Coronary artery anomalies: a practical approach to diagnosis and management

Mohammed Ali,1 Alan Hanley,1 Eugene P McFadden,1,2 Carl J Vaughan1

ABSTRACT
The authors deal with common coronary anomalies, discuss their anatomy and some diagnostic and clinical aspects, and describe some of the principles of management.

INTRODUCTION
Coronary artery anomalies (CAA) are usually encountered incidentally during coronary angiography. Here, we review common coronary anomalies, discuss their anatomy with particular reference to their angiographic appearance and describe the principles of management.

Incidence
Coronary artery anomalies occur in 0.3–0.9% of the population without structural heart defects and in 3–6% of those with congenital heart defects.1 2 They are encountered in 1% of those undergoing cardiac catheterisation.3 The largest angiographic series, comprising 126,595 coronary angiograms,3 detected 1,686 coronary anomalies, with a prevalence of 1.3%; there were 22 (0.01%) cases with anomalous left main coronary artery (LMCA) arising from the right coronary sinus (RCS) and 136 (0.08%) with anomalous right coronary artery (RCA) arising from the left coronary sinus (LCS). These data likely underestimate the true incidence, as they are based on a review of a large angiographic database. Most people with underlying CAA will never have an angiogram, as they are generally asymptomatic. There is evidence of familial clustering of CAA, but no gene defects have yet been identified.5

Definition and classification of CAA
We classify these anomalies based on the origin of the anomalous artery that is from the opposite coronary sinus of Valsalva. In addition, the anomalies can be further characterised based on their course in relation to other cardiac structures, especially the great vessels (box 1). This is a convenient anatomical scheme but also provides important anatomical and prognostic information on anomalies associated with coronary ischaemia and sudden death.

‘Normality’ in the coronary tree
One definition of anomalous coronary arteries proposed by Angelini and colleagues6 is based on the relative frequency of anatomical variations in the general population. They define an ‘anomaly’ as a morphological feature seen in less than 1% of the population. Each coronary artery is conventionally named according to its anatomical position and course rather than the portion of myocardium subtended. Angelini suggested defining the normal coronary anatomy as having two to four coronary ostia arising from the right and left coronary cusps, originating from the aortic wall at 45°–90° with a ‘direct’ extramural course between the ostia and destination, with capillaries sufficient to supply the relevant myocardium.7 The LMCA arises from the LCS of the aortic root, usually from the upper third of the sinus, and it is usually less than 10 mm long. The LMCA then divides into the left anterior descending (LAD), left circumflex (LCx) and, in 30% of the population, to a third branch called the Ramus intermediate artery. The LAD supplies blood to the anterior wall and anterior half of the septum. The LCx supplies the lateral wall and, if dominant, will supply the posterior wall and the posterior half of the septum. The LAD gives rise to diagonal branches that supply the anterior free wall of the heart and septal branches which supply the interventricular septum. The LCx gives rise to obtuse marginal branches that supply the lateral wall of the heart. The RCA is dominant in 85% of people, usually arises from the RCS and supplies the right ventricle, posterior left ventricle and posterior septum.8

Coronary angiography: general principles
From a practical standpoint, we will describe CAA for each coronary artery in turn, rather than resort to traditional and exhaustive classification strategies.

During coronary angiography, there are two clues that should raise suspicion of a coronary anomaly: (1) the ‘unperfused myocardium’ sign, a myocardial region that is not supplied by any visualised vessel; and (2) the ‘aortic root’ sign, a vessel that appears to cross the aorta and the pulmonary artery at the level of the aortic root on ventriculography or proximal root injection in the right anterior oblique (RAO) projection, which is seen with most anomalies with an ectopic origin from the contra-lateral sinus.9

There are challenges when performing angiography in patients with CAA. There may be difficulty in locating and engaging the ostium of the artery. In addition, there may be difficulty determining the precise course of the artery, and CT angiography (CTA) is increasingly employed in these circumstances to provide accurate anatomical information on origin and course. When there is difficulty in cannulating the LMCA, a ‘cuspogram’ (injecting in the aortic cusp) to visualise and partly opacify the artery may be performed. If this is unsuccessful, we suggest proceeding to injection in the right or the non-coronary aortic cusps for LMCA arising from the right or the non-coronary cusps respectively. To visualise the slit-like orifice of
**Box 1 Classification of coronary artery anomalies.**

