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Clinical outcome of anomalous coronary artery with interarterial course in adults: Single-center experience combined with a systematic review

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ABSTRACT

Background: Anomalous coronary artery originating from the opposite sinus of Vasalva with interarterial course (ACAOS-IAC) is associated with sudden cardiac death (SCD) in young athletes. If identified in adulthood prognosis is usually more benign, resulting in a dilemma regarding revascularization.
Methods: This is a retrospective observational single-center study, including adults with ACAOS-IAC. Medical records between 2012 and 2019 were reviewed for management approach, mortality, cardiac death and coronary related adverse events. Coronary computed tomographic angiography (CCTA) were reviewed. We provide a literature review in regard to clinical outcome.
Results: We identified 40 patients with ACAOS-IAC (mean age 51). Presentation was acute in 7/40 (18%). Ischemia detection with single photon emission tomography (SPECT), cardiac magnetic resonance (CMR) or dobutamine stress echocardiography were performed in 25/40 (63%) patients. Ischemia in the vascular territory of the anomaly was present in 2/25 (8%). In 39/40 (98%) patients were treated expectative. During median follow-up of 2.7 years (IQR 1.5–5.3) no cardiovascular death was observed. Mortality occurred in 1/40 (3%) and coronary related adverse events in 2/40 (5%). We identified 20 studies describing 1194 patients. Revascularization was performed in 376/1154 (32.6%) patients. Mortality stratified for clinical management was 23/431 (5.3%) in the non-revascularization versus 16/253 (6.3%) in the revascularization group during 4.0 years follow-up (weighted median). Cause of death was cardiovascular in 10/596 (1.7%) in 4.2 years (weighted median) follow up.
Conclusions: Both revascularization and non-invasive management have good prognosis in adults with ACAOS-IAC during early follow up. There is need for guidelines and long-term surveillance.

1. Introduction

Anomalous origin of the coronary artery originating from the opposite sinus of Valsalva with an interarterial course (ACAOS-IAC) between the aorta and pulmonary artery is a rare congenital cardiac abnormality. The prevalence is 0.23% for the right coronary artery (RCA) and 0.03% for the left coronary artery (LCA) [1]. ACAOS-IAC is often classified as malignant because it is associated with sudden cardiac death (SCD) in young athletes [2]. Identification of this coronary anomaly in adults is believed to be usually more benign but long-term follow-up is missing. Finding ACAOS-IAC in adults therefore results in a dilemma regarding the need for revascularization. Little is known about the risk of SCD and for whom surgery provides benefit at adult age. Criteria for the necessity of surgical treatment in adults remain controversial and existing guidelines are not always being followed [3–5]. Although this is a rare congenital anatomic variant, findings are likely to increase due to a more widespread use of coronary computed tomographic angiography (CCTA).

Imaging is used for risk stratification which rely on anatomical (vessel morphology and course) and functional (testing for myocardial ischemia) findings. Anatomical features believed to be associated with increased risk of ischemia include involvement of the LCA, intramural course, slit-like orifice, acute angle take-off and high IAC course [2,3,6,7]. However, these features are not univocally endorsed, and some studies failed to prove a correlation [7–9]. Demonstrating myocardial ischemia in the vascular territory of the anomaly by e.g. cardiac single photon emission computed tomography (SPECT) or cardiovascular magnetic resonance (CMR) is believed to be associated with SCD [10]. Since the exact pathophysiological mechanism is not completely

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understood, it remains uncertain if these tests reflect a reliable representation of the risk [1].

We conducted a retrospective study to analyze the diagnostic work-up used and chosen management in our hospital in correlation with clinical outcome. Also, a systematic review was performed of the existing literature to summarize all reported clinical outcome data in relation to treatment.

2. Methods

2.1. Retrospective observational study

We selected all patients with ACAOS-IAC referred to our tertiary hospital for consultation of the multidisciplinary congenital heart team between 2012 and 2019. Since this is a purely observational and retrospective study, the need for ethics committee approval was waived by the Medical Research Ethics Committee of the Erasmus Medical Center.

Data from our standard diagnostic work-up were collected including evaluating electronic medical records with baseline demographics, clinical history, exercise tests, surgery reports, clinical management and results of diagnostic imaging tests (i.e. SPECT, CMR, CCTA, invasive coronary angiography (ICA)). From 2017 diagnostic work-up was standardized with retrospectively ECG-gated CCTA and adenosine stress CMR if no other ischemia detection was already performed in the referral center.

