The Ross procedure: an excellent option in the right hands

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The ideal approach to managing aortic valve disease in the young patient remains controversial. Although valve repair should be considered, it is frequently not anatomically possible, especially in the setting of aortic stenosis. The requirements for aortic valve replacement (AVR) in the young patient are simple—the replacement should be durable, not require anticoagulation, and have a very low incidence of stroke and other valve-related complications. Options for AVR in the young patient include a mechanical or biological valve, a cryopreserved allograft, and the pulmonary autograft.

Mechanical valve replacement has the purported advantage of long durability, but requires anticoagulation to prevent valve thrombosis, thromboembolism and other valve-related complications. Even with adequate anticoagulation, a not insignificant number of young patients with mechanical aortic valves require reoperative AVR in their lifetimes, and the annualized risk of bleeding and/or thromboembolism is 1–2% per year. Biologic valves (porcine, bovine, equine) have the advantage of not requiring life-long anticoagulation, but the significant disadvantage of valve deterioration requiring reintervention generally within 15–20 years (if not earlier). To make the decision between these two options more difficult, several recent studies have shown that balancing the risk-benefit ratio between these two choices in the young patient is complicated (1,2). Although the risk of reoperative AVR in the setting of a deteriorated bioprosthetic valve is higher than in the initial operation, the cumulative risk of anticoagulation, thrombosis, thromboembolism and other valve-related complications associated with a mechanical valve, make the life-time risks of valve associated morbidity and mortality for a young patient in need of an AVR relatively equal with these two options (2). The recent introduction of percutaneous valve-in-valve AVR technology makes the advantage of not requiring anticoagulation even more attractive for the tissue AVR. Of course, long term durability of percutaneously inserted tissue valves, especially in the young patient and in the situation where it is placed inside a previously place bioprosthetic valve is unknown.

Cryopreserved allografts are another option for replacement of the aortic valve and have the advantage of not requiring anticoagulation and low rates of thromboembolism, however, the requirement for root replacement, the limited durability of the allograft and the difficulty of reoperation makes the use of this option use in the young patient less than ideal (3). The pulmonary autograft procedure for replacement of the aortic valve, in which the aortic root is replaced with the patient's own native pulmonary root and a cryopreserved allograft is used to establish right ventricle to pulmonary artery continuity (Ross procedure) has the potential advantage of freedom from thromboembolism without the need for anticoagulation, excellent hemodynamic performance, growth over time, and the assumption that replacement of the aortic valve with a living autologous tissue is preferential

to prosthetic or xenogenic materials (4). Unfortunately, this procedure is technically complex, and potentially creates both aortic and pulmonary valve disease. Results with the procedure have also proven difficult to translate to the broad cardiac surgery community. El-Hamamsy *et al*. recently reported one of the only prospective randomized trials involving these two techniques. This group randomized 228 adults (age 18–69 years) to an autograft or a homograft. At 10 years, survival was 97% in the autograft group versus 83% in the homograft group, suggesting that a living valve placed in the aortic position can significantly improve long-term outcomes (3).

The study by Mazine *et al*. from the University of Toronto recently published in *Circulation* reports a 20-plus year propensity matched comparison of 208 pairs of young to middle-aged adults who underwent either a Ross procedure or a mechanical aortic valve for primary aortic valve disease (5). While several other propensity score analyses have been reported, this series appears to have the longest follow-up in the literature. Bouhout *et al*. from the Montreal Heart Institute reported equal perioperative outcomes between 70 propensity matched Ross and mechanical AVR patients (average age 52 years) but no follow up data was reported (6). The largest propensity matched study with long-term follow up was from Mokhles *et al*. at Erasmus Medical Center in the Netherlands in which 253 patients (mean age 47 years) were compared in each group. Late survival was equal between groups at a mean of 5.1–6.3 years (7). In a non-matched analysis form the Vienna group, Andreas *et al*. reported 15-year survival of 93% in 159 Ross patients and 75% in 177 mechanical aortic valve recipients, suggesting a possible benefit of the Ross procedure as compared to a mechanical aortic valve in the relatively young patient (8).

