Aortic Root Dilatation After Repair of Tetralogy of Fallot
Pathology From the Past?

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Repair of tetralogy of Fallot (TOF) has been performed since 1954 and adult survival is expected. Long-term problems include arrhythmias, both supraventricular and ventricular, and residual hemodynamic problems, which are generally well tolerated for many years; these include residual ventricular septal defect and pulmonary stenosis but, most commonly, pulmonary regurgitation, with its consequent right ventricular dysfunction and tricuspid regurgitation. Although the most common reason for repeat surgery in the adult after TOF repair relates to problems in the right ventricular outflow tract, the aortic root is often forgotten. In this issue of Circulation, Niwa et al report a series of 32 patients who demonstrated a dilated aortic root after surgical repair of tetralogy of Fallot (TOF). Aortic root size measured echocardiographically was >1.5 expected diameter by standard nomogram. This “dilator” group comprised almost 15% of their TOF patient population. Characteristics of these patients with TOF compared with age-matched controls included a higher prevalence of pulmonary atresia, a longer shunt-to-repair interval, and a right aortic arch. Other features were consequent on the dilated aorta rather than causal, moderate-to-severe aortic regurgitation and a larger left ventricle both echocardiographically and radiographically. Two of these patients needed aortic valve replacement and root repair.

These observations are not new. Progressive aortic root dilatation after complete uncomplicated repair of TOF has been noted previously, and others have reported aortic regurgitation. In the majority of patients, however, the aortic regurgitation is mild and of little or no clinical consequence. In the Mayo Clinic series, 16 patients had aortic valve replacement after TOF repair of whom 4 also had aortic root replacement. Eleven of these 16 patients had pulmonary atresia. The mean age at repair in this series was also relatively advanced (13.5 years), although 1 patient was only 3 months old. The echocardiographic morphology of the aortic root is usually abnormal and is manifest by both enlargement and effacement of the sinotubular ridge in about three-fourths of adult tetralogy patients. This anatomy results in some degree of aortic regurgitation in 74%, usually mild-to-moderate but occasionally severe.

Why does progressive aortic root dilatation occur in some patients? It is postulated that increased flow through the aorta for years prior to repair sets the stage for progressive dilatation. This premise is supported by the observation that these patients reported by Niwa et al were repaired relatively late in life (mean 14 years of age) and had a longer time from insertion of a palliative aortopulmonary shunt to definitive repair than did the control group. In addition, 6 patients had pulmonary atresia, which when compared with the control group suggests that, at least in part, the greater volume load on the aorta predisposes to dilatation. Because a right aortic arch is more common in pulmonary atresia than TOF, this would suggest that it is the primary hemodynamic abnormality itself that predisposes to the dilatation rather than the sidedness of the aortic arch.

Underlying this tendency to aortic root dilatation and distortion are histological changes of the media in the dilated aortic root of tetralogy patients that resemble those observed in both bicuspid aortic valve disease and Marfan syndrome. So-called “cystic medial necrosis” is a misnomer because necrosis is seldom encountered and there are no true cysts; nonetheless, there is a noninflammatory loss of smooth muscle cells, mucoid degeneration, and fragmentation of the elastic fibers within the media. Whether these changes result from a primary or intrinsic medial abnormality inherent in TOF itself or are secondary to the antecedent volume load through the aorta before repair remains unknown. Certainly, familial thoracic aortic aneurysms and dissections, unrelated to TOF have been found to be genetically heterogeneous diseases that can be mapped to various chromosomes.

Apoptosis may be an important mechanism underlying the loss of smooth muscle cells in the ascending aorta of patients with bicuspid aortic valve and contributes to aortic dilatation in those patients. In addition to intrinsic genetic or cellular signals precipitating apoptosis, perhaps triggers for programmed cell death may originate in the aortic wall from mechanical forces, such as shear stresses, which are secondary to increased flow and could account for the dilatation seen in some TOF patients. Such apoptotic medial changes have been observed under the stimuli of hypertension and atherosclerosis. In fact, it may be a combination of an intrinsic capacity for premature injury or cell death and secondary...
stress-induced activation of tissue enzymes or cell death that causes the end result.

Alternatively, there may be one or more cellular abnormalities of the aorta in patients with conotruncal abnormalities. During embryogenesis, occipital neural crest cells derived from the cranial neural fold migrate into the cardiac outflow tract and participate in outflow tract septation.14 Perhaps in some way these neuroectodermal immigrants into the ascending aorta influence medial degeneration and aortic dilation.15 Recently, cellular proteinases have been found to degrade many components in the arterial wall. The findings that increases in particular metalloproteinase (elastin or collagen) expression has been linked with size and expansion of abdominal aortic aneurysms are intriguing.16

When should aortic root replacement be considered in these patients? If reoperation is being performed for aortic valve replacement or pulmonary valve replacement, it would appear prudent to consider aortic root repair or replacement if the aortic root is >50 mm in diameter. Suppose, however, that there is no other indication for operation other than aortic root dilatation? Should the aortic root be replaced using the same criteria as for Marfan syndrome? In the Mayo Clinic series, the largest aortic root was 85 mm in diameter without dissection, and to our knowledge, spontaneous dissection has never been observed in any patient with a conotruncal abnormality. Whether β-blockade may limit the progression of aortic dilatation in these patients is also unknown.

These observations serve to emphasize that adults with TOF, even after a good intracardiac repair, require meticulous lifelong follow-up; comprehensive assessment should include a clinical and echocardiographic evaluation not only of the right ventricular outflow tract but also the aorta. The present impetus to operate on TOF patients early in life might mean that aortic root dilatation may be a pathology of the past and not of future generations of TOF patients. Early surgical repair offers many advantages: it may prevent the right ventricular fibrosis that occurs when the right ventricle is exposed to systemic pressure through the large ventricular defect. It also obviates the need for a palliative arteriopulmonary shunt, which may distort the pulmonary arteries. Avoiding the long-standing volume load on the aorta inherent in the right-to-left shunt, or resulting from a surgically created shunt, may be another advantage. As such, even if there is an intrinsic developmental tendency to medial pathology, limiting the exposure to hemodynamic stress may obviate or reduce future aortic dilatation as well as progression of aortic regurgitation. Thus, this aortic dilatation may be a pathological process in current adult TOF populations but not in future ones.

References


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