Table 1: Classification and prevalence of coronary artery anomalies in 5634 consecutive patients undergoing CCTA.

Classification		Cases n	Cases %	Prevalence (%)
Anomalies of vessel origin and course (n = 107)	Separate ostium for LAD and LCX	27	(18.6)	0.48
	Single coronary artery	7		0.12
	Absent LCX	2	(1.4)	0.04
	Bland-White-Garland syndrome	1	(0.7)	0.02
	High take off LAD	1	(0.7)	0.02
	High take off RCA	3	(2.0)	0.05
	ACAOS	66		1.17
	ACAOS with interarterial course	36		0.64
	ACAOS with prepulmonary course	3		0.05
	ACAOS with retroaortic course	27		0.37
	LM from noncoronary sinus	5	(3.5)	0.09
	RCA from noncoronary sinus	1	(0.7)	0.02
Anomalies of intrinsic coronary arterial anatomy (n = 33)	Duplication of LAD	6	(4.1)	0.11
	Duplication of RIM	2	(1.4)	0.04
	Duplication of RCA	1	(0.7)	0.02
	Ectasia	12	(8.3)	0.21
	Hypoplasia of LCX	8	(5.5)	0.14
	Hypoplasia of RCA	4	(2.8)	0.07
Anomalies of vessel termination (n = 5)	Coronary artery fistula	5		0.09
	LAD to pulmonary artery	3	(2.1)	0.05
	LAD and RCA to pulmonary artery	1	(0.7)	0.02
	LCX to Coronary Sinus	1	(0.7)	0.02

LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; RCA = right coronary artery; LCS = left coronary sinus of Valsalva; RCS = right coronary sinus of Valsalva; LM = left main stem; RIM = ramus indermedius artery. Adapted with permission of EMH Swiss Medical Publishers Ltd. from Ref. [2]

tients and controls. Interestingly, the annual event rate of ACAOS patients compared with controls was not significantly different at 4.9 versus 4.8% and a hazard ratio of 0.94 (95% confidence interval [CI] 0.39–2.28, p = 0.89). In the subgroup with ACAOS with an interarterial course (40 patients, 65%), the annual event rate was also not significantly different from their matched controls, at 5.2 and 4.3%, respectively and a hazard ratio of 1.01 (95% CI 0.39–2.58, p = 0.99) (fig. 4) [14]. Thus, in this middle-aged population with newly diagnosed ACAOS and possible concomitant CAD, mid-term outcome was favourable and not statistically different from the matched control cohort without an anomalous coronary artery, regardless of whether or not ACAOS with an interarterial course were present. Whether older patients with ACAOS are less susceptible to adverse cardiac events, or whether a selection bias towards low-risk patients who survived childhood may have influenced our results remains unclear. Whichever is the case, it may be hypothesised that with ageing the risk for cardiovascular morbidity and mortality due to ACAOS moves into the background compared with the increasing risk of CAD-related events [15] and that surgery of ACAOS might not be mandatory for all these incidental findings. Indeed, when a subgroup of this middle-aged population with ACAOS who underwent hybrid imaging with CCTA and single photon emission computed tomography (SPECT) was analysed, myocardial ischaemia due to ACAOS was exceedingly rare and was more likely attributable to concomitant CAD [15].

Table 2: Different imaging modalities in evaluating anomalous coronary arteries.

		TTE	TEE	CCTA	CMR	Invasive angiography and IVUS
	Spatial resolution	++	++	+++	++	++++
	Temporal resolution	++	+++	++	++	+++
Anatomy of coronary arteries	Proximal	+++	+++	++++	++++	+++
	Distal	+	+	++++	++	+++
Anatomical high-risk features in anomalous coronary arteries	Interarterial course	++	++	++++	++++	++
	Slit-like ostium	+	+	++++	++	+++
	Take-off angle	++	+	++++	++++	+
	Intramural course	++	++	++++	+++	++++
	Proximal narrowing	++	++	+++	++	+++
	Elliptical shape	++	++	+++	++	+++

IVUS = intravascular ultrasound; TEE = transoesophageal echocardiography; TTE = transthoracic echocardiography. Adapted with permission of Elsevier from Ref. [7]

