Anomalous right coronary artery in a middle-aged patient
A case report and review of the literature

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Abstract
Background: An anomalous right coronary artery originating from the left sinus of Valsalva is rare, but often incidental, finding in middle-aged to elderly people. Prevalence is difficult to define, as well as determining potential harmful hemodynamic consequences. Moreover, the optimal treatment remains debatable.

Case summary: The authors present a case of a middle-aged patient diagnosed with an anomalous right coronary artery causing ischemia, who was treated surgically.

Conclusion: By reviewing literature, the authors conclude that choice of treatment depends on age, symptoms, and certain anatomic features of this anomaly. However, there are no randomized trials available in this field.

Abbreviations: ALCA = anomalous left coronary artery, ARCA = aberrant right coronary artery, CA = coronary angiography, CMP = cardiac magnetic resonance, ECG = electrocardiogram, IVUS = intravascular ultrasound, MACE = major adverse cardiac event, MDCT = multidetector computed tomography, MRA = magnetic resonance angiography, RCA = right coronary artery, RVOT = right ventricular outflow tract, SCD = sudden cardiac death, SPECT = single photon emission computed tomography.

Keywords: aberrant right coronary artery, ARCA, case report, coronary anomaly, sudden cardiac death

1. Introduction
In middle-aged to elderly patients, a coronary anomaly is often an incidental finding. The clinical presentation varies from asymptomatic up to presentation as an acute myocardial infarction or even sudden cardiac death (SCD). Coronary anomalies are the second most frequent cause of SCD in young athletes.1,2

Many coronary anomalies are truly benign. Nevertheless, in a large group of anomalies, it is difficult to determine if and how dangerous they are. There is no strict consensus about which treatment should be recommended.

We present a case of an aberrant right coronary artery (ARCA) and reviewed the literature concerning the best diagnostic and therapeutic strategy.

2. Case
A 40-year-old male farmer attended the outpatient clinic complaining of chest pain during work. When he tilted heavy straw bales he felt a piercing and oppressive left-sided thoracic pain, which ceased at rest. The episodes tended to increase in frequency. Syncope or dyspnea was present.

Cardiovascular risk factors consisted of a familial predisposition for coronary artery disease (father had coronary bypass at age of 65) and hypercholesterolemia. His medical history was uneventful.

Physical examination was unremarkable. Resting electrocardiogram (ECG) showed a regular sinus rhythm at 65 bpm, without further abnormalities.

During his first visit, a treadmill exercise test and echocardiography were performed. During the maximal treadmill test (Fig. 1) up to 200 W, he mentioned the chest pain, he felt when working and tilting heavy weights. This was associated with ST depression up to 1.5 mm in leads V5 and V6 and some solitary monomorphic premature ventricular complexes. Echocardiography (Fig. 2) revealed a normal left and right ventricular function with normal function of the heart valves. The right ventricle showed a mild degree of hypertrabeculation.

A further diagnostic work-up was initiated with stress echocardiography and cardiac magnetic resonance (CMR).

Supine bicycle stress echocardiography once again provoked recognizable chest pain, electrocardiographic ST depression in leads V5 to V6, and revealed severe hypokinesia in the inferoposterior region. A coronary angiography (CA) was subsequently planned.

Angiography revealed nonsignificant atherosclerosis in the 3 main coronary arteries in a right dominant coronary system. However, an anomalous take off of the right coronary artery (RCA) in the left sinus of Valsalva was diagnosed (Fig. 3).

CMR confirmed some hypertrabeculation of the right ventricle, without signs of arrhythmogenic right ventricular...
dysplasia or noncompaction syndrome. The left and right ventricular function was preserved and no delayed enhancement or myocardial fibrosis was visualized. This imaging technique confirmed the aberrant origin of the RCA, originating from the left coronary cusp and with a course of the proximal RCA between the pulmonary artery and aorta.

In conclusion, our patient presented with recurrent stable angina and only an ARCA could explain the symptoms. This was clearly confirmed by the abnormal myocardial ischemia tests (treadmill exercise ECG and stress echocardiography) in the territory of the RCA. The case was debated in the heart team, and the patient was referred for a surgical correction.

