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Valve Surgery

Outcome of Mild Periprosthetic Regurgitation Detected by Intraoperative Transesophageal Echocardiography

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OBJECTIVES The goal of this study was to determine the outcome of trivial or mild periprosthetic regurgitation (PPR) identified by intraoperative transesophageal echocardiography (TEE).

BACKGROUND The clinical significance, natural history and correlates of trivial or mild PPR detected early after surgery are unknown.

METHODS Between 1992 and 1997, 608 consecutive patients underwent isolated aortic valve replacement or mitral valve replacement at Dartmouth-Hitchcock Medical Center. Of these, 113 patients (18.3%) were found to have trivial or mild PPR at surgery by TEE. Follow-up transthoracic echocardiograms (early TTEs) were obtained within six weeks of surgery in 99.0% of patients and late TTEs (mean 2.1 years) in 54.3%. Clinical, intraoperative and outcome variables associated with PPR were identified using *t* test, chi-square and logistic regression analyses.

RESULTS By univariate analysis, compared with patients without PPR, patients with PPR were older, of smaller body surface area (BSA), had degenerative valve disease more often and were more likely to receive a bioprosthetic valve. By multivariate analysis, smaller BSA and the use of a bioprosthesis were the strongest predictors of PPR ($p < 0.01$). At early TTE, PPR was not observed ($n = 56$) or remained unchanged ($n = 44$) in all patients. At late TTE, four patients were found to have progression of their PPR. All four patients had bioprosthetic valves. Two of these patients had endocarditis, and one had primary valvular degeneration. The fourth patient had progressive PPR.

CONCLUSIONS Trivial or mild PPR is a frequent finding on intraoperative TEE. Smaller body size and the use of a bioprosthetic valve are significantly associated with PPR. The clinical significance and natural history of PPR is benign in most cases. (J Am Coll Cardiol 2001;38:163–6) © 2001 by the American College of Cardiology

The incidence of periprosthetic regurgitation (PPR) identified early after surgery has varied widely from a low of 1% to 5% (1,2) to as high as 53% to 73% (3–6). Although these studies suggest that patients with mild PPR had a benign course during long-term follow-up, they were limited by small sample size, variation in the time interval between valve surgery and detection of the regurgitant leak, the duration of follow-up and the method used to detect PPR—transthoracic echocardiography (TTE) versus transesophageal echocardiography (TEE) (2,7).

The clinical correlates of trivial or mild PPR are unknown. Causes of periprosthetic leak are believed to be mainly technical. The purpose of this study was to determine the clinical significance, natural history and correlates of trivial or mild PPR identified by intraoperative TEE.

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METHODS

Between January 1, 1992 and December 31, 1997, 608 patients underwent isolated aortic valve replacement (AVR) or mitral valve replacement (MVR) at Dartmouth-Hitchcock Medical Center. From these 608 patients, two groups of patients were identified based on the presence (group 1; $n = 113$) or absence (group 2; $n = 495$) of PPR.

At our institution, all patients who have valvular surgery have a complete TEE examination performed intraoperatively by biplane or multiplane imaging after separation from cardiopulmonary bypass. A follow-up TTE at six weeks is routinely obtained in all patients who have undergone valve surgery. Additionally, for those patients who are followed long-term at our institution, a yearly TTE is often obtained. Echocardiographic findings are entered into and maintained in a database.

The echocardiographic database was searched to identify patients classified as having trivial or mild PPR intraoperatively. Clinical and surgical characteristics are collected on all patients undergoing valve surgery as part of the Northern New England Cardiovascular Disease Study Group (8). The

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Abbreviations and Acronyms

AVR = aortic valve replacement
BSA = body surface area
MVR = mitral valve replacement
PPR = periprosthetic regurgitation
TEE = transesophageal echocardiography
TTE = transthoracic echocardiography

information from this database and the echocardiographic database were merged for analysis.

The TEE studies of all patients with trivial or mild PPR were reviewed by an independent echocardiographer to verify the presence of a leak. All of the intraoperative TEEs originally classified as having trivial or mild PPR were subsequently confirmed as having that degree of leak on review of the tapes. A random sample (n = 75) from the control group (group 2) without reported PPR were independently reviewed and verified to have no leak. The presence or absence of PPR on follow-up TTEs was obtained from the clinical reports in our echocardiographic database. Regurgitation was considered periprosthetic if the jet of regurgitation was identified as originating between the prosthetic valve sewing ring and the native valve annulus. The severity of PPR was assessed semiquantitatively using visual estimation. All PPR was subsequently measured off-line to confirm the initial visual assessment of severity. These measurements confirmed that the severity of PPR was trivial or mild in the mitral position, as all jet areas were less than 3.0 cm^2, which is within the accepted value (9–12). Periprosthetic regurgitation in the aortic position was considered to be trivial or mild if the ratio of the regurgitant jet to left ventricular outflow tract diameter was less than 25% (13). No patient was identified as having moderate or severe PPR. At our institution, all instances of moderate or severe PPR are repaired at the time of initial operation.

Statistical analysis. Standard statistical tests (*t* test, chi-square and analysis of variance) were used to compare the characteristics between the two groups. Differences were identified by univariate analysis ($p < 0.05$) and then entered into a multivariate model. Logistic regression was used to identify those variables that were significant correlates of PPR ($p < 0.05$). All analyses were performed using Stata Statistical Software (Stata Corporation, College Station, Texas).

RESULTS

Of the 608 consecutive patients who underwent isolated AVR or MVR at our institution between January 1, 1992 and December 31, 1997, 113 (18.3%) were found to have trivial or mild PPR at surgery by TEE. The valves implanted included: Carpentier-Edwards (n = 46) and Hancock (n = 247) bioprostheses; Medtronic-Hall (n = 237) and St. Jude (n = 73) mechanical prostheses and a small number of other types (n = 5). The incidence of PPR for AVR was 17.7% (89/502) and for MVR was 22.6% (24/106), which was not statistically different (p = 0.41). There was no difference in overall mortality at six weeks (Table 1).

Table 1. Outcome of Periprosthetic Regurgitation

Mortality	Group 1 PPR Present (n = 113)	Group 2 No PPR (n = 495)	p Value
Six week (%)	10.6	8.1	0.32
Progression of PPR	**n**		
Intraoperative TEE			
Trivial or mild PPR	113		
Early TTE (within 6 weeks)	100		
No PPR	56		
Trivial or mild PPR	44		
Moderate PPR	0		
Severe PPR	0		
Late TTE (between 6 months and 5 years; mean 2.1 yr)	50		
No PPR	27		
Trivial or mild PPR	19		
Moderate PPR	3		
Severe PPR	1		

PPR = periprosthetic regurgitation; TEE = transesophageal echocardiogram; TTE = transthoracic echocardiogram.

The natural history of PPR was evaluated by echocardiography. Transthoracic echocardiograms were obtained within six weeks after valve replacement (early TTE) and at late follow-up (mean 2.1 years). Of the 101 patients remaining at early follow-up, 100 patients had a TTE (99.0%). At early TTE, PPR was not observed and, therefore, probably not significant (n = 56) or remained unchanged (n = 44) in all patients (Table 1). At late follow-up, an additional nine patients had died leaving 92 patients available for follow-up. Of these 92 patients, TTEs were obtained in 54.3%. Of those undergoing late TTE, four of 50 (8.0%) patients had progression of their PPR. All four patients had bioprosthetic valves. Three of the four patients had no PPR on early TTE. Of the three who did not have PPR on early TTE, two had infective endocarditis, and one had primary valvular degeneration. The fourth patient, who had mild PPR at six weeks, had progression of his periprosthetic leak. Therefore, only one patient of the original 113 patients with trivial or mild mitral regurgitation (0.9%) had significant progression of PPR. This patient subsequently had his bioprosthetic aortic valve replaced approximately three years after his initial valve implantation.

Univariate analysis was used to determine the clinical and surgical characteristics that were correlates of trivial or mild PPR (Tables 2 and 3). Variables found to be significantly associated with PPR on univariate analysis included older age ($p < 0.0001$), smaller body surface area (BSA) ($p < 0.0001$), underlying valve disease-degenerative valve disease ($p = 0.05$) and valve type-bioprosthetic valve implantation ($p < 0.0001$). These variables were then used in a multivariate model. On multivariate analysis, smaller BSA and

Table 2. Clinical Characteristics

Clinical Characteristics	Group 1 PPR Present (n = 113)	Group 2 No PPR (n = 495)	p Value
Mean age (yr)	73.9	67.1	< 0.0001
Gender (% male)	54.0	59.0	0.33
Body surface area	1.7	1.9	< 0.0001
History of diabetes (%)	5.4	8.1	0.35
History of hypertension (%)	37.1	43.0	0.44
History of smoking (%)	13.9	18.0	0.30
Known coronary artery disease (%)	53.7	47.5	0.24
History of coronary angioplasty (%)	2.8	1.4	0.14
History of bypass surgery (%)	5.6	4.7	0.70
History of heart failure (%)	75.0	67.1	0.16
NYHA class			
I	2.8	3.1	0.17
II	12.9	14.6	
III	71.4	60.8	
IV	12.9	21.5	
History of stroke (%)	8.3	9.0	0.83
History of atrial fibrillation	52.8	50.3	0.81
History of valve surgery (%)	11.0	8.7	0.46
Preoperative creatinine (mg/dl)	1.1	1.1	0.51

NYHA = New York Heart Association.

the use of a bioprosthetic valve were the strongest correlates of PPR ($p < 0.01$).

DISCUSSION

Our study found that the incidence of PPR was 17.7% for aortic prostheses and 22.6% for mitral prostheses. In the majority of patients, PPR resolved or remained unchanged during subsequent echocardiographic follow-up. The presence or absence of PPR had no effect on six-week mortality. Several univariate correlates of PPR were identified including older age, smaller body size, degenerative valve disease and the use of a bioprosthetic valve. However, by multivariate analysis, small body size and the use of a bioprosthetic valve were the strongest predictors of trivial or mild periprosthetic leak. Significant progression of PPR requiring repeat valve surgery occurred in only one (0.9%) patient at late follow-up (mean 2.1 years). In three other patients with progression of PPR at late follow-up, a new etiology was identified, either infective endocarditis or primary valve deterioration.

Natural history of periprosthetic regurgitation. The natural history of PPR is beginning to be elucidated. Two small studies have recently reported a benign prognosis in patients with a small periprosthetic leak detected at the time of surgery. Murthy et al. (2) found that, of 48 patients with small periprosthetic leaks identified intraoperatively, no patients had progression of their PPR over a mean follow-up of 3.5 years. Rallidis et al. (4) reported that the severity of the PPR in all 40 patients initially identified as having a small aortic periprosthetic leak remained un-

Table 3. Surgical Characteristics and Outcome

Surgical Characteristics	Group 1 PPR Present (n = 113)	Group 2 No PPR (n = 495)	p Value
Surgical indication (%)			
Degenerative	75.9	63.9	0.05
Rheumatic	10.2	13.4	
Other	13.9	22.7	
Surgical priority			
Elective	59.2	61.3	0.58
Urgent	39.7	36.5	
Emergent	0.1	2.2	
Preoperative left ventricular end-diastolic pressure	18.1	19.6	0.10
Intraaortic balloon pump inserted intraoperatively (%)	5.6	4.7	0.92
Valve type			
Bioprosthetic (%)	80.0	43.0	< 0.0001
Mechanical (%)	20.0	57.0	
Valve size (mean, cm)			
Aortic	22.2	22.2	0.88
Mitral	29.2	29.3	0.87

changed during five years of follow-up. We found that the majority of cases of trivial or mild PPR identified by intraoperative TEE were not visualized or remained stable over time on follow-up TTE.

Incidence of periprosthetic regurgitation. The reported incidence of PPR has varied widely depending on the timing of the echocardiogram used to detect the periprosthetic leak, the method of echocardiographic evaluation, the valve type implanted and its location (1–6). In our study, we found that the incidence of PPR associated with aortic (17.7%) and mitral prostheses (22.6%) was not statistically different and was comparable to that reported by other investigators (5,6). However, despite the common finding of trivial or mild PPR on intraoperative TEE, the long-term clinical significance and natural history of the PPR was favorable and comparable to that of patients without PPR.

Predictors of periprosthetic regurgitation. To our knowledge, there has been no previous study that has attempted to determine the clinical and surgical characteristics associated with PPR. Using univariate analysis, older age, smaller body size, degenerative valve disease and the use of a bioprosthetic valve were found to be correlates of trivial or mild PPR. By multivariate analysis, smaller BSA and the use of a bioprosthesis were the strongest correlates. It is reasonable to postulate that people with smaller body size are more likely to have a smaller heart and, therefore, a smaller valve annulus that would only accommodate a small prosthesis. The smaller annulus may pose technical problems for the surgeon in suture placement and seating of the prosthesis in comparison with a patient with a large annulus resulting in trivial or mild PPR.

Study limitations. First, a late TTE was obtained in 50% of the study patients. Therefore, it is possible that some patients with progressive PPR were not identified. Second, the TEEs for the 495 patients comprising the control group were not retrospectively reviewed to verify the absence of a periprosthetic leak. It is possible that some of these patients had a trivial or mild periprosthetic leak that was not originally detected. However, no patients in the control group subsequently required repeat valve surgery for progressive PPR, and long-term mortality between the two groups was not significantly different. Third, nonvolumetric methods for assessing mitral regurgitation were used, which may have resulted in underestimating the severity of the leak. However, semiquantitative measures, that is, visual and jet area, have been shown to perform very well in recognizing trivial to mild MR (11,12).

Conclusions. Trivial or mild PPR is a common finding on intraoperative TEE. Smaller body size and use of a bioprosthetic valve were found to be significantly associated with the development of a periprosthetic leak. The clinical outcome and natural history of PPR is benign in the majority of cases.

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