Review Article

Imaging options for defining anomalous origin of the coronary artery from the pulmonary artery

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Contributions: (I) Conception and design: M Zhu; (II) Administrative support: M Zhu; (III) Provision of study materials or patients: H Xin; (IV) Collection and assembly of data: H Xin; (V) Data analysis and interpretation: Both authors; (VI) Manuscript writing: Both authors; (VII) Final approval of manuscript: Both authors.

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Abstract: Anomalous origin of the coronary artery from the pulmonary artery is a rare type of congenital heart disease (CHD). According to the establishment of collateral circulation and the abnormal anatomy of coronary arteries, there are several clinical types. In some clinical types, serious cardiac insufficiency can arise in the early stage of the condition, which, if not promptly treated, can endanger the patient's life. Up to 90% of infants with an anomaly involving the left coronary artery die within the first year of life. The treatment of the disease is to restore the double coronary circulation as soon as possible by surgery after early detection by diagnostic imaging. Presently, medical imaging is the most commonly used examination method for a diagnosis of the disease. The comprehensive application of various imaging modalities is the basis for the diagnosis and follow-up of coronary artery origin from the pulmonary artery. The current review mainly summarized the common signs and application advantages of different imaging techniques in the diagnosis of anomalous origin of the coronary artery from the pulmonary artery. It also highlights existing problems and provides an important theoretical basis and practical guidance for imaging techniques about the coronary artery originating from the pulmonary artery's diagnosis and treatment.

Keywords: Anomalous origin of coronary artery; pulmonary artery; transthoracic echocardiography (TTE); CT angiography; magnetic resonance imaging

Submitted May 18, 2022. Accepted for publication Oct 18, 2022. Published online Nov 11, 2022.
doi: 10.21037/qims-22-502
View this article at: https://dx.doi.org/10.21037/qims-22-502

Introduction

Anomalous coronary artery from the pulmonary artery (ACAPA) is a rare form of congenital heart disease (CHD). Anatomically, it presents as the coronary artery originating abnormally from the lateral or posterior wall of the pulmonary artery. The condition accounts for approximately 0.25–0.50% of CHDs, and its incidence rate is approximately 1/300,000 in the normal population (1). Early diagnosis and treatment of the disease can effectively preserve patients' cardiac function but will not necessarily improve their quality of life.

With the development of imaging technology, the ACAPA detection rate has been significantly improved. This review summarizes the current literature on common imaging types applied for ACAPA detection to help ensure early identification and diagnosis.

Classification and the hemodynamics of anomalous origin of the coronary artery from the pulmonary artery

Coronary artery development

In week nine of embryonic development, the angioblast buds pass through the endocardium to form the distal end of the coronary system. The proximal coronary arteries form a ring near the arterial trunk and connect with the coronary buds at the primitive aortic sinus to form the aorta. The arterial vascular plexus remodels under hypoxic control and the influence of growth factors and finally matches with the coronary sinus at the aortic root under the stimulation of vascular factors (e.g., vascular endothelial growth factor and platelet endothelial cell adhesion molecule 1) (2). The coronary artery can abnormally originate from the pulmonary artery if the proximal portion is displaced during the formation process.

Anatomical and epidemiological characteristics of abnormal coronary arteries

Generally, ACAPA can be classified based on its origination into three distinct types, i.e., anomalous left coronary artery arising from the pulmonary artery (ALCAPA), anomalous right coronary artery arising from the pulmonary artery (ARCAPA), and anomalous circumflex (LCX), or left anterior descending (LAD) artery arising from the pulmonary artery.

Among the above, ALCAPA is the most common type of ACAPA. The incidence of ALCAPA is approximately 0.008% (3), accounting for almost 90% of this serious condition (4). This type is one of the causes of neonatal myocardial infarction and adult sudden death (5). In contrast, ARCAPA is a rare condition with an incidence rate of approximately 0.002% and in contrast with ALCAPA, most patients have no obvious clinical symptoms at the early stage, and the condition is typically diagnosed in combination with other cardiovascular diseases (6). The coronary LAD or LCX originating from the pulmonary artery is very rare and its incidence remains unknown (3); at present, 97 such cases have been identified worldwide (7) and, compared with ALCAPA, the symptoms of this type are not typically obvious in infancy.

