EDITORIAL COMMENT

“Repaired” Aortic Coarctation in Adults: Not a “Simple” Congenital Heart Defect*

Gerald Ross Marx, MD
Boston, Massachusetts

Long-term follow-up of adult patients after surgical intervention for aortic coarctation has been associated with systemic arterial hypertension, recoarctation, and progressive aortic and/or mitral valve disease from congenital abnormalities (1). Increased morbidity and shortened life span have resulted from aneurysms at the site of previous coarctation repair; aneurysm rupture at the circle of Willis; and premature atherosclerotic coronary artery (1).

Paradoxically, cardiologists have often ascribed aortic coarctation as “simple” rather than “complex” congenital heart disease. Nothing could be further from the truth. The complexity of aortic coarctation becomes evident when caring for the adolescent or adult who has had previous surgical or balloon dilation angioplasty “repair.” To reduce the associated morbidity and mortality, Therrien and colleagues (2) explore, in this issue of the Journal, the “most cost-effective” strategy for following adult patients who have undergone surgical and/or catheter intervention for aortic coarctation. In particular, the authors focus on a cost-effective strategy based on detection of two specific parameters, recoarctation and/or aneurysm formation.

In analysis of sensitivity, specificity and cost, the authors investigated separately, and in combination, factors including symptoms, electrocardiogram, physical examination, chest radiograph, exercise testing, and transthoracic echocardiography. Magnetic resonance imaging (MRI) was used as the “gold standard.” The authors conclude that a clinic visit with MRI was the most “cost-effective” approach to follow this patient group. However, a clinical visit with a screening echocardiogram, and an MRI on patients with positive results, was an acceptable alternative.

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Can we truly determine the most cost-effective approach when the development, progression, and intervention for the medical condition are all obscure? Cost-effectiveness analysis is more straightforward for evaluation of a medical condition such as appendicitis. The latter condition has a narrow time frame for presentation; it occurs once, and following diagnosis has a definitive intervention (i.e., appendectomy). Tests with high sensitivity seem appropriate because appendectomy is a relatively “benign” intervention, and is certainly favorable over missed diagnosis. However, the same may not be true for recoarctation, or aneurysm formation, after catheter or surgical intervention. Both entities can progress in severity over time. Uncertainties remain regarding the parameters for clinically significant residual coarctation or aneurysm, as well as the criteria for intervention. The need for serial evaluation might influence the cost-effective strategy.

Does the information about the coarctation or aneurysm alone provide sufficient information in caring for these patients? Even “simple” coarctation is associated with a high incidence of aortic and mitral valve pathology. Bicuspid aortic valve has been reported to occur in up to 85% of patients with aortic coarctation (3). Two-dimensional echocardiography has delineated mitral valve disease occurring in over 50% of patients with aortic coarctation, with approximately 20% having major disease (4). The term “complex” coarctation, occurring in up to 50% of patients (3), has been reserved for conditions in which coarctation is associated with other major lesions. More “complex” lesions include ventricular septal defects, subvalvar aortic stenosis, d-transposition of the great arteries with ventricular septal defect, double outlet right ventricle, “corrected” or L-transposition of the great arteries, single ventricles, and hypoplastic left heart syndrome. Those in whom coarctation occurs in conjunction with a systemic right ventricle, or single ventricle, are at particular risk of developing ventricular dysfunction. Patients with physiologically “corrected” or L-transposition of the great arteries, in whom the aorta arises from the right ventricle, often have associated tricuspid valve pathology. Such patients would be increasingly vulnerable to increased afterload that accompanies coarctation. Complete evaluation of these associated anatomic abnormalities is essential to better understand the clinical importance of the aortic coarctation.

Investigators have determined that residual coarctation is associated with increased left ventricular wall mass and abnormal Doppler indices of left ventricular filling, regardless of the gradient measurement (5–8). Certainly, ventricular systolic function may affect the gradient measurement. Likewise, the coarctation, by increasing arterial resistance, will affect left ventricular function. Increased stroke volume from aortic regurgitation may increase coarctation gradients. In turn, aortic coarctation may exacerbate the severity of aortic regurgitation. Therrien et al. (2) do acknowledge that noninvasive testing such as echocardiography may offer additional information, not readily available from MRI, and its use must be tailored to the individual patient. Although

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From the Harvard Medical School, Boston, Massachusetts.
one could argue whether echocardiography or MRI best provides such additional information, the severity of aortic coarctation, be it related to restenosis or aneurysm formation, can only be fully comprehended by evaluation of associated anatomic and hemodynamic alterations in individual patients.

