Do stentless valves make a difference?

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Summary

Stentless glutaraldehyde-preserved bioprosthetic valves for the aortic position were introduced into clinical practice in 1988. Their introduction coincided with the publication of several long-term observational studies of aortic homografts, which showed superior freedom from structural valve damage compared to the first generation stented porcine bioprosthesis. There followed 10 years of intensive investigation into the haemodynamic characteristics of stentless valves. These studies have demonstrated superior haemodynamic features in terms of transvalvular pressure gradients, effective orifice area, and more complete regression of left ventricular hypertrophy. Despite these advantages, stentless valves have yet to be adopted widely. This review seeks to explain this paradox.

Keywords: Aortic valve; Stentless valve; Bioprosthesis; Haemodynamics

1. Introduction

Aortic stenosis is the predominant lesion in the majority of adult patients who present with clinically important aortic valve disease. Aortic valve replacement (AVR) is recognized as the only definitive treatment for critical aortic stenosis and presently accounts for 15% of all adult cardiac surgery in the UK (6000 operations per year). Bioprosthetic valves are commonly employed in the elderly, in patients for whom the risk of bleeding complications are high, and in patients whose desired way of life precludes the discipline of anticoagulation. Evidence from the hypertension literature suggests a strong correlation between left ventricular hypertrophy (LVH) or elevated left ventricular mass index (LVMI) and sudden death, congestive heart failure, stroke, myocardial infarction, coronary artery disease and cardiovascular mortality [1]. After AVR, incomplete regression of LVH has been shown to significantly reduce 10-year survival [2]. Such persistent hypertrophy may be due to the obstructive nature of the valve sewing ring and stent, or to patient–prosthesis mismatch. The free sewn aortic homograft circumvents most of these problems but its limited availability prevents its widespread use. McGriffin et al. [3] reported on 2100 patients undergoing 2366 AVRs between 1967 and 1990. Actuarial survival at 12 years was 59.6% (70% CL: 57.8–61.4). Risk factor analysis revealed a deleterious impact on long-term survival resulting from impaired left ventricular function due to aortic valve disease. No valve type used in that study was a risk factor for death.

Despite the enthusiasm with which stentless valves have been developed over the last 10 years, the attitude of surgeons has shown a wide divergence. The use of stentless valves is limited to a few surgeons who are experienced in performing this type of surgery within a few cardiac surgical units across Europe. This has prompted us to undertake an objective review of the physiological and clinical benefits provided by the stentless aortic bioprosthesis as well as the surgical challenges and operative risks with which stentless valve replacement may have been associated.

2. Effect of valve substitutes

In the early 1960s Ross and Barratt-Boyce separately introduced the aortic homograft into clinical practice. In those early days only a few skilled surgeons were able to obtain predictable results with a free-sewn valve. In 1965, Binet et al. [4] introduced a stentless porcine bioprosthesis but this was not pursued due to difficulties with implantation at a time when myocardial protection was in its infancy.

Stented bioprostheses were therefore developed as this required a much simpler surgical technique and resulted in a reproducible performance. Nevertheless, the transvalvular gradients and limited durability became major concerns of the stented bioprosthesis. The original free-sewn homograft circumvents most of these problems but its limited avail-
ability prevents its widespread use. This eventually prompted a reconsideration of stentless design, intended to reduce residual obstruction to trans-aortic flow by maximizing the available cross-sectional area. The removal of the stent has brought several advantages: (a) a larger valve can be implanted into a given size of aortic annulus [5]; (b) the distensibility and dynamic nature of the aortic annulus is preserved [6,7]; (c) it is possible to remodel the native aortic root and preserve the sinotubular junction. [8]. Our preferred approach is to use a longitudinal in preference to a transverse aortic incision, which facilitates reduction of the non-coronary portion of the sinotubular junction as this is the portion of the circumference most commonly enlarged.

In 1988, the Toronto stentless porcine valve was introduced as an alternative to stented tissue valves. Two years later, the same group reported that the mean pressure gradients and effective orifice area (EOA) of the Toronto SPV valve were significantly superior to those of the Hancock II [9]. In 1991, Haussman et al. [10] reported favourable haemodynamic results of stentless valves at 3-year follow-up in comparison to the aortic homograft.