Pathophysiology

Anomalous origin of the coronary artery can be divided into infant and adult types, based on hemodynamics. In the neonatal period, pressure in the pulmonary artery is high, and the coronary artery can rely on the forward blood perfusion of the pulmonary artery for blood supply; as such, no evident symptoms will be observable within one month after birth (8). At one month following birth, due to the closure of arterial ducts and other reasons, the pressure in small pulmonary vessels and pulmonary arteries decreases, resulting in the "pulmonary stealing" phenomenon. At this point, infant-type collateral circulation has not been fully established, resulting in a decrease in antegrade coronary blood flow and myocardial perfusion, thus enabling clinical symptoms to be observed at an early stage (9).

Based on international studies, the vast majority of ALCAPA patients present clinical symptoms that include weight loss two years after birth (10). In adults, collateral circulation is fully established, and the pathogenic coronary artery can rely on abundant collateral circulation for blood supply.

Clinical symptoms in cases of anomalous origin of the coronary artery from the pulmonary artery

The main clinical symptoms of ACAPA are cardiac murmur, dysfunction of the cardiac valves and accessory structures, and congestive heart failure. The time at which symptoms present rely mainly on the establishment of collateral circulation (11,12).

The anterolateral papillary muscle is the most ischemic region in patients with ALCAPA because it is the most distant area that is supplied by the left and right coronary systems. Therefore, a systolic murmur can be heard in the auscultation area of the mitral valve in most patients with this condition (10), while a diastolic murmur will manifest in the presence of papillary muscle insufficiency or mitral valve prolapse (13).

Electrocardiographic imaging has a high sensitivity for the diagnosis of ALCAPA. Pathological Q-waves were observed in leads I and the augmented unipolar limb leads, while a decrease in R-wave was present in precordial leads V3–6 with/without ST-T changes, which suggested myocardial ischemia (14).

Adult patients showed better collateral circulation; however, continuous myocardial ischemia may significantly reduce their mobility (11). Adult ALCAPA is an important cause of sudden cardiac death, which may be related to long-term chronic ischemia of the left ventricular subendocardial myocardium, leading to malignant arrhythmia events. Peña

et al. (4) found that patients who were at risk of sudden death represented approximately 80% of adult ALCAPA cases.

Patients with ARCAPA are often diagnosed due to the presence of other cardiovascular diseases (6,15). There are typically no obvious symptoms in infant patients; the reason for this may be because the oxygen consumption of the right ventricle is lower compared with the left, rendering the requirements for a collateral circulation blood supply of the right ventricle relatively flexible (15).

Cases in which the LAD or LCX branches originate from the pulmonary artery are extremely rare; in these cases, the onset among patients is approximately 25 years of age (7), and the clinical symptoms are very similar to myocardial ischemia (angina pectoris, shortness of breath, and palpitation); a small number of patients may be asymptomatic. In more than half of patients with anomalous origin of the LAD branch from the pulmonary artery, murmurs could be heard in the mitral auscultation and systolic areas, and the patient's cardiac function was typically significantly improved after surgical intervention (7).

Diagnostic imaging

As a routine ACAPA detection method, imaging can be used for disease diagnosis and the evaluation of postoperative outcomes. The 2020 European Society of Cardiology guidelines for the management of adult CHD notes that non-pharmacological functional imaging techniques, such as echocardiography and cardiac magnetic resonance (CMR) are recommended for patients with coronary artery abnormalities to confirm or exclude myocardial ischemia (grade I recommendation) (16).

