etmek için enfekte dokuların radikal rezeksiyonu önemlidir. Öncesinde çift kapak replasmanı yapılmış hastalarda yalnızca enfekte olan kapağın değiştirilmesi tercih edilebilir. Yeniden yapılan replasman işlemlerinde mekanik kapaklar veya biyoprotezler tercih edilebilir.

Anahtar sözcükler: İnfektif endokardit, protez kalp kapağı, cerrahi tedavi.

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The incidence of prosthetic valve endocarditis (PVE) has been estimated as 0.3 to 1.2% per patient year. Its prevalence is also 1 to 6% in patients with valve prostheses. About 10 to 30% of infective endocarditis (IE) cases are PVE. Prosthetic valve endocarditis is a challenging situation with certain difficulties in diagnosis and treatment with poor prognosis. It also similarly affects mechanical and bioprosthetic valves.[1]

Pathogenesis differs due to the type of contamination and the prosthesis type. Early PVE mostly occur with preoperative contamination and the junction between the annulus and the sewing ring is usually involved. This leads to pseudoaneurysms, perivalvular abscesses, valvular dehiscence, and fistula formation. The pathogenesis of mechanical PVE is similar to early PVE due to the fact that the leaflets which are free from the thrombotic material cannot be adhered by the microorganisms. Therefore, infection occurs around the periannular area frequently with an abscess formation. On the other hand, infection is frequently seen on the leaflets in bioprostheses, leading to cusp rupture, perforation, and vegetations.[2]

In the present study, we aimed to evaluate the surgical outcomes of PVE.

PATIENTS AND METHODS

A total of 21 patients (6 males, 15 females; mean age 58.9±12.6 years; range, 33 to 79 years) who were surgically treated for prosthetic valve endocarditis in our clinic between January 2013 and January 2018 were retrospectively analyzed. A written informed consent was obtained from each patient. The study protocol was approved by Pamukkale University Faculty of Medicine Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

The diagnosis for PVE was made according to the culture and echocardiographic findings. Patients with persistent fever with positive blood cultures and/or vegetation on the prosthetic valve and/or a new periprosthetic leak were considered to have PVE. If there was a suspicion of PVE, particularly in patients with persistent fever without positive blood culture with suspicious or absent echocardiographic criteria, positron emission tomography/computed tomography (PET/CT) and single-photon emission computed tomography (SPECT) with radiolabelled leucocytes (99mTc-hexamethylpropyleneamine oxime) were used for the diagnosis. Surgical decision was done on consultation of cardiology, cardiac surgery, and infectious diseases departments. The presence of one or more of the following criteria was considered a surgical indication: persistent fever for more than seven days after antibiotherapy, congestive heart failure refractory to medical treatment, vegetations larger than 1 cm on echocardiography, the presence of fungal endocarditis, severe valvular leak and valvular dysfunction, and staphylococcal PVE. Demographic data, previous operations, operative procedures, culture results, and antibiotherapy details were recorded. Surgical outcomes were collected.

Surgical techniques

Standard cardiopulmonary bypass techniques were used for the operation. The patients who were hemodynamically unstable were urgently operated at the time of diagnosis. The infected prosthesis was replaced with a new prosthesis. If the native valve besides the infected prosthesis was also infected, all infected valves were, then, replaced. If one valve was infected in a previously replaced two valves, then only the infected one was replaced. All surgical debrided tissues and prostheses were sent for culture. The remaining annulus and surroundings were rinsed by povidone-iodine solution. Surgical radical debridement and re-replacement was done for all patients. All of the prosthetic materials, sutures, and pledgets were resected. Before the re-replacement procedure, the surgical instruments and clothes were changed, and rifampicin was applied to the surgical site.

Statistical analysis

PASW 17.0 statistical software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Continuous variables were expressed as the mean±1 SD.

