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# Prevalence and Severity of Paravalvular Regurgitation in the Artificial Valve Endocarditis Reduction Trial (AVERT) Echocardiography Study

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**OBJECTIVES** The purpose of this study was to determine the prevalence and severity of paravalvular regurgitation (PVR) in the Artificial Valve Endocarditis Reduction Trial (AVERT) cohort.

**BACKGROUND** The initial AVERT cohort consisted of 807 patients randomized to receive either a Silzone-coated prosthetic valve or a conventional prosthetic valve; early clinical reports showed higher rates of valve explant caused by PVR for Silzone-coated prosthetic valve.

**METHODS** Of the 678 eligible patients, 575 (85%) underwent postoperative transthoracic echocardiograms. The presence and severity of PVR were identified by color flow Doppler. Reviewers were blinded to the type of prosthetic valve and the demographic and clinical variables.

**RESULTS** Among those who underwent echocardiography (Silzone-coated prosthetic valve, n = 285 and conventional prosthetic valve, n = 290), 59% had prosthetic aortic valves, 32% prosthetic mitral valves, and 9% had both; demographic and clinical findings (i.e., prosthetic valve endocarditis, thromboembolism, bleeding, and all-cause death) were similar for the two groups. Echocardiographically determined PVR was present in 50 valves: Silzone-coated prosthetic valve, 29 of 285 (10%) and conventional prosthetic valve, 21 of 290 (7%, p = NS); the severity of PVR was similar in both groups. Kaplan-Meier analysis showed no significant differences in PVR at 24 months from valve implantation between the two groups (24-month event-free rate: 93% Silzone-coated prosthetic valve vs. 94% conventional prosthetic valve, p = NS).

**CONCLUSIONS** Excluding those patients who had initial prosthetic valve explant, the two-year echocardiographic follow-up of the AVERT cohort shows no statistically significant differences in the prevalence or severity of PVR in the Silzone-coated prosthetic valve compared with the conventional prosthetic valve. Further monitoring is warranted to determine whether these clinical outcomes remain similar on long-term follow-up. (J Am Coll Cardiol 2004;44: 1467–72) © 2004 by the American College of Cardiology Foundation

The Artificial Valve Endocarditis Reduction Trial (AVERT) was designed to evaluate the efficacy of the Silzone-coated prosthetic valve silver-coated sewing ring to reduce prosthetic valve endocarditis (PVE), based on studies documenting the safety and efficacy of silver for antimicrobial protection (1–3). The purpose of the AVERT study was to assess long-term outcomes and evaluate for adverse events (i.e., thromboembolic, bleeding, PVE and/or prosthetic valve dysfunction). The initial study cohort consisted of 807 patients randomized to receive either a Silzone-coated prosthetic valve or a conventional prosthetic valve. Although no differences in thromboembolic events between the two valves were found by the AVERT Data and Safety Monitoring Board, reports of a higher incidence of early prosthetic valve explant caused by paravalvular regurgitation (PVR) in the Silzone-coated prosthetic valve study arm led to a discontinuation of recruitment and a worldwide voluntary recall of the prosthesis (4,5).

The prevalence and/or clinical significance of PVR after prosthetic valve replacement has not been well characterized. Recent studies seem to suggest that PVR is rather common. When assessed by intraoperative transesophageal echocardiography, PVR has been reported to be 18% for aortic valve replacement (AVR) and 23% for mitral valve replacement (MVR) (6–8). Furthermore, two-year follow-up of patients with PVR suggests a benign clinical course, with re-operation required in <1%, usually because of increased severity of regurgitation.

