Is a high-intensity exercise test better than a graded exercise test in eliciting exercise-related arrhythmias?

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Introduction

Exercise stress tests are commonly used to evaluate symptoms, such as palpitations, that occur during exercise. The most commonly used exercise stress test in both children and adults is a graded exercise test (GXT) that starts at a slow pace and increases the speed and incline in a stepwise fashion. However, a GXT does not often accurately reproduce the cardiovascular conditions that result in symptoms, particularly in children and young athletes. A high-intensity exercise test (HIXT) protocol that consists of short durations at higher speeds may more accurately simulate the cardiovascular conditions likely to elicit patient symptoms. Herein, we present 2 cases in which a HIXT led to the diagnosis of exercise-related arrhythmias, previously unrecognized by GXT.

KEY TEACHING POINTS

- Current graded exercise test protocols were initially designed to assess for myocardial ischemia in adults. In pediatric and young adult patients, the incidence of arrhythmias during these tests is very low, including patients with exercise-related symptoms.
- Given the characteristics of the physical activity during childhood, high-intensity exercise test protocols may better represent the cardiovascular conditions that trigger symptoms.
- High-intensity exercise test protocols may lead to a higher catecholaminergic state. This is why a repetitive sprint-based high-intensity protocol, tailored to the physical training level of the patient, may be more suitable than graded tests in the attempt to reproduce arrhythmias in patients with exercise-related symptoms.

Case report

Case 1

A previously healthy 12-year-old female subject with no significant past medical history and no concerning family history was seeking cardiac clearance to participate in competitive sports after premature ventricular contractions (1% of total beats) and 1 asymptomatic 4-beat run of monomorphic ventricular tachycardia (VT) at a rate of 185 beats per minute (BPM) were seen on an ambulatory electrocardiogram (ECG) monitor (Figure 1a). After a normal echocardiogram and a resting ECG showing sinus bradycardia at 46 BPM, a GXT utilizing an institutional accelerated Naughton protocol (2 metabolic equivalent increments every 2 minutes) was performed. This showed a limited peak oxygen uptake (VO2 max was 64% of predicted) and limited heart rate response (maximal heart rate 148 BPM, 74% of predicted) despite a near-maximal effort (respiratory exchange ratio of 1.1). Peak exercise occurred at 3 mph with a 12.5% incline. The rhythm remained sinus throughout except for a 4-beat run of wide complex rhythm fusing with sinus at a rate just slightly faster than the underlying sinus rate, and occasional single premature ventricular complexes near peak exercise (Figure 1b).

The following day a HIXT was performed. After a warmup period of 3 minutes at 2.5 mph, speed was abruptly increased to 5 mph with no incline. Frequent premature ventricular complexes developed, followed by polymorphic VT at 160 BPM (Figure 1c). The diagnosis of catecholaminergic polymorphic VT (CPVT) was strongly suspected and genetic testing ultimately confirmed the diagnosis, revealing a pathologic de novo mutation in *RYR2 gene*.

KEYWORDS Arrhythmia; Exercise; Exercise stress test; High-intensity exercise test; Pediatric
(Heart Rhythm Case Reports 2021;7:549–552)

Funding: No funding was needed for this study. Conflict of Interest: The authors have no conflicts to disclose. **Address reprint requests and correspondence:** Dr Ezequiel Sagray, Gonda 6335, Mayo Clinic, 200 First St – SW, Rochester, MN 55905. E-mail address: Sagray.Ezequiel@mayo.edu.

