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RESEARCH LETTER

Exploring the Hidden Side of Ventricular Arrhythmias in Elite Athletes With Structural Normal Hearts

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Ventricular ectopic beats (VEBs) during exercise are a common finding in athletes, representing a challenging issue when unassociated with structural cardiac diseases, leaving the etiological and management issues unsolved.[1]

We sought to investigate the spectrum of potential determinants associated with VEBs in a large cohort of Olympic athletes with structurally normal hearts.

We enrolled 763 athletes prior to their participation in the 2024 Olympic Games, engaged in 32 different sporting disciplines, grouped into skill (n=183, 24%), power (n=221, 28.9%), mixed (n=175, 22.9%), and endurance (n=184, 24.1%) according to the 2020 ESC Sport Cardiology classification.[2]

Athletes with VEBs at cardiopulmonary exercise test underwent a comprehensive investigation, including 24-hour Holter ECG monitoring and cardiac magnetic resonance or coronary CT scan, when indicated.[3]

The study was approved by the Ethical Committee of Sapienza University of Rome (IRB number 0208/2024). All data are maintained in an institutional database, available upon reasonable request. The subjects gave informed consent.

The overall sample had a mean age of 25.8±5.1 years; 358 were females (47.1%), mostly White (98%), with a mean body mass index of 23.1±3 kg/m^2. Fifty-one (6.7%) were smokers, while 254 (33.4%) had a positive family history of CVD. Three athletes were excluded from our study due to detection of structural cardiac disease (2 cases of left ventricular nonischemic scar, 1 case of arrhythmogenic cardiomyopathy).

At cardiopulmonary exercise test, 148 athletes (19.5%) had VEBs. Athletes with VEBs were older (27±4.5 versus 25.5±5.2 years; P=0.002), with a lower prevalence of females (39.8% versus 48.9%; P=0.049), and included a higher proportion of endurance athletes (31.7% versus 22.2%; P=0.014). At 24-hour Holter ECG monitoring, in 121 athletes (80%) VEBs were confirmed with a broad burden of 624±3198 beats. At echocardiography, athletes with VEBs had a larger left ventricular end-diastolic volume indexed: 74.2±18.9 versus 69.1±14.8 mL; P=0.001, a thicker interventricular septum: 9.23±1.1 versus 8.94±1.1 mm; P=0.001, and posterior wall: 8.55±1.2 versus 8.3±1.2 mm; P=0.024. Moreover, at cardiopulmonary exercise test athletes with VEBs attained a higher peak systolic blood pressure (177.2±16.2 versus 172.8±20.3 mm Hg; P=0.016), higher VO_2 max (44.8±9.5 versus 42.9±9.5 mL/min per kg; P=0.033), and higher O_2 pulse (20±5.3 versus 18.6±5.4 mL/beat; P=0.004). After excluding cardiac diseases by cardiac magnetic resonance and coronary CT scan, extracardiac causes of VEBs were investigated.

Athletes with VEBs had lower hemoglobin values (14±1.2 versus 14.3±1.2 g/dL; P=0.008), lower values of serum iron concentrations (89.1±40.5 versus 108.7±44.8 µg/dL; P<0.0001), and higher prevalence of iron deficiency (15.5% versus 6.2%; P=0.0002), compared with athletes without arrhythmias.

Key Words: athletes ■ blood pressure ■ inflammation ■ prevalence ■ smokers

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Nonstandard Abbreviations and Acronyms

OR	odds ratio
SII	systemic immuno-inflammation index
VEB	ventricular ectopic beat

No statistically significant difference in electrolyte balance was noted, except for relatively lower serum Ca++ concentrations (9.62±0.35 versus 9.73±0.38 mmol/L; *P*=0.001) in those with VEBs. Moreover, higher cortisol concentrations were observed in athletes with VEBs (20.7±10.2 versus 18±6 µg/dL; *P*<0.0001), as well as higher inflammatory parameters, including higher neutrophils (3.39±1.5×10³/µL versus 2.94±1.1×10³/µL; *P*<0.0001), and platelet counts (253.7±54×10³/µL versus 238.6±48.6×10³/µL; *P*=0.0009), and a higher systemic immuno-inflammation index (SII; 438.4±341.7 versus 344.1±180.6; *P*<0.0001), a new additional marker of systemic inflammation calculated as neutrophils×platelets/lymphocytes.[4]

At multivariable analysis (adjusted for gender, left ventricular end-diastolic volume indexed, LVESVi, interventricular septum, PWT, VO_2 max, O_2 pulse, hemoglobin, serum calcium, cortisol, SII index, serum iron, peak systolic blood pressure), VEBs were independently and positively correlated with left ventricular wall thickness (odds ratio (OR), 1.565 [95% CI, 1.110–2.206]; *P*=0.010), serum cortisol levels (OR, 1.066 [95% CI, 1.037–1.096]; *P*<0.0001), and SII index (OR, 1.002 [95% CI, 1.001–1.003]; *P*<0.0001), and inversely correlated with serum Ca++ (OR, 0.419 [95% CI, 0.232–0.759]; *P*=0.004) and serum iron (OR, 0.991 [95% CI, 0.985–0.996]; *P*<0.0001) concentrations (Figure).

