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Reoperation for bioprosthetic mitral valve dysfunction early and late-term risk analysis

Mitral biyoprotez kapak disfonksiyonu reoperasyonlarında erken ve geç dönem risk analizi

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Background: Assessment of risk factors affecting early and late outcomes of reoperation for bioprosthetic mitral valve dysfunction in patients with rheumatic heart disease and analysis of long-term prognosis of such operations.

Methods: Between 1985 and 2004, we performed reoperations for bioprosthetic valve dysfunction to 104 patients (95 women, 9 men; mean age 48.5±11.3 years; range 20 to 73 years). Causes of bioprosthetic valve dysfunction were structural degeneration in 99 patients, infective endocarditis in two patients and paravalvular leak in three patients.

Results: The hospital mortality was 8.7% (9 patients). Multivariate analysis showed that tricuspid repair in the first operation (p=0.03; Odds ratio 22.7, 95%CI 1.2-423.7), pulmonary hypertension (p=0.03; Odds ratio 24.8, 95%CI 1.3-475.8), and concomitant tricuspid valve repair in the reoperation (p=0.03, Odds ratio 22.7, %95CI 1.2-423.8) were significant risk factors for early mortality. Patients with initial tricuspid disease at the first operation had worse early outcome compared to patients without tricuspid pathology (p=0.038). Late mortality was 2.9% (3 patients). No statistically significant risk factor for late mortality was identified. The ten-year survival rate was 85.6%±4.35.

Conclusion: Our study suggests that reoperation for bioprosthetic mitral valve dysfunction should be performed prior to development of pulmonary hypertension. Rheumatic tricuspid valve disease requiring repair at first operation and/or at reoperation has a poor effect on the early outcome of reoperation.

Key words: Bioprosthesis; mitral valve; reoperation; tricuspid valves.

Amaç: Mitral biyoprotez kapak replasmanı uygulanmış romatizmal kalp hastalarında biyoprotez kapak disfonksiyonu için yapılan reoperasyonların erken ve geç dönem sonuçlarını etkileyen risk faktörleri değerlendirildi ve bu ameliyatların uzun dönem seyri incelendi.

Çalışma planı: 1985-2004 yılları arasında biyoprotez kapak disfonksiyonu nedeniyle toplam 104 hastaya (95 kadın, 9 erkek; ort. yaş 48.5±11.3; dağılım 20-73) reoperasyon uygulandı. Biyoprotez kapak disfonksiyonu 99 hastada yapısal dejenerasyona, ikisinde enfektif endokardite ve üçünde periprostetik kaçağa bağlıydı.

Bulgular: Hastane mortalitesi %8.7 (n=9) oldu. Multivariate analizde erken mortalite ile ilişkili bulunan durumlar, ilk ameliyatta triküspid kapak girişimi yapılmış olması (p=0.03; odds ratio 22.7, %95 CI 1.2-423.7), pulmoner hipertansiyon (p=0.03; odds ratio 24.8, %95 CI 1.3-475.8) ve reoperasyonlarda eşzamanlı triküspid kapak onarımı (p=0.03, odds ratio 22.7, %95 CI 1.2-423.8) olarak saptandı. İlk ameliyatta triküspid kapak girişimi uygulananlarda, uygulanmayanlara kıyasla daha kötü sonuçlar alındı (p=0.038). Geç mortalite %2.9 (n=3) oldu. Geç mortalite ile ilişkili bir risk faktörü saptanamadı. On yıllık sağkalım %85.6±4.35 idi.

Sonuç: Mitral biyoprotez kapak disfonksiyonlarında reoperasyon pulmoner hipertansiyon gelişmeden önce yapılmalıdır. Hastada ilk ameliyatta ve reoperasyonda girişim gerektiren triküspid kapak patolojisi varlığı, reoperasyonun erken dönem mortalitesi üzerine etkilidir.

Anahtar sözcükler: Biyoprotez; mitral kapak; reoperasyon; triküspid kapak.