Follow up data were collected by evaluating electronic medical records until October 2020 and consisted of all-cause mortality, cardiovascular death and coronary related adverse events (coronary surgery, PCI, myocardial infarction, sudden cardiac death). To ensure no events outside of our hospital were missed, patients were contacted with a telephone questionnaire.

2.2. Imaging

CCTA images were reviewed by one trained observer (MSHB). Since our study population was referred by other hospitals and primarily scanned elsewhere, different scanners were used, all with prospective cardiac gating and on scanners with at least 64-slices. If additional retrospectively ECG-gated CCTA was performed, a Siemens Somatom Force dual source scanner was used. The following anatomical features were evaluated: 1) Proximal vessel morphology: minimum diameter at the most narrowed point of the IAC, compared with a distal reference segment. The percentage of narrowing was calculated as: %narrowing = 1 – (minimum diameter IAC/minimum diameter distal reference segment).

Proximal vessel morphology was defined as normal (<10% narrowing), oval (≥10% and < 50%) and slit-like (≥50%). 2) Take-off angle: measured between 5 mm along the centerline of the anomalous coronary artery and the tangent line at level of the aorta coronary ostium. Measurements were performed in a multi-planar axial reconstruction at the level of the coronary ostium [11]. Acute angle was defined as angle <30°. 3) Intramural course: defined as present or absent and length of the intramural course was measured in mm [11]: 4) If retrospective ECG-gated CCTA was available, variation of the minimum diameter at the most narrowed point of the interarterial segment between the systolic and diastolic phase was measured. Dynamic compression was defined as >0.5 mm difference.

Exercise ECG, SPECT, adenosine stress CMR, and dobutamine stress echocardiography were analyzed for any ischemia. If applicable, ischemia in the vascular territory of the coronary anomaly was scored.

2.3. Systematic literature review

A comprehensive search of MEDLINE (Pubmed) was performed electronically in July 2019 and updated in December 2020 for all published reports of outcome for patients with ACAOS-IAC. Details of MESH terms combination are given in the appendix. One reviewer (MSHB) screened titles and abstracts, and then examined the full text of relevant publications.

Studies describing ≥20 patients with ACAOS-IAC in combination with clinical outcome with mean or median follow up of at least 1 year were included. Both adult and pediatric populations were included. Articles published in languages other than English, non-human studies and surgical cohort studies were excluded.

Data collection included: Age, gender, total number of patients with coronary anomalies, number of patients with ACAOS-IAC, follow up time. Specifically, for patients with ACAOS-IAC we collected the following data: involvement of LCA or RCA and choice of treatment (revascularization vs. other).

The following secondary outcomes were recorded: mortality, cardiac or cardiovascular death, late revascularization, re-operation, ventricular rhythm disorders, syncope, ischemic symptoms, ischemia, acute myocardial infarction. Outcomes were stratified for two groups regarding treatment. The revascularization group included all patients treated with PCI or cardiac surgery and a non-revascularization group included patients treated otherwise (non-invasively).

2.4. Statistical analysis

Results are summarized reporting the absolute numbers and percentages. For categorical variables, mean with standard deviation (SD) when normally distributed, or median with interquartile range (IQR) are given. In the systematic literature review median follow-up duration of the entire study population reported in the articles was used for the IAC subpopulation if the follow-up of this subpopulation was not described separately. To calculate the pooled follow-up, the weighted median was calculated based on the number of patients with ACAOS-IAC. If only mean follow up was reported this was used as median. Weighted mean age was calculated based on number of patients with ACAOS-IAC. If only median was reported this was used as mean. Statistical analyses were performed using SPSS (version 25, IBM SPSS Statistics, IBM corporation, Armonk, New York, USA).

3. Results

3.1. Retrospective observational study

We identified 40 patients (age 51, mean) with an ACAOS-IAC. Patient information is presented in Table 1. RCA involvement was present in 36/40 (90%) patients and LCA in 4/40 (10%). Mean age at time of diagnosis was 51 years (range 16–73). One or more cardiovascular risk factors were present in 28/40 (70%). The main indication for initial cardiac evaluation was mainly stable chest pain 28/40 (70%). A minority of 6/40, (13%) patients were diagnosed with ACS. One patient presented with sudden cardiac arrest and ventricular fibrillation after a running competition. Emergency ICA was performed which showed a left ACAOS-IAC and suspicion of a dissected interarterial segment which was treated with PCI. Post-procedure CCTA showed proximal from the coronary stent tapering of the anomalous coronary artery either due to residual dissection or proximal intramural course. ICA during follow up showed patent coronary stent and tapering of the proximal anomalous LCA with fractional flow reserve measurement of 0.87. Patient was asymptomatic and further treatment was expectative with good clinical outcome.

