Do Ventricular Arrhythmias in Athletes Subside Over Time?

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ABSTRACT: **Background:** Sudden death in athletes can occur during sport activities and is presumably related to ventricular arrhythmias.
Objectives: To investigate the long-term follow-up of athletes with ventricular arrhythmias during an exercise test.
Methods: From a database of 56,462 athletes we identified 192 athletes < 35 years old who had ventricular arrhythmias during an exercise test. Ninety athletes had ≥ 3 ventricular premature beats (VPB) (group A) and 102 athletes had ventricular couplets or non-sustained ventricular tachycardia (NSVT) during an exercise test (group B). A control group of 92 athletes without ventricular arrhythmias was randomly selected from the database (group C). Of the 192 athletes 39 returned for a repeat exercise test after a mean follow-up period of 70 ± 25 months and they constitute the study population.
Results: Twelve athletes from group A, 21 from group B and 6 from group C returned for a repeat exercise test. The athletes reached a significantly lower peak heart rate during their follow-up exercise test ($P = 0.001$). More athletes were engaged in competitive sports during their initial exercise test than in the follow-up test ($P = 0.021$). Most of the athletes who had VPB and/or ventricular couplets and/or NSVT during their initial exercise test had far fewer ventricular arrhythmias in the follow-up exercise test ($P = 0.001$).
Conclusions: Athletes engaged in competitive sports are more likely to develop ventricular arrhythmias during exercise. These arrhythmias subside over time when athletes are engaged in non-competitive sports.

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KEY WORDS: arrhythmias, ventricular premature beats (VBP), exercise testing, competitive sports

Sudden death in young athletes has a major impact on the lay and medical communities. Identifying athletes at risk of sudden death remains a major challenge. Ventricular premature beats occur among athletes with the same frequency as in the general population, but they usually disappear with exercise. In contrast, complex ventricular arrhythmias should prompt a search for underlying heart disease. In the majority of cases these arrhythmias are supposedly part of the "athlete's heart syndrome" and do not increase the risk of sudden death in an athlete with an apparently normal heart [1-4]. The data available in the literature deal with ventricular arrhythmias assessed mainly by 24 hour ambulatory electrocardiograms [5,6]. A previous study in this population of athletes showed that VA during exercise were more commonly associated with cardiovascular abnormalities in young competitive athletes [7]. The aim of the current study was to investigate the long-term follow-up of athletes with ventricular arrhythmias by means of an exercise test.

PATIENTS AND METHODS

We reviewed the athletes' records at the Wingate Institute of Sport from January 1995 to August 2007. Athletes were referred by different athletic organizations for preparticipation screening before engagement in sport activities. This was not part of a prospective organized national screening program for athletes.

According to the Israeli guidelines for sports medicine, all athletes should undergo a physical examination before engaging in sports activities prior to each game season. Additionally, each athlete must undergo an exercise test at age 17, 23, 27, 32, 34 and yearly thereafter. Athletes with an abnormal physical examination, an abnormal ECG and/or an abnormal exercise test are referred for further workup as needed.

All the records of the athletes' clinical data in our study were kept in a database maintained by the Wingate Institute. The exercise tests were retrospectively analyzed by an electrophysiologist for the purpose of this study. All VPB, ventricular couplets and runs of non-sustained ventricular tachycardia were counted from the tracings obtained during the exercise test and during the recovery period. (NSVT was defined as ≥ 3 consecutive ventricular beats). The athletes' baseline ECG were analyzed according to the most recent recommendations for interpretation of 12-lead electrocardiogram in athletes [8]. Athletes with VPB only at rest before

VA = ventricular arrhythmias
VPB = ventricular premature beats

Table 1. Classification of sports

	A: Low dynamic component	B: Moderate dynamic component	C: High dynamic component
High static component	Gymnastics, sailing, climbing, water skiing, weight lifting, windsurfing	Body building, wrestling	Boxing, canoeing, cycling, rowing, speed skating, triathlon
Moderate static component	Horse riding, motorcycling	Football, jumping, figure skating, rugby, running, surfing, swimming	Basketball, ice hockey, lacrosse, running (middle distance), swimming, handball
Low static component	Bowling, cricket, golf	Baseball, softball, fencing, table tennis, volleyball	Squash, running (long distance), soccer, tennis

Modified from the 36th Bethesda conference, task force 8 [9]

exercise were excluded from the study. Athletes older than 35 years at their initial exercise test were also excluded from the study in order to decrease the likelihood of enrolling athletes with coronary artery disease.

