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Proximal Anomalous Connections of Coronary Arteries in Adults

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1. Introduction

Isolated proximal **ANO**malous connections of **COR**onary arteries (ANOCOR) are not rare with an angiographic prevalence and tomographic prevalence of 0.5% and 1.3% respectively, in adult populations. The diagnosis of ANOCOR is sometimes fortuitous in adults undergoing a coronary angiography to detect a coronary artery disease (CAD). The absence of diagnosis in young people may have severe consequences with sudden death occurring frequently during intensive exertion. The prognosis depends mainly on the initial course of the ectopic coronary vessel. Preaortic course with intramural segment is recognized as high risk for sudden death in children or young adults. Management of ANOCOR with intramural course may be difficult in patients >35 years of age and with no evidence of myocardial ischemia. The mechanisms of life-threatening cardiac events are still not well understood even if anatomical risk factors are identified. Fortunately, most cases of ANOCOR are simply incidental anatomical findings. Multidetector computed tomography (CT) is recognized as the best imaging technique for identifying ANOCOR. Intravascular ultrasonography (IVUS) may help to quantify the severity of high-risk ANOCOR. In the ACC/AHA 2008 guidelines for the management of adults with congenital heart disease, surgical repair is the treatment of choice for high-risk ANOCOR (Warnes et al. 2008). However, this therapeutic management is based on little solid data with limited long-term follow-up. Percutaneous coronary intervention (PCI) has been proposed in some ANOCOR. The limited experience of most angiographers in detection of ANOCOR may explain non infrequent misdiagnoses with erroneous interpretations of ANOCOR. Large-scale prospective multicenter studies are needed to improve screening and imaging strategies and to better define the treatment of these potentially lethal congenital coronary abnormalities.

Today, prospective registries are ongoing in France and North and South America with the goal of assessing the natural history of ANOCOR, as well as the long-term impact of surgical repair or PCI. The present review will focus on recent imaging modalities allowing us to revisit previous concepts and definitions.

2. Embryology and normal anatomy

The basics of cardiac development are needed to understand congenital coronary malformations and to avoid incorrect interpretation leading sometimes to erroneous diagnoses (Gittenberger-de Groot et al. 2005).

2.1 Embryology

The looping of the heart and the completion of the great vessels occur before the connection of coronary arteries to the aorta. Neural crest cells play an essential role in the outflow tract septation and coronary artery development. An additional element is the contribution of extracardiac cell populations like epicardium-derived cells. Coronary vascular formation occurs relatively late in development after covering of the myocardium by the epicardium. A plexus of epicardially derived vessels connects to the aortic root. It is generally considered that the initial segment of the coronary arteries develops by endothelial ingrowth from the peritruncal ring rather than by endothelial outgrowth from the aorta (Bogers et al., 1989). That is why the expression *anomalous connection* will often be used in this review. Otherwise, the concept of ingrowth permits a better understanding of the numerous ANOCOR patterns. Proximal left and right coronary arteries connect to the left posterior and anterior sinuses which are closest to the right ventricular outflow tract and pulmonary trunk. In the normal heart, the left posterior sinus is also known as the left sinus, and the anterior sinus, the right sinus. Recent experimental insights suggest that multiple endothelial strands penetrate the three sinuses at the onset of the proximal coronary vascular formation (Ando et al., 2004). Then, the left and the right stems develop by fusion of endothelial strands, and the strands connecting the right posterior sinus disappear. Therefore, the right posterior sinus is also known as the non-coronary sinus. Anomalous origin of coronary arteries may occur in isolation without abnormal myocardial outflow tract development. Inconsistencies exist with regard to the exact mode of development of these congenital abnormalities in otherwise normal hearts.

2.2 Normal anatomy

On an axial cross-sectional CT view, the origin of the left coronary arises at the 3- to 5-o'clock position and the right coronary at the 10- to 12-o'clock position (figure 1). Knowledge of the position of the heart within the mediastinum is essential for appropriate analysis of imaging tools (Anderson & Loukas, 2009). Due to the orientation of the aorta, the origin of the coronary arteries is not well visualised simultaneously on the same axial image. The left ostium is more cranial in comparison with the right ostium. Shortly after their origin, the coronary arteries run across the epicardial surface of the heart surrounded by fat. The proximal segment of the right coronary artery (RCA) courses directly in the right atrioventricular groove, whereas the left coronary artery (LCA) courses initially between the pulmonary trunk and the left appendage.

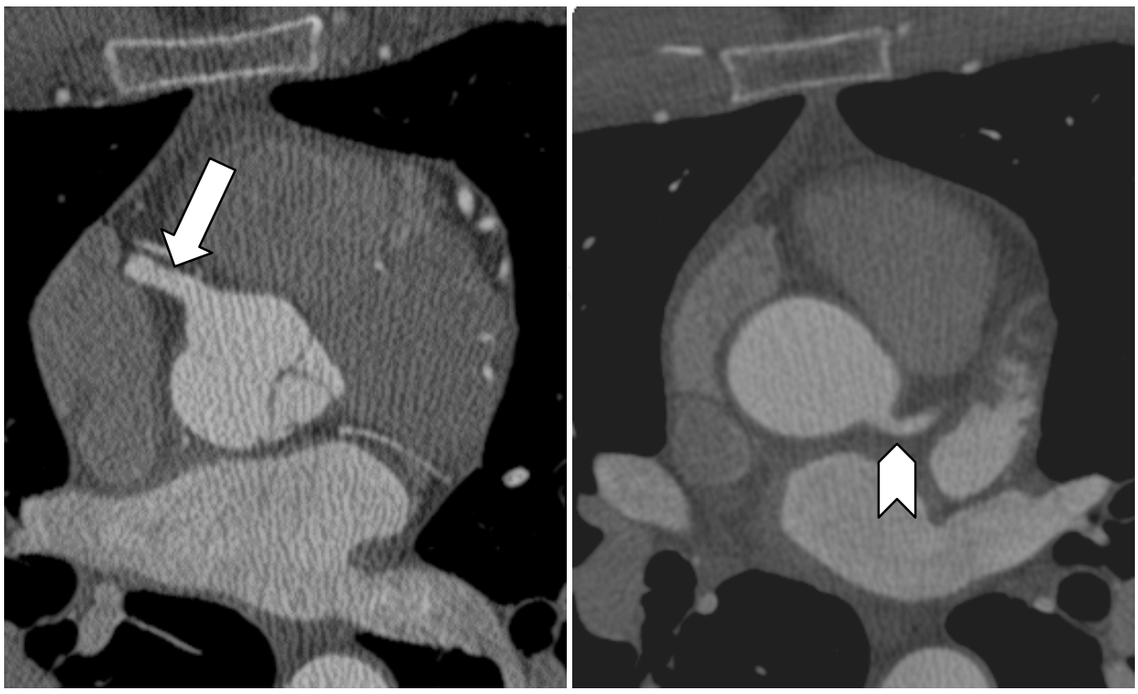

Fig. 1. Axial cross-sectional computed tomography views showing normal origin of the right coronary artery (arrow) and left coronary artery (arrow head).

Cardiologists and radiologists should be aware of the normal origin and anatomical variants (Angelini, 2007) of the coronary arteries (table 1) in order to make an accurate diagnosis of ANOCOR.

Normal connections	
Left coronary	Left main dividing into LAD and CX coronary arteries
Right artery	Single ostium
Site of left connection	In mid-left sinus
Site of right connection	In mid-right sinus
Level of connection	Upper half of sinus
Ostium shape	Circular
Angulation with aorta	45 to 90°
Initial course to aorta	Extramural
Anatomical variants	
Left coronary	Separate origin of LAD and CX coronary arteries in left sinus
Right coronary	Separate origin of conus artery in right sinus
Site of left connection	Close to the right sinus
Site of right connection	Close to the non-coronary sinus
Level of connection	Up to 10 mm above the level of the sinotubular junction
Ostium shape	Ovoid
Angulation with aorta	90 to 135°

Table 1. Normal connections and anatomical variants of the coronary arteries. CX: circumflex, LAD: left anterior descending.

In the normal heart, the coronary arteries arise from the upper half of sinuses, close to the sinotubular junction in most of cases (Muriago et al., 1997). A connection above the level of the sinotubular junction is possible. The coronary orifices are not always located in the centre of aortic sinuses. The left coronary ostium may lie near the junction between the left and right aortic sinuses, whereas the right ostium may lie near the junction between the right and the non-coronary aortic sinuses (Muriago et al., 1997). The discrimination between a common variant and an anomalous origin from an unusual site within the appropriate sinus is often difficult. It is inappropriate to use the notation of left and right aortic sinuses when there is an anomalous aortic origin of one of the coronary arteries. The categorisation proposed by the working group of Leiden (Gittenberger-de Groot et al., 1983) is based on the view by an observer positioned in the sinus farthest from the pulmonary trunk. The sinus at the right hand of the observer is named sinus 1 and gives rise to the right coronary artery in the normal heart, whereas the sinus at the left hand is named sinus 2 and normally gives rise to the left coronary artery. Another classification is used in this review with the two sinuses adjacent to the pulmonary trunk called respectively appropriate sinus and opposite sinus. The origin of mistakes that occur in the literature is often due to the confused interpretation describing the relationships of the ectopic coronary arteries with the adjacent structures, mainly the great vessels. The schematic representation, often cited, with a cross-section view of the aortic and pulmonary valves is erroneous. Indeed, the aortic and pulmonary annuluses are not in the same plane and the latter is more superior. Therefore, it is easy to understand that the initial path of the RCA is facing the subpulmonary infundibulum and not the pulmonary trunk (figure 2). According to the position and the

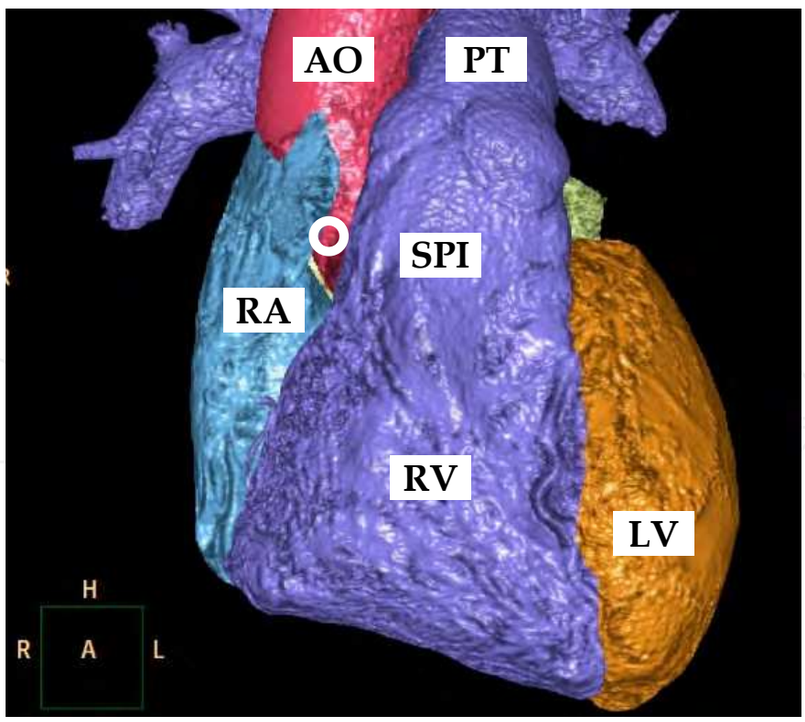

Fig. 2. Volume-rendered computed tomography image of the heart with the normal origin of the right coronary artery (white circle) marked. AO: aorta, LV: left ventricle, PT: pulmonary trunk, RA: right atrium, RV: right ventricle, SPI: subpulmonary infundibulum.

orientation of the initial pulmonary trunk, the origin of the LCA is hidden by the pulmonary trunk. Consequently, it is crucial to accept that the initial preaortic course of an ectopic coronary artery may be in contact with the subpulmonary infundibulum or pulmonary trunk or both. Thus, the definition of the so-called interarterial course is too simplistic in our opinion. Another major pitfall in this field is the confused anatomical interpretation of the space between the aortic and pulmonary roots. In fact, there is no muscular septum between the origins of the great vessels (Loukas et al., 2009). Therefore, the visualization of an ectopic coronary artery coursing between the subpulmonary infundibulum and the interventricular septum does not necessarily imply an intramyocardial course. The ectopic vessel passes rather on the myocardial septum and close to the subpulmonic infundibulum. Thus, for the reasons discussed above, we chose to identify 4 ectopic courses regarding their relationships with the great vessels: preinfundibular, retroinfundibular, preaortic and retroaortic courses, in opposition to the usual definition with 4 ectopic courses: prepulmonary, intraseptal, interarterial and retroaortic courses (Roberts & Shirani, 1992).

At the level of the aortic and pulmonary valves, the aortic and pulmonary walls are in close contact surrounded by large fatty tissues. The adjacent area between the great vessels may vary according to age, intrathoracic deformations, and acquired heart diseases. A clockwise or counter-clockwise rotation of the aortic root can modify the relationship of a normal coronary origin with the pulmonary trunk or subpulmonary infundibulum.

3. Classification

So far, no consensus exists to define and classify easily the wide spectrum of the congenital coronary artery abnormalities (Angelini, 2002). Numerous, sometimes long or complex, descriptions have been presented in the literature (Angelini 2007, Dodge-Khatami et al., 2000, Jacobs & Mavroudis, 2010, Rigatelli et al., 2009, Roberts, 1986). We propose, in this review focused on the proximal anomalous connections of the coronary arteries, a simplified classification with 8 types (table 2). This classification is based on an anatomical view with the contribution of postmortem data (Frescura et al., 1998) and recent imaging modalities. By definition, the abnormalities involve the orifices of the LCA and RCA, and their branches. Different types of ANOCOR may be observed in the same patient. Diagnosis of ANOCOR is sometimes uncertain, especially in cases of an incomplete or poor-quality imaging. We consider that an accurate anatomical diagnosis should be the first step when an ANOCOR is suspected.

type I	anomalous connection with the opposite sinus
type II	anomalous connection with the contralateral artery
type III	anomalous connection with the appropriate sinus
type IV	anomalous connection with the non-coronary sinus
type V	anomalous connection above the sinotubular junction
type VI	single coronary artery
type VII	anomalous connection with the pulmonary artery
type VIII	other abnormalities

Table 2. Simplified classification of proximal anomalous connections of the coronary arteries.

3.1 Anomalous connection with the opposite sinus (type I)

The ectopic orifice may be in contact with the ostium in right location or close to the latter (figure 3). The main anomalies involve a RCA arising from the opposite sinus, a left main coronary artery (LMCA), or a left anterior descending (LAD) coronary artery and/or circumflex (CX) coronary artery arising from the opposite sinus.

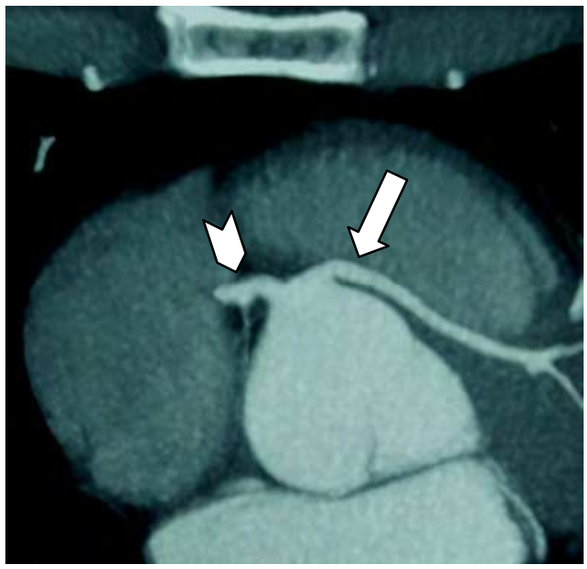

Fig. 3. Axial computed tomography image showing an anomalous connection of the left main coronary artery (arrow) with the opposite sinus close to the normal origin of the right coronary artery (arrow head).

3.2 Anomalous connection with the contralateral artery (type II)

By definition, the RCA is the contralateral artery of the LCA, and the LCA the contralateral artery of the RCA. In most cases, an anomalous connection in the contralateral artery results in a unique coronary ostium (figure 4).