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<tr>
<th>Left circumflex coronary artery</th>
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<tr>
<td>1. Arising from the right sinus of Valsalva (retroaortic course)</td>
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<tr>
<td>2. Separate ostium of left circumflex from left sinus of Valsalva</td>
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<td>3. Rudimentary left circumflex (super-dominant right coronary)</td>
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<td>4. Absent left circumflex (super-dominant right coronary)</td>
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<th>Right coronary artery</th>
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<td>1. Anterior location in the right sinus of Valsalva</td>
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<td>2. Posterior location in the right sinus of Valsalva</td>
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<td>3. Arising from the left sinus of Valsalva (intra-arterial course)</td>
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<td>4. Absent right coronary artery (super-dominant left circumflex)</td>
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<th>Left main coronary artery</th>
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<tbody>
<tr>
<td>1. Separate ostia of the left anterior descending and left circumflex</td>
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<tr>
<td>2. Aberrant location in the left sinus of Valsalva (anterior or posterior)</td>
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<td>3. Superior origin above the left sinus of Valsalva</td>
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<td>4. Arising from the right sinus of Valsalva:</td>
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<tr>
<td>a. Interarterial</td>
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<td>b. Septal</td>
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<td>c. Anterior</td>
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<td>d. Retroaortic course</td>
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<td>5. Arising from the pulmonary artery</td>
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In many cases, the anomalous RCA may be fortuitously diagnosed when it is opacified while injecting the LMCA. In these circumstances, the ostium lies in close proximity to the LMCA ostium, and there is sufficient reflux of contrast to opacify the aberrant RCA. During normal coronary angiography, cannulation of the RCA may require some catheter manipulation, particularly if the RCA ostium has either a posterior or anterior location. After the appropriate time and exclusion of these possibilities, the likelihood of an anomaly should be entertained. Then, the LCS can be explored again using a multipurpose or Amplatz catheter, or with an aortogram performed in the LAO projection. On RAO projections, the interarterial course will be seen as a ‘dot’ anterior to the aorta.

**LEFT CIRCUMFLEX ANOMALIES**

These are relatively common and usually benign. They are often encountered after cannulation of the LMCA when a true LCx is not apparent, raising suspicion that it may be anomalous. When one encounters ‘absence’ of the LCx during injection of the LMCA, two possibilities should be entertained: an absent LCx or an aberrant origin; (1) separate LCx from the LCS or (2) LCx arising from the RCA or from the RCS originating near the RCA ostium. In the latter situation, the course is usually retroaortic and clinically benign. When the LCx arises from the RCS, it can usually be cannulated with the Judkins right catheter or right Amplatz. A multipurpose catheter is useful when the coronary artery origin is low and has a sharp inferior course; after engaging the ostium of the RCA, a clockwise rotation will engage the anomalous LCx.

In many instances, it will be visualised coursing to the left upon injection of the right coronary ostium, and it will be seen as a ‘dot’ posterior to the aorta on RAO projections.

In the case of separate left coronary ostia, changing to a different Judkins left catheter will often permit cannulation of the anomalous RCA, a steep right anterior oblique (RAO) and cranially angulated antero-posterior view can be helpful.

In 1985, Ishikawa constructed a protocol for determination of the true course of the CAA radiologically, the ‘dot and eye method’. He demonstrated that an injection in the RAO view will separate the normally positioned aorta and pulmonary artery, and allows excellent localisation of the initial course of the anomalous coronary arteries relative to the great vessels; the ‘eye’ refers to an ellipse formed by the LMCA and the initial portion of the LCx, and the ‘dot’ refers to a radiopaque dot formed by the contrast column in the coronary artery, seen ‘on end’ posterior or anterior to the aorta (figure 1). Details are explained with each anomaly.

**Right coronary artery anomalies**

Anomalous origin of the RCA from the LCS is an important anomaly with a reported incidence of 0.1%. Because this anomaly involves a course between the aorta and pulmonary artery, it has been implicated in sudden cardiac death, and some recent studies have reported a prevalence of 30% among asymptomatic adolescents who have suffered sudden cardiac death.

In many cases, the anomalous RCA may be fortuitously diagnosed when it is opacified while injecting the LMCA. In these circumstances, the ostium lies in close proximity to the LMCA ostium, and there is sufficient reflux of contrast to opacify the aberrant RCA. During normal coronary angiography, cannulation of the RCA may require some catheter manipulation, particularly if the RCA ostium has either a posterior or anterior location. After the appropriate time and exclusion of these possibilities, the likelihood of an anomaly should be entertained. Then, the LCS can be explored again using a multipurpose or Amplatz catheter, or with an aortogram performed in the LAO projection. On RAO projections, the interarterial course will be seen as a ‘dot’ anterior to the aorta.

**Figure 1** Diagrammatic angiographic illustration of the four possible left main coronary artery courses arising from the right coronary cusp. Illustration of the coronary angiographic images in right anterior oblique projection (redrawn from Ishikawa10) showing the four possible courses of an aberrant left main coronary artery (LMCA) arising from the right coronary cusp or the right coronary artery. LAD, left anterior descending; LCx, left circumflex.
Left main coronary artery anomalies
Split origin or separate ostia LAD and LCx or absent LMCA is a common finding during coronary angiography; this is a clinically benign variant.