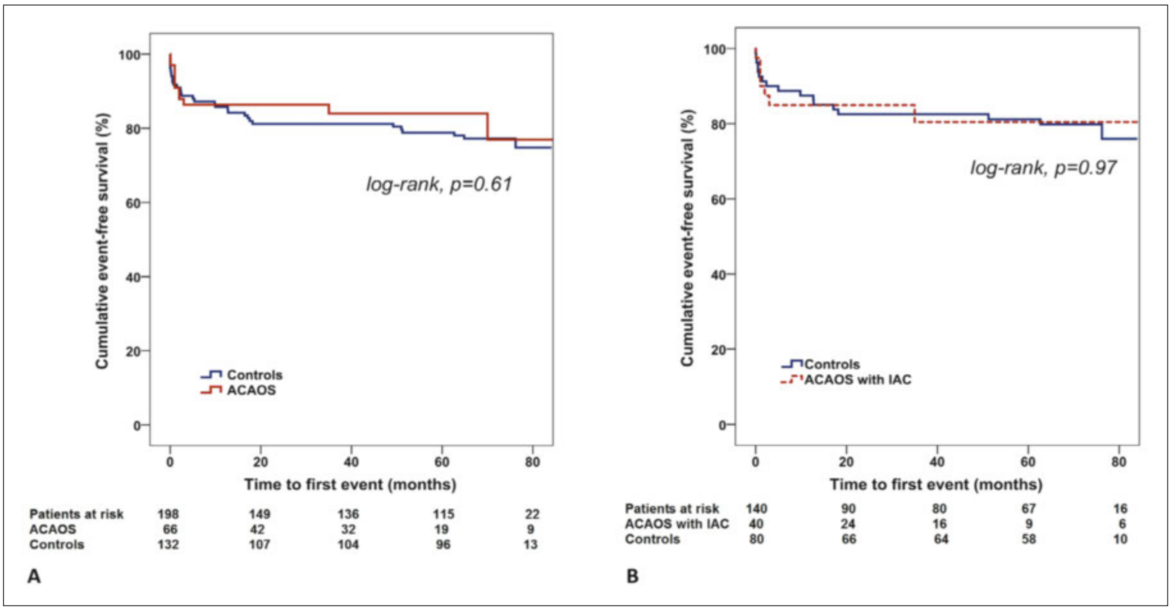

Figure 4: Kaplan-Meier cumulative event-free survival for patients with ACAOS vs controls (A) and ACAOS and IAC vs Controls (B). IAC = interarterial course. Adapted with permission of the Oxford University Press from Ref. [14].

Imaging modalities in the assessment of coronary artery anomalies

CCTA has undergone substantial technical advances over the last decade, particularly with regard to spatial resolution and reduction of patients' exposure to radiation to an average range of 0.21 to 0.5 mSv in daily clinical routine [16]. Therefore in most centres, CCTA has become the first-line imaging modality to assess the anatomy, i.e., the full course, of coronary artery anomalies [2]. Cardiac magnetic resonance imaging (CMR) also offers three-dimensional imaging at high spatial resolution (slightly lower than coronary CCTA), but without radiation exposure, and allows visualisation of the origin and the full course of the ACAOS, including its relationship to the great vessels. Furthermore, CMR offers other additional relevant information including valvular function, ventricular function, regional contractility and myocardial viability, all of which could be important considerations during the pre- or postoperative evaluation [17]. Echocardiography is also a valid alternative for assessing primarily the origin of ACAOS.

If an anomalous coronary artery with a high-risk anatomical feature is detected, downstream imaging for assessment of haemodynamic relevance is indicated. As pharmacological (adenosine) testing would not adequately represent strenuous exercise, maximum physical stress imaging, using SPECT (or also physical stress echocardiography, especially in children) is preferred in patients with ACAOS [15, 18, 19]. Alternatively, stress testing with dobutamine – which mimics physical exercise better than adenosine [20] – with use of other imaging modalities can also be considered where, for technical and procedural reasons, adequate maximum intensity exercise stress testing is not possible (e.g., stress-CMR, positron emission tomography [PET]). However, there is no evidence comparing the different imaging modalities in this particular clinical setting. Beside the advantage of the feasibility of physical stress imaging, SPECT also allows fusion of the functional imaging with the anatomical information from CCTA (fig. 5) [15, 21]. In more than half of patients with no coronary anomalies, the so-called standard distribution of myocardial perfusion territories does not correspond with individual anatomy [22], and it is even more challenging in patients with ACAOS to correctly assign territories to the subtending coronary arteries. Therefore, hybrid CCTA/SPECT and hybrid CCTA/PET represents a valuable noninvasive tool for discriminating the impact of ACAOS from that of concomitant CAD on myocardial ischaemia and correctly allocating ischaemia to the subtended anomalous or nonanomalous vessel.

