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RAPID COMMUNICATIONS

Cardiac magnetic resonance in the assessment of the anomalous right coronary artery originating from the left sinus of Valsalva

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Risk stratification and therapeutic management of patients with an anomalous right coronary artery originating from the left sinus of Valsalva (R-ACAOS) represent a clinical challenge.[1] According to guidelines, a thorough clinical workup of patients with R-ACAOS is recommended using multi-modality imaging to characterize the anatomy of the origin and course of the anomalous coronary artery and stress testing to assess the ischaemic potential, which are considered key determinants of the risk of sudden cardiac death (SCD).[2–4] Unlike patients with left ACAOS, those with R-ACAOS are diagnosed incidentally as they are usually asymptomatic, rarely have evidence of myocardial ischaemia on provocative tests, and are deemed at a lower risk of SCD.[2,3] Previous autopsy series showed the presence of a myocardial scar in the myocardial territory tributary of R-ACAOS in a significant number of SCD victims.[5,6] Hence, the current study was designed to evaluate the prevalence and clinical meaning of a myocardial scar in a cohort of living R-ACAOS patients using cardiac magnetic resonance (CMR) imaging with the late gadolinium enhancement (LGE) technique.

We retrospectively screened the clinical database of patients with congenital coronary anomalies from two institutions (Padua and Milan, Italy), to include only those with a final diagnosis of R-ACAOS based on coronary computed tomography angiography (CCTA; $n = 73$), who underwent LGE–CMR between 2015 and 2023 ($n = 48$). Patients with coronary artery disease due to obstructive atherosclerosis, dissection or inflammation ($n = 3$), and coronary embolisms from either atrial fibrillation ($n = 1$) or patent foramen ovale ($n = 1$) were excluded. Late gadolinium enhancement technique protocol and image interpretation are reported in detail elsewhere.[7,8] The study was approved by the Local Ethics Committee of the University Hospital of Padua, Italy (protocol number 4901/AO/20).

Forty-eight CMR scans of patients with R-ACAOS [81% males, median age 24 years (interquartile range 14–44), 41% were <16 years] were included in this analysis. Indications for CMR were symptoms, abnormal electrocardiogram (ECG) or echocardiogram in 29 patients, ventricular arrhythmias (VAs) in 13 patients (i.e. isolated or repetitive exercise–induced premature ventricular beats on ECG stress testing in 7 patients, or resting ventricular tachycardia [≥3 consecutive ventricular beats] on 24 h ECG monitoring in 6 patients), and known R-ACAOS in 6 patients. Except for these latter 6 patients, in the remaining 42, the presence of R-ACAOS was suspected ($n = 35$) or diagnosed ($n = 7$) by CMR on the cine left ventricular (LV)/aortic short-axis stack. In all patients, the diagnosis of R-ACAOS was confirmed and refined according to CCTA results for anatomic details. Late gadolinium enhancement was identified in 10 of 48 patients (21%) and showed an ischaemic pattern in all (sub-endocardial in 9 and transmural in 1). The

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	R-ACAOS with no LGE N=38	R-ACAOS with LGE N=10	p
Age, y	21 (16; 28)	45 (32; 55)	0.001
Male gender	29 (76)	10 (100)	0.17
Symptoms	9 (24)	3 (30)	0.67
Exercise-induced VAs	3 (8)	4 (40)	0.027
Interarterial course	36 (95)	10 (100)	1.00
Intramural course	16 (42)	7 (70)	0.16
Other high-risk features*	25 (66)	8 (80)	0.47
Positive stress test	11 (29)	3 (30)	1.00

