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Retrospective Study

Outcomes after asystole events occurring during wearable defibrillator-cardioverter use

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Abstract**AIM**

To examine whether wearable cardioverter defibrillator (WCD) alarms for asystole improve patient outcomes and survival.

METHODS

All asystole episodes recorded by the WCD in 2013 were retrospectively analyzed from a database of device and medical record documentation and customer call reports. Events were classified as asystole episodes if initial presenting arrhythmia was asystole (< 10 beats/minor \geq 5 s pause). Survival was defined as recovery at the scene or arrival to a medical facility alive, or not requiring immediate medical attention. Episodes occurring in hospitals, nursing homes, or ambulances were considered to be under medical care. Serious asystole episodes were defined as resulting in unconsciousness, hospital transfer, or death.

RESULTS

Of the total 51933 patients having worn the WCD in

2013, there were 257 patients (0.5%) who had asystole episodes and comprised the study cohort. Among the 257 patients (74% male, median age 69 years), there were 264 asystole episodes. Overall patient survival was 42%. Most asystoles were considered "serious" ($n = 201$ in 201 patients, 76%), with a 26% survival rate. All 56 patients with "non-serious" asystole episodes survived. Being under medical care was associated with worse survival of serious asystoles. Among acute survivors, 20% later died during WCD use (a median 4 days post asystole episode). Of the 86 living patients at the end of WCD use period, 48 (56%) received ICD/pacemaker and 17 (20%) improved their condition.

CONCLUSION

Survival rates after asystole in patients with WCD are higher than historically reported survival rates. Those under medical care at time of asystole exhibited lower survival.

Key words: Asystole; Bradycardia; Cardiac arrest; Defibrillator; LifeVest

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Core tip: Survival rates after asystole, including serious episodes, in patients being treated with wearable cardioverter-defibrillators is higher than historically reported survival rates in the emergency medicine literature. Wearable cardioverter-defibrillators may improve outcomes by alarming and alerting bystanders to assist patients with asystole events.

Liang JJ, Bianco NR, Muser D, Enriquez A, Santangeli P, D'Souza BA. Outcomes after asystole events occurring during wearable defibrillator-cardioverter use. *World J Cardiol* 2018; 10(4): 21-25 Available from: URL: <http://www.wjgnet.com/1949-8462/full/v10/i4/21.htm> DOI: <http://dx.doi.org/10.4330/wjc.v10.i4.21>

INTRODUCTION

Survival to hospital discharge for out-of-hospital cardiac arrest (OHCA) victims found to be in bradycardia or asystole is low (2%). The wearable cardioverter-defibrillator (WCD) has been increasingly utilized to detect and treat potentially fatal ventricular arrhythmias in high-risk patients with cardiomyopathy and low left ventricular ejection fraction (LVEF). Most life-threatening arrhythmias recorded by the WCD are ventricular arrhythmias (VA) such as ventricular tachycardia (VT) and ventricular fibrillation (VF). The WCD can deliver treatment shocks to terminate these tachyarrhythmias. However, a significant percentage of recorded episodes with WCD have been asystole or severe bradycardia episodes; 24.5% of SCAs in the study by Chung *et al*^[1]. The WCD does not have

antibradycardia pacing capabilities, but does alarm and instruct bystanders to call for help and perform CPR.

Patients with OHCA due to bradycardia or asystole are less likely than those with VT or VF to arrive to the hospital alive and survive to discharge^[2,3]. Shorter time intervals between collapse to initiation of bystander cardiopulmonary resuscitation (CPR) and notification of emergency medical services (EMS) are associated with improved overall survival as well as neurologically favorable survival^[4-9]. Since the WCD alerts for asystole, it may contribute to improved outcomes in patients who suffer from severe bradycardia or asystolic cardiac arrest by alerting bystanders to perform CPR and contact EMS. We examined the incidence of WCD alerts related to outcomes in patients with asystole and/or severe bradycardia.

MATERIALS AND METHODS

Patient population and definitions

All patients prescribed a WCD between January 1, 2013 and December 31, 2013 were analyzed using a corporate database (ZOLL LifeVest). This database includes indications for WCD prescription, baseline demographics (age and gender), complaints, and all device-recorded events. All patients signed consent to use their data and all data were de-identified.

