Catheterization and Cardiovascular Interventions

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Catheterization Techniques for Anomalous Aortic Origin of Coronary Arteries

Xavier Halna du Fretay[1,2] | Olivier Boudvillain[2] | Athanasios Koutsoukis[3] | Philippe Degrell[4] | Patrick Dupouy[5] | Pierre Aubry[2,6]

[1]Department of Cardiology, Pôle Santé Oreliance, Saran, France | [2]Department of Cardiology, Assistance Publique-Hôpitaux de Paris, Hôpital Bichat, Paris, France | [3]Department of Cardiology, Hôpital Marie-Lannelongue, Groupe Paris Saint-Joseph, Le Plessis-Robinson, France | [4]Department of Cardiology, Institut National de Chirurgie Cardiaque et de Cardiologie Interventionnelle, Luxembourg, Luxembourg | [5]Pôle Cardiovasculaire Imagerie et Interventionnel, Clinique les Fontaines, Melun, France | [6]Department of Cardiology, Centre Hospitalier de Gonesse, Gonesse, France

Correspondence: Pierre Aubry (pcaubry@yahoo.fr)

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Keywords: anomalous coronary artery | coronary computed tomography angiography | coronary pressure indices | intracoronary imaging | invasive coronary angiography

ABSTRACT

Anomalous aortic origin of a coronary artery (AAOCA) is a rare congenital anomaly with a large spectrum of anatomical variations. Selective engagement of an AAOCA can present challenges during cardiac catheterization. A comprehensive understanding of the characteristics of major AAOCA can effectively assist operators for selecting and maneuvering catheters. This review outlines the recommended catheter manipulations based on the site of ectopic coronary origin. Identifying the initial course (prepulmonic, subpulmonic, interarterial or retroaortic course) is crucial for classifying each AAOCA. Besides invasive coronary angiography, coronary computed tomography angiography is frequently utilized to enhance the diagnostic assessment. Cardiac catheterization enables the use of intracoronary imaging and physiologic tools for accurately assessing the significance of AAOCA identified as at risk, mainly the anomalies associated with an interarterial course. Intravascular ultrasound is recognized as the gold standard for analyzing AAOCA with interarterial course. Optical tomography coherence imaging can be interesting to evaluate the rare AAOCA with a subpulmonic course, which are associated with ischemic symptoms or myocardial ischemia. Invasive physiological indices using pressure wires can be employed, with the caveat that their threshold values remain uncertain. Decision-making can be challenging for patients with AAOCA. Both non-invasive and invasive imaging tools are essential to support the final choice.

1 | Introduction

Anomalous aortic origin of a coronary artery (AAOCA) represents a rare congenital anomaly, with an angiography prevalence of 0.8% [1]. Diagnosing AAOCA in adults involves different modalities such as coronary computed tomography angiography (CCTA), invasive coronary angiography (ICA), or less commonly, echocardiography. Encountering an unknown AAOCA poses challenges for interventional cardiologists, affecting catheter choice, engagement maneuvers, contrast

Abbreviations: AAOCA, anomalous aortic origin of coronaries arteries; AL, amplatz left; AR, amplatz right; CAD, coronary artery disease; CCTA, coronary computed tomography angiography; CCW, counterclockwise; CW, clockwise; Cx, circumflex; EBU, Extra Back-Up; FFR, fractional flow reserve; ICA, invasive coronary angiography; JL, Judkins left; JR, Judkins right; LAD, left anterior descending; LAO, left anterior oblique; LM, left main; MP, multipurpose; RAO, right anterior oblique; RCA, right coronary artery; SCD, sudden cardiac death; TAVI, transcatheter aortic valve implantation.

media administration, and percutaneous coronary intervention procedures [2–4]. The complexity of AAOCA catheterization not only extends procedure duration and contrast medium use, but also may delay intervention in acute coronary syndromes. While ICA offers 2-dimensional imaging, it often falls short in accurately analyzing certain AAOCA. Interventional cardiologists can leverage CCTA's 3-dimensional visualization of cardiac structures to enhance procedural planning and catheterization. Literature on the AAOCA catheterization techniques remains limited [5]. This review aims to address common AAOCA scenarios through an artery-by-artery approach. The first part outlines strategies to improve diagnostic catheterization success rates. In the second part, the role of intracoronary imaging and coronary physiology assessment during catheterization is discussed. Additionally, the contribution of CCTA in AAOCA diagnosis and work-up, is presented. This review will focus on adult population.

2 | General Diagnostic Catheterization Strategy

2.1 | Identifying AAOCA Origin

Switching to the contralateral vessel is recommended if the coronary artery cannot be visualized in its usual location. Many cases of AAOCA arise from the contralateral artery or sinus. If the origin is near the contralateral ostium, a highly selective catheter engagement may miss an AAOCA (Figure 1). An aortic root angiogram can provide valuable information about coronary artery origins and catheter selection. While radial access is the preferred route for ICA, a femoral approach may be necessary in cases of hostile brachial access. Using guide catheters instead of diagnostic catheters can improve stability and facilitate the use of guidewires or guide extension catheters. If the ectopic artery remains elusive despite standard angiographic attempts, patients without ST elevation myocardial infarction should avoid prolonged procedures and consider scheduling a CCTA.

While modified guide catheters have been developed for specific AAOCA cases [6], their availability varies by country. Therefore, the strategies described below are based on the use of standard catheters, which can be adapted through manual maneuvers to change the distal tip orientation [7, 8]. Additionally, CCTA imaging, sometimes with inverted views as seen by the operator, were added to provide valuable insights into coronary anatomy and catheter maneuvers. The Central Illustration 1 summarizes the suggested catheters according to the site of origin of each AAOCA.

2.2 | Considerations for AAOCA Ectopic Course

Familiarity with various ectopic courses associated with AAOCA is crucial to avoid misdiagnosis. Four primary ectopic courses based on their relationships to the great vessels have been identified: prepulmonic, subpulmonic, interarterial, and retroaortic [1, 9, 10]. The frequency of each ectopic course varies depending on the type of coronary artery involved. Generally, the circumflex (Cx) artery, right coronary artery (RCA), and left main (LM) or left anterior descending (LAD) artery account for approximately 50%, 30%, and 20% of AAOCA angiographic cases, respectively [11]. AAOCA must be categorized based on their associated risks. Those with an interarterial course are identified as having a risk of myocardial ischemia, sudden cardiac death (SCD) or aborted cardiac arrest [12]. Few AAOCA with subpulmonic course are associated with potential myocardial ischemia [13].

3 | Artery-Specific Catheterization Strategy

3.1 | Anomalous Origin of the Cx Artery

This AAOCA is the most frequent, with an angiographic prevalence of 5/1000 [11]. Its anatomic phenotype is well-established, typically originating in the RCA or right sinus, almost always associated with a retroaortic course [11]. The origin of a Cx artery arising from the RCA is in close proximity to the right ostium (Figure 1). Engagement of the Judkins right (JR) 4 catheter in the RCA, coupled with a clockwise maneuver and slow withdrawal, is recommended. Alternatively, Amplatz

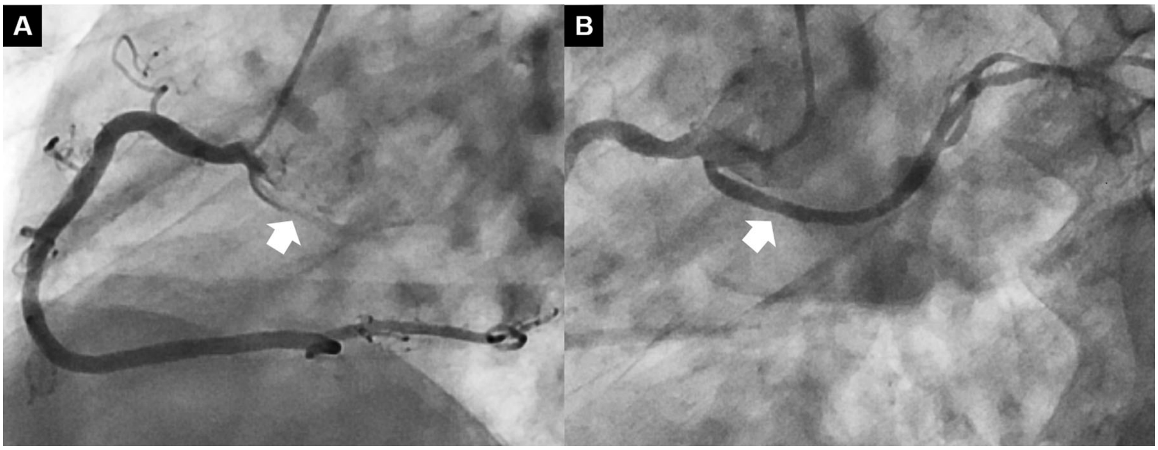
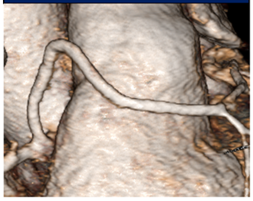


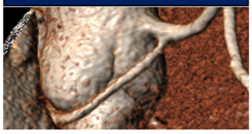
FIGURE 1 | Anomalous circumflex artery. (A) Angiographic image (left anterior oblique) depicting a deep engagement of the catheter in the right coronary artery, with the visualization of a shadow indicating the presence of an anomalous circumflex artery (white arrow). (B) Angiographic image (left anterior oblique) showing an anomalous circumflex artery (white arrow) after the pullback of the catheter.