An estimated 36,000 patients worldwide have received Silzone-coated prosthetic valve mechanical valves. A recent report on the AVERT cohort has shown that the overall survival in both groups is similar (5). However, the preva-

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**Abbreviations and Acronyms**

AVERT = Artificial Valve Endocarditis Reduction Trial
AVR = aortic valve replacement
LAA = left atrial area
LV = left ventricular
LVOT = left ventricular outflow tract
MVR = mitral valve replacement
PASP = pulmonary artery systolic pressure
PVE = prosthetic valve endocarditis
PVR = paravalvular regurgitation
RJA = regurgitant jet area
TTE = transthoracic echocardiography
TVI = time-velocity integral

lence and severity of PVR in those whose prosthetic valves were not explanted early are not known. Long-term follow-up of the AVERT study cohort is important to identify the prevalence of adverse events, including PVR. Furthermore, long-term follow-up of the AVERT cohort allows one to further define the rate of progression of PVR. This report includes demographic, clinical, and transthoracic echocardiography (TTE) findings of the available AVERT cohort since the beginning of the study until June 30, 2002. The primary end point of the present study was to determine the prevalence and severity of PVR in the Silzone-coated prosthetic valve and conventional prosthetic valves. Secondary end points include other TTE-derived variables (i.e., ventricular size and function, prosthetic valve function) and clinical events (i.e., thromboembolism, bleeding, PVE, and all-cause death).

## METHODS

**Study protocol.** The study design, sample-size determination, and early clinical findings have been presented previously (4,5). Briefly, the AVERT trial was developed to determine whether Silzone-coated prosthetic valve coating of prosthetic valve sewing rings reduced the risk of PVE. The trial began recruitment of patients in July 1998, with the original goal of randomizing 4,400 patients at 12 North American and 7 European centers, based on a power analysis to detect a 50% reduction in risk of PVE. Recruitment ended in January 2000 because of higher rates of early prosthetic valve explant resulting from PVR in patients receiving a Silzone-coated prosthetic valve. The echocardiographic study was initiated in June 1, 2000, to determine the prevalence and severity of PVR in the remaining AVERT cohort.

**Patient population.** The AVERT study population comprised 807 patients who underwent AVR, MVR, or double (AVR and MVR) valve replacement in North America (n = 446) and Europe (n = 361); of these, 129 patients were not included in the present study because they had either died (n = 57), had their valves explanted (n = 19), withdrew consent (n = 10), or had not signed informed consent for the echocardiography substudy (n = 43). Thus, the cohort available for echocardiographic follow-up was 678 patients; this report describes 575 (85%) of these patients who had at least one postoperative TTE study performed by June 30, 2002. The mean age of the patients was 61 years (range 21 to 85 years), and 214 (43%) were women.

**Study end points.** The primary end point of the study was to determine the incidence and severity of echocardiographically determined PVR. The following classification was used to assess for PVR: 1) definitive PVR: a regurgitant jet was clearly identified by color flow Doppler as originating between the prosthetic valve sewing ring and the native valve annulus; a high-velocity mitral or aortic valve regurgitant jet was identified by continuous-wave spectral Doppler; and 2) possible PVR: for MVR, a systolic regurgitant jet was identified within the left atrium, or for AVR a diastolic jet was identified in the left ventricular outflow tract (LVOT) that appeared but could not be clearly identified as originating between the prosthetic valve sewing ring and the native valve annulus.

The semiquantitative assessment of PVR severity (when present), included measurements based on the color flow Doppler, as follows: 1) for MVR, the regurgitant jet area (RJA) was evaluated in multiple views, and the largest RJA was measured. The RJA was expressed as a percentage of the left atrial area (LAA) obtained in the same plane as the maximum regurgitant area (9,10). Mild mitral PVR was defined as maximum RJA/LAA <20%; moderate mitral PVR between 20% and 40%; and severe mitral PVR as >40%; and 2) for AVR, the prosthetic aortic valve regurgitation required a measurement of the proximal jet width evaluated in multiple views, and the widest proximal jet width was measured. The proximal jet width was expressed as a ratio to the LVOT diameter obtained from the parasternal long-axis view. Mild aortic PVR was defined as a ratio of <24%; moderate aortic PVR between 25% and 64%; and severe aortic PVR as >65% (11). Disagreements between the two observers in terms of the primary end point were settled by consensus.

