Aortic valve replacement in young and middle-aged adults: looking beyond the tree that hides the forest

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Introduction

The burden of heart valve disease is increasing worldwide. This increase is mainly driven by aging of the world population, and a failure to eradicate rheumatic heart disease in the developing world (1). In western countries, aortic stenosis is the most common form of valvular heart disease and aortic valve replacement (AVR) is the standard treatment for these patients (2). Up to 85,000 AVRs are performed annually in the United States alone.

When replacing the aortic valve, a number of valve substitutes are available. In choosing the optimal replacement option, patients—and a fortiori young patients—must be counselled carefully, as the choice of aortic valve substitute has been shown to affect long-term outcomes. One of the options available, the Ross procedure (pulmonary autograft replacement), was first described by Donald Ross in 1967 (3). This operation consists in the replacement of the aortic valve with the patient’s own pulmonary root (pulmonary autograft), and subsequent implantation of a homograft in the pulmonary position. The Ross procedure has several advantages. It is the only operation that allows replacement of the diseased aortic valve with a living substitute, thus allowing adaptive remodeling (4), better hemodynamics (5,6), and guaranteeing long-term viability of the aortic valve substitute (7). In addition, the Ross procedure is the only operation that has demonstrated the potential to restore a long-term survival equivalent to that of the age- and gender-matched general population in young and middle-aged adults with aortic valve disease (8,9). Patients undergoing the Ross operation enjoy enhanced quality of life compared to those undergoing mechanical AVR (10), and a number of recent studies have demonstrated superior long-term outcomes compared to other valve replacement options (11,12).

The tree

Despite the aforementioned advantages and recent evidence suggesting improved long-term outcomes, the Ross procedure has all but disappeared from the surgical menu. After an initial wave of enthusiasm in the 1990s, use of this operation has rapidly dwindled in the last 15 years. In 2010, the Ross procedure accounted for only 0.09% of all adult AVRs performed in the United States (13).

Further contributing to the decrease in the use of the Ross operation are current guidelines, which in certain cases fail to mention the option of pulmonary autograft
replacement altogether in their recommendations (European guidelines) (17). Major society guidelines that do comment on the Ross procedure give it a class IIB recommendation (2014 American College of Cardiology/American Heart Association Guidelines) (2), or even a class III recommendation (2013 Society of Thoracic Surgeons guidelines) (18). Importantly, these guidelines insist heavily on the increased perioperative risk and potential for late failure associated with the Ross procedure, and fail to take into account recent evidence suggesting improved long-term outcomes.

The forest

The advantages and shortcomings of the Ross procedure must be put in perspective. These considerations should be analyzed in light of the available alternatives. While the Ross operation is closely scrutinized and severely criticized, the cardiovascular and surgical communities have traditionally been much more lenient towards the more frequently performed operations of bioprosthetic and mechanical AVR. These operations are simpler, more reproducible, and most complications associated with their use occur well after patients have left the hospital. This leniency is reflected in the terminology used by surgeons to describe so-called “valve-related complications”, thus exonerating the operator from adverse events that occur after patient leaves their care. However, when one decides to implant a prosthetic valve in a young patient with a long anticipated life expectancy, one must be aware that he or she is subjecting the patient to potential lifelong exposure to adverse events.

In this age of increased scrutiny, quality control metrics of nationally published databases focus heavily on perioperative outcomes, at the expense of long-term results (19). The focus on institutional death rates and short-term survival may be appropriate for elderly patients, who have a limited life expectancy. However, young and middle-aged adults represent a special population. Due to their longer anticipated life expectancy, these patients present a higher cumulative lifetime risk of prosthesis-related complications.

The nature of these complications varies depending on the type of prosthetic valve implanted. For bioprosthetic aortic valves, the main complication is structural valve deterioration, requiring reoperation. This deterioration occurs earlier in younger patients and translates into excess mortality compared to the general population. Several studies have shown that this excess mortality is inversely proportional to the age of the patients at the time of surgery—i.e., younger patients have the highest hazard of long-term excess mortality—and is further compounded by the insertion of a small prosthesis (20,21). The higher excess mortality observed in young patients is likely related to higher functional demand and a longer period of exposure to valve-related complications.

Several randomized and observational studies have demonstrated superiority of mechanical valves over bioprostheses in younger patients (22-24). Despite these data, over the last 15 years, the use of bioprosthetic heart valves has increased significantly in the United States, at the expense of mechanical valves (25). This trend—which was observed across all age groups, including younger adults—might be due, at least in part, to the promise of valve-in-valve transcatheter aortic valve replacement (TAVR) as a potential therapeutic option for the treatment of failed bioprostheses. This prospect must be considered prudently, however, as valve-in-valve TAVR has shown suboptimal outcomes in elderly patients (26), and has yet to demonstrate its efficacy in young adults with failed bioprosthetic surgical valves. In addition, the durability of transcatheter devices implanted in patients who are in their seventh decade of life or earlier remains entirely unknown.

