



Exercise-induced intraventricular pressure gradient may be the cause of sudden cardiac death in patients with unknown cardiac disease

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ARTICLE INFO

Keywords:

Exercise stress echocardiography
Intra-ventricular pressure gradient
Sudden cardiac death
Sports medicine

ABSTRACT

Sudden cardiac death (SCD) is a tragedy at any age and under any circumstances, but it is especially poignant, and fortunately very rare, when it takes the life of an athlete, a person who represents health and a healthy lifestyle. Sports cardiologists worldwide have worked to quantify the incidence of SCD in athletes, identify risk factors, develop pre-participation screening tools, and formulate plans to address on-field SCD. While progress has been made, there is still much to do to make both competitive and recreational sports safer for individuals with known cardiac disease and athletes without known or suspected cardiac abnormalities.

We recently published the case of an athlete who practices triathlon and underwent medical evaluation after an episode of aborted sudden death. The complete diagnostic workup including a complete genetic study for myocardial pathology had normal results. An exercise stress echocardiogram (ESE) was finally performed during which he developed a significant intraventricular pressure gradient (IVPG) – a possible cause of ischemia – over 100 mmHg with an end-systolic peak at the end of exercise that was associated with frequent premature ventricular complexes.

We hypothesize the possible role of ESE for IVPG assessment in athletes who have unexplained symptoms related to exercise or aborted sudden death. In our opinion, it should be considered useful and used by routine to improve the clinical approach of this group of patients, detecting possible high-risk athletes.

Introduction

We know that intraventricular pressure gradients, of low magnitude are a common and normal occurrence. Three mechanisms have been put forward [1] for them to rise significantly during physical exertion: an increase in non-obstructive physiological gradients; end-systolic obstruction secondary to ventricular cavity eradication; and mid-systolic obstruction caused by systolic anterior movement (SAM) of the mitral valve impeding ejection. However, for the SAM of the mitral valve to come about, there must be some variation in the geometry of the ventricular chamber or the mitral valve apparatus. This was not the case in the athlete we studied after aborted sudden death [2]. It has been demonstrated that IVPG can be caused by maneuvers that change loading conditions in structurally normal hearts [1], and it is known that participating in sports can elicit such changes.

The hypothesis

Significant intraventricular pressure gradient development during exercise is rare and more frequently associated with left ventricular hypertrophy [3]. The association between intraventricular gradient and myocardial ischemia with angina and ST segment alterations has been reported in the literature [4–13] and exemplified in Figs. 1, 2, and 3 from an athlete without left ventricular hypertrophy, with angina pectoris that we have studied [14]. We suggest that this phenomenon is likely caused by subtle changes — when compared to hypertrophic cardiomyopathy — in the geometric shape and dimensions of the left ventricle, possibly due to more anterior implantation of the papillary muscles. During exercise, these changes can lead to abnormal systolic anterior motion of the chordae and mitral valve and papillary muscle ischemia. The resulting outflow obstruction in the left ventricle, and the

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<https://doi.org/10.1016/j.mehy.2024.111552>

Received 6 April 2024; Received in revised form 22 December 2024; Accepted 22 December 2024

Available online 24 December 2024

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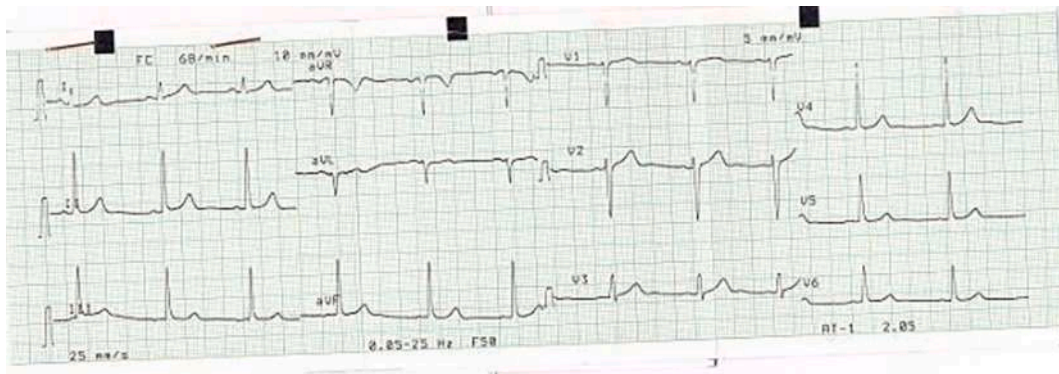


Fig. 1. [14]: Normal ECG before exercise.