RESULTS

Five patients had previous aortic valve replacement and three of the aortic prostheses were re-replaced. Two patients had coexisting native mitral valve endocarditis and double valve replacement was done. Thirteen patients had previous mitral valve replacement and 12 of the mitral prostheses were re-replaced. One patient had coexisting native aortic valve endocarditis and double valve re-replacement was done. Three patients had previous aortic valve replacement + mitral valve replacement. One of the double valve replacement patients had previous additional ascending aortic replacement. Mitral valve endocarditis was diagnosed in two patients and these patients had only mitral valve re-replacement. The other patient had double valve endocarditis, and double valve replacement was done. Twenty of previous valves were mechanical and

Table 1. Demographic and clinical characteristics of patients

Patient	Age (year)	Gender	T_1 (year)	Previous AVR	Previous MVR	AVR for IE	MVR for IE	T_2 (day)
1	50	F	3	N	Y	Y	Y	7
2	67	F	7	N	Y	N	Y	7
3	40	F	7	N	Y	N	Y	1
4	55	F	8	N	Y	N	Y	1
5	55	M	7	Y	N	Y	Y	16
6	59	M	7	Y	N	Y	N	25
7	76	F	1	N	Y	N	Y	3
8	68	F	4	N	Y	N	Y	7
9	69	F	15	N	Y	N	Y	11
10	79	F	8	N	Y	N	Y	0
11	52	F	6	N	Y	N	Y	3
12	60	M	5	Y	N	Y	Y	2
13	67	F	2	Y	N	Y	N	3
14	59	F	22	N	Y	N	Y	7
15	44	F	4	Y	N	Y	N	3
16	33	M	5	N	Y	N	Y	3
17	66	M	22	Y	Y	Y	Y	15
18	73	M	3	N	Y	N	Y	30
19	45	F	8	N	Y	N	Y	30
20	47	F	5	Y	Y	N	Y	15
21	72	F	6	Y	Y	N	Y	30

F: Female; M: Male; T_1: Time from initial operation to diagnosis of endocarditis (year); T_2: Time from initial diagnosis to operation (day); AVR: Aortic valve replacement, MVR: Mitral valve replacement; Y: Yes; N: No; IE: Infective endocarditis.

one was bioprosthetic. However, six of the mechanical valves were re-replaced with a bioprosthetic valve (Tables 1 and 2). In total, seven patients (33%) were implanted a bioprosthetic valve. In the remaining 12 patients (67%), mechanical valves were used for reimplantation.

Positive blood culture for microorganism was found in 16 patients and/or vegetation on the valve and/or new valvular dehiscence. In five of the culture-negative patients, the diagnosis was based on new valvular dehiscence and/or vegetation on the valve besides fever without any other etiology. All of the prosthetic valves were sent to the culture. Only one patient had a positive culture from the prosthetic valve extracted (Table 2). All patients had late prosthetic valve endocarditis.

The mean time from the first operation to the development of endocarditis was 7.3±5.7 (range, 1 to 22) years. The mean time from the initial diagnosis to operation was 10.4±10.2 (range, 0 to 30) days. The mean postoperative length of hospital stay was 36.9±21.7 (range, 1 to 105) days. The mean duration of antibiotherapy was 47.9±25.6 (range, 1 to 116) days (Table 1). Of five lost patients, two died from multiple organ failure, one from low cardiac output, one from pneumonia, and one from respiratory failure.

DISCUSSION

Prosthetic valve endocarditis is one of the most severe complications of prosthetic valves. It is more difficult to diagnose PVE than to diagnose native valve endocarditis.[1] Echocardiography and blood cultures are the main diagnostic tools. However, these may be negative in certain PVE cases. A negative echocardiogram does not rule out the diagnosis. A new-onset periprosthetic leak is the major criterion for the diagnosis.[1] In our study, we confirmed diagnosis using PET/CT and SPECT with radiolabelled leucocytes in the patients in whom the cultures were negative and echocardiography gave little data. All of our patients had late PVE diagnosed minimally one year after the first valve implantation. Electrocardiography-gated CT may give information of perivalvular extension of infection in addition to

