Reminder: Tetralogy of Fallot is not just a right-sided cardiac problem

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Keep an eye on the aortic root after tetralogy of Fallot repair!

Central Message

The dynamics of the aortic root in tetralogy of Fallot is abnormal even after repair and even if the root is not dilated. This finding raises the possibility of late left-sided circulatory problems.

See Article page 2239.

Pediatric cardiac surgeons are familiar with the “generous” aortic root observed in patients with tetralogy of Fallot (TOF). In one cohort at a median follow-up of 27 years after TOF repair, maximal aortic diameter was greater than 4 cm in 39% of patients and greater than 5 cm in 8%.¹ Focusing on right-sided pathology, we usually ignore the finding unless the root becomes frankly aneurysmal. Limiting our exposure to patients in the first few decades of life, we only infrequently see clinical complications of the enlarged TOF aorta. We treat it more as a curiosity.

There is, however, additional, hidden pathology in the TOF root. In this issue of the *Journal*, Schäfer and colleagues² report 4-dimensional flow magnetic resonance imaging measurements of aortic size, distensibility, and wall shear stress (WSS) in a small cohort of adolescents who underwent repair of TOF in infancy. In their comparison with an age-matched control group, Schäfer and colleagues² found the following: (1) aortic root size did not differ between the groups, (2) aortic distensibility was decreased, (3) WSS was elevated, and (4) helical flow was qualitatively increased.

Why are these observations important? WSS and degree of helical flow are primarily determined by the velocity field of the inflow to the aorta and are thus generated in the left ventricle (LV), the LV outflow tract, and the aortic valve. Elevated WSS and helical flow are transduced by endothelial cells, which signal the vessel wall to thicken and increase in diameter. Changes in the architecture of the wall decrease distensibility. Although increased diameter may tend to decrease WSS, decreased distensibility tends to increase WSS.³⁻⁵ The interplay of these factors is complex. This interplay and normal changes with somatic growth make the evolution of the aortic root in TOF uncertain but potentially concerning. Perhaps decades later, the root may again begin to dilate and become aneurysmal. Decreased aortic distensibility will increase LV afterload,

blunt normal small vessel pulse pressure, and compromise coronary perfusion, ultimately resulting in an increased risk of cardiovascular morbidity and mortality associated with the *left*-sided circulation.

What is the origin of this problem? Interestingly, the aortic valve and root are already dilated at birth in TOF. Aortic specimens obtained at TOF repair at a median age of 6 months show abnormal fibrosis in 45% of patients.⁶ In fact, dilation is evident in the second-trimester fetus. Recently, Taketazu and coworkers⁷ reported that aortic distensibility was significantly less in 22- to 39-week fetuses with TOF than in normal fetuses (Figure 1). Aortic root pathology is not limited to TOF but also occurs in other conotruncal anomalies, including double-outlet right ventricle, truncus arteriosus, and transposition of the great arteries.⁸ These observations suggest that at least the *prediction* for root dilation is intrinsic to conotruncal anomalies through abnormal genetic signaling during heart formation and development.⁹ On the other hand, early repair of TOF is associated with lack of progression, or even regression, of root dilation. Because WSS is primarily determined by the inflow velocity field, perhaps repair alters this velocity field and thus the impact of WSS on the root. The key finding of the study of Schäfer and colleagues² is that repair does not completely normalize WSS and distensibility. What remains is to determine the precise reason for the

FIGURE 1. Comparison of z score of aortic compliance (AC) between normal fetuses (N) and fetuses with congenital cardiac anomalies. Compliance is significantly decreased in fetuses with tetralogy of Fallot (TOF) relative to that of normal fetuses. Arrows indicate aortic compliance of sample patients with Marfan and Noonan syndromes. TGA, Transposition of the great arteries; SV, single ventricle; VSD, ventricular septal defect; CoA/IAA, coarctation of the aorta/interrupted aortic arch; tr18, trisomy 18 with ventricular septal defect. (Used with permission from Elsevier.⁷)

elevated WSS in this cohort—is it the underlying persistent decreased distensibility, or is it a persistently abnormal inflow velocity field, resulting from the patched anterior malalignment defect, or an interaction of the LV and the right ventricle? Detailed computational modelling may be required to answer this question. Likewise, measurements were made only at one time per patient. The time-dependent behavior of the root will lend further to our understanding of this phenomenon, as well as its potentially significant clinical impact. TOF is not just a right-sided problem.

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