Chest radiographic findings

A chest X-ray film is used as a method for the preliminary evaluation of heart size and pulmonary blood flow. The choice of film position is different between children and adults. For children, supine anteroposterior and left-view positions are typically adopted, while for adults, a standing position is preferable. On a chest radiograph, the main manifestation of ACAPA is an enlarged heart shadow; enlargement of the heart mediastinum shadow can be observed on an anteroposterior view of the heart, which can also indicate an absence of the retrocardiac anterior esophageal space, while increased pulmonary blood flow can be observed on the lateral view (17), suggesting enlargement of the cardiac chamber and pulmonary congestion. However, a chest X-ray film provides no specificity in the diagnosis of ACAPA; accordingly, other imaging examinations are needed to establish a more definitive diagnostic foundation.

Echocardiography

Transthoracic echocardiography (TTE) is one of the most commonly used methods for diagnosing heart disease and evaluating cardiac function. This method can observe the cardiac cavity structure, valve motion, and myocardial motion. The diagnosis of ACAPA by TTE can be summarized according to direct and indirect signs.

Direct signs typically include no detection of a coronary ostium in the appropriate sinus, while the ectopic opening of the coronary artery and the blood-stealing phenomenon at the pulmonary artery can be observed by two-dimensional (2D) imaging and color Doppler flow imaging (CDFI) (*Figure 1A*,*1B*) (14). The left coronary artery in ALCAPA patients often originates from the left posterior sinus of the pulmonary artery; in a small number of patients, it may originate from the right posterior sinus of the pulmonary artery (18). When the coronary artery ectopically originates from the right posterior sinus of the pulmonary artery, a 2D TTE will reflect the illusion of the presence of the left coronary artery at the left coronary sinus; however, a reverse blood-flow signal to the pulmonary artery in the left coronary artery will be detected by CDFI in such a case (*Figure 1B*) (11,14,19).

Indirect abnormal signs of ACAPA by TTE can roughly be divided into abnormal cardiac cavity structure, abnormal myocardial motion, abnormal valve and accessory structures, abnormal vascular structure, and abnormal CDFI blood-flow direction. In terms of myocardial structure, the left ventricle is severely dilated, and the ventricular end-diastolic dimension and left ventricular end-diastolic volume are both increased (20-23).

The quality of coronary blood perfusion can also be observed by myocardial motion. In infant patients with ALCAPA, pulmonary blood-stealing and insufficient forward blood flow occurred in the left coronary artery. Left ventricular myocardial systolic function was observed to have been significantly weakened and mobility was reduced; additionally, if severe myocardial ischemia led to myocardial infarction, a ventricular aneurysm could form at the infarct location (11,14). Extensive left ventricular fibrosis was observed on 2D echocardiography in some