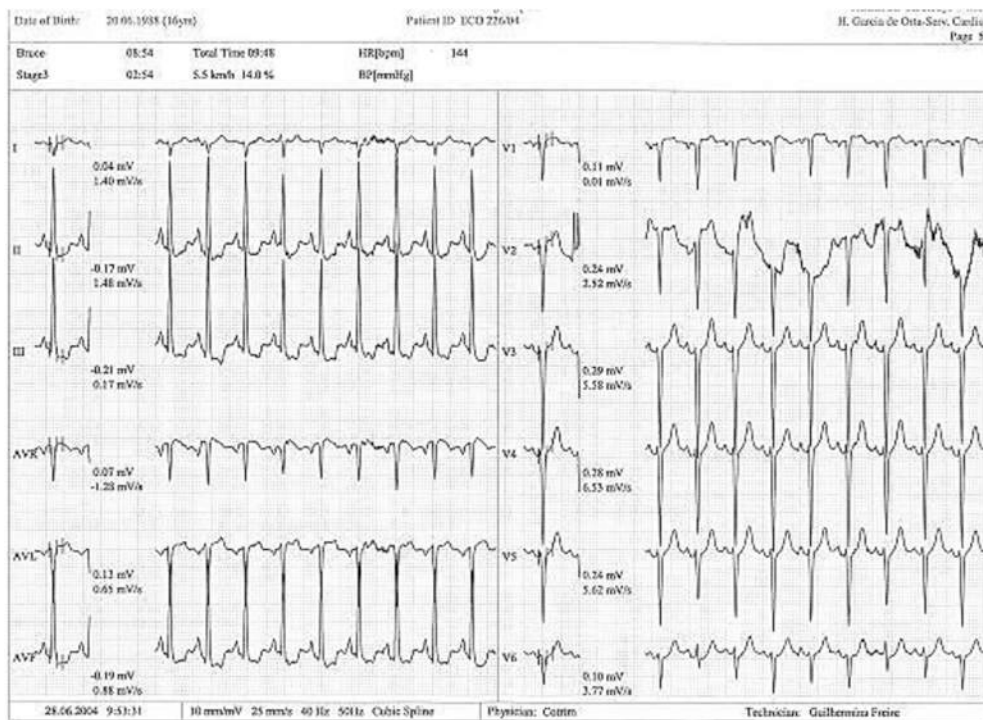


Fig. 2. [14]: Exercise test with alteration in ST segment in DII, DIII, and avF.

subsequent increase in intraventricular pressure with extravascular compression and perfusion reserve impairment, may contribute to left ventricular strain and ST depression as indicators of subendocardial ischemia in these patients [15,16].

Scientific recommendations also highlight that exercise-induced symptoms and/or ischemic-like ECG signs are frequently associated with a significant intraventricular gradient (50 mmHg during or after exercise) in the absence of wall motion abnormalities in athletes [14,17–21].

This situation somewhat resembles the “suicide left ventricle” in a hypercontractile state, which can occur during and after transaortic valve implantation or aortic valve surgery. In such cases, careful management of heart rate, intravascular fluid volume, and the inotropic state of the left ventricle is crucial for the procedure’s success. [22].

Similarly, the connection between ischemia, arrhythmias, and the risk of sudden death is well-established [13–16]. Taking into consideration this knowledge, along with the case of the athlete we published [2], we hypothesize that exercise-induced intraventricular gradients causing ischemia may trigger the onset of fatal/malignant arrhythmias.

Evolution of the hypothesis

Sudden death among young athletes has been extensively researched, with a consensus emerging that hereditary or congenital factors are typically implicated [21]. Nonetheless, in certain studies [22], approximately 30 % of autopsy findings reveal no discernible abnormalities, raising concerns about the effectiveness of existing screening protocols in averting sudden fatalities. In the instance under consideration [2], we report that the athlete had a normal echocardiogram, coronary computed tomography angiography, and cardiac magnetic resonance which means that his heart would likely exhibit no morphological irregularities upon autopsy examination. The lack of understanding surrounding cases of sudden death without an apparent cause highlighted the need for new explanations of this phenomenon, ultimately giving rise to our hypothesis.