Several points concerning the tests employed in the study by Therrien et al. (2) are worthy of discussion. Can we rely on two-dimensional (2-D) echocardiography to provide clinically accurate data about aortic arch abnormalities, in particular aneurysm formation or recoarctation? For years, 2-D echocardiography (9) with color flow mapping (10) has been accepted as a reliable noninvasive tool in the anatomic assessment of aortic coarctation, especially in infants and children. However, with the advent of MRI, excellent views of the entire aortic arch could also be displayed (11–15). This prompted several comparative studies in which measurements of the aortic arch, isthmus, and coarctation were similar for echocardiography and MRI, as compared to angiography (12–15). However, in these studies, nearly 50% of older adolescents or adults could not be adequately imaged by echocardiography, yet MRI provided detailed composite views of the aortic arch and coarctation (13–15).

In a study of adult patients, transesophageal imaging provided comparable details of the isthmus and coarctation site as MRI, but only MRI adequately demonstrated the aortic arch (16). Moreover, MRI has been reported to provide additional information including the ability to detect (15), and quantify, collateral flow (17). In older, larger adolescent or adult patients with known poor ‘‘echocardiographic images,’’ MRI as a first study would be cost-effective for detection of recoarctation (15). In contrast, when optimal imaging is feasible, the literature supports 2-D echocardiography to image the aortic arch, isthmus, and coarctation site.

No studies have been reported comparing MRI with echocardiography for the detection and delineation of aortic aneurysms in this patient group. Therrien et al. used the echocardiographic determination of a ‘‘mention of a bulge’’ as an indicator of a ‘‘possible aneurysm’’ (2). The MRI criterion to confirm the echocardiographic finding was a discrete bulging of the aorta >150% of the diameter of the descending aorta at the level of the diaphragm. Interestingly, the investigators (2) found chest X-ray was 67% and echocardiography was 29% sensitive for aneurysm detection. Bromberg et al. (18) compared chest X-ray, 2-D echocardiography, and computerized chest tomography for the detection of aortic aneurysms in children, adolescents and young adults who had undergone prior surgery for aortic coarctation. Sensitivities for the detection of aneurysm formation for chest X-ray, echocardiography, and chest computed tomography were 100%, 71%, and 66%, respectively. As compared to Therrien’s findings, Bromberg’s higher sensitivity of echocardiography may have been related to enhanced imaging in some pediatric patients. Bromberg and colleagues emphasized, however, that the relatively low sensitivities of chest computerized tomography and echocardiography were attributable to the ‘‘arbitrary nature of the definition of an aneurysm.’’ Importantly, the researchers emphasized that if progressive aneurysm dilation of the aorta is documented, surgical resection is probably indicated, but that the natural history of such aneurysms remains unknown. As previously mentioned, the lack of specific parameters for aneurysm diagnosis, knowledge about progression, and indications for intervention may hamper the development of cost-effective strategies for this clinical entity.

Therrien and colleagues define a resting Doppler echocardiographic maximal instantaneous gradient of 25 mm Hg to be indicative of recoarctation. Nonimaging continuous-wave Doppler velocimetry, without incorporation of proximal velocities in the modified Bernoulli equation, was used to measure the pressure drop. Although several investigators have reported that Doppler echocardiography can accurately determine coarctation gradients, this concept remains controversial.

Initially, Doppler echocardiography was found to be accurate in the determination of the pressure drop across coarctations in pediatric (19–21) and adult patients (19), at both rest and during exercise (15,19). Although certain investigators (19–21) reported that Doppler echocardiography provided a good estimate of coarctation gradients as compared to simultaneously obtained cardiac catheterization measurements, lack of incorporation of proximal velocities overestimated gradient determination at the specific coarctation site. Preobstruction velocities as high as twice normal, attributed to residual hypoplasia of the transverse aortic arch, were reported (21). The potential for overestimation might not be considered important for purposes of the study by Therrien et al. (2), as the investigators readily accepted a high false-positive rate.

However, several investigators have refuted the accuracy of Doppler echocardiography to measure coarctation gradients accurately. Poor correlation and limits of agreement between Doppler maximal instantaneous gradients and catheterization maximal instantaneous and peak-to-peak gradients have been reported (22–24). In an intricate study design, however, excellent agreement was obtained by comparing simultaneous measured continuous-wave Doppler and catheterization maximal instantaneous velocities (25). Catheterization maximal velocities were obtained using dual micromanometer catheter-tipped pressure transducers, and the maximal velocities were calculated from the simultaneous pressure differences. A slight overestimation was found by Doppler, which investigators attributed both to lack of incorporation of proximal velocities and to differences related to pressure recovery phenomenon.

Can Doppler echocardiography underestimate the pressure gradient? Several investigators have maintained that, occasionally, coarctation may have the properties of a long-segment stenosis, which would result in additional energy loss due to viscous resistance (26). Such energy loss
were less than 0.25 cm², and tunnel lengths were greater. Measured pressure gradients did not occur until tunnel areas were less than 0.25 cm², and tunnel lengths were greater than 4 cm (26). It remains to be determined in the clinical arena which aortic coartations have similar properties.