3.1.1. CCTA evaluation

Anatomical assessment with CCTA was performed in all patients. One CCTA evaluation performed after emergency PCI was not suitable for proximal morphology review and one CCTA was not available for review. Occurrence and examples of proximal vessel morphology, intramural course, take-off angle and dynamic compression are

Table 1
Patient information for patients with ACAOS-IAC.

	All patients ($n = 40$)	RCA ($n = 36$)	LCA (n = 4)
Demographics, n(%)			
Age mean, years ± SD	51 ± 13	51 ± 13	54 ± 16
Female	17 (43)	14 (39)	3 (75)
Diabetes mellitus	4 (10)	3 (8)	1 (25)
Hyperlipidemia	8 (20)	8 (22)	0
Hypertension	14 (35)	12 (33)	2 (50)
Current Smoker	7 (18)	7 (18)	0
Family history	13 (33)	13 (36)	0
Presenting symptoms, n(%)			
Chest pain	28 (70)	25 (69)	3 (75)
Acute coronary syndrome	6 (15)	6 (17)	0
Dyspnea	5 (13)	4 (11)	1 (25)
Palpitations/arrhythmia	2 (5)	2 (6)	0
Coincidental finding at extra cardiac evaluation	4 (10)	3 (8)	1 (25)
Asymptomatic	4 (10)	3 (8)	1 (25)
Aborted sudden cardiac death	1 (3)	0	1 (25)
Diagnostic imaging, n (%)			
CCTA	40 (100)	36 (100)	4 (100)
Retrospective ECG-gating CCTA	28 (70)	26 (72)	2 (50)
Invasive coronary angiography	17 (43)	15 (42)	2 (50)
Obstructive CAD, n(%)	2 (5)	2 (6)	0
Agatson score, n/N (%)			
0	20/34 (59)	18/32 (50)	2/2 (100)
1–400	13/34 (38)	13/32 (36)	0/2
≥ 400	1/34 (3)	1/32 (3)	0/2
Positive results ischemia detection, n/N (%)			
Exercise ECG	1/27 (4)	1/24 (4)	0/3
SPECT	2/15 (13)	1/14 (8)	1/1 (100)
Adenosine stress CMR perfusion	0/12	0/12	0
Dobutamine stress echocardiography	0/1	0/1	0
Clinical management, n (%)			
PCI	1 (3)	0	1 (25)
Cardiac surgery	0	0	0
Expectative management	39 (98)	36 (100)	3 (75)

ACAOS-IAC: anomalous coronary arteries originating from the opposite sinus of Vasalva with interarterial course; SD: standard deviation; RCA: right coronary artery; LCA: left coronary artery; CCTA: coronary computed tomography angiography; ECG: electrocardiogram; CCTA: coronary computed tomography angiography; CAD: coronary artery disease; SPECT: single photon emission computed tomography; CMR: cardiac magnetic resonance; PCI:,percutaneous coronary intervention.

summarized in Fig. 1. Median angle of the proximal anomalous coronary artery was 25° (IQR 22–31) and was <30° in 25/38 (66%). Intramural course was present in 17/38 (45%) with a mean length of 11.9 ± 4.8 mm. Retrospectively ECG-gated CCTA was performed in 29/40 (73%) patients and dynamic compression was found in 4/27 (15%). Calcium score was performed in 34/39 (89%) and was ≥400 in 1/34 (3%).

3.1.2. Ischemia detection

Exercise ECG was performed in 27/40 (68%) and showed suspicion of ischemia in 1/27 (4%). Additional ischemia detection was performed in 25 patients, with SPECT in 15/25 (60%), adenosine stress CMR in 12/25 (48%) and dobutamine stress echocardiography in 1/25 (4%).