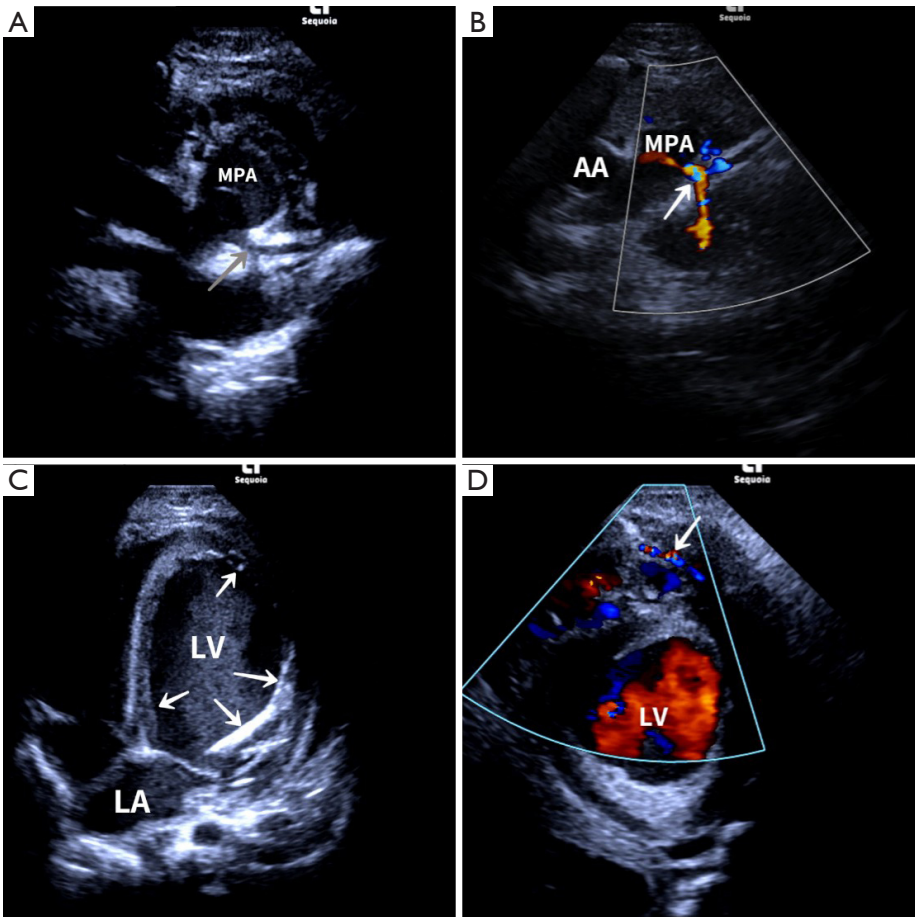

Figure 1 Echocardiographic imaging of infant type anomalous left coronary artery arising from the pulmonary artery. (A) A parasternal view shows the left coronary artery of abnormal origin (grey arrow). (B) A color Doppler echocardiographic image reveals reversed flow (red color) in the left coronary artery (white arrow) in a case of infant-type anomalous left coronary artery arising from the pulmonary artery. (C) An apical four-chamber echocardiogram shows the echogenic valve structure and endocardium with ischemic damage-induced fibrosis (white arrows). (D) An apical short-axis echocardiographic image demonstrates characteristic inter-coronary collateral arteries (arrow) in the apex. Notably, the left atrium and left ventricle are enlarged. MPA, main pulmonary artery; AA, ascending aorta; LA, left atrium; LV, left ventricle.

ALCAPA patients, particularly in the subendocardial region (8,24). Attention should be paid to distinguishing this from endocardial fibroelastosis (22,25,26), a CHD caused by an increase in collagen and elastic fibers and characterized by thickening of the endocardium, enlargement of the cardiac chambers, and decreased myocardial motor function.

In infant-type ALCAPA, the mitral valve and its accessory structures (the valve leaflet, chordae tendineae, and papillary muscle) are fibrotic and an echo will be enhanced (*Figure 1C*) (22). Furthermore, ACAPA is supported by the blood supply of coronary collateral with normal origin. Therefore, 2D echocardiography can observe the compensatory thickening and tortuosity of normal-origin coronary arteries.

CDFI can directly reflect the movement of blood flow in a 2D plane. When patients with ACAPA underwent CDFI, a full cardiac cycle reverse blood-flow signal was observed in an abnormal coronary artery, primarily from the diastole to the pulmonary heartbeats, and the blood flow signal in the pulmonary artery presented as a multicolored turbulence signal (*Figure 1B*) (27). Continuous diastolic blood flow signals were observed in the myocardium at the junction of the left and right coronary arteries in a short-axis isometric view of the left ventricle, particularly in the ventricular septum and the apical region (*Figure 1D*) (6,11,24).