https://doi.org/10.1016/j.hrcr.2021.05.001

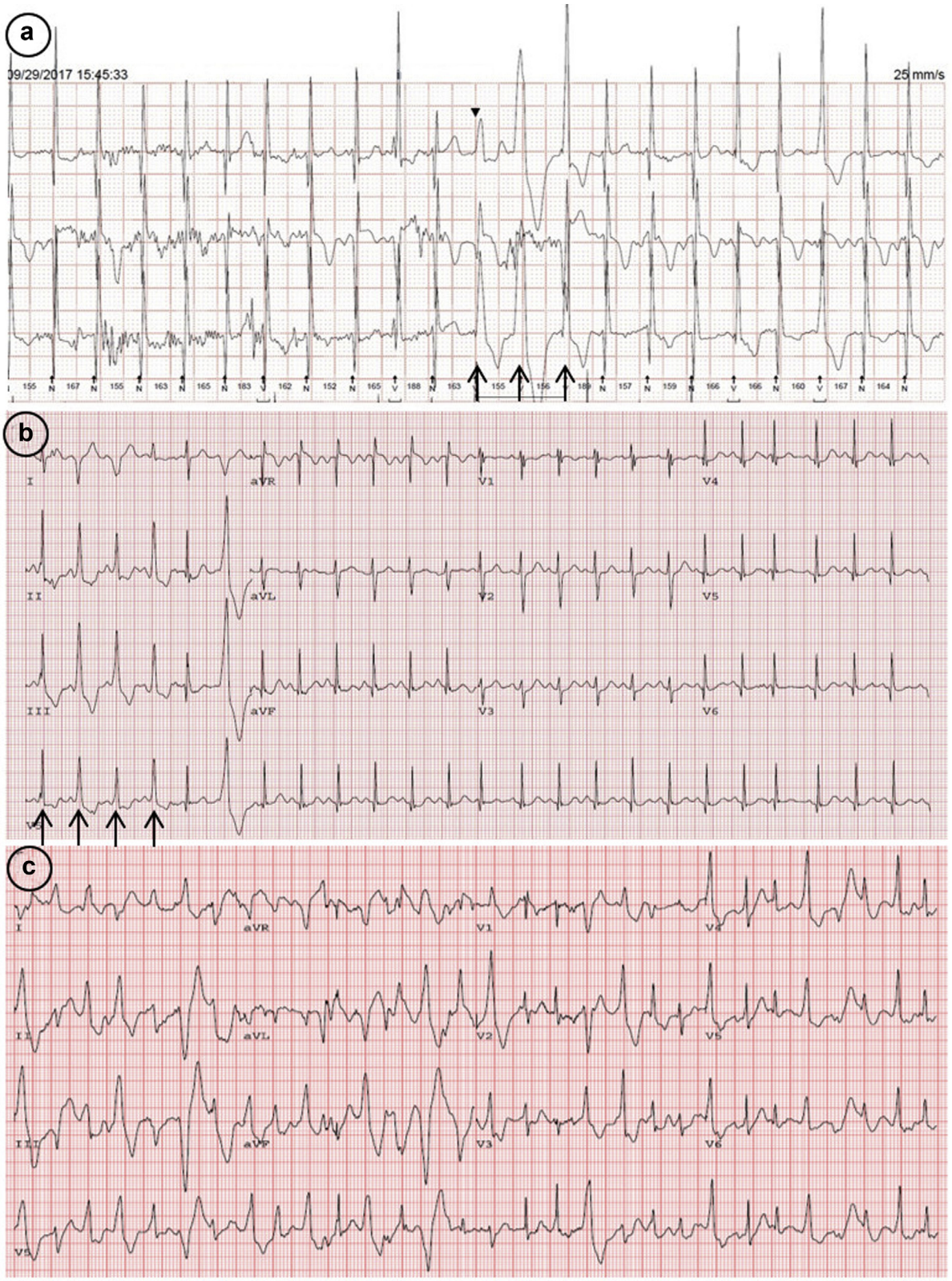

Figure 1 **a:** Tracing from Holter monitor showing asymptomatic 3-beat run of ventricular tachycardia at 159 beats per minute (BPM) (*arrows*). **b:** Electrocardiogram at peak exercise during graded exercise test, with arrows pointing at 4-beat run of wide complex QRS fusing with sinus at 150 BPM. **c:** Polymorphic ventricular tachycardia at 160 BPM during HIXT.