Adenosine stress CMR tests and dobutamine stress echocardiography found no ischemia. Ischemia in the vascular territory of the anomaly was found with SPECT in 2/15 (13%). The first patient had an anomalous RCA with acute take-off angle of 17°, slit-like orifice and 9 mm intramural course. Due to the small affected area of ischemia this patient was treated expectative. The second patient had a left ACAOS-IAC and ischemia in the anterior wall caused by severe intramyocardial bridging of the LAD for which surgical repair was performed.

Adenosine CMR was performed after initial SPECT in 3/25 (12%) patients to confirm findings on SPECT interpreted as artifacts or to analyze old myocardial infarction. On both modalities findings of ischemia were negative.

3.1.3. Management and follow-up

One patient with left ACAOS-IAC received emergency PCI as detailed above. All other patients 39/40 (98%) were treated expectative with no revascularization with regard to the coronary anomaly and no restrictions on physical activities. Two patients with ACS showed significant stenosis in the LCA which was treated with PCI, the anomalous RCA was not treated. In all other patients with ACS no significant coronary stenosis was found and ischemia tests were negative.

During a median follow-up of 2.7 years (IQR 1.5–5.3) no CV death was recorded and mortality occurred in 1/40 (3%). Autopsy showed major cerebral infarction in the left hemisphere.

Coronary related adverse event occurred in 2/40 (5%) patients. The first patient, described earlier, with surgical repair for intramyocardial bridging received PCI of the LAD during follow up, the anomalous proximal LCA was not treated. The second patient presented with stable angina during follow-up. ICA showed a proximal LAD stenosis for which PCI was performed. The anomalous RCA showed no significant stenosis with FFR and expectative management was continued.

3.2. Systematic literature review

Among 8471 studies in our search of published reports, we eventually identified 19 studies in addition to our own study. Selection of studies is illustrated in a flowchart in the appendix. Results are summarized in Table 2. Total number of patients with ACAOS-IAC was $n = 1194$. Weighted mean age was 43 years. Treatment was specified for 1154/1194 (96.6%) patients. Revascularization was performed in 376/1154 (32.6%) patients including surgical repair in 365/376 (97.1%) and PCI in 11/376 (2.9%). Mortality stratified for clinical management was 23/431 (5.3%) in the non-revascularization group vs. 16/253 (6.3%) in the revascularization group, during a weighted median follow-up of 4.0 years. Cardiac or CV death occurred in 10/596 (1.7%) during a weighted median follow up of 4.2 years. CV death was attributed to non-ischemic cardiomyopathy in 1/10 (10%) and severe aortic stenosis in 1/10 (10%) [11]. Other cases of cardiac or CV death were not described.

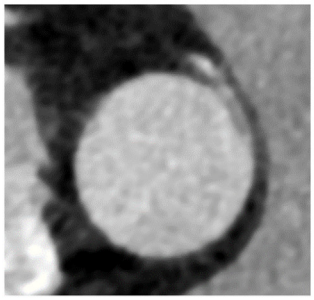
Secondary endpoints occurred in the non-revascularization group in 7/423 (1.7%) patients and in 6/195 (3.1%) in the revascularization group, during a weighted median follow up of 3.5 years. For description of the endpoints see Table 2. Risk factors could not be identified due to the low number of events.

4. Discussion

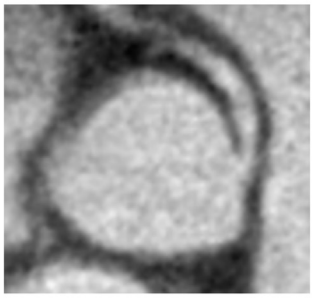
This is a single-center retrospective observational study of adult patients with a coronary anomaly running between the aorta and pulmonary artery and in addition a systematic review of literature. In our own data we found no cardiac death or coronary adverse event caused by the coronary anomaly during follow up. One patient with an left ACAOS-IAC presented with an acute presentation after a running match was treated with an emergency PCI. All other patients (39/40 (98%)) were treated with no revascularization with regard to the coronary anomaly and no restrictions on physical activities. We compared our results in a systematic literature review which also showed a low incidence of cardiac or cardiovascular death during 4 years of follow up. Furthermore, in our literature review mortality and clinical outcome was similar for patients treated with revascularization (surgical or PCI) versus other management. These findings are similar to early results of a multicenter study including 182 ACAOS-IAC which found no statistical difference in coronary related events between surgically treated (median age 37) and medically treated patients (median age 13) during a follow-up of 18 months [12].

