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ORIGINAL ARTICLE

Long-Term Risk Assessment in Athletes With Complex Ventricular Arrhythmias

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BACKGROUND: Ventricular arrhythmias (VAs) are a major concern in athletes. We sought to determine the prognostic role of noninvasive and invasive assessments in athletes with complex VAs.

METHODS: One-hundred-ninety athletes (82% male; 28 [19–43] years; 148 [78%] competitive athletes) with frequent or exercise-induced premature ventricular complexes or nonsustained ventricular tachycardia were included in a multicenter cohort study and categorized based on VA ECG morphology into common (n=99) and uncommon (n=91) VA groups. Each athlete underwent a comprehensive diagnostic workup, including cardiac magnetic resonance in 94% (n=178) and electrophysiology study/electroanatomical mapping in 87% (n=166). The primary end point was the occurrence of sudden death or sustained VAs during long-term follow-up.

RESULTS: Athletes with uncommon VA morphology had higher rates of abnormal findings at multimodality assessment and more final diagnoses of structural heart disease. Over a median follow-up of 6.2 (4.3–8.1) years, 7 (4%) athletes experienced a primary outcome event, including 1 sudden death. Interestingly, no events occurred in athletes with common morphology VAs. In univariable Cox models, factors associated with the primary end point included uncommon VA morphology (P=0.003), lack of VA suppression (P=0.049), and nonsustained ventricular tachycardia/ventricular tachycardia induction (P=0.010) during stress testing, late gadolinium enhancement (P=0.045), electroanatomical scar regions (P=0.022), and sustained VA inducibility by electrophysiology study (P<0.001). Incorporating findings of invasive tests improved prediction of primary outcome events over clinical/noninvasive findings in isolation (log-likelihood ratio for nested models, P=0.004). A survival tree model based on VA morphology, late gadolinium enhancement, VA response to exercise testing, and electroanatomical mapping allowed risk stratification, identifying subgroups of athletes without primary outcome events during follow-up. Among 148 competitive athletes, 101 (68%) regained eligibility after 3 months of detraining, but only 42 (28%) continued long-term.

CONCLUSIONS: A comprehensive diagnostic assessment integrating ECG, stress testing, and imaging findings, along with the selective use of invasive electrophysiology assessments, may help refine the prognostic evaluation of athletes with complex VAs.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: athletes ■ exercise test ■ gadolinium ■ prognosis ■ risk assessment

The finding of ventricular arrhythmias (VAs) in otherwise healthy athletes is an important and not uncommon clinical issue.[1–3] A 12-lead ECG screening can detect at least one premature ventricular complex (PVC) in 0.24% of young athletes.[1] In addition, the prevalence of complex VAs during 24-hour ambulatory ECG

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WHAT IS KNOWN?

- Complex ventricular arrhythmias (VAs) may be a key clinical indicator of an underlying cardiomyopathy in athletes.
- Although previous studies suggested that a comprehensive diagnostic evaluation, including magnetic resonance imaging and invasive electrophysiology tests, may lead to diagnostic reclassification in athletes with complex VAs, the long-term prognostic value of these different diagnostic modalities is less well understood.

WHAT THE STUDY ADDS

- Our study confirms that the simple classification of VAs into common (ie, infundibular or fascicular) versus uncommon (ie, other morphologies including polymorphic ventricular arrhythmias) morphologies may facilitate risk stratification, as no life-threatening arrhythmic events were observed during long-term follow-up among athletes with common morphology premature ventricular complexes/nonsustained ventricular tachycardia.
- In addition to premature ventricular complex/nonsustained ventricular tachycardia morphology, factors associated with increased risk of life-threatening arrhythmic events included regional wall motion abnormalities on echocardiogram, VA induction or persistence during exercise testing, late gadolinium enhancement, scar regions on electroanatomical mapping, and sustained VA inducibility by electrophysiology study.
- An integrated model that begins with the evaluation of arrhythmia morphology (common versus uncommon) and reserves cardiac magnetic resonance imaging and electroanatomical mapping for selected cases may facilitate risk stratification.

Nonstandard Abbreviations and Acronyms

CMR	cardiac magnetic resonance
EAM	electroanatomical mapping
EPS	electrophysiology study
ICD	implantable cardioverter defibrillator
LBBB	left bundle branch block
LGE	late gadolinium enhancement
NSVT	nonsustained ventricular tachycardia
PES	programmed electrical stimulation
PVC	premature ventricular complex
RBBB	right bundle branch block
VA	ventricular arrhythmia
VF	ventricular fibrillation
VT	ventricular tachycardia

monitoring, including a training session, is 6% in athletes under 30 years of age and 7% to 18% in those over 30 years of age.[2,3]

The main concern for clinicians assessing athletes with VAs is the need to exclude an underlying arrhythmogenic substrate, which may lead to cardiac arrest and sudden cardiac death during sports activities.[4] Among VA features, ECG morphology appears to be especially important, and an arrhythmogenic substrate should be suspected in the uncommon case of VAs of multiple ECG morphologies or with right bundle branch block (RBBB) and intermediate/superior axis configuration.[5,6] By contrast, some types of VAs (ie, infundibular and fascicular VAs) are considered idiopathic and benign, and do not mandate further diagnostic assessments or sports restriction according to recent consensus statements, in which these VAs have been referred to as common.[5,6] However, these recommendations lack validation, and recent work from our group demonstrated that a comprehensive multimodality assessment applied to athletes with complex VAs of any morphology may uncover an underlying heart disease and change the final diagnosis in a high proportion of cases, with implications for sports eligibility assessment.[7]

In the present study, we sought to investigate the long-term clinical outcomes and sports eligibility in a cohort of athletes presenting with nonsustained ventricular tachycardia (NSVT) or frequent/exercise-related PVCs, aiming to establish the prognostic implications of noninvasive (arrhythmia ECG morphology, cardiac magnetic resonance imaging [CMR]) and invasive (electrophysiology study [EPS]/electroanatomical mapping [EAM]) assessments.

METHODS

Study Population and Definitions

We conducted a multicenter, observational cohort study including all consecutive athletes referred to 3 Italian high-volume centers (University Hospital Azienda Ospedaliero-Universitaria delle Marche, Ancona, Italy; Centro Cardiologico Monzino IRCCS, Milan, Italy; Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy) for the diagnostic assessment of complex VAs between January 2010 and December 2021.

Throughout the study, a competitive athlete is defined as one who participates in an organized team or individual sport that requires regular competition against others as a central component, places a high premium on excellence and achievement, and requires some form of systematic (and usually intense) training.[8] A leisure-time athlete is defined as a physically active person engaging in a range of exercise levels from modest to vigorous on a regular basis, not desiring to excel against others and, therefore, not facing the same psychological and physical pressures as the competitive athlete.[9] A professional athlete is defined as a competitive athlete for whom the practice of sport constitutes the main occupation and the principal source of income.

In the present study, complex VAs are defined as NSVT and frequent (>500/day) or exercise-related PVCs of any morphology detected by ECG monitoring or exercise stress testing.[7]

For each patient, we collected demographics, clinical and imaging information, details of invasive procedures, and follow-up data. The study was performed according to institutional standards, national legal requirements, and the Declaration of Helsinki, and patient data were collected in an institutional review board-approved database. Informed consent was obtained from all patients, and the data that support the findings of this study are available from the corresponding author upon reasonable request. The study flowchart is shown in Figure 1.

Classification of Patients According to VA Characteristics

VA morphology was defined based on findings from 24-hour ambulatory ECG monitoring, maximal exercise stress testing, and in-hospital telemetry (when performed). VAs were classified as monomorphic in the case of a single dominant QRS morphology, or polymorphic in the case of PVCs with ≥2 morphologies accounting for ≥10% of all PVCs or NSVT with changing QRS contours.[5,10] The definitions of left bundle branch block (LBBB)/RBBB-like VAs and of VA axis are reported in the Supplemental Methods.

According to arrhythmia ECG morphology, 2 groups of athletes were identified: athletes with common morphology VAs, which included infundibular (monomorphic LBBB-like PVCs/NSVTs with inferior axis) and fascicular (monomorphic PVCs/NSVTs with a QRS duration ≤130 ms resembling a typical RBBB/left or right axis deviation) VAs; and athletes with uncommon VAs, including polymorphic VAs (polymorphic PVCs or NSVTs) or VAs of other morphologies (monomorphic PVCs/NSVTs with LBBB with superior/intermediate axis, monomorphic PVCs/NSVTs with RBBB morphology and without criteria for fascicular VAs).[5,6]

In addition, VA response to exercise testing was recorded in all but 14 athletes, in whom a step-test without continuous ECG monitoring was performed. VA response was considered abnormal in the case of persistence/induction of PVCs during exercise, or in the presence of NSVT/sustained ventricular tachycardia (VT).