Uneventful reimplantation of the RCA was performed. Medication at the time of discharge included low-dose aspirin, a statin, and a beta-blocker. After 4 weeks the patient was already slowly resuming daily life, including his work as a farmer.

Four months after the operation, the patient consulted because of exertional shortness of breath (New York Heart Association Class II). There were no obvious signs of ischemia during exercise treadmill test. Coronary multidetector computed tomography (MDCT) (Fig. 4) showed a patient reimplanted RCA without significant coronary artery disease. Repeat stress echocardiography was normal, confirming the treadmill and MDCT scan findings. Cardiac rehabilitation was prescribed. During all follow-up visits, the patient remained asymptomatic and 5 years after presentation there were no cardiac events.

3. Discussion

Several forms of anatomical variants in coronary arteries exist. Some are believed to be potentially dangerous, others are benign.

Potential malignant coronary artery anomalies are an ectopic coronary origin from the pulmonary artery, an ectopic coronary origin from the opposite sinus of Valsalva, a single coronary artery, and large coronary fistulae or muscular bridging.[3]

3.1. Aberrant right coronary artery

The proximal course of an ARCA may vary: preaortic, interarterial (between aorta and pulmonary artery, as in our patient), retrocardiac, retroaortic, intraseptal, and precardiac (pulmonary).
The hemodynamic important variant (i.e., interarterial course) runs between the aorta and pulmonary artery, either intramural (within the aortic wall) or separated from the aortic wall (like 2 distinct arteries). It is supposed that only this interarterial course can cause symptoms or is potentially dangerous.[4]

With newer imaging techniques, newer anatomical variants of the proximal course of an ARCA were distinguished. The coronary takeoff can be high (above the level of the pulmonary valve with a course between the aorta and pulmonary artery) or low (below the level of the pulmonary valve with a course between the aorta and right ventricular outflow tract [RVOT]). This high takeoff variant is believed to be more hostile than an ARCA with low takeoff.[5] Post hoc analysis of the CMR images of our case, revealed a low takeoff.

### 3.2. Prevalence and mortality

During CA studies, the incidence of an ARCA ranges from 0.09% to 0.92%.[6–8] An ARCA has a higher incidence than an anomalous left coronary artery (ALCA) (0.02–0.15%) and is presumed to be the most common type of hemodynamically significant coronary anomalies.[9,10]

In MDCT coronary studies, the incidence of an ARCA is comparable (0.54%).[5]

Among 18,950 autopsy cases in a Los Angeles hospital, 54 cases of coronary anomalies were detected of whom 39 with anomalies of the coronary ostia, totaling to an incidence of 0.206%.[11] In young athletes, 12% of SCDs is caused by an ARCA.[12] In young athletes, coronary anomaly becomes a less frequent cause of SCD.[13]

Mortality data derived from autopsy studies (risk on SCD in ARCA 0–57%, in ALCA 30–100%) are far too high when converted to the general population. These numbers can obviously not be extrapolated from autopsy studies to the general population and are probably severely overestimated as mortality rates are biased as we are not aware of the exact prevalence of an ARCA in asymptomatic patients.[14,15] Notwithstanding, it is assumed that there is a 3- to 6-fold increased risk for SCD in people with an ARCA doing physical activity.[14]

### 3.3. Pathophysiology

The exact pathophysiological mechanism remains unclear. There are several hypotheses: a slit-like orifice caused by an acute angle of takeoff, which could cause reduced coronary flow during exercise[16,17]; compression of the interarterial segment caused by systolic compression between the aorta and pulmonary artery, aggravated during increased flow, for example, with exercise; ventricular arrhythmias caused by ischemia; acute or repetitive ischemia provoking myocardial fibrosis or reperfusion; intramural proximal intussusception of the anomalous artery at the aortic-root wall, as proposed by Angelini et al during intravascular ultrasound (IVUS) studies.[18] Presumably it is even a combination of these different mechanisms. On the other hand, studies showed that a coronary anomaly is not associated with an increased risk for development of coronary atherosclerosis.[19]