Patients with ARCAPA had better collateral circulation

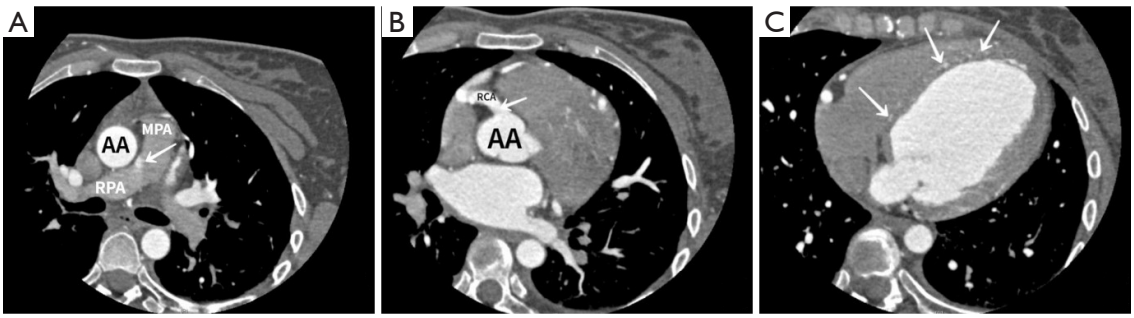

Figure 2 Computed tomography angiography of infant-type anomalous left coronary artery arising from the pulmonary artery. (A) A short-axis image shows the left coronary artery (white arrow) originating from the right wall of the main pulmonary artery. (B) A short-axis image shows the right coronary artery originating from the aorta with an enlarged lumen (white arrow). (C) A short-axis image shows multiple collateral circulations (white arrows) in the interventricular septum. MPA, main pulmonary artery; RPA, right pulmonary artery; AA, ascending aorta; RCA, right coronary artery.

than those with ALCAPA. In the former, the left and right ventricles could not be significantly expanded, but cardiac function was good (28); other signs were similar to those that present for ALCAPA.

The 2008 American College of Cardiology and American Heart Association Guidelines for the Management of Adult Congenital Heart Disease propose that patients with ACAPA undergo TTE and non-invasive clinical examination every 3–5 years after surgery (29). The postoperative follow-up of ACAPA patients by TTE revealed that patients' left ventricles began to remodel approximately one year after surgery. At this time, mitral insufficiency and the ischemic enlargement of left ventricular volume will have recovered (11,30,31). Valvuloplasty may be considered if there is no significant improvement in valvular regurgitation after surgery (30,32-36).

Echocardiography has the advantages of safety, non-invasiveness, and convenience. It can display information, such as the origin and course of coronary arteries, cardiac chamber structure, and valve activity, which play important roles in the early diagnosis, surgical decision-making, prognosis evaluation, and follow-up observation of ALCAPA.

Coronary computed tomography angiography (CCTA)

CCTA utilizes post-processing technology to visually display the types and details related to coronary artery anatomical variation and is considered one of the preferred imaging methods for diagnosing a coronary artery of anomalous origin (37-39). This method can show the structural relationship between coronary and pulmonary arteries, the state of collateral circulation connection between coronary arteries, and other possible cardiac structural abnormalities.

CCTA can be divided into direct and indirect signs in the diagnosis of the disease (40). The direct sign is where the contrast medium flows from the normal coronary artery to the abnormal coronary artery through collateral circulation before finally flowing into the pulmonary artery, giving rise to the blood-stealing phenomenon (*Figure 2A*); notably, there is also no detection of a coronary ostium in the appropriate sinus. The indirect sign is where the coronary vessels of normal origin are thickened (*Figure 2B*) (17), and abundant collateral circulation can be observed in the apex of the heart (*Figure 2C*).

CCTA can utilize a multi-temporal reconstruction technique to evaluate left ventricular volume and cardiac function indexes within a complete cardiac cycle (41). Myocardial survival was evaluated according to late iodine enhancement CT, approximately 10 min after intravenous injection of an iodine contrasting agent (42). Different post-processing techniques present diverse abilities for displaying the lumen and its anatomical structure. During an inspection, appropriate reconstruction methods must be adopted according to the patient's needs. A volume-rendering image can completely display the overall anatomical structure of the heart and large blood vessels (*Figure 3A*), while the maximum intensity projection and multiplanar reconstruction images can show the origin and shape of coronary arteries (*Figure 3B,3C*) (17,40).