Comprehensive Diagnostic Assessments and CA

Each athlete underwent a prespecified comprehensive diagnostic assessment, following a recently published diagnostic

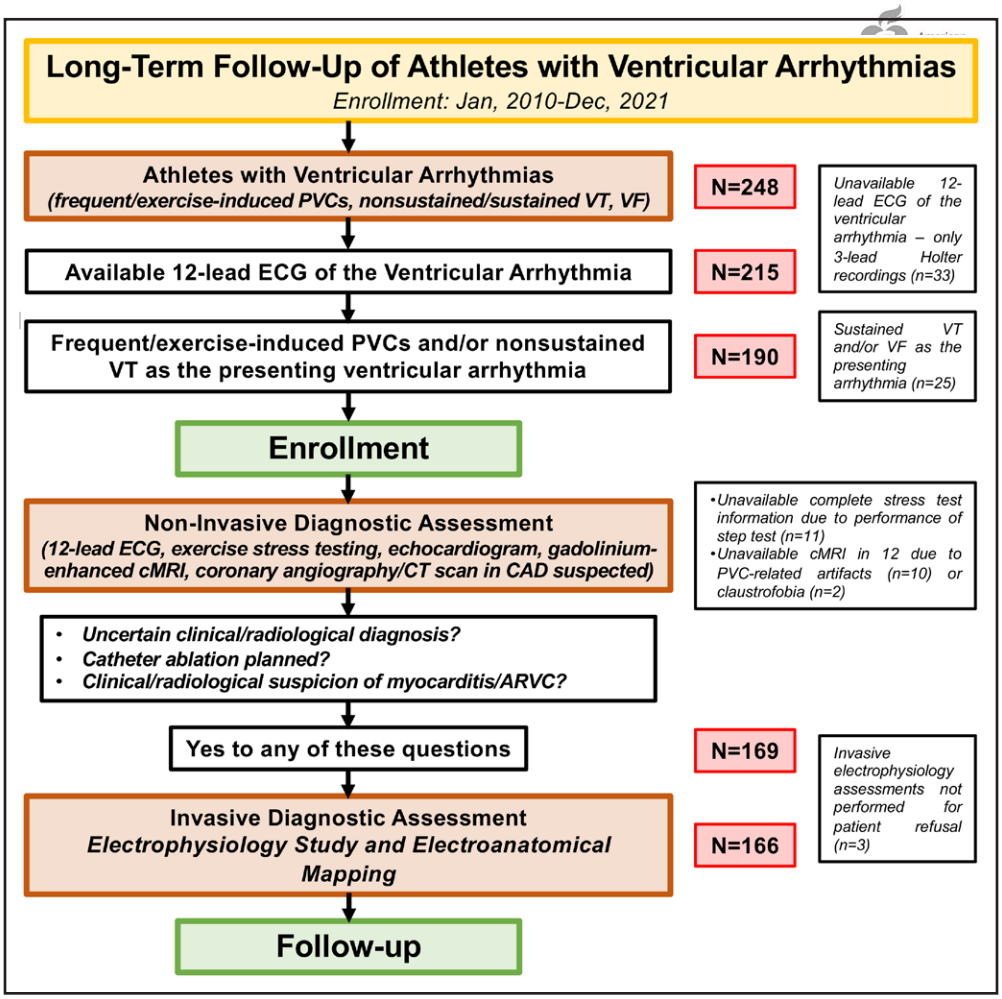

Figure 1. Patient selection and diagnostic workup.
ARVC indicates arrhythmogenic right ventricular cardiomyopathy; CAD, coronary artery disease; cMRI, cardiac magnetic resonance imaging; CT, computed tomography; PVC, premature ventricular complex; VF, ventricular fibrillation; and VT, ventricular tachycardia.

workflow.[7] Briefly, 12-lead ECGs were interpreted according to the international recommendations for interpretation of the athlete's ECG,[11] while the use of echocardiography and gadolinium-enhanced CMR was recommended in each case. EPS with programmed electrical stimulation (PES) and ventricular EAM were performed during a single procedure in the index hospitalization in case of diagnostic doubts after noninvasive tests or, in case of diagnostic certainty after noninvasive tests, as a preliminary step to catheter ablation (CA) procedures (Figure 1).[7] Details regarding CMR, EPS, and EAM are described in the Supplemental Methods. The indications for CA were in accordance with international guidelines on the treatment of VAs.[12] Final diagnoses of heart diseases were made on the basis of all available information, according to international guidelines/recommendations (Supplemental Methods).

Study End Points and Follow-Up

The primary study end point was the occurrence of sudden death or sustained VT/ventricular fibrillation (VF) during long-term follow-up, which lasted until December 2023. Furthermore, information concerning return to play after an initial 3-month detraining period and at last follow-up was systematically collected. Outcome data were retrieved from office visits, remote monitoring (for patients implanted with cardiac implantable electronic devices), and phone calls, and end points were adjudicated by investigators at participating institutions, who documented all VT/VF episodes.

Statistical Analysis

Categorical data were expressed as absolute and relative frequencies, and compared using the χ^2 or Fisher exact test, as appropriate. Continuous variables were checked for normality with the Shapiro-Wilk test and reported as mean and SD, if normally distributed, or median and 1st to 3rd quartile, if not normally distributed. Continuous variables were compared with Student *t* or Wilcoxon tests, as appropriate. Predictors of CMR-proven LV scar among patients presenting with common VAs were identified using logistic regression models and receiver operating characteristic curve analysis. The time to the first primary outcome event was assessed using the Kaplan-Meier method, beginning from the index hospitalization until the end of follow-up. Comparisons between the groups of patients with common and uncommon VAs were evaluated with the permutation log-rank test. After verifying standard proportional hazards assumption testing criteria, univariable Cox proportional hazard regression analyses were fitted to identify predictors of primary outcome events. Furthermore, due to the small number of primary outcome events, propensity score-weighting based upon noninvasive predictors of primary outcome events in univariable Cox models was used to test the independent prognostic role of invasive electrophysiological assessments.[13] The discrimination of Cox proportional hazard models for the prediction of primary outcome events was assessed using a nonparametric concordance-based *C*-statistic, and the added value of invasive predictors over clinical/noninvasive findings was assessed using log-likelihood ratio testing for nested models. The sensitivity, specificity, positive predictive value, and negative predictive value of factors associated with the primary end point were calculated according to previously published methods for estimating these test metrics in survival data.[14] To summarize study findings in a unifying model, we applied an exploratory survival tree method that included all variables associated with the primary end point identified in univariable Cox models. A $P<0.05$ was considered statistically significant. All statistical analyses were performed with the software R, version 4.2.0 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study Population

During the study period, 248 athletes with complex VAs were identified and underwent diagnostic assessment. Of these athletes, 33 who had undergone 3-lead ambulatory ECG monitoring lacked 12-lead ECG VA morphology documentation during exercise testing or the index hospitalization and were therefore excluded (Figure 1). Furthermore, 25 athletes who presented with sustained VT (n=18) or VF (n=9) were also excluded. The final study population comprised 190 athletes (male gender, 82%; median age, 28 [19–43] years). The characteristics of the overall study population are presented in Table 1.

The proportion of professional, competitive, and leisure-time athletes was 12% (n=23), 66% (n=125), and 23% (n=42), respectively, while the most commonly practiced sports were soccer (n=54, 28%), athletics (n=43, 23%), and cycling (n=28, 15%). Ninety athletes (47%) were symptomatic for VAs (palpitations, n=79; syncope, n=11), while the remaining 100 subjects (53%) were asymptomatic and referred after VA detection at preparticipation screening.

Common and Uncommon Morphology VA Groups: Clinical, ECG, and Imaging Characteristics

According to ECG VA morphology, 99 athletes (52%) were included in the common VA group, while the uncommon VA group comprised 91 athletes (48%; Table 1). The proportions of infundibular and fascicular morphologies in the common VA group were 92% (n=91) and 8% (n=8), respectively, while arrhythmia types were frequent PVCs and NSVTs in 89 (90%) and 47 (47%) athletes, respectively. Of the 91 athletes in the uncommon VA group, polymorphic, LBBB superior/intermediate axis, and RBBB morphologies were found in 49 (54%), 17 (18%), and 25 (27%) subjects. The types of VAs in the uncommon group were PVCs and NSVTs in 79 (87%) and 46 (51%) subjects, respectively.