It would be interesting to identify specific anatomical or clinical risk factors for SCD in order to predict the possible hemodynamic significance. Logically, the dominance of an anomalous coronary artery is an important risk factor.[20] In a large pathology study of 30 cases of anomalous arteries, it was not possible to identify a certain anatomical feature related to increased mortality.[21] In an MDCT study, clinical symptoms were not related to the relative luminal narrowing nor angle of takeoff.[17,22] However, a significant difference in the prevalence of major adverse cardiac events (MACE) and typical angina was observed in a retrospective review of 22,925 consecutive MDCT scans, in which 124 cases with an interarterial anomalous coronary artery were found. They differentiated the anatomical takeoff in a high and a low takeoff (above or below the level of pulmonary valve). The group with high takeoff (coursing between aorta and pulmonary artery) proved to have a significant higher prevalence of typical angina (43% vs 6%, P = 0.001) and MACE (28% vs 6%, P = 0.012) compared to those with a low takeoff (coursing between aorta and RVOT). Age is an important clinical parameter that is related with the risk of SCD. Under the age of 30, there is an increased risk for SCD in patients with a coronary anomaly. This risk decreases with age.[23] It has been hypothesized that the aortic wall stiffens with age, which reduces compression.[10,21] As mentioned above, exercise is a risk factor for SCD in people with an ARCA.[14]

### 3.4. Clinical presentation and diagnosis

In a necropsy study of 242 patients who died suddenly, 62% of the patients were asymptomatic until the event.[25]

In a Japanese review of 56 patients with coronary anomalies of whom 44 with an ARCA and with a mean age of 55.9 years old, clinical patterns were reviewed. Of 22 patients with an ARCA who had undergone a treadmill test, 10 proved abnormal. Three out of 4 had a positive myocardial perfusion single photon emission computed tomography (SPECT) exercise test. Two patients even suffered ventricular tachycardia during stress testing.[24] These latter results show a much higher rate of positive stress testing than seen in other studies. Stress testing is often inadequate to identify ischemia. This is why a negative stress test
does not exclude a potentially dangerous coronary anomaly.\(^{125}\) When a stress test proves negative but symptoms are suspicious (e.g., exertional syncope or chest pain) anatomical examinations (i.e., MDCT scan) should be considered.

In young patients, or ephrogenic patients, a transhoracic echocardiography could be useful in determining the proximal coronary origin.\(^{26}\) One study showed significant 2D strain impairment in 25 patients with a coronary anomaly (of whom 15 with ARCA), suggesting subtle left ventricular contractility disorder in these patients.\(^{27}\)

One study evaluated the accuracy of coronary artery calcium scanning for detecting coronary anomalies, which was found out to have a great diagnostic accuracy.\(^{28}\) However, nowadays, MDCT CA is accepted as the “gold standard” for the evaluation of coronary anomalies.\(^{29}\)

Magnetic resonance angiography (MRA) is similar successful, but the identification of the distal coronary course can be more difficult.\(^{30}\) Some disadvantages of MRA are also to be considered: availability is less, MRA is not useful in patients with pacemakers or claustrophobia, and total study time takes much longer. One large benefit of MRA is that it can assess and locate scarred tissue and viability in the course of the affected artery, which could have an important prognostic value.\(^{31}\)

A conventional CA is an invasive test. During CA it is not always possible to define the exact proximal anatomical course of the coronary anomaly. In a CA study, only in 53% of the cases the exact proximal course could be defined.\(^{32}\) IVUS showed in some studies intussusception or lateral compression during systole, aggravated by saline, atropine, or dobutamine infusion.\(^{33,34}\) Fractional flow reserve (FFR) was tested by Angelini et al, and showed results within normal limits during adenosine provocation (FFR > 0.9, cutoff 0.8),\(^{10}\) indicating that FFR is not a good parameter to diagnose hemodynamic significance in this setting.

Stress-rest myocardial perfusion SPECT can be used to detect reversible perfusion defects,\(^{35}\) although results are often negative, as it is for stress ECG.

