Current Selection of Optimal Prosthetic Aortic Valve Replacement in Middle-Aged Patients

Still Dealer’s Choice*

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Selection of the type of prosthetic aortic valve replacement (AVR) is frequently a difficult judgment decision affecting the majority of patients who require surgical AVR. The choices generally include bioprosthetic valves (stented or stentless porcine bioprosthesis, stented pericardial prosthesis) and mechanical prosthetic valves (bileaflet or monoleaflet) (1,2). Mechanical valves have the advantage of structural stability but the disadvantage of requiring anticoagulation with warfarin, whereas bioprostheses have the advantage of not requiring anticoagulation with warfarin but the disadvantage of being subject to time-related structural valve failure (2). Although some patients are clearly better served with one valve type or another, as noted below, the choice for many patients has been at the discretion of the patient or physician. A number of landmark studies over the past 30 years have shed critical light on the outcome of patients who received one design or another (3–8), and guidelines have been formulated and more recently updated (2). Many of the patients in the previous long-term follow-up studies that were used to create the current guidelines, however, received their AVR in the late 1970s and early 1980s, and surgical techniques, valve design, and concomitant medications have improved substantially since that time (2). An update concerning clinical outcomes after AVR in the current therapeutic era with more current valve designs would be of enormous value.

Some complications associated with AVR are similar between bioprosthetic and mechanical prostheses, whereas others are more unique to one valve type or another.

Systemic thromboembolism. Systemic thromboembolism has been consistently similar in patients receiving either a tissue or a mechanical prosthesis (3,4), although the responsible mechanisms might be different in the 2 types of valves: inadequate anticoagulation in the setting of a mechanical prosthesis versus structural valve degeneration in the setting of a bioprosthetic valve.

Hemorrhage. Hemorrhage is typically related to anticoagulation therapy and is generally increased in patients with a mechanical prosthesis, which requires lifelong anticoagulation, compared with patients with a bioprosthesis, in whom anticoagulation is typically not used or used routinely only early post-operatively (2–4). The bleeding events in patients with a mechanical prosthesis are most often due to excessive anticoagulation, which generally can be adequately managed with careful management of the level of anticoagulation (1,2).

Structural valve degeneration. Structural valve degeneration primarily affects leaflets of bioprosthetic valves, although mechanical failure of mechanical prostheses occurred with older generations of mechanical valves (1). Newer generations of bioprosthetic and pericardial valves have been reported to have less structural degeneration than earlier generations of bioprosthetic valves (1,2,9–11), but other studies suggest that there is no difference (2). Host-related factors are critically important to determine the likelihood of structural valve degeneration, and age is probably the most important factor. The rate of bioprosthetic valve failure is <10% at 10 years in patients >65 years of age but is 20% to 30% in patients <40 years of age (1,2,10,12). Other important predictors of structural valve degeneration include systemic hypertension, renal insufficiency, left ventricular hypertrophy, poor left ventricular function, and prosthetic valve size (1,9,10).

The most recently updated guidelines indicate that the existing information does not necessarily obligate one type of valve over another in most patients (Class IIa, Level of Evidence: C) and emphasize that patient and physician preference is an important determinant of prosthesis selection (2). Age also importantly influences the recommendation: in patients <65 years of age in whom there is no contraindication for warfarin therapy a mechanical prosthesis is generally recommended, whereas in older patients >65 years of age a bioprosthetic valve is generally recommended (1,2).

The most definitive way to address the comparative value of tissue versus mechanical valve prostheses is a randomized clinical trial, but the only 2 previous randomized trials (the Edinburgh Heart Valve Trial [4] and the Veterans Affairs Cooperative Study on Valvular Heart Disease [3]) enrolled patients in a very different era of surgical technique (1975 to 1982) and compared prosthetic valves that are no longer

*Editorials published in the Journal of the American College of Cardiology reflect the views of the authors and do not necessarily represent the views of JACC or the American College of Cardiology.