Generally, this abnormality is not separated from the anomalous connection with the opposite sinus. In our opinion, it seems interesting to make a difference between these abnormalities. Firstly, a connection of the ectopic coronary artery with the proximal segment of the contralateral involves, almost without exception, the LCA or their branches. Secondly, in theory, the risk of intramural course can be excluded. Finally, this classification may include an anomalous origin distant from the aorta. In theses uncommon cases, the classification used in this study implies that an anomalous connection can exist between two coronary arteries whatever the level of the connection from the origin to the distal segment. The anomalous connections of the LCA with the opposite sinus or contralateral artery are generally associated with an absent LMCA in the appropriate sinus. However, rare cases of atresia of the LMCA originated from the left coronary sinus have been described (Levisman et al., 2009) with an embryonic small vessel often solely visible by CT.

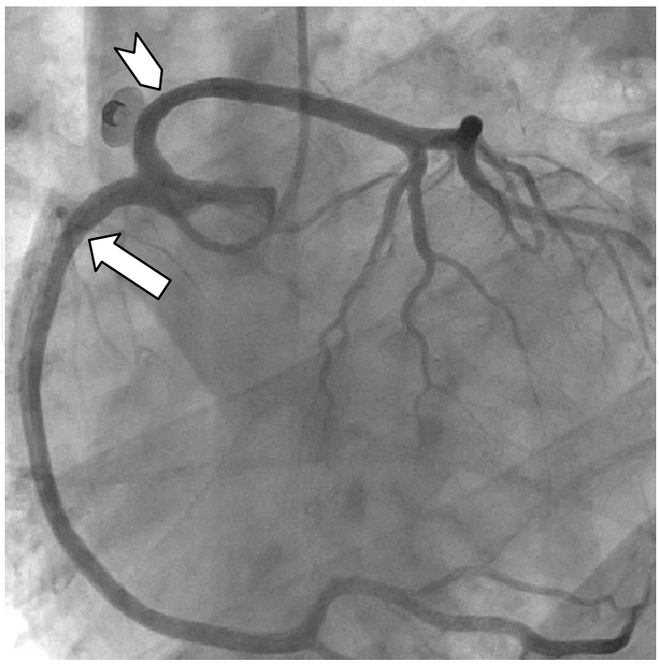

Fig. 4. Angiographic view showing an anomalous connection of the left main coronary artery (arrow head) with the proximal right coronary artery (arrow).

3.3 Anomalous connection with the appropriate sinus (type III)

An anomalous orifice of a coronary artery is usually linked with an ectopic ostium. Nevertheless, in rare postmortem observations (Frescura et al., 1998), a valve-like stenosis has been described with a ridge, consequence of an aortic wall fold that is in contact with an ostium in right position. Recently, a LMCA originated from the left sinus in the usual site, but with a slit-like orifice due to a tangential initial course associated with a short intramural segment, has been described (Angelini et al., 2010). An ectopic origin of a coronary artery in the appropriate sinus remains possible, but the limit between a true abnormality and a common variant may be tenuous, such as a connection in the lower half of the sinus, or near the commissural junction between the left and right cusps.

3.4 Anomalous connection with the non-coronary sinus (type IV)

ANOCOR from the non-coronary sinus proved by surgical or postmortem examination were previously described as exceptional. Nevertheless, a higher frequency of the latter is noticed in recent studies using tomographic imaging.

3.5 Anomalous connection above the sinotubular junction (type V)

A high take-off from the aorta at least 10 mm above the sinotubular junction is generally considered as an anomalous connection (Hlavacek et al., 2010). However, the height of take-off judged to represent the abnormality is based on few solid data. Indeed, a level of 4 mm has been reported in a postmortem study (Frescura et al., 1998). Therefore, the criteria to determine an anomalous aortic origin above the sinotubular junction should be redefined with the contribution of non-invasive imaging. Usually, the ectopic vessel continues to arise above the appropriate sinus (figure 5).

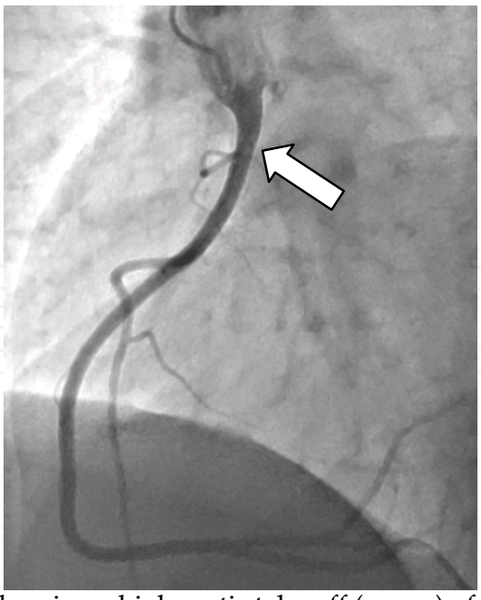

Fig. 5. Angiographic view showing a high aortic take-off (arrow) of the right coronary artery.

3.6 Single coronary artery (type VI)

The definition of a single coronary artery is often ambiguous in the literature. In our view, a single coronary should be clearly differenced from an ANOCOR with a single ostium, as described on figure 5. In both cases, the solitary vessel supplies the entire coronary circulation. Nevertheless, the flow is always antegrade beyond a single ostium, while a single artery supplies the coronary circulation of a part of the myocardium by a retrograde filling (figure 6). Moreover, with our definition, a single coronary artery is never associated with an abnormal proximal course.

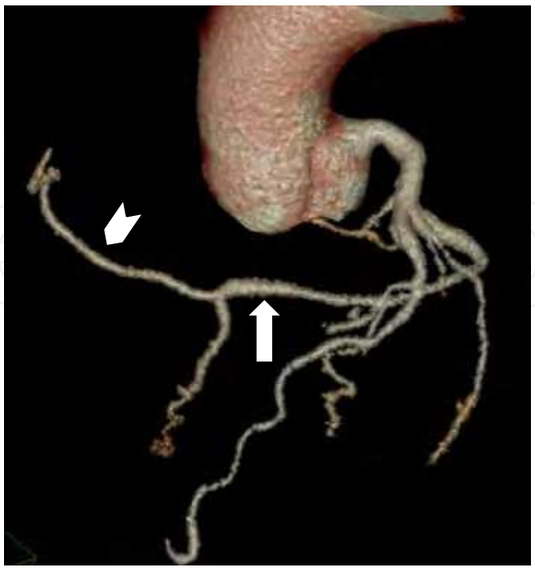

Fig. 6. Volume-rendered computed tomography image showing a single coronary artery with a normal left ostium, and a circumflex coronary artery (arrow) supplying the myocardium usually fed by the right coronary artery (arrow head).

3.7 Anomalous connection with the pulmonary artery (type VII)

In patients with anomalous connection with the pulmonary artery, the most commonly artery is the LMCA. Usually, the latter is connected with the left posterior pulmonary sinus, facing the left posterior aortic sinus. Numerous epicardial collateral vessels are observed between the anomalous coronary artery that arises from the pulmonary artery and the normal contralateral coronary artery that arises from the aorta (fig 7). An origin of the RCA from the pulmonary artery is less frequently than the LCA.

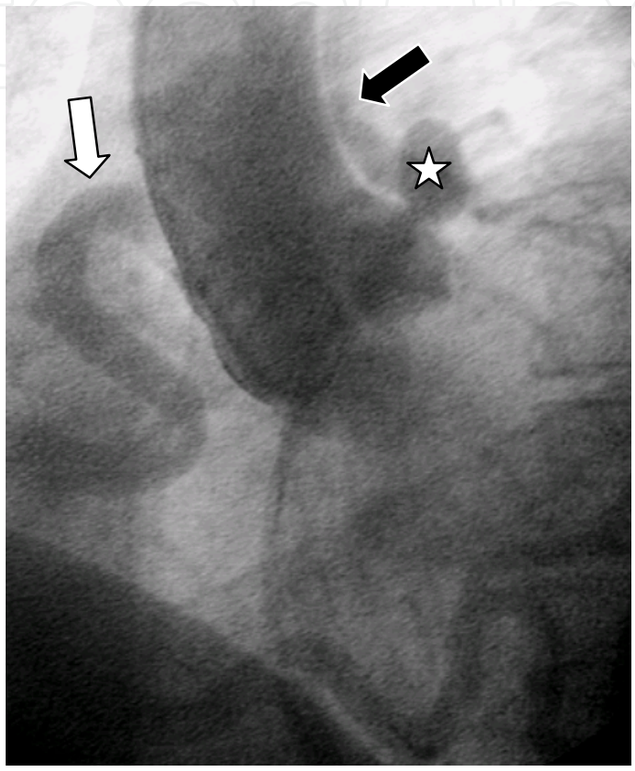

Fig. 7. Aortic angiography view showing an anomalous connection of the left main (white star) with the pulmonary trunk (black arrow) with an enlarged right coronary artery (white arrow) filling by a retrograde flow the left coronary circulation.

3.8 Other abnormalities (type VIII)

Numerous other ANOCOR have been reported in the literature, but with a very low incidence. Beside anomalous connections in the aorta or the pulmonary artery, an ectopic origin from a brachiocephalic artery, bronchial artery or internal mammary artery is possible, but anecdotal. A rotation of the aortic root may modify the position of normal coronary origin regarding the pulmonary trunk or subpulmonary infundibulum. The latter is on the border between a true ANOCOR and an acquired anomaly.

4. Prevalence

Data are numerous in literature about the angiographic prevalence of congenital coronary abnormalities. The latter are found in >1% including abnormalities of origin and

distribution, anomalies of coronary termination, and often some anatomical variants. If any anatomical pattern observed in >1% of an unselected population is considered as normal or variant of normal, then an anomalous origin of the coronary arteries is not exceptional. Indeed, the angiographic prevalence is around 0.5% in a cohort pooling several studies published since 1990 (Angelini et al., 1999, Aydinlar et al., 2005, Cieslinski et al., 1993, Garg et al., 2000, Kardos et al., 1997, Ouali et al., 2009, Rigatelli et al., 2003, Tuncer et al., 2006, Yamanaka et al., 1990) and with the possibility to individualise clearly the following ANOCOR: anomalous connection with the opposite sinus or non-coronary sinus, anomalous connection with the contralateral coronary artery, single coronary artery, and anomalous connection with the pulmonary artery. The latter was excluded in one study (Ouali, 2009). In this large (n=236,694) and relatively homogeneous cohort of adults with no structural congenital defect, 1 067 anomalous origins were identified, therefore a mean prevalence of 0.45% (table 3). The latter is ranged between 0.2 and 1.7%. The highest prevalence is observed in the sole prospective study, rather performed by a well-renowned team, recognized as an expert in the field of ANOCOR (Angelini et al., 1999). Otherwise, a misdiagnosis (as in most cases of "missing" coronary arteries) may explain some differences of prevalence, especially in the old retrospective studies. The high take-off from the aorta and the anomalous connection with an unusual site of the appropriate sinus were not included in this cohort.

Authors	Coronary angiograms n	Anomalous connections n	Anomalous connections %
Angelini, 1999	1,950	34	1.7
Aydinlar, 2005	12,059	39	0.3
Cieslinski, 1993	4,016	22	0.5
Garg, 2000	4,100	35	0.9
Kardos, 1997	7,694	39	0.5
Ouali, 2009	7,330	20	0.3
Rigatelli, 2003	5,100	34	0.7
Tuncer, 2006	70,850	110	0.2
Yamanaka, 1990	126,595	734	0.6
Total	236,694	1,067	0.45

Table 3. Angiographic prevalence of proximal anomalous connections of the coronary arteries in adult populations.

The prevalence of ANOCOR varies according to the type of coronary artery and connection (table 4). The most frequent anomaly involves the CX coronary artery with a prevalence of 3/1 000, while the anomalous connection with the pulmonary artery is the less frequent abnormality with a prevalence of 8/100 000. Both anomalous connections of the LMCA and of the LAD coronary artery are observed with a prevalence of 2/10 000. The prevalence of an ectopic origin of the RCA is of 1/1 000. The related frequency (4/10 000) of a single artery is certainly overestimated in the cohort. Indeed, contrary to the classification used in our review, most previous studies categorized a single ostium with an abnormal proximal course, as a single artery. Some patterns, generally not counted, are identified with difficulty by angiography. That is the case of an abnormal origin above the sinotubular junction. Two-

hundred-and four (0.2%) high take-off from the aorta, most commonly the RCA, were reported in a large study (Yamanaka et al., 1997). In only one study (Angelini et al., 1999), an anomalous connection with an unusual site of the appropriate sinus was noticed, regarding the RCA without exception, with a prevalence of 1.1%. Few studies distinguished origin from the opposite sinus and from the contralateral artery. In the CASS study, among 71 anomalous origins, 52 (73%) arose from the opposite sinus and 19 (27%) from the contralateral artery (Click et al., 1988).

Type of anomaly	Number	%
Anomalous aortic connection of the left main coronary artery	49	0.02
Anomalous aortic connection of the left anterior descending coronary artery	55	0.02
Anomalous aortic connection of the circumflex coronary artery	636	0.3
Anomalous aortic connection of the right coronary artery	226	0.1
Anomalous connection with the pulmonary artery	18	0.008
Single artery	83	0.04

Table 4. Angiographic prevalence of abnormalities of the coronary arteries according to the type of coronary artery and connection in a population of 236,694 adults.

A more accurate analysis of ANOCOR needs other imaging modalities. The diagnosis of some ANOCOR suspected during conventional angiography should be confirmed by cardiac CT scan. The studies (Fujimoto et al., 2011, Rodriguez-Granillo et al. 2009, Schmitt et al., 2005) assessing the prevalence of ANOCOR with CT scan reported a higher rate of abnormalities, even if the patients referred for CT following selective coronary angiography were excluded (table 5). This fact is due on several reasons. On the one hand, a more accurate diagnosis of ANOCOR is performed with CT scan in comparison with conventional coronary angiography. On the other hand, some patterns of ANOCOR are easily discovered only by CT scan, such as anomalous connection with an unusual site of the appropriate sinus, high take-off form the aorta or orthotropic origins from the clockwise or counter-clockwise rotated aortic root (Schmitt 2005). With these additional abnormalities, the CT prevalence of ANOCOR, in a cohort pooling 8,184 adults from 3 studies (table 5), is of 1.3%.

Authors	Computed tomography n	Anomalous connections n	Anomalous connections %
Fujimoto, 2011	5,869	74	1.3
Rodriguez-Granillo, 2009	577	6	1.0
Schmitt, 2005	1,738	24	1.4
Total	8,184	104	1.3

Table 5. Computed tomography prevalence of anomalous connections of the coronary arteries in adult populations.

The prevalence of ANOCOR in a general population, for example at birth, remains unknown. Large studies based on an autopsy population without methodological biases are lacking. Otherwise, the aforementioned angiographic prevalence involves, almost without exception, adult populations.

5. Orifices, initial and ectopic courses

An exact analysis of the orifices and courses of ANOCOR is of crucial importance, while the pathophysiological mechanisms of cardiac adverse events are mainly based on anatomical findings.

5.1 Orifices

A normal coronary orifice is more or less round, or slightly ovoid. Our knowledge about orifices of ANOCOR is mostly taken from postmortem (Frescura et al., 1998, Kragel et al., 1988) and individual peroperative examinations. The invasive coronary arteriography has understandable limitations for the visualization of the orifice shape. More recently, qualitative and quantitative assessment of the orifices and initial paths of ANOCOR has been documented by IVUS during conventional coronary angiography (Angelini et al., 2003). It is important to consider that an anomalous origin of a coronary artery does not imply systematically an abnormal shape of its orifice. The ANOCOR connected with the contralateral artery must have, in theory, a normal coronary orifice. Indeed, the initial segment, the first millimetres at least, of the ectopic coronary has a normal angulation (>45°) with the contralateral artery. On the contrary, the anomalous origins from the inappropriate sinus with an initial course tangential to aorta are most often associated with an abnormal orifice. A slit-like ostium is generally described in the postmortem descriptions. A similar feature is found by surgeons through an intra aortic view (figure 8). Rare selective coronary angiograms suggest the presence of a membrane-like ostial stenosis (Angelini et al., 2006). As mentioned above, an abnormal orifice of a coronary artery connected with the usual site of the appropriate sinus has been described, but rarely (Frescura et al., 1998).