Clinical characteristics and the results of ECG, imaging tests, and invasive electrophysiological assessments by VA group in the overall study cohort are presented in Table 1. CMR data were available for 178 athletes (94%) in the overall cohort (Figure 1); in the remaining 12 athletes, CMR images were not interpretable due to

Table 1. Baseline Clinical, Electrocardiographic, Imaging, and Electrophysiological Characteristics of Patients in the Overall Study Population and According to the Morphology of Ventricular Arrhythmias (Common vs Uncommon)

	Overall (n=190)	Common ventricular arrhythmias (n=99)	Uncommon ventricular arrhythmias (n=91)	*P* value*
Age, median (1st–3rd quartile)	28 (19–43)	25 (18–41)	29 (20–46)	0.143
Male gender, n (%)	156 (82)	77 (78)	79 (87)	0.156
Level of training				
Leisure-time athlete, n (%)	42 (23)	22 (22)	20 (22)	1.000
Competitive athlete, n (%)	125 (66)	71 (72)	54 (59)	0.100
Professional athlete, n (%)	**23 (12)**	**6 (6)**	**17 (19)**	**0.015**
Type of sport				
Cycling, n (%)	**28 (15)**	**8 (8)**	**20 (22)**	**0.013**
Soccer, n (%)	54 (28)	27 (27)	27 (30)	0.838
Athletics, n (%)	43 (23)	25 (25)	18 (20)	0.467
Swimming, n (%)	12 (6)	7 (7)	5 (5)	0.883
Basketball, n (%)	14 (7)	7 (7)	7 (8)	1.000
Symptoms				
None, n (%)	100 (53)	49 (49)	51 (56)	0.449
Palpitations, n (%)	79 (42)	47 (47)	32 (35)	0.116
Syncope, n (%)	11 (6)	3 (3)	8 (9)	0.122
Arrhythmia morphology				
Infundibular, n (%)	**91 (48)**	**91 (92)**	**0 (0)**	…
Fascicular, n (%)	**8 (4)**	**8 (8)**	**0 (0)**	…
Polymorphic, n (%)	**49 (26)**	**0 (0)**	**49 (54)**	…
LBBB superior/intermediate axis, n (%)	**17 (9)**	**0 (0)**	**17 (19)**	…
Atypical RBBB, n (%)	**25 (13)**	**0 (0)**	**25 (27)**	…
Arrhythmia at baseline				
Frequent PVCs, n (%)	168 (88)	89 (90)	79 (87)	0.662
NSVT, n (%)	93 (49)	47 (47)	46 (51)	0.781
12-lead ECG				
Normal, n (%)	**108 (57)**	**70 (71)**	**38 (42)**	**<0.001**
Borderline, n (%)	32 (17)	18 (18)	14 (15)	0.749
Abnormal, n (%)	**50 (26)**	**11 (11)**	**39 (43)**	**<0.001**
Exercise stress test, n (%)	**179 (94)**	**89 (90)**	**90 (99)**	**0.011**
PVC suppression/absent arrhythmias, n (%)†	119 (66)	67 (75)	52 (58)	0.177
PVC persistence/induction, n (%)†	**43 (24)**	**16 (18)**	**27 (30)**	**0.040**
Nonsustained VT, n (%)†	15 (8)	6 (7)	9 (10)	0.479
Sustained VT, n (%)†	2 (1)	0 (0)	2 (2)	0.228
Echocardiogram				
Normal, n (%)	**133 (70)**	**83 (84)**	**50 (55)**	**<0.001**
Abnormal, n (%)	**57 (30)**	**16 (16)**	**41 (45)**	**<0.001**
LVEF<50%, n (%)	17 (9)	6 (6)	11 (12)	0.230
MVP, n (%)	17 (9)	7 (7)	10 (11)	0.490
LV RWMA, n (%)	**13 (7)**	**1 (1)**	**12 (13)**	**<0.001**
RV RWMA, n (%)	7 (4)	4 (4)	3 (3)	1.000
CMR				
CMR performed, n (%)	178 (94)	91 (92)	87 (96)	0.377
LGE, n (%)‡	**62 (33)**	**14 (15)**	**48 (53)**	**<0.001**
LV LGE, n (%)‡	**56 (31)**	**13 (14)**	**43 (49)**	**<0.001**
Stria, n (%)	**37 (21)**	**11 (12)**	**26 (30)**	**0.006**
Patchy, n (%)	**19 (11)**	**2 (2)**	**17 (20)**	**<0.001**

(*Continued*)

Table 1. Continued

	Overall (n=190)	Common ventricular arrhythmias (n=99)	Uncommon ventricular arrhythmias (n=91)	*P* value*
RV LGE, n (%)‡	**9 (5)**	**1 (1)**	**8 (9)**	**0.016**
Edema, n (%)‡	**5 (3)**	**0 (0)**	**5 (6)**	**0.026**
Fat infiltration, n (%)‡	**8 (4)**	**1 (1)**	**7 (8)**	**0.032**
Programmed electrical stimulation, n (%)	166 (87)	84 (85)	82 (90)	0.383
Inducibility of sustained VT/VF, n (%)§	**7 (4)**	**0 (0)**	**7 (8)**	**0.002**
Catheter ablation, n (%)	**84 (44)**	**57 (58)**	**27 (30)**	**<0.001**
Electroanatomical mapping, n (%)	166 (87)	84 (85)	82 (90)	0.383
RV electroanatomical mapping performed, n (%)	143 (75)	76 (77)	67 (74)	0.739
Bipolar RV scar, n (%)¶	28 (20)	10 (13)	18 (27)	0.064
Unipolar RV scar, n (%)¶	**31 (22)**	**10 (13)**	**21 (31)**	**0.015**
Regional distribution of RV scar, n (%)¶				
RVOT	21 (15)	9 (12)	12 (18)	0.432
Subtricuspid RV	**16 (11)**	**3 (4)**	**13 (19)**	**0.006**
RV apex	**9 (6)**	**1 (1)**	**8 (12)**	**0.013**
RV septum	**4 (3)**	**0 (0)**	**4 (6)**	**0.046**
LV electroanatomical mapping performed, n (%)	**62 (33)**	**24 (24)**	**38 (42)**	**0.016**
Bipolar LV scar, n (%)#	**17 (27)**	**2 (8)**	**15 (39)**	**0.009**
Unipolar LV scar, n (%)#	22 (35)	5 (21)	17 (45)	0.064
Regional distribution of LV scar, n (%)#				
LV inferolateral wall	18 (29)	4 (17)	14 (37)	0.150
LV septum	10 (16)	1 (4)	9 (24)	0.073
LVOT	2 (3)	1 (4)	1 (3)	1.000
LV anterior wall	2 (3)	0 (0)	2 (5)	0.518
LV apex	3 (5)	0 (0)	3 (8)	0.277
Epicardial mapping performed, n (%)	1 (1)	0 (0)	1 (1)	1.000
Late potentials, n (%)**	**10 (6)**	**0 (0)**	**10 (12)**	**<0.001**
Final diagnoses				
Idiopathic VA, n (%)	**99 (52)**	**71 (72)**	**28 (31)**	**<0.001**
Myocarditis, n (%)	**24 (13)**	**6 (6)**	**18 (20)**	**0.009**
Arrhythmogenic cardiomyopathy, n (%)	**40 (21)**	**9 (9)**	**31 (34)**	**<0.001**
Dilated cardiomyopathy, n (%)	12 (6)	7 (7)	5 (5)	0.883
Mitral valve prolapse, n (%)	12 (6)	6 (6)	6 (7)	1.000
Hypertrophic cardiomyopathy with gray-zone (13–14 mm) maximal septal thickness, n (%)	3 (2)	0 (0)	3 (3)	0.108
Left ventricular noncompaction, n (%)	1 (1)	0 (0)	1 (1)	0.479

CMR indicates cardiac magnetic resonance; LBBB, left bundle branch block; LGE, late gadolinium enhancement; LV, left ventricular; LVEF, left ventricular ejection fraction; MVP, mitral valve prolapse; NSVT, nonsustained ventricular tachycardia; PVC, premature ventricular complex; RBBB, right bundle branch block; RV, right ventricular; RWMA, regional wall motion abnormalities; VA, ventricular arrhythmia; VF, ventricular fibrillation; and VT, ventricular tachycardia.

*For the comparison between the Common and Uncommon Morphology Arrhythmia Groups.

†Percentages were calculated considering the total number of patients in whom exercise stress testing information was available.

‡Percentages were calculated considering the total number of patients in whom CMR data were available.

§Percentages were calculated considering the total number of patients in whom electrophysiology study was performed.

¶Percentages were calculated considering the total number of patients in whom RV EAM was performed.

#Percentages were calculated considering the total number of patients in whom LV EAM was performed.

**Percentages were calculated considering the total number of patients in whom EAM was performed.

PVC-related artifacts (n=10), or the exam was prematurely interrupted due to claustrophobia (n=2). Abnormal findings from ECG, echocardiography, exercise stress testing, and CMR were significantly more prevalent in the uncommon group (Table 1).

According to the prespecified protocol (Figure 1), 166 (87%) athletes underwent a comprehensive invasive assessment, including EPS and EAM. Sustained VA inducibility by PES was documented in a higher proportion of athletes in the uncommon group (common: n=0

[0%]; uncommon: n=7 [8%]; *P*=0.002). RV EAM was performed in a similar proportion of athletes with common and uncommon VA morphologies (common: n=76 [77%]; uncommon: n=67 [74%]; *P*=0.739), while LV EAM was more commonly performed in the latter group (common: n=24 [24%]; uncommon: n=38 [42%]; *P*=0.016). Athletes in the uncommon VA morphology group had a higher prevalence of bipolar LV and unipolar RV scar and late potentials. Regarding the regional distribution of electroanatomical scars, the RVOT and the inferolateral LV wall were the most commonly involved RV and LV regions, respectively.