Table 2. Patient data

Patient	Postoperative hospitalization duration (day)	Antibiotherapy duration (day)	Culture from surgical material	Blood culture	Antibiotherapy	Result	Previous valve	Implanted valve
1	30	37	None	None	Vancomycin Gentamicin Rifampicin	Cure	Mechanical	Mechanical
2	40	47	None	*S. aureus*	Vancomycin Gentamicin Rifampicin	Cure	Mechanical	Bioprosthesis
3	30	31	None	None	Vancomycin Gentamicin Rifampicin Ampicillin/Sulbactam	Cure	Mechanical	Mechanical
4	14	15	S. aureus	*S. aureus*	Vancomycin Gentamicin Meropenem daptomycin	Exitus	Mechanical	Mechanical
5	40	41	None	Coagulase negative staphylococcus	Penicilin G Gentamicin Rifampicin	Cure	Mechanical	Mechanical
6	40	56	None	Coagulase negative staphylococcus	Meropenem Ampicillin Rifampicin	Cure	Mechanical	Mechanical
7	35	38	None	None	Vancomycin Gentamicin Rifampicin	Cure	Bioprosthesis	Bioprosthesis
8	40	47	None	Enterococcus faecalis	Vancomycin Gentamicin Rifampicin	Cure	Mechanical	Mechanical
9	105	116	None	Gram positive coccus	Vancomycin Gentamicin Rifampicin	Exitus	Mechanical	Mechanical
10	1	1	None	*S. aureus*	Vankomicin Gentamicin	Exitus	Mechanical	Mechanical
11	35	41	None	Gram positive coccus	Vancomycin Gentamicin Rifampicin Cefazolin	Cure	Mechanical	Mechanical
12	58	60	None	Coagulase negative staphylococcus	Ampicillin/Sulbactam Gentamicin	Exitus	Mechanical	Bioprosthesis
13	30	33	None	Gram positive coccus	Vancomycin Gentamicin Rifampicin	Cure	Bioprosthesis	Bioprosthesis
14	16	47	None	None	Vancomycin Gentamicin Rifampicin	Cure	Mechanical	Bioprosthesis
15	20	38	None	Gram positive coccus	Vancomycin Gentamicin Rifampicin	Cure	Mechanical	Mechanical
16	20	43	None	Gram positive coccus	Penicilin G Gentamicin Rifampicin	Cure	Mechanical	Mechanical
17	45	60	None	Streptococcus anginosus	Ampicillin/Sulbactam Gentamisin Rifampicin	Cure	Mechanical	Mechanical
18	21	30	None	Staphylococcus intermedius	Meropenem Daptomycin Rifamycin	Exitus	Mechanical	Mechanical
19	60	90	None	Coagulase negative staphylococcus	Meropenem Ampicillin Rifampicin Linezolide	Cure	Mechanical	Bioproshesis
20	35	45	None	None	Ampicillin/Sulbactam Gentamycin	Cure	Mechanical	Mechanical
21	60	90	None	Candida parapsilosis	Amphotericin B Piperacillin-tazobactam	Cure	Mechanical	Bioprosthesis

be a non-invasive coronary angiogram.[3] None of our patients needed to be examined with ECG-gated CT in our series.

Atypical clinical presentation is frequent in the early postoperative period in most PVE cases. Fever and inflammatory syndromes are commonly seen in the absence of IE. In this case, persistent fever should lead to suspicion of PVE.[1] In our study, all patients had persistent fever.