We have discussed the angiographic approach to this anomaly above. In addition to separate ostia, occasionally the LMCA will have either a posterior or anterior location in the LCS that requires some additional catheter manipulation to obtain selective engagement and proper opacification or a change to a Judkins left catheter of a different size. Similarly, one will occasionally encounter a high origin of the LMCA (this refers to an origin above the sino-tubular junction). High coronary ostia have been reported in up to 6% of adult hearts.12 This may lead to difficulty in cannulating the artery during conventional angiography and may also theoretically reduce diastolic coronary artery blood flow.13

Anomalous origin of the LMCA from the RCS is quite rare, with an estimated incidence of 0.03–0.15%. In this case, it may take four possible courses14 (figures 1, 2):

(a) Interarterial course: Between the aortic root and the pulmonary artery. The LMCA initially courses up toward and then behind the right ventricular outflow tract before travelling anteriorly to its normal point of bifurcation. During RAO injections, the contrast column of the LMCA will be seen on end as a ‘dot’ anterior to the aorta.

(b) Septal course. The LMCA may course intramyocardially or subendocardially, along the floor of the right ventricular outflow tract. It will then surface in the midseptum, at which point it branches into the LAD (only the mid and distal segments are present) and LCx (the initial portion courses toward the aorta). During 30° RAO injection, the LCx will form an ellipse to the left of the aorta similar to an ‘eye’, with the LMCA forming the inferior portion and the LCx forming the superior portion. Another clue is the presence of the unusual septal perforator branches arising from the LMCA; this is well demonstrated (figure 5) in an example of a septal course.

(c) Anterior (to the right ventricular outflow tract) course. The LMCA passes anteriorly over the right ventricular outflow tract, making a cranial anterior loop in which the artery passes initially rightward then up and over the right ventricular infundibular free wall in the RAO view before reaching the interventricular groove and then dividing normally. During the 30° RAO injections, the LMCA and the initial portion of the LCx will form an ellipse (‘eye’) to the left of the aorta with the LMCA forming the superior portion and the LCx forming the inferior portion.

(d) Retroaortic (posterior to the aortic root) course. The LMCA may arise to the right of the RCA and pass posterior to the aortic root. In an RAO view, the LMCA takes a caudal posterior loop, and the contrast column of the LMCA will be seen ‘on end’ posterior to the aorta and will appear as a radiopaque ‘dot’.

This anomaly is clinically significant, as it is associated with sudden cardiac death, especially during vigorous exercise.15 The potential lethality of this anomaly is due to the course followed by the LMCA on arising from the RCS.

Mechanisms of sudden death in CAA
There are a number of postulated mechanisms to explain the mechanisms of ischaemia associated with LMCA anomalies. The normal coronary artery arises at a perpendicular angle to the aorta, in contrast to the anomalous coronary artery arising from the opposite coronary sinus, which comes off at an acute angle and bends over itself to reach its normal supply territory. Because of this, the ostium of the abnormal coronary artery is smaller, with a slit-like ostium, as compared with the normal circular ostium. The magnitude of ischaemic risk is related to the degree of angulation. These complications commonly occur during or immediately after exercise. Exercise leads to expansion of the aortic root and pulmonary trunk, stretching the aortic wall and leading to compression and exaggeration of the slit-like ostium causing further ischaemia.16 17

Another theory refers to the initial course of the CAA. When the anomalous artery course is interarterial, between the aorta and pulmonary artery, the increase in the pressure in the two vessels occurring during exertion would produce a compression of the vessel, myocardial ischaemia and carries a high risk for sudden cardiac death in both adults and teenagers.18 If the initial pathway is an intramural course, that segment of the coronary artery may be compressed and deformed within the aortic wall during periods of hypertension.11 19

With respect to RCA anomalies, the acute angulation at the coronary takeoff may increase or become kinked during exertion; the slit-like orifice may become compressed by exercise-induced aortic dilatation; the intramural segment may be compressed by the aortic valve commissure; and the presence of an ostial ridge functioning as a ‘valve’ which restricts flow during exertion.20 21

Angelini has demonstrated with intravascular ultrasound lateral luminal compression of the intramural portion of the coronary artery and compression of the coronary artery between the aorta and the pulmonary artery.6 20

Some authors suggest that anomalous pathways may result in endothelial damage and dysfunction leading to coronary artery spasm contributing with other mechanisms (mentioned above) to myocardial ischaemia.22
CAA and atherosclerosis

Some studies suggest that anomalous arteries, in particular circumflex artery anomalies, have a selective predisposition to focal accelerated atherosclerotic disease, possibly due to repetitive mechanical buffeting, abnormal wall stress or abnormal flow strain.23 The published literature examining this issue is inconclusive, with studies both supporting24 and refuting25 excess atherosclerotic involvement of the anomalous coronary.