CCTA is essentially recommended, as it can not only

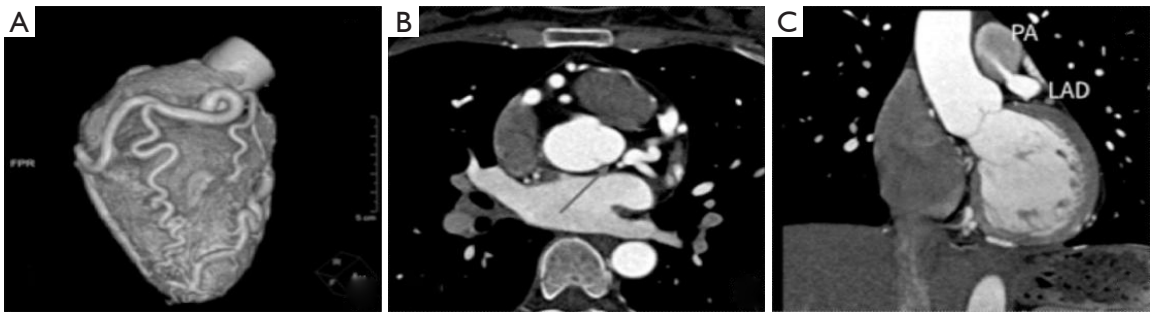

Figure 3 Computed tomography angiography of infant-type anomalous left coronary artery arising from the pulmonary artery. (A) A volume reproduction view shows thickening and tortuosity of the coronary vessels and large anastomotic vessels at the apex. (B) A maximum intensity projection view shows that the left main trunk does not communicate with the left coronary sinus (grey arrow). (C) A multiplanar reconstruction view shows the contrast escaping from the left anterior descending artery to the pulmonary artery through the window. PA, pulmonary artery; LAD, left anterior descending artery.

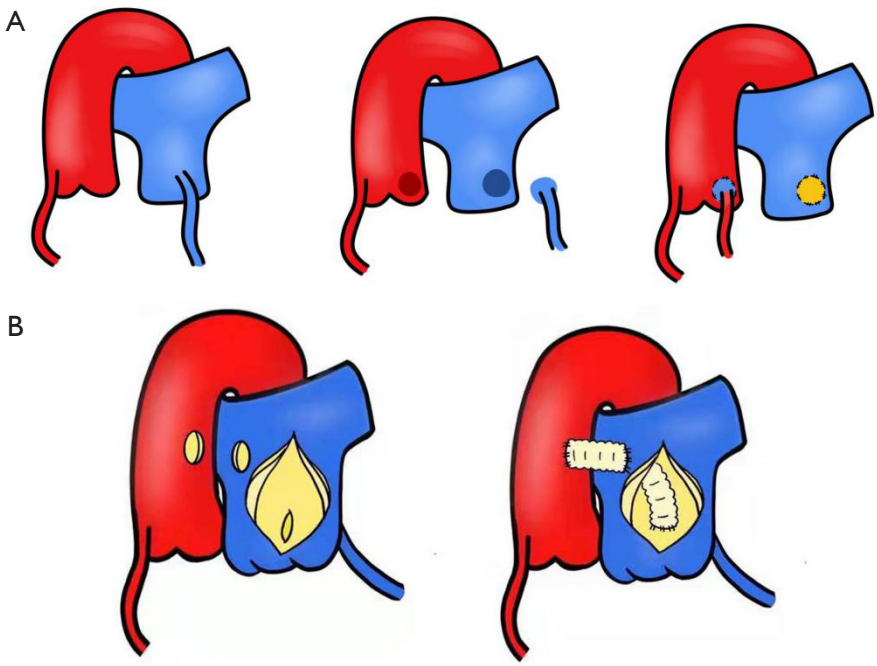

Figure 4 The difference between direct coronary implantation and Takeuchi implantation. (A) Direct coronary implantation. (B) Coronary implantation using the Takeuchi method.

provide imaging evidence but also a basis for subsequent surgical selection because the spatial relationship between the anomalous coronary artery and the aortic sinus is critical for planning an appropriate surgical procedure. In the case of a small number of patients, for whom the anomalous coronary artery opens on the left side of the pulmonary trunk and presents abundant collateral branches, it may be difficult to perform coronary artery transplantation. In these cases, the Takeuchi procedure will be performed (43) (*Figure 4*). Following surgery, CCTA can be used to assess the patient's surgical outcome and the occurrence of postoperative complications (44-48).