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In spite of the recent developments in treatment of cardiac valve diseases, an ideal prosthetic valve has not yet been manufactured to replace the malfunctioning native valve. Mechanical valves require continuous use of anticoagulants and carry the risk of anticoagulant-related bleeding and thrombo-embolic complications. Although bioprosthetic valves do not require anticoagulation, limited durability is an important disadvantage.[1] Despite recent improvements in material technology and design, structural degeneration of the valves remains the most important complication that requires reoperation.[2,3] Bioprostheses have better long-term results in aortic position than mitral position, especially in older age groups and reoperation is rarely indicated. On the other hand, bioprostheses bear higher risk for structural deterioration in younger patients, especially in mitral position. Several studies reported the risk factors for mitral valve reoperations.[4,5] Risk factors for mortality at reoperation are age, sex, preoperative New York Heart Association (NYHA) class, type of prosthetic valve, position of replacement, previous operations, timing of operation and renal insufficiency.[6-8]

There are only few articles looking at repeat mitral valve surgery for failed bioprostheses specifically in cases with rheumatic heart disease. In this study, we investigated the risk factors for hospital mortality and analyzed the long-term results of these operations.

PATIENTS AND METHODS

Between 1985 and 2004, 483 patients (predominantly female) underwent bioprosthetic mitral valve replacement. One hundred four (21.5%) patients were reoperated due to bioprosthetic valve dysfunction (Table 1). Of those, 95 (91.3%) were female and nine were males. The mean age was 48.5±11.3 years with a range of 20 to 73 years. In all cases, the etiology of the valve lesion at the first operation was rheumatic valvular disease. Women at childbearing age and young male patients who cannot use warfarin received bioprosthetic valves. These patients initially underwent isolated mitral valve replacement with or without tricuspid valve repair and all had received a bioprosthesis in mitral position (Table 2). Tricuspid valve pathology had been detected in 59 patients and 18 of them had tricuspid valve repair at the first operation. Tricuspid DeVega suture annuloplasty was performed in 14 patients that had significant tricuspid regurgitation (> 2°), and tricuspid commissurotomy and combined commissurotomy / annuloplasty in two

Table 1. Preoperative variable

Variable	Alive		Early mortality		*p*
	n	%	n	%	
	95	91.4	9	8.6	
Sex (female)	79	83.2	9	100	0.208
Age (years)	46.7±11.3		52.2±11.4		0.162
Functional class (NYHA)	2.4±0.5		3.4±0.7		<0.001
II	55	57.9	1	11.2	0.008
III	38	40	3	33.3	0.495
IV	2	2.1	5	55.5	<0.001
Indication					
Tissue failure	90	94.7	9	100	0.573
Paravalvular leak	3	3.2	0	–	0.760
Endocarditis	2	2.1	0	–	0.834
Urgency of operation	0	–	2	22.2	0.007
Creatinine level (> 1.6 mg/dL)	4	3.8	2	22.2	0.058
Rhythm (atrial fibrillation)	73	76.8	7	77.7	0.385
Left ventricular ejection fraction (50%)	58.3±6.2		55.9±6.4		0.262
Pulmonary artery pressure	53.3±11.4		61.1±13.9		0.057
Pulmonary hypertension (systolic ≥ 60 mmHg)	28	29.5	6	66.6	0.032
Aortic cross clamp time (min)	83.3±32.1		111±43.8		0.018
Cardiopulmonary bypass (time)	113.4±39.4		187.1±81.3		<0.001
Aortic valve intervention	12	12.6	0	–	0.240
Tricuspid repair					
Reoperation (total=34)	27	28.4	7	77.7	0.005
First + Reoperation (n=9)	5	5.3	4	44.4	<0.001
First operation (total=18)	14	–	4	44.4	0.028

Table 2. Implanted bioprosthetic valves

Biocor Porcine	80
Liotto	11
Carpentiar-Edwars	9
Hancock II	4

patients each. No coronary bypass grafting or aortic intervention was performed at the first operation.