In previous studies, blood cultures have been found to be negative in 2.5 to 31% of endocarditis cases due to previous antibiotic therapy and intracellular bacteria, fungi, and fastidious pathogens.[4] Staphylococci and enterococci are the most common pathogenic microorganisms in PVE.[1] In our patients, staphylococcal PVE was more predominant. However, valve cultures taken from the patients with IE are positive in only 39.4% and only 25.4% is true positive. For patients without endocarditis, false positive culture is seen in 28.4%. Therefore, routine culture of heart valves is not recommended by some authors.[5]

For the medical treatment of PVE, antimicrobial therapy is similar to treatment in native valve endocarditis (NVE). For the *Staphylococcus aureus*, PVE treatment should be prolonged (≥6 weeks) with an antibiotic regimen (with the addition of aminoglycosides and frequently rifampicin).[1] In the present study, we also treated the patients with staphylococcal PVE with prolonged antibiotherapy.

Negative prognostic factors of PVE include alder age, staphylococcal infection, early PVE, congestive heart failure, stroke, and intracardiac abscess.[2] In our study population, four of the five deaths had staphylococcal PVE. Surgery is recommended in cases of heart failure, uncontrolled infection, and PVE with a high embolism risk.[4] Complicated and staphylococcal PVE have a worse prognosis, if treated without surgery.[1] In a meta-analysis of retrospective studies comparing medical treatment with surgical treatment, surgery had a lower 30-day mortality (25% vs. 34%; $p<0.00001$), and higher survival at follow-up (69% vs. 58%; $p=0.01$).[6] Emergency surgery is needed, when there is refractory congestive heart failure leading to pulmonary edema or shock.[1] Persistent fever for more than seven days following antibiotherapy, congestive heart failure refractory to medical treatment, vegetations larger than 1 cm on echocardiography, fungal endocarditis, severe valvular leak and valvular dysfunction, and staphylococcal PVE were the surgical indications in our study.

In aortic PVE, homografts, stentless valves, or autografts can be used for re-replacement. Homograft or xenograft root replacement is indicated for aortic root distortions. A valved Dacron conduit can be also used alternatively.[1] Transcatheter aortic bioprosthetic valve infections should be managed as the other prosthetic valves.[7] In our study, we did not replace the aortic root in our study population. We used stented bioprostheses or mechanical valves. In a study, surgery was shown to be more beneficial, when all infected tissues were extirpated. The type of the prosthesis has less impact on the outcome.[8] We also believe that radical resection is critical to achieve satisfactory surgical outcomes.

In the literature, there are few studies for decision making of surgical procedure in case of double prosthetic valves. Whether to replace the non-involved valve still remains to be elucidated. According to the previous studies, operative mortality is higher in double-valve replacement than a single-valve replacement and replacement of only the involved prosthesis is reported to be a convenient and safe strategy.[9] In our study, we only replaced the infected valves. The surgical outcomes of this decision were favorable in our three patients.

In redo surgeries, particularly in endocarditis, coronary angiography was done in four of our patients. Nonetheless, it is questionable, particularly for aortic prosthesis endocarditis with vegetations. Catheters may lead to detachment of the vegetations and lead to embolization. However, in mitral valve endocarditis, coronary angiography may be discussed as well, due to the fact that catheter may worsen the cardiac failure in endocarditis and particularly in aortic insufficiency. Many studies, on the other hand, concludes that cardiac catheterization and coronary angiography can be performed safely in IE and should be performed, if necessary, unless the patients are hemodynamically unstable with exacerbating heart failure and require emergency surgery.[10] In the present study, we were only able to evaluate the patients with coronary symptoms through coronary angiography. None of our patients had previous coronary artery bypass grafting.

Furthermore, for the diagnosis of IE and its complications, CT may serve a complementary role to transesophageal echocardiogram for perivalvular involvement of abscesses and pseudoaneurysms.[11] However, we believe that routine evaluation of patients with CT is unnecessary.

This is a small population size study. Its retrospective design is a limitation. However, this complication

is seen in limited numbers and therefore our study population may give some ideas for such a challenging complication.

In conclusion, radical resection of the infected tissues is critical to achieve favorable surgical outcomes. In addition, single valve replacement of the infected valve may be preferred in patients having previous double valve replacement. Mechanical valves or bioprostheses can be used for re-replacement procedures.

Declaration of conflicting interests

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