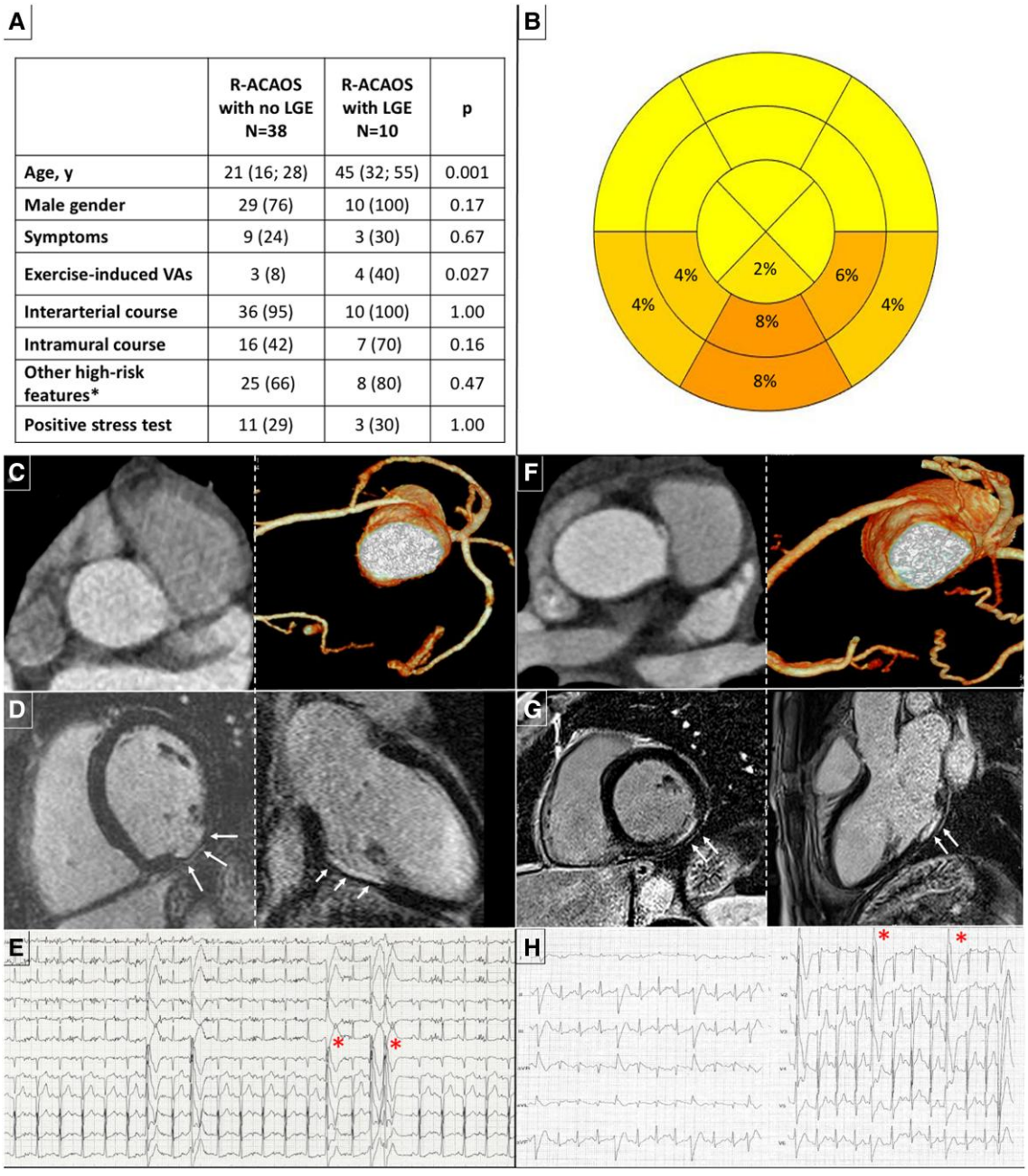

Figure 1 (*A*) Demographics of the study population with a comparison between an anomalous right coronary artery originating from the left sinus of Valsalva patients with/without ischaemic late gadolinium enhancement. Ages of the groups are expressed as median (interquartile range) and compared using the Mann–Whitney *U* test. Other categorical variables are expressed as absolute numbers and percentages and compared using the Fisher's exact test. (*B*) The regional distribution of ischaemic late gadolinium enhancement in the study cohort. (*C–H*) Imaging features of two representative anomalous right coronary artery originating from the left sinus of Valsalva patients with ischaemic late gadolinium enhancement. (*C*) Coronary computed tomography angiography images of a 36-year-old male showing an anomalous right coronary artery originating from the left sinus of Valsalva with an inter-arterial course, an acute exit angle, and an elliptical-shaped cross section throughout the short proximal intramural aortic course. (*D*) Post-contrast cardiac magnetic resonance images (short-axis and long-axis views) of the same patient demonstrating a sub-endocardial late gadolinium enhancement involving the basal-mid inferior wall of the left ventricle. (*E*) A stress electrocardiogram strip showing single and coupled exercise-induced ventricular arrhythmias with a right-bundle branch block morphology and superior axis of the ectopic QRS. (*F*) Coronary computed tomography angiography images of a 42-year-old male showing an anomalous right coronary artery originating from the left sinus of Valsalva with an inter-arterial course, significant ostial narrowing, acute exit angle, and a short intramural course. (*G*) Post-contrast cardiac magnetic resonance images of the same patient demonstrating a focal transmural late gadolinium enhancement involving the mid-inferior wall of the left ventricle. (*H*) A twenty-four–hour Holter ambulatory 12-lead electrocardiogram monitoring detecting isolated exercise-induced ventricular arrhythmias with right-bundle branch block morphology and superior axis of the ectopic QRS. *High-risk features include a slit-like ostium, acute exit angle, and significant proximal narrowing.[1]

