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Aerobic Fitness and Risk of Ventricular Arrhythmia Following Physical Exertion

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Abstract

Background—Brief episodes of physical exertion are associated with an immediately higher risk of cardiovascular events. Prior studies on the risk of ventricular arrhythmia (VA) shortly after exertion have not assessed if this risk differs by level of aerobic fitness or sedentary behaviour. Therefore, we conducted a prospective cohort study of patients with implantable cardioverter-defibrillators (ICD) with a nested case-crossover analysis to examine the risk of VA shortly after exertion and whether this risk is modified by aerobic fitness and sedentary behaviour.

Methods—97 consecutive patients were recruited at the time of ICD implant and 30 confirmed events occurred among patients who completed interviews about physical exertion preceding ICD

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therapy. We compared the frequency of exertion within an hour of ICD discharge to each patient's usual frequency of exertion reported at the time of ICD implant.

Results—Within an hour of episodes of exertion, the risk of VA was 5.3 (95% CI 2.7 – 10.6) times greater compared to periods of rest. The association was higher among patients with aerobic fitness below the median (RR[relative risk]=17.5, 95% CI 5.2 – 58.5) than for patients with aerobic fitness above the median (RR=1.2, 95% CI 0.4 – 4.2, p-homogeneity = 0.002) and higher among patients who were sedentary (RR=52.8, 95% CI 10.1 – 277) compared to individuals who were not sedentary (RR=3.2, 95% CI 1.3 – 7.6, p-homogeneity=0.0002).

Conclusions—Within one hour of episodes of exertion, there is an elevated risk of VA, especially among individuals with lower levels of aerobic fitness and with sedentary behaviour.

Introduction

There is consistent evidence that discrete episodes of physical exertion are associated with a transient rise in the risk of cardiovascular events, including myocardial infarction and stroke.^{1,2} Prior studies have described this association with ventricular arrhythmia, but have not examined if this risk varies by level of aerobic fitness or sedentary behaviour.

Although appropriate anti-tachycardia pacing (ATP) and shocks delivered by implantable cardioverter-defibrillators (ICD) may be life-saving, ICD therapy can be associated with psychological distress and reduced quality of life.^{3, 4} Reducing sedentary behaviour is important for healthy aging in older adults,⁵ but patients with ICDs commonly report concerns that physical exertion will elicit a shock and may therefore abstain from or engage in lower levels of physical activity.⁶

In this study, we evaluated whether there is a higher risk of ventricular arrhythmia during and shortly after episodes of physical exertion compared to rest. We hypothesized that lower levels of aerobic fitness, measured by peak VO₂, and sedentary behaviour would be associated with a higher risk of ventricular arrhythmia following isolated bouts of physical exertion.

Methods

Study population

The MOVE-IT study is a prospective cohort of 97 consecutive ICD patients recruited at the time of implant at the London Health Sciences Centre in London, Ontario, Canada from May 2008 to July 2012 and followed until January 2015. Patients with ischemic or dilated cardiomyopathy received Medtronic™ ICDs (St. Paul, MN) for primary or secondary prevention based on standard criteria.⁷ Patients were ineligible for the study if they met any of the following criteria: < 18 years of age, comorbid non-cardiac condition associated with anticipated survival < 2 years, or physical limitations precluding moderate exercise. The study protocol was approved by the Health Sciences Research Ethics Board (REB) and all patients provided informed consent. Thirty therapies (ATP or shock) among 22 patients were delivered for symptomatic ventricular arrhythmias, which make up the sample for analysis.

Study design

The case-crossover design was selected to examine the transient effect of an intermittent exposure on events with acute onset.⁸ Rather than comparing different people at the same time, the case-crossover design compares the same person at different times. As a result, there is no confounding by fixed or slowly varying characteristics such as sex, age, and prior medical history. This design involves collecting information on exposure (e.g. physical exertion) immediately preceding the event (e.g. ventricular arrhythmia) and comparing this with the expected frequency of exposure over a similar time period based on the study patient's habitual pattern.