**TTE protocol.** Complete transthoracic echocardiograms (M-mode, two-dimensional, pulse-wave, continuous-wave, and color flow Doppler) were performed in the four standard views (i.e., parasternal long- and short-axis, and apical four- and two-chamber views) using commercially available ultrasound systems. All studies were performed by experienced cardiac sonographers at their respective clinical sites, following a rigorous echocardiographic protocol designed to ensure uniformity of studies, which included optimal visualization of the left and right ventricular endocardial borders, the cardiac chambers, and the native and prosthetic valves (12,13). Echocardiographic images were stored on 1/2 inch videotape (VHS), and the studies were sent to the AVERT Echocardiography Core Laboratory at Washington University for independent review and completion of measurements by experienced echocardiographers who were blinded to the type of prosthetic valve and the demographic

and clinical data. The AVERT Coordinating Center at the University of Pittsburgh performed all statistical analyses.

**TWO-DIMENSIONAL ECHOCARDIOGRAPHY.** Transthoracic echocardiography was used to obtain measurements of chamber structure and function and to assess native and prosthetic valve function. Specifically, the prosthetic valves were evaluated for abnormal motion suggestive of dehiscence and for abnormal echogenic patterns suggestive of endocarditis or thrombosis (13). Measurements of left ventricular (LV) ejection fraction were derived from the apical four-chamber view at end-diastole and -systole to obtain the LV cavity areas and volumes, by the method of summation of disks (14). The LAA was measured at end-systole in patients with MVR from the apical four-chamber view. The LVOT diameter was measured just below the aortic valve leaflets at early systole from the parasternal long-axis view. All echocardiographic measurements were made in three cardiac cycles, and these were averaged.

**PULSE-WAVE, CONTINUOUS-WAVE, AND COLOR FLOW DOPPLER.** The Doppler studies were performed following previously described techniques for the assessment of native and prosthetic mitral and aortic valves (15–18). In patients with MVR, the peak diastolic early inflow velocity (E-wave) and the diastolic time-velocity integral (TVI) (to determine mean transvalvular gradient) were obtained by either pulse-wave or continuous-wave Doppler from the apical four-chamber view. The ratio of mitral valve TVI to LVOT-TVI was derived as an index of prosthetic mitral valve regurgitation, with normal values defined as <2.2 (19).

The peak LVOT systolic velocity and TVI were obtained from the apical five-chamber view. In patients with AVR, the peak systolic aortic valve velocity was obtained by continuous-wave Doppler. In patients with tricuspid regurgitation, the pulmonary artery systolic pressure (PASP, in mm Hg) was calculated from the continuous-wave Doppler echocardiography velocity as follows: $PASP = 4(V)^2 + 10$, where V is the peak tricuspid regurgitant jet velocity (in m/s), and 10 mm Hg is the estimated right atrial pressure (20).

Color flow Doppler was performed in all imaging planes to assess for the presence of native and prosthetic valve regurgitation. The normal bileaflet prosthetic valve has a characteristic central regurgitant jet along the closure line of the disks that is less than that occurring from the leaflet hinge points. These regurgitant jets can be detected by use of color flow Doppler according to their characteristic pattern that arise peripherally and converge (inverted V-shape), and/or the origin from the center of the valve and diverge (V-pattern) (21). Deviations from this pattern, including large, asymmetric, or eccentric jets that originated outside of the sewing ring were considered indicative of PVR. The qualitative assessment, as described previously, defined the presence or absence of PVR, and the semiquantitative assessment defined the severity of PVR.

**Statistical analysis.** All measurements are expressed as mean ± SD. Comparison between groups was performed by chi-square analysis for categorical variables and unpaired *t* tests for continuous variables. Estimation of rates of PVR and postoperative events was made using Kaplan-Meier analysis. All statistical calculations were performed using the SAS statistical software (Version 8, SAS Institute, Cary, North Carolina).