Lack of studies with long-term follow-up after identification of an ACAOS-IAC in adult patients provide a gap in evidence who are at risk

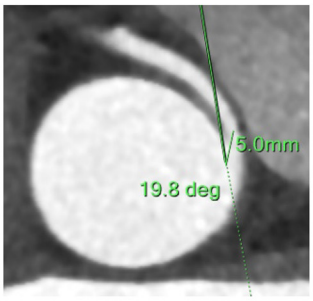
A.Intramural segment
Present 17/38 (45%)
Mean length 11.9mm (+/- 4.8mm)



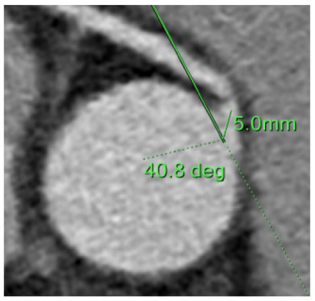
No intramural segment
Absent 21/38 (55%)



B. Acute angle
Present 25/38 (66%)

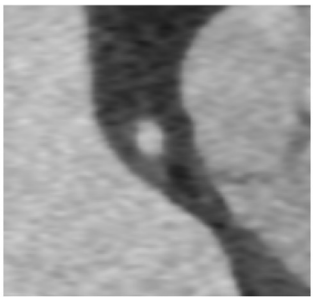


No acute angle
Absent 13/38 (34%)

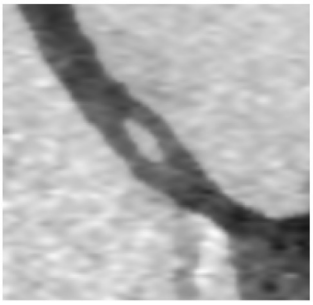


C. Proximal vessel morphology

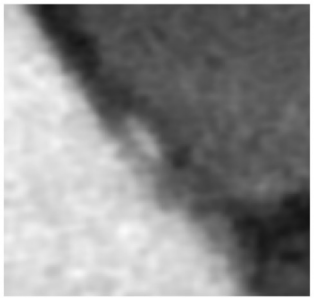
Normal
5/38 (13%)



Oval
28/38 (74%)

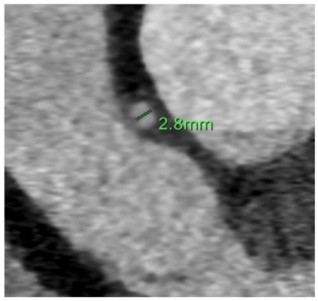


Slit-like
5/38 (13%)

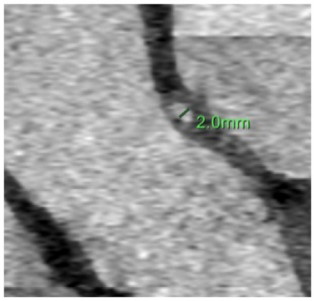


D. Dynamic Compression

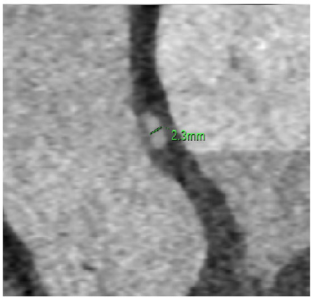
Present 4/29 (14%)
Diastolic



Systolic



Absent 25/29 (86%)
Diastolic



Systolic

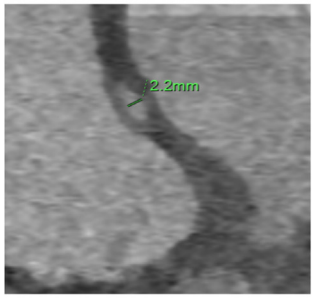


Fig. 1. High-risk anatomic features coronary anomaly with interarterial course. A. Intramural course, defined as present or absent. Length of the intramural course is given when present. B. Acute angle of take-off, defined if <30°. Take-off measured between 5 mm along the centerline of the anomalous coronary artery and the tangent line at the level of the aorta coronary ostium. C. Proximal vessel morphology, defined as normal (<10% narrowing), oval (≥10% and < 50%) and slit-like (≥50%). Minimum diameter at most narrowed point of the interarterial course compared with distal reference segment. D. Dynamic compression, defined present if difference > 0.5 mm between systolic vs. diastolic diameter of th most narrowed point of the interarterial segment.

Table 2
Result systematic review.