Left main or Left anterior descending artery



Site	Frequency	Ectopic course	Catheters
Right sinus	++++	Prepulmonic or subpulmonic or retroaortic	JR 4, AR 1-2, AL 1, MP
Right sinus	+	Interarterial	Standard left, JR 4, EBU
Right coronary artery	++	Prepulmonic or subpulmonic or retroaortic	Standard right
Right coronary artery	+	Interarterial	Standard right
Aorta	+	Absent or interarterial	AL 1-2, MP
Left sinus	+	Absent or interarterial	Standard left
Non-coronary sinus	+	Retroaortic	Standard left/right
Single coronary	+	Not applicable	Standard right

Circumflex artery



Site	Frequency	Ectopic course	Catheters
Right sinus	+++++	Retroaortic	JR 4, AR 1-2, AL 1, MP
Right coronary artery	+++++	Retroaortic	JR 4, AR 1-2, AL 1
Single coronary	+	Not applicable	Standard right

Right coronary artery

Site	Frequency	Ectopic course	Catheters
Left sinus	+++++	Interarterial	EBU, AL 0.75-1-2, XB, CLS
Left main	+	Interarterial	Standard left
Left anterior descending	+	Prepulmonic	Standard left
Aorta	+	Absent or interarterial	AL 1-2, MP
Right sinus	+	Absent or interarterial	Standard right
Non-coronary sinus	+	Retroaortic	Standard right/left
Single coronary	+	Not applicable	Standard left

CENTRAL ILLUSTRATION 1 | Site of Origin and ectopic course of anomalous aortic origin of coronary arteries with suggested catheters. AL, amplatz left; AR, amplatz right; CLS, contralateral support; EBU, Extra Back-Up; JR, Judkins right; MP, multipurpose. [Color figure can be viewed at wileyonlinelibrary.com]

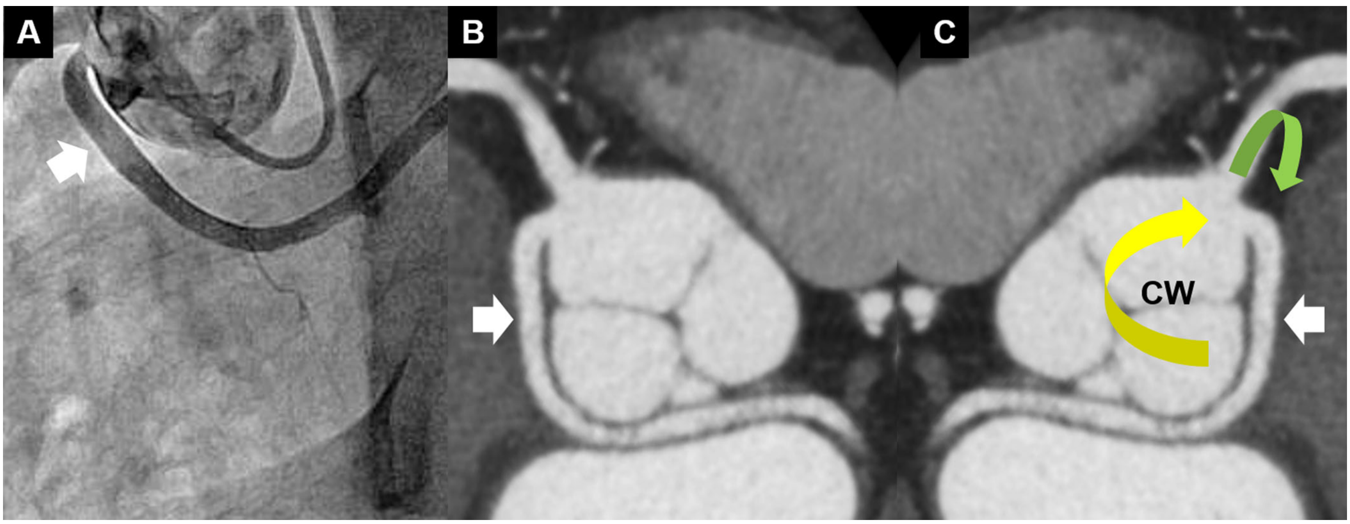


FIGURE 2 | Catheter Maneuver To Engage Anomalous Circumflex Artery From Right Sinus. (A) Angiographic image (left anterior oblique view) displaying a circumflex artery (white arrow) arising from the right sinus near and below the right ostium. Circumflex artery engaged with an Amplatz left catheter. (B) Computed tomographic image illustrating a circumflex artery (white arrow) arising from the right sinus with a retroaortic course. (C) Inverted computed tomographic image demonstrating the maneuver to guide the catheter (green arrow) from the right coronary artery to the circumflex artery using a clockwise (CW) rotation (yellow arrow). [Color figure can be viewed at wileyonlinelibrary.com]

right (AR) 1 or 2 catheters may be used. If necessary, placement of a 0.014-in. guidewire in the distal RCA can stabilize the catheter. An anomalous Cx artery origin in the right sinus lies near, below, and to the right of the RCA ostium. Engaging the catheter in the RCA and slowly withdrawing it from the RCA ostium with a clockwise rotation is optimal (Figure 2). Catheters such as JR 4, AR 1 or 2, Amplatz left (AL), or Multipurpose (MP) should be used. The retroaortic course is characterized by a long path with a marked downwards concave curve, typically visible in left anterior oblique (LAO) or right anterior oblique (RAO) incidence. During the left ventriculography in RAO incidence, the "dot-sign" can be observed, that is, the mid ectopic CX artery appears as a dot behind the aorta and below the RCA There is speculation that the retroaortic course is associated with a higher incidence of coronary artery disease (CAD) compared to other ectopic courses [14].

3.2 | Anomalous Origin of the RCA

The prevalence of this AAOCA is close to 3/1000 in the general population [15]. The most common anatomical phenotype involves an anomalous origin within the left sinus, typically near the left ostium (Figure 3). In over 90% of cases, the ectopic course is interarterial [11]. Rare alternative courses include a retroaortic course in cases of origin within the non-coronary sinus, or a prepulmonic course in cases of origin within the mid LAD artery (Figure 3). A high take-off from the ascending aorta (> 5 mm above the sinotubular junction) can be observed (Figure 3). In such cases, the initial course may be normal (ectopic ostium above the appropriate sinus) or interarterial (ectopic ostium above the contralateral sinus). An exceptional anomaly is a single coronary artery (Figure S1) with a single left ostium and retrograde filling of the RCA by the left network [16]. Catheterization of a right AAOCA is always challenging due to the tangential aortic pathway often associated with an intramural aortic passage [17]. This can result in coronary morphological deformation, particularly with an ostial slit-like shape, which makes selective engagement rare. To increase the success rate of visualizing a right AAOCA, the recommended maneuvers are described in Figure 4. An Extra Back-Up (EBU) 3.5 (or equivalent) is often the first choice. From the left ostium a clockwise rotation is optimal to engage the right ostium (Figure 5). A guide extension catheter can be utilized to improve opacification of the right AAOCA (Figure S2). Alternatively, AL 0.75, 1, 2, or XB 3, or Contralateral Support 3 guide catheters can be used. An intramural aortic passage can be suspected based on angiographic views, characterized by an enlarged and hypodense appearance in the initial arterial millimeters in LAO incidence, and a flute mouthpiece shape in RAO incidence (Figure 6). A lack of intramural aortic passage is characterized by a mild narrowing in RAO incidence (Figure S3). A remarkable finding is the rare occurrence of RCA originating in the proximal LM artery, always associated with