Complications due to the invasive electrophysiology procedure occurred in 4 patients (2%; common: n=3 [3%]; uncommon: n=1 [1%]; *P*=0.622) who underwent CA. These included 2 conservatively managed vascular complications (1 small femoral arteriovenous fistula and 1 hematoma), 1 transient LBBB, and 1 conservatively managed pericardial effusion.

The most common final diagnoses after comprehensive evaluation were idiopathic VAs in the common VA group (n=71, 72%) and arrhythmogenic cardiomyopathy (n=31, 34%) in the uncommon VA group. During the index hospitalization, 10 (5%) patients underwent implantable cardioverter defibrillator (ICD) implantation for the primary prevention of SCD. All of the patients implanted with ICDs were in the uncommon VA group (*P*<0.001 for the comparison of ICD implantation rates between common and uncommon VA groups).

Noninvasive Predictors of LGE in the Common VA Group

Notably, the prevalence of late gadolinium enhancement (LGE) was almost fourfold in the uncommon group, compared with the common VA group (53% versus 15%; *P*<0.001). Nonetheless, LV LGE was evident in 13 athletes in the common VA group, mostly involving the inferior-lateral LV (n=10, 71%) with a midmyocardial-epicardial stria pattern (n=11, 79%; Table 1 and Table S1; Figure 2).

Of clinical, ECG, exercise test, and echocardiography parameters, only left ventricular ejection fraction <50% (*P*=0.030) was significantly associated with LGE at CMR in the common VA group in univariable analysis (Table S2). However, the diagnostic performance of left ventricular ejection fraction <50% was suboptimal, with an area under the receiver operating characteristic curve of 0.59 (95% CI, 0.47–0.70; NPV, 87%; PPV, 50%; SE, 21%; SP, 96%; Figure 2).

Long-Term Clinical Outcomes

During a median follow-up of 6.2 (1st–3rd quartile, 4.3–8.1) years, 7 (4%) athletes experienced a primary outcome event, all of whom were in the uncommon VA group (permutation log-rank test for the comparison between common and uncommon VAs, *P*<0.001; Figure 3), while no events occurred in patients with common VAs. No athlete reported syncope during follow-up. Additional details on patients experiencing sudden cardiac death and resuscitated cardiac arrest are provided in the Supplemental Results.

Among the 9 subjects who were implanted with ICDs during the index hospitalization, none received ICD therapies during follow-up. In addition, 9 athletes underwent ICD implantation during follow-up, after a median of 1.0 (0.5–1.6) years; all of these patients were in the uncommon VA group (permutation log-rank test *P*<0.001).

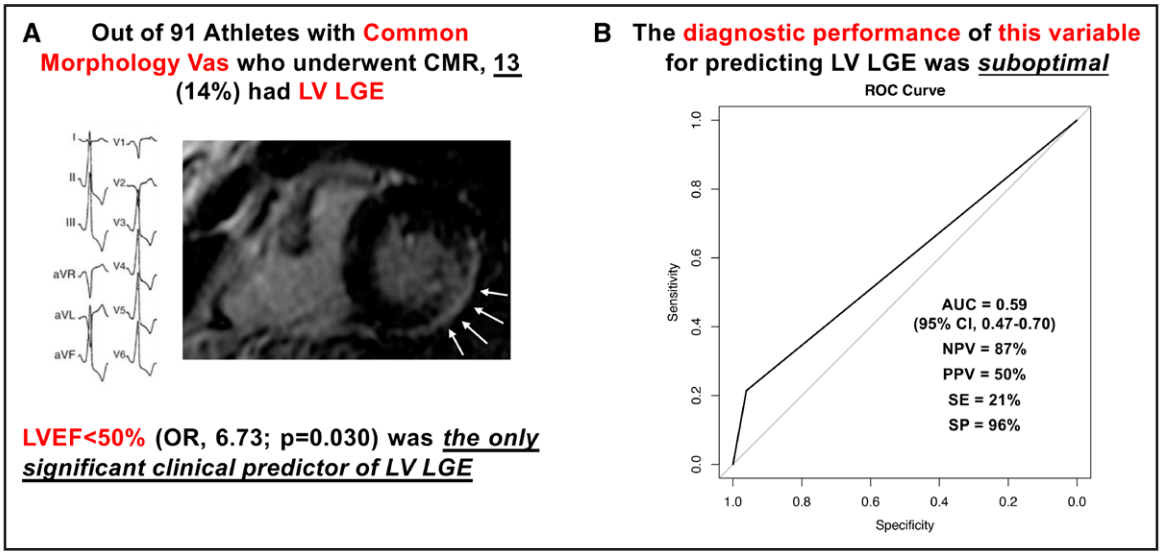

Figure 2. Prevalence and predictors of left ventricular (LV) late gadolinium enhancement (LGE) among athletes with common morphology ventricular arrhythmias (VA).
LVEF indicates left ventricular ejection fraction.

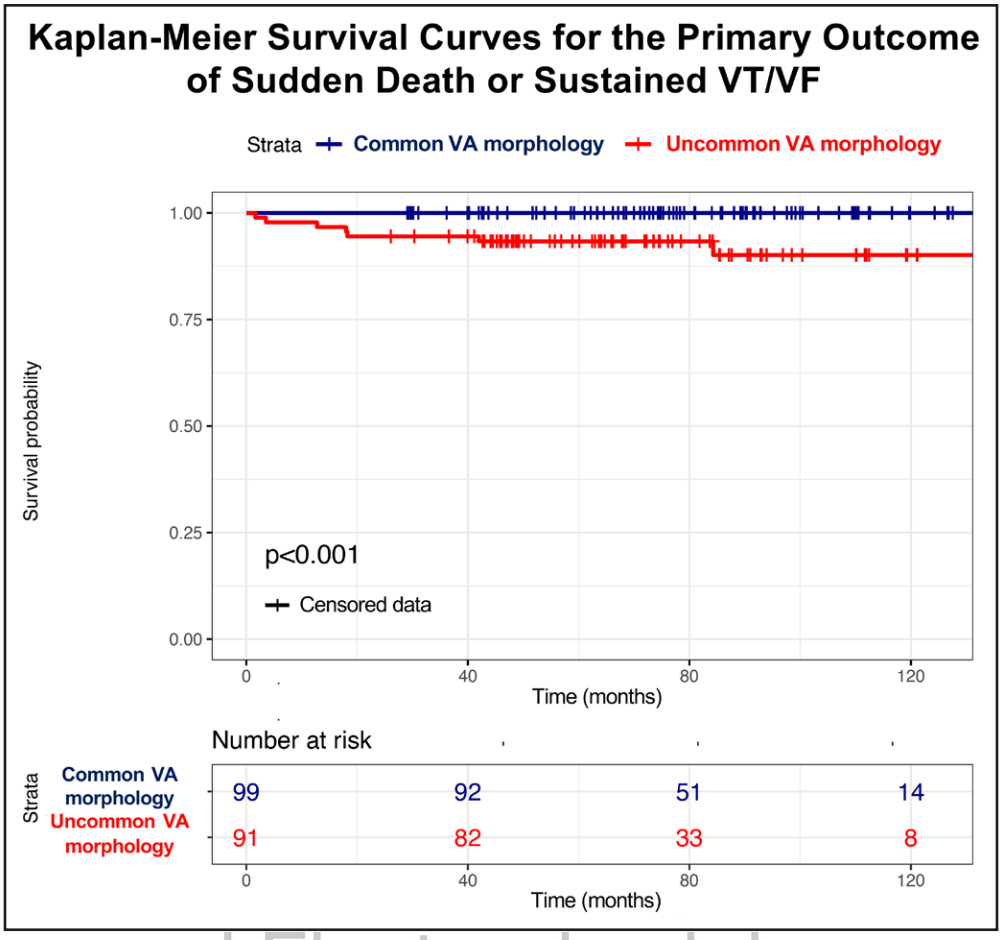

Figure 3. Primary outcome: survival free from sudden death or sustained ventricular tachycardia (VT)/ventricular fibrillation (VF) during follow-up according to the 12-lead ECG morphology of ventricular arrhythmias (VA).