Physical exertion

At the initial study visit, patients estimated their average frequency and duration of light, moderate, and vigorous exertion activities over the last 6 months using the 15-point (scores ranging from 6–20) visual analogue Borg scale⁹ to gauge exertion intensity. Examples of exertion were provided for each category such as light gardening, brisk walking, and shoveling, which are associated with light, moderate, and vigorous exertion respectively. Patients who reported no moderate to vigorous exertion in the past 6 months were classified as sedentary and patients who reported any moderate to vigorous exertion were deemed not sedentary. Information on timing of physical exertion and exposure to other possible behavioural precursors was also collected.

Patients who experienced symptomatic ventricular arrhythmia completed a semi-structured questionnaire within 72 hours of device therapy by telephone or at the clinic. Patients reported the last time prior to device discharge that they had engaged in light, moderate, and vigorous exertion with the following response options: never, at the time of therapy, 1/2 hour before, 1 hour before, 2 hours before, 3–6 hours before, 6–24 hours before, 1–2 days before, 3–4 days before, or 5 days before. Patients described their specific activity at the time of and immediately preceding ICD therapy, and their symptoms surrounding the event as well. Information on other potential triggers was also collected from the questionnaire and information on age, medical history, and medications was abstracted from medical records.

Cardiopulmonary exercise stress test

A modified Bruce protocol¹⁰ was conducted 2 weeks after ICD implant to measure peak VO_2 . An initial 3 minute stage of 1.7 mph and 0% gradient was followed by 3 minute stages as follows: 1.7 mph at 5% grade, 1.7 mph at 10% grade, 2.5 mph and 12% grade, 3.4 mph and 14% grade, 4.2 mph and 16% grade, 5 mph and 18% grade. VO_2 was measured continuously throughout the treadmill test using computerized online rapid gas analyzers for oxygen and carbon dioxide¹¹ of the VmaxTM Encore Metabolic Cart (CareFusion, San Diego, CA). Peak VO_2 was the VO_2 measured at peak exercise. The treadmill test was performed adhering to accepted standards,¹² with continuous 12 lead ECG monitoring and recordings at rest prior to exercise, at least every 3 minutes during exercise, peak exercise, and at 1-minute intervals for 6 minutes during recovery. Symptoms of chest pain, leg fatigue, and dyspnea were quantified using the Borg Scale. The exercise test was terminated when the subject could not continue due to symptoms (such as fatigue, dyspnea or chest pain) or if it was deemed medically necessary due to any of the following clinical findings: > 2 mm of

horizontal or downsloping ST segment depression; persistent 10 mm Hg decline in systolic blood pressure (SBP); a hypertensive (SBP > 280 mm Hg, diastolic blood pressure > 120 mm Hg) blood pressure response; or the development of significant arrhythmias. Written informed consent was obtained from each patient prior to exercise testing.

ATP or shock

All ICDs were programmed in a standard manner, detecting heart rates 188bpm or faster. Rates between 188–250bpm were considered ‘fast ventricular tachycardia’ and treated with one burst of 8 paced beats at 84% the cycle length of the tachycardia, followed by up to five 35J shocks. Rates faster than 250bpm were considered ‘ventricular fibrillation’ and treated with burst pacing during charge, followed by delivery of up to six 35J shocks. Interrogation of the ICD provides a summary of detected arrhythmias; date, time, duration, therapies, and rhythm prior to onset are stored in the device memory. Electrograms were also available for each episode. The lead investigator (LJG) reviewed all stored electrograms to confirm included events.

Statistical analysis

In the case-crossover design, data are stratified on each individual event.^{8, 13} In each stratum, the patient’s exposure within an hour of the event (hazard period) is compared to their expected frequency of exposure in a random hour based on their usual exposure time. We multiplied the usual frequency of activity by the usual duration of activity to calculate annual exposure time and we subtracted this value from total hours in a year to calculate annual non-exposure time. Using methods for sparse data,¹⁴ we calculated the Mantel-Haenszel incidence rate ratio (RR) for person-time and 95% confidence intervals comparing the observed exposure in the hazard period to the expected frequency of exposure. We evaluated whether this association was different between people above and below the median level of peak VO₂ in this sample and between individuals who were and were not sedentary. We compared these subgroups using a Wald χ^2 test of homogeneity.¹⁴