Each athlete completed a detailed questionnaire and underwent a thorough physical examination by a sports physician. All athletes performed an exercise test adhering to the Astrand protocol (maximal exercise test with change of speed and steepness of the treadmill every minute). At the time of the initial exercise test no athlete was taking a beta-blocker agent or antiarrhythmic drug. Athletes who developed VA during the exercise tests underwent a more thorough cardiovascular workup: Holter monitoring (n=37), echocardiogram (n=182), magnetic resonance imaging (n=3) and electrophysiologic study (n=4).

Table 2. Comparison between the initial and follow-up exercise test

	Study I (Group A+B+C) (N=39)	Study II (Group A+B+C) (N=39)	*P* value
Mean age (yr)	25.2 ± 4.96	31.2 ± 4.97	0.001
Sports class A B C	 7.7% (n=3) 25.6% (n=10) 66.7% (n=26)	 5.1% (n=2) 17.9% (n=7) 76.9% (n=30)	 0.250
Competitive	46.2% (n=18)	20.5% (n=8)	0.021
Hours of training	6.71 ± 5.13	4.81 ± 3.79	0.132
VA ex+recovery			
No arrythmia › 3 VPB Couplets and NSVT	15.4% (n=6) 30.8% (n=12) 53.8% (n=21)	82.1% (n=32) 10.3% (n=4) 7.7% (n=3)	 0.001
Arrhythmia morphology RBBB LBBB	 40% (n=4) 60% (n=6)	 40% (n=4) 60% (n=6)	 1.00
Arrhythmia axis Right Left	 70% (n=7) 30% (n=3)	 80% (n=8) 20% (n=2)	 1.00
Peak HR (bpm)	190.7 ± 9.5	185.4 ± 10.3	0.001
Ventricular tachycardia cycle length (msec)	284.8 ± 69.5	0	
Coupling interval (msec)	313.3 ± 33.3	335.6 ± 63.1	0.063
Abnormal ECG	23.7% (n=9)	23.7% (n=9)	1.00
Abnormal Echo	15.4% (n=2)	15.4% (n=2)	1.00

VPB = ventricular premature beats, VA ex = ventricular arrhythmia during exercise, NSVT = non-sustained ventricular tachycardia, LBBB = left bundle branch block, RBBB = right bundle branch block

The athletes were engaged in different sport disciplines. These activities were divided into three groups: low (class A), moderate (class B), high (class C), according to the task force for the classification of sports [9]. This classification was used to simplify the data analysis [Table 1].

Of the 192 athletes 39 returned for a repeat exercise test after a mean follow-up period of 70 ± 25 months. The athletes were still engaged in athletic activity during the follow-up period. Table 2 shows the different variables in the three groups of athletes during the first and the second exercise test.

STUDY DESIGN

We conducted a matched case-control study that compared the long-term outcomes in athletes who had VPB, ventricular couplets and NSVT during an exercise test with the outcomes in a similar group of athletes who had no VA during an exercise test. The results of the study were published previously [7]. Thirty-nine athletes from the previous study agreed to participate in the present study and had a repeat exercise test. The study design was approved by the review boards of the Wingate Institute and the Assaf Harofeh Medical Center. Written informed consent was obtained from all the athletes.

STATISTICS

Statistical analysis was performed using SPSS version 13 software. Data are expressed as mean ± standard deviation. Differences between means were assessed by paired Student's *t*-test or one-way ANOVA. Differences between proportions were assessed with the Pearson chi-square test, the Fisher exact test, McNemar test or Wilcoxon signed ranks test as appropriate. A two-tailed P value < 0.05 was considered to indicate statistical significance.

RESULTS

A total of 56,462 athletes underwent an exercise test for prepaticipation screening at the Wingate Sports Institute between January 1995 and August 2007. From this database we identified 192 athletes who were less than 35 years old and had VA during an exercise test. Ninety athletes had ≥ 3 VPB

NSVT = non-sustained ventricular tachycardia

(group A) and 102 athletes had VPB and ventricular couplets or NSVT (range 3–30 consecutive beats) during an exercise test (group B). The control group comprised 92 athletes who were randomly selected from the group of athletes who had no VA during their exercise test (group C).

Of the 192 athletes 39 returned for a repeat exercise test after a mean follow-up of 70 ± 25 months [Table 2]. The data show that the athletes reached a significantly lower peak heart rate during their follow-up exercise test ($P = 0.001$). There was no significant difference in the sports class between the two periods in which the exercise tests were performed. More athletes were engaged in competitive sports during their initial exercise test compared to the follow-up test ($P = 0.021$). There was no significant difference in the number of training hours between the period of their first exercise test and the period of the second. Most of the athletes who had VPB and/or ventricular couplets and/or NSVT during their initial exercise test had much fewer ventricular arrhythmias in the follow-up exercise test ($P = 0.001$). In fact, none of the athletes had ventricular couplets or NSVT during the follow-up exercise test. Two athletes from group B who had a full follow-up were taking beta-blockers after their initial exercise test.