Predictors of Primary Outcome Events

In univariable Cox proportional hazards regression models (Table 2), uncommon VA morphology, induction/persistence of VAs at exercise testing, NSVT/VT during exercise testing, presence of regional LV wall motion abnormalities at echocardiogram, LGE, presence of scar regions at EAM, and sustained VA induction by PES were all associated with increased risk of primary outcome events (Figure 4). After propensity score-weighting based on all noninvasive variables associated with primary outcome events in univariable Cox proportional hazards models (uncommon VA morphology, induction/persistence of VAs and NSVT/VT at exercise testing, presence of regional LV wall motion abnormalities at echocardiogram, and LGE),[13] sustained VA induction at PES (hazard ratio, 25.64 [95% CI, 6.68–76.74]; $P<0.001$) retained a significant association with higher risk of death or sustained VA during follow-up. By contrast, the presence of scar regions at EAM was not significantly associated with primary outcome events after propensity score-weighting (hazard ratio, 3.94 [95% CI, 0.82–1.12]; $P=0.082$).

The performance measures of variables associated with the primary end point at the median follow-up duration of 6.2 years are reported in Table 3. Positive and negative predictive values should be interpreted considering the low prevalence of primary outcome events in the study population. Notably, sustained VA induction by PES had the highest specificity (97% [95% CI, 93–98]), followed by the presence of regional LV wall motion abnormalities by echocardiography (94% [89–96]); however, both factors exhibited low sensitivity. The presence of electroanatomical scar had a sensitivity of 82% (46–96) and a specificity of 71% (64–77).

The model combining invasive (PES inducibility, presence of scar regions and late potentials at EAM) with noninvasive predictors (sustained VT/VF at presentation, uncommon VA morphology, syncope, abnormal 12-lead ECG in sinus rhythm, induction/persistence of VAs and NSVT/VT at exercise testing, LGE; *C*-statistic, 0.95) was superior to the nested model including only noninvasive predictors of primary outcome events (*C*-statistic, 0.90; log-likelihood ratio; $P=0.004$).

Summary Model

Based on our findings, to facilitate the clinical application of our observations, an exploratory integrated model was

Table 2. Univariable Cox Proportional Hazards Analysis of Predictors of Primary Outcome Events

Variable	Univariable analysis		
	HR	95% CI	*P* value
Age (per year change)	1.01	0.97–1.06	0.538
Sex (male vs female)	0.54	0.10–2.79	0.463
Competitive athlete (vs leisure-time)	0.68	0.13–3.52	0.649
Professional athlete (vs leisure-time)	1.33	0.16–11.10	0.793
VA characteristics			
Uncommon morphology VA (vs common)	**17.87**	**2.17–383.43**	**0.003**
NSVT (yes vs no)	2.63	0.51–13.54	0.248
PVC number (per unit change)	1.00	0.99–1.00	0.594
Clinical presentation			
Any symptoms (vs asymptomatic)	0.47	0.09–2.46	0.374
Palpitations (yes vs no)	0.11	0.01–2.35	0.051
Syncope (yes vs no)	2.68	0.32–22.23	0.362
ECG			
Borderline ECG (vs normal ECG)	1.80	0.16–19.84	0.632
Abnormal ECG (vs normal ECG)	4.64	0.85–25.33	0.077
Exercise testing			
Persistence/appearance of VAs (vs VAs suppression/absent VAs)	**5.00**	**1.01–25.78**	**0.049**
NSVT/VT during exercise testing (vs no NSVT/VT during exercise testing)	**7.13**	**1.59–31.90**	**0.010**
Echocardiography			
Any abnormalities (yes vs no)	3.30	0.74–14.77	0.118
LVEF ≤50% (vs >50%)	1.86	0.22–15.53	0.565
Regional LV WMA (yes vs no)	**6.13**	**1.19–31.66**	**0.030**
Mitral valve prolapse (yes vs no)	0.65	0.03–13.91	0.755
LGE (yes vs no)	**5.42**	**1.04–28.34**	**0.045**
Sustained VA induction by PES (yes vs no)	**20.03**	**4.47–89.61**	**<0.001**
EAM details			
Presence of electroanatomical scar (yes vs no)	**7.03**	**1.33–37.07**	**0.022**
Late potentials (yes vs no)	2.47	0.30–20.55	0.403
Catheter ablation performed (yes vs no)	1.64	0.37–7.32	0.519

EAM indicates electroanatomical mapping; LGE, late gadolinium enhancement; LV, left ventricular; LVEF, left ventricular ejection fraction; NSVT, nonsustained ventricular tachycardia; PES, programmed electrical stimulation; PVC, premature ventricular complex; VA, ventricular arrhythmia; VT, ventricular tachycardia; and WMA, wall motion abnormalities.

generated to predict the occurrence of primary outcome events in our population. The results are summarized in Figure 5.

In particular, VA morphology (common versus uncommon) was the most important predictor of primary outcome events, followed by LGE. Further risk stratification was allowed by using electroanatomical voltage mapping among patients with uncommon morphology PVCs/NSVTs and LGE: patients with electroanatomical scar regions were at higher risk (5 events/29 patients) than patients with normal electroanatomical voltage maps (0 events/22 patients; permutation log-rank test *P*=0.045), with this latter group experiencing no primary outcome events during follow-up. The other variables associated with primary outcome events (NSVT/VT during exercise testing, LV regional wall motion abnormalities, and PES inducibility) were not retained in the final survival tree model.

Sports Eligibility During Follow-up

Of the 148 athletes practicing competitive or professional sports at baseline, 101(68%) regained competitive sports eligibility according to Italian law after an initial 3-month detraining period, and 42 (28%) continued practicing competitive sports until the last follow-up. Among the 59 (40%) athletes who discontinued practicing competitive sports during follow-up, the reasons for the interruption included aborted cardiac arrest due to VF (n=1), ICD implantation (n=1), or personal preferences (n=57). Factors associated with long-term practice of competitive sports are reported in Table S2.

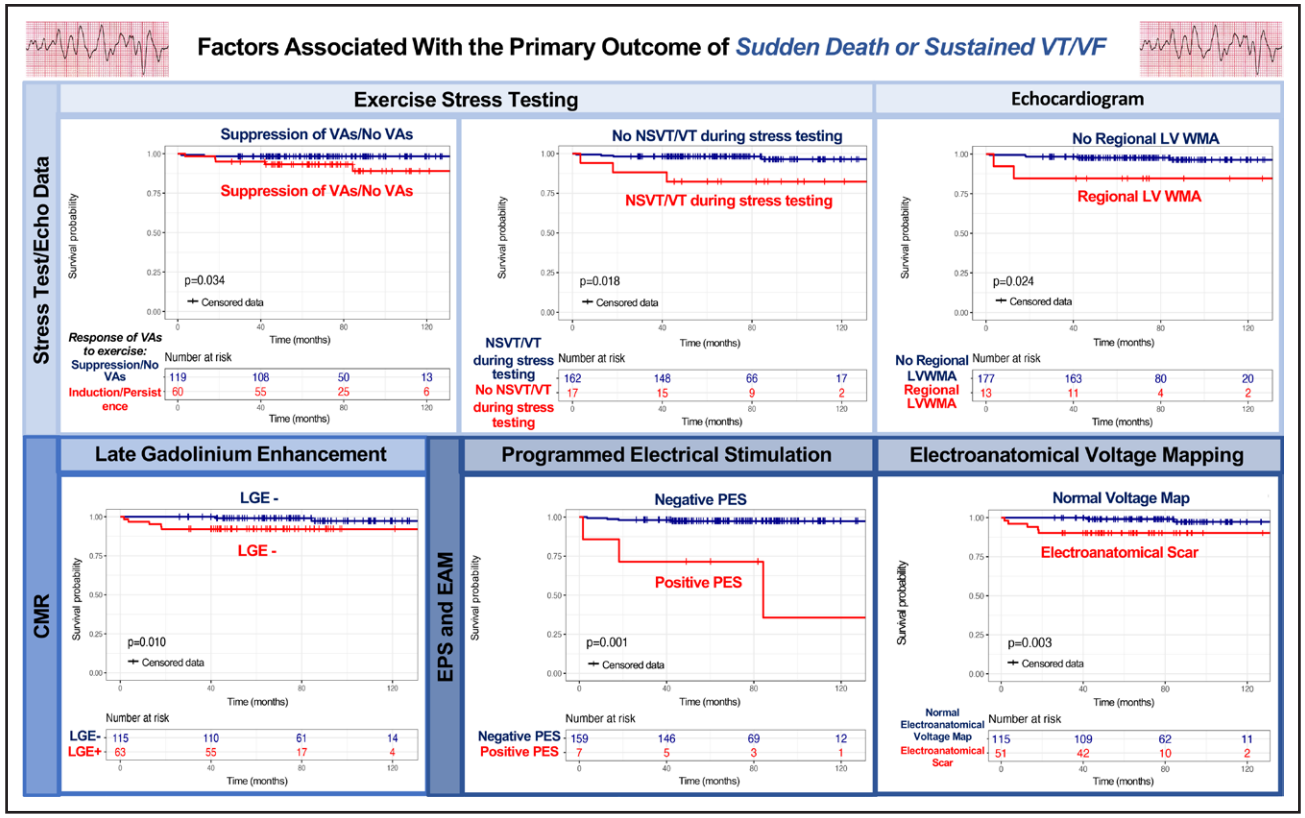

Figure 4. Factors associated with the primary outcome of sudden death or sustained ventricular tachycardia (VT)/ventricular fibrillation (VF) in univariable Cox models.
For each parameter, Kaplan-Meier Survival Curves with corresponding permutation log-rank test *P* values are displayed. CMR indicates cardiac magnetic resonance imaging; LGE, late gadolinium enhancement; NSVT, nonsustained ventricular tachycardia; PES, programmed electrical stimulation; VA, ventricular arrhythmia; and WMA, wall motion abnormality.