The main cause for bioprosthetic valve dysfunction was structural deterioration (Table 1). This manifested as cusp rupture and/or calcification leading to severe regurgitation or stenosis. Cusp rupture alone was identified in 62 (59.6%) patients, calcification alone in 21 (20.2%) patients and both of these were identified in 21 patients (20.2%). Two patients underwent emergency reoperation for bioprosthetic rupture secondary to infective endocarditis. The mean interval between the first mitral valve replacement and reoperation was 126.5±34.5 months with a range of 12 to 193 months. None had signs of right heart failure (no hepatomegaly or edema).

Surgical management. In elective reoperations, first median sternotomy with an oscillating saw and than limited dissection on the aorta and the right atrium were performed. Femoral artery and vein were explored and prepared for cannulation in patients who had severe sternal adhesion on the chest roentgenogram or in the emergency cases. Cardiopulmonary bypass was performed by cannulation of the ascending aorta and both of vena cavae through right atrium. All operations were performed with moderate (32°) hypothermia. Myocardial protection was provided by intermittent antegrade blood cardioplegia, however, continuous retrograde cardioplegia through the coronary sinus was preferred in cases with concomitant aortic valve intervention. Left heart venting was performed via a left atrial vent catheter through right upper pulmonary vein. After the standard left atriotomy, the degenerated bioprosthetic valve was extracted carefully and was replaced by a mechanical valve using a simple suture technique (2/0 polyesther). The superior transseptal approach was used in three patients, who also needed tricuspid repair. 34 (32.1%) patients with significant regurgitation (> 2°) during reoperation underwent tricuspid annuloplasty. We performed aortic valve replacement in 9 patients and aortic valve repair (resuspention in 2 and leaflet thinning in 1) in 3 patients for newly developed aortic valve pathology. Ascending aorta replacement with a composite graft was performed in one patient because of ascending aortic dissection. In one patient, the left anterior descending artery was bypassed with a saphenous vein graft.

Acetyl salicylate 150 mg/day and sodium warfarine were given to all patients on the first postoperative day.

Statistical analysis. Follow-up information was obtained directly from patients, their close relatives or from hospital records. The mean follow-up time was 45.6±35.4 months with a total of 361.3 patient ayear, and all surviving patients are still under follow-up. Statistical analysis was performed using the statistical software SPSS 11.0 for windows (SPSS Inc., Chicago, IL). The data are expressed as mean value ± standard deviation for continuous variables, as numbers with percentage for categorical variables. Differences between categorical variables were tested using the χ^2 test; differences between continuous variables were tested using unpaired t-test. The following variables were analyzed in this study: sex, age, indication for reoperation, functional class, left ventricular ejection fraction (LVEF), pulmonary hypertension (≥60 mmHg), preoperative or postoperative renal insufficiency (creatinine >1.6 mg/dL), cardiac rhythm, number of previous operation(s), tricuspid repair in the first operation, tricuspid repair in reoperation, urgency of operation, extracorporeal circulation (ECC) time, aortic cross-clamp (ACC) time, postoperative inotropic support, requirement of a pacemaker. Univariate and multivariate analyses were used to assess risk factors as independent predictors of early mortality. Actuarial survival was calculated by the Kaplan-Meier method and the result is expressed as mean value ± standard error. Cox proportional hazard regression analysis was used to assess risk factors as independent predictors of patient survival. A p value of 0.05 or less was considered to be significant.

RESULTS

Hospital mortality. Hospital mortality was 8.7% (nine patients). The main cause of death in six patients was low cardiac output (LCO). Two patients died because of multiorgan failure. One patient died during median sternotomy due to right ventricular rupture. Univariate analysis revealed that tricuspid repair at the first operation (p=0.004), advanced NYHA class (p=0.006), urgent operation (p<0.001), preoperative renal dysfunction (p=0.014), ECC time ≥120 minutes (p=0.007), ACC time ≥85 minutes (p=0.039), pulmonary hypertension (p=0.016), concomitant intervention to tricuspid valve at reoperation (p=0.004), inotropic support (p=0.017) and postoperative renal insufficiency (p=0.004) were the risk factors associated with early mortality. Stepwise logistic regression analysis showed that tricuspid repair in the first operation (p=0.036; Odds 22.7, 95% CI 1.2-423.7), pulmonary hypertension (p=0.03; Odds 24.8, 95% CI 1.3-475.8) and concomitant intervention to the tricuspid valve at reoperation

(p=0.036; Odds 22.7, 95% CI 1.2-423.8) were significant predictors of hospital mortality.