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implanted (Bjork-Shiley tilting-disc valve or first-generation porcine heterografts). In this issue of the Journal, Stassano et al. (13) present the results of a new landmark, prospective, randomized trial of prosthetic aortic valves in patients who were enrolled from 1995 to 2003. These investigators focused their trial on patients with aortic valve disease between 55 and 70 years of age because, as noted in the preceding text, patients younger than 55 years of age are generally recommended to have a mechanical valve prosthesis and patients older than 70 years of age are generally recommended to have a bioprosthetic valve. Patients in this “middle-age” group could potentially be well served with either type of valve, and the investigators enrolled only those patients who left the decision concerning which valve type to be implanted to the discretion of the surgeon. Of 392 patients (35% of all patients with aortic valve disease) in this age group, 310 were randomized to receive either a bioprostheses (Carpentier-Edwards SAV or Pericardial valve, Irvine, California) or a mechanical bileaflet valve (St. Jude Medical, Seattle, Washington, or CarboMedics, Austin, Texas), valve choices that remain in widespread use today. Coronary artery bypass graft was concomitantly performed in approximately 25% of patients in each group. Patients with a mechanical AVR received lifelong warfarin, and patients with a bioprosthesis received warfarin for only 8 to 12 weeks. Medication management was left to the discretion of the local treating physician. Perioperative mortality was low and similar in both mechanical and bioprosthetic groups (2.6% vs. 3.9%, respectively, \( p = 0.4 \)). At late follow-up (mean 106 ± 28 months) the outcomes were also similar in both groups: overall mortality (27.5% vs. 30.6%), cardiac–related mortality (16.7% vs. 21.7%), valve–related mortality (6.7% vs. 8.1%), and major adverse prosthesis-related events (23.4% vs. 28.6%). Independent predictors of late mortality were related to host characteristics (New York Heart Association functional class, low ejection fraction, or concomitant coronary artery bypass graft performed) and not to valve type implanted. There were no differences in morbidity (thromboembolism, bleeding, endocarditis, valve thrombosis, and nonstructural dysfunction) between the 2 randomized groups, although—as expected—the bioprosthetic valve group exhibited more frequent structural valve dysfunction (2.17%/patient-year vs. 0%/patient-year, \( p = 0.0001 \)) and more frequently required reoperation (2.32%/patient-year vs. 0.62%/patient-year, \( p = 0.0003 \)) compared with the mechanical prosthesis group. The occurrence of major adverse prosthesis-related events began to show an important divergence beginning at 10 years, when structural valve degeneration and reoperation became more frequent in the patients who received a bioprosthetic AVR.

The results of this important study reinforce and expand a number of major observations from the prior era. Although perioperative mortality has improved since the late 1970s and early 1980s, the long-term outcomes comparing the 2 types of valves are generally as similar now with more modern generations of the respective valve types as they were with earlier generations of the valves 30 years ago. An interesting issue from the Stassano et al. (13) study is that the difference in bleeding between the 2 groups was only a statistical trend (\( p = 0.08 \)), in contrast to previous trials in which bleeding was significantly more common in the mechanical prosthesis group in whom lifetime warfarin therapy is required (3,4). As the authors suggest, the explanation might be that 21% of patients in the bioprosthetic group received long-term warfarin therapy and 26% received antiplatelet therapy. They note that the use of warfarin was dictated by the local treating physician and was likely initiated for a variety of indications necessitating anticoagulation that middle-aged patients with aortic valve disease acquire regardless of prosthetic valve type implanted. Bleeding primarily occurred in those patients who were taking warfarin, regardless of valve type implanted.

It should also be emphasized that these patients were only followed for a mean of 106 months. In the randomized Veterans Administration trial (3), the significantly increased mortality associated with implantation of a bioprosthetic valve only became evident after 10 years of follow-up when increased mortality associated with reoperation for structural valve degeneration occurred. The very long-term outcomes will be very important to follow in the Stassano trial to further guide valve selection, because most of the middle-aged patients enrolled can be expected to survive well beyond 10 years post-operatively.

How are the results from this new randomized trial to be incorporated into our management decisions with patients with aortic valve disease who require AVR? I think very little has changed. The authors have provided an invaluable update with a randomized clinical trial format and current generations of mechanical and bioprosthetic valves. As the current guidelines recommend (2), even before an awareness of the Stassano et al. (13) trial, patient and physician preference concerning valve selection remains paramount. There are no major differences in terms of mortality between the 2 valve types, but patients receiving a bioprosthetic valve can be assured of developing structural valve deterioration after approximately 10 years and will require reoperation, whereas those patients taking warfarin (primarily the patients receiving a mechanical valve) will likely develop more bleeding. Patients and physicians can now decide on valve choice based on experience in the current therapeutic era and the current generations of the respective valve types.

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Key Words: aortic valve replacement ▪ biological valve ▪ mechanical valve ▪ valve outcomes.