Incorporating current knowledge of the literature of ACAOS, we propose the following imaging evaluation steps, treatment options and sport restriction recommendations (fig. 6) [7]. In "benign" ACAOS with absent high-risk anatomical features, no downstream testing, treatment and follow-up is generally needed. In "ma-

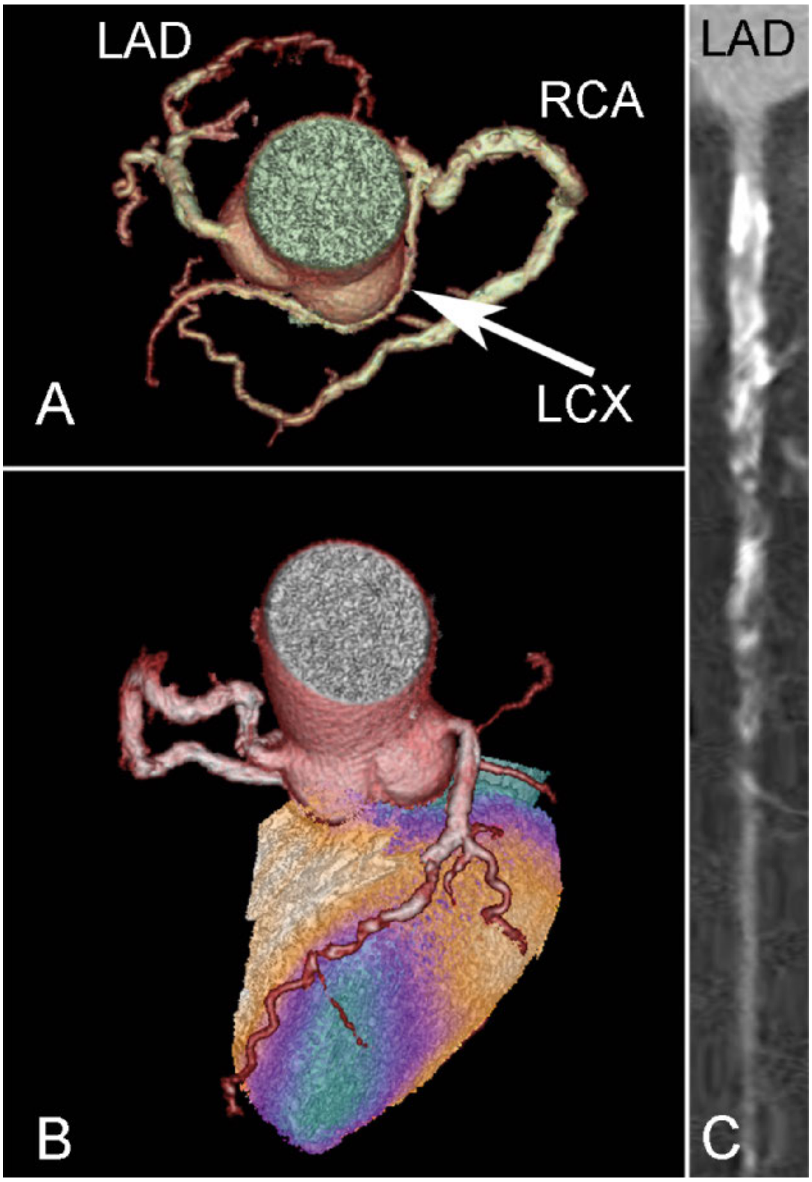

Figure 5: CCTA shows a patient with a benign ACAOS variant and a retroaortic course of the LCX (A). Hybrid CCTA/SPECT (using the CT attenuation-corrected stress dataset) reveals an anteroapical ischaemia matching the perfusion area of the LAD (B). CCTA demonstrates severe coronary atherosclerosis with subtotal stenosis of the middle LAD (C). LAD = left anterior descending artery; LCX = left cirumflex artery; RCA = right coronary artery. Reproduced with permission of Springer from Ref. [15].

lignant" ACAOS with high-risk anatomical features, further imaging evaluation is needed in order to rule out ischaemia. Whether no finding of ischaemia fully reassures the physician and prognosticates absence of ACAOS-related future adverse cardiac events, remains unclear to date.