The necessity for tricuspid repair was increased in patients who had tricuspid intervention at first operation compared to patients without initial tricuspid pathology (50% vs 29.1%; p=0.0027). Tricuspid re-repair was performed in nine (50%) out of eighteen patients who had received tricuspid repair at first operation. Four (44.4%) of them died after reoperation (Table 1). Twenty-five patients (29.1%) of a total of eighty-six patients who had not had tricuspid intervention at first operation, underwent tricuspid repair at reoperation. Three (12%) of those patients died. Patients with initial tricuspid disease have a worse early outcome compared to patients without tricuspid involvement at first operation (p=0.038).

Early morbidity. Re-exploration for bleeding was necessary in two patients (1.9%). One patient developed a permanent hemiplegia. Intraaortic balloon-pump support was used for LCO in two patients. One of them was discharged from hospital whereas the other died during early postoperative period. Renal failure requiring hemodialysis was present in two patients, one had renal insufficiency before the operation. A temporary pacemaker support to complete an atrioventricular block was necessary in three patients, two of them required a permanent pace maker implantation. The mean duration of stay in intensive care unit was 3.6±2.6 days.

Late outcome. Actuarial freedom from death was 85.6%±4.3 at 10 years. Three patients were lost at long-term follow-up. The cause of deaths was cardiac failure in two patients. One patient was reoperated a third time for newly developed aortic regurgitation, however she died because of LCO on postoperative day one. No risk factors for late mortality were found by Cox regression model. Paravalvular leak was detected in two patients but they were followed medically with periodic echocardiographic checks. Mechanical valve thrombosis was observed in two patients and they were treated with thrombolytic drugs. Anticoagulant related gastrointestinal bleeding was observed in two patients. Eighty-eight surviving patients had NYHA Class I or II functional capacity whereas four patients had NYHA class III functional capacity.

DISCUSSION

The major disadvantages of bioprosthetic valves are the limited durability due to structural deterioration and increased reoperation rate. Degeneration progresses slowly and allows early diagnosis and elective intervention without acute and fatal complications, however this eventually may require a second intervention.[9,10] Nevertheless emergency surgery may be required in some bioprosthetic valve dysfunctions. In the previous studies, stress related tears and perforations secondary to dystrophic calcifications have been reported to be the most important causes of reoperation. Young age, renal insufficiency, low LVEF and development of coronary lesions are the most frequent risk factors affecting reoperations. Both mortality and morbidity rates are higher at reoperations than at initial operation. Mortality rates of reoperations for bioprosthetic and mechanical valves at mitral position range between 10% and 15.3%.[5,6,10-12] Tyers et al.[13] detected 10.6% mortality rate for bioprosthetic valves at all positions. The improved mortality rates in the recent decades reveal that current models of bioprostheses have better durability than the older models. The mortality rate of reoperations for mitral bioprosthetic valves has been reported between 3.4% and 6.8%.[8,14-16] In our series, the overall hospital mortality rate was 9/104 (8.7%). The univariate analysis identified impaired functional capacity and urgent operation as independent predictors of hospital mortality. The early mortality rate seems a bit high, but when we exclude urgent operations early mortality rate of elective patients is 6.8%, which is within the limits of the presented mortality rates. The NYHA functional capacity is one of the most important predictors of mortality.[10,17,18] Likewise, the requirement of inotropic support during early postoperative period (reflecting early postoperative ventricular dysfunction) is associated with early mortality. All of these well-known risk factors could impair surgical outcomes, but using multivariant analysis we did not find any risk factor to be statistically significant. Our study revealed that the left ventricular dysfunction was not associated with higher mortality.