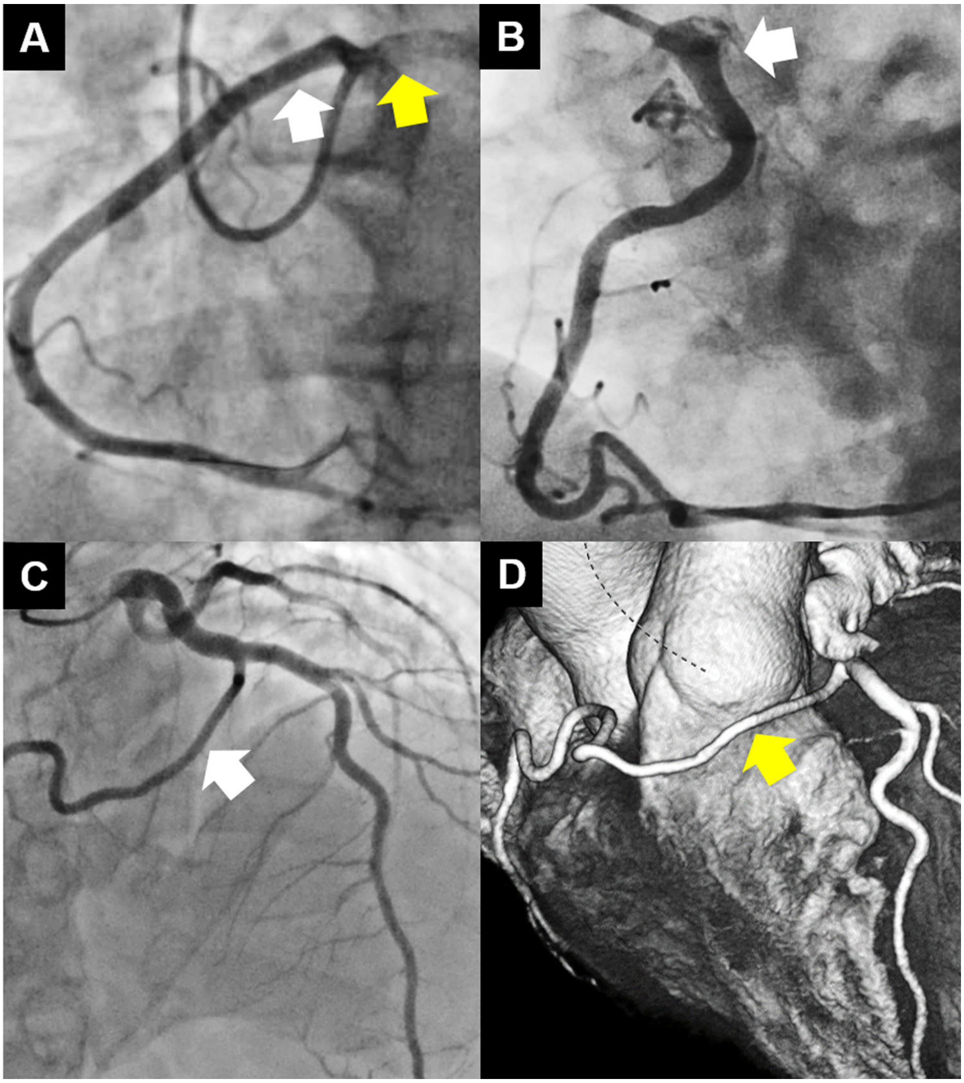


FIGURE 3 | Anomalous right coronary artery from left sinus, ascending aorta or left anterior descending artery. (A) Angiographic image (left anterior oblique view) showing a right coronary artery (white arrow) arising from the left sinus in close proximity to the left ostium (yellow arrow). Right coronary artery engaged with an Amplatz left catheter. (B) Angiographic image (left anterior oblique view) depicting of a right coronary artery arising from the ascending aorta. Note the funnel-like appearance of the ostium (white arrow). (C) Angiographic image (right anterior oblique view) illustrating a right coronary artery (white arrow) arising from the left anterior descending artery. (D) Computed tomographic image (volume rendering) showing a prepulmonic course (yellow arrow). [Color figure can be viewed at wileyonlinelibrary.com]

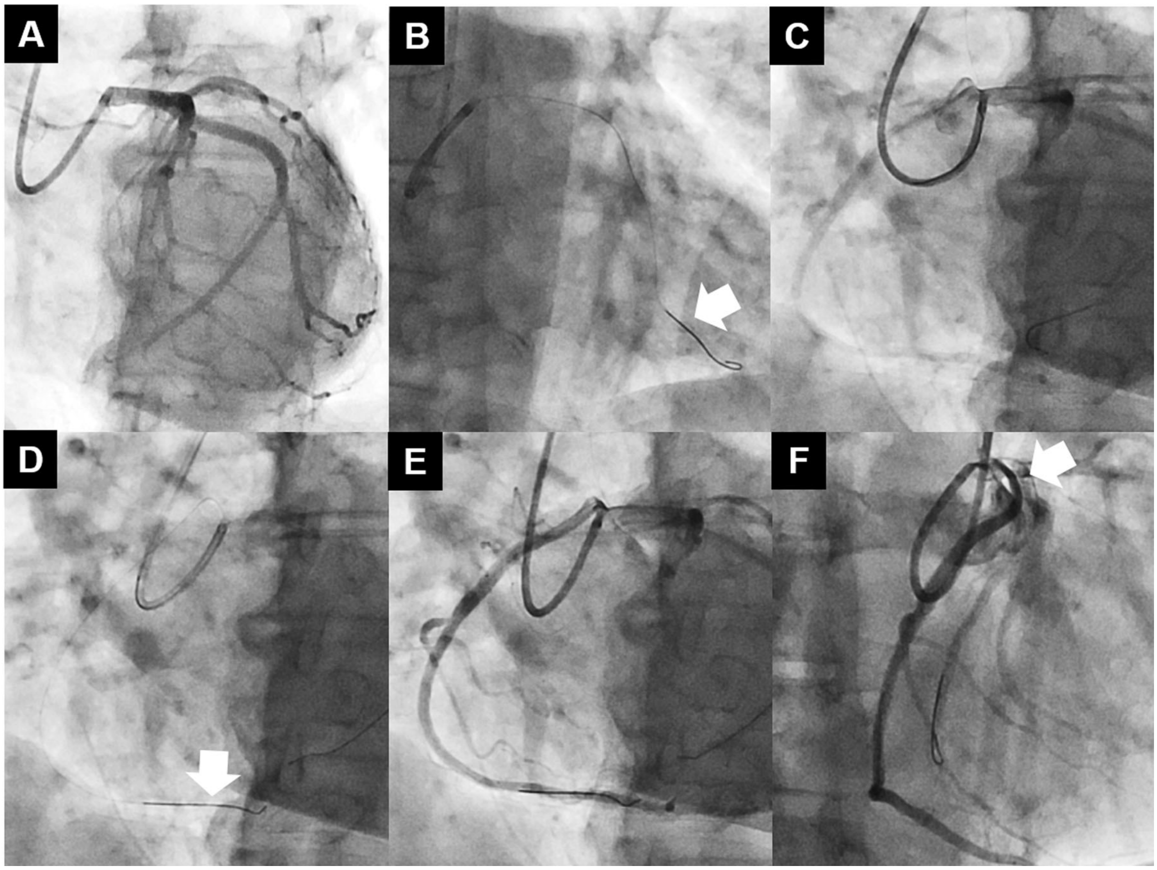


FIGURE 4 | Catheterization of anomalous right coronary artery from left sinus. Angiographic images demonstrating the catheterization of a right coronary artery arising from the left sinus. (A) Engage the left main artery with an Extra Back-Up 3.5 catheter. (B) Insert a guidewire (white arrow) down the left coronary to stabilize the guide catheter. (C) Push gently the guide catheter to disengage from the left main with a slow clockwise maneuver. (D) Upon reaching the right ostium, insert a guidewire (white arrow) down the distal right coronary artery. (E) Carefully advance the guide catheter and begin injecting contrast media in left anterior oblique view. (F) Right anterior oblique view revealing a proximal coronary narrowing with a tapered appearance (white arrow).