After propensity matching, the group of patients recently reported by Mazine *et al*. were remarkable similar. There were more patients with aortic insufficiency in the mechanical aortic valve group and more bicuspid aortic valves in the Ross group, which is not unexpected given the selection criteria used at this center for the Ross procedure. Cross-clamp and cardiopulmonary bypass times were also approximately 25 and 50 minutes longer in the Ross group (which is both not unexpected and quite respectable given the added complexity of the Ross procedure as compared to a mechanical AVR). The patient population was relatively young (37.2±10.2 years), male (63%) and mean follow-up was an impressive 14.2±6.5 years, with clinical follow-up available in 98.3% of patients. The similarity of the groups and long term follow-up make this the best comparative analysis of these two techniques available.

The primary outcome was early (30 day) and late mortality, early mortality was 0.5% in both groups, and there was no difference in long-term mortality between groups (Ross versus AVR: hazard ratio 0.91; 95% confidence interval, 0.38–2.16; P=0.83). Fifteen-year survival in both groups was over 90%. If one just considers cardiac and valve-related mortality, the Ross group had superior outcomes as compared to the mechanical aortic valve group (Ross versus AVR: hazard ratio 0.22; 95% confidence interval, 0.034–0.86; P=0.0.03).

The secondary outcomes of bleeding and stoke, were as expected more common with a mechanical aortic valve (Ross versus AVR: hazard ratio 0.09; 95% confidence interval, 0.02–0.31; P<0.001). These events are not trivial and although data as to effects on quality of life are not provided, there is no doubt significant morbidity occurred in some patients.

While mechanical aortic valves are assumed to infrequently require reintervention, this is a common concern with the Ross procedure, especially since both pulmonary and aortic valves are susceptible to deterioration. Surprisingly, the study reported by Mazine *et al*. showed that freedom from operated valve reintervention (aortic valve in the mechanical AVR group and aortic or pulmonary valve in the Ross group) was equivalent between groups (Ross versus AVR: hazard ratio 1.86; 95% confidence interval, 0.76–0.94; P=0.18). In addition, of the 17 patients in the Ross group that required valve reintervention, there were no operative mortalities, while 2 of the 10 patients died at reoperation in the mechanical AVR group.

These results are impressive, and support the potential advantage of the Ross procedure for young adults with aortic valve disease, however, they should be viewed with caution. Our own results with the Ross procedure were recently reported (9). Although overall follow up was shorter, overall survival at 8 years was excellent at 92% (includes infants). In the comparable age groups presented in the study of Mazine *et al*. (adults), our 8-year survival was 100 and 90% in the 20–40 and >40 year cohorts.

The need for autograft reintervention after the Ross procedure remains a concern. Mazine *et al*. report and incidence of pulmonary autograft dysfunction and the need for aortic valve reintervention of approximately 6% at 10 years. The primary reason was structural deterioration of the pulmonary autograft. In our series, 15% required autograft reintervention during a mean follow-up of

8.2 years, of which in 47% the autograft valve could be salvaged (valve-sparring root replacement or valve repair), while the remaining 53% required replacement of the aortic root or valve alone (10). The failure of the autograft appears to occur in a bimodal distribution with early failure commonly due to a leaflet issue without root dilatation requiring valve replacement, while those who present later typically have root dilatation and are often amenable to a valve-sparring procedure.

Unfortunately, the report of Mazine *et al*. suffers from the same limitation of nearly every report of excellent outcomes with the Ross Procedure—all procedures were performed by a very small number of master surgeons, and in most cases, a single surgeon. All Ross procedures in our experience have been performed by the senior author (VAS), while 96% of the Ross procedures in the report of Mazine *et al*. were performed by Dr. David. Given the question of universal reproducibility of these outcomes, we agree with the authors that one cannot advocate the performance of the Ross procedure, except in the hands of a true expert. It is perhaps unfortunate that the Ross procedure is so technically demanding and has proven so difficult to reproducibly teach, as one could argue that in the right hands it is an excellent option in the young patient in need of an AVR.

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None.

Footnote

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

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