DISCUSSION

This study reports the long-term clinical outcomes of a large cohort of athletes with complex VAs undergoing a comprehensive multimodality assessment. The findings suggest several key messages:

1. Athletes with PVCs/NSVTs of common morphology have a low risk of major arrhythmic events, as no such events occurred in our cohort during long-term follow-up.
2. LV LGE can rarely be present in athletes with common VA morphologies, though its clinical significance remains uncertain. Clinical variables such as reduced left ventricular ejection fraction have limited value in identifying athletes with VAs of common morphology and LV scar.
3. Several factors are associated with a higher risk of arrhythmic events during follow-up in univariable analyses, including uncommon VA morphology, lack of VA suppression, and NSVT/sustained

Table 3. Accuracy Measures of Factors Associated With Primary Outcome Events at the Median Follow-Up Duration of 6.2 Years

Variable	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive predictive value % (95% CI)	Negative predictive value % (95% CI)
Uncommon morphology VA (vs common)	100 (65–100)	59 (51–65)	8 (7–9)	100 (98–100)
Persistence/appearance of VAs (vs VAs suppression/absent VAs)	67 (43–86)	66 (59–73)	7 (5–9)	98 (95–99)
NSVT/VT during exercise testing (vs no NSVT/VT during exercise testing)	51 (21–80)	91 (86–94)	17 (12–18)	98 (97–99)
Regional LV wall motion abnormalities by echo (yes vs no)	33 (10–68)	94 (89–96)	16 (10–19)	97 (96–99)
LGE (yes vs no)	82 (46–96)	71 (64–77)	10 (7–10)	99 (97–100)
Sustained VA induction by PES (yes vs no)	49 (20–79)	97 (93–98)	36 (33–39)	98 (97–99)
Presence of electroanatomical scar (yes vs no)	82 (45–96)	76 (70–82)	12 (9–14)	99 (98–100)

LGE indicates late gadolinium enhancement; LV, left ventricular; NSVT, nonsustained ventricular tachycardia; PES, programmed electrical stimulation; VA, ventricular arrhythmia; and VT, ventricular tachycardia.

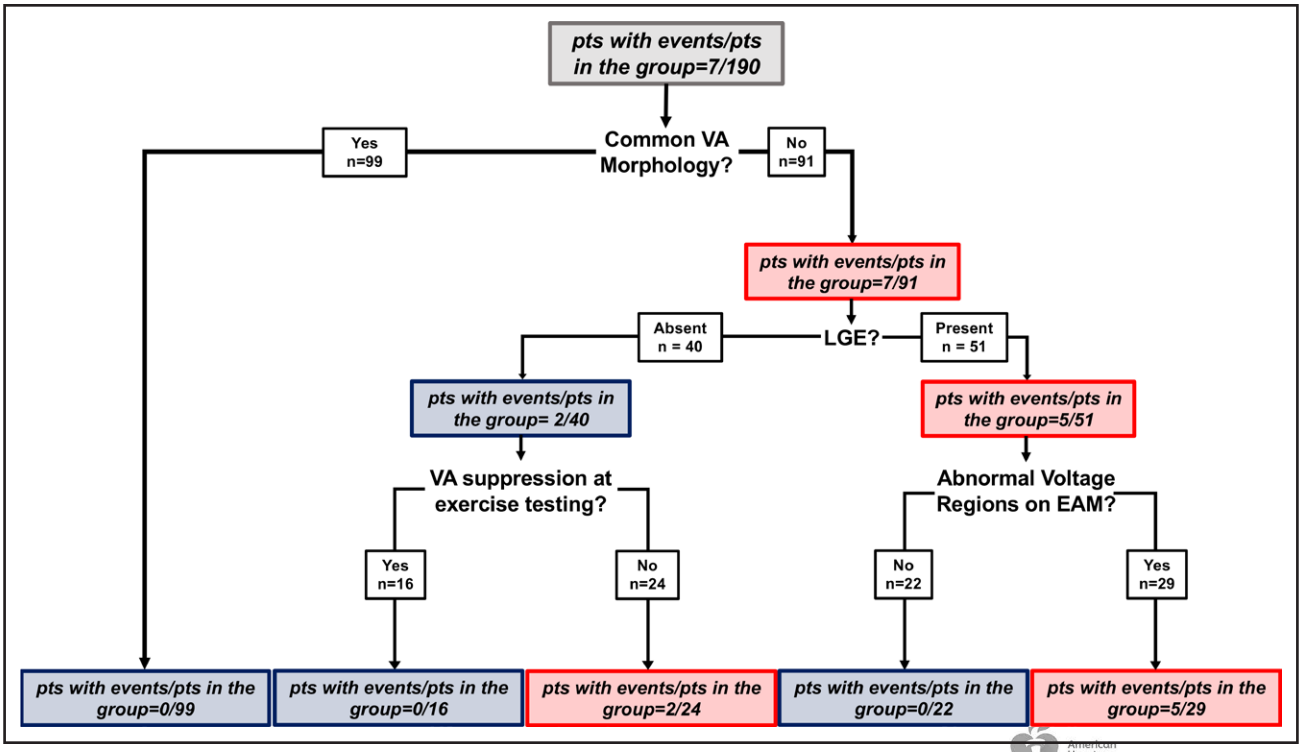

Figure 5. Integrated model for risk stratification.
To summarize the main study findings, an exploratory survival tree method was applied to predict the occurrence of primary outcome events during follow-up. The following variables were tested as candidate predictors of events: ventricular arrhythmia (VA) morphology (common vs uncommon), VA suppression at exercise testing, nonsustained ventricular tachycardia (NSVT)/ventricular tachycardia (VT) during exercise stress testing, late gadolinium enhancement (LGE), sustained VA inducibility by programmed electrical stimulation (PES), and presence of electroanatomical scar. Following automated discard of less relevant variables, the model suggests that, following VA morphology, LGE is the most important variable; VA suppression at exercise testing and presence of electroanatomical scar may allow further risk stratification in selected cases. PVC indicates premature ventricular complex; and VF, ventricular fibrillation.

VT during exercise stress testing, LV regional wall motion abnormalities on echocardiogram, LGE, inducibility of sustained VAs by PES, and the presence of electroanatomical scar on EAM.

4. Survival tree analysis showed that the prognostic assessment of athletes with frequent/exercise-related PVCs and NSVT should always start with the evaluation of VA morphology, reserving CMR and EAM to refine prognostication in selected cases.

The Importance of ECG Morphology and VA Complexity

Our data provide additional validation for previously proposed expert recommendations concerning the assessment of athletes with VAs, suggesting that 12-lead ECG arrhythmia morphology is a key parameter associated with the underlying myocardial substrate and, therefore, with the risk of major arrhythmic events, especially during training or competition.[5,6] Previous observational data have suggested that the uncommon ECG VA morphology is a key factor associated with CMR-proven LV scar in athletes with apparently idiopathic frequent or exercise-induced VAs.[10,15]

Our data confirm these observations and further validate the prognostic value of arrhythmia ECG morphology: athletes presenting with infundibular or fascicular PVCs and NSVTs at baseline—as confirmed by ambulatory ECG monitoring and maximal exercise stress testing—experienced no major arrhythmic events during long-term follow-up. This supports the notion that common morphology VAs may be considered clinically benign, especially in the absence of other clinical, ECG, or imaging risk markers.[1,16]

Although the prevalence of a final diagnosis of underlying cardiomyopathy was lower among athletes with common morphology VAs compared with those with uncommon morphologies, 28% of athletes in the former group were ultimately diagnosed with structural heart disease, including 9% with arrhythmogenic cardiomyopathy. These findings are consistent with previous studies reporting a prevalence of structural heart disease ranging from 9% to 24% in young athletes with common morphology PVCs/NSVTs,[17,18] and underscore the importance of comprehensive clinical, ECG, and imaging assessment, as well as periodic reevaluation during follow-up to detect potential disease progression.