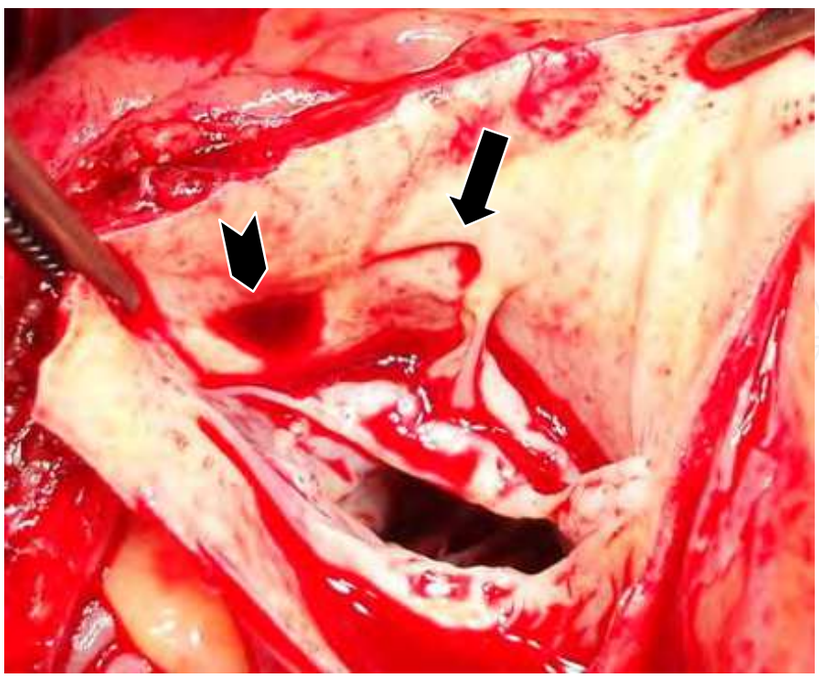

Fig. 8. Peroperative view showing an ectopic origin of the right coronary artery (arrow) from the left sinus close to the origin of the left coronary artery (arrowhead).

5.2 Initial courses

It is admitted that a slit-like orifice, almost without exception, is associated with an intramural course. The latter means a course of the first millimetres of the ectopic vessel in the aortic media. Therefore, no adventitia exists between the coronary media and aortic media. The length of the intramural path is ranged from 5 to 25 mm, much longer for the left ANOCOR (Angelini & Flamm, 2007). An intramural course is not synonymous with a preaortic course, and inversely (Houyel & Planché, 2008). The ANOCOR arising from the opposite sinus, and without a preaortic or retroaortic course, have generally a normal orifice, while they move quickly from the aorta, and their initial courses are therefore extramural. The ANOCOR with a retroaortic course have in most cases a juxtamural course regarding the aorta, although rare observations with abnormal orifice and/or intramural course have been reported. The ANOCOR with a high take-off above the sinotubular junction may have an abnormal orifice with a vertical intramural initial course. Generally, the orifice of the anomalous connections with the pulmonary artery is circular with an extramural or juxtamural initial course. Coronary IVUS, now easily available, gives important quantitative parameters regarding the orifices and initial courses of ANOCOR (Angelini & Flamm 2007). The ellipsoid shape of an ectopic orifice is well visualized. Also important, coronary IVUS highlighted systematically a hypoplasia of the intramural segment in comparison with the more distal, extramural segment.

5.3 Ectopic courses

The ectopic course of an ANOCOR may be defined as the coronary path between the orifice and the point where the ectopic artery meet up with an appropriate myocardial area. The length of the ectopic course varies considerably regarding the site of ectopic ostium and relationships with the adjacent structures. The definitions of different ectopic courses are still used in an ambiguous fashion. Usually, 4 subgroups of anomalous origin of the LCA from the opposite sinus are described: anterior to pulmonary trunk, between aorta and pulmonary trunk, in ventricular septum, and posterior to aorta courses (Roberts & Shirani, 1992). For the purpose of being close to the anatomical descriptions and recent imaging contributions, we classify the ANOCOR into 7 courses relating to their links with the great vessels and/or ventricles (table 6). We chose to define each course according to the closest adjacent cardiac structure (figure 9).

type A	preinfundibular course
type B	retroinfundibular course
type C	preaortic course with intramural path
type D	preaortic course without intramural path
type E	retroaortic course
type F	absent proximal ectopic course
type G	other ectopic courses

Table 6. Different courses of anomalous origins of the coronary arteries.

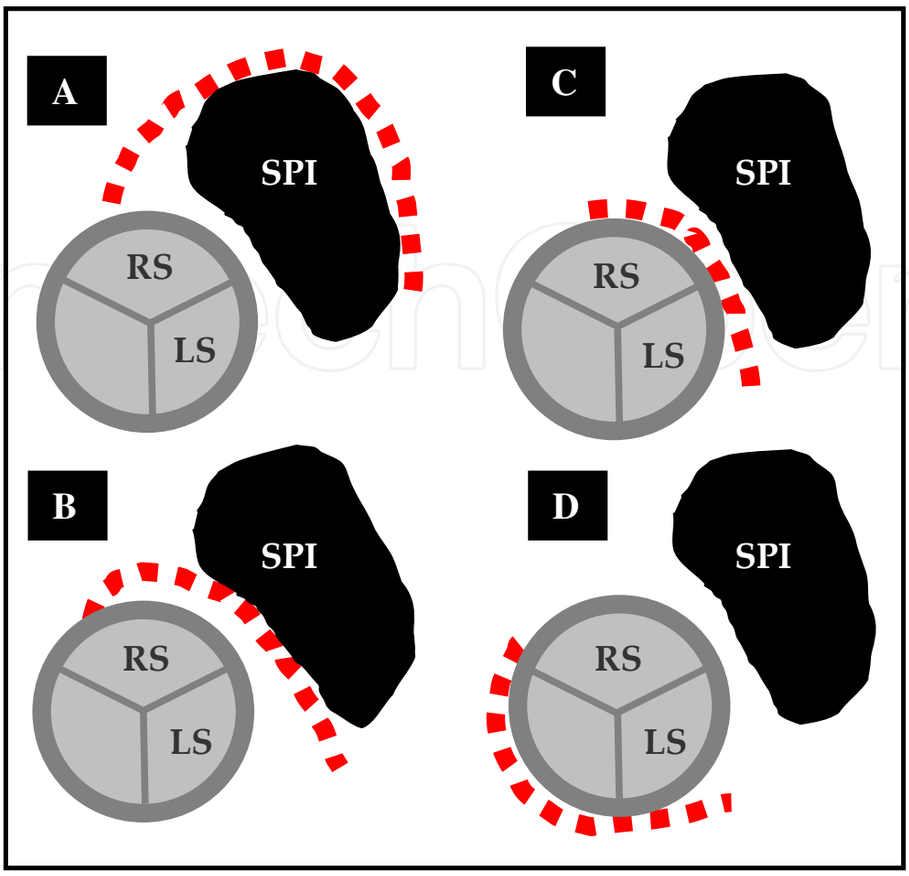

Fig. 9. Anatomic representation of the courses of an anomalous left coronary artery arising from the right sinus. A: preinfundibular course, B: retroinfundibular course, C: preaortic course, D: retroaortic course. LS: left sinus, RS: right sinus.

5.3.1 Preinfundibular course (type A)

The prepulmonary course involves the ectopic paths coursing on the surface of the pulmonary trunk or subpulmonary infundibulum. The latter is mostly concerned. In case of a long and sinuous course, both pulmonary trunk and subpulmonary infundibulum may be in contact with the ectopic vessel. The vessel coursing with a prepulmonary path, almost without exception, is the left coronary artery (LMCA or LAD or septal branch arising from the opposite sinus or the RCA).

5.3.2 Retroinfundibular course (type B)

A clear understanding of the retroinfundibular course remains difficult. Due to a low risk of lethal cardiac events, examinations of heart specimens with a retroinfundibular course are rare. However, tomographic imaging allowed a better analysis of their relationships with the adjacent structures (figure 10). The retroinfundibular course, without exception, involves the LCA and their branches. The ectopic vessel first courses behind the subpulmonary infundibulum, then crosses between the latter and the ventricular septum, and finally emerges from the interventricular space to join the left ventricle on the epicardial surface at the mid LAD level. In the literature, the retroinfundibular course is also known as

subpulmonic or intraseptal or intraconal course. The nomenclature used in this review appears more appropriate regarding the cardiac anatomy. The left coronary artery (LMCA or LAD) with retroinfundibular course provide always one or more septal branches in the floor of the right ventricular outflow tract.

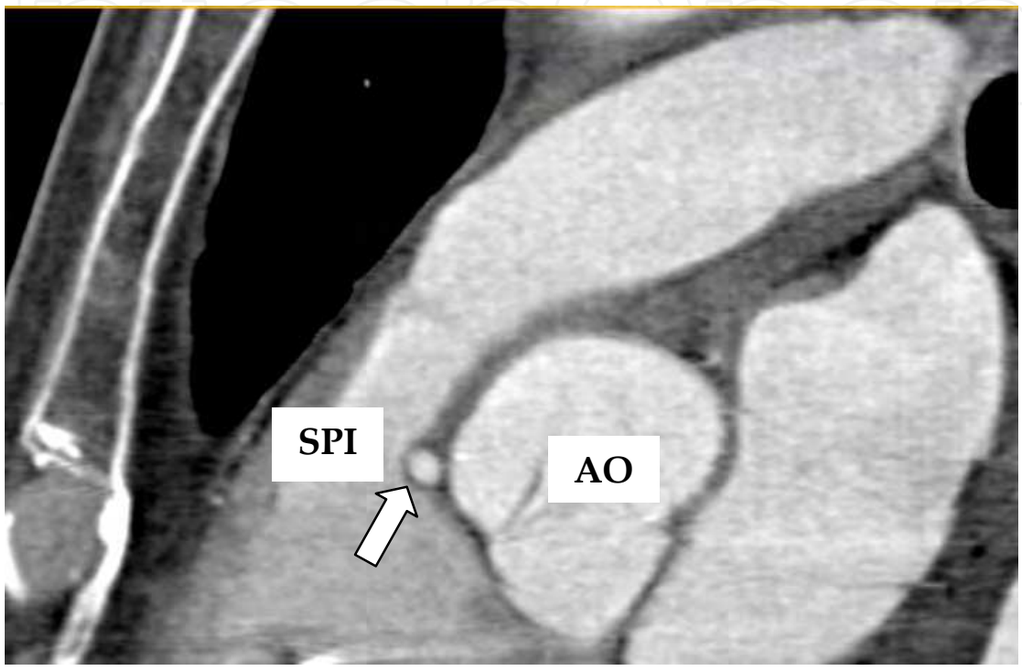

Fig. 10. Computed tomography imaging of an ectopic left main coronary artery (arrow) arising from the right sinus with a retroinfundibular course. AO: aorta, SPI: subpulmonary infundibulum.

5.3.3 Preaortic course with intramural segment (type C)

The typical preaortic course is tangential to the aorta through the fibroadipose tissue separating the arterial roots, (figure 11). Nomenclatures using the so-called interarterial course, in other words between the aorta and the pulmonary artery, may be ambiguous. In fact, a LCA connected in the opposite sinus or contralateral artery, and coursing anterior to the aorta, is in contact first with the subpulmonary infundibulum. A close contact with the pulmonary trunk is also possible because a LCA arising from the opposite sinus with a preaortic path, courses distally near the usual origin of the vessel before to join the interventricular groove. Conversely, an ectopic RCA is in contact first with the pulmonary trunk and then with the subpulmonary infundibulum before to join the atrioventricular groove. ANOCOR with high take-off from the aorta above the sinuses have, by definition, a preaortic course. The presence of an intramural segment, as defined above, must be systematically looked for in order to stratify the risk.

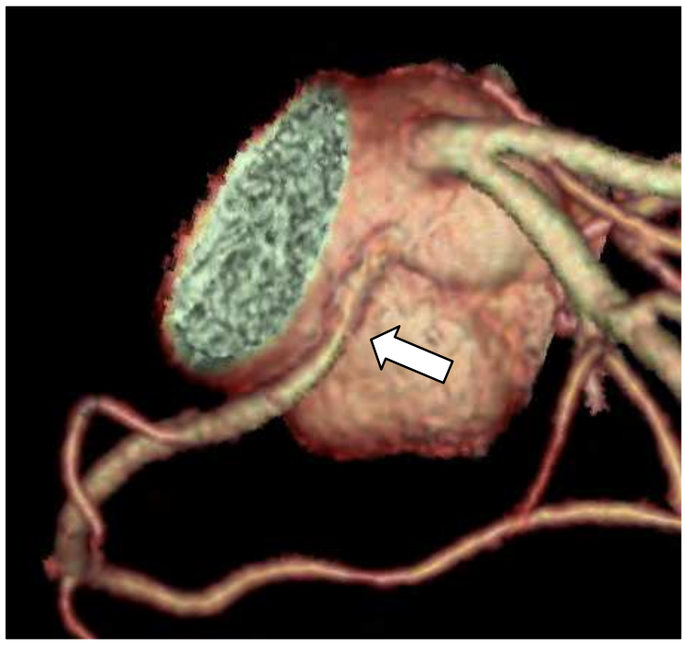

Fig. 11. Volume-rendered computed tomography images of an ectopic right coronary artery (arrow) arising from the left sinus with a preaortic course tangential to the aorta.

5.3.4 Preaortic course without intramural segment (type D)

As mentioned before, a preaortic course without intramural segment is possible, for example an ectopic vessel with an orthogonal take-off from the contralateral or a high origin from the aorta. The ectopic course is juxtamural with the aorta. Making a distinction between preaortic course without intramural segment and preaortic course with intramural course is essential, while the latter has a recognized higher risk of life-threatening symptoms.

5.3.5 Retroaortic course (type E)

The retroaortic course, the most commonly encountered ectopic course, is also the easier to diagnose. This course involves, almost without exception, the LCA. Unlike other coronary arteries, the CX coronary artery is associated, to the exclusion of uncommon patterns, with the same ectopic course, i.e. a retroaortic course. The ectopic vessel courses first behind or more precisely below the aorta, then crosses between the aortic root and the left atrium with a juxtamural course, and finally emerges into the left atrioventricular groove between the left atrial appendage and the left atrium (figure 12).

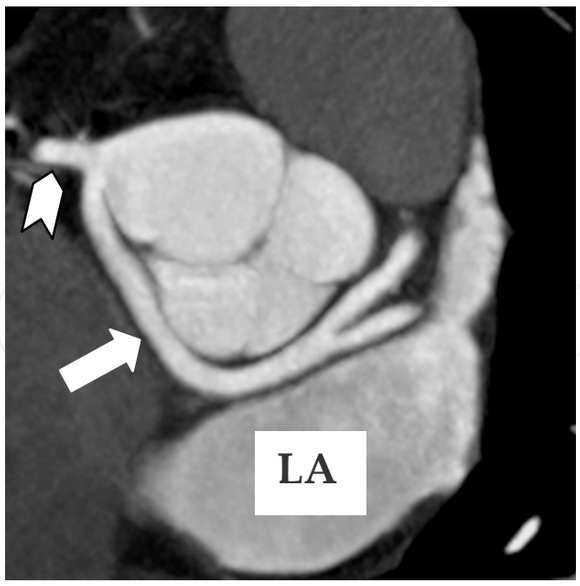

Fig. 12. Computed tomography imaging of anomalous connection of the left main coronary artery (arrow) with the right sinus close to the right coronary artery (arrowhead). LA : left atrium.

5.3.6 Absent proximal ectopic course (type F)

As mentioned above, a single coronary artery is never associated with an abnormal proximal course. The myocardium usually dependant on the absent coronary artery is fed by a retrograde flow using a coronary network, near normal. Besides, a coronary artery, connected with the contralateral artery far from the proximal segment of the latter, may have normal relationships with the cardiac structures.

