Finding Asymptomatic People With a Coronary Artery Arising From the Wrong Sinus of Valsalva

Consequences Arising From Knowing the Anomaly to Be Familial*

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The article in this issue of the Journal by Brothers et al. (1) is the first study to show convincingly that the anomalous aortic origin of a coronary artery, that is, the left main coronary artery arising from the right sinus of Valsalva (ALCA) or the right coronary artery arising from the left sinus of Valsalva (ARCA), is familial. It is no surprise that coronary anomalies are familial. Given the fact that the embryology of coronary artery development, in both the course they take on the epicardium and their origin from the aorta, is according to genetic plan, a mutation in the genetic coding can result in these anomalies of coronary origin. If the mutation is in the somatic cells after germ cell differentiation, then the anomaly is confined to that individual, but if it involves the germ cells, then it can be passed on to future generations and becomes a familial anomaly.

The reason that we have not encountered examples of this familial association until now involves a number of circumstances. These anomalies are relatively rare and the vast majority of patients who have these anomalies are asymptomatic and never suffer any complications. Thus the anomalies remain silent and overlooked.

To determine that the incidence of sudden death or aborted sudden death is rare in patients with these anomalies, we must look at the prevalence of the anomalies in the population and compare this number with the number of people with these anomalies, that series underestimates the prevalence of those coronary anomalies of origin in the population. Another problem is that not all ALCA or ARCA are at risk of sudden death—only those anomalous arteries that pass obliquely between the aortic root and the pulmonary outflow tract or the pulmonary trunk.

A consecutive autopsy series, if large enough, should give a better approximation of the prevalence of these anomalies in the population. The problem with autopsy series is that with a routine autopsy it is easy to miss an anomalous coronary origin from the noncoronary sinus and even from the wrong sinus of Valsalva. From autopsy series, the prevalence of coronary anomalies is 0.2% to 1.2% (3). Assuming the same low incidence of anomalous origin of the coronary arteries from the wrong sinus, the prevalence in the general population of ALCA and ARCA is 0.02% to 0.11% of approximately 4 million live births in the U.S. annually (4). Adapting data from a letter by Colin K. L. Poon (5) in a previous issue of the Journal, with 2,000 children born with this anomaly each year by age 30, when almost all of the sudden deaths occur with these anomalies, there are about 60,000 people with these anomalies in the U.S. alone. In the U.S. there are 275,000 to 500,000 sudden deaths annually, the majority over the age of 40 years and due to coronary artery disease. Maron et al. (6) reported the prevalence of sudden cardiac death during competitive sports activities in Minnesota high school athletes. The authors used a circumstance where the exact number of participants and deaths due to cardiovascular disease were known over a considerable period of time because of a long-standing insurance program for catastrophic injury or death. Over a period of 12 years, there were 3 sudden deaths due to cardiovascular disease in athletes in grades 10 to 12 during competition or practice, 1 of which was due to ALCA. During this same period there were 1,453,280 overall sports participants and 651,695 student athlete participants. The risk of sudden death in a population of high school athletes was estimated at 1 in 200,000 per year. The number dying suddenly with these anomalies is minuscule compared with the number of people with these

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anomalies. The most likely conclusion from these data is that most people with these anomalies go through life without any difficulty or catastrophic event related to the coronary anomaly.

Even with technically excellent 2-dimensional (2D) echocardiography, reliable identification of both coronary origins is not sought in the 2D echocardiogram done for the usual request for cardiac imaging. On the other hand, at least in children, when there has been a concerted effort to identify coronary origins this can be achieved with a high degree of reliability. For example, Davis et al. (7) prospectively determined the prevalence of coronary artery anomalies of origin in 2,388 asymptomatic children using transthoracic 2D echocardiography. They found 4 (0.17%) with coronary anomalies of origin, 2 with ALCA, and 2 with ARCA. In adults, finding the origin of both coronary arteries is not as successful as it is in children. However, magnetic resonance imaging (MRI) is highly successful in imaging both the origins and initial courses of these anomalously arising coronary arteries (8).

The extremely rare person with anomalous origin of a coronary artery who does have difficulty may suffer the ultimate complication, that of sudden death or aborted sudden death, which is the way that the probands of the coronary anomaly die. The most likely conclusion from these data is that most of these patients would never have had a life-threatening event during or after exercise, it does not seem possible to reliably provoke ischemia by duplicating the exercise.

Fourth, ALCA is more often associated with sudden death than is ARCA (9,10). It is understandable that, whatever the pathophysiological mechanism by which the proximal coronary artery is suddenly occluded, if this happens to the left main coronary artery, massive left ventricular ischemia occurs, followed by ventricular tachycardia or ventricular fibrillation, or, if the patient survives, a massive myocardial infarction. If the proximal right coronary artery suddenly occludes, the inferior wall is affected, and with an inferior wall myocardial infarction the patient usually survives.

Fifth, sudden death in patients with these coronary anomalies is very unusual over the age of 30 years, and the vast majority of patients dying suddenly are teenagers or young adults in their twenties (6,9,10). It appears that if the individual survives these early years without a catastrophe, they will not have the mechanistic substrate necessary for the precipitation of malignant arrhythmias and sudden death.

Given all of the above facts, including the extremely low risk of patients with these coronary anomalies of origin experiencing sudden death, the following guidelines to managing these patients are suggested.

First, any patient with one of these coronary anomalies, regardless of age, who has an unexplained syncope, palpitation, or malignant arrhythmia or aborted sudden death, should have surgical correction, usually unroofing of the coronary ostium and creating a funnel-like opening to both coronary arteries (12,13).

Second, because asymptomatic young patients are the ones most at risk, patients under the age of 30 years, if found to have one of these coronary anomalies, should have surgical correction.

Third, patients over the age of 30 years with one of these coronary artery anomalies of origin, who have nonspecific symptoms such as chest pain, fatigue, or palpitations, should have as part of their work-up a stress myocardial perfusion scan. If myocardial ischemia is demonstrated in a myocardial region supplied by the anomalous coronary artery, surgical correction is indicated. If no ischemia is found, the patient should be followed medically.

Fourth, asymptomatic patients over the age of 30 years should be followed medically.

It is probable that screening first-degree relatives of patients found to have these coronary anomalies of origin will find a relatively large number of asymptomatic patients with one of these coronary artery anomalies. Given the fear of sudden death if the anomaly is not surgically “corrected” in the patients <30 years old and the fact that exercise testing frequently fails to provoke ischemia or malignant arrhythmias, the present approach, especially in children, is to surgically “correct” the problem. The overwhelming probability is that most of these patients would never have any difficulty from the anomaly, and so most of the surgery would have been unnecessary. In addition, there is a danger in unroofing the ostium of damaging an aortic commissure and causing aortic regurgitation (13). Unfortunately, we
cannot tell who would and who would not benefit from surgery at the present time. Another approach, since the vast majority of sudden deaths occur during or immediately after vigorous exercise, is to inform the patient and, if the patient is a child, the parents that he or she must avoid the type of activity that could precipitate problems (i.e., vigorous exercise). Unfortunately, with children and young people, this kind of advice is rarely followed. Until we better understand the pathophysiological mechanisms by which the proximal artery is suddenly occluded, we will not be able to risk-stratify these patients and predict which of them are at greatest risk of sudden death and would be well served by surgery and who should be followed medically.

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