An "asystole episode" was defined as bradycardia with heart rate < 10 beats/min, or having a pause lasting ≥ 5 s. To identify patients with asystole episodes, the database was retrospectively screened to identify all episodes of primary asystole ECG recordings. Episodes of post-shock asystole or asystole following untreated VT episodes were excluded from the study. All episodes were manually adjudicated to ensure that a true asystole event had occurred. For the purposes of this study, a "serious asystole episode" was defined as any life-threatening asystole episode which either required hospitalization or led to unconsciousness or death. "Acute survival" was defined as recovery at the scene or arrival to a medical facility alive, or not requiring immediate medical attention. For the purposes of this study, asystole episodes occurring in a "health care setting" were defined as any events in a hospital, nursing home, or ambulance. Survival was determined by customer call reports at the end of WCD use, or by a mortality search of the Social Security death index if the customer call report at the end of WCD use did not indicate death (data available to 2/28/2014).

Statistical analysis

Descriptive statistics were utilized to describe this population based on data collected at the time of referral for WCD prescription or during use. All continuous values were reported as mean \pm SD, or median and range for skewed distributions. Categorical values were expressed as absolute numbers and percentages. To test for differences in the proportions

Table 1 Patient demographics at the start of wearable cardioverter defibrillator use

Parameter	All (<i>n</i> = 257)	Not serious (<i>n</i> = 56)	Serious (<i>n</i> = 201)
Age, yr (median, range)	69 (25-90)	69 (25-82)	69 (39-90)
Sex			
Male (%)	191 (74.3)	41 (73.2)	150 (74.6)
Female	65 (25.3)	15 (26.8)	50 (24.9)
NA	1 (0.4)	0 (0)	1 (0.5)
LVEF % (median, range) (<i>n</i> = 241 reported)	25 (10-65)	25 (10-65)	27.5 (10-60)
Primary indication, <i>n</i> (%)			
MI/NICM	198 (77.0)	43 (76.8)	155 (77.1)
ICD Explant	22 (8.6)	6 (10.7)	16 (8.0)
VT/SCA	35 (13.6)	7 (12.5)	28 (13.9)
Genetic risk	1 (0.4)	0 (0)	1 (0.5)
NA	1 (0.4)	0 (0)	1 (0.5)
History of diabetes mellitus			
Yes	128 (49.8)	18 (32.1)	110 (54.7) ^c
No	111 (43.2)	38 (67.9)	73 (36.3)
NA	18 (7.0)	0 (0)	18 (9.0)
History of ESRD/HD			
Yes	34 (13.2)	5 (8.9)	29 (14.4)
No	204 (79.4)	51 (9.1)	153 (76.1)
NA	19 (7.4)	0 (0)	19 (9.5)
History of arrhythmias ¹	237	54	183
Patients reported			
Any arrhythmia listed below	169 (71.3)	41 (75.9)	128 (69.9)
Sustained VT/VF	68 (28.7)	19 (35.2)	49 (26.8)
Bundle branch block	49 (20.7)	18 (33.3) ^b	31 (16.9)
AFib/Aflutter/SVT/AT	98 (41.4)	23 (42.6)	75 (41.0)
Bradycardia/Heart Block/PEA	31 (13.1)	6 (11.1)	25 (13.7)

¹Percentages were calculated based on patients with information. ^b $P < 0.05$ as no serious group compared to serious group using Fisher's exact test, P -value are calculated based on patients with information; ^c $P < 0.001$ as no serious group compared to non-serious group using Fisher's exact test. AFib: Atrial fibrillation; Aflutter: Atrial flutter; SVT: Supraventricular tachycardia; AT: Atrial tachycardia; PEA: Pulseless electrical activity; NA: Not reported.

of clinical variables between serious and non-serious asystole episodes, Fisher's exact test was used. Univariate logistical regression analysis was used to identify potential variables associated with survival of serious asystole episodes, where a P value of 0.05 was considered statistically significant.

RESULTS

Of the total 51933 patients having worn the WCD in 2013, there were 257 patients (0.5%) who had isolated asystole episodes and comprised the study cohort (Supplemental Figure). The cohort wore the WCD for 40.8 total patient-years during which a total of 264 asystole episodes occurred (one asystole episode in 251 patients, 2 asystole episodes in 5 patients, 3 asystole episodes in 1 patient). The cohort was 74% male and had a median age of 69 years. Over three-fourths of WCD prescriptions were for recent myocardial infarction (MI) or non-ischemic cardiomyopathy (NICM). Table 1 summarizes the baseline characteristics. A greater proportion of patients having a serious event had a history of diabetes mellitus ($P < 0.001$), while more patients with non-serious asystole episodes had a history of a bundle branch block ($P < 0.05$).

Overall survival for patients with asystole episodes was 42%. The majority of patients had asystole episodes that were considered serious (201; 78%).

The rate of acute survival in patients with serious asystole episodes was 26%, while all 56 patients with non-serious asystole episodes survived. Further analysis for patients with serious asystole episodes suggested that survival was worse when the location was in a healthcare setting (Supplemental Table).