## RESULTS

**Patient characteristics.** Of the 678 available patients, 575 (85%) had at least one echocardiographic study after surgery; clinical follow-up was available for all 678 patients. Initial valve implants included AVR in 59%, MVR in 32%, and both AVR and MVR in 9%. The majority of studies (90%) were performed between 12 and 30 months after prosthetic valve surgery; only a small number of studies were performed between 1 and 12 months (4%) or after 30 months (6%) postoperatively. With the exception of in-

**Table 1.** Clinical Characteristics of AVERT Patients by Echocardiographic Study*

| | Echocardiographic Study (n = 575) | No Echocardiographic Study (n = 166*) |
|---|---|---|
| Age (yrs) | 61 ± 10 | 60 ± 13 |
| Gender (% male) | 58 | 66 |
| NYHA functional class, I/II/III/IV (%) | 10/41/42/7 | 7/42/41/10 |
| Systolic blood pressure (mm Hg) | 129 ± 20 | 130 ± 23 |
| Diastolic blood pressure (mm Hg) | 72 ± 12 | 72 ± 13 |
| Preoperative LVEF (%) | 58 ± 14 | 56 ± 16 |
| Past medical/surgical history (%) | | |
| Neurologic events (stroke/RIND/TIA) | 5 | 6 |
| Diabetes mellitus | 13 | 15 |
| Coronary artery disease | 31 | 36 |
| Myocardial infarction | 7 | 13† |
| Congestive heart failure | 21 | 26 |
| Carotid artery disease | 3 | 6 |
| Coronary artery bypass surgery | 4 | 7 |
| Heart valve surgery | 11 | 7 |
| Endocarditis (inactive or recent) | 8 | 8 |
| Clinical events after valve implant (%) | | |
| Thromboembolism (all reported) | 9 | 11 |
| Bleeding | 8 | 12 |
| Prosthetic valve endocarditis | 2.6 | 1.8 |
| All-cause death | 2 | 7† |

All numbers shown are mean ± SD, unless noted otherwise. *Excludes patients who died or had their prosthetic valves explanted before the start of the echocardiographic study. †$p < 0.01$.

AVERT = Artificial Valve Endocarditis Reduction Trial; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; RIND = reversible ischemic neurologic deficit; TIA = transient ischemic attack.

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creased rates of myocardial infarction and all-cause death, the baseline characteristics of the group who underwent TTE studies were similar to those who did not (Table 1). Of the 575 patients who underwent TTE, 285 were in the Silzone-coated prosthetic valve valve group and 290 were in the conventional prosthetic valve group. The two groups were similar in terms of demographic and clinical characteristics (Table 2).

**TTE.** The results of the TTE studies for patients in the Silzone-coated prosthetic valve and the conventional prosthetic valve groups are shown in Table 3. Patient follow-up times, LV volumes and ejection fraction were similar between groups. Definitive PVR was slightly higher in the Silzone-coated prosthetic valve group compared with the conventional prosthetic valve group, but this difference did not achieve statistical significance. Paravalvular regurgitation was higher in Silzone-coated prosthetic valves in both mitral and aortic positions compared with the respective conventional prosthetic valves, but these differences likewise did not achieve statistical significance. Studies with possible PVR were similar between the groups. The severity of PVR was mild-moderate in nearly all cases. The prevalence of PVR was higher in patients who had MVR (regardless of valve type) compared with those with AVR (23 of 230 vs. 27 of 397, respectively, p = 0.15). There was no echocardiographic evidence of PVE or thrombosis in either group.

The echocardiographic parameters of the AVERT patients by type of valve are shown in Table 4. There were no statistically significant differences between patients who received a Silzone-coated prosthetic valve or a conventional prosthetic valve in any of the TTE-derived parameters, including LV volumes, ejection fraction, peak velocities, and time velocity integrals across the prosthetic valves.