Symptoms

Most CAAs are asymptomatic and are detected incidentally during angiography. Some anomalies present as sudden cardiac death in young subjects. Maron et al reported that 19% of deaths in athletes are attributable to CAA.26

When symptomatic, modes of presentation include episodic chest pain, syncope, dyspnoea, heart failure, ventricular arrhythmias, myocardial infarction and sudden death. Symptoms typically occur after heavy exercise and are usually associated with an anomalous origin of the LMCA or the RCA from the opposite coronary sinus.

DIAGNOSIS

To evaluate a patient with suspected CAA, we would need to establish the exact anatomical course of the anomalous artery and then to stratify the risk of sudden death associated with it. If we consider the mechanism of death in patients with CAA to be ischaemia provoked as a consequence of the haemodynamic changes of exercise, a functional assessment in addition to an imaging test would be required.

Coronary angiography and cardiac CTA would provide radiological information on coronary anatomy at a resting heart rate. Saline injection and Dobutamine infusion have been tried during coronary angiography to simulate exercise physiology in addition to the use of pressure wire and intravascular ultrasound (IVUS),7 but this work is so far still experimental.

Functional assessment in the form of an exercise stress test or radionuclide stress or dobutamine stress echo is useful in some patients.

CT coronary angiogram

Novel advances in CT have led to provision of a non-invasive technique offering an accurate diagnostic modality.

The advantages of CT include non-invasiveness of the study, visualisation of both vessel wall and lumen, and simultaneous study of all coronary arteries, valves and all cardiac chambers.

The disadvantages of CT angiogram are the radiation dose and the use of contrast. The radiation dose with current 64 multislice computed tomography (MSCT) for a retrospective ECG-gated CTA is 13–15 mSv for males and 18–21 mSv for females.27

The current indications for CT angiogram include asymptomatic high-risk patients, particularly those with inconclusive stress tests.28 CT angiography is also indicated as a part of the investigative process for CAA: multidetector computed tomography (MDCT) is superior to conventional angiography in delineating the ostial origin and proximal course of anomalous coronary arteries as well as in patients with myocardial bridging who present with chest pain or even myocardial infarction.

The origin and course of abnormal coronary arteries can be visualised with a three-dimensional anatomical display using axial reconstructions from multidetector CTA. Some authors advocate using CT as the first-line investigation when CAA are suspected, as the exact position and course of the anomalous artery can be viewed in relation to the aortic root and pulmonary artery.29

MRI, despite inferior resolution, holds the greatest appeal because it avoids radiation and yields interpretable images in most cases. MRI may surpass conventional angiography for isolated coronary anomalies.30

MANAGEMENT

The management of patients with CAA is controversial, and the decision process should be individualised, taking into account the type of anomaly.

Patients with anomalies from the opposite coronary sinus, because of the potential risk of sudden death, should first be prevented from participating in competitive sports, and then a decision should be made as to whether these patients would need revascularisation. The aim in treating patients with CAA <35 years of age is to prevent sudden death. If these patients are asymptomatic, most authors would advise revascularisation. If these patients are asymptomatic, the literature is less clear, but we feel that these patients should be considered for revascularisation unless they opt for conservative management. In that event, adopting a sedentary lifestyle and annual follow-up with a thallium scan or dobutamine stress echocardiogram may be
advisable. In patients older than 35 years of age, the risk of sudden death is probably not clinically significant, so our aim in these patients is to treat symptoms like ischaemia. However, each patient should be considered separately, and the risk is still of unknown magnitude.

Surgical repair of coronary arteries with anomalous origin has generally been the standard of practice. Multiple surgical techniques have been utilised, including coronary bypass graft placement, reimplantation of the anomalous coronary artery to the appropriate sinus and the unroofing procedure. The unroofing procedure was initially reported by Mustafa in 1981 and has been used for anomalous origin of both the LMCA and the RCA arising from the opposite coronary sinus when the anomalous coronary artery has an intramural course.11

Aortocoronary bypass grafting has been strongly criticised because of its ‘limited’ patency and the inevitable competitive flow between the bypass and the CAA. Thus, the unroofing technique, which would appear to be more physiological, is increasingly being adopted.17

Percutaneous intervention, with implantation of stents in the region of the compression between the large vessels and in the anomalous ostium, has been performed in several cases, in adults, with short-term success. To date, surgical revascularisation is preferred in young patients, and the percutaneous procedure is performed only in adults. Evidently, in both cases, long-term follow-up is necessary.17

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REFERENCES