These early reports signaled the beginning of a decade of intensive clinical investigation. Several important haemodynamic advantages of stentless valves have been established. Using Echo-Doppler measurement, the mean transvalvular pressure gradient of stented or mechanical prostheses at rest is usually within the range of 10–20 mmHg [11–15] but this can significantly increase during exercise. Van der Brink et al. studied a group of patients following AVR who had received single disk valves, either Bjork–Shiley or Medtronic–Hall [16]. All patients studied were in NYHA Class I or II and had normal left ventricular function on echo. Doppler-measured peak and mean gradients increased from 44 and 24 mmHg at rest, to 68 and 39 mmHg, respectively, soon after a symptom-limited Master two-step test. Recently, Freis et al. compared mean pressure gradients across 23-mm Freestyle stentless valves and 23-mm Carpentier–Edwards stented valves at rest (6 ± 2 versus 12 ± 3 mmHg, respectively, P = 0.009) and on exercise (9 ± 3 versus 22 ± 8 mmHg, P = 0.0004, respectively). The comparative peak gradients at rest (11 ± 4 versus 21 ± 10 mmHg, P = 0.02) and on exercise (18 ± 6 versus 40 ± 11 mmHg, P = 0.0004) told the same story [17]. Prospective studies have confirmed that stentless valves not only have a lower pressure gradient and a greater EOA early after implantation but these indices show further improvement during the first year of follow-up [18]. In a study comparing stented Medtronic Mosaic and Carpentier–Edwards Perimount valves with the Freestyle stentless valve, during exercise on a bicycle the increase in mean pressure gradients was less than 20% from the resting value, while the corresponding increase for the stented valves was nearly 100% [19]. Likewise when patients who had received Toronto SPV or Freestyle stentless valves were compared to patients with St. Jude Medical or Sorin Bicarbon mechanical valves during simulated exercise with dobutamine; both stentless valves showed no change in mean gradient on exercise, whereas for the mechanical stented valves the mean gradient doubled [20]. The lower pressure gradient seen with stentless valves during exercise has to be attributed in part to a flow-related increase in EOA [8], which is due to a predominant inertial flow and a more uniform flow velocity profile when transvalvular pressure gradient of stentless valves is below 5 mmHg. These haemodynamic characteristics of stentless valves have distinguished themselves from their stented counterparts in which flow characteristics are predominantly resistive and turbulent in nature.

Despite these advantages, many surgeons are not persuaded to alter their practice and are put off by several practical concerns. One of these surrounds the technical difficulties of implantation and a longer cross-clamp time. Yet when we looked carefully at perioperative left ventricular function in patients with aortic stenosis matched for age, gender and valve size, a 20 min longer cross-clamp time (51 min versus 72 min) had no effect on postoperative left ventricular function, morbidity or mortality [21,22]. The current level of public and institutional scrutiny of cardiac surgical audit makes the traditional ‘learning curve’ for a new procedure virtually impossible. But with the use of ‘wet-labs’ and experienced proctors, these problems can be overcome, provided that hypertrophic myocardium with or without coronary artery disease is effectively protected by a modern cardioplegia method. Another concern is the incidence of regurgitation after stentless AVR which is best dealt with by assuring that the sinotubular junction size is within 115% of implanted valve size [6] and by routine use of transthoracic echocardiography during these procedures. Peri-operative transthoracic echocardiography has become part of surgical practice necessary to deliver high quality surgery and care to patients undergoing valve operations. In this way, unsatisfactory surgical results can be detected early and corrected effectively and promptly.

The experience of removing calcified homografts from the aortic position has deterred some from embarking on stentless valve surgery. Although the reports of removing stentless porcine valves are currently anecdotal, the limited experience of ourselves and others is that it is considerably easier than dealing with a calcified homograft, as the calcification is less severe and the Dacron sleeve provides a convenient plane of dissection.

3. Left ventricular function and hypertrophy

Although significant regression of hypertrophy and improvement in left ventricular function commonly occur after AVR, even with a small (19 mm) size bioprosthesis [11], the residual pressure drop across a valve prosthesis and the associated non-physiological flow profile still unfavourably influences long-term results, particularly with a small
Valve [23,24]. After AVR, incomplete regression of LVH has been shown to significantly reduce 10-year survival [2]. Such persistent hypertrophy may be due to the obstructive nature of the sewing ring and stent, or to patient–prosthesis mismatch. Prosthesis-related left ventricular pressure increase is an important reason for incomplete regression of ventricular and cellular hypertrophy and the development of increased interstitial fibrosis postoperatively [25]. In 44 patients studied 10–17 years after isolated AVR, a higher peak pressure gradient with the Starr–Edwards valve was associated with a lower fractional shortening (FS) (30 versus 37%) compared to patients with a Björk–Shiley valve [15].