**Table 2.** Clinical Characteristics of AVERT Patients With Echocardiographic Study by Type of Valve

| | Silzone-Coated Valve Prosthesis (n = 285) | Conventional Valve Prosthesis (n = 290) |
|---|---|---|
| Age (yrs) | 62 ± 10 | 61 ± 10 |
| Gender (% male) | 60 | 56 |
| NYHA functional class, I/II/III/IV (%) | 11/43/39/7 | 9/39/46/6 |
| Systolic blood pressure (mm Hg) | 129 ± 21 | 129 ± 19 |
| Diastolic blood pressure (mm Hg) | 72 ± 12 | 72 ± 13 |
| Past medical/surgical history (%) | | |
| Neurologic events | 9 | 7 |
| Diabetes mellitus | 15 | 11 |
| Coronary artery disease | 30 | 32 |
| Myocardial infarction | 5 | 9 |
| Congestive heart failure | 21 | 21 |
| Carotid artery disease | 3 | 3 |
| Coronary artery bypass surgery | 5 | 4 |
| Heart valve surgery | 9 | 12 |
| Endocarditis (inactive or recent) | 7 | 9 |
| Clinical events after valve implant (%) | | |
| Thromboembolism | 9 | 9 |
| Bleeding | 8 | 9 |
| Prosthetic valve endocarditis | 1 | 4 |
| All-cause death | 2 | 2 |

All numbers shown are mean ± SD, unless noted otherwise.
There were no statistical differences between the two groups. Abbreviations as in Table 1.

**Table 3.** Echocardiographic Parameters of AVERT Patients, by Type of Valve

| | Silzone-Coated Valve Prosthesis (n = 285) | Conventional Valve Prosthesis (n = 290) |
|---|---|---|
| Echocardiographic follow-up (months) | 23 ± 7 | 22 ± 8 |
| LVEDV (ml) | 112 ± 44 | 108 ± 42 |
| LVESV (ml) | 48 ± 38 | 44 ± 35 |
| LVEF (%) | 61 ± 12 | 62 ± 12 |
| All prosthetic valve regurgitation, n (%) | | |
| Definitive | 29 (10.2%) | 21 (7.2%) |
| Possible | 8 (2.8%) | 11 (3.8%) |
| Severity of PVR | | |
| Mild | 13 (4.6%) | 13 (4.5%) |
| Moderate | 13 (4.6%) | 9 (3.1%) |
| Severe | 2 (0.7%) | 0 (0.0%) |
| PVR, mitral valve | n = 111 | n = 119 |
| Definitive | 13 (11.7%) | 10 (8.4%) |
| Possible | 4 (3.6%) | 8 (6.7%) |
| PVR, aortic valve | n = 201 | n = 196 |
| Definitive | 16 (8.0%) | 11 (5.6%) |
| Possible | 4 (2.0%) | 3 (1.5%) |

All numbers shown are mean ± SD, unless noted otherwise. There were no statistical differences between the two groups.
AVERT = Artificial Valve Endocarditis Reduction Trial; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; PVR = paravalvular regurgitation.

The PVR-free rates for both types of prosthetic valves (Kaplan-Meier analysis) showed no significant differences between the two valves (Fig. 1). In fact, after 24 months of follow-up, the two curves virtually overlap each other, with similar PVR-free rates for the Silzone-coated prosthetic valve and conventional prosthetic valves (91% [95% confidence interval: 88% to 95%] vs. 94% [95% confidence interval: 91% to 97%], respectively, p = 0.6).

