JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
PUBLISHED BY ELSEVIER ON BEHALF OF THE AMERICAN
COLLEGE OF CARDIOLOGY FOUNDATION

VOL. 69, NO. 12, 2017
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2017.01.031

THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

Anomalous Aortic Origin of a Coronary Artery From the Inappropriate Sinus of Valsalva

Michael K. Cheezum, MD,[a,b] Richard R. Liberthson, MD,[c] Nishant R. Shah, MD, MPH, MSc,[d] Todd C. Villines, MD,[e] Patrick T. O'Gara, MD,[a] Michael J. Landzberg, MD,[f] Ron Blankstein, MD[a]

ABSTRACT

Anomalous aortic origin of a coronary artery (AAOCA) from the inappropriate sinus of Valsalva is increasingly recognized by cardiac imaging. Although most AAOCA subtypes are benign, autopsy studies report an associated risk of sudden death with interarterial anomalous left coronary artery (ALCA) and anomalous right coronary artery (ARCA). Despite efforts to identify high-risk ALCA and ARCA patients who may benefit from surgical repair, debate remains regarding their classification, prevalence, risk stratification, and management. We comprehensively reviewed 77 studies reporting the prevalence of AAOCA among >1 million patients, and 20 studies examining outcomes of interarterial ALCA/ARCA patients. Observational data suggests that interarterial ALCA is rare (weighted prevalence = 0.03%; 95% confidence interval [CI]: 0.01% to 0.04%) compared with interarterial ARCA (weighted prevalence = 0.23%; 95% CI: 0.17% to 0.31%). Recognizing the challenges in managing these patients, we review cardiac tests used to examine AAOCA and knowledge gaps in management. (J Am Coll Cardiol 2017;69:1592–608) Published by Elsevier on behalf of the American College of Cardiology Foundation.

Congenital coronary artery anomalies (CAA) are rare and may be broadly classified as abnormalities of coronary artery origin, course, destination, and size or number of vessels (1,2). This review focuses on anomalous aortic origin of a coronary artery (AAOCA) arising at or above the inappropriate sinus of Valsalva. Although classification of these cases varies (1–4), AAOCA arise from the aorta by a separate ostium, shared or common ostium, or as a branch vessel (5). Among subtypes, our discussion will focus on anomalous left coronary artery (ALCA) arising at or above the right sinus of Valsalva and anomalous right coronary artery (ARCA) arising at or above the left sinus of Valsalva. Rarely, AAOCA vessels may also arise from the "noncoronary" sinus. AAOCA are further characterized by 1 of 5 course subtypes as interarterial, subpulmonic (intraconal or intraseptal), pre-pulmonic, retroaortic, or retrocardiac (**Central Illustration**). Additionally, AAOCA may have an early intramural segment (within the aortic wall), as seen in the majority of interarterial cases. Among course subtypes, the potential for sudden cardiac death (SCD) has been largely attributed to an interarterial course between the aorta and pulmonary

Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

From the [a]Departments of Medicine and Radiology, Cardiovascular Division, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; [b]Department of Medicine, Cardiology Service, Fort Belvoir Community Hospital, Ft. Belvoir, Virginia; [c]Department of Medicine, Division of Cardiology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; [d]Lifespan Cardiovascular Institute, Division of Cardiovascular Medicine, Department of Medicine, Brown University Alpert School of Medicine, Providence, Rhode Island; [e]Department of Medicine, Cardiology Service, Walter Reed National Military Medical Center, Bethesda Maryland; and the [f]Department of Cardiology, Boston Children's Hospital, Boston, Massachusetts. The opinions and assertions herein are those of the authors alone, and do not represent the views of the U.S. Army, Office of the Surgeon General, Department of Defense, or the U.S. Government. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received October 7, 2016; revised manuscript received December 5, 2016, accepted January 3, 2017.

artery (**Figure 1A**) (6). By comparison, a subpulmonic course exits the aorta below the pulmonic valve and traverses the right ventricular outflow tract, pulmonary infundibulum, and interventricular septum (**Figure 1B**) (7). Although prior studies with invasive angiography and echocardiography provide limited visualization of these course subtypes, coronary computed tomography angiography (CTA), magnetic resonance angiography (MRA), and intravascular ultrasound (IVUS) are improving characterization of AAOCA vessels.