5.3.7 Other ectopic courses (type G)

Rare ANOCOR, such as abnormal origin from the aortic arch, may have another ectopic course, often complex, in contact with several structures. A LMCA with an anomalous connection with the pulmonary trunk courses usually facing the left side of the latter.

6. Angiographic diagnosis of ectopic vessels and courses

6.1 Angiographic diagnosis of ectopic vessels

The diagnosis of ANOCOR in adult patients is usually suspected or achieved during a selective coronary angiography scheduled to evaluate or to rule out a CAD. The invasive coronary angiography is no longer considered the method of choice, in other terms *the gold standard*, for an accurate diagnosis of ANOCOR. Studies have described the correlations between invasive angiography and CT angiography but always in small populations. Correct identification of the ectopic vessel was achieved by conventional angiography in 69% (9/13) of ANOCOR (Shi et al., 2004). Selective catheterization and precise vessel determination was possible in only 53% (8/15) of ANOCOR (Schmitt et al., 2005). The coronary abnormality was accurately depicted in 44% (4/9) of ANOCOR (de Jonge et al., 2008). Several shortcomings of the conventional angiography are obvious, such as a difficult canulation of the abnormal orifice, a two-dimensional interpretation of the ectopic course, or

an incomplete visualization of the ectopic vessel, leading to an erroneous diagnosis, particularly if the angiographer is not aware with the congenital coronary abnormalities. In addition, the selective coronary angiography is not able to analyse the shape of the ectopic orifice, to quantify a hypoplasic segment exactly, or to identify an intramural course. Despite these limitations, often some angiographic views typically make an interpretation easier.

6.1.1 Angiographic diagnosis of anomalous connection with the opposite sinus (type I)

Selective angiography of some ANOCOR arising from the opposite sinus may be a challenge, especially with the RCA. The origin of the latter is often characteristic with an orifice at the level of the sinotubular junction and close to the commissural zone between the right and the left coronary cusps. The two ostia are generally non adjacent, which explains why the catheter used for the LCA does not generally find the ectopic right orifice. Other catheters (Judkins right, Amplatz left) are required. Nevertheless, the ellipsoid shape of the orifice and the lack of orthogonal take-off, explain the non rare failures of satisfactory angiography. Instead of an additional aortography, usually not very contributory, a tomographic imaging will allow the diagnosis of ANOCOR to be confirmed or not. When selective angiography is possible, the views of an ectopic RCA originated from the left sinus are typical, with a normal or slightly enlarged ostial lumen in the 30° left anterior oblique (LAO) projection, while a narrowing of the first segment is visible in the 30° right anterior oblique (RAO) projection, expressing the ellipsoid shape of the orifice and the initial intramural course (figure 13).

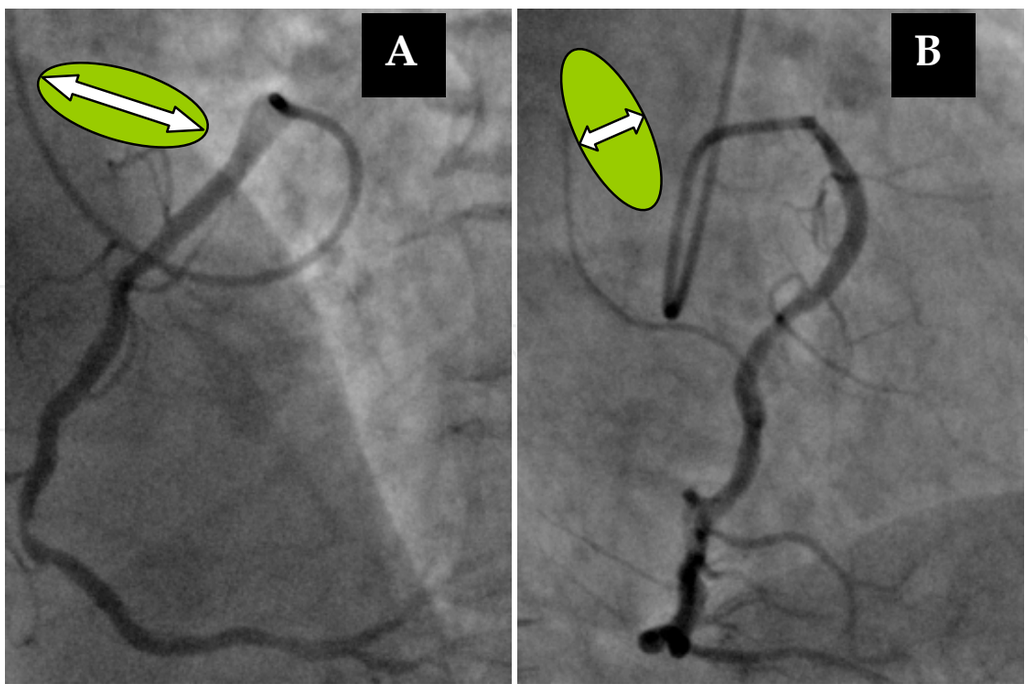

Fig. 13. Selective angiogram of an anomalous connection of the right coronary artery with the left sinus in 20° left anterior oblique projection (A) and left 30° right anterior oblique projection (B) with a schematic representation of X-ray plane (arrow).

The ectopic orifice of the left coronary artery (LMCA, LAD coronary artery or CX coronary artery) is in most cases very close to the right coronary orifice, and sometimes contiguous. Thus, a selective angiography is generally easier using Judkins right catheter or Amplatz left or right catheters. A multipurpose catheter may be useful to catheterize the orifice of an aberrant circumflex coronary artery.

6.1.2 Angiographic diagnosis of anomalous connection with the contralateral artery (type II)

Obviously, angiographic diagnosis of anomalous connection with the contralateral artery is usually easy, with the exception of a too selective angiography leading to a misdiagnosis, for example an ectopic CX coronary artery originated from the proximal segment of the RCA.

6.1.3 Angiographic diagnosis of anomalous connection with the appropriate sinus (type III)

A lack of identification remains possible. Diagnosis of anomalous connection with the appropriate sinus is usually only suspected with X-ray coronary angiography, and contribution of tomographic imaging is essential.

6.1.4 Angiographic diagnosis of anomalous connection with the non-coronary sinus (type IV)

Angiographic diagnosis of anomalous origin from the non-coronary sinus is always challenging with frequent difficulties of a selective canulation. Moreover, the interpretation of angiographic views is often ambiguous and needs complementary imaging.

6.1.5 Angiographic diagnosis of anomalous connection above the sinotubular junction (type V)

Difficulties in identifying a high take-off from the aorta by conventional angiography are non unusual. Many catheters, similar to these used for saphenous vein grafts, are often required. Moreover, an initial intramural course may make selective injections more difficult. Finally, the distinction between a normal variant of origin and a high take-off at least 10 mm above the sinotubular junction is ambiguous in most cases. Once again, the coronary CT angiography will be able to delineate accurately the level of the coronary ostia.

6.1.6 Angiographic diagnosis of single coronary artery (type VI)

The diagnosis of a single coronary artery is easy with a single orifice in the appropriate sinus and the lack of ectopic proximal course. All major coronary arteries course the atrioventricular and interventricular grooves. Coronary angiography needs large fields to visualize the whole coronary circulation.

6.1.7 Angiographic diagnosis of anomalous connection with the pulmonary artery (type VII)

Conventional angiography of anomalous connection with the pulmonary artery is not always easy. Indeed, the contralateral artery, mostly the RCA, is considerably enlarged with an ostial diameter around 10 mm and a diffused dilation of the artery, making a selective

intubation and an adequate opacification with regular coronary catheters difficult. An aortography in LAO projection is useful allowing simultaneous visualization of the aorta and the pulmonary trunk. The most common site of drainage is the pulmonary trunk. Multiple collateral vessels coursing the subpulmonary infundibulum and the right ventricle are present, as well as a large collateral circulation through the interventricular septum, between the RCA and the LCA.

6.1.8 Angiographic diagnosis of other anomalies (type VIII)

Rare abnormal origins, apart from aorta, contralateral coronary artery and pulmonary artery, are generally never identified by conventional angiography.

6.2 Angiographic diagnosis of ectopic courses

As mentioned above, the rate of an accurate diagnosis of ANOCOR is relatively low (<70%) with conventional angiography. Correct angiographic identification of the different possible courses followed by an ectopic vessel is achievable, but requires special training. Numerous examples of misinterpretation of the ectopic course in the literature imply that the rate of erroneous delineation is certainly high in the real life. Before the wide growth of non-invasive imaging, some authors have proposed interesting methods to identify the different anomalous courses of ANOCOR quickly and correctly (Ishikawa & Brandt, 1985, Serota et al., 1990). As the ectopic course of RCA and CX, almost without exception, is typical with a preaortic course and a retroaortic course respectively, these methods are only dedicated to the LCA (LCMA or LAD coronary artery) originated from the opposite sinus or the contralateral artery. The LCA may follow 1 of 4 previously described paths: preinfundibular, retroinfundibular, preaortic and retroaortic. The angiographic criteria used by Serota et al. are based on selective coronary angiograms in the RAO and LAO projections. The method suggested by Ishikawa et al. use angiographic features derived from a selective coronary angiogram in RAO projection and from a 30° RAO ventriculography. The lateral projection may be helpful in some cases. The main features are summarized in table 7. Despite of a meticulous analysis, these methods are sometimes incorrect.

6.2.1 Angiographic diagnosis of preinfundibular course

The LCA courses on the surface of the subpulmonary infundibulum and sometimes the root of the pulmonary artery, and reaches the interventricular septum at the mid LAD level. Therefore, the LAD coronary artery is relatively short. In RAO and LAO projections, the initial course of the LCA passes anteriorly and upward. The LMCA and the proximal segment of the CX coronary artery form an “eye” with the LMCA as the superior edge and the CX coronary artery as the inferior edge (figure 14).

6.2.2 Angiographic diagnosis of retroinfundibular course

The LCA courses behind the subpulmonary infundibulum, then in contact with the left ventricular septum, and finally emerges at mid LAD level. Thus, the LAD coronary artery is relatively short. In RAO and LAO projections, the initial course of the LCA passes anteriorly and downward. The upward loop of the CX coronary artery and the LMCA form an “eye”. Septal branches arising from the LMCA are an additional clue (figure 15).

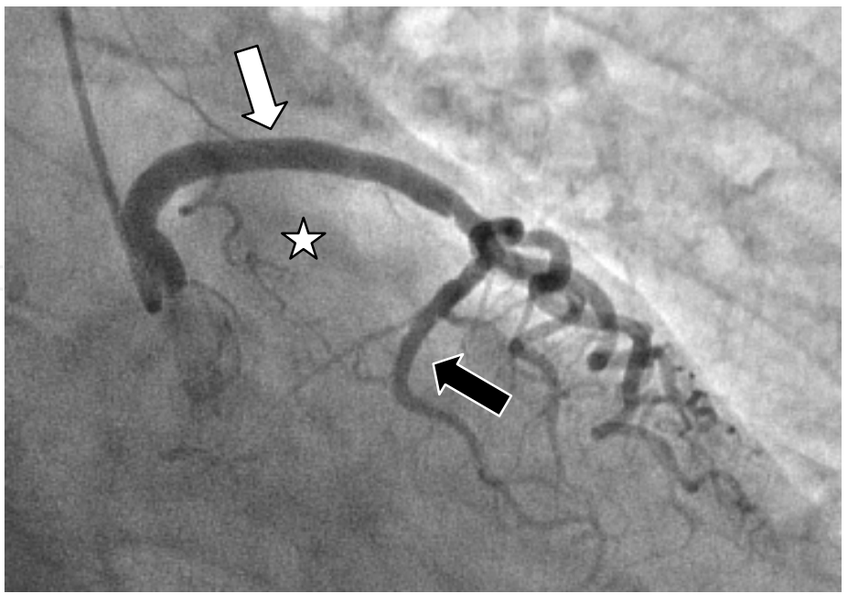

Fig. 14. Angiographic view (right anterior oblique projection) showing a preinfundibular course of a left main coronary artery (white arrow) forming an "eye" (star) with the circumflex coronary artery (black arrow).

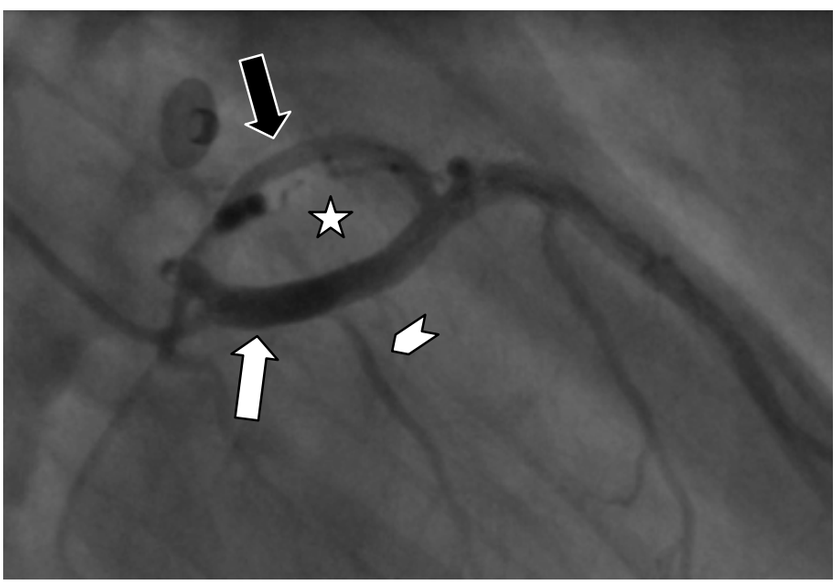

Fig. 15. Angiographic view (right anterior oblique projection) showing a retroinfundibular course of a left main coronary artery (white arrow) forming an "eye" (star) with the circumflex coronary artery (black arrow). Note a septal branch (arrow head) originated from the left main coronary artery.

6.2.3 Angiographic diagnosis of preaortic course

The LCA courses initially between the aorta and subpulmonary infundibulum, and behind the pulmonary trunk at left coronary sinus level. Then, the LMCA follows a normal course to its bifurcation. Therefore, all segments of the LAD coronary artery are visualized, and the

orientation of the CX coronary artery is normal. The initial course of the LMCA is upward and slightly posterior in RAO and LAO projections (figure 16). During 30° RAO ventriculography, the distal LMCA appears as a radiopaque "dot", anterior to the aorta.

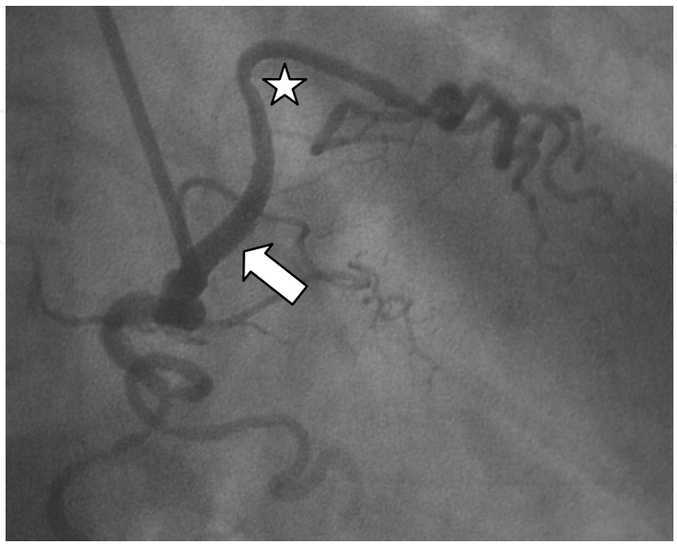

Fig. 16. Angiographic view (right anterior oblique projection) showing a preaortic course of a left main coronary artery (white arrow) arising from the right sinus with a posterior and upward loop (star).

6.2.4 Angiographic diagnosis of retroaortic course

The LCA courses behind or beneath the aorta and emerges at the left atrioventricular groove. In RAO and LAO projections, the LCA passes posteriorly and downward (figure 17). During 30° RAO ventriculography, the mid LCA appears as a radiopaque "dot", posterior to the aorta.