## DISCUSSION

Echocardiographic follow-up in this AVERT substudy demonstrates that among patients with study valves in place at a mean follow-up of 23 months after prosthetic valve implant, there were no statistically significant differences in the prevalence or severity of PVR between the Silzone-coated prosthetic valve and conventional mechanical valves in either the mitral or aortic positions. The baseline clinical characteristics and postoperative events in this echocardiographic substudy were similar in both groups. Transthoracic two-dimensional and color flow Doppler echocardiography disclosed PVR (combined definite and possible) in 10.9% for Silzone-coated prosthetic valves versus 8.3% for conventional prosthetic valves. The severity of PVR for both MVR and AVR was similar in both prosthetic valve groups. In the original AVERT study cohort of 807 patients, major PVR resulting in early prosthetic valve explants was significantly

**Table 4.** Echocardiographic Parameters of AVERT Patients, by Type of Valve

| | Silzone-Coated Valve Prosthesis | Conventional Valve Prosthesis |
|---|---|---|
| Mitral valve prosthesis (n = 230) | n = 111 | n = 119 |
| Prosthetic valve size (mm) | 29 ± 2 | 29 ± 2 |
| LVEDV (ml) | 114 ± 52 | 107 ± 38 |
| LVESV (ml) | 51 ± 46 | 46 ± 31 |
| LVEF (%) | 59 ± 13 | 60 ± 13 |
| Peak E-wave velocity (m/s) | 1.6 ± 0.4 | 1.6 ± 0.3 |
| MV TVI (cm) | 36 ± 9 | 36 ± 9 |
| MV mean gradient (mm Hg) | 4.0 ± 1.4 | 4.0 ± 1.7 |
| Ratio of: MV TVI/LVOT TVI | 1.80 ± 0.47 | 1.80 ± 0.46 |
| TR jet velocity (m/s) | 2.6 ± 0.4 | 2.7 ± 0.4 |
| PASP (mm Hg) | 39 ± 9 | 39 ± 9 |
| Aortic valve prosthesis (n = 397) | n = 201 | n = 196 |
| Prosthetic valve size (mm) | 23 ± 2 | 23 ± 2 |
| LVEDV (ml) | 111 ± 38 | 109 ± 44 |
| LVESV (ml) | 46 ± 30 | 43 ± 36 |
| LVEF (%) | 62 ± 11 | 63 ± 11 |
| LVOT TVI (cm) | 21 ± 5 | 21 ± 5 |
| LVOT peak velocity (m/s) | 1.0 ± 0.2 | 1.0 ± 0.2 |
| AoV peak velocity (m/s) | 2.3 ± 0.5 | 2.4 ± 0.5 |
| Ratio of: LVOT velocity/ AoV velocity | 0.43 ± 0.09 | 0.44 ± 0.11 |

All numbers shown are mean ± SD, unless noted otherwise. There were no statistical differences between the two groups.

AoV = aortic valve; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; LVOT = left ventricular outflow tract; MV = mitral valve; PASP = pulmonary artery systolic pressure; TR = tricuspid regurgitation; TVI = time-velocity integral; other abbreviations as in Table 3.

greater in patients receiving the Silzone-coated prosthetic valve prosthesis compared with those receiving a conventional prosthetic valve at two-year follow-up (4.4% vs. 1%) (5). The present study excluded those patients who died before receiving an echocardiogram, those whose valves had been explanted early, and those who withdrew study consent or who had not consented to the echocardiographic substudy. In addition to PVL, echocardiographic parameters such as LV volumes and ejection fraction, and pulse-wave and continuous-wave spectral Doppler-derived measurements of prosthetic valve function were similar between the two groups, regardless of implant site. These findings suggest that at an intermediate postoperative follow-up period of approximately two years, ventricular function and prosthetic valve function are similar in the Silzone-coated prosthetic valves compared with the conventional prosthetic valves. Furthermore, clinical events such as thromboembolism, bleeding, PVE, and all-cause mortality were similar in both groups.