Therapeutic options in individuals with coronary artery anomalies

Although there are no long-term follow-up data showing a benefit of surgery over conservative treatment, it is generally recommended that, especially young patients with left-ACAOS and an interarterial course or documented ischaemia, should undergo surgery [23]. These patients also should be restricted from any competitive sports before surgery, based on the recent American Heart Association / American College of Cardiology Task Force 4 recommendations [24]. As an exception, participation in low static or low dynamic (class IA sports, such as bowling, cricket, curling, golf, rifle shooting and yoga) is allowed. This applies to patients with symptomatic or asymptomatic ACAOS diagnosed in either intentional or incidental conditions. This recommendation applies also to patients with right-ACAOS and either symptoms or a positive exercise stress test. In athletes with uncorrected right-ACAOS who exhibit symptoms, arrhythmias, or signs of ischaemia on exercise stress testing, participation in all competitive sports, except for class IA sports, is also not recommended before a surgical repair. For patients with right-ACAOS but no symptoms or ischaemia on an adequately performed exercise stress test, participation in competitive sports can be considered after adequate counselling of the athlete or the athlete's parents [24].

The operative correction technique most used is so-called unroofing, where the intramural segment in the aorta is opened and a neo-ostium is created. Alternatively, re-implantation of the aberrant coronary artery or bypass surgery can be performed. However, this last technique is usually less effective as the bypass graft is prone to closure because of competing flow in the native vessel [7].

In other haemodynamically relevant coronary artery anomalies, namely Bland-White-Garland Syndrome, an operation is almost always indicated [23]. The primary aim is to re-implant the aberrant coronary artery in the aortic root or to tunnel aortic blood flow through the pulmonary artery to the ostium of the aberrant coronary artery (Takeuchi operation). Large coronary artery fistulas should be corrected with an operation or interventionally [23]. In smaller fistulas, pre-interventional ischaemia, left ventricular dysfunction or arrhythmia should be documented [23].

The evidence on which therapeutic recommendations in patients with anomalous coronary arteries is scarce and mainly based on anecdotal reports, case series