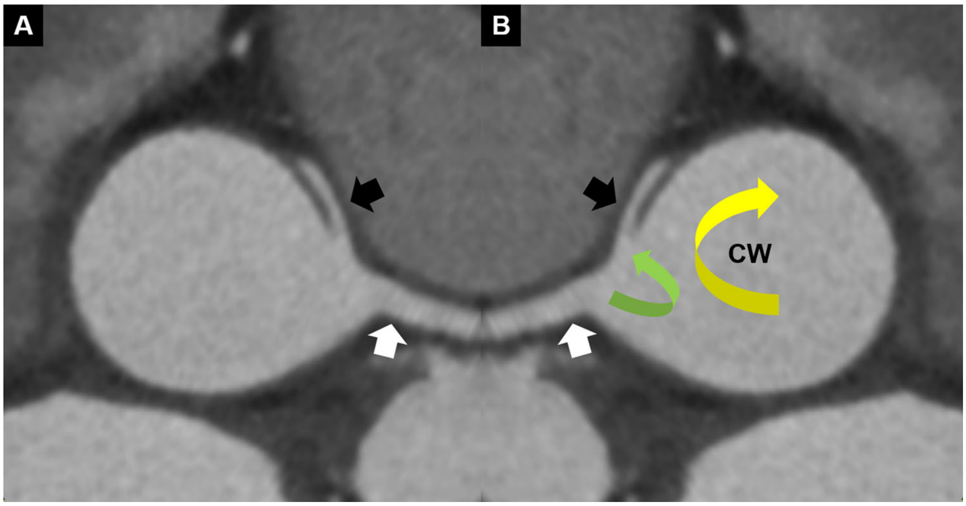


FIGURE 5 | Catheter maneuver to engage anomalous right coronary artery from left sinus. (A) Computed tomographic image displaying a right coronary artery (black arrow) arising from the left sinus with an interarterial course. (B) Inverted tomographic image illustrating the maneuver to move the catheter (green arrow) from the left main artery (white arrow) to the right coronary artery with a clockwise (CW) rotation (yellow arrow). [Color figure can be viewed at wileyonlinelibrary.com]

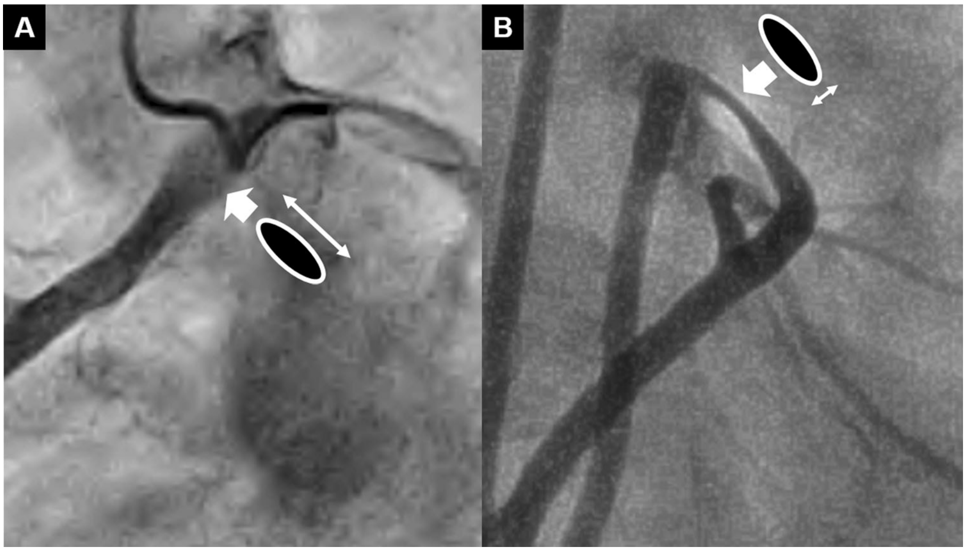


FIGURE 6 | Anomalous right coronary artery with intramural aortic passage. Angiographic images displaying an anomalous right coronary artery (white arrowhead) arising from the left sinus, presenting an interarterial course and intramural aortic passage. (A) Left anterior oblique incidence with enlarged and hypodense appearance (white arrow) of proximal arterial segment (long axis of lumen). (B) Right anterior oblique incidence with flute mouthpiece shape (white arrow) of proximal arterial segment (short axis of lumen).

an interarterial course (Figure S4). In the case of anomalous high take-off from the aorta, the use of AL or MP catheters is advised, employing techniques similar to those used for saphenous vein graft engagement. A common observation is the funnel-like appearance observed between the aorta and the ectopic coronary artery (Figure 3).

3.3 | Anomalous Origin of LM or LAD Artery

LM and LAD artery encompasses a wide spectrum of anatomical variations, with a global angiographic prevalence estimated at 2/1000 cases [11]. The ectopic ostium can be situated in the proximal RCA, the right sinus, or the ascending aorta. Four ectopic courses have been identified: prepulmonic, subpulmonic, interarterial, and retroaortic [9] (Figure 7). Notably, the subpulmonic course is the most frequently encountered in the adult population, while the interarterial course is relatively rare [11, 18]. In instances of a prepulmonic course, the LM or LAD artery arises from the proximal RCA or the right sinus, either adjacent to, above, or at the level of the right ostium, and to the left of it. Conversely, in cases of a subpulmonic course, the LM or LAD artery originates from the proximal RCA or the right sinus, typically below or at the level of the right ostium, and to the left of it. In both scenarios, when the JR 4 catheter is engaged in the RCA, it should be gently pulled back while executing a counterclockwise maneuver (Figure 8). In cases of a retroaortic course, the LM or LAD artery arises from the proximal RCA or the right sinus, positioned near or below the right ostium and to the right of it. To engage the LM or LAD artery with a retroaortic course, a slow withdrawal of the JR 4 catheter engaged in the RCA is essential, accompanied by a clockwise maneuver (Figure 9). Occasionally, an MP catheter can be used for LM or LAD artery with a subpulmonic or retroaortic course. An EBU guide catheter may be more suitable for LM or LAD artery with a prepulmonic course. Selective engagement of a LM with an interarterial course may be facilitated due to a less deformed ostium compared to a RCA. Typically, a JL 3.5 catheter or EBU 3.5 guide catheter suffices (Figure 10). An intramural aortic passage may be present solely on the mid part of the ectopic LM. To engage the LM with a JR 4 catheter, a counterclockwise maneuver is required after withdrawal from the right ostium. With experience, different ectopic courses of the LM or LAD AAOCA can be discerned through angiography [10, 19]. In LAO incidence with a subpulmonic or retroaortic course, a long path with a downwards concave marked curve may be observed (Figure S5). Identification of a septal artery in the ectopic segment indicates a subpulmonic course, distinguishing it from a retroaortic course (Figure S5). In RAO view, the eye sign formed by the ectopic LM and Cx artery is indicative of a left AAOCA with a prepulmonic or retropulmonic course (Figure S5). In RAO incidence with a prepulmonic or interarterial course, a path with an upwards convex marked curve may be observed (Figure S5). Compared to the interarterial course, the path of a prepulmonic course is typically longer and more meandering, while an interarterial course is generally associated with a straight course. For anomalous high take-off from the aorta, AL or MP catheters are necessary. Multiple ectopic connections may coexist in a single patient, necessitating the use of various catheters (Figure S6).

3.4 | Other Anomalies

Several other uncommon AAOCA have been documented. A single coronary artery represents a distinct abnormality previously described, which should be distinguished from other AAOCA with a single ostium [16]. An abnormal coronary origin in the appropriate sinus, but very eccentric, may include an RCA ostium located near the right-left commissure, or a LM ostium situated near the left-non-coronary commissure. In such cases, the RCA may exhibit a short interarterial course, while the LM artery may demonstrate a short retroaortic course.