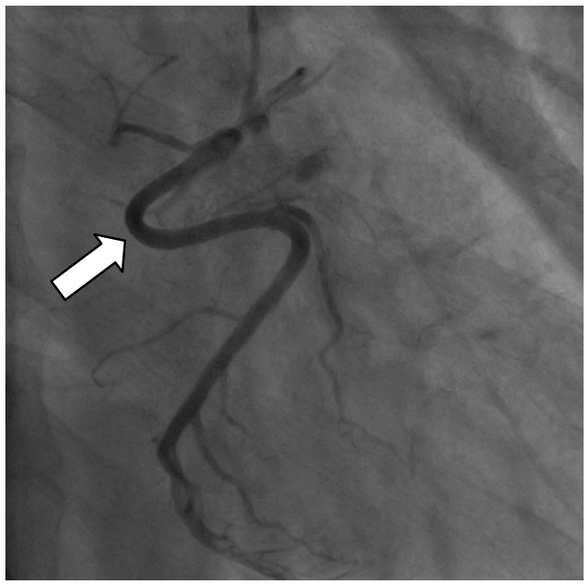

Fig 17. Angiographic (right anterior oblique projection) view showing a retroaortic course of an ectopic circumflex coronary artery (arrow) arising from the right sinus.

	ectopic course	initial loop	eye sign	dot sign	LAD length	septal branches
type A	preinfundibular	anterior and upward	yes	no	short	no
type B	retroinfundibular	anterior and downward	yes	no	short	yes
types C and D	preaortic	posterior and upward	no	yes	normal	no
type E	retroaortic	posterior and downward	no	yes	normal	no

Table 7. Main angiographic characteristics of ectopic courses of anomalous connections of the left coronary artery with the opposite sinus or contralateral artery. LAD: left anterior descending coronary artery.

7. Intravascular ultrasonography (IVUS)

IVUS is an intracoronary imaging technique which provides qualitative and quantifiable features of the coronary anatomy in ANOCOR. Its high spatial resolution about 0.15 mm achieves a good anatomic visualization of the coronary artery wall. Other imaging modalities are not too competitive to analyse the shape and area of the ectopic orifice, and to identify an intramural segment. In this field, the contribution of the group of Angelini has been essential with a routinely use of IVUS in ANOCOR with a suspected intramural course (Angelini et al., 2003, Angelini et al., 2006, Angelini, 2007, Angelini & Flamm, 2007). In ANOCOR with intramural segment, IVUS imaging often visualizes the aortic wall at the level of the ectopic orifice. Several features, similar to histological and anatomical characteristics of ANOCOR with an intramural course, are well depicted by IVUS. Pharmacologic provocative tests may be associated during IVUS procedure. IVUS use is mentioned in ACC/AHA 2008 guidelines for adults with congenital heart disease, with a recommendation of class IIa and a level of evidence C, in order to delineate potential mechanisms of flow restriction (Warnes et al., 2008). Angelini et al. have defined several consistent IVUS characteristics regarding to ANOCOR with intramural segment (Angelini & Flamm, 2007).

7.1 Abnormal orifice

The orifice is never circular with an ovoid or ellipsoidal shape. The area of the slit-like ostium is not necessary significantly reduced, like during selective coronary angiography. It is the fact that the longest diameter of the orifice may be as long as the diameter of the distal segment. Importantly, the IVUS shows a normal intima tunica without atherosclerotic plaque.

7.2 Intramural hypoplasia

An IVUS hypoplasia of the intramural segment is demonstrated with a ratio <1.0 between the intramural minimal circumference and the distal reference circumference. The length of the intramural segment, generally ranged from 5 to 15 mm, may vary depending of the site of the ectopic orifice. The narrowing diameters and surfaces must be compared with the distal reference parameters. The baseline area of stenosis is the ratio between the distal area (mm^2) minus the intramural area (mm^2), and the distal area (mm^2). The degree of area obstruction varies between 30 and 70%.

7.3 Lateral compression

The intramural segment of the ectopic has an abnormal shape (figure 18), resulting from a shared media with the aorta and a probably incomplete growth of the ectopic vessel in the aortic wall. The cross section is more or less oblong. The lateral compression is defined as a smaller area than that possessed by a circle of the same circumference. This parameter is quantified with the asymmetric ratio of the smallest to the largest diameter <1.0.

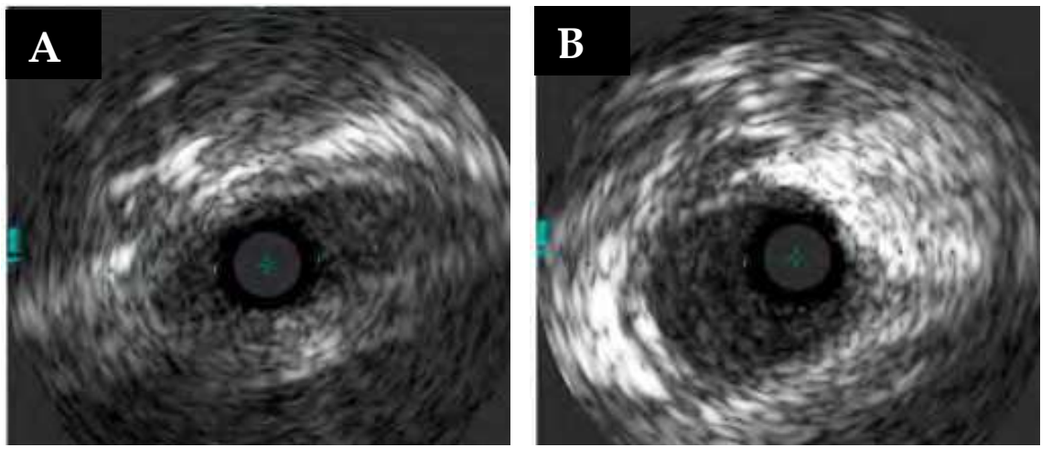

Fig. 18. Intravascular ultrasound images showing the intramural segment (A) and the extramural segment (B) of an ectopic right coronary artery connected with the left sinus.

Despite first promising results, the IVUS imaging tool has several limits. Non selective canulation of the vessel may disrupt the procedure. The possibility of artefacts has been pointed out, as well as the decreasing in the precision of measurements, due to the tangential orientation of the vessel (Angelini & Flamm, 2007). Moreover, ST-T changes and angina may occur during IVUS manoeuvres.

8. Non-invasive imaging modalities

Selective coronary angiography does not always assure the diagnosis of ANOCOR, particularly to identify accurately the origin of the RCA from the left sinus, or to delineate the initial course of an ectopic vessel. Over the last decade, the multislice tomographic imaging made dramatically breakthroughs, so much that the electrocardiography-gated multidetector coronary CT angiography has become the method of choice for evaluation of known or suspected ANOCOR (Sundaram et al., 2010). Tomographic reconstructed images provide useful supplemental information with volumetric views allowing an analysis of ANOCOR in 3-D spatial orientation (Gharib et al., 2008, Manghat et al., 2005). However, other non-invasive methods have been used to diagnose or evaluate ANOCOR.

8.1 Echocardiography

Transthoracic echocardiography (TTE) is not commonly used to examine the coronary arteries. The parasternal short-axis plane, with the help of the colour flow mapping, is the best view for an echographic visualization of the coronary origins (Frommelt et al., 2003). Nevertheless, the ability of the TTE to identify the coronary origins with confidence becomes less easy with age and increase in the body mass. Transoesophageal

echocardiography (TEE) may improve the imaging quality (figure 19) but not necessarily the diagnostic ability. Several studies have reported the echocardiographic prevalence of ANOCOR particularly in paediatric populations or young adults. An anomalous connection with the opposite sinus was found in 4 cases (0.2%) in a series of 2388 children or adolescents referred for innocent murmurs or functional assessments (Davis et al., 2001), and in 3 cases (0.09%) in 3504 (mean age, 30 years) asymptomatic athletes (Zeppilli et al., 1998). In the latter study a clear visualization of both ostia was obtained in 90% of cases. Therefore, the echographic prevalence is lower than those reported with selective coronary angiography and tomographic imaging techniques. The limited discriminating power of TTE to distinguish some ANOCOR may explain this discrepancy. TTE lacks reliability to identify a small RCA or CX coronary artery with an ectopic origin. Besides, an ectopic vessel with preaortic course crosses very closely the appropriate sinus, and thus may pretend a normal origin. Nevertheless, in young adults or in patients with a satisfactory acoustic window, several echographic characteristics must be known (Cohen et al., 2010). An abnormal diastolic colour flow between the aorta and the pulmonary trunk is often the first identification of an ANOCOR with a preaortic course. However, only the first millimetres of the ectopic vessel are visualized, and, often, the TTE is inconclusive in ruling out some ectopic paths. Thus, a suspected retroinfundibular or preaortic course with TTE should be always confirmed with other imaging modalities. In addition, TTE is not able to describe the shape of an ectopic orifice and to measure a possible ostial narrowing. TEE may identify some high take-off above the sinotubular junction with the long-axis view. Echographic diagnosis of anomalous origin of the LCA from the pulmonary trunk is mainly based on indirect features with a dilation of the RCA and a multiple collateral flow through the interventricular septum. In practice, the management of an ANOCOR should never be discussed with only echocardiographic imaging in adult patient.

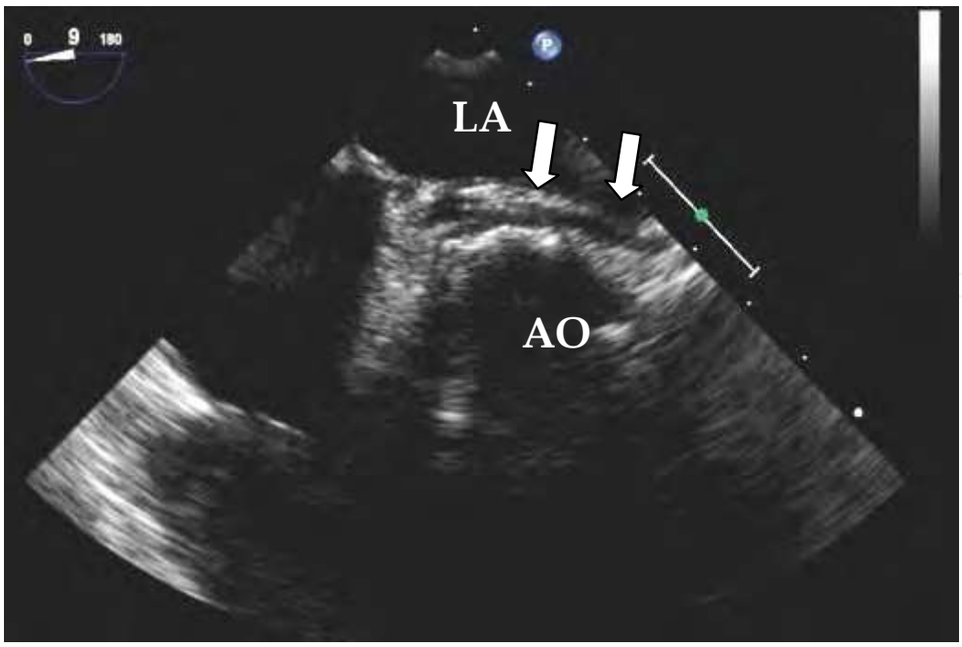

Fig. 19. Short-axis transoesphageal echocardiographic view showing an ectopic circumflex coronary artery (arrows) coursing between the aorta (AO) and the left atrium (LA) with a retroaortic course.

8.2 Magnetic resonance angiography

Magnetic resonance (MR) angiography is a non invasive imaging technique that does not expose to ionizing radiation and to potentially nephrotoxic contrast media. Cardiac MR angiography allows 3-D reconstruction of the heart and can identify the origin of coronary arteries (figure 20). The relationships with neighbouring structures are well visualized. Nonetheless, due to insufficient spatial resolution and cardiac movements, this imaging technique fails sometimes to describe accurately the anatomy of the ectopic course of the ANOCOR, especially the orifice and the visualization of a lateral compression in the aortic wall. Otherwise, MR angiography is a less available technique in comparison to the CT angiography, and identifies not as good the degree of atherosclerotic associated lesions. Nevertheless, coronary MR angiography remains an attractive option in young population to avoid ionizing radiation. Several studies have shown the feasibility of coronary MR angiography to identify ANOCOR. In a selected population of 19 patients with known ANOCOR by a previous selective coronary angiography, sensitivity and sensibility for detecting anomalous origins and ectopic courses were 100% with MR angiography (Post et al., 1995). Delineation of the ectopic course was erroneous in 3 of 19 patients (16%) with the conventional coronary angiography. The hypothesis that MR angiography may be useful in the identification of ANOCOR was confirmed in 12 of 14 patients (86%) with a known anomaly (Mc Connell et al., 1995). A series of 21 patients with known or suspected ANOCOR (9 LMCA or LAD coronary arteries, 6 CX coronary arteries and 6 RCA) underwent a MR angiography (Bunce et al., 2003). All patients had undergone a selective coronary angiography but in 11 patients (52%) the proximal course was uncertain.

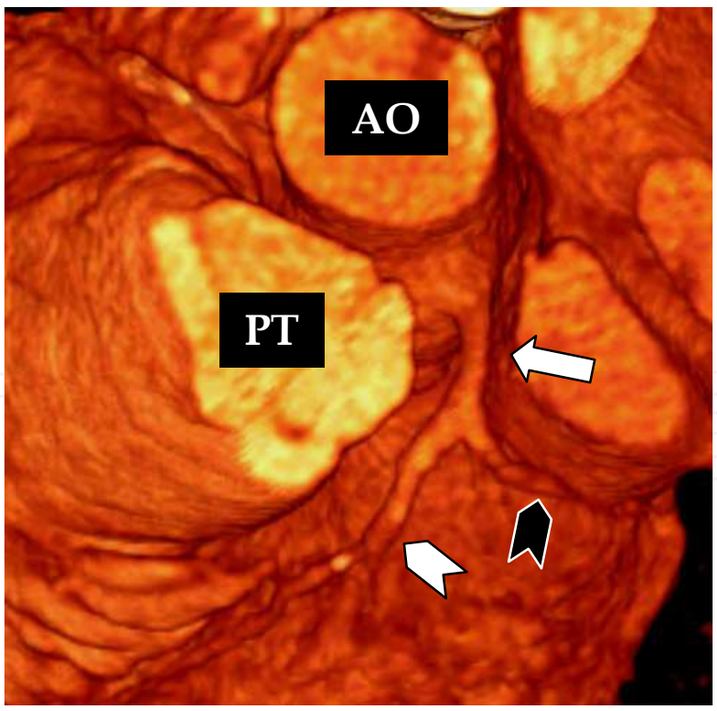

Fig. 20. Volume-rendered magnetic resonance angiography showing a normal origin of the left main coronary artery (arrow) dividing into left anterior descending coronary artery (white arrow head) and circumflex coronary artery (black arrow head). AO: aorta, PT: pulmonary trunk.

In addition, selective canulation of ectopic vessel was not possible in 3 cases, and the ectopic artery was not identified in 1 case. MR angiography depicted correctly all ANOCOR, and in 13 patients (62%) a preaortic course, which passes between the aorta and right ventricular outflow tract, was affirmed. MR angiography seems to be an accurate tool as primary investigation in symptomatic young patients. In older population, due to a higher prevalence of the coronary artery disease, the CT angiography is generally preferred.

8.3 Multidetector computed tomography angiography

In comparison with aforementioned non-invasive tools imaging, multidetector CT angiography has the major advantage of a better spatial resolution. Despite, the need of administration of contrast media and the use of ionizing radiation, the CT angiography is becoming for most practioners the preferred test in adult patients with known or suspected ANOCOR. The impressive 3-D ability of CT angiography to identify unambiguously the origin and the ectopic course of an ANOCOR (figure 21) explain easily its wide use. However, it must be remembered that the production of consistent and reliable imaging is one thing, and that the correct interpretation of the latter is another thing. In ACC/AHA 2008 guidelines for adults with congenital heart disease, CT and MR angiography are recognized useful as the initial screening method in centers with expertise in such imaging (Warnes et al. 2008).