LGE was limited to LV *Bull's eye* segment in the territory tributary of the R-ACAOS with a regional distribution involving the inferoseptal ($n = 1$), inferior ($n = 4$), and inferolateral ($n = 5$) segments. Patients with ischaemic LGE were all males and significantly older than those without LGE (44 vs. 23 years, $P = .001$). On CCTA, all R-ACAOSs associated with ischaemic LGE had an inter-arterial course and more often showed an intramural course (70% vs. 42%) with >1 additional high-risk anatomic feature(s) such as a slit-like ostium, acute exit angle, or significant proximal narrowing (80% vs. 66%). The R-ACAOS patients with ischaemic LGE more frequently had exercise-induced VAs (40% vs. 8%), most commonly (75%) with a right-bundle branch block (RBBB) morphology of the ectopic QRS (*Figure 1*). Three of 10 (30%) R-ACAOS patients with LGE had a positive provocative test result (cyclo-ergometer stress scintigraphy $n = 3$); the remaining 7 patients had no evidence of inducible myocardial ischaemia at ≥1 of the following tests: ECG exercise testing $n = 5$, dipyridamole stress echocardiogram $n = 1$, adenosine stress CMR $n = 3$, dipyridamole stress scintigraphy $n = 2$, and cyclo-ergometer stress scintigraphy $n = 2$. All R-ACAOS patients were restricted from sports activity, those with VAs were treated medically with beta-blockers, and those with inducible myocardial ischaemia underwent surgical intervention. During a median follow-up of 49 (34–70) months, there were no deaths or major cardiovascular events.

Risk assessment of patients with R-ACAOS relies on characterization of anatomical features and testing of myocardial ischaemia inducibility. However, such an approach often leads to false-negative results with episodes of SCD occurring in patients with previously non-inducible ischaemia on available provocative tests. To our knowledge, the present study was the first to systematically investigate *in vivo* the presence of an ischaemic myocardial scar in the territory tributary of R-ACAOS by using the CMR technique of LGE. The finding of ischaemic myocardial LGE/scar in approximately one-fifth of our patients is in keeping with those of previous pathological studies showing myocardial fibrosis in a sizeable proportion of R-ACAOS patients,[5,6] which suggests that ischaemia might precede the terminal event. Left ventricular myocardial fibrosis was previously detected on a histologic examination at a post-mortem examination in 45% R-ACAOS, mainly with a subendocardial distribution.[6] Although in our study the presence of an ischaemic LGE/scar was associated with high-risk anatomical features, including inter-arterial and proximal intramural aortic course, the majority of patients was asymptomatic and most often had a negative provocative test. This finding may indicate a discrepancy between a lack of inducibility of myocardial ischaemia and structural signs of ischaemic damage in patients with R-ACAOS, suggesting that myocardial necrosis may have a silent clinical course with mechanisms that differ from those of atherosclerotic coronary artery disease. That LGE was observed in older R-ACAOS patients may reflect a process of damage characterized by cumulative episodes of ischaemic myocardial injury over time. Of interest, patients with LGE frequently showed VAs with an RBBB/superior QRS axis morphology, consistent with the origin from the LV infero-lateral region, where the ischaemic LGE/scar was demonstrated by CMR. This concordance between VA morphology and ischaemic scar location supports the concept of a scar-related arrhythmogenesis and the potential for an arrhythmic cardiac arrest in patients with R-ACAOS, similar to that occurring in patients with a post-myocardial infarction scar.

Study limitations include the retrospective/observational study design and the inconsistency of provocative stress tests. No patient with LGE underwent an imaging dobutamine stress test.

The results of our study suggest that CMR may be a useful tool for improving risk stratification for SCD in R-ACAOS patients with at-risk anatomy, by providing evidence of an ischaemic LGE/scar underlying scar-related VAs that may occur in the absence of inducible myocardial ischaemia. Validation by further studies of our preliminary results on the role of LGE/scar for risk assessment may have a significant impact on future guidelines for indication of surgical correction of R-ACAOS in asymptomatic patients with non-inducible myocardial ischaemia.

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Declarations

Disclosure of Interest

All authors declare no disclosure of interest for this contribution.

Data Availability

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Ethical Approval

The study was approved by the Local Ethics Committee of the University Hospital of Padua, Italy (protocol number 4901/AO/20).

Pre-registered Clinical Trial Number

Not applicable.

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