Residual hypertrophy has an important effect on ventricular function and late outcome. In a 22-year follow-up after AVR for aortic stenosis, Lund [26] found that the completeness with which LVH regressed was a dominant mechanism determining overall late outcome. In particular, impaired left ventricular diastolic function identified at late reinvestigation related to significant residual hypertrophy, and was the sole predictor of fatal congestive heart failure irrespective of the ejection fraction. Unresolved left ventricular hypertrophy may also result in more frequent and severe ventricular arrhythmias. In 96 patients with aortic valve disease undergoing 24-h electrocardiogram (ECG) monitoring, 37% who had severe ventricular arrhythmias (Lown Class III or IV) before AVR proved to have a greater LVMI and lower ejection fraction than the remaining 63% [27]. Eighteen months after AVR, the incidence of severe ventricular arrhythmia had fallen to 27%; these patients had a significantly lower ejection fraction and larger cavity dimension.

Suboptimal left ventricular function after AVR not only increases morbidity and compromises quality of life but also increases mortality when redo operation becomes necessary [28]. In a retrospective study of 177 patients who underwent repeat AVR using an aortic homograft characterized by a low transvalvular pressure gradient [29], the early mortality rate was 5.1% and the actuarial 10-year survival was 71%. Those patients in whom an aortic homograft had been implanted at their first operation had a significantly improved long-term survival compared with those who had received a mechanical valve.

On the basis of a large body of evidence in support of superior haemodynamics of stentless valves, it was reasoned that this would permit a more complete resolution of LVH, and therefore an improvement in LV function. This would be expected to reduce the risk of sudden death and congestive heart failure after AVR and thus improve long-term outcome [2,30,31]. Left ventricular function in the early postoperative hours was similar to that of a stented valve despite the longer aortic cross-clamp time required for its implantation [22]. But the fall in LV wall stress was significantly greater following stentless compared to stented valve replacement for aortic stenosis. This resulted in a more rapid and more complete resolution of LVH in the same group of patients followed out to 2 years [32].

Both systolic and diastolic functions improve to a greater extent after stentless valve replacement [32]. These findings have been confirmed by several randomized studies [5,33]. The beneficial effects of stentless valves on LV function were also confirmed by Cohen et al. [34]. They found that FS and velocity of circumferential shortening (Vcf) were greater in the stentless valve patients at 3 and at 6 months ($P = 0.0004$ and $P = 0.0001$, respectively) when compared with stented valves. More recently, we have preliminary observations, which suggest that the transvalvular pressure gradients may have a significant impact on the coronary artery flow profile after AVR. The possibility that stentless valves provide a more physiological coronary perfusion warrants further investigation.

4. Operative risk

If the physiological benefits of stentless valves are accepted, the results of stentless AVR will depend on the perioperative mortality and morbidity and the long-term durability. The perioperative risk of AVR in patients with very marked concentric hypertrophy is known to be increased. Carroll et al. [35] have shown in an elderly population with aortic stenosis, a subgroup of women who could be identified with higher FS and a higher ratio of wall thickness to cavity dimension even though men had a greater LV mass index. Further support for these observations is the finding that in spite of the greater ejection fraction in women with aortic stenosis, overall wall stress–endocardial shortening relations were within the normal range and similar to those in men [36]. Furthermore, there was no difference in circumferential midwall fibre shortening. Differences between endocardial and mid-wall shortening were directly related to the differences in relative wall thickness, in other words to altered geometry. Orsinelli [37] reported that marked hypertrophy expressed as increased relative wall thickness was associated with a higher in-hospital mortality after AVR and especially high among women with greater septal and posterior wall thickness. LV mass/volume ratios have been extensively used for both humans and animals and show an excellent correlation with peak LV systolic pressure [35,36] and as an index of the degree of hypertrophy [38]. Women had higher LV mass/volume ratios (P = 0.001) even though they had significantly lower LVMI. Women respond to chronic pressure overload in a distinct way characterized by a disproportional greater degree of left ventricular hypertrophy relative to volume increase [39].

In a meta-analysis of 20 published series of stentless valves, the hospital mortality varied from 0 to 7.5% [40]. In a comparison of two contemporaneous but non-randomised series from studies performed specifically for Federal Drug Administration (FDA) approval, the stented mosaic valve was associated with a lower mortality (2.5%) than the stentless freestyle (5.5%) used in a subcoronary position.
in 82% of patients, but this was not statistically significant at the 95% level [41].