Contrary to bioprosthetic valves, mechanical valves are durable and present a virtually inexistent risk of structural valve deterioration. However, these valves are thrombogenic and require lifelong anticoagulation with warfarin, which exposes patients to a small but substantial and continuous lifetime risk of bleeding, thromboembolism and death. This continuous risk results in progressive excess mortality compared to the general population (27,28). In addition, the use of mechanical valves is problematic in women of childbearing age who are contemplating pregnancy (29).

Several strategies have been proposed to mitigate the thromboembolic and hemorrhagic risks associated with the use of mechanical valves. One of these strategies, home INR monitoring using point-of-care devices, has garnered a lot of enthusiasm. However, most of the evidence supporting the efficacy of home INR monitoring is derived from observational studies. The largest randomized controlled trial on the subject—the Home INR Study (THINRS)—failed to demonstrate any advantage of weekly self-testing, as compared with monthly high-quality clinic testing, in delaying the time to a first stroke, major bleeding episode or death (30).

Similarly, there has been a lot of interest in recent years regarding the development of mechanical valves requiring
lower INR targets for anticoagulation. The recent publication of the PROACT trial has garnered a lot of interest within the cardiovascular community (31). In this multicenter trial, 375 patients undergoing AVR with the On-X bileaflet mechanical prosthesis were randomized to receive either lower dose warfarin (target INR 1.5–2.0) or standard dose warfarin (target INR 2.0–3.0). Patients in the lower INR group experienced significantly lower rates of minor and major bleeding, with no significant increase in thromboembolic complications (31). This study generated a lot of enthusiasm, as it demonstrated the safety of maintaining an INR between 1.5 and 2.0 in patients undergoing mechanical AVR with the On-X bileaflet valve. However, a closer look at the data reveals a more sobering picture. In this relatively young—mean age was 55 years—and prospectively followed population, the linearized rate of major adverse event (i.e., major bleeding, thromboembolism, thrombosis) was 4.44%/patient-year in the lower INR group. This suggests that even with lower INR targets, the burden of thromboembolic and hemorrhagic complications associated with mechanical valves is significant. In an otherwise healthy 40-year-old patient undergoing AVR, this represents a very high lifetime probability of at least one major adverse valve-related event.

Moving forward

The suboptimal outcomes associated with the use of conventional prosthetic valves in young and middle-aged adults forces us to reconsider the role of the Ross procedure in today’s armamentarium. A careful and objective assessment of the currently available literature reveals that the two main limitations of the Ross operation—i.e., increased operative risk and late autograft failure—have been largely mitigated in the modern era.

While data from the Society of Thoracic Surgeons have demonstrated a significantly higher perioperative mortality with the Ross procedure as compared to prosthetic AVR, these data are mainly driven by low volume centers (13). In contrast, several series from expert centers have demonstrated that the Ross operation can be carried out with very low rates of operative mortality (8,9), similar to those achieved with prosthetic AVR (11,32). Interestingly, the surgical group from the Montreal Heart Institute recently reported their inaugural experience with a Ross program that was started in 2011 by a young surgeon during his first year of practice (33). Between 2011 and 2016, the Ross procedure was carried out in 200 patients, with two operative deaths, yielding a 1% early mortality rate. Both these deaths occurred early in the experience and were related to suboptimal patient selection. Of note, no operative mortality was observed in the last 150 patients undergoing a Ross procedure at the Montreal Heart Institute. This experience clearly demonstrates that while the Ross procedure is a technically complex operation, it can be performed with excellent early outcomes—including by early-career surgeons—provided that the right conditions are met (i.e., adequate surgical volumes, dedication to the technique, etc.). These excellent results notwithstanding, the learning curve and surgical volume required to achieve proficiency with this operation should not be underestimated. The learning curve of the Ross procedure has been estimated to be around 75–100 cases. In addition, this operation should not be carried out sporadically. We recommend a minimum annual volume of 10 to 15 of these operations, along with other aortic root procedures.

The second drawback of the Ross procedure is the potential for late failure of two valves, i.e. the pulmonary autograft and the pulmonary homograft. This late failure is most often due to dilatation of the pulmonary autograft. Risk factors include a large annulus (≥27 mm) and presence of aortic regurgitation (34). Furthermore, presence of connective tissue disorder is a contraindication to the Ross operation.