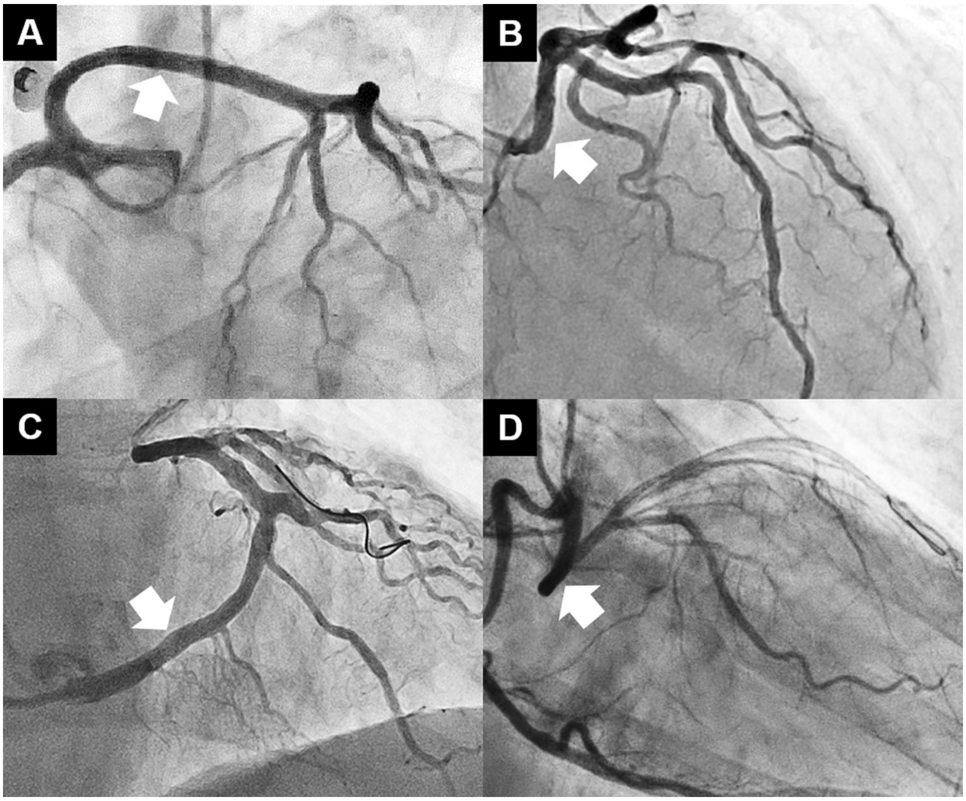


FIGURE 7 | Anomalous left main from right coronary artery or right sinus. Angiographic images showing various ectopic courses of an anomalous left main artery (white arrow) arising from the right coronary artery or right sinus. (A) Prepulmonic course (left anterior oblique view). (B) Interarterial course (right anterior oblique view). (C) Subpulmonic course (right anterior oblique view). (D) Retroaortic course (right anterior oblique view).

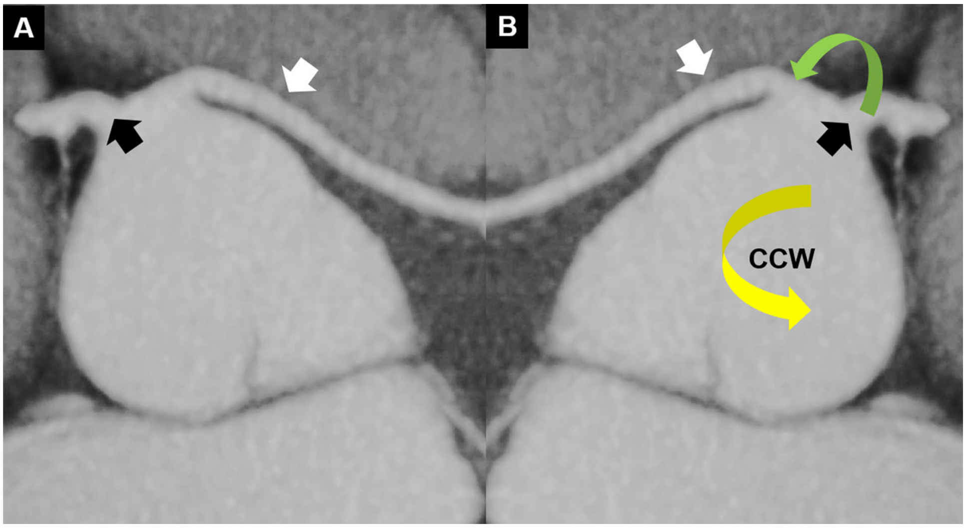


FIGURE 8 | Catheter maneuver to engage left main or left anterior descending artery with retropulmonic course. (A) Computed tomographic image displaying an anomalous left anterior descending artery (white arrow) arising from the right sinus near the right ostium (black arrow) and exhibiting a retropulmonic course. (B) Inverted tomographic image demonstrating the maneuver to move the catheter (green arrow) from the right ostium to the left anterior descending artery using a counterclockwise (CCW) rotation (yellow arrow). [Color figure can be viewed at wileyonlinelibrary.com]

Achieving selective engagement in these locations might prove challenging, often necessitating the use of non-standard diagnostic catheters such as AL, AR, MP, or 3DRC. A detailed plan may not always be applicable to this type of abnormality. Instances where the LM or RCA arises from the non-coronary sinus, typically associated with a more or less long retroaortic course, are also observed (Figure S7). Standard diagnostic catheters can be employed in such cases, with a

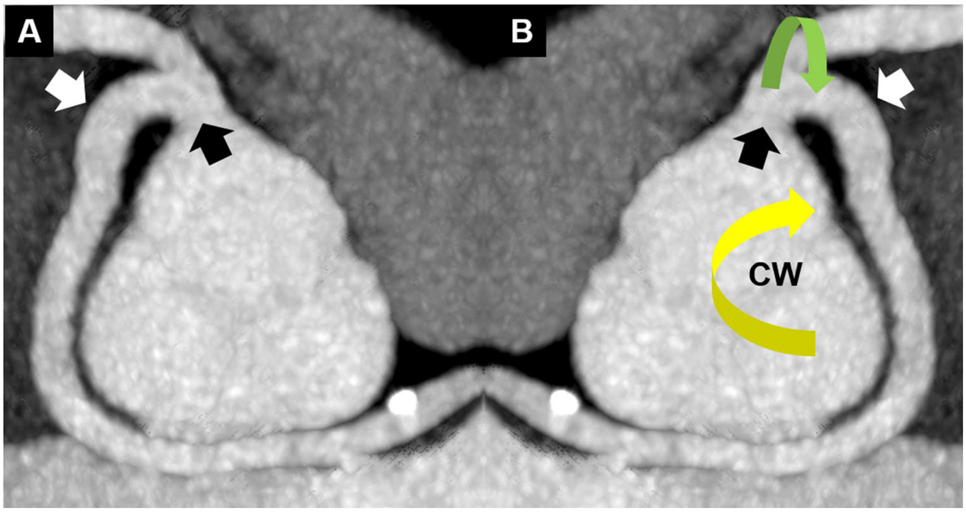


FIGURE 9 | Catheter maneuver to engage left main with retroaortic course. (A) Computed tomographic image depicting an anomalous left main artery (white arrow) arising from the right coronary artery (white arrow) with a retroaortic course. (B) Inverted tomographic image demonstrating the maneuver to move the catheter (green arrow) from the right coronary ostium to the left main artery employing a clockwise (CW) rotation (yellow arrow). [Color figure can be viewed at wileyonlinelibrary.com]

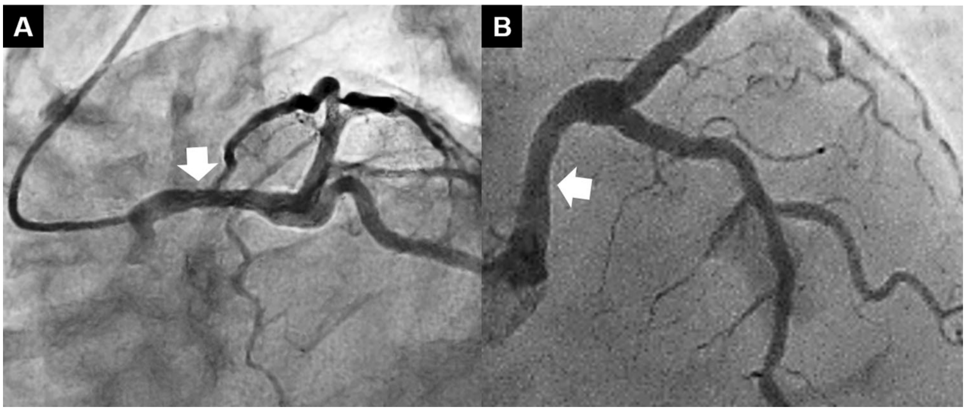


FIGURE 10 | Anomalous left main from right sinus. (A) Angiographic image (spider view) displaying an anomalous left main artery (white arrow) arising from the right sinus with an interarterial course. (B) Left main engaged with a Judkins left catheter.

counterclockwise maneuver often required to move the catheter tip posteriorly. Differentiate between an ostial hypoplasia/atresia and an ostial occlusion related to CAD can be challenging. The presence of an ostial stump, a non-tortuous collateral network, and the absence of CAD typically align with the definition of coronary ostial hypoplasia or atresia. Nevertheless, this is often not possible by ICA alone and requires a further evaluation by CCTA.

