Diagnostic Accuracy of Echocardiography in ALCAPA: Is It Always Correct to Rely Only on Echocardiography? The Issue of False Negatives

To the Editor:

We read with interest the article by Patel *et al*[1] titled "Echocardiographic Diagnosis, Surgical Treatment, and Outcomes of Anomalous Left Coronary Artery from the Pulmonary Artery." We congratulate the authors, who brilliantly highlighted the need for a careful and systematic diagnostic approach in children with anomalous left coronary artery origin from the pulmonary artery (ALCAPA), providing additional pediatric experience to the ongoing discussion of the best imaging modality in such patients.

In their report, Patel *et al*[1] stated that the echocardiographic findings were highly suggestive for ALCAPA in 85% of cases, including retrograde flow within the left coronary artery (CA) (in 91% of cases), color Doppler findings of collateral coronary vessels (in 85% of cases), right CA dilatation (in 81% of cases), abnormal blood flow within the CAs (in 79% of cases), mitral regurgitation (in 74% of cases), left ventricular dysfunction (in 66% of cases), and endocardial fibroelastosis (in 57% of cases). However, the origins of the CAs were clearly visualized in only 54% of cases overall; coronary origins were seen clearly in 31% of the patients imaged between 1990 and 2000 and in 74% of those imaged after 2000. Because imaging of CA origins was imperfect, this diminishes enthusiasm regarding the accuracy of echocardiography in diagnosing CA anomalies in children. Indeed, CA imaging remains a great challenge for sonographers, despite advances in techniques and medical knowledge. In fact, Benavidez *et al*,[2] reviewing 50,660 echocardiograms from 2004 to 2007 at Boston Children's Hospital, showed that 16% of echocardiographic misdiagnoses (in total 87 cases) were CA anomalies. In addition, other studies have produced contrasting results in terms of the diagnostic accuracy of echocardiography in CA anomalies in the setting of transposition of the great arteries, as low as 81% to 86%.[3-5]

Whether physicians should rely on echocardiography alone when ALCAPA is suspected or instead should proceed to further imaging modalities is a subject of ongoing debate.[6-10] Whether to refer a patient for computed tomography, magnetic resonance imaging, or contrast angiography is an additional source of debate. In any event, the issue of false-negative results on echocardiography[7-10] and the potential catastrophic consequences of missing the diagnosis[2] are key concerns.

In the study of Patel *et al*,[1] about half of the patients (19 of 37) underwent surgery on the basis of only echocardiographic findings, while the remaining patients underwent further imaging examinations (angiography in 17 and magnetic resonance imaging in one). More important, after 2005, all patients were successfully imaged using only echocardiography.

Most recent literature[6-11] supports the accuracy of echocardiography, but interestingly, the diagnosis was further confirmed by angiography[6,7,10,11] and/or computed tomography.[7-9] In a recent study, Li *et al*[7] showed that in 22 patients with ALCAPA, the diagnostic accuracy of echocardiography was 90.9%, while accuracy of coronary angiography (17 patients) and coronary computed tomographic angiography (nine patients) increased to 100%. It is true that, unlike other forms of CA anomalies (i.e., transposition of the great arteries), diagnosis of ALCAPA by echocardiography may also be suggested by functional signs, even when the coronary origin cannot correctly visualized.[1] However, there are a few reports of cases in which ALCAPA was misdiagnosed as cardiomyopathy when children were examined using only echocardiography,[1,7,9,10] resulting in life-threatening clinical consequences. Of interest, a false-negative finding of ALCAPA (incidentally discovered during operation for mitral insufficiency) was described also by Patel *et al*[1]

In summary, we consider that at present, the diagnosis of CA anomalies in children can be reliably made only with echocardiography[1,3] and that ALCAPA represents a "favorable" anomaly because of its peculiar clinical presentation and associated echocardiographic and electrocardiographic findings (i.e., ischemic lesions).[1,6-11] However, relying on echocardiography alone to rule out ALCAPA is not justified in uncertain cases, because other imaging modalities offer higher diagnostic accuracy in CA visualization[7,9,10] and may reduce the false-negative rate of echocardiography.[7-10] In this setting, computed tomography should be preferred, as it is less invasive, highly accurate, and cost effective in coronary imaging.[7-9]

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Authors' Reply

To the Editor:

We thank Cantinotti *et al* for their thoughtful letter regarding our work on the echocardiographic diagnosis of anomalous left coronary artery from the pulmonary artery (ALCAPA) in children.[1] We believe that their letter emphasizes a fundamental point from our work that we are pleased to readdress and highlight.

As the authors have pointed out, the current literature recognizes the challenge of precisely defining coronary artery origins using only transthoracic echocardiography in every patient with ALCAPA. We certainly agree that if the only criterion used in the echocardiographic diagnosis of ALCAPA is clear two-dimensional identification of the anomalous coronary origin, patients will remain at risk for missed diagnosis. However, our data emphasize the additional echocardiographic markers present within these studies, which highlight hemodynamic and ischemic changes key to the understanding of the unique pathophysiology of ALCAPA and valuable in making a timely diagnosis.

The additional markers of ALCAPA described in our report include the following[1]:

1. retrograde flow by color Doppler in the left coronary artery toward the pulmonary artery and away from the aortic root (found in 91% of cases);
2. linear color Doppler flow signals within the myocardium, indicating collateral coronary vessels (in 85% of cases);
3. right coronary artery dilatation from excessive collateral flow (in 81% of cases);
4. abnormal color Doppler signals in the pulmonary artery where the anomalous coronary empties into the pulmonary artery (in 79% of cases);
5. pathologic mitral regurgitation from watershed papillary muscle ischemia (in 74% of cases);
6. left ventricular systolic dysfunction (in 66% of cases); and
7. endocardial fibroelastosis from chronic subendocardial ischemia (in 57% of cases).

These markers, in concert with the ability of echocardiography to identify the anomalous coronary origin from the pulmonary artery directly (in 74% of cases), will confirm diagnosis in virtually every case of ALCAPA if applied correctly. If the coronary artery origins are not clearly shown, the additional markers provide further data that should raise the level of concern for ALCAPA and suggest a more concerted effort to identifying the coronary origins. As Cantinotti *et al* accurately pointed out from our work, transthoracic echocardiography has been the primary diagnostic tool used in our laboratories in the diagnosis of ALCAPA since 2005, reflecting a commitment to the full description of abnormalities found within ALCAPA. We encourage other laboratories to apply these criteria in the diagnosis of ALCAPA as well.

Although dated, the gold standard in the diagnosis of ALCAPA has been coronary angiography.[2] This technique is diagnostic but comes with important risks, especially for infants with severe myocardial dysfunction, which is commonly associated with ALCAPA.[3] Other imaging techniques can also accurately identify ALCAPA, as Cantinotti *et al* note in their letter. None of these techniques, however, can provide the immediate, risk-free, and accurate bedside diagnosis available with transthoracic echocardiography for this critical life-threatening disease. It has been 34 years since the initial publication describing echocardiographic identification of ALCAPA,[4] and we believe echocardiography remains a very reliable diagnostic modality when the current technology and knowledge is applied thoughtfully and carefully.

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