Bioprosthetic aortic valve replacement: a telltale from the young

Athanasios Antoniou, Amer Harky, John Yap, Kulvinder Lall, Mohamad Bashir

Department of Cardiac Surgery, Barts Heart Centre, St Bartholomew's Hospital, London, UK

Correspondence to: Mohamad Bashir, MD, PhD, MRCS. Department of Cardiac Surgery, Barts Heart Centre, St Bartholomew's Hospital, West Smithfield, EC1A 7BE, London, UK. Email: Mohamad.Bashir@bartshealth.nhs.uk.

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Patients younger than 50 years of age constitute 20% of overall patients with severe aortic valve disease (1). This represents a challenge perhaps due to the choice of the prosthesis elected and the need to provide the patient with some degree of balanced quality of life, interspersed with maintaining and upholding an extent of their life routine and engagements. This challenge also entails knowing for which valve substrate is the best substitute which will consequentially impact the durability and long-term results. The substantial evidence that dictated superiority of bioprosthetic valve over mechanical valves allowed for the surge of bioprosthetic valves implantation in this age referenced group. This brings us to the point of discussion which was entertained by Schnittman *et al.* (1) demonstrating in the United States the mid and long-term outcomes of young patients that underwent replacement of the AV with a bioprosthesis.

In their report, there was no significant difference in survival at 15 years with Biological valve (BV) versus mechanical valve (MV), the long-term risks of stroke and major bleeding events were greater with MV compared to BV, whereas MV replacement had improved freedom from reoperation compared with BV. Hence, in patients aged 18–50 years, BV present a reasonable alternative to MV replacement.

Surely, this indicates a new impetus to review the literature regarding the choice of prosthesis in this specific group of patients, raising at the same time, some points that need to be highlighted in this editorial. According to the 2017 AHA/ACC guidelines for the management of patients with valvular heart disease (2) the choice of the type of prosthetic heart valve should be a shared decision-making process that accounts for the patient's values and preferences and includes discussion of the indications for and risks of anticoagulant therapy and the potential need for and risk associated with re-intervention [Class of recommendation (COR): I, Level of evidence (LOE): C-LD]. Due to the improved durability of BVs and the desire of patients to avoid long-term anticoagulation, there is a significant trend towards the use of BVs in younger patients. As, Schnittman *et al.* (1) reported, the annual number of implanted BV in patients aged 18 to 50 years, has been increased from 14.3% in 1997 to 47.1% in 2014.

However, this opens Pandora's Box as to which choice of the prosthesis in young patients accounts for long-term results? There have been only few randomized clinical trials comparing biological and mechanical prostheses. In most of series, there was no significant difference in overall survival between the 2 valve types.

On the contrary, Schnittman *et al.* were diligent in their findings which were slightly better with BVs. More specifically, in the United States Veterans Administration (USVA) Cooperative Study on Valvular Heart Disease, Hammermeister *et al.* (3) randomized either MVs or BVs for patients, who were in their 50s or 60s, undergoing aortic valve replacement (AVR). They concluded that patients with MVs had better survival at 15 years than those who received BVs (34% *vs.* 21%). Weber *et al.* (4) reported that in young patients, AVR group with BV were associated with reduced mid-term survival compared with survival after AVR with

MV. On the other hand, in the Edinburgh trial, Oxenham *et al.* (5) conducted a prospective randomized study in which they found no differences in the 20-year survival rate between mechanical and bioprosthetic valves. Similarly, McClure *et al.* (6) and Minakata *et al.* (7) reported that there was no difference in overall survival between the two types of valves. In contrast, with the slightly controversial statement regarding the survival, it seems that there is an agreement of most of the studies that the major bleeding events are more common in MVs.

This very much coincides with Schnittman's findings, but there are no significant differences in thromboembolic events and endocarditis in between the two types of prosthesis. One limitation that needs to be mentioned is that many studies have included on the young population patients who are younger than 60 years old compared to this article in which the cut off has been placed on 50 years of age.

The need for reoperation is another entity that we to need to draw a close up look. The 2017 AHA/ACC guidelines (2) states that the predicted risk of needing reoperation is inversely proportional to the age and more specifically is quite high on the first two age groups (18–30, 31–40 years of age) and is lower on the last group age (41–50 years of age). Jamieson *et al.* (8) reported a rate of degeneration of the bioprosthesis in the aortic valve position at 3.7%/pt-yr for patients <50 years. Anselmi *et al.* (9) reported that the 15-year freedom from reoperation for structural valve deterioration (SVD) was 55.4%±5.6% by Kaplan-Meier analysis and 67.1%±4.2% by completing analysis. These rates are significantly worse from the cumulative incidences of reoperation after BV replacement which are reported by Schnittman *et al.* and are 4.3%, 13.6% and 24.5% in 5, 10 and 15 years respectively after the operation. It's imperative to note that there are also an increasing number of published series which reported similar results. For instance, David *et al.* (10) found that the freedom from SVD is as high as 98.9%±1.0% in 5 years, 89.5%±2.2% in 10 years, 64.6%±4.6% in 15 years for patients <60 years.