4 | Transcatheter Aortic Valve Implantation (TAVI) and AAOCA

With the development of TAVI, operators have become aware of the risk of external compression of AAOCA during valve expansion [20]. The retroaortic course, mainly observed with LM and Cx artery, is particularly at risk due to its close anatomical relationship with the aortic valve annulus (Figure S8). The risk of extrinsic compression can occur at the middle part of the ectopic course. Before TAVI, balloon aortic valvuloplasty with simultaneous coronary injection can be performed to assess tolerance. During the TAVI procedure, placement of a guidewire and an unexpanded stent in the ectopic coronary artery is advised for AAOCA at risk of compression (Figure S9). The TAVI procedure should be carried out as usual practice for other AAOCA.

5 | Evaluation of Coronary Morphology and Physiology

Approximately one-third of AAOCA, predominantly right AAOCA, diagnosed in the adult population are deemed at risk of myocardial ischemia or SCD. Although rare, left AAOCA with a subpulmonic course, especially when associated with coronary hypoplasia (Figure S10) or deep intramyocardial passage, have been linked to myocardial ischemia. The absolute annual risk of SCD is exceedingly low in patients with AAOCA, however poorly known and estimated at 0.02%–0.05% and 0.1%–0.2% for right and left AAOCA with an interarterial course, respectively [12, 21–23]. Furthermore, this risk is predominantly observed in athletic populations and decreases significantly after the age of 35 years [24, 25]. Conducting individual risk assessments can be challenging, particularly when AAOCA is incidentally discovered. In addition to the information provided by CCTA, supplementary morphological and physiological evaluations during cardiac catheterization may prove beneficial for informed decision-making.

5.1 | Morphologic Evaluation

The invasive morphological evaluation of AAOCA relies on intracoronary imaging techniques, that is, optical coherence tomography (OCT) or intravascular ultrasound (IVUS). OCT has a higher axial resolution and pullback speed compared to IVUS. However, the latter remains the gold standard for assessing AAOCA with an interarterial course [10, 26, 27]. IVUS allows simultaneous visualization of the arterial lumen, arterial wall, and adjacent structures. Certain probes equipped with the ChromaFlo function facilitate accurate analysis of the anatomical relationships of an interarterial course with the aorta and pulmonary artery. This type of imaging also aids in understanding the morphological adaptations of an interarterial course, where the ectopic coronary artery must navigate a constrained space between the arterial trunks, smaller than the normal arterial diameter. As the artery traverses behind the pulmonic structures to reach the aorta, the arterial surface area diminishes, transitioning first to an oval shape with a ratio (degree of eccentricity) between the long and short axis < 2.0. Then an intramural aortic passage leads to an ellipsoid arterial deformation with a ratio between the long and short axis ≥ 2.0. The ostium then has a slit-like shape (Figure 11). IVUS allows a quantitative assessment of an AAOCA with an interarterial course (Figure S11). The absence of perivascular cell density, resulting from the lack of adventitia, and the segmental disappearance of the typical 3-layered aspect may also suggest an intramural passage. In resting conditions, IVUS imaging may reveal a dynamic area narrowing (approximately of 5%−10% in systole) of the intramural segment due to aortic expansion [28]. Conversely, such dynamic changes are generally absent in AAOCA without an intramural aortic passage [29]. Unlike OCT, IVUS allows for manual pullback, specifically targeting the ectopic ostium, making it the preferred method for ruling in or ruling out an intramural aortic passage (Figure S12). Insufficient flushing of the blood vessel, which is not uncommon during AAOCA evaluation, may result in poor quality OCT images. Nevertheless, it can be used to evaluate left AAOCA with an interarterial course, as the ostium is often oval, allowing selective injections (Figure 12). OCT also remains valuable for assessing intramyocardial segments often found in AAOCA with a subpulmonic course, where a small or moderate reduction in diameter and lumen area may be observed (Figure 13).

5.2 | Physiological Assessment

The challenge of inducing myocardial ischemia with non-invasive tests is well recognized, even in high-risk individuals with symptomatic AAOCA. The limited reduction in luminal area, typically not exceeding 70%, may account for the high incidence of negative results in non-invasive tests. A two-tier concept has been proposed to elucidate the occurrence of myocardial ischemia [30]. This concept delineates a dynamic component in addition to the fixed component. The latter refers to a similar physiological behavior as the atherosclerotic stenotic lesions. Microvascular dilation induced by adenosine predominantly evaluates the fixed component of narrowing. Physiological measurements utilizing a pressure guidewire during pharmacological vasodilation-induced hyperemia reveal a fractional flow reserve (FFR) value generally ranging between 0.80 and 0.90 [31, 32] when the decrease in luminal diameter exceeds 50%, but rarely falling below 0.80 (Figure 14). While the physiologic assessment AAOCA via invasive methods has yet to be fully validated, an uncertain threshold value persists. Because the administration of a vasodilator via non-selective catheterization may be incomplete, intravenous administration can potentially overcome this limitation. It has been suggested that inotropic stress induced by dobutamine is more adept at evaluating the dynamic component of narrowing. A compression of the intramural segment can be induced, resulting in decreased luminal area and increased vascular resistance, ultimately leading to impairment of coronary flow reserve. To enhance the effects of a dobutamine stepwise infusion up to 40 µg/kg/min, atropine (0.5−1 mg intravenously) and volume expansion (up to 3 L of saline) can be added, to counteract the side effect of dobutamine to decrease the cardiac preload, and thus the blood pressure [30, 33]. This protocol, however, may not be applicable for every patient and cannot fully replicate vigorous and prolonged physical exercise. Nevertheless, the use of dobutamine slightly increases the incidence of positive invasive FFR results compared to adenosine. IVUS imaging can be employed at rest and during dobutamine infusion, with short round trips to identify increased dynamic compression. Resting indices measurement, such as instantaneous wave-free ratio or iFR, resting full-cycle ratio or RFR, or diastolic hyperemia-free ratio or DFR, have not been extensively evaluated yet. Additionally, angiography-derived FFR calculation can be performed using quantitative flow ratio (QFR). Even though this technology is not validated for ostial lesions, a recent study has shown that a non-significant QFR value in RCA with interarterial course was associated with a good clinical outcome at 5 years [34]. QFR calculation utilizing the Medis QFR software is based on 3-dimensional quantitative coronary angiography and computational fluid dynamics, employing contrast medium progression in the coronary artery (Figure S13). Beyond AAOCA with an interarterial course, invasive evaluation of certain AAOCA with a subpulmonic course may be beneficial in cases of ischemic symptoms and/or non-invasive functional testing-induced ischemia (Figure 13). A decrease in luminal area due to a deep intramyocardial passage can result in a positive invasive test.

5.3 | CCTA

CCTA has emerged as the primary imaging modality for visualizing the origin and initial course of AAOCA [12, 18, 35, 36]. Except an abnormal CX artery origin, CCTA is recommended following the discovery of AAOCA with ICA in the adult population. Utilizing volume rendering with 3-dimensional images facilitates the identification of ectopic courses, and clarifies their relationships with the great vessels