Study	Year	Number of patients	Sex (male/female)	Age (years)	Follow-up (years)	Selection of patients with interarterial course**							
						Number of patients (RCA/LCA)	Treatment				Outcome		
							Non-revasc.	Revasc.			Mortality (Non-revasc./revasc.)	Cardiac or cardiovascular death	Combined endpoints (non-revasc./revasc.)
								Total	RCA/LCA	Surgical/PCI			
Blomjous et.al.	2020	40	23/17	51 ± 13	2.7 [1.5–5.3]	40 (36/4)	39	1	0/1	0/1	1 (1/0)	0	2 (2/0) (PCI)
Padalino et.al. [12]	2019	217	124/93	37 [13–53]	1.5 [0.5–4.0]	182 (135/47)	47	135	*	135/0	4 (0/4)	*	5 (0/5) (PCI, ICD, surgical resection)
Nagashima et.al. [14]	2019	65	48/17	41 ± 23	5.0 [1.8–7.0]	65 (47/18)	30	35	*	26/9	0	0	*
Driesen et.al. [8]	2018	30	19/11	52 ± 8	3.0 [1.0–3.9]	30 (25/5)	18	12	10/2	12/0	*	0	0 (MI, revascularization, ventricular rhythm disorders, syncope)
Palmieri et.al. [20]	2017	23	17/6	19 ± 14	5.4 ± 5.8	23 (17/6)	17	6	3/3	6/0	0	0	0 (ischemic symptoms)
Alkhulaifi et.al. [21]	2017	33	19/4**	43 ± 15***	Range 2–5	23 (20/3)	23	0	0	0	*	*	0 (angina pectoris)
Cheezum et.al. [11]	2017	103	65/38	52 ± 17	5.8 [3.8–7.8]	43 (40/3)	36	7	7/0	7/0	3 (3/0)	2	*
Gräni et.al. [22]	2017	66	48/18	56 ± 11	4.0 ± 2.8	40 (33/7)	*	*	*	*	*	0	*
Layser et.al. [23]	2016	172	38/41**	64 ± 12***	4.5 ± 3.3****	79 (68/11)	58	21	17/4	21/0	9 (3/6)	3	3 (2/1) (myocardial infarction)
Lee SE et.al. [28]	2016	119	70/49	55 [*]	4.0 [IQR *]	119 (119/0)	112	7	7/0	6/1	2 (2/0)	*	1 (1/0) (late surgical repair)
Fabozzo et.al. [24]	2016	155	101/54	9, range 0–50	1.9, range 0–12.7	151 (*)	81	70	*	70/0	*	*	*
Amado et.al. [25]	2016	53	30/23	58 ± 10	3.8 ± 2.4	21 (17/4)	21	0	0	0	0	0	*
Nasis et.al. [7]	2015	114	77/37	58 ± 13	2.3 ± 1.3	46 (36/10)	38	8	6/2	8/0	*	0	0 (acute coronary syndrome)
Ripley et.al. [26]	2014	116	*	57, range 1–85***	4.3 [2.5–7.8]	64 (*)	41	23	*	23/0	*	3	*
Opolski et.al. [27]	2013	72	37/35	55 ± 12	1.3 ± 1.0	24 (20/4)	22	2	1/1	2/0	*	*	*
Lee HJ et.al. [6]	2012	87	51/36	56, range 20–80	2.5 [0.8–3.9]	87 (87/0)	79	8	8/0	8/0	*	1	*
Krasuski et.al. [29]	2011	301	36/18**	52 ± 13***	9.2 [3.3–16.4] ****	54 (*)	26	28	8/0	28/0	17 (12/5)	*	*
Lytrivi et.al. [30]	2008	166	93/73	6, range 0–50	1.5 (0.2–3.6)	27 (23/4)	21	6	5/1	6/0	1 (1/0)	0	*
Osaki et.al. [19]	2007	31	25/6	6 range 0–16	4.2, range 0–9.0	31 (18/13)	24	7	0/7 *	7/0	2 (1/1)	1	0 (ischemia)
Kaku et.al. [31]	1996	56	41/15	60 ± 12	5.6 ± 4.2	45 (44/1)	45	0	0	0/0	*	*	2 (2/0) (acute myocardial infarction, syncope)
Total		2019	962/591	43	3.5	1194	778/1154 (67%)	376/1154 (33%)	71/22	365/376 (97%)/ 11/376 (3%)	39/684 (5.7%) (23/431 (5.3%)/16/253 (6.3%))	10/596 (1.7%)	13/618 (2.1%) (7/423 (1.7%)/6/195 (3.1%))

