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EDITORIAL COMMENT

Aortic dilatation in repaired tetralogy of Fallot: Can an old problem be solved?

Dilatação da aorta na tetralogia de Fallot reparada. Resolveremos um velho problema?

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Tetralogy of Fallot (TOF) is the most common cyanotic heart disease in infancy, representing nearly 10% of all cyanotic heart disease.[1] The earliest reports of successful surgical repair date back to 1954, since when corrective surgery has changed in both technique and in age of intervention. The consequent reductions in mortality and morbidity now enable most patients with TOF to survive into adulthood.[2] However, in follow-up, more than 30% of these patients present arrhythmias and some degree of residual defects including shunts, right ventricular obstruction, pulmonary regurgitation and right ventricular dysfunction, with negative impact on ventricular coupling and left ventricular function, leading in some cases to adverse outcomes. These complications are the main cause for repeated interventions in this population.[3–5]

Aortic root dilatation has been identified even in the fetus and is considered a marker of TOF in fetal echocardiography.[6] Progressive aortic dilatation is known to occur in unrepaired TOF, but more interestingly, several studies have demonstrated that a subset of repaired TOF patients also present aortic root and ascending aorta dilatation, sometimes leading to aortic regurgitation. However, the majority of repaired TOF patients present mild to moderate regurgitation and only a minority will require aortic root repair.[7–9] Rarely, the dilated ascending aorta is also at risk of dissection and rupture.[10,11]

A more important issue is why the aortic root continues to dilate in some patients with repaired TOF. Increased aortic overflow because of late repair or previous palliative shunt surgery, and intrinsic anomalies of the aortic wall, have been considered as causative mechanisms. Niwa et al.[9] reported a positive association between aortic dilatation and male gender, longer time from palliation to repair and the presence of pulmonary atresia and right aortic arch, but they did not find that age at repair or time from repair were significantly associated with this complication. Abnormalities of the arterial media, consistent with intrinsic aortopathy, have been seen in different congenital heart defects, from Marfan syndrome to bicuspid aortic valve, and in conotruncal anomalies such as TOF and truncus arteriosus.[12,13] In a subset of patients with TOF these have been demonstrated to be present from an early age, suggesting that intrinsic histological abnormalities may have a role in aortic dilatation.[14] Other studies have shown, for instance, that fibrillin-1 gene mutations in TOF patients are associated with histological abnormalities

and larger aortic size, suggesting that a genetic predisposition may contribute to aortic dilatation.[14–16] Such changes in the arterial wall structure could significantly alter its mechanical properties, possibly by increasing aortic stiffness and reducing strain and distensibility, which would also exert a negative effect on left ventricular diastolic function, potentially with long-term effects on clinical status.[17–19] Additionally, increased aortic wall stiffness contributes to aortic wall remodeling by stimulating vascular smooth muscle to increase collagen synthesis[20] and is considered a significant predictor of aortic dilatation.[17]

In their article in this issue of the *Journal*, Cruz et al.[21] aimed to assess aortic dimensions and elasticity and to find predictors of aortic dilatation in 126 adult patients with repaired TOF, compared with 63 matched healthy controls, prospectively analyzing aortic diameter and arterial hemodynamics. The authors decided to exclude patients with pulmonary atresia and genetic syndromes, in order to avoid bias, because both tend to be associated with aortic root dilatation. They found a significant prevalence of aortic dilatation (29-24%), lower strain and higher stiffness index in the study population compared with controls. Also, male gender had a strong correlation with aortic root dilatation (odds ratio of 6.3). Although the research and results are not new, corroborating the results of previous studies, they are important because they reflect for the first time the reality of a grown-up congenital heart (GUCH) center in Portugal, the particular characteristics of which, as the authors point out, are reflected in their results in terms of diagnostic accuracy, referral and surgical policies, and patients' social background.

Of the TOF population, 10% had had surgical repair at the age of 18 or older, median age being five or seven years (without and with dilatation, respectively). Moreover, 48% of patients had a previous shunt operation performed later than infancy, with a mean time between palliation and correction of three years. Neither of these were predictors of aortic dilatation.

These results might not be reproduced in the overall adult repaired TOF population, because of differences between centers in clinical referral and surgical policies. In fact, even 20-25 years ago, a palliative shunt was rarely considered necessary in classical TOF after one year of age in some centers, and primary correction was performed preferably before the age of two years. This is a major issue, as several authors have described better outcomes for patients undergoing corrective surgery during early infancy. Baht et al.[22] reported the first prospective study that addressed trends in aortic root growth according to age at definitive repair, and concluded that root dimensions in patients repaired in infancy had normalized by mid-childhood. This was further demonstrated by other studies on larger datasets, such as those of François et al.,[23,24] who showed regression of aortic root diameters at different levels, with the fastest size regression at the level of the aortic annulus and sinotubular junction, in the first three years after repair. Size decrease at the aortic sinus appears to be slower but consistent at late follow-up.

Variations in the prevalence of aortic dilatation in the literature have been shown to depend largely on the imaging tool used and the sizing criteria. Echocardiography is the first-line imaging modality and previous studies have established reference values for aortic size after correction of TOF. Cardiac magnetic resonance (CMR) is also a routine follow-up tool in these patients, and is more accurate for volumes, regurgitation fraction and aortic measurements. Recent studies using CMR in children and young adults after correction of TOF have established values for aortic dimensions in these patients.[25,26]

There is no gender predominance in TOF, but the present study revealed a strong correlation between male gender and aortic dilatation. Other studies have revealed the same association, as well as lower strain and higher stiffness index in males. Interestingly, the influence of gender and age on aortic distensibility and stiffness, which are worse in males, is well known.[27,28]

The present study, along with several others, highlights the need for appropriate and meticulous lifelong follow-up for adults with TOF, even if they appear to be asymptomatic and underwent technically correct surgical repair. This requires teams of specialists in congenital heart disease, intervention and surgery working in integrated reference centers for treatment of GUCH patients. Follow-up should include not only clinical and imaging assessment of right ventricular and outflow tract function, but also thorough assessment of left chamber function and the aorta.

We can only hope that the present tendency toward correction of TOF in early infancy, avoiding palliative surgery, will prevent ventricular fibrosis, aortic root dilatation and related complications in future generations. Only then may aortic dilatation after repaired TOF become a ghost from the past.

Conflicts of interest

The author has no conflicts of interest to declare.

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