Remarkably, the generally benign prognostic meaning of common morphology VAs was confirmed in our study despite a 47% prevalence of NSVT, which is regarded as a marker of increased risk of sudden cardiac death in athletes, mainly based on data obtained in patients with arrhythmogenic right ventricular cardiomyopathy,[19,20] arrhythmic myocarditis,[21,22] or arrhythmic mitral valve prolapse.[23] Our results align with previous CMR studies conducted in nonathletic subjects with apparently idiopathic VAs, in which NSVTs were not associated with abnormal myocardial substrates or increased risk of major arrhythmic outcomes during follow-up.[24]

Clinical and Electrophysiological Predictors of Major Arrhythmic Events in Athletes With Complex VAs

Besides VA morphology and complexity, other noninvasive markers—lack of VA suppression and NSVT/VT during exercise stress testing, the presence of LV regional wall motion abnormalities on echocardiogram, and LGE—emerged as key factors associated with major arrhythmic events during follow-up. These observations confirm previous studies suggesting that maximal exercise stress testing is important not only to confirm the VA morphology (common versus uncommon), but also to evaluate the response of PVCs to exercise and NSVT inducibility. These parameters are, in turn, associated with CMR-proven LV scar.[10] The importance of CMR-proven myocardial scar cannot be overstated: LV LGE, especially with a nonischemic stria pattern, may be the substrate for life-threatening VAs and sudden death in athletes, and should be suspected in those with uncommon VAs, especially when they present with an RBBB-superior axis pattern.[25]

In our cohort, sustained VT/VF inducibility at EPS was also significantly associated with major arrhythmic events in the propensity score-weighted analysis. Heidbüchel et al[26] previously reported that EPS may enable risk stratification among endurance athletes with complex LBBB-pattern VAs and exercise-induced arrhythmogenic cardiomyopathy. Our results extend this observation to a less selected cohort of athletes with complex VAs.

Although analyses concerning the long-term prediction of the study end point are hypothesis-generating due to the small number of outcomes, the results suggest that, especially in competitive athletes with uncommon PVCs/NSVTs and unclear findings after noninvasive tests including CMR, who place a high value on precise diagnostic definition to inform a safe return to play, referral for invasive electrophysiological assessments may have prognostic as well as diagnostic value, in line with what was recently suggested by a task force of Italian sports cardiology experts.[27]

The extent of electroanatomical scar and sustained VT/VF inducibility at EPS are key electrophysiological hallmarks of the arrhythmogenicity of myocardial fibrosis.[28] These factors reflect the propensity of the electroanatomical scar to favor sustained VAs and point to the presence of slow conduction zones and conduction barriers in the myocardium, which are crucial mechanistical determinants of reentrant VAs.[28] The lack of association between the presence of late potentials and primary outcome events in our sample may reflect the exclusion of patients with a history of sustained VAs at baseline, in whom late potentials are more commonly detectable.[28] This finding suggests the need for future research to explore the prognostic value of additional functional substrate mapping strategies for better electrophysiological characterization of myocardial scars in athletes referred for complex VAs.[29]

As summarized in Figure 5, our data allowed for the development of an exploratory unifying model to assist clinicians in identifying athletes with complex VAs at risk of life-threatening arrhythmic events. This model may enable rapid risk stratification, particularly in the subgroup of athletes with common morphology PVCs/NSVTs who lack other risk markers, for whom further testing may not be necessary for prognostic purposes.[1,30] Based on our findings, EAM may have prognostic value among athletes with uncommon PVCs/NSVTs and LGE, suggesting that limited CMR-proven myocardial scars that cannot be detected by bipolar and unipolar EAM may not be associated with an increased risk of sustained VT/VF during follow-up.[8,28]

Limitations

Several limitations of our work should be acknowledged. The comprehensive diagnostic assessment was performed in high-volume referral centers for the care of patients with VAs, potentially limiting the generalizability of our findings. Some athletes were excluded from the present analysis due to lack of data on 12-lead ECG morphology of the VAs, and some refused invasive diagnostic assessments. Furthermore, the low rate of events limited the statistical power of all analyses concerning prognostic factors, and the survival tree model needs further validation in other cohorts. Nonetheless, to our knowledge, this is the largest report concerning the multimodality characterization of athletes with complex VAs in which the long-term prognostic value of a comprehensive diagnostic workup was evaluated. Future studies enrolling larger cohorts of athletes are needed to better elucidate the prognostic significance of the workup in the context of specific underlying diagnoses of structural heart disease. Epicardial mapping was only performed when clinically indicated for CA of epicardial VT, potentially limiting our ability to detect late potentials confined to the epicardium in athletes with nonischemic cardiomyopathies.

Conclusions

The prognostic assessment of athletes with VAs requires the integration of ECG, imaging, and, in selected cases, electrophysiology data. A comprehensive diagnostic workup may facilitate risk stratification in athletes with complex VAs and inform safe return-to-play decisions.

ARTICLE INFORMATION

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REFERENCES

1. Gomez SE, Perez MV, Wheeler MT, Hadley D, Hwang CE, Kussman A, Kim DS, Froelicher V. Classification of premature ventricular contractions in athletes during routine preparticipation exams. *Circ Arrhythm Electrophysiol.* 2024;17:e012835. doi: 10.1161/CIRCEP.124.012835
2. Zorzi A, De Lazzari M, Mastella G, Niero A, Trovato D, Cipriani A, Peruzza F, Portolan L, Berton G, Sciacca F, et al. Ventricular arrhythmias in young competitive athletes: prevalence, determinants, and underlying substrate. *J Am Heart Assoc.* 2018;7:e009171. doi: 10.1161/JAHA.118.009171
3. Zorzi A, Mastella G, Cipriani A, Berton G, Del Monte A, Gusella B, Nese A, Portolan L, Sciacca F, Tikvina S, et al. Burden of ventricular arrhythmias at 12-lead 24-hour ambulatory ECG monitoring in middle-aged endurance athletes versus sedentary controls. *Eur J Prev Cardiol.* 2018;25:2003–2011. doi: 10.1177/2047487318797396
4. Pelliccia A, Sharma S, Gati S, Bäck M, Börjesson M, Caselli S, Collet JP, Corrado D, Drezner JA, Halle M, et al; ESC Scientific Document Group. 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease. *Eur Heart J.* 2021;42:17–96. doi: 10.1093/eurheartj/ehaa605
5. Corrado D, Drezner JA, D'Ascenzi F, Zorzi A. How to evaluate premature ventricular beats in the athlete: critical review and proposal of a diagnostic algorithm. *Br J Sports Med.* 2020;54:1142–1148. doi: 10.1136/bjsports-2018-100529
6. Zorzi A, D'Ascenzi F, Andreini D, Castelletti S, Casella M, Cavarretta E, Cipriani A, Compagnucci P, Delise P, Dello Russo A, et al. Interpretation and management of premature ventricular beats in athletes: an expert opinion document of the Italian Society of Sports Cardiology (SICSPORT). *Int J Cardiol.* 2023;391:131220. doi: 10.1016/j.ijcard.2023.131220
7. Dello Russo A, Compagnucci P, Casella M, Gasperetti A, Riva S, Dessanai MA, Pizzamiglio F, Catto V, Guerra F, Stronati G, et al. Ventricular arrhythmias in athletes: Role of a comprehensive diagnostic workup. *Heart Rhythm.* 2022;19:90–99. doi: 10.1016/j.hrthm.2021.09.013
8. Maron BJ, Zipes DP, Kovacs RJ; American Heart Association Electrocardiography and Arrhythmias Committee of Council on Clinical Cardiology, Council on Cardiovascular Disease in Young, Council on Cardiovascular and Stroke Nursing, Council on Functional Genomics and Translational Biology, and American College of Cardiology. American Heart Association Electrocardiography and Arrhythmias Committee of Council on Clinical Cardiology, Council on Cardiovascular Disease in Young, Council on Cardiovascular and Stroke Nursing, Council on Functional Genomics and Translational Biology, and American College of Cardiology. Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Preamble, Principles, and General Considerations: A Scientific Statement From the American Heart Association and American College of Cardiology. *Circulation.* 2015;132:e256–e261. doi: 10.1161/CIR.0000000000000236
9. Maron BJ, Chaitman BR, Ackerman MJ, Bayés de Luna A, Corrado D, Crosson JE, Deal BJ, Driscoll DJ, Estes NA 3rd, Araújo CG, et al; Working Groups of the American Heart Association Committee on Exercise, Cardiac Rehabilitation, and Prevention. Recommendations for physical activity and recreational sports participation for young patients with genetic cardiovascular diseases. *Circulation.* 2004;109:2807–2816. doi: 10.1161/01.CIR.0000128363.85581.E1
10. Crescenzi C, Zorzi A, Vessella T, Martino A, Panattoni G, Cipriani A, De Lazzari M, Perazzolo Marra M, Fusco A, Sciarra L, et al. Predictors of left ventricular scar using cardiac magnetic resonance in athletes with apparently idiopathic ventricular arrhythmias. *J Am Heart Assoc.* 2021;10:e018206. doi: 10.1161/JAHA.120.018206
11. Sharma S, Drezner JA, Baggish A, Papadakis M, Wilson MG, Prutkin JM, La Gerche A, Ackerman MJ, Borjesson M, Salerno JC, et al. International recommendations for electrocardiographic interpretation in athletes. *J Am Coll Cardiol.* 2017;69:1057–1075. doi: 10.1016/j.jacc.2017.01.015
12. Zeppenfeld K, Tfelt-Hansen J, de Riva M, Winkel BG, Behr ER, Blom NA, Charron P, Corrado D, Dagres N, de Chillou C, et al; ESC Scientific Document Group. 2022 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Eur Heart J.* 2022;43:3997–4126. doi: 10.1093/eurheartj/ehac262
13. Olmos A, Govindasamy P. A practical guide for using propensity score weighting in R. *Pract Assess Res Eval.* 2015;20:1–8
14. Gasperetti A, Carrick RT, Costa S, Compagnucci P, Bosman LP, Chivulescu M, Tichnell C, Murray B, Tandri H, Tadros R, et al. Programmed ventricular stimulation as an additional primary prevention risk stratification tool in arrhythmogenic right ventricular cardiomyopathy: a multinational study. *Circulation.* 2022;146:1434–1443. doi: 10.1161/CIRCULATIONAHA.122.060866
15. Cipriani A, Zorzi A, Sarto P, Donini M, Rigato I, Bariani R, De Lazzari M, Pilichou K, Thiene G, Iliceto S, et al. Predictive value of exercise testing in athletes with ventricular ectopy evaluated by cardiac magnetic resonance. *Heart Rhythm.* 2019;16:239–248. doi: 10.1016/j.hrthm.2018.08.029
16. Delise P, Sitta N, Lanari E, Berton G, Centa M, Allocca G, Cati A, Biffi A. Long-term effect of continuing sports activity in competitive athletes with frequent ventricular premature complexes and apparently normal heart. *Am J Cardiol.* 2013;112:1396–1402. doi: 10.1016/j.amjcard.2013.06.032
17. Biffi A, Pelliccia A, Verdile L, Fernando F, Spataro A, Caselli S, Santini M, Maron BJ. Long-term clinical significance of frequent and complex ventricular tachyarrhythmias in trained athletes. *J Am Coll Cardiol.* 2002;40:446–452. doi: 10.1016/s0735-1097(02)01977-0
18. Di Florio A, Fusi C, Anselmi F, Cavigli L, Focardi M, Cameli M, Felici A, Capitani M, Valente S, Bonifazi M, et al. Clinical management of young competitive athletes with premature ventricular beats: a prospective cohort study. *Int J Cardiol.* 2021;330:59–64. doi: 10.1016/j.ijcard.2021.02.021
19. Gasperetti A, Cappelletto C, Carrick R, Targetti M, Tichnell C, Martino A, Murray B, Compagnucci P, Stolfo D, Bisson J, et al. Association of premature ventricular contraction burden on serial holter monitoring with arrhythmic risk in patients with arrhythmogenic right ventricular cardiomyopathy. *JAMA Cardiol.* 2022;7:378–385. doi: 10.1001/jamacardio.2021.6016