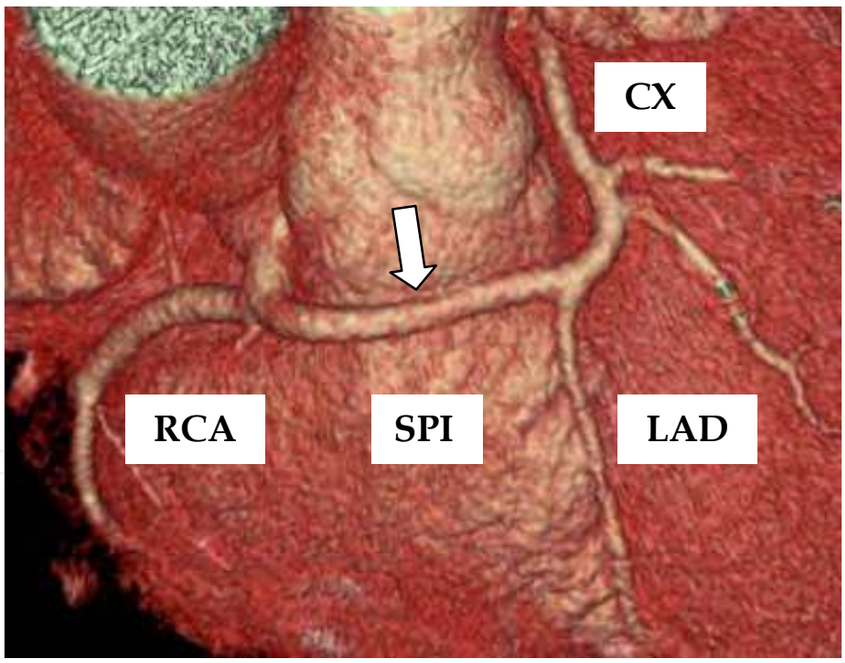

Fig. 21. Three-dimensional volume-rendered reconstruction of computed tomography showing an ectopic origin of the left main coronary artery (white arrow) arising from the right coronary artery with an ectopic course coursing on the subpulmonary infundibulum. CX: circumflex coronary artery, LAD: left anterior descending coronary artery, RCA: right coronary artery, SPI: subpulmonary infundibulum.

Numerous studies, often with small populations, have described the interest of CT angiography in the ANOCOR field. Some of them have been already mentioned above

(Fujimoto et al, 2011, Schmitt et al. 2005, Rodriguez-Granillo et al, 2009). In a series of 28 patients with known ANOCOR (4 LMCA, 15 CX coronary arteries and 9 RCA), the origin and ectopic course was correctly identified in all patients (Ropers et al., 2001). All patients had had previously an X-ray coronary arteriography. A correct analysis was achieved in only 3 patients (11%) with the latter. Nine-teen ANOCOR in 12 patients were correctly analysed with CT angiography in another small series (Datta et al., 2004). Twelve ANOCOR (1 LMCA, 1 LAD coronary artery, 4 CX coronary arteries, 5 RCA and 1 single artery) in adults patients (mean age 63 years) were analysed retrospectively with invasive (11 patients) and non-invasive tests (Leddet et al., 2008). All ANOCOR were well identified with CT angiography. However, the interpretation of one photo is ambiguous in the paper with a listed preinfundibular course instead of a retroinfundibular course. Selective coronary angiography identified accurately the origin and the ectopic course of ANOCOR in 8 of 10 cases (80%) and in 2 of 10 cases (20%), respectively. The position of CT angiography cannot be ignored either before or after invasive coronary angiography. The latter and the CT imaging are complementary in most cases of ANOCOR in adult patients (Kim et al., 2006). The main characteristics of invasive and non-invasive imaging techniques are summarized in the table 8.

Characteristics	TTE	MRA	CTA	SCA	IVUS
Invasive	no	no	no	yes	yes
Ionizing radiation	no	no	yes	yes	yes
Iodine contrast media use	no	no	yes	yes	no
Spatial resolution (mm)	0.8	1.2 x 1.8	0.5	0.3	0.15 (axial)
Visualization of adjacent structures	++	+++	+++	no	no
3-D reconstruction	no	yes	yes	no	no
Visualization of orifice	no	+	+	+	+++
Identification of intramural segment	+	+	+	+	+++
Identification of ectopic course	+	+++	+++	++	no
Identification of CAD	no	+	++	+++	+++ (limited)

Table 8. Comparison of imaging techniques in adult populations. 3-D: three-dimensional, CAD: coronary artery disease, CTA: computed tomography angiography, IVUS: intravascular ultrasonography, MRA: magnetic resonance angiography, SCA: selective coronary angiography.

Regarding to tomographic studies, the analysis of the literature shows non rare erroneous interpretations of ectopic courses of some ANOCOR, especially anomalous origins of LMCA or LAD coronary artery arising from the opposite sinus, with a misinterpretation between the preaortic course and retroinfundibular course.

9. Clinical presentations

ANOCOR are rarely recognized in infancy, except for anomalous connections with the pulmonary artery (Richard et al., 2005). Numerous clinical presentations are possible leading to the diagnosis of ANOCOR in young people and adults, but the situation seems different between < 30-year old and ≥ 30-year old. In populations with a known high prevalence of coronary artery and valvular diseases, the ANOCOR is usually diagnosed fortuitously during a selective coronary angiography. The clinical presentations are similar to those observed with symptomatic acquired heart diseases, and the association of an

ANOCOR with a significant CAD is common. Sudden ANOCOR-related death is rare in such patients. Some ANOCOR may also be identified late in patients referred for evaluation of various atypical symptoms. In young populations, the latter can lead also to the diagnosis of ANOCOR. Nevertheless, serious symptoms usually related to exertion, are possible. Last but not least, a sudden death related to a high risk ANOCOR may be the first event in the life of a young patient. Fortunately, only a small subgroup of ANOCOR, including mainly anomalies with an intramural segment and anomalous connections with the pulmonary artery, may entail life-threatening adverse events. In patients with significant acquired heart disease, relationships between the coronary abnormality and clinical status should be made clear as far as possible. The clinical presentations of anomalous origins from the pulmonary artery differ from that of anomalous origins form the aorta.

9.1 Sudden deaths

Analysis of necropsy cases has been crucial to highlight the lethal risk of some ANOCOR (Frescura et al. 1998, Kragel & Williams, 1988). In a postmortem series of 242 congenital abnormalities of coronary arteries, 49 anomalous connections of the LCA and 52 anomalous connections of the RCA with the opposite sinus were identified (Virmani et al., 2001). Sudden death was observed in 57% of LCA abnormalities and 25% of RCA abnormalities. Most of them had a preaortic course. The profile of the patients suffered from sudden death is often typical: young age, frequent intensive exercise, and non systematic premonitory symptoms. In a necropsy study of 150 consecutive sudden deaths occurring in a population ≤ 35-year old, 16 sudden deaths related to non-atherosclerotic coronary disease were identified (Corrado et al., 1992). Three (19%) of them were ANOCOR (11, 22 and 29 year-old patients). Sudden death occurred during effort. In a series of 27 ANOCOR (23 LMCA and 4 RCA from the opposite sinus) identified at autopsy in young athletes, sudden death occurred during intense exertion in 25 cases or immediately after in 2 cases (Basso, et al. 2000). In 126 nontraumatic sudden deaths collected during a 25-year autopsy study of military recruits, there were 21 (17%) ANOCOR, all LCA originated from the opposite sinus, with a preaortic course (Eckart et al. 2004). Thus, sudden death, especially during exercise, is a fairly common mode of revealing high-risk ANOCOR in young populations. Some sudden cardiac arrests may survive up to hospitalization with public education and emergency care systems. The individual incidence of sudden death in asymptomatic patients with high risk ANOCOR remains unknown.

9.2 Other symptoms

All usual cardiac symptoms are possible, i.e. angina, chest pain, dyspnea, syncopes, palpitations. In autopsy studies mentioned above, prodromal symptoms before sudden death were noted in up to 56% of patients (Eckart et al., 2004) but often underestimated or hidden owning to the patient profile (athlete or military). In another study, only 55% of patients had no cardiac history (Basso et al., 2000). Syncope and chest pain, exercise-related almost without exception, are the most frequent symptoms However, it must be remembered that the population studied was subjected to extreme exercise, unusual for a general population. In the latter, symptoms leading to the diagnosis of ANOCOR are variable and sometimes no such typical with chest discomfort or palpitations. Obviously, stable angina and acute coronary syndromes are possible if a significant CAD is associated. In a retrospective study, 301 anomalous origin from the opposite sinus were identified among

210,700 adult patients underwent selective coronary angiography (Krasuski et al., 2011). The mean age (58 ± 14 years) was relatively high in the ANOCOR cohort. As presenting symptoms, chest pain and dyspnea were common (66% and 58% of patients, respectively), as well as a myocardial infarction (24% of patients). However, the prevalence of significant CAD was of 68% in this population. Clinical presentations similar to CAD-related presentations are possible in ≥ 50-year old patients free of significant CAD (Angelini et al., 2006).

9.3 Anomalous connection with the pulmonary artery

The clinical presentation of anomalous connections with the pulmonary artery is different in children and adult populations. The mortality rate is high in infancy. In anomalous connection of the LCA with the pulmonary artery, an intermediate survival is possible with a major enlargement of the RCA and multiple intercoronary collaterals. In patients who survive into childhood, left ventricular enlargement and/or dysfunction, mitral valve incompetence, heart failure, myocardial infarction, or ventricular arrhythmias are reported, usually before 35 years age. Dyspnea and/or angina on exertion are the most frequent presenting symptoms (Kottayil et al., 2011). However, sudden death due to malignant ventricular arrhythmias may be the first cardiac event (Frapier et al., 1999). Fortuitous discovery is rare in asymptomatic patients with a continuous murmur due to interventricular collateral flow.

10. Screening and risk identification

Screening of ANOCOR in young populations and risk identification of known ANOCOR are both, two great challenges in order to impact on the incidence of life-threatening cardiac events.

10.1 Screening

In view of the fairly rare nature of ANOCOR it would be inappropriate to screen an unselected population. Moreover, the economic impact of screening in large populations should always be taken in consideration. Major obstacle of large-scale screening is the substantial number of young athletes eligible for evaluation (Maron et al. 2005). The subgroup of young athletes is certainly an interesting population in which to develop screening strategies. In a review of 387 sudden death in young athletes <35 years of age (Maron, 2003), the third most frequent cause is congenital anomalies of coronary arteries (13.7%) after hypertrophic cardiomyopathy (26.4%) and commotio cordis (19.9%). Among athletes suffering from an ANOCOR-related sudden death, a considerable number of anomalies were clinically silent. Although an intense exertion remains sometimes difficult to quantify, it would be reasonable to select among the young athletes those who will be exposed to competitive and high-intensity sports. However, time and content of such screening remain debatable. In the absence of specific European guidelines, the Study Group on Sports Cardiology of the Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology proposed recently, through a consensus statement, a screening project of young competitive athletes for prevention of sudden death (Corrado et al. 2005). The latter, based mainly on the large Italian experience, includes medical history, physical examination and 12-lead ECG. The screening should start at the beginning of competitive activity, which usually corresponds to an age of 12-14 years. This strategy seems useful in diagnosing an early hypertrophic cardiomyopathy. Otherwise, a

resting ECG is unable to identify young people with ANOCOR except some anomalous connections in pulmonary artery (Cohen & Berger, 2010). Exercise stress test, with a known low sensibility in symptomatic high risk ANOCOR, is clearly inadequate for screening of an asymptomatic population. Among non-invasive imaging tools, ETT has the potential to identify some ANOCOR. Nevertheless, capacity for ETT should be dramatically increased and cardiologist should be trained to visualize coronary ostia. Meanwhile, better information among young athletes of frightening cardiac symptoms, i.e. chest pain or syncope in exertion, appears probably as a useful preventive measure to reduce the calamitous impact on the well-know sport benefits of each exercise-related sudden death. In addition, the visualization (or at least a meticulous search for) of origins of coronary arteries should be a routine part of any echocardiographic procedure in young population referred for functional assessments. Recently, the first series of familial ANOCOR was published with identification of 5 families in which a child or a young person <30-year old was diagnosed with preaortic ANOCOR generally symptomatic and another family member was identified with a preaortic ANOCOR through echocardiographic screening (Brothers et al., 2008). A systematic TTE screening for children and young people in families with a history of a major cardiac ANOCOR-related event (sudden death or aborted sudden death) may be discussed.

10.2 Risk identification

It is insufficient to note an abnormal origin of a coronary artery. A complete diagnosis with the orifice and the course of the ANOCOR will allow an accurate prognostic stratification. Risk identification is a major stage after a diagnosis of ANOCOR, because important therapeutic decisions and restrictive recommendations on lifestyle may follow from the final classification of the coronary abnormality. Usually, ANOCOR are identified at low-risk or high-risk with a strong evaluation criterion (sudden death). Nevertheless, one have to keep in mind that low-risk does not signify no risk. This classification is based first on postmortem examinations, because many of the patients with high-risk ANOCOR were previously diagnosed at autopsy. Now, with a better knowledge of these abnormalities and the development of imaging tools allowing an early diagnosis, it is mandatory that cardiologists and radiologists be familiar with the spectrum of congenital coronary abnormalities and their potential clinical relevance. However, the angiographers may be faced with difficult decisions for example a symptomatic patient with a low-risk ANOCOR or an asymptomatic patient with a high-risk ANOCOR. So far, no solid data are available on the natural history of ANOCOR with abnormal origin from the aorta. Several characteristics and parameters allow evaluation of sudden-death risk in most ANOCOR. However, in some cases, the classification may be difficult, and without enough information, it seems preferable to avoid too strict therapeutic rules. Indeed, it is always intriguing and not clear that among patients with the same high-risk ANOCOR, some will suffer from early sudden death, while others will die later in life of unrelated cause .

10.2.1 Type of coronary abnormality

Despite its rare frequency, the natural history of anomalous connections with the pulmonary artery is better known, and the latter are classified as high-risk. The risk of sudden death is related to malignant arrhythmias or acute myocardial infarction. Progressive left ventricular dilatation and dysfunction secondary to chronic myocardial ischemia is the trigger for rhythmic disturbances occurring usually before 35 years of age. The main subgroup of high-

risk ANOCOR includes abnormalities with a preaortic course associated with an intramural segment, especially anomalous connections of LCA and RCA from the opposite sinus. If initially, the LCA with preaortic course has been recognized as the most frequent sudden death-related ANOCOR, it is clear that the RCA arising from the opposite sinus may also be a cause of sudden death (Frescura et al, 1998, Kragel & Roberts, 1988, Taylor et al., 1992). As previously discussed, almost without exception, the RCA originating from the left sinus has a preaortic course and thus a high-risk profile. The smaller myocardial territory at risk in right versus left ANOCOR is hypothesized to explain the lower incidence of sudden death in right ANOCOR despite it being more frequent than left ANOCOR. Universally, anomalous connection of the CX coronary artery, with an almost exclusive retroaortic course, is classified as low-risk ANOCOR. The subgroup of ectopic LMCA or LAD coronary artery represents certainly the greatest challenge for angiographers to accurately identify the ectopic course. As mentioned above, ANOCOR with preaortic course and ANOCOR with retroinfundibular course were previously often confused. The latter are recognized as low-risk in contrast to the ANOCOR with preaortic course. In the young population, a misdiagnosis may lead to dramatic consequences. Currently, the widely used tomographic tools allow an easy and flexible image interpretation, which should limit the risk of mistake. Other courses of LMCA or LAD coronary artery, i.e. preinfundibular and retroaortic courses are classified as low-risk. Surprisingly, anomalous origins in the opposite sinus and anomalous origins in the contralateral artery are rarely distinguished. As aforementioned, frequency of an intramural segment may be different between an abnormal connection near the orifice of the contralateral artery and an abnormal connection in the contralateral artery.