Hypothesis testing

As a center with extensive experience in exercise stress echocardiography, particularly in the evaluation of IVPG [1], we propose the

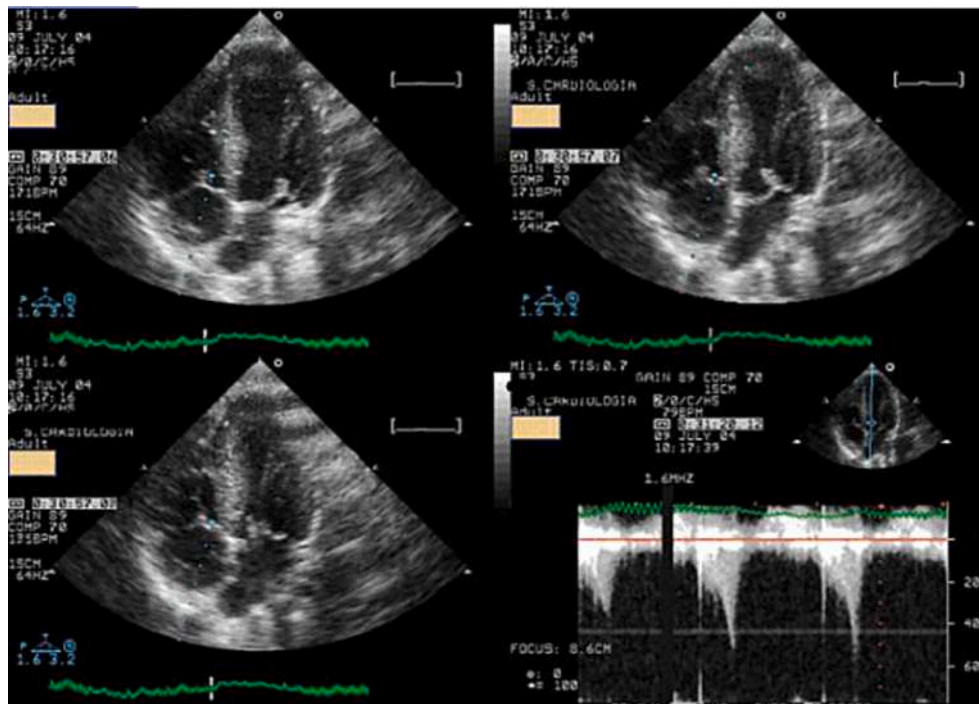


Fig. 3. [14]: At peak exercise, systolic anterior movement of mitral valve and significant intraventricular pressure gradient was detected. Copyright of the figures from Carlos Cotrim as co-author from reference,[14].

following: firstly, conduct an exercise stress echocardiography on all eligible patients/athletes [12–14] experiencing symptoms without an identifiable cause after undergoing the standard-of-care diagnostic approach and accompany them when they develop intraventricular gradient. The results of this follow-up include the assumption that most of them will be treated with beta-blockers by their cardiologists [8,25] and this treatment may influence the outcomes. Secondly, exercise stress echocardiography to identify intraventricular gradient in all possible cases of aborted sudden death related to exercise, where a comprehensive medical assessment was normal [2].

Conclusion

Our experience tells us that if we do not search for IVPG we will not find them. Our published experience [1] and the present hypotheses imply that the search for IVPG should be done routinely with the proper candidates.

Therefore, when appropriate, the exercise stress protocol should, systematically include the search for intraventricular pressure gradient [1,21,22,23,24]. This is particularly crucial concerning the hypothesized correlation between intraventricular pressure gradient and sudden cardiac death, as well as with unexplained exercise-induced symptoms.

CRediT authorship contribution statement

Nuno Cotrim: Writing – original draft, Supervision, Project administration, Investigation, Data curation, Conceptualization. **Hugo Café:** Writing – review & editing, Methodology. **Pedro Cordeiro:** Writing – review & editing. **Jorge Guardado:** Writing – review & editing. **Luís Baquero:** Writing – review & editing. **Carlos Cotrim:** .

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

None declared.

Statement Regarding Ethics Approval

This is because the study does not involve human or animal participants, nor does it include any procedures, experiments, or interventions that necessitate approval from an ethics committee. The research solely relies on theoretical analysis, publicly available data, or similar non-invasive methodologies that are exempt from ethical review.

This conclusion aligns with established guidelines for ethical review requirements in academic research.

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