RCA: right coronary artery; LCA: left coronary artery; ICD: implantable cardioverter defibrillator; SD: standard deviation; IQR: interquartile range; PCI: percutaneous coronary intervention; MI: myocardial infarction; Revasc: revascularization; Non-revasc.; non-revascularization.
Data is presented as number (percentage), mean ± SD, median [IQR], or otherwise stated, * data missing/not possible to extract from reference ** sex specific for subgroup ACOAS-IAC *** age specific for subgroup ACAOS-IAC **** follow-up specific for subgroup ACAOS-IAC.

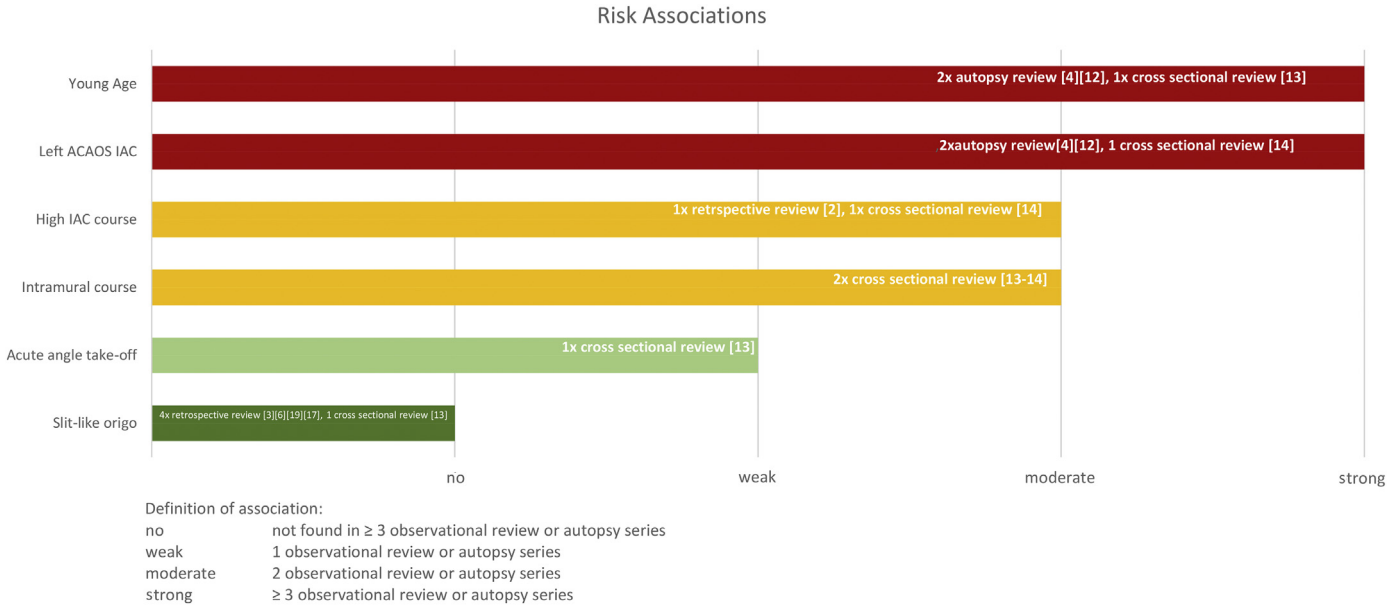


Fig. 2. Prognostic value of anatomic feature of an anomalous coronary artery and interarterial course based on results of our retrospective cohort study, systematic literature review and other literature. No. Not found in ≥3 observational review or autopsy series. Weak. 1 observational review or autopsy series Moderate. 2observational review or autopsy series Strong. ≥ 3 observational review or autopsy series.

for SCD and for whom surgery provides benefit at adult age [3,5]. Based on level C evidence, the 2020 ECS guidelines for management of adult congenital heart diseases recommend to consider surgery for symptomatic patients regardless of presence of myocardial ischemia and for specific populations (left-ACAOS and young patients with high-risk anatomy) even in absence of myocardial ischemia and symptoms. These recommendations are largely similar to previous American College of Cardiology/American Heart Association 2008 guidelines and expert consensus guidelines American Association for Thoracic Surgery 2017 [4,5].