Results

A total of 30 appropriate therapies occurred among 22 patients (20 men, 2 women). Six (20%) were ventricular tachycardia, 12 (40%) were fast ventricular tachycardia, and 12 (40%) were ventricular fibrillation. Seven (23%) events were terminated by ATP alone, 12 (40%) by shock alone, and 11 (37%) by shock after ATP. The characteristics of the 22 patients who experienced symptomatic ventricular arrhythmia are presented in Table 1. The mean age of these study patients was 62.2 ± 7.6 . The mean left ventricular ejection fraction was 26.9%, ranging from 15–42%. Twelve patients (55%) had a history of myocardial infarction, 6 patients (27%) had diabetes mellitus, and 21 (96%) were on beta blocker medication. Fourteen (64%) patients received primary prevention ICD, and 8 (36%) received ICD for secondary prevention.

Most ICD therapy (77%) occurred between 6AM and 6PM and an equal proportion of events occurred before and after 12:00PM. Seven (23%) events occurred on Mondays.

Sixteen (53%) therapies were delivered within an hour of physical exertion (14 light or moderate, 2 vigorous), 13 (43%) of which occurred during the episode of physical exertion.

The results of the case-crossover analyses are presented in Table 2. The risk of ventricular arrhythmia within an hour of any exertion was 5.3 (95% CI 2.7 – 10.6) times greater compared to periods of rest. The risk of ventricular arrhythmia was 23.3 (95% CI 5.8 – 91.9) times greater within an hour of vigorous exertion compared to other times. The risk of ventricular arrhythmia within an hour of any exertion was higher among patients with lower levels of aerobic fitness (peak $\text{VO}_2 < 18.2 \text{ mL/kg/min}$) than for patients with higher levels of aerobic fitness ($p\text{-homogeneity}=0.002$). Similarly, this risk was higher among sedentary patients compared to patients who were not sedentary ($p\text{-homogeneity}=0.0002$). The results were not substantially different from sensitivity analyses that were restricted to shock events.

Discussion

In this study, there was a higher risk of ventricular arrhythmia within an hour of exertion compared to periods of rest. This association was stronger for patients below the median peak VO_2 than for patients with peak VO_2 above the median, with otherwise similar baseline characteristics. The association between an episode of exertion and ventricular arrhythmia was also stronger among those who were sedentary compared to those who were not sedentary, suggesting that higher aerobic fitness and habitual physical exertion may lower the risk of ventricular arrhythmia following episodes of exertion.

Our results are consistent with prior research on exertion as an acute trigger of ventricular arrhythmia. Lampert et al.¹⁵ and Fries et al.¹⁶ reported a higher risk of ICD therapy immediately following an episode of exertion compared to other times. Additionally, previous research has shown that the relative risk of myocardial infarction and sudden cardiac death following episodes of physical exertion is higher among people who are sedentary.^{1, 17} This is the first study to show that there is a higher risk of ventricular arrhythmia following episodes of physical exertion among those with lower levels of aerobic fitness and sedentary behaviour. Based on our findings that the immediate risk of ventricular arrhythmia is lower among patients with higher levels of aerobic fitness and those who are not sedentary, it is possible that an exercise regimen with an incremental increase in the intensity of exertion may help to minimize the risk of ventricular arrhythmia associated with isolated episodes of physical exertion by improving aerobic fitness. These improvements can be achieved among patients with ICDs. In a randomized controlled trial (RCT) of 52 men with chronic heart failure who had ICDs, Belardinelli et al.¹⁸ demonstrated that exercise training improved aerobic fitness and quality of life within 8 weeks. In a post-hoc analysis of over 1000 patients with heart failure and ICDs enrolled in an RCT, Piccini et al.¹⁹ found that randomizing sedentary individuals to exercise 3 times a week was not associated with the combined endpoint of appropriate and inappropriate shocks and all-cause mortality. By increasing the frequency of exertion, the time at risk of exertion-induced ventricular arrhythmia would be higher in the intervention group than the control group. Therefore, the fact that there was no difference in risk of ventricular arrhythmia between the two groups may suggest that the exertion regimen improved fitness and thereby attenuated the risk of exertion-induced ventricular arrhythmias. Even habitual activity at low levels of intensity is

associated with a lower baseline risk of cardiovascular events,^{20–22} and it is possible that it also lowers the risk of ventricular arrhythmia from each episode of exertion.