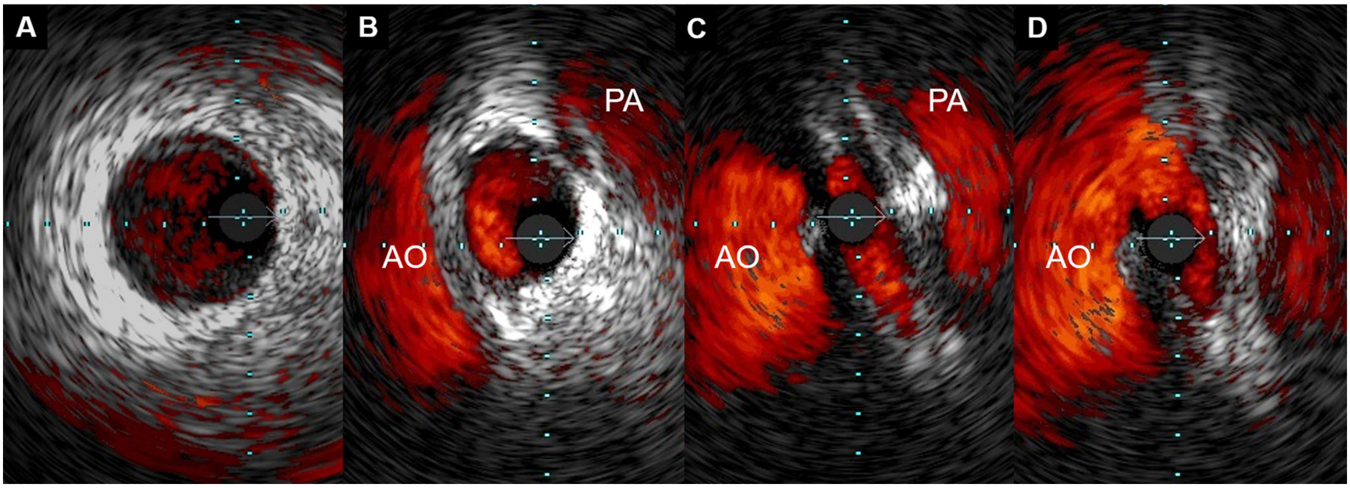


FIGURE 11 | Intravascular ultrasound imaging of anomalous right coronary artery with intramural aortic passage. Intravascular ultrasound images of an anomalous right coronary artery arising from the left sinus with a pullback from the non-ectopic segment (A) to the ostium (D). (B) Distal interarterial segment with an oval lumen shape. (C) Proximal interarterial segment with an elliptic lumen shape due to an intramural aortic passage. Note the use of a probe with Chromaflo function (Eagle Eye Platinum, Volcano, Philips Healthcare) facilitating the visualization of the aorta (AO) and pulmonary artery (PA). [Color figure can be viewed at wileyonlinelibrary.com]

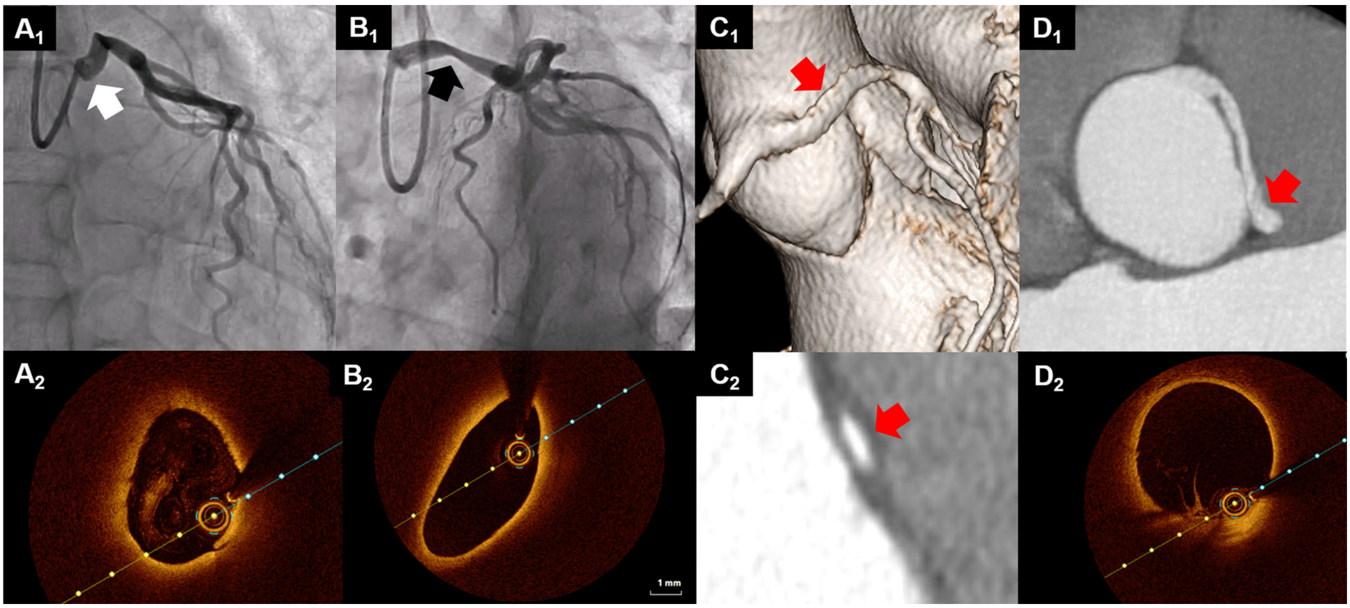


FIGURE 12 | Anomalous left main with intramural aortic passage. Angiographic images displaying an anomalous left main artery arising from the right sinus with interarterial course. Left main (white arrow) engaged with Extra Back-Up guide catheter. (A_1) Right anterior oblique view. (B_1) Left anterior oblique view showing a narrowing (black arrow) on the mid part of the left main artery. Optical coherence tomographic (OCT) images depicting the left ostium (A_2) with an oval shape and the mid left main artery (B_2) with an elliptic shape. Computed tomographic images with volume rendering (C_1) and coronal reconstructed view (C_2) showing a slit-like narrowing (red arrow) due to an intramural aortic passage. Computed tomographic image (D_1) and optical coherence tomographic image (D_2) of the distal left main artery. [Color figure can be viewed at wileyonlinelibrary.com]

when ICA 2-dimensional imaging remains ambiguous (Figure 15). It is crucial to distinguish between a subpulmonic or interarterial course (Figure S14) to avoid inappropriate decision-making regarding a left AAOCA. A more (> 2 mm) or less deep intramyocardial passage can be observed in left AAOCO with a subpulmonic course (Figure S15). A reduction of diameter and lumen area is often noticed in cases where an intramyocardial passage is present (Figure S16). Multiplanar reformatted images play a main role in evaluating anatomical features of AAOCA with interarterial course, such as luminal shape deformation, vessel narrowing (both diameter and area), and take-off angle (Figure S17). The diagnosis of intramural aortic passage generally relies on the association of the following criteria: degree of eccentricity ≥ 2.0, lumen diameter reduction ≥ 50%, and acute take-off angle (< 45°). CCTA serves as the cornerstone of multimodality imaging, significantly contributing to the evaluation of individuals with AAOCA and guiding patient management [27, 37, 38]. The identification of