10.2.2 Symptoms and induced-myocardial ischemia

The numerous ANOCOR-related sudden deaths reported in the literature suggest that they are in most cases unpredictable. However, a more accurate analysis of the data shows that in more than half of patients suffering from sudden death, premonitory symptoms were identified after the fatal event, especially chest pain and syncope on exertion. These deaths are always to be deplored but some characteristics of the exposed population can explain an absence of diagnosis. On the one hand, young athletes may hide or underestimate symptoms, and they do not systematically interfere with usual intensive and repetitive efforts. On the other hand, medical teams can misinterpret some clinical presentations in a young and healthy population with a low prevalence of CAD, as unimportant. In addition, exercise stress tests are usually reassuring. Difficulties in inducing myocardial ischemia with the usual tools are well-described, even in symptomatic high-risk ANOCOR. In as series of 27 sudden deaths in young athletes, due to ANOCOR, all maximal exercise stress tests (6/6) were judged within normal limits (Basso et al. 2000). In addition, intermittent ischemia was described in rare cases (Brothers et al., 2010). The experience of fractional flow reserve (FFR) assessment with a pressure-wire during coronary catheterization remains limited. Angelini and coworkers speculated that functional tests suggested usually in patients with CAD are probably not appropriate for risk evaluation in patients with ANOCOR, and proposed pharmacologic tests simulating extreme exercise efforts (Angelini et al. 2003). In order to increase dramatically cardiac output and stroke left ventricular volume, concomitant administration of saline, atropine and dobutamine may lead to a significant systolic expansion of aorta. IVUS can identify the impact of this on the degree of lateral compression in the intramural segment, with sometimes a visualization of >50% area stenosis.

10.2.3 Age

Age at the time of anomaly discovery is an important parameter in risk identification. In anomalous connections with the pulmonary artery, the risk of major adverse cardiac events exists probably during the entire life, even if this risk is more pronounced in early childhood. In contrast, for anomalous origins from the aorta, most sudden deaths occur between 10 and 35 years of age. Clinicopathologic presentations of 142 cardiac deaths in patients with congenital coronary anomalies were reviewed (Taylor et al., 1992). Sudden death occurred in 78 patients (32%). Younger patients (≤ 30-year old) died suddenly more frequently in comparison with older patients, 62% versus 12%, p=0.001, respectively, despite a lower frequency of CAD, 1% versus 40%, p = 0.00001, respectively. In a series of 690 sudden deaths occurred between 14 and 40 years of age, prevalence of ANOCOR identified as sole cause of death was of 8% between 14 and 20 years of age, of 4% between 21 and 30 years of age, and of 0.5% between 31 an 40 years of age (Virmani et al., 2001). Risk of sudden death in the absence of CAD seems very low after the age of 50 years, including so-called interarterial high-risk ANOCOR. However, some ANOCOR with intramural segment may be symptomatic late requiring interventional and/or surgical treatment (Angelini et al., 2006).

10.2.4 Associated coronary artery disease

Obviously, the presence of CAD will interfere with the management of ANOCOR. A significant ostial or juxtaostial narrowing due to an intramural segment should not be confused with a fixed atherosclerotic stenosis. Sites of significant atherosclerotic lesions should be clearly distinguished, especially between ectopic segment and normal path. Association of CAD with ectopic segment of ANOCOR with a single ostium or with proximal path of a single coronary increases the risk. A higher prevalence of CAD has been suggested in CX coronary arteries but the location of atherosclerotic lesions is not always defined accurately in studies. However, most of them seem concordant with a higher incidence of atherosclerotic lesions in CX coronary arteries (Click et al., 1989, Wilkins et al. 1988). Table 9 summarizes the main characteristics of low-risk and high-risk ANOCOR in young and adult populations.

	Low-risk	High-risk
Anomalous connection with the pulmonary artery	-	+
Preaortic course with intramural segment	-	+
Other courses with intramural segment	-	+
Other courses without intramural segment	+	-
Valve-like ostial stenosis	-	+
Other anomalous connections	+	-
History of aborted sudden death	-	+
History of chest pain related to exertion	-	+
History of syncope related to exertion	-	+
History of severe ventricular arrhythmias	-	+
Induced-myocardial ischemia	-	+
Any anomaly above age of 50 years*	+	-
Ectopic segment with significant atherosclerotic lesion	-	+

* Except anomalous connections with the pulmonary artery.

Table 9. Main characteristics of low-risk and high-risk proximal anomalous connections of the coronary arteries.

11. Pathophysiological mechanisms

The degree of understanding of the pathophysiological mechanisms differs between the different types of ANOCOR.

11.1 Anomalous connections with the pulmonary artery

For the first clinical description of an anomalous connection with the pulmonary artery (Bland et al., 1933), pathophysiological mechanisms were established and well understood (Edwards, 1964). In anomalous connections of the LCA with the pulmonary trunk, the most frequent abnormality, the left ventricular myocardium is initially fed by less saturated blood under high pulmonary vascular resistances. Then, the antegrade flow to the LCA decreases with an eventual reversal of flow due to the decrease in pulmonary vascular resistances, leading to a coronary steal phenomenon. A long asymptomatic period until adulthood is possible in patients with dominant RCA and multiple large intercoronary collaterals between RCA and LCA. However, permanent myocardial hypoperfusion progressively impairs left ventricular function with occurrence of dyspnea and/or heart failure in young age. Mitral insufficiency, generally mild or moderate, is frequent, due to papillary muscle ischemia. Hibernating myocardium is possible requiring myocardial viability studies in order to rule out idiopathic dilated cardiomyopathy. As aforementioned, low ventricular function and/or myocardial infarction sequelae may be the trigger for malignant ventricular arrhythmias revealing the coronary abnormality.

11.2 Anomalous connections with the aorta

In subgroups of anomalous origins from the aorta, mechanisms of life-threatening cardiac events are less clear. Even if most sudden deaths are almost due to ventricular fibrillation, the accurate sequence leading to lethal arrhythmic disturbance often remains unknown or debated. Hypotension and extreme bradycardia seem to occur before the malignant ventricular arrhythmia. Experimental studies are lacking in the field of ANOCOR. Numerous hypotheses have been speculated. The oldest of them, still often widely held, is the compression of the ectopic vessel between the aorta and the pulmonary artery. However, such mechanism has never been demonstrated. Extrinsic compression of the LCA in normal location, from a markedly dilated pulmonary artery trunk has been described (Caldera et al., 2009, de Jesus Perez et al., 2009, Lyndsey et al., 2008). Nevertheless, relationships between an ANOCOR with preaortic course and a non dilated pulmonary artery are different. As previously discussed, RCA or LCA with preaortic course are not necessary close to the pulmonary artery. Therefore, anatomical characteristics of ANOCOR with preaortic course and intramural segment are probably more interesting for comprehension of induced-myocardial ischemia (Angelini, 2007). It is important to consider that myocardial ischemia is not necessarily the result of significant differences between supply and demand of myocardial oxygen. In the absence of fixed atherosclerotic stenosis, the determinants of myocardial ischemia are not truly reproducible in patients with ANOCOR. Most young athletes are able to perform intensive and repetitive efforts which do not interfere with their performances until the occurrence of a life-threatening cardiac event. Thus, the subject continues to intrigue pathologists and physiologists. Invasive approach with IVUS advocated by Angelini et al. permitted a better comprehension between anatomical features of ectopic vessel and pathophysiological mechanisms of ischemia. If symptoms are a suggestive of a compressive etiology, one must consider IVUS as it is the

gold standard anatomical technique. A slit-like orifice may have a large area, but can collapse with a valve-like manner, during an abrupt increase in pressure and/or volume in the aorta. Vessel hypoplasia is another potential cause of decrease in blood supply under extreme conditions. CT imaging and IVUS are useful to demonstrate a non atherosclerotic reduction of the lumen vessel in the initial ectopic path (figure 22). Another abnormality contributing to myocardial ischemia is the intramural segment of the ectopic vessel. Histology and ultrasonography demonstrated the non circular shape of intramural segment thoroughly. The oblong area of the latter may be more exposed to the dynamic changes of the aortic wall.

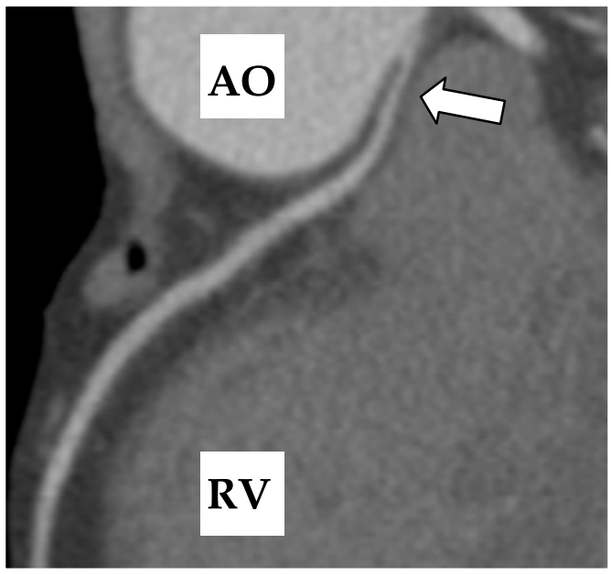

Fig. 22. Multiplanar reconstruction of computed tomography showing an hypoplasia of the initial path (arrow) of a right coronary artery arising from the left sinus. AO: aorta, RV: right ventricle.

If numerous anatomical risk factors were identified, the relative contribution of each factor is not clear. In a study, no significant differences were found in length of intramural segment, coronary ostial size, or angle of coronary take-off between right or left ANOCOR arising from the opposite sinus, with (n=12) and without (n=18) sudden death (Taylor et al., 1997). Age ≥ 30 years was the only factor with a lower incidence of sudden death. Apart from the fact that intensive exercises are preferably performed during the young age, the dramatic reduction of sudden death risk after the age of 30 years remains surprising. The progressive hardening of the aortic wall has been suggested as a pathophysiological mechanism, with less dynamic changes of the aortic media during exertion. Otherwise, clotting and spasm have often been suspected but rarely proven as further mechanisms leading to acute coronary events. Furthermore, large sequelae of transmural myocardial infarction are rare in necropsy cases. Nevertheless, chronic myocardial ischemic damage may occur and lead to fatal arrhythmias. Histologic examination of heart specimens of young athletes suffering from sudden death may show patchy replacement-type fibrosis (Basso et al., 2000) or scattered foci of contraction band necrosis (Corrado et al., 1992). CX coronary artery arising from the opposite sinus or the RAC is a well-known abnormality deemed benign. Nevertheless, suspicion exists about an earlier atherosclerotic formation in

the proximal path of ectopic CX coronary arteries. Angiographic demonstration of a reduction of the lumen is not rare. However, besides atherosclerotic narrowing, a distortion of CX coronary artery may also be suspected in case of enlarged aortic root due to their close relationships. The mechanism of a potentially higher incidence of CAD of ectopic CX coronary artery in the retroaortic segment remains unclear.

12. Management, recommendations, and treatments

If most of ANOCOR are benign and require no specific investigation or treatment, other abnormalities such ANOCOR classified as high-risk or symptomatic ANOCOR require a meticulous and accurate analysis in order to offer the best management in the present state of our knowledge.

12.1 Management

First of all, the coronary abnormality should be clearly defined with a correct interpretation of ectopic origin, initial course regarding to aortic wall, and ectopic course regarding to adjacent structures. Uncertain diagnosis or high-risk ANOCOR need always complementary imaging investigation allowing a useful confrontation. All cardiologists and radiologists are not familiar with the large spectrum of congenital coronary abnormalities, and the opinion of a practitioner experienced in the field of ANOCOR should be mandatory before decision-making. Recent investigation conducted by the Anomalous Coronary Artery Working Group of the Congenital Heart Surgeon's Society showed a heterogeneous management of young adults with ANOCOR associated with a preaortic course (Brothers et al., 2009). In 36th Bethesda Conference focused on trained athlete with an identified cardiovascular abnormality, detection of coronary anomalies of wrong sinus origin in which a coronary artery passes between the aorta and pulmonary artery should result in exclusion from all participations in competitive sport (Graham et al., 2005). Participation in all sport 3 months after successful operation would be permitted for an athlete without ischemia, ventricular or tachyarrhythmia, or dysfunction during maximal exercise testing was another recommendation of the 36th Bethesda Conference. As previously mentioned, presence of symptoms, high-risk anatomical features and young age are the main criteria requiring a special attention in order to prevent a sudden cardiac death. Even if false-negative cases are frequent, stress exercise tests with nuclear imaging are necessary in this population exposed. More aggressive investigations, such pharmacological tests simulating extreme exercise have been suggested but are not without dangers (Angelini et al., 2003). According to current understanding, only an intramural segment seems to be clearly related with a high-risk of sudden death, and the best means in identifying intramural segment is IVUS. The definition of a cut-off age in deciding a population as high-risk remains difficult in practice. If the literature gives relatively clear information in < 30-year old and > 50-year old patients, the management of patients between 30 and 50 years of age is often problematic. Restriction of activity, particularly competitive sport and intensive exertion, is often recommended if a surgical repair is not indicated. Medical treatment with essentially beta-blockers is sometimes associated. Due to possible but rare late deaths or subclinical myocardial ischemia after surgical repair of ANOCOR, long-term follow-up with regular cardiovascular evaluation is needed (Brothers et al., 2007, Brothers et al., 2009). Presence of significant atherosclerotic coronary disease or valvular disease requiring cardiac surgery permits sometimes a concomitant treatment of a high-risk ANOCOR. Furthermore, identification of

ANOCOR is crucial before aortic surgery in order to avoid an injury of the ectopic vessel or to compress along its course by a valvular prosthesis.

12.2 Recommendations

ACC/AHA 2008 guidelines for the management of adults with congenital heart disease (Warnes et al., 2008) give recommendations for congenital coronary abnormalities of ectopic aortic origin and for anomalous left coronary artery from the pulmonary artery (table 10).

Recommendations for congenital coronary anomalies of ectopic aortic origin		
	Class	Level of evidence
Surgical coronary revascularization should be performed in patients with any of the following indications:		
a. Anomalous left main coronary artery coursing between the aorta and pulmonary artery.	1	B
b. Documented coronary ischemia due to coronary compression (when coursing between the great vessels or in intramural fashion).	1	B
c. Anomalous origin of the right coronary artery between aorta and pulmonary artery with evidence of ischemia.	1	B
Surgical coronary revascularization can be beneficial in the setting of documented vascular wall hypoplasia, coronary compression, or documented obstruction to coronary flow, regardless of inability to document coronary ischemia.	IIa	C
Surgical coronary revascularization may be reasonable in patients with anomalous left anterior descending coronary artery coursing between the aorta and pulmonary artery.	IIb	C
Recommendations for anomalous left coronary artery from the pulmonary artery		
	Class	Level of evidence
In patients with an anomalous left coronary artery from the pulmonary artery, reconstruction of a dual coronary artery supply should be performed. The surgery should be performed by surgeons with training and expertise in congenital heart disease at centers with expertise in the management of anomalous coronary artery origins.	1	C

Table 10. ACC/AHA 2008 recommendations for anomalous connections with aorta and pulmonary artery.

Surgical repair is indicated for LMCA with preaortic course regardless of symptoms. Surgical repair is also indicated for RCA with preaortic course in association with symptoms and/or inducible ischemia. A conservative approach is recommended in asymptomatic in patients with ectopic RCA in association with preaortic course. Position of PCI with limited experience and without long-term follow-up is not established in the ACC/AHA guidelines. Furthermore, the risk stratification with age is not clearly exposed. Only, a young patient is

defined as a patient with an age less than 50 years. Despite of absence of randomized studies and limited information about long term follow-up in high risk patients, current guidelines are fairly directive in favor of large surgical indications in high–risk ANOCOR with ectopic origin from the aorta. In accordance with its well-described natural history, an anomalous LCA connected with pulmonary artery should be repaired surgically regardless of age. Surprisingly, congenital coronary abnormalities do not appear on the list of specific congenital heart defects in the recent European 2010 guidelines (Baumgartner et al., 2010).