Association between SCD and ACAOS-IAC is largely based on previous autopsy studies of military recruits and competitive athletes indicating an increased risk of sudden death due to a coronary anomaly, especially for left ACAOS-IAC [2,13]. During a 25-year review of 126 military recruits with sudden death, identifiable cardiac abnormalities were found in 51% ($n = 64$) and in a third of these cases left ACAOS-IAC was present. Besides the involvement of LCA, several other pathophysiologic mechanisms in addition to the proximal vessel course have been proposed to explain the increased risk of sudden cardiac death. These include: a slit-like ostium due to believed risk of valve-like occlusion, an acute take-off angle which might cause kinking, high interatrial course and intramural course which might increase the vulnerability of dynamic compression. Despite such theoretical considerations, several observational studies included in our literature review failed to show correlation between these anatomic features and clinical outcome [7,8]. Only high inter-arterial course did show a correlation with major adverse events in one observational study [6]. In a multicenter cross-sectional study including patients with symptomatic presentation, an association with acute take-off angle was found, but no correlation with slit-like ostium was demonstrated [14]. Another multicenter cross-sectional study that was not included in our literature review showed positive ischemia tests of patients with left ACAOS in correlation with intramural course, high orifice and slit-like orifice. However, the same findings could not be demonstrated for right ACAOS [15]. In Fig. 2 we propose an interpretation of the prognostic value of these anatomic features based on the results of our own retrospective cohort study, the systematic literature review and other literature.

Different imaging modalities can be used for evaluating anomalous coronary arteries. Given the technical improvement of CT-scanners in spatial and temporal resolution it has become the first-line imaging modality in most centers to visualize the origin and course of coronary anomalies in adult patients [16]. ICA in combination with intravascular ultrasound (IVUS) may be of value to assess the intramural course during the cardiac cycle but is inevitably limited by dependence on operating physicians and evaluation of other high-risk features. To assess changing morphology during the cardiac cycle we uniquely performed retrospectively ECG-gated CCTA in 29 patients revealing subtle changes of proximal vessel morphology between systole and diastole.

Evaluation of the hemodynamic effects when finding ACAOS in adults is always indicated [3]. Exercise ECG may have false negative results according to a study including 27 young athletes with SCD and previous 6/6 normal exercise ECG results [17]. SPECT with physical stress is preferred over pharmacological testing because this simulates the normal situation better and is included as class 1 recommendation in the 2020 ECS guidelines [3]. In a study including 26 patients with hybrid CCTA/SPECT myocardial ischemia was found once believed to be caused by concomitant CAD [18]. We found a small area of ischemia caused by the anomaly in 1/15 with SPECT in a patient with several high-risk anatomic features on CCTA. The absence of myocardial ischemia on stress testing may suggest that in adult population myocardial ischemia due to ACAOS is rare and hence results in better clinical outcome in this population. Although the exact pathophysiological mechanism is not completely understood, it remains uncertain if these tests reflect a reliable representation of the risk and more research is necessary to examine possible false negative results.

4.1. Study limitations

In interpreting our findings, the following limitations should be considered. This is a single-center observational study at a tertiary center with a selected population of patients and therefore subject to referral bias. The follow up period is comparable to similar studies but a longer follow up is clearly desirable. Due to the retrospective nature of this study, we evaluated coronary adverse events as clinical outcome and development of initial presenting symptoms could not be examined. A relatively aged population was presented in our cohort as in most studies included in the systematic literature review. Patients at the highest risk of fatal complications may be underrepresented as their first

presentation may be a fatal one at younger age. Because this is a retrospective study, these patients might be missed. Revascularization is often chosen for patients in worse (clinical) condition and is a biased in the comparison to non-revascularized treated patients. In the systematic literature we focused on clinical outcome and therefore we did not elaborate on diagnostic approach of included studies.

5. Conclusion

Adults are believed to have a better prognosis then young patients when presenting with an ACAOS-IAC. Management with revascularization in adults is therefore debatable. We have shown an excellent prognosis in adults that do no undergo surgery during 2.7 years follow up. The systematic review could not demonstrate any claimed protective effect of revascularization. Prognostic value of high-risk anatomic features shows conflicting results in several studies. Long follow-up is needed to demonstrate the contributing role of revascularization in adults with ACAOS-IAC.

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Declaration of Competing Interest

None.

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