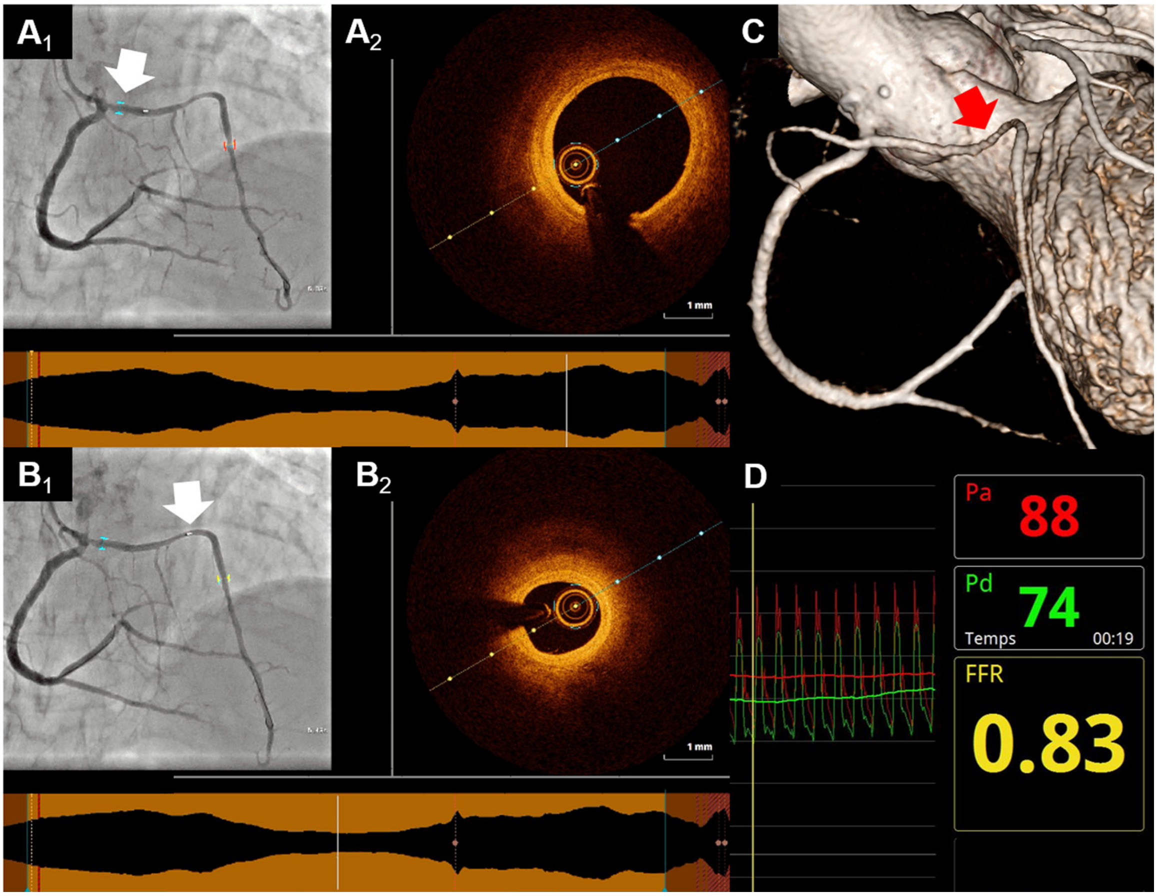


FIGURE 13 | Anomalous left anterior descending artery with subpulmonic course. Angiographic and optical coherence tomographic (OCT) images illustrating an anomalous left anterior descending artery (white arrow) arising from the right coronary artery with a subpulmonic course. (A_1) and (A_2) Analysis of the proximal ectopic segment. (B_1) and (B_2) Analysis of the distal ectopic segment free of atheroma and with lumen diameter reduction. (C) Computed tomographic image with volume rendering showing a narrowing (red arrow) of the distal ectopic segment. (D) Invasive assessment with fractional flow reserve (FFR) under adenosine. [Color figure can be viewed at wileyonlinelibrary.com]

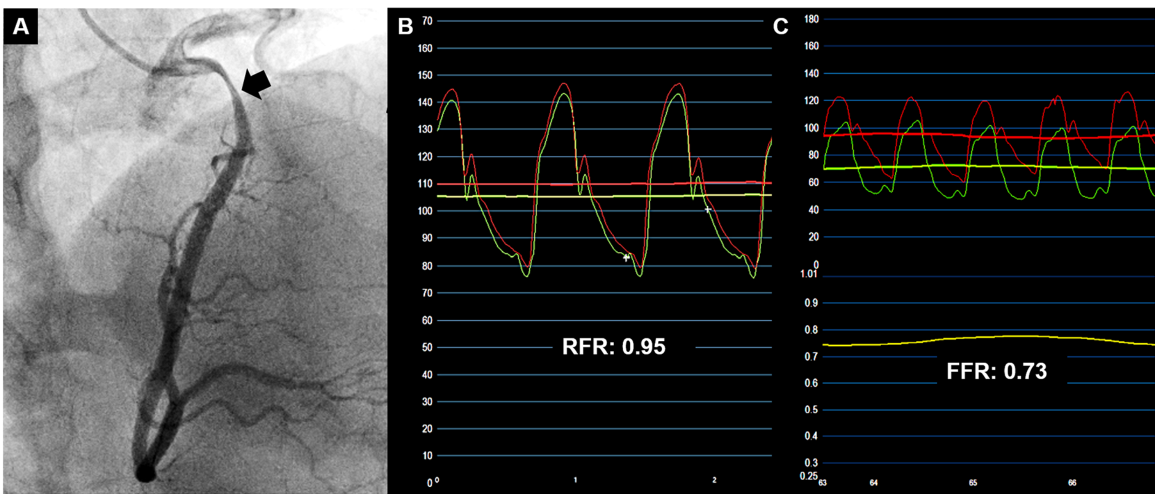


FIGURE 14 | Invasive physiologic evaluation of anomalous right coronary artery. (A) Angiographic image displaying an anomalous right coronary artery arising from the left sinus with a severe proximal narrowing (black arrow). (B) and (C) Invasive assessement with resting full-cycle ratio (RFR) and fractional flow reserve (FFR) under adenosine. [Color figure can be viewed at wileyonlinelibrary.com]

an intramural aortic passage is crucial for ensuring appropriate management of AAOCA with an interarterial course. CCTA can be extended beyond the scope of anatomical evaluation. Computational fluid dynamics simulations, such as those offered by HeartFlow Inc. (Redwood City, California), now provide physiological assessment (Figure S18) through FFR measurement (FFR_{CT}) [39]. However, it's important to note that while this non-invasive approach offers valuable insights, it may

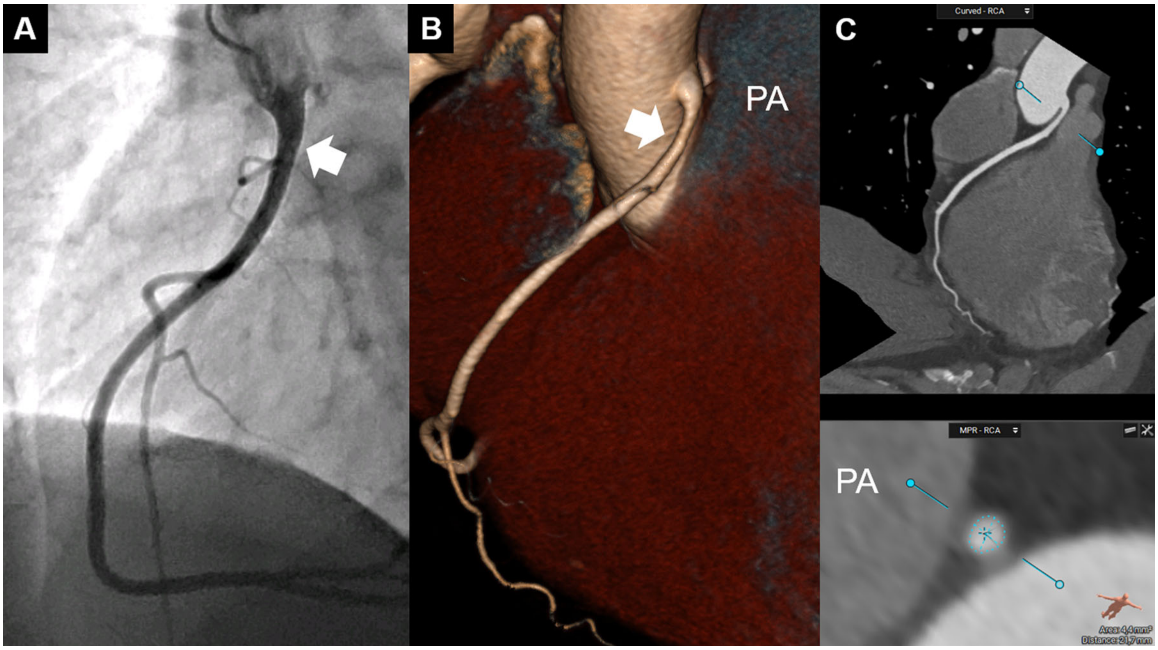


FIGURE 15 | Anomalous right coronary artery with high take-off. (A) Angiographic image (right anterior oblique view) and computed tomographic images showing an anomalous right coronary artery (white arrow) arising from the ascending aorta (high take-off) without interarterial course. (B) Volume rendering view. (C) Multiplanar reconstructed views. PA, pulmonary artery. [Color figure can be viewed at wileyonlinelibrary.com]

not fully capture the spectrum of pathophysiologic changes observed in AAOCA during a strenuous physical exertion [40].

6 | Conclusions

Locating and engaging an AAOCA during ICA can pose challenges. Having knowledge about the prevalence, site of connection, and initial ectopic course of different AAOCA can assist physicians in selecting the appropriate catheter and executing the most effective maneuvers. If necessary, a CCTA can provide more precise anatomical information. In cases of AAOCA with an interarterial course, evaluating coronary morphology and physiology using specific tools such as intravascular imaging and intracoronary hemodynamic measurements can aid in risk stratification. Continued research and clinical experience will further refine the current making decision algorithms of AAOCA.

Acknowledgments

This paper is dedicated to the memory of Dr. Paolo Angelini (1941–2023), a pioneering figure in the field of anomalous coronary arteries. His legacy continues to inspire and guide the efforts of clinicians and researchers worldwide, ensuring improved outcomes for patients with anomalous coronary arteries.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.