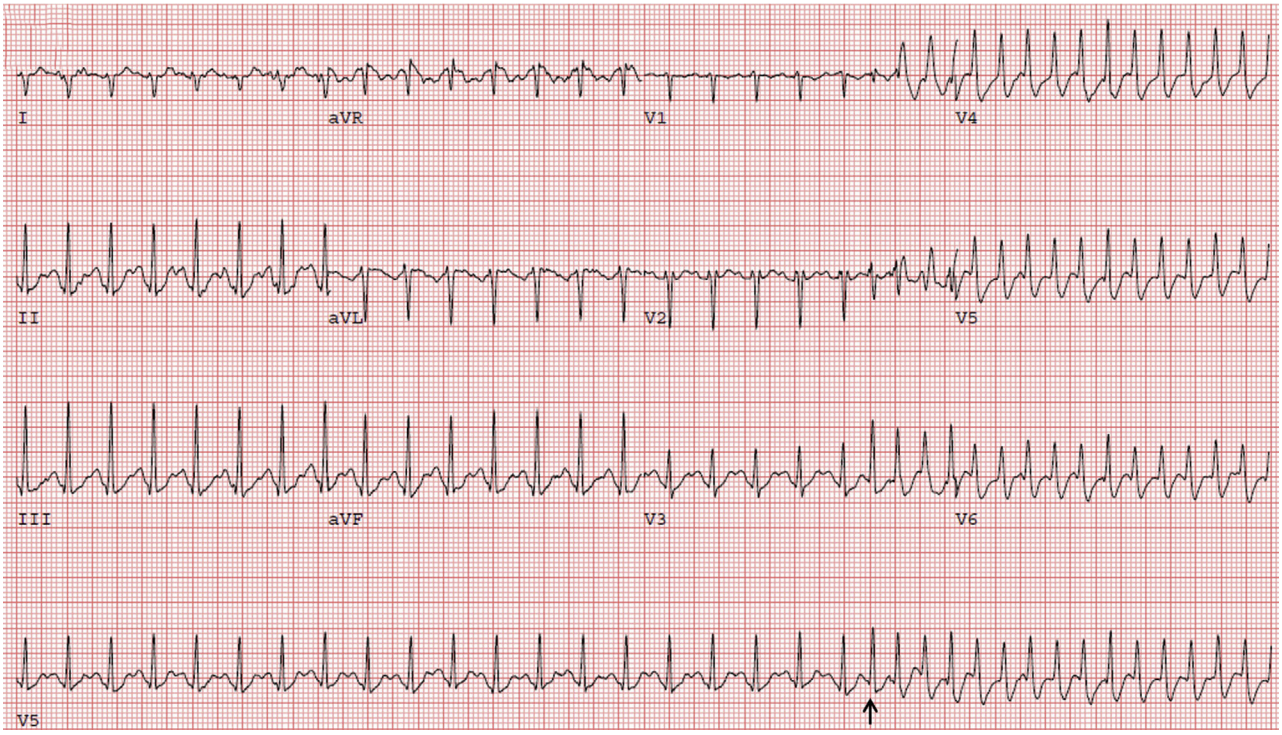

Figure 2 Electrocardiogram obtained during active recovery after high-intensity exercise test, showing sinus rhythm at 167 beats per minute (BPM), followed by narrow QRS tachycardia at 285 BPM (*arrow pointing to onset of tachycardia*).

Case 2

A 20-year-old female professional dancer, with a history of supraventricular tachycardia (SVT) and 2 previous ablations for AV nodal reentrant tachycardia and orthodromic reciprocating tachycardia utilizing a concealed para-Hisian accessory pathway, presented with recurrent palpitations during exercise and a standard GXT was done with a Bruce protocol. This showed an exercise time of 16 minutes with a peak heart rate of 193 BPM (95% of predicted). There were no rhythm abnormalities and this test did not reproduce her symptoms. A third electrophysiology study was performed, and no SVT could be induced despite utilizing no anesthesia and an isoproterenol infusion.