Aerobic exercise is typically performed continuously at low-to-moderate intensity, but recent studies suggest that High Intensity Interval Training (HIIT) may be more effective.²³ In HIIT, short bursts of aerobic exercise at a high intensity are interspersed with rest periods. Studies conducted in patients with heart failure have shown greater improvements in cardiorespiratory fitness among people randomized to HIIT compared to those who performed continuous aerobic exercise. Alternatively, Iellamo et al.²⁴ attributed the larger benefits from HIIT to an uneven comparison in the training load between the exercise routines. In their study of patients with heart failure, they matched training loads for intensity using heart rate and blood lactate levels, and found no difference in cardiorespiratory or metabolic adaptations between HIIT and continuous exercise. HIIT has not been studied in the ICD population and a predisposition for ventricular arrhythmia has been suggested as a contraindication to HIIT.²³ A greater intensity of exertion has previously been associated with a larger relative risk of acute myocardial infarction.²⁵ With the present study in mind, we bring attention to the risk of ventricular arrhythmia associated with exertion, particularly during the early stages of conditioning.

Exercise confers numerous long-term benefits,²⁶ but isolated episodes of exertion are accompanied by transient changes that may induce ventricular arrhythmia.²⁷ Activation of the sympathetic nervous system from exertion leads to several mechanical, metabolic, and electrophysiological changes.²⁸ Increased heart rate, inotropy, blood pressure, and afterload increase myocardial oxygen demand, that may lead to ischemia and in turn precipitate ventricular arrhythmia.²⁷ In addition, changes in electrolytes and pH may potentiate the risk of arrhythmia.²⁸ Elevated levels of circulating catecholamines increase myocardial conduction velocity and membrane refractoriness, that may increase susceptibility to ventricular arrhythmia.²⁷ Further, increased sympathetic activity increases calcium influx that may increase the amplitude of delayed afterpotentials, which can cause triggered automaticity and enhanced automaticity.²⁷ As well, vagally-mediated recovery is typically delayed in patients with low ejection fraction,^{29,29} creating an elevated period of risk longer than the episode of exertion itself. The impact of these changes ultimately varies by individual characteristics; arrhythmic substrate may influence susceptibility to arrhythmia, but participation in habitual physical exertion may attenuate the risk associated with each episode of exertion.

Strengths and limitations

By using each patient as his or her own control, the case-crossover design eliminates between-person confounding by all fixed and slow-varying characteristics – both measured and unmeasured. However, confounding by time of day is possible because ventricular arrhythmias are more likely to occur in the morning, when physical activity may also be more likely. However, the timing of both ventricular arrhythmias and physical activity among MOVE-IT patients were spread across the day. We prospectively collected usual frequency and duration of physical exertion at the initial study visit so that occurrence of symptomatic ventricular arrhythmia could not influence a patient's perspective on their

physical exertion habits. Further, in addition to assessing sedentary behaviour by self-report, we studied the impact of peak VO_2 , an objectively collected measure of aerobic fitness.

This study enrolled a small number of patients who were primarily of older age with depressed left ventricular systolic function, which may limit generalizability of its conclusions. As patients had ischemic or dilated cardiomyopathy, these results do not necessarily apply to other clinical populations (e.g. familial cardiomyopathies). In addition, reported exertion was based on self-report, and is therefore susceptible to recall bias. Patients who reported activity at the time of therapy were classified as active by the ICD's activity sensor, which senses mechanical vibration using a single-axis accelerometer. However, several patients who reported being at rest during therapy were also classified as active by the ICD activity sensor. Although self-reported exertion at the time of ICD therapy may be over-reported or under-reported by some patients, we used this measure because of concerns that the objectively recorded accelerometer data was too sensitive to small movements, does not measure exertion intensity, and only records activity at the time of device discharge.

Conclusions

Within one hour of episodes of exertion, there is an elevated risk of ventricular arrhythmia, especially among individuals with lower levels of aerobic fitness and with sedentary behaviour. Further research is necessary to design activity recommendations that maximize the benefits of habitual physical activity and exercise training while minimizing the risk of ventricular arrhythmia associated with each episode of exertion.