In this study, right heart dysfunction was identified as the main cause of hospital mortality for patients with rheumatic disease. This study group consists of younger patients when compared with studies in patients who have degenerative mitral valve disease. Right heart failure is the main risk factor for early and late outcome in patients with rheumatic valve disease. The major determinant is significant tricuspid insufficiency which reflects the right heart failure, whereas severe tricuspid stenosis indicates the severity of rheumatic disease which will impair cardiac functions. In our study, concomitant tricuspid valve repair at first operation and reoperation were identified as risk factors. Such patients usually have severely compromised cardiac functions. On the other hand, a significant increase in pulmonary hypertension is a sign of left heart problems or end stage valvular disease. Pulmonary artery systolic pressure was also identified in this study as a significant risk factor for early mortality. However, some authors do not indicate any influence of median and systolic pulmonary artery pressures on mortality.[8,14] We think

that increased pulmonary hypertension with rheumatic involvement of the tricuspid valve impair the right heart functions more so than isolated pulmonary hypertension. As previously stated, functional tricuspid regurgitation could improve after surgical treatment of the mitral valve in patients with isolated left heart rheumatic involvement without severe pulmonary hypertension (<50 mmHg).[19] However, a de novo tricuspid insufficiency can develop after bioprosthesis replacement in young patients with rheumatic disease, because bioprosthesis dysfunction and progression of rheumatic disease worsened the right heart dysfunction and tricuspid function. Both can cause tricuspid insufficiency that needs intervention at reoperation. In this study, one quarter of patients without tricuspid pathology at first operation needed tricuspid annuloplasty at reoperation. Early mortality rate was four times higher among these patients compared to patients that did not need tricuspid intervention at reoperation, but this was not statistically significant (p=0.1). The patients that underwent two tricuspid repairs (both at first operation and reoperation) had the worst early outcome after reoperation. Similarly, tricuspid valve replacement at reoperation was identified as a predictor of early mortality in various studies.[20]

Identification of high pulmonary artery pressure and concomitant tricuspid valve procedure as risk factors suggest that elective and earlier reoperations for bioprosthetic valve dysfunctions should be performed before development of right ventricular dilatation and failure in patients with rheumatic disease. The preoperative clinical status of patients and additional concomitant procedures dictate the success of operation. Tricuspid valve involvement and right heart function status must be taken into consideration in younger patients who require mitral valve replacement due to rheumatic disease. In this group of patients, mechanical prosthesis is a good alternative to bioprosthetic mitral valve replacement at first operation because it is not associated with structural deterioration thus preventing the development of right heart failure caused by bioprosthesis dysfunction.

REFERENCES

1. Bloomfield P, Wheatley DJ, Prescott RJ, Miller HC. Twelve-year comparison of a Bjork-Shiley mechanical heart valve with porcine bioprostheses. N Engl J Med 1991;324:573-9.
2. Eichinger WB, Botzenhardt F, Gunzinger R, Kemkes BM, Sosnowski A, Maiza D, et al. European experience with the Mosaic bioprosthesis. J Thorac Cardiovasc Surg 2002; 124:333-9.
3. Kirali K, Guler M, Tuncer A, Daglar B, Ipek G, Isik O, et al. Fifteen-year clinical experience with the biocor porcine bioprostheses in the mitral position. Ann Thorac Surg 2001; 71:811-5.
4. Matsuyama K, Matsumoto M, Sugita T, Nishizawa J, Kawansihi Y, Uehara K. Long-term results of reoperative mitral valve surgery in patients with rheumatic disease. Ann Thorac Surg 2003;76:1939-43.
5. Potter DD, Sundt TM 3rd, Zehr KJ, Dearani JA, Daly RC, Mullany CJ, et al. Risk of repeat mitral valve replacement for failed mitral valve prostheses. Ann Thorac Surg 2004;78:67-72.
6. Lytle BW, Cosgrove DM, Taylor PC, Gill CC, Goormastic M, Golding LR, et al. Reoperations for valve surgery: perioperative mortality and determinants of risk for 1,000 patients, 1958-1984. Ann Thorac Surg 1986;42:632-43.
7. Glower DD, Landolfo KP, Cheruvu S, Cen YY, Harrison JK, Bashore TM, et al. Determinants of 15-year outcome with 1,119 standard Carpentier-Edwards porcine valves. Ann Thorac Surg 1998;66(6 Suppl):S44-8.
8. Akins CW, Buckley MJ, Daggett WM, Hilgenberg AD, Vlahakes GJ, Torchiana DF, et al. Risk of reoperative valve replacement for failed mitral and aortic bioprostheses. Ann Thorac Surg 1998;65:1545-51.
9. Loisance DY, Mazzucotelli JP, Bertrand PC, Deleuze PH, Cachera JP. Mitroflow pericardial valve: long-term durability. Ann Thorac Surg 1993;56:131-6.
10. Bortolotti U, Milano A, Mossuto E, Mazzaro E, Thiene G, Casarotto D. Early and late outcome after reoperation for prosthetic valve dysfunction: analysis of 549 patients during a 26-year period. J Heart Valve Dis 1994;3:81-7.
11. Demirag M, Kirali K, Omeroglu SN, Mansuroglu D, Akinci E, Ipek G, et al. Mechanical versus biological valve prosthesis in the mitral position: a 10-year follow up of St. Jude Medical and Biocor valves. J Heart Valve Dis 2001;10:78-83.
12. Ruel M, Kulik A, Rubens FD, Bedard P, Masters RG, Pipe AL, et al. Late incidence and determinants of reoperation in patients with prosthetic heart valves. Eur J Cardiothorac Surg 2004;25:364-70.
13. Tyers GF, Jamieson WR, Munro AI, Germann E, Burr LH, Miyagishima RT, et al. Reoperation in biological and mechanical valve populations: fate of the reoperative patient. Ann Thorac Surg 1995;60(2 Suppl):S464-8.
14. de Almeida Brandao CM, Pomerantzeff PM, Souza LR, Tarasoutchi F, Grimberg M, Ramires JA, et al. Multivariate analysis of risk factors for hospital mortality in valvular reoperations for prosthetic valve dysfunction. Eur J Cardiothorac Surg 2002;22:922-6.
15. Jamieson WR, Burr LH, Miyagishima RT, Janusz MT, Fradet GJ, Lichtenstein SV, et al. Reoperation for bioprosthetic mitral structural failure: risk assessment. Circulation 2003;108 Suppl 1:II98-102.
16. McGrath LB, Fernandez J, Laub GW, Anderson WA, Bailey BM, Chen C. Perioperative events in patients with failed mechanical and bioprosthetic valves. Ann Thorac Surg 1995;60(2 Suppl):S475-8.
17. Piehler JM, Blackstone EH, Bailey KR, Sullivan ME, Pluth JR, Weiss NS, et al. Reoperation on prosthetic heart values. Patient-specific estimates of in-hospital events. J Thorac Cardiovasc Surg 1995;109:30-48.
18. Pansini S, Ottino G, Forsennati PG, Serpieri G, Zattera G, Casabona R, et al. Reoperations on heart valve prostheses: an analysis of operative risks and late results. Ann Thorac Surg 1990;50:590-6.
19. Kirali K, Omeroglu SN, Uzun K, Erentug V, Bozbuga N,

Eren E, et al. Evolution of repaired and non-repaired tricuspid regurgitation in rheumatic mitral valve surgery without severe pulmonary hypertension. Asian Cardiovasc Thorac Ann 2004;12:239-45.

20. Glower DD, White WD, Smith LR, Young WG, Oldham HN, Wolfe WG, et al. In-hospital and long-term outcome after porcine tricuspid valve replacement. J Thorac Cardiovasc Surg 1995;109:877-83.