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Editorial

Congenital Heart Disease and Coronary Atherosclerosis: A Looming Concern?

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See article by Guerri-Guttenberg et al., pages 849-857 of this issue.

The relationship between congenital heart disease and coronary artery lesions may involve different pathophysiological mechanisms, be they direct or indirect, acquired or iatrogenic, depending, in part, on the type of defect and surgical intervention. For example, congenital anomalies of the coronary arteries can result in myocardial hypoperfusion and infarction.[1] Congenital coronary fistulae, which most commonly involve a right coronary artery shunting into a right atrium, coronary sinus, or right ventricle, may be complicated by right-sided volume overload, myocardial infarction, and sudden death.[2] In addition, rare cases have been described of coronary artery compression due to sinus of Valsalva aneurysms,[3] stents in pulmonary artery conduits,[4] and surgically[5] or percutaneously[6] implanted pulmonary valves. Intracardiac shunts can allow emboli to transit into the coronary circulation, with increased incidence in patients with intracardiac thrombogenic material.[7] Surgical repairs, such as the arterial switch procedure for transposition of the great arteries, which involves reimplanting coronary arteries, may be complicated by obstructive coronary flow and myocardial infarction.[8] Other forms of congenital heart disease, such as aortic coarctation, are associated with hypertension, a risk factor for premature coronary atherosclerosis.[9] Whether coronary artery disease in adulthood may be linked to a sedentary lifestyle resulting from functional limitations implicit in severe forms of congenital heart disease remains a topic of investigation.[10]

Within this context, Guerri-Guttenberg and colleagues contributed a welcomed and timely addition to the growing literature exploring the association between coronary and congenital heart disease.[11] While prior studies demonstrated the existence of coronary artery intimal hyperplasia in infants and children with otherwise normal hearts,[12-14] to our knowledge, Guerri-Guttenberg et al.'s investigation is the first to systematically examine the prevalence of preatherosclerotic coronary lesions in a necropsy series of children with congenital cardiac defects. Coronary artery sections were assessed in 98 children with congenital heart defects and 10 controls.[11] The coronary arteries were immunohistochemically stained for the expression of transforming growth factor β1 (TGF-β1). It is interesting that 61% of children with congenital heart disease and all controls had evidence of intimal hyperplasia in at least 1 coronary artery, usually the left main. Analysis of patients with congenital defects found no difference in the prevalence of coronary intimal hyperplasia in those with cyanotic vs acyanotic cardiac lesions. However, the subgroup of patients with surgical repair of their heart defects, and those having left heart obstructive lesions or left ventricular hypertrophy, were significantly more likely to have intimal coronary hyperplasia. TGF-β1 immunostaining was negative in all controls and no different between those with cyanotic or acyanotic defects, but significantly greater in those with repaired vs unrepaired congenital heart disease. The authors contend that coronary lesions expressing TGF-β1 could represent precursors of coronary atherosclerotic disease, and they surmise that hypoxia-ischemia induced vascular injury occurring prior to or during cardiac surgery (such as with hemodynamic instability, cardioplegic arrest, or manipulation of the coronaries) may be responsible for this phenomenon.

As with many interesting studies, Guerri-Guttenberg et al.'s thought-provoking analysis raises many questions. Since congenital heart disease encompasses a heterogeneous assortment of loosely connected defects, it remains to be determined which single or group of surgically repaired malformations is associated with intimal hyperplasia. The hypothesis that factors such as cardioplegia may lead to intimal hyperplasia remains to be demonstrated. While an increased prevalence of intimal hyperplasia was previously described in association with certain surgical interventions, such as those involving coronary manipulation,[15] it is unlikely that all forms of congenital heart disease incur a higher risk. Moreover, without knowledge of the time interval between cardiac surgery and death, it may be biologically implausible to implicate surgery as a risk factor for TGF-β1 expression in coronary arteries of patients with early postoperative deaths.

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A more detailed description of cardiac anatomy, defects associated with left ventricular hypertrophy and left heart obstruction, and types and timing of surgical repair may shed further light on these important issues. It is difficult to imagine that a palliative operation such as the placement of an aorto-pulmonary shunt (eg, modified Blalock-Taussig shunt), which may be performed off-pump and requires no coronary manipulation, is in any way comparable in risk of coronary injury to an arterial switch operation.

The varied types of congenital defects, underlying physiologies, operative approaches, and postoperative sequelae obscure speculations as to whether the culprit for intimal hyperplasia was primarily the underlying cardiac malformation itself, or the hemodynamic disturbance it produced, or still, the surgical repair of the said defect. Considering the marked heterogeneity in key exposure variables, lesion-specific analyses may best inform the relationship between congenital heart disease and coronary intimal hyperplasia. As 1 example of nonuniform risks, it has been postulated that cyanotic congenital heart disease actually protects against coronary atherosclerosis by virtue of the salutary effects of associated hypocholesterolemia, hypoxemia, low platelet counts, hyperbilirubinemia, and upregulation of nitric oxide.[16]

Guerri-Guttenberg et al. are to be commended for their foray into potential determinants of intimal hyperplasia in children with congenital heart disease. It is important that they have drawn attention to the enigma of coronary complications in this growing and aging population and have identified avenues for further research.

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