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Table 1

Baseline characteristics for 22 MOVE-IT patients experiencing symptomatic ventricular arrhythmia, mean $\pm$ SD or n (%)

	Full cohort n=22	Aerobic fitness below median [§] n=9	Aerobic fitness above median n=9
Age (years)	62.2 $\pm$ 7.6	60.9 $\pm$ 10.2	63.3 $\pm$ 6.0
Men	20 (91%)	7 (78%)	9 (100%)
Ejection fraction (%) [†]	26.9 $\pm$ 7.3	28.0 $\pm$ 12.5	24.8 $\pm$ 5.3
Blood pressure (mmHg)			
Systolic	116.6 $\pm$ 71.4	105.9 $\pm$ 11.1	115.6 $\pm$ 17.1
Diastolic	71.4 $\pm$ 12.0	65.7 $\pm$ 9.3	73.9 $\pm$ 13.3
Body mass index (kg/m ²)	29.3 $\pm$ 4.9	30.2 $\pm$ 6.3	29.2 $\pm$ 3.9
Peak VO ₂ [‡] (mL/kg/min)	18.73 $\pm$ 5.80	13.9 $\pm$ 2.8	23.5 $\pm$ 3.4
Sedentary behaviour	8 (37%)	5 (55%)	1 (11%)
Indication for ICD			
Primary prevention	14 (64%)	7 (78%)	6 (67%)
Secondary prevention	8 (36%)	2 (22%)	3 (33%)
Cardiovascular history			
Ischemic heart disease	12 (55%)	4 (44%)	5 (56%)
Prior revascularization	7 (32%)	2 (22%)	3 (33%)
Myocardial infarction	12 (55%)	3 (33%)	6 (67%)
Non-Ischemic cardiomyopathy	8 (36%)	4 (44%)	3 (33%)
Congestive heart failure	12 (55%)	6 (67%)	5 (56%)
Valvular heart surgery	3 (14%)	1 (11%)	2 (22%)
Congenital heart surgery	1 (5%)	1 (11%)	0
Other medical history			
Diabetes mellitus	6 (27%)	3 (33%)	3 (33%)
Hypertension	12 (55%)	5 (56%)	5 (56%)
Hyperlipidemia	6 (27%)	3 (33%)	2 (22%)
Cardiac medication history			
Beta blocker	21 (96%)	9 (100%)	8 (89%)
ACE inhibitors	17 (77%)	7 (78%)	6 (67%)
Angiotensin receptor blocker	5 (23%)	2 (22%)	3 (33%)
Diuretic	14 (64%)	7 (78%)	5 (56%)
Digoxin	7 (32%)	4 (44%)	3 (33%)
Calcium channel blocker	2 (9%)	1 (11%)	1 (11%)
Class 1 antiarrhythmic	3 (14%)	1 (11%)	1 (11%)

ICD = implantable cardioverter-defibrillator.

[†] 4 patients did not have information on ejection fraction

[‡] 4 patients did not consent to cardiopulmonary exercise stress test to determine peak VO₂

[§] Median aerobic fitness (peak VO₂) = 18.2 mL/kg/min

Table 2

Relative risk and 95% confidence intervals of symptomatic ventricular arrhythmia within 1 hour of exertion among 22 MOVE-IT patients

	Ventricular arrhythmia within 1 hour of exertion	Patients	Relative risk (95% CI)	P-heterogeneity
Any exertion	16	22	5.3 (2.7 – 10.6)	
Light or moderate exertion	14	22	4.9 (2.5 – 9.7)	
Vigorous exertion	2	22	23.2 (5.8 – 91.9)	
Aerobic fitness (peak VO ₂)				
Above median [†]	3	9	1.2 (0.4 – 4.2)	0.002
Below median	9	9	17.5 (5.2 – 58.5)	
Sedentary behaviour [‡]				
No	10	14	3.2 (1.3 – 7.6)	0.0002
Yes	6	8	52.8 (10.1 – 277)	

CI = Confidence interval

[†]Median aerobic fitness (peak VO₂) = 18.2 mL/kg/min

[‡]At initial assessment, patients who reported no moderate to vigorous exertion in the past 6 months were classified as sedentary and patients who reported any moderate to vigorous exertion were deemed not sedentary