In a subsequent subanalysis of VEB morphology, that is, common (LBBB/inferior axis, typical RBBB and narrow QRS [<130 ms]) versus uncommon (LBBB/intermediate-superior axis, atypical RBBB and wide QRS [≥130 ms]), 76 (51.4%) had an uncommon morphology.[3,5] In those with uncommon morphology, an even higher SII index was noted (509.8±419.4 versus 371.7±227.3; *P*=0.014), with similar values of iron (91±40.1 versus 87.1±40.7 µg/dL; *P*=0.563), serum calcium (9.64±0.34 versus 9.60±0.36 mmol/L; *P*=0.466), and cortisol (9.60±0.36 versus 20.6±12.1 µg/dL; *P*=0.931) concentrations.

Finally, we analyzed the hematologic condition in relation to sport discipline and sex. Indeed, no statistically significant differences were found in hematologic parameters between different disciplines (hemoglobin, *P*=0.719; neutrophils, *P*=0.354; platelets, *P*=0.869; lymphocytes, *P*=0.078; and SII index, *P*=0.80). Moreover, no gender differences were highlighted, with similar values in hemoglobin (*P*=0.473), neutrophils (*P*=0.235), platelets (*P*=0.411), lymphocytes (*P*=0.0529), and SII index (*P*=0.175).

In conclusion, this study sheds a new light on the multifactorial nature of VEBs in elite athletes, emphasizing a possible contribution of extracardiac determinants, primarily systemic inflammation, iron deficiency, and calcium metabolism, in their genesis. Our study highlights that arrhythmias in athletes can stem from various causes, which are not necessarily pathological cardiac conditions.

These findings suggest the need for an integrated approach that considers both cardiac and extracardiac factors in the evaluation of arrhythmias in athletes. Future research should explore the mechanisms linking these parameters to arrhythmogenesis and assess the impact of targeted interventions on the prevalence and management of VEBs in this population.

ARTICLE INFORMATION

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All authors have approved the final article. Drs Di Gioia and Daniello were responsible for the conception and design of the study. Drs Monosilio, Maestrini, Pelliccia, Serdoz, Lanza, and Paoletti were involved in the acquisition of data or the analysis and interpretation of data. Drs Ferrera, Lanza, Squeo, and Serdoz contributed to drafting the article or revising it critically for important intellectual content. Drs Di Gioia and Pelliccia provided the final approval of the version to be submitted.

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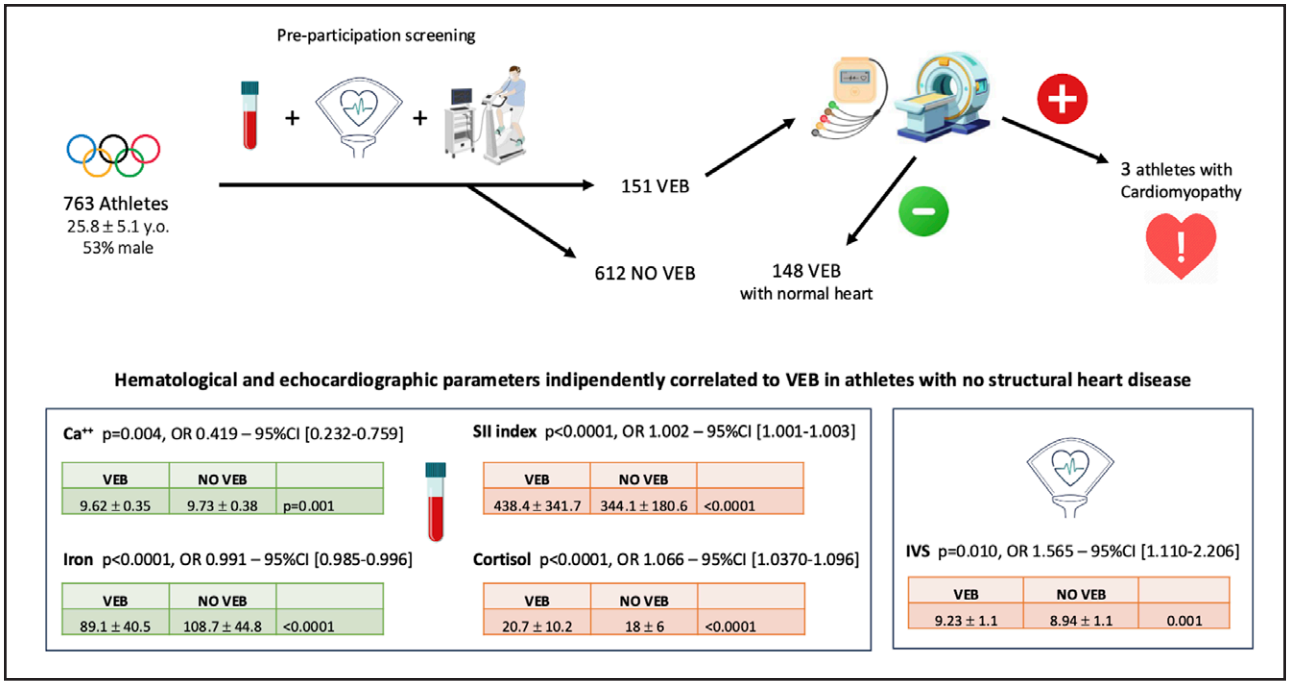

Figure. Summary of the study that show our protocol.
Athletes with cardiomyopathies were excluded. Athletes with ventricular ectopic beat (VEB) and structural normal heart were enrolled. Hematologic (Ca++, systemic immune inflammation (SII) index, iron, and cortisol) and echocardiographic (interventricular septum [IVS]) parameters were independently correlated to VEB.OR indicates odds ratio.