Long-term Holter monitoring can be helpful in screening for arrhythmia, although being an aspecific tool.

In summary, MDCT CA seems to be the best examination for anatomical diagnosis and ischemic testing proves often negative.

### 3.5. Treatment

The 2008 American Heart Association guidelines for the management of adults with congenital disease,\(^{135}\) recommend that surgical coronary revascularization should be performed when there is evidence of ischemia in an anomalous RCA coursing between aorta and pulmonary artery (level of evidence class I, B).

There are no prospective studies available to determine the best treatment option. Indication to treat should be individualized, and depends on age, symptoms, the anatomical variant, and ischemic testing.

In literature, patients are separated by age (younger and older than 35 to 40 years old). New anatomical understandings separate high and low coronary takeoff of the ARCA (above or under level of pulmonary valve) as a possible prognostic finding.

Lee et al suggest to operate all patients, younger than 40 years old, with high takeoff, regardless of symptoms. Symptomatic patients older than 40 years old and with high takeoff should be operated if symptomatic, following their ideas. In patients with a low takeoff, close observation is suggested, unless when related symptoms are present surgery might be considered.\(^{36}\)

In a Japanese retrospective study of 56 patients (mean age 55.9 years old), with anomalous origin of coronary artery (78% ARCA) and without coexisting atherosclerosis, a conservative treatment was applied (nitrates, calcium channel blockers, beta-adrenergic antagonists, or antiarrhythmic drugs).\(^{34}\) During follow-up (2 months to 14.5 years), there were no cardiac-related deaths. The authors concluded that the prognosis of middle-aged to elderly patients with an anomalous origin of the coronary artery is relatively good. A few other studies proved comparable results, suggesting a conservative approach (beta-blockers and physical restriction) may be safe.\(^{13,36,37}\)

This somehow conflicting evidence illustrates that further research is warranted, matching anatomical with clinical and functional test data.

### 3.6. Invasive management

A percutaneous approach has been applied in the past. One case series of 14 patients with proximal coronary artery stenting showed a normalization of stress test results and angiographical patency 6 months after the percutaneous coronary intervention was demonstrated.\(^{38}\)

There are also different surgical strategies: reimplantation of the RCA (as in our case), unroofing of the intramural course with creation of a neo-orifice, the modified unroofing technique, patch augmentation, and classical bypass grafting. With patch augmentation, the proximal interarterial course is not relieved. Bypass grafting demonstrated graft failure because of competitive flow.\(^{39,40}\)

The unroofing technique is mostly applied in children. Unroofing of the anomalous artery can be applied when the proximal course runs intramural, and when there is no involvement of aortic valve commissures, which otherwise could create aortic insufficiency. This technique relieves the ostial stenosis, creates a large neo-orifice, and removes the intramural segment. In the modified unroofing technique, the anomalous orifice is closed, a neo-orifice is created in the appropriate sinus, without extensive unroofing of the proximal intramural part of the anomalous coronary artery. This technique is used to avoid aortic regurgitation when there is commissural involvement.

### 4. Conclusion

The interarterial form of an anomalous RCA (coursing between the aorta and pulmonary artery) can lead to symptoms or even SCD. A high takeoff of the ARCA is a high-risk anatomical feature.

The incidence of an ARCA varies from 0.09% to 0.92%. Coronary anomaly is the second most common cause of cardiac sudden death in young athletes, which demonstrates that young age and vigorous exercise are risk factors for sudden death in patients with an ARCA.

Coronary MDCT is the gold standard for anatomical diagnosis. Further ischemic testing can help to guide the therapy strategy, although functional tests often prove negative.

In middle-aged patients, this anomaly is often an incidental finding. Notwithstanding the lack of randomized trials, we consider it advisable to operate when an ARCA is seen in young patients (<40 years old) or, in older patients with proven related symptoms or positive ischemic testing. Reimplantation of the RCA or unroofing the proximal course of the anomalous artery seems to be the best surgical strategies. When a conservative approach is proposed, avoidance of vigorous exercise and prescribing beta-blockers are advised.
Nevertheless, further research is warranted to determine the optimal treatment strategy.

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