In addition to appropriate patient selection, the Ross procedure requires attention to minute technical details that have an important impact on long-term outcomes. These technical refinements rely on a thorough understanding of the anatomy and physiology of the aortic and pulmonary roots. While certain technical considerations are beyond the scope of this article, a few critical points should be emphasized. First, unlike the aortic root, the pulmonary valve does not have a true fibrous annulus, and is supported by 360 degrees of infundibular muscle. When harvesting the pulmonary autograft, one should visualize the line of attachment of the pulmonary leaflets, and take only a thin rim of muscle below the valve. Harvesting too much infundibular muscle weakens the right ventricular outflow tract and predisposes to arrhythmia. Furthermore, once harvested from the right side, this infundibular muscle becomes avascular and unable to provide any structural support to the neo-aortic root. Thus, it is imperative that the pulmonary autograft be implanted within the native aortic annulus in order to provide proximal support. Similarly, to avoid dilatation of the sinotubular junction, the pulmonary autograft is harvested only a few millimetres above the commissural level, in order to minimize the amount of
pulmonary artery tissue exposed to systemic pressures. With regards to the pulmonary homograft used to reconstruct the right ventricular outflow tract, the risk of premature degeneration can largely be mitigated by oversizing the homograft. In our experience, the homograft selected for implantation is virtually always larger than the pulmonary autograft, and rarely smaller than 25 mm in diameter. Finally, tight arterial blood pressure control is critical during the first 3 to 6 months after the operation to allow the pulmonary autograft to adapt to its new environment.

Using these technical refinements, several centers have reported excellent long-term freedom from valve deterioration and reintervention (8,9,35,36). The Harefield group, led by Sir Magdi Yacoub, reported a 99% freedom from aortic valve reoperation at 13 years (35). Similarly, our group recently reported an 87% freedom from valve reintervention at 20 years (including any surgical or percutaneous reintervention of either the pulmonary autograft or the pulmonary homograft) (11). This freedom from reintervention was not significantly different from that observed in a propensity-matched cohort of mechanical AVR patients. Furthermore, no deaths were observed at reoperation in the Ross group, while two of ten patients died at reoperation in the mechanical AVR group.

Despite the important strides made in refining the surgical technique of the Ross procedure, several important questions remain unanswered. For instance, differences in long-term outcomes between the subcoronary implantation technique—as originally described by Donald Ross in 1967—and the full root replacement technique have not been thoroughly studied. Furthermore, in an effort to prevent late dilatation, certain groups have advocated inclusion of the pulmonary autograft in a Dacron tube prior to its implantation in the aortic position (37). While this simple technical modification is appealing, the reduced expansibility of the autograft within the Dacron tube might affect aortic and coronary flow dynamics and impair the autograft’s ability to mimic the native aortic root. It remains to be seen whether this will translate into loss of some of the long-term benefits of the Ross operation in terms of left ventricular remodeling and long-term clinical outcomes.

**Conclusions**

The ideal aortic valve substitute remains elusive. It is widely held that all forms of AVR represent a palliative approach. Conventional prosthetic valves expose the young patient to the virtual inevitability of a reoperation or the continuous hazards of thrombosis and bleeding. In the long run, this translates into excess mortality compared to the general population. The Ross procedure offers unique advantages and is the only operation that has shown the potential to restore the survival of young and middle-aged adults with aortic valve disease to that of the general population. Despite these advantages, its use has declined dramatically in recent years due to concerns over technical complexity, perioperative complications, and long-term autograft failure. These drawbacks can be largely mitigated by adequate patient selection and careful attention to minute technical details. In the current era, the Ross procedure can be performed safely and reproducibly in centers of excellence where complex aortic root operations are performed regularly. Concentrating the care of young adults with aortic valve disease in such centers of excellence may ultimately improve outcomes.

We believe the Ross procedure is the best option for the treatment of aortic valve disease in the vast majority of patients younger than 50 years of age. For patients between 50 and 65 years of age, we recommend the Ross procedure for those who are most likely to derive a benefit from the advantages of this operation. Specifically, these are patients who have an anticipated life expectancy of at least 15 years, pursue an active lifestyle and do not have any major cardiovascular co-morbidities. Finally, the Ross procedure is especially valuable in patients with a small aortic annulus, who are at higher risk of prosthesis-patient mismatch.

The suboptimal outcomes associated with the use of bioprosthetic and mechanical aortic valves in young and middle-aged adults—as well as the growing body of evidence suggesting improved long-term outcomes with the Ross procedure compared to conventional AVR—make it increasingly difficult for clinicians to simply dismiss the pulmonary autograft when considering options for AVR in young and middle-aged adults. When choosing the optimal aortic valve substitute in a young patient, one should consider the lifetime benefits and risks of each option instead of focusing solely on perioperative outcomes.

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**Footnote**

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