Owing to the persistence of palpitations with exercise despite a negative electrophysiology study, she was evaluated in our institution. She underwent HIXT utilizing a constant 2.5% incline, with 1-minute stages of rapidly increasing speeds up to 8 mph before increasing the incline to 7.5% for the final minute. Maximal heart rate during HIXT protocol was 196 BPM (101% of predicted). Just after reaching peak exercise, within the initial stage of recovery, at a sinus rate of 167 BPM, SVT at 285 BPM developed (Figure 2). The patient ultimately underwent successful cryoablation of a concealed anterolateral accessory pathway.

Discussion

Currently, the most widely used exercise stress test protocols in both children and adults are GXTs, which consist of linear workload increase until reaching the maximal tolerated exertion, allowing for determination of maximal VO2.[1–3] Such GXT protocols were not specifically designed to assess for arrhythmia. In fact, the protocol designed by Bruce and colleagues[4] in 1973 (*Bruce protocol*) was initially proposed to assess cardiac impairment owing to coronary artery disease in adult patients. Despite its aim, the Bruce protocol (or a variation of it) remains the most commonly used exercise test, and has been validated for pediatric patients.[2,5]

An exercise stress test is often indicated in the evaluation and/or characterization of exercise-induced arrhythmias.[2,3] However, the incidence of arrhythmias in patients undergoing GXT, even when considering patients with exertional symptoms, is very low.[6,7] In this manner, Draper and colleagues[8] described how in patients with exercise-related symptoms and documented SVT or ventricular preexcitation, GXT reproduced tachycardia in only 12% of cases.

It is likely that a GXT may not accurately represent the physiologic cardiovascular and/or metabolic responses during the type of physical exertion that more commonly results in symptoms.[8] This could be particularly true for younger adults who practice predominantly anaerobic sports, or in children, whose physical activity mainly involves short-duration bursts of intense activity, neither of which would be properly represented by GXT protocols.[9,10] Other protocols that better assess anaerobic performance have been proposed, but to our knowledge no HIXT protocol has been specifically designed to assess for exercise-induced arrhythmias.

A HIXT could be superior to a GXT in the evaluation of exercise-related arrhythmias, as it may elicit a higher catecholaminergic state. During physical activity, activation of

the sympathetic efferent and blunted vagal input lead to increased heart rate, altered afterload, and elevated circulating catecholamines, which in turn change the underlying electrophysiological properties of the heart.[9] In this setting, ventricular and atrial tachyarrhythmias can occur,[6,7] caused by adrenergic-induced enhanced automaticity, reentry, triggered activity, or critically timed premature ventricular/atrial beats, either alone or in combination.[8,11–13] Inherited conditions such as long QT syndrome, CPVT, and arrhythmogenic right ventricular cardiomyopathy may also predispose to exercise-induced tachyarrhythmias.[8,14] Furthermore, in patients with underlying accessory pathways and/or dual AV node physiology, increased catecholamines can facilitate SVT by shortening the refractory period of an accessory pathway and enhancing AV node conduction.[12] However, the degree of sympathetic activation during exercise is not uniform, but is rather influenced by several factors. Exercise intensity is the primary determinant of catecholaminergic response to exercise, so that for a given exercise duration, catecholamines exponentially increase with higher intensity, in particular when high intensity is achieved quickly and performed beyond the maximal aerobic power.[15] Other lesser factors are longer duration of exercise, which is associated with continuously increasing catecholamine concentrations if performed at submaximal levels, and prior physical training, with higher adrenaline concentrations in trained vs untrained subjects at the same relative intensity.[15] It is also important to mention that catecholamines continue to rise after cessation of exercise, reaching a peak level within the first minute after exercise termination.[13] These observations support the concept that a HIXT, and most likely a repetitive sprint-based running protocol, tailored to the physical training level of the patient, may be more suitable than GXT in the attempt to reproduce arrhythmias in patients with exercise-related symptoms.

Conclusion

We presented 2 cases in which a HIXT triggered adrenergic-related arrhythmias that were previously unprovoked by a standard GXT. We highlight that for the evaluation of possible exercise- or adrenergic-related arrhythmias, more of a sprint-based HIXT tailored to the physical training level of the subject might be superior to a GXT when trying to reproduce exercise-related symptoms.

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