The study by Therrien et al. (2), used MRI as the "gold standard" rather than catheterization anatomy or gradients. Interesting, gradients measured by Doppler echocardiography have compared favorably with MRI velocity gradients (16,17). Coarctation gradients measured by both techniques are done in a more natural physiologic state than gradients measured at catheterization. Potentially maximal instantaneous or perhaps mean gradients will provide a more meaningful index of severity than conventional catheterization measured peak-to-peak gradients. Employing hemodynamic measurements that more closely simulate normal physiologic states, at rest or with exercise, will enhance our understanding of cardiovascular disease, be it coarctation or otherwise.

This introduces a further question: What is the clinically important gradient in aortic coarctation? Therrien and colleagues used a gradient ≥25 mm Hg as an indicator of significant residual coarctation. However, gradients at which medical, catheterization, or surgical interventions are performed may be related to other factors, including symptoms, systemic hypertension, or ventricular function. Additionally, several investigators have reported that patients with "successfully repaired" coarctation may continue to be at risk for increased morbidity and early mortality. Weber and colleagues (27) reported that patients with normal resting blood pressures, and a continuous-wave Doppler gradient <20 mm Hg developed systolic hypertension and increased ascending to descending aortic Doppler gradients during exercise. These patients underwent catheterization, angiography revealed significant narrowing of the transverse aortic arch. Similarly, Cyran and colleagues (28) reported that one-third of patients with resting Doppler coarctation gradients ≤25 mm Hg developed systolic hypertension and increased Doppler descending aorta velocities with exercise. These patients had widely patent aortic arches, prompting investigators to conclude that altered "compliance" of the transverse aortic arch resulted in the "abnormal" response to exercise.

A plethora of investigations have now reported increased left ventricular wall mass in patients after "successful" coarctation surgery (5–8). Johnson et al. (5) reported that postoperative coarctation patients had increased left ventricular wall mass despite normal resting blood pressure and Doppler gradients <20 mm Hg. Although the increased wall mass was noted in patients operated as neonates as well as early childhood, this phenomenon seemed to be progressive with advancing age. Again, the investigators attributed the increased wall mass to residual aortic arch narrowing. Moskowitz (7) and Kimball (6) have reported abnormal Doppler indices of left ventricular filling in addition to increased wall mass.

In a related study by Leandro et al. (8), although the "successfully repaired" coarctation patients had normal resting blood pressures and normal peak exercise systolic blood pressure, these patients had elevated blood pressure on 24-h ambulatory monitoring. The coarctation group had increased aortic arch gradients with exercise, increased left ventricular wall mass, and abnormal Doppler trans-mitral E/A ratios. All patients had narrowed transverse aortic arches. Therrien did not employ 24-h ambulatory blood pressure monitoring in their study. Perhaps this would have revealed underlying hypertension. However, the cost-effectiveness of such monitoring might preclude application in this particular clinical setting.

Conjecturally, patients after coarctation repair, with low to "normal" resting gradients, and normal resting systolic blood pressure, may have clinically important aortic coarctation that leads to shortened life spans. Such patients may have systemic hypertension that becomes manifest during increased levels of physical activity, eventually resulting in increased left ventricular wall mass. This latter phenomenon has been identified as a significant risk factor for cardiovascular disease in adult patients (29). In part, systemic hypertension that manifests during increased "activity" may be related to coarctation narrowing, aortic arch narrowing, or decreased compliance of the aortic arch. This is not to imply that such patients would necessarily require catheterization or surgical intervention for lower gradients. Potentially, these patients would best be treated with antihypertensive medications. Importantly, an echocardiogram or MRI gradient greater <25 mm Hg, or normal resting blood pressures, may be insufficiently sensitive for detection of clinically important aortic coarctation that may insidiously culminate in increased morbidity and/or mortality.

In summary, cost-effectiveness, accounting for the ability to detect significant disease, is not merely about balancing the budget, but rather about improvement in the quality of care. Therrien and colleagues are to be commended for this unique and innovative study, which will become a signature article for many similar studies. Personally, I am also pleased that the investigators included a clinical visit in their “best” cost-effective strategies. As medicine becomes more technologically oriented we must never “cost-out” the human and compassionate physician to patient relationship. Finally, the article by Therrien et al. forces us to reassess the most appropriate manner in which to provide care for adult patients who have interventions for aortic coarctation. The available data certainly support Dr. Somerville’s contention that “such patients will best be followed in specialized centers that concentrate the multitude of resources for caring for the specialized adult patients with congenital heart disease” (2).
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Reprint requests and correspondence: Dr. Gerald Ross Marx, Boston Children’s Hospital, 300 Longwood Avenue, Boston, Massachusetts 02030. E-mail: marx@cardio.tch.harvard.edu.

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