Transvalvular regurgitation in the closed mechanical valve prosthesis is an intrinsic feature of normal valve function. This has been described as "physiologic" regurgitation and is detected in most bileaflet mechanical valves by use of color flow Doppler echocardiography (21). Physiologic regurgitant jets are small and confined to the closure margins or at the hinges of the prosthesis regardless of valve size and are hemodynamically insignificant. In the normal bileaflet prosthesis in the mitral position, physiologic regurgitant orifice areas range from 0.2 to 1.1 $mm^2$ (21). When assessed by intraoperative TEE, PVR is common after prosthetic valve replacement, and has been reported as high as 18% for AVR and 23% for MVR (6–8). Follow-up studies suggest a benign long-term prognosis in these patients, with progression of regurgitation requiring re-operation in <1% of patients at follow-up >1 to 2 years (6–8,22). The relatively benign clinical course of the patients in these previous studies suggests that incidental findings of PVR in the absence of symptoms may be managed conservatively. A strategy that includes frequent clinical follow-up appears justified, with surgical intervention warranted only for those who develop clinical symptoms. Previous studies suggest that clinical progression is more common in patients with a history of previous endocarditis and/or those with severe valve annulus calcification (23).

Mechanisms responsible for the development of early PVR in the Silzone-coated prosthetic valve have not been well defined. It has been suggested that silzone-coating inhibits normal fibroblast growth into the prosthetic valve sewing cuff; this is supported by the findings of poor tissue ingrowth and loosening of sutures in explanted valves in the AVERT study (5). In contrast, PVR that is associated with significant clinical symptoms and/or a rapidly progressive course is often the result of active endocarditis (8). The present AVERT echocardiography study, one of the largest prosthetic valve follow-up studies to date (1,823 valve-years of follow-up), showed similar PVR rates for both valve types, and combined PVR rates that are lower than those previously reported in large series (combined PVR rate of 8.7% in the present study). Furthermore, the majority of cases were of mild or moderate severity (mild: 4.5%, moderate: 3.8%, severe: 0.3%). Thus, it is possible that some patients experienced inadequate fibroblast growth into the prosthetic valve sewing cuff that resulted in the high incidence of early valve explants. After a high prosthetic valve explant rate for the Silzone-coated prosthetic valve, this intermediate follow-up suggests a similar prevalence of

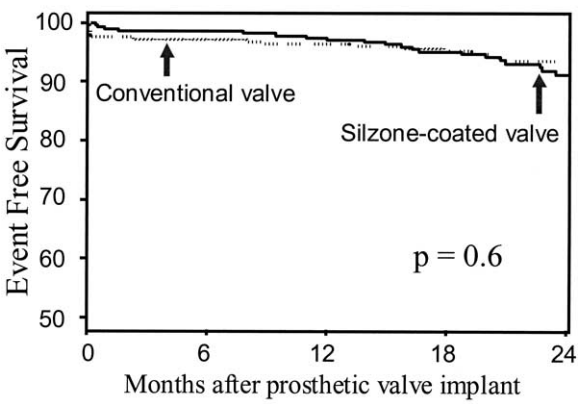


**Figure 1.** Kaplan-Meier curves for definite paravalvular regurgitation for all valves in the AVERT echocardiography substudy (both mitral and aortic valve replacement).

PVR for both prosthetic valves. Whether the severity of PVR in these prosthetic valves increases over time leading to valve explant is unknown and is the subject of continued clinical and echocardiographic monitoring in the AVERT cohort.

**Study limitations.** Assessment of mechanical prosthetic mitral valve regurgitation by TTE is limited because of attenuation and acoustic shadowing of the prosthesis in the left atrium. To minimize this potential problem, a number of well-validated Doppler-derived indices that have been shown to correlate with significant prosthetic mitral valve regurgitation were performed, and no differences were found between the two groups (19). Transesophageal echocardiography would have been a more sensitive test for PVR detection in mitral valve prosthesis, but this test was not routinely performed owing to its semi-invasive nature.

**Conclusions.** Intermediate two-year follow-up of the AVERT cohort shows that among patients with study valves in place, there are no significant differences by valve type in the prevalence or severity of PVR in either the aortic or mitral valve positions. Although the incidence of reported PVR leading to early prosthetic valve explant was higher in Silzone-coated prosthetic valves, the prevalence of echocardiographically determined parameters (including PVR) as well as other clinical parameters were similar among the two groups. Further monitoring is warranted to determine whether these clinical outcomes remain similar on long-term follow-up.

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