20. Jordà P, Bosman LP, Gasperetti A, Mazzanti A, Gourraud JB, Davies B, Frederiksen TC, Weidmann ZM, Di Marco A, Roberts JD, et al. Arrhythmic risk prediction in arrhythmogenic right ventricular cardiomyopathy: external validation of the arrhythmogenic right ventricular cardiomyopathy risk calculator. *Eur Heart J*. 2022;43:3041–3052. doi: 10.1093/eurheartj/ehac289
21. Compagnucci P, Volpato G, Falanga U, Cipolletta L, Conti MA, Grifoni G, Ciliberti G, Stronati G, Fogante M, Bergonti M, et al. Myocardial inflammation, sports practice, and sudden cardiac death: 2021 update. *Medicina (Kaunas)*. 2021;57:277. doi: 10.3390/medicina57030277
22. Casella M, Gasperetti A, Compagnucci P, Narducci ML, Pelargonio G, Catto V, Carbucicchio C, Bencardino G, Conte E, Schicchi N, et al. Different phases of disease in lymphocytic myocarditis: clinical and electrophysiological characteristics. *JACC Clin Electrophysiol*. 2023;9:314–326. doi: 10.1016/j.jacep.2022.10.004
23. Compagnucci P, Selimi A, Cipolletta L, Volpato G, Gasperetti A, Valeri Y, Parisi Q, Curcio A, Natale A, Dello Russo A, et al. Arrhythmic mitral valve prolapse and sports activity: pathophysiology, risk stratification, and sports eligibility assessment. *J Clin Med*. 2024;13:1350. doi: 10.3390/jcm13051350
24. Nucifora G, Muser D, Masci PG, Barison A, Rebellato L, Piccoli G, Daleffe E, Toniolo M, Zanuttini D, Facchin D, et al. Prevalence and prognostic value of concealed structural abnormalities in patients with apparently idiopathic ventricular arrhythmias of left versus right ventricular origin: a magnetic resonance imaging study. *Circ Arrhythm Electrophysiol*. 2014;7:456–462. doi: 10.1161/CIRCEP.113.001172
25. Zorzi A, Perazzolo Marra M, Rigato I, De Lazzari M, Susana A, Niero A, Pilichou K, Migliore F, Rizzo S, Giorgi B, et al. Nonischemic left ventricular scar as a substrate of life-threatening ventricular arrhythmias and sudden cardiac death in competitive athletes. *Circ Arrhythm Electrophysiol*. 2016;9:e004229. doi: 10.1161/CIRCEP.116.004229
26. Heidbüchel H, Hoogsteen J, Fagard R, Vanhees L, Ector H, Willems R, Van Lierde J. High prevalence of right ventricular involvement in endurance athletes with ventricular arrhythmias. Role of an electrophysiologic study in risk stratification. *Eur Heart J*. 2003;24:1473–1480. doi: 10.1016/s0195-668x(03)00282-3
27. Dello Russo A, Compagnucci P, Zorzi A, Cavarretta E, Castelletti S, Contursi M, D'Aleo A, D'Ascenzi F, Mos L, Palmieri V, et al. Electroanatomic mapping in athletes: why and when. An expert opinion paper from the Italian Society of Sports Cardiology. *Int J Cardiol*. 2023;383:166–174. doi: 10.1016/j.ijcard.2023.05.013
28. Haqqani HM, Kalman JM, Roberts-Thomson KC, Balasubramaniam RN, Rosso R, Snowdon RL, Sparks PB, Vohra JK, Morton JB. Fundamental differences in electrophysiologic and electroanatomic substrate between ischemic cardiomyopathy patients with and without clinical ventricular tachycardia. *J Am Coll Cardiol*. 2009;54:166–173. doi: 10.1016/j.jacc.2009.04.024
29. Vlachos K, Letsas KP, Srinivasan NT, Frontera A, Efremidis M, Dragasis S, Martin CA, Martin R, Nakashima T, Bazoukis G, et al. The value of functional substrate mapping in ventricular tachycardia ablation. *Heart Rhythm O2*. 2022;4:134–146. doi: 10.1016/j.hroo.2022.10.013
30. Lampert R, Chung EH, Ackerman MJ, Arroyo AR, Darden D, Deo R, Dolan J, Etheridge SP, Gray BR, Harmon KG, et al. 2024 HRS expert consensus statement on arrhythmias in the athlete: evaluation, treatment, and return to play. *Heart Rhythm*. 2024;21:e151–e252. doi: 10.1016/j.hrthm.2024.05.018
31. Casella M, Perna F, Dello Russo A, Pelargonio G, Bartoletti S, Ricco A, Sanna T, Pieroni M, Forleo G, Pappalardo A, et al. Right ventricular substrate mapping using the Ensite Navx system: accuracy of high-density voltage map obtained by automatic point acquisition during geometry reconstruction. *Heart Rhythm*. 2009;6:1598–1605. doi: 10.1016/j.hrthm.2009.07.040
32. Caforio AL, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, Fu M, Heliö T, Heymans S, Jahns R, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur Heart J*. 2013;34:2636-48, 2648a–2636-48, 2648d.
33. Towbin JA, McKenna WJ, Abrams DJ, Ackerman MJ, Calkins H, Darrieux FCC, Daubert JP, de Chillou C, DePasquale EC, Desai MY, et al. 2019 HRS expert consensus statement on evaluation, risk stratification, and management of arrhythmogenic cardiomyopathy. *Heart Rhythm*. 2019;16:e301–e372. doi: 10.1016/j.hrthm.2019.05.007
34. Casella M, Pizzamiglio F, Dello Russo A, Carbucicchio C, Al-Mohani G, Russo E, Notarstefano P, Pieroni M, D'Amati G, Sommariva E, et al. Feasibility of combined unipolar and bipolar voltage maps to improve sensitivity of endomyocardial biopsy. *Circ Arrhythm Electrophysiol*. 2015;8:625–632. doi: 10.1161/CIRCEP.114.002216