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EDITORIAL COMMENT

The Fate of the Aortic Root After the Arterial Switch Operation*

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The arterial switch operation (ASO) for transposition of the great arteries (TGA) is arguably the most successful surgical innovation for any congenital heart defect, turning what is almost universally a lethal condition into one with >95% survival to adulthood with low (1-3%) surgical mortality.[1] After the ASO, most patients have normal left ventricular function (average ejection fraction 61%)[2], near-normal exercise capacity (average peak VO_2 of 88% of predicted)[2], and quality of life comparable to that of the general population.[3] However, due to the nature of the arterial switch technique, complications predictably occur in 3 domains: the coronary artery ostia, the pulmonary artery and its branches, and the aortic root. While coronary complications typically manifest in infancy and pulmonary artery complications often develop during childhood, aortic root complications tend to occur later, impacting some older children and increasingly adults after the ASO.

In this issue of *JACC: Advances*, the meta-analysis and systematic review by Jacquemyn et al.[4] of 6,169 TGA patients after ASO describe the incidence and risk factors for aortic root complications, including neo-aortic root dilatation, neo-aortic regurgitation, and the need for reoperation on the neo-aortic root. The authors included 30 studies that reported outcomes in the neo-aortic root over at least 10 years, encompassing 13 countries, and employed a "curve approach" to reconstruct individual patient data based on published Kaplan-Meier graphs. As a large compilation of postoperative survivors of the ASO, the report by Jacquemyn et al. provides granular data about the fate of the neo-aortic root over an extended time frame up to 30 years after the ASO. The study found mild neo-aortic regurgitation is common by adulthood (only 47.7% freedom from ≥mild neo-aortic regurgitation at 20 years, cumulative incidence of 67.5% at 30 years); however, more significant neo-aortic regurgitation is uncommon (87.8% freedom from ≥moderate neo-aortic regurgitation at 20 years, cumulative incidence of 21.4% at 30 years). Neo-aortic root dilatation is present in half of children and the majority of adults after ASO (34.9% freedom from neo-aortic root dilatation at 20 years) and appears to be progressive over time. Reassuringly, surgery to address the neo-aortic root is rare (96.5% freedom from neo-aortic valve surgery at 20 years).

As expected, the authors found larger aortic root sizes in those who developed neo-aortic regurgitation, suggesting that aortic root dilation is causally linked to aortic regurgitation in this population. Based on their meta-analysis, risk factors for the development of any neo-aortic regurgitation after ASO include a prior pulmonary artery band (PAB), presence of a ventricular septal defect (VSD), aorto-pulmonary size discrepancy, bicuspid pulmonary valve, and neo-aortic regurgitation being present at the time of discharge after the ASO; risk factors for ≥ moderate aortic regurgitation are VSD and PAB.

Due to the nature of systematic review and meta-analysis, the study of Jacquemyn et al[4] does not provide any new data, but it does give a clearer picture of the fate of the aortic root, which can be helpful in counseling patients and their families after the

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ASO: most patients will have neo-aortic root dilation and mild neo-aortic regurgitation by adulthood, a fifth will have moderate or greater aortic regurgitation, and a little more than 5% will require surgery on the aortic root by age 30 years. Unlike earlier single-center reports of aortic root outcomes, the meta-analysis includes data from diverse geographic centers across 3 continents, which should improve the generalizability of the estimates. Limitations of this work include the era effect, as the data is derived from patients undergoing the ASO between 10 and 30 years ago. Evolution in surgical technique plausibly means that contemporary cohorts may have improved outcomes from these patients. Although the overall cohort in the study by Jacquemyn et al[4] was large, complete data was not available for all patients. Beyond age 20 years, the reported outcomes are based on just a few studies with a much smaller sample size, making the estimates less certain. Examination of the Kaplan-Meir curves for neo-aortic regurgitation suggests the curves may flatten after 25 years of age, while the curve for aortic dilatation continues to decline. However, given the scant amount of data in adults, there is not much certainty about what happens after age 25 years; thus, there will be a continuing need to study the fate of the aortic root after ASO in adult cohorts as they age.

Data from the meta-analysis of Jacquemyn et al[4] provide potential insight into mechanisms of neo-aortic root dilatation and neo-aortic regurgitation after ASO. The most important preoperative factors affecting the neo-aortic root appear to be the presence of a bicuspid pulmonary valve and a VSD. Bicuspid pulmonary valve is present in up to 7% of patients with TGA and is not a contraindication to ASO, with bicuspid pulmonary valve patients having similar early outcomes after ASO to other patients.[5] Bicuspid pulmonary valve prior to ASO has been associated with earlier neo-aortic regurgitation and increased prevalence of neo-aortic regurgitation at hospital discharge.[5] The data by Jacquemyn et al[4] confirm that over the longer term, bicuspid pulmonary valve and neo-aortic regurgitation at hospital discharge confer increased risk of late neo-aortic valve regurgitation. The presence of a VSD in TGA is a well-known risk factor for adverse outcomes. Early left-to-right shunting across the VSD enlarges the size of the native pulmonary artery and may necessitate PAB. PAB increases pressure and causes distension and distortion of the native pulmonary artery. Increased volume and pressure in the native pulmonary artery results in a size discrepancy between vessels, leading to a larger native pulmonary artery and a smaller native aorta. After the ASO, these changes in neo-aortic size and shape contribute to late neo-aortic regurgitation, as PAB and aorto-pulmonary size discrepancies were found to be risk factors for late neo-aortic regurgitation by Jacquemyn et al[4] Notably, Taussig-Bing Anomaly (TBA) did not arise as a risk factor for neo-aortic regurgitation in the meta-analysis, possibly because of the small number of patients with TBA or incomplete data. The large VSD that usually accompanies TBA is associated with more aorta-pulmonary size mismatch, and the side-by-side position of the great vessels in TBA often results in distortion of the neo-aortic root after coronary re-implantation. The TBA subgroup of ASO patients merits additional study, as these patients may be at particular risk for late neo-aortic root dilatation and neo-aortic regurgitation.

In light of the report of Jacquemyn et al,[4] are there any lessons to be learned to improve the fate of the neo-aortic root after ASO? The use of a PA band has decreased significantly in the current era, which could decrease the incidence of neo-aortic root dilation. It is unlikely that refinements in surgical technique can substantially mitigate neo-aortic regurgitation immediately after the ASO, as early regurgitation is mostly related to bicuspid valve, aorto-pulmonary size mismatch, or distortion of the aortic root after coronary reimplantation. Adult congenital cardiologists are assessing and treating patients many years after the ASO. Little is known about the role acquired factors play in the progression of neo-aortic root dilatation and regurgitation. One recent report[6] suggests that being overweight is a risk factor for neo-aortic root dilation after ASO. Hypertension, diabetes, dyslipidemia, sedentary lifestyle, smoking, and drug use are all potentially modifiable targets that merit study in large adult cohorts to see if they will emerge as contributors to neo-aortic root dilatation and regurgitation. Furthermore, there is no evidence or even consensus recommendations about the role of medical therapy (such as beta-blockers and angiotensin receptor blockers) to treat neo-aortic root dilatation. Additional areas of uncertainty are the thresholds for reoperation on the aortic root after ASO. Most programs use adult guideline recommendations on aortic regurgitation and aortic dilatation to determine indication for and timing of surgery. Whether earlier, prophylactic surgery to remodel the aortic root before it is severely dilated would prevent aortic valve replacement in this patient population is unknown.

While the systematic review and meta-analysis of Jacquemyn et al[4] add to our understanding of outcomes in the neo-aortic root, many areas of uncertainty remain. There is a continuing need to follow contemporary cohorts of ASO patients past the third decade, ideally by prospective multicenter cohorts with detailed imaging and clinical characterization to better understand the fate of the aortic root after the ASO.

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REFERENCES

1. Fricke TA, Konstatinov IE. Arterial switch operation: operative approach and outcomes. *Ann Thorac Surg*. 2019;107:302–310.

2. van Wijk SW, Driessen MM, Meijboom FJ, et al. Left ventricular function and exercise capacity after arterial switch operation for transposition of the great arteries: a systematic review and meta-analysis. *Cardiol Young*. 2018;28(7):895–902.

3. Morfaw F, Leenus A, Mbuagbaw L, et al. Outcomes after corrective surgery for congenital dextro-transposition of the arteries using the arterial switch technique: a scoping systematic review. *Syst Rev*. 2020;9(1):231.

4. Jacquemyn X, Van den Eynde J, Schuermans A, et al. Neoaortic regurgitation detected by echocardiography after arterial switch operation: a systematic review and meta-analysis. *JACC: Adv*. 2024;3:100878.

5. Irwin M, Binney G, Gauvreau K, et al. Native bicuspid pulmonary valve in D-Loop transposition of the great arteries: outcomes of the neo-aortic valve function and root dilation after arterial switch operation. *J Am Heart Assoc*. 2021;10:e021599.

6. Muneuchi J, Watanabe M, Sugitani Y, et al. Being overweight is related to Neoaortic Sinus dilatation after arterial switch operation. *Texas Hear Inst J*. 2022;49(5):e207508.

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