Although evidence demonstrates that interarterial ALCA and ARCA may be associated with an increased risk of SCD among AAOCA subtypes (6), the prevalence of AAOCA and their associated absolute risk of SCD in the general population is unknown. Thus, controversy remains regarding the optimal approach to risk stratify and manage these patients. With increasing recognition of AAOCA, we aimed to review the following: 1) the observed prevalence of AAOCA arising at or above the inappropriate sinus of Valsalva with attention to the interarterial course subtype; 2) the use of cardiac testing to examine AAOCA; 3) outcomes of interarterial ALCA and ARCA patients; and 4) recommendations and knowledge gaps in current management.

OBSERVED PREVALENCE OF AAOCA IN CLINICAL PRACTICE

We performed a comprehensive review of published reports to examine the observed prevalence of AAOCA arising at or above the inappropriate sinus of Valsalva on cardiac testing with the course subtypes shown in the **Central Illustration**. Studies were included if they examined patients by invasive coronary angiography (ICA), transthoracic echocardiography (TTE), coronary CTA, or MRA. Detailed methods, and inclusion and exclusion criteria are described in Online Appendix A, incorporating evidence from 77 studies and >1 million patients undergoing cardiac testing (Online Figure 1).

In **Figure 2**, we summarize the observed prevalence of AAOCA arising at or above the inappropriate sinus of Valsalva as the combined rate of all course subtypes (interarterial, subpulmonic, pre-pulmonic, retroaortic, and retrocardiac) across included studies. As shown, there is significant variability in the observed prevalence of AAOCA, which may be attributed to inherent referral bias, differences in age groups and presentation of various cohorts, variable inclusion criteria and AAOCA course descriptions, and limitations in the ability of each modality to examine AAOCA. To date, few studies have screened patients for AAOCA in the absence of a clinical indication for testing (Online Appendix A, Online Table 1) (8–12). Consequently, the true prevalence of AAOCA in the general population remains unknown.

In **Figure 3**, we focus specifically on the observed rate of interarterial ARCA and interarterial ALCA cases among included studies. As shown, the frequency of interarterial ALCA is rare (weighted prevalence = 0.03%; 95% confidence interval [CI]: 0.01% to 0.04%) by comparison with interarterial ARCA (0.23%; 95% CI: 0.17% to 0.31%). The observed prevalence of the remaining course subtypes is listed in Online Table 2, with a retroaortic course comprising the most common subtype (prevalence = 0.28%; 95% CI: 0.21% to 0.35%).

EVALUATION OF AAOCA

TRANSTHORACIC AND TRANSESOPHAGEAL ECHOCARDIOGRAPHY. TTE is a common technique used to evaluate young patients with suspected or known cardiac disease, as a noninvasive, rapid, and widely available test with low cost (**Figure 4**). Yet TTE has limited accuracy to detect AAOCA, requiring experienced operators to identify coronary ostia. In a study by Thankavel et al. (13), a standardized TTE protocol improved AAOCA detection from 0.02% to 0.22% of patients. TTE also depends on patient habitus for optimal image quality. Across studies designed to visualize AAOCA, 6% to 10% of patients were excluded on the basis of an uninterpretable TTE (8,9). Even after excluding unsatisfactory cases, Pelliccia et al. (8) were unable to visualize the RCA ostium in 20% of young athletes, a population expected to have good image quality. Lastly, TTE has limited spatial resolution and lacks detailed characterization of AAOCA features and surrounding structures (14). Among 159 AAOCA patients in the CHSS (Congenital Heart Surgeon's Society) registry, there was limited agreement (weighted kappa) between institutional and expert TTE reports and surgical findings of AAOCA measures (i.e., interarterial course, intramural course, and acute angle takeoff) (15).

Transesophageal echocardiography has been used to identify AAOCA (15–23) and may be useful to visualize CAA perioperatively (24). With the addition of 3-dimensional transesophageal echocardiography, visualization of AAOCA and their relation to surrounding anatomy may improve (25). At this time, however, transesophageal echocardiography is not a

ABBREVIATIONS AND ACRONYMS

AAOCA = anomalous aortic origin of a coronary artery

ALCA = anomalous left coronary artery

ANOCOR = anomalous connections of coronary arteries

ARCA = anomalous right coronary artery

CAA = coronary artery anomaly

CI = confidence interval

CTA = computed tomography angiography

FFR = fractional flow reserve

ICA = invasive coronary angiography

IVUS = intravascular ultrasound

MRA = magnetic resonance angiography

PCI = percutaneous coronary intervention

SCD = sudden cardiac death

TTE = transthoracic echocardiography