CMR imaging

CMR imaging can comprehensively evaluate cardiac

structure and myocardial and valve motion through rapid imaging, myocardial perfusion imaging, strain imaging, and late gadolinium-enhanced imaging (49,50). Compared with conventional CT, CMR does not produce ionizing radiation and can more clearly show myocardial perfusion and myocardial viability. Cardiovascular magnetic resonance based tissue tracking (CMR-TT) can use algorithms to analyze the myocardial coordination, especially at the global level of the left ventricle (51). However, it is challenging to provide an accurate anatomical diagnosis for surgery in infants (the most common population with this disease) with ACAPA using CMR because of its limitations related to spatial and time resolutions (52). In this regard, gadolinium-enhancement CMR is useful for evaluating the myocardial scar and coronary flow pattern in this population (53) and can also be used to monitor the recovery of cardiac function following ACAPA surgical repair (17,50). Four-dimensional Flow MRI is a novel magnetic resonance angiography technique that can visualize the morphology and hemodynamics of blood vessels. Compared with conventional three-dimensional angiography, the time dimension is added to demonstrate the changes in hemodynamics in different cardiac cycles (54). Recently, four-dimensional flow MRI has been used to detect the retrograde flow from the LAD artery into the main pulmonary artery in a patient with Bland-White-Garland syndrome (55).

Single-photon emission computerized tomography

Single-photon emission computerized tomography and other radionuclide myocardial imaging techniques can be used to evaluate blood perfusion and whether a myocardial injury is reversible; however, the sensitivity and specificity of these methods are low (52).

Considerations and future prospects

Clinically, the incidence rate of ACAPA is very low. However, in cases of anomalous origin of the left coronary artery from the pulmonary artery, patients may be at risk of left ventricular myocardial infarction and valve insufficiency caused by the blood-stealing behavior of the pulmonary artery. Currently, there remain several issues in ACAPA research as follows. (I) The statistical time of the true prevalence of ACAPA in the general population is too early to reflect the prevalence of the condition in the population at this stage. (II) The large error range involved in using imaging to evaluate the abnormal anatomical position of ACAPA (e.g., the origin and shape of the coronary artery, and the relative distance between an abnormal coronary artery and aortic sinus) compared with direct observation under surgery. (III) Echocardiography is the most commonly used imaging method for the clinical diagnosis of structural heart disease; however, the accuracy of the technique's results is limited by the experience of sonographers and the physical condition of patients. The key points for distinguishing ACAPA from other structural heart diseases are as follows: patients with severe heart failure or myocardial ischemia in early childhood should be routinely examined in terms of coronary structure and blood flow signals in the coronary artery. In children with severe pneumonia, the blood-stealing phenomenon, effected by the pulmonary artery, may be weakened due to high pressure in this artery (56); when this is the case, other imaging examinations should be performed to help make a definitive diagnosis. (IV) The related imaging indexes that affect the survival rate of patients after ACAPA requires further study. (V) Patients with severe preoperative mitral regurgitation should be followed-up over an extended time to observe imaging signs related to whether their valves will subsequently require surgical repair (57).

In summary, an accurate imaging diagnosis and timely restoration of intracoronary hemodynamics are key in the diagnosis and treatment of ACAPA. Accordingly, radiologists should be familiar with the common imaging manifestations of the disease and provide clinicians with relevant diagnoses and treatment strategies.

Acknowledgments

This article was edited by a native English speaker Amanda Merritt.

Funding: This work was supported by Provincial Key Research and Development Program of Shandong, China (No. 2018GSF118112).

Footnote

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-502/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related

to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Xin H, Zhu M. Imaging options for defining anomalous origin of the coronary artery from the pulmonary artery. Quant Imaging Med Surg 2023;13(2):1164-1173. doi: 10.21037/qims-22-502