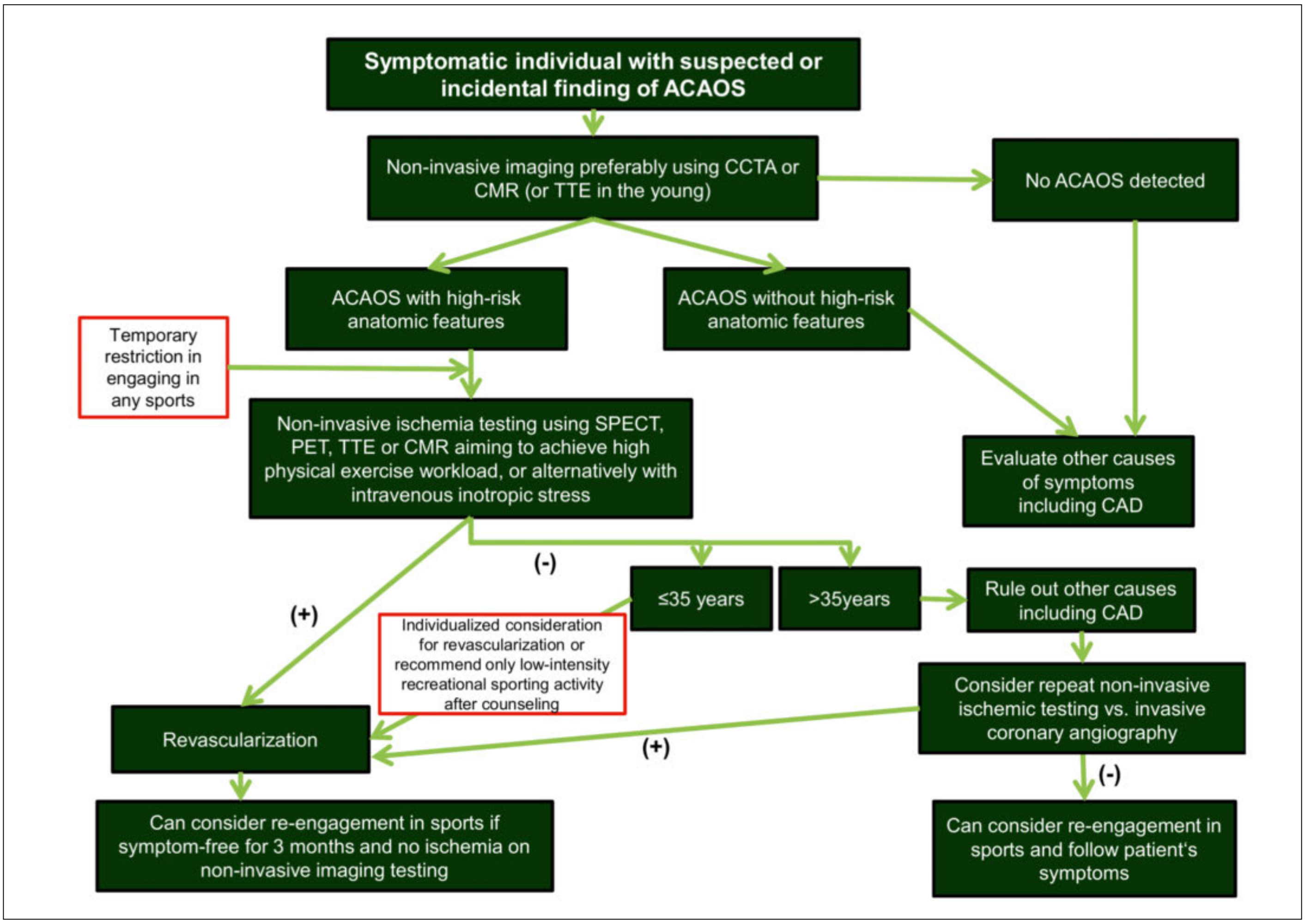

Figure 6: Flow chart for evaluation of symptomatic individuals with suspected or incidental finding of ACAOS. Initial steps are CCTA (or alternatively CMR or echocardiography) for evaluation of cases with high-risk anatomical features, followed by noninvasive ischaemia testing, preferably with use of maximum physical exercise to mimic real life conditions. Alternatively, dobutamine stress testing can be used to achieve high heart rates and imitate physical exercise. Beside SPECT, PET and CMR, stress-echocardiography might also play a role, especially in children to assess hemodynamic relevance [18, 25]. TTE = transthoracic echocardiography. Adapted with permission of Elsevier from Ref. [7].

Conclusions and key messages

- Increased use of noninvasive imaging results in increasing absolute numbers of patients detected with ACAOS
- In middle-aged individuals with newly diagnosed ACAOS, outcome is not statistically different from that of a matched control cohort without anomalies
- Hybrid CCTA/SPECT discriminates the impact of ACAOS from concomitant CAD on myocardial ischaemia/scarring. Impairment of myocardial perfusion due to ACAOS *per se* seems to be exceedingly rare and such impairment is much more likely attributable to concomitant CAD.
- In patients with ACAOS, any presumed prognostic benefits from surgical repair and sports restriction should be individually carefully balanced against the risk of a surgery and possible impairment of quality of life
- Decisions about patient management should be made after considering all available information, such as symptoms, age, sports behaviour, and imaging of high-risk anatomical features and possible haemodynamic consequences
- More evidence based on prospective trials and multicentre registries with follow-up studies is imperatively needed to modify current recommendations.

and experts' opinions. There are no prospective, randomised multicentre trials. Mostly, the choice of surgery, sports restriction or no treatment is made on a case-by-case discussion. The combination of clinical symptoms, age, sports behaviour and presence or absence of high-risk features / ischaemia, and individualised discussion between the treating physician, patient and heart surgeon leads to the final decision. In order to adapt current recommendations, more evidence, based on multicentre registries and prospective trials with follow-up studies are needed.

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