Although the reported rates of SVD and the need of reoperation as demonstrated by Schnittman *et al.* are promising, further long-term data are required before we recommend that BV as an equivalent alternative to MV replacement. At this point, this remains equivocal and open to more than one interpretation. Considering also the rate of SVD which is related to the age of implantation of the AV (10) and the fact that less patients have been included in Schnittman *et al.* study in the subgroup (18–30 years) with "fast progress" of SVD and more patients on the subgroup (41–50 years) with "slow progress" of SVD, the cumulative incidence of reoperation should be more accurate if the patients had been matched in 1:1 ratio not only for the type of prosthesis, but also for the age subgroups.

Again, according to the 2017 AHA/ACC guidelines (2), the replacement of the AV by a pulmonary graft (the Ross procedure), when performed by an experienced surgeon, may be considered for young patients when vitamin K antagonists (VKA) anticoagulation is contraindicated or undesirable (COR: IIb, LOE:C). One of the advantages of this operation is the freedom from thromboembolism without the need for anticoagulation.

Moreover, the valve seems to grow while the younger patient grows and has favourable haemodynamics in the absence of foreign valve material. The Harefield group, led by El-Hamamsy *et al.* (11), reported a 99% freedom from AVR at 13 years. Similarly, Mazine *et al.* (12) recently reported an 87% freedom from valve re-intervention at 20 years (including any surgical or percutaneous re-intervention of either the pulmonary autograft or the pulmonary homograft).

Although the reported limitations of the Ross procedure—i.e., increased operative risk and late autograft failure—surgeons should be thought of for patients <50 years, especially on those with patient-prosthesis mismatch. It's still a viable option in the armamentarium amongst patient substrate with small aortic root who are on high risk for patient-prosthesis mismatch.

So it becomes plainly imperative to dwell on the current options of reoperation versus the transcatheter valve-in-valve replacement (TVIVR available). A recent series of 3,380 patients from the Society of Thoracic Surgeons database (13) underwent re-operative AVR showed that the operative mortality is acceptable but higher than that of the first surgery (4.6% *vs.* 2.2%). Re-operative AVR was associated also with a higher rate of major morbidities (21.6% *vs.* 11.8%), including postoperative stroke, aortic insufficiency, pacemaker requirement, and vascular complications. On the other hand, the Valve-in-Valve International Registry (14), showed 30-day mortality of 8.4% and the 1-year follow-up revealed 85.8% survival of treated patients. The TVIVR is not also without any limitation; adverse events reported on the VIVID Registry are device mal-positioning (15%—mainly in stentless surgical valves), coronary obstruction (~3%) and elevated (defined as >20 mmHg) residual transvalvular gradient

(28.4%) which, inherently presents with PPM (14).

The conclusions from all the above could be summarized in that mortality and morbidity risk of re-intervention, independently of the type of the approach (surgical replacement *vs.* TVIVR) are significantly higher from those of the primary operation. In young patients who choose to avoid mechanical valves, surgeons when obtaining informed consent needs to inform this group of population about the potential and increased risk of a reoperation quantifying the current evidence and their matched-up results. TVIVR as an alternative to reoperation in young patients, based on the current evidence, is that it should be limited to second or subsequent re-operative procedures where the risk of operative mortality increases.

The surge of new generation of BV with longer durability, is also met with new types of MVs, which require lower INR and therefore are more "friendly" for the patient.

Schnittman *et al.* certainly ameliorated the controversial fact of valve requisite in the young needing to undergo AVR, however, we are witnessing surge in innovative valves with longer durability and less valve-related complications. But, till we have longer outcome data regarding these valves, we need to follow the recommendations that have been included in the 2017 AHA/ACC guidelines for the choice of the type of prosthesis. A bioprosthesis is recommended in patients of any age for whom anticoagulant therapy is contraindicated, cannot be managed appropriately, or is not desired (COR: I, LOE: C) and also, an aortic mechanical prosthesis is reasonable for patients less than 50 years of age who do not have a contraindication to anticoagulation (COR: IIa, LOE: B-NR).

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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