DISCUSSION

Sudden death in young and healthy-appearing athletes is a rare event, but its occurrence creates an immense impact on the lay and medical communities [10-14]. According to a study by Corrado et al. [15], sports activity in adolescent and young adults is associated with an approximate threefold greater risk of sudden cardiovascular death. The same investigators showed that there was a decline in sudden cardiovascular death in young competitive athletes following the implementation of preparticipation cardiovascular screening in Italy [15,16].

The mechanism of VA in athletes is unclear [17-20]. Some arrhythmias may be secondary to the high sympathetic tone during exercise, and others to structural heart disease. Since sudden death occurs in most cases during sports activities, what is the significance of VA during a preparticipation screening exercise test in an athlete? Clinicians are faced with the dilemma of considering these arrhythmias as either a benign finding, which is part of the "athlete's heart," or as potentially life threatening. A similar dilemma arises when an athlete's ECG is abnormal. Some of these ECG changes may be part of the "athlete's heart," while some may represent the initial expression of a cardiovascular disease [21].

In the present study, VA during an exercise test occurred in 11% of the athletes (192/1712) who were < 35 years of age. The athletes with the more severe forms of VA were automatically disqualified from competitive athletic activities and, therefore, it is unclear whether disqualification reduced the incidence of cardiovascular events in this group.

Biffi et al. [22] studied 70 trained athletes who had ventricular arrhythmias on a Holter monitor. After a period of 12 to 24 weeks of deconditioning there was a significant decrease in the frequency and complexity of ventricular arrhythmias in the athletes (with and without cardiovascular abnormalities). Their study is different from the present research which assessed arrhythmias using an exercise test. Additionally, the athletes in the present study continued with their training and the lack of competitiveness decreased the number of their arrhythmias.

Our study has several limitations due to the fact that only a small percentage of athletes were engaged in competitive sports. Also, not all athletes had an echocardiogram, and athletes with VA were more likely to have a workup. It is possible that disqualification from intensive training and competition could have favorably influenced the outcome and prevented cardiac events in the athletes with severe forms of VA. Therefore, the risk of engaging in competitive sports with such arrhythmias cannot be assessed from our data.

In conclusion, athletes engaged in competitive sports are more likely to develop ventricular arrhythmias during exercise. These arrhythmias subside over time when athletes are engaged in non-competitive sports, despite the fact that they continue with their athletic activities.

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Capsule

Efficacy of remission-induction regimens for ANCA-associated vasculitis

The 18 month efficacy of a single course of rituximab as compared with conventional immunosuppression with cyclophosphamide followed by azathioprine in patients with severe (organ-threatening) antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis is unknown. Specks and team enrolled 197 patients. As reported previously, 64% of the patients in the rituximab group, as compared with 53% of the patients in the cyclophosphamide-azathioprine group, had a complete remission by 6 months. At 12 and 18 months, 48% and 39%, respectively, of the patients in the rituximab group had maintained the complete remissions, as compared with 39% and 33%, respectively, in the comparison group. Rituximab met the prespecified criteria for non-inferiority ($P < 0.001$, with a non-inferiority margin of 20%). There was no significant difference between the groups in any efficacy measure, including the duration of complete remission and the frequency or severity of relapses. Among the 101 patients who had relapsing disease at baseline, rituximab was superior to conventional immunosuppression at 6 months ($P = 0.01$) and at 12 months ($P = 0.009$) but not at 18 months ($P = 0.06$), at which time most patients in the rituximab group had reconstituted B cells. There was no significant between-group difference in adverse events. In patients with severe ANCA-associated vasculitis, a single course of rituximab was as effective as continuous conventional immunosuppressive therapy for the induction and maintenance of remissions over the course of 18 months.

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Capsule

Model therapies for cancer

If cellular signaling pathways were discrete and linear, controlling signals gone awry – like those from growth-promoting receptor tyrosine kinases often linked to cancer – would be straightforward. But these pathways form entangled and dynamic networks, and inhibiting signal transmission at one node, although successful in the short term, is often thwarted by regulatory mechanisms that keep cells healthy by rendering them robust to perturbations. Two groups have used a combination of mathematical modeling and experiments to identify strategies that may more effectively fight excess signaling by the ErbB family of receptors, which is associated with breast cancer. Kirouac et al. used their model to search for combinations of two or three inhibitors that would overcome adaptive feedback and validated these effects in cell and animal models of cancer. Meyer et al. used a model, data from public databases, and their own experiments to identify a second receptor, AXL, which allowed cancer cells to resist the effects of ErbB receptor inhibitors. In this scenario, ligand-independent activating interactions between receptors of the ErbB family and AXL appeared to be crucial, suggesting that reducing receptor number or activity is more likely to be effective than treatments that target ligand-induced activation of the receptors.

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