12.3 Treatments of anomalous connections with the pulmonary artery

Correction of anomalous connections with the pulmonary artery should always be proposed regardless symptoms and age, with as possible establishment of a dual coronary system. The restitution of an antegrade flow in the LCA is associated with an improvement of the left ventricular function and a reduction of the ischemic mitral regurgitation. At mid-term, regression of the intercoronary collateral network and decrease in size of dilated RCA are observed. Numerous surgical methods have been attempted to repair coronary abnormality, including Takeuchi tunnel procedure, venous or arterial bypass grafts, or direct aortic reimplantation. The latter, although technically more challenging, appears today as the method of choice in patients with favorable anatomy (Kottayil et al., 2011). The implantation of the LMCA into the aorta is a more physiological correction and avoids the late risks of venous grafts. Takeuchi procedure is a technique of repair with the creation of a baffle within the pulmonary artery to divert the blood from the origin of the ectopic LMCA to the aorta (Takeuchi et al., 1979). Due to a high rate of reoperations for supravalvular pulmonary stenosis, baffle leak or obstruction of the intrapulmonary channel, the Takeuchi procedure is almost no longer used. Ectopic LCA usually originates from the left posterior pulmonary sinus facing the left side of the aorta. The excised ectopic coronary is directly implanted just above the sinotubular junction. The site of pulmonary excision is repaired with autologous pericardium. Sometimes, strategies to lengthen the anomalous coronary artery are necessary. Mitral repair or replacement is recommended in patients with severe mitral regurgitation. Establishment of a satisfactory left myocardial perfusion may resolve mild and some moderate mitral insufficiencies (Fehrenbacher et al., 2010). Mechanical circulatory support should be considered in patients with intractable left ventricular failure in postoperative setting (Dodge-Khatami et al., 2002). With increased experience with direct aortic implantation technique and better postoperative management, the perioperative mortality rate, initially up to 20%, decreased dramatically of about 10%. Due to the rare frequency of patients with a coronary artery arising from pulmonary artery who survive into childhood, large prospective studies in adults who underwent surgical repair are lacking. Studies, pooling generally children and adult populations, reported a 10-year survival rate between 85 and 95% (Ben Ali et al., 2009, Brown et al., 2008, Fehrenbacher et al., 2010). Close long-term follow-up after surgical repair is recommended to detect residual ischemia.

12.4 Treatments of anomalous connections with the aorta

12.4.1 Surgical treatment

Surgical treatment is recommended in patients with high-risk anomalous connections with the aorta (Warnes et al, 2008). However, an inhomogeneous management of high-risk ANOCOR is observed in practice (Brothers et al., 2009). Surgical repair techniques are

numerous and current therapeutic strategies may vary among clinicians due to marked heterogeneity in physician opinions. Obviously, the left high-risk ANOCOR are easier entrusted to surgeon. Nevertheless, surgical repair of right high-risk ANOCOR has been reported (Garcia-Rinaldi et al., 2004). In contrast to anomalous connections with pulmonary artery, direct aortic reimplantation is rarely possible due to an, almost without exception, intramural segment. Several techniques have been proposed (Said et al. 2010): unroofing of the coronary artery, creation of a neo-ostium, reimplantation of the coronary artery, translocation of the pulmonary artery with patch angioplasty of the coronary artery and coronary bypass grafting. Unroofing consists to a longitudinal excision of the common wall between the aorta and the ectopic coronary artery coursing tangentially with an intramural segment (figure 23). Excision starts at the anomalous ostium and continues into the appropriate sinus. To create a neo-ostium, a probe passed through the intramural segment and the coronary artery is opened at the location at which the probe exits the aortic wall (figure 23). In the absence of intramural segment, reimplantation of the coronary artery is possible. The ectopic ostium is excised and implanted in the appropriate sinus above the sinotubular junction. Another technique may be used in the absence of intramural segment, with a translocation of the pulmonary trunk anteriorly and leftward to avoid a compression of the ectopic artery. This technique may be associated with patch angioplasty of the ectopic coronary artery (Karl et al., 2010). The coronary artery is open well beyond the intramural segment and a patch of autologous pericardium creates a large neo-ostium. Finally, coronary artery bypass grafting with saphenous vein or internal mammary artery is another possibility. Thus, correction of intramural segment is not systematically. The choice of the technique depends of surgeon's preference, anatomical pattern of ANOCOR, and existence of CAD requiring myocardial revascularization. Coronary artery bypass grafting is proposed in older adults with concomitant CAD. The use of venous or arterial conduits in young people exposes to a long-term patency concern, because of competitive flow. For most operators, the creation of a neo-ostium is the more physiological treatment without the risk of take-down of the commissural junction between the right and left coronary sinuses observed sometimes with the unroofing technique. No comparative data exist about these different surgical methods. Surgical practice has evolved in the time from coronary artery bypass grafting to direct surgical repair. To date, unroofing technique seems the more used in young people (Davies et al., 2009, Frommelt et al., 2011, Mainwaring et al. 2011). The rate of perioperative death is near to zero in small series of children and young people (Davies et al., 2009, Erez et al., 2006, Karl et al., 2010). Recently, Krasuski et al. reported the impact of surgery in patients with ANOCOR from the opposite sinus (Krasuski, et al., 2011). A cohort of 301 adults from 210,700 cardiac catherizations performed over a 35-year period was retrospectively analysed. The incidence of anomalous connections with the opposite sinus was of 0.14%, and in 54 of 301 patients (18%) an interarterial course between the aorta and pulmonary artery was identified, thus an incidence of 3/10.000 of high-risk ANOCOR with 18 left ANOCOR (33%) and 36 right ANOCOR (67%). Surgical management was chosen in 28 of 54 patients (52%), and in 8 of 18 left ANOCOR (44%) and 20 of 36 right ANOCOR (56%). Coronary artery bypass grafting was used as treatment in most of cases (71%). At 10 years, no difference in survival was observed between interarterial ANOCOR managed surgically or medically. Some characteristics of the cohort studied may explain the lack of benefit associated with surgical repair. As aforementioned, the study population consisted of relatively old patients with a mean age of 58 years and with a high prevalence of CAD.

The latter was present in 86% of ANOCOR managed surgically and in 50% of ANOCOR managed medically. Abnormal stress tests were more frequent in surgical patients (90%) versus 43% in patients with medical management. Moreover, whether the primary indication for surgery was CAD or coronary abnormality was not clarified. The authors concluded that the results of their study must not be applied to younger patients because the mortality risk is not the same. Mainwaring et al. reported medium-term results after surgical repair of ANOCOR in 50 patients with a mean age of 14 years (Mainwaring, et al., 2011). Congenital cardiac abnormalities were associated in 14 patients. Interarterial and intramural courses were present in 100% and 70% of patients, respectively. An unroofing procedure was performed in 36 of 50 patients (72%). All patients (n=9) with single coronary ostium and without an intramural path underwent pulmonary artery translocation. With a mean follow-up of 5.3 years, satisfactory follow-up was obtained in 47 patients, and all have remained free of cardiac symptoms. Functional results of modern surgical methods are recognized as good in young people with most of patients free of symptoms at a medium-term follow-up (Erez et al., 2006, Karl, et al. 2010). However, Brothers et al. reported that subclinical ischemia may occur after surgical repair of anomalous aortic origin of a coronary artery (Brothers et al., 2007). In this study, 9 asymptomatic children or adolescents (5 to 18 years) had post operative evaluations (range 2 to 48 months) suggestive of silent ischemia. This data highlight the need of long-term follow-up in young people undergoing surgical repair of ANOCOR.

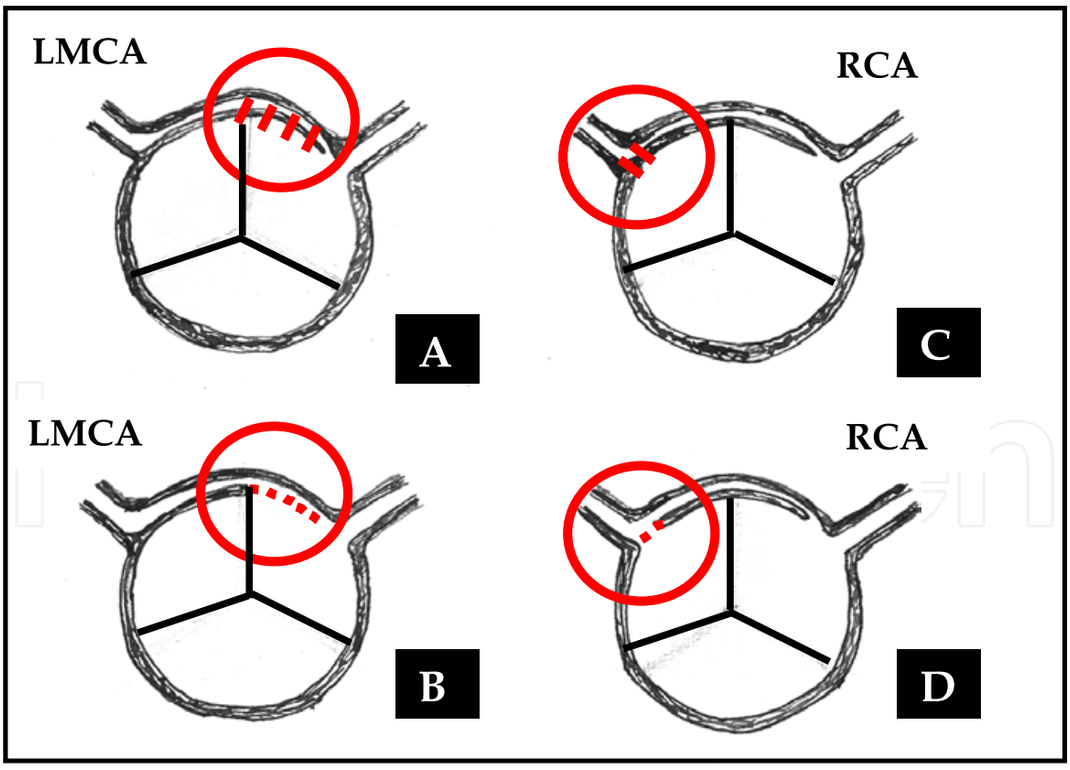

Fig. 23. Diagram representation of surgical repair of an anomalous left main coronary artery (LMCA) arising from the right sinus and associated with an intramural segment. A and B: unroofing technique. C and D: creation of a neo-ostium. RCA: right coronary artery.

12.4.2 Interventional treatment

Coronary angioplasty with stenting is a more recent therapeutic method in the field of ANOCOR. So far, only cases report or small groups of ANOCOR have been reported. Percutaneous coronary intervention (PCI) in ANOCOR with and without associated CAD must be distinguished. In fact, most of PCI are performed in ANOCOR with significant atherosclerotic lesions within or distal to ectopic course, and sometimes during acute coronary syndrome (Jaffe et al., 2009). PCI may be attractive as an alternative to surgical repair in young patients without CAD. Nevertheless, the capacities of a stent to adapt to anatomical characteristics of an ANOCOR with an intramural segment should be accurately analyzed before its use can be recommended. Hariharan et al. displayed potential concerns with canulation difficult, incomplete coverage of ostium without protruding into the aorta, uncertainly regarding the true diameter, risk of aortic dissection, and unknown restenosis risk (Hariharan et al. 2002). Angelini et al. suggest the use of PCI in patients with symptomatic right ANOCOR associated with ischemia induced by a nuclear stress test (Angelini et al., 2007). During cardiac catheterization, IVUS is crucial to evaluate the minimal lumen area, length of intramural segment, arterial diameters and results after stent deployment. However, evaluation data of interventional treatment of right ANOCOR are currently too poor to envisage on extension of this technique to left ANOCOR. In AHA/ACC 2008 guidelines, PCI is not recommended in therapeutic management (Warnes et al., 2008).

13. Perspectives

Among the wide spectrum of congenital abnormalities of coronary arteries, proximal anomalous connections of coronary arteries (ANOCOR) represent a significant subgroup, which continues to promote debate. A more simple classification, and recognized by all, would have the advantage to avoid confusions. A non insignificant prevalence of about 1% in the general population and, in particular, the presence of anatomical patterns associated with a risk of sudden death require that the current research supplies data sufficiently robust in order to improve the management of ANOCOR. Young competitive athletes are a well-known population which pays a heavy toll to high-risk ANOCOR. Cooperation between physicians is necessary in order to prevent sport-related fatalities and to determine the modalities of cost-effective screening. From a diagnostic point of view, tomographic techniques, especially CT angiography, represent today an unrivaled tool by their ability to supply multiple volumetric reconstructions. Therefore, accurate diagnosis of the ectopic origin and non-ambiguous interpretation of the ectopic course are possible in most of cases. However, ANOCOR are still often discovered fortuitously in adult populations during selective coronary angiography by angiographers with sometimes a limited experience in the field of ANOCOR. It seems that the knowledge of angiographers should be improved in order to limit the risk of misinterpretation. Systematic usage of tomographic imaging solves this problem, while at the same time educating angiographers. Currently, high-risk ANOCOR are identified well, however the management of them is heterogeneous, specially the timing and mode of treatment. There clearly remains a gap between the practices and the recommendations, sometimes due to misunderstanding, but also relating to physician opinion. The absence of long-term follow-up after surgical repair and the difficulties of undertaking randomized studies, and as the unknown natural history of ANOCOR all may explain the divergence between clinical practice and current guidelines. Surgical treatment demonstrates a preference for the unroofing technique in ANOCOR arising from the aorta

and direct aortic implantation for ANOCOR connected with the pulmonary artery. Perioperative risks are low, except in some anomalous connections with the pulmonary artery, but the long-term evaluation is lacking. To date, the role of PCI remains undetermined. The low incidence of ANOCOR requiring a percutaneous or a surgical repair would justify that these congenital abnormalities being taken care off in a center specialized in the management of ANOCOR. Several attempts have been made to set up observational registries to determine the outcome of different strategies in the field of ANOCOR (Angelini 2007, Aubry et al., 2008, Brothers et al., 2007, Pelliccia, 2001). To date, two registries are ongoing, one in North and South America, and one in France. The registry of anomalous aortic origin of the coronary artery of The Congenital Heart Surgeons' Society (www.chssdc.com) has been set up to determine the outcome of children or young adults (≤ 30-year old) with high-risk ANOCOR. This registry includes those managed conservatively and with surgical intervention. The ANOCOR with interarterial, intramural, and/or intraseptal courses are classified as high-risk. The registry consists of a retrospective cohort of patients diagnosed between 1 January, 1998 and 20 January, 2009 and a prospective cohort of patients newly diagnosed from 21 January, 2009. The registry of proximal anomalous connections of coronary arteries (ANOCOR Registry) of the French Society of Cardiology (www.sfcardio.fr) is a prospective observational study of patients (≥ 15-year old) diagnosed with an ANOCOR. The main objective of this registry is to describe the chosen therapeutic strategies according to the type of ANOCOR. The secondary objectives are to describe the cardiac morbidity and mortality and to estimate the impact of different therapeutic strategies at a 5-year follow-up. The ANOCOR registry started 31 January, 2010 with an inclusion period of 3 years. With such multicenter registries dedicated to ANOCOR, evidence-based guidelines will probably be easier to establish in an attempt to achieve a better understanding of the clinical profile and the impact of interventional correction on the natural history of these congenital coronary abnormalities.

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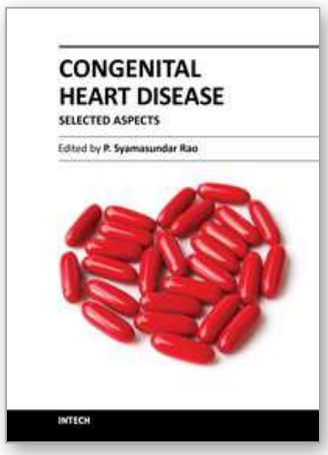

Congenital Heart Disease - Selected Aspects

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There are significant advances in the understanding of the molecular mechanisms of cardiac development and the etiology of congenital heart disease (CHD). However, these have not yet evolved to such a degree so as to be useful in preventing CHD at this time. Developments such as early detection of the neonates with serious heart disease and their rapid transport to tertiary care centers, availability of highly sensitive noninvasive diagnostic tools, advances in neonatal care and anesthesia, progress in transcatheter interventional procedures and extension of complicated surgical procedures to the neonate and infant have advanced to such a degree that almost all congenital cardiac defects can be diagnosed and "corrected". Treatment of the majority of acyanotic and simpler cyanotic heart defects with currently available transcatheter and surgical techniques is feasible, effective and safe. The application of staged total cavo-pulmonary connection (Fontan) has markedly improved the long-term outlook of children who have one functioning ventricle. This book, I hope, will serve as a rich source of information to the physician caring for infants, children and adults with CHD which may help them provide optimal care for their patients.

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