Furthermore, based on the established haemodynamic advantages of stentless valves in the first few years after implantation, we believe that it is the high-risk patient with impaired left ventricular function and severe hypertrophy who will benefit from the unique features of these valves [42]. Our own audited but unpublished figures reveal a hospital mortality of 6.1% in this group of patients, 87% of whom required concomitant coronary bypass.

5. Valve durability and patient survival

For patients over the age of 65, several stented porcine valves have been shown to have a freedom from structural deterioration of greater than 90% at 10 years [43]. Experimental studies [44] had suggested that stentless porcine valves were less likely to calcify than stented valves. In our 10-year follow-up, we have seen only one patient with calcification of porcine cusps after stentless valve replacement [45]. Even taking the initial clinical series of stentless porcine valves, valve durability has been excellent in the first 6–8 years with freedom from primary valve tissue failure greater than 97% [46,47]. But there are concerns regarding the long-term competence of these valves. A small number of early explants were performed because of significant transvalvular regurgitation caused by the dilation of the sinotubular junction [48]. This may reflect the learning curve regarding the indication for the use of a stentless valve and the skill of its implantation. The durability of a stentless valve is determined not just by valve manufacture and patient factors but also on the accuracy of its implantation by the surgeon. This is a distinguishing feature from stented valves.

The incidence of aortic regurgitation after AVR is routinely assessed as trivial/mild or moderate by transthoracic echocardiography. In a recent series of reports from experienced centers, the incidence of trivial/mild leak in the first year ranged from 2 to 4%, rising to 14–30% by the eighth postoperative year [47–51].

Do the benefits of stentless valves enumerated already, translate into improved long-term survival? To answer this question, we and others are undertaking randomized controlled trials of stented versus stentless bioprosthetic valves in aortic stenosis, focusing on the smaller aortic root. Meanwhile, we have to rely on non-randomised retrospective data. Emerging evidence from non-randomised studies is supporting the notion of an improved survival in patients with stentless valves owing to its lower valve-related mortality [52]. A case-matched study from Toronto [53] which compared the Hancock with the Toronto stentless valve showed significant differences in intermediate term survival in favour of the stentless valve. Recently, further data from the same group showed that patients with an EOA/BSA ratio <0.75 cm²/M² experienced a higher operative mortality and a worse survival at 12 years [54].

Furthermore the benefits of a stentless valve may be greater in patients younger than 65 years [55].

But there are opposing views. An extremely detailed analysis from the Cleveland Clinic of 892 patients undergoing primary isolated AVR for aortic stenosis showed that survival (mean 5.0 ± 3.9 years) was not adversely affected by moderate patient–prosthesis mismatch down to 4 SDs below normal. A prosthetic valve orifice within this range appeared to be an efficient size [56]. The end-point chosen, all-cause mortality, was robust but not cardiac-specific and no information was available on exercise capacity or symptomatic state. Furthermore, no analysis was made of LV mass index or ejection fraction. Despite their conclusion, the authors do concede that there may be individual patients for whom prosthesis size is important, for example, patients wanting increased physical activity. Nevertheless, any study of the effects of valve size on patient outcome faces the difficulty that patients implanted with a larger valve size are more likely to have poorer LV function. In an observational study of stentless valves, it has been shown that although a larger valve size offers a lower mean pressure gradient and a greater EOA, there is a lower left ventricular ejection fraction (LVEF) and greater LVMI when compared with small (less than 23 mm diameter) size stentless valves, which persists several years after the operation [57]. Thus, this kind of background bias can significantly mask the real physiological impact of valve size on LV function and long-term survival.

6. Conclusion

The 10-year results of large-scale observational studies and the results of randomized studies of stentless versus stented aortic valves will not be available for another 2 years. In the meantime, we can confirm that stentless valves in the aortic position are associated with greater regression of LVMI than stented options. Residual LV hypertrophy after AVR impairs LV diastolic function which leads to late congestive cardiac failure, and diastolic function can be markedly improved by using stentless valve implantation. It remains uncertain whether stentless valve replacement is definitely associated with improved long-term survival. With encouraging data of stentless valve durability, the practice that stentless valves should be reserved for patients over the age of 70 years has become debatable. Nevertheless, with more mature surgical skills and a more established long-term benefit in terms of patient mortality and morbidity, stentless aortic bioprostheses may become the valve of choice for elderly patients requiring AVR.

References

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