For the 108 patients that survived the acute event, twenty-two (20%) of them later died (median 4 d post-asystole episode), while 86 (80%) survived post-WCD use. Information regarding reason for WCD discontinuation is shown in Table 2. Overall, 44% of patients were implanted with an ICD or pacemaker a median of four days after the asystole episode.

DISCUSSION

This study examines the outcomes of asystole and severe bradycardia during WCD use among patients who were prescribed the device to prevent sudden death due to ventricular arrhythmias. In this population, asystole episodes were infrequent, occurring in 0.5% of patients treated with WCD during the time period. Over three quarters of these asystole episodes were serious enough to result in unconsciousness, hospitalization, or death. Survival rates after asystole episodes and serious asystole episodes were 44% and 26% respectively. These rates are significantly higher than those reported in the literature for non-shockable cardiac arrest.

Table 2 Wearable cardioverter defibrillator discontinuation among acute survivors

Reason	Patients [<i>n</i> = 108, <i>n</i> (%)]	Days post-asystole (median, range)
Received ICD or pacemaker	48 (44.4)	4 (0-175)
Condition improved	17 (15.7)	39 (3-525)
Condition deteriorated	10 (9.3)	4 (0-44)
Patient decision	5 (4.6)	73 (12-80)
Unknown/other	5 (4.6)	33 (0-96)
Died	22 (20.4)	4 (0-44)
Still wearing	1 (0.9)	NA

Due to the increased incidence of life-threatening ventricular arrhythmias in patients with cardiomyopathy and low ejection fraction, a WCD is often recommended for patients who are not immediate candidates for ICD therapy^[10]. These patients may possess a history of palpitations or syncope which may cause concern for sustained VAs. However, it is important to recognize that in such patients with structural heart disease there is also a high incidence of conduction disease; furthermore, conduction disease may be exacerbated by the concomitant use of medications such as beta-blockers, digoxin, or antiarrhythmic drugs (*i.e.*, amiodarone, sotalol, dofetilide, *etc.*).

The WCD appears to serve as an effective monitoring device for severe bradycardic events. While the WCD has been shown to prevent sudden cardiac death due to VAs in certain patients^[1,11-16], our study suggests that it may also provide an additional benefit in improving outcomes in patients who suffer from bradycardic conditions both in the acute setting as well as long-term by helping to determine which patients qualify for permanent pacemaker devices. Of the 86 patients surviving to WCD discontinuation, 48 (56%) of them were implanted with an ICD or pacemaker, a median of four days after the asystole episode. Although the device does not provide antibradycardia treatment, it does aid patients by alerting bystanders with an audible tone, thus potentially decreasing time to CPR and EMS notification. Shorter time to CPR and EMS arrival have been repeatedly shown to correlate with improved survival and neurologic outcome after cardiac arrests^[8]. Just as pacemakers or rhythm monitors may detect sustained ventricular arrhythmias which would meet indications for ICD implantation or upgrade, the WCD may detect symptomatic bradycardic rhythms which would lead to permanent pacemaker or ICD implantation.

Limitations

This was an observational retrospective study and data was derived from the manufacturer's database. While rhythm strips for each recorded event was adjudicated to assure that a bradycardic/asystolic event meeting criteria for device detection had occurred, the clinical details surrounding the asystole episodes for each patient were limited. The WCD database included a

limited amount of patient information, and information regarding patient comorbidities, medical therapy, and outcomes. For example, the fact that the overall survival rates among patients with serious episodes was lower in patients whose event occurred in a location under medical care (*i.e.*, hospital, emergency room, dialysis center, rehabilitation center, or long-term care nursing facility) could be due to the fact that patients already under medical care may have had more comorbidities than those whose serious asystole episode occurred outside of a medical facility. Thus our findings, while interesting, should be considered hypothesis-generating.

In conclusion, while the current indication for WCDs in high-risk patients is to detect and treat VAs, patients with reduced LVEF are also at increased risk of having severe bradycardic events. The WCD may improve survival in patients with severe bradycardic/asystolic episodes by alerting bystanders to notify EMS and to perform early CPR, as well as to detect episodes leading to appropriate permanent device implantation.

ARTICLE HIGHLIGHTS

Research background

Outcomes in patients with asystole and severe bradycardic events is poor. The wearable cardioverter defibrillator (WCD) can deliver shocks to terminate ventricular tachycardia and fibrillation, and also alarms for asystole and severe bradycardia events which can alert bystanders to help.

Research motivation

Minimal data exists on whether WCD improves outcomes and survival in patients with asystole and severe bradycardia events.

Research objectives

This study aimed to examine whether WCD alarms for asystole improve patient outcomes and survival.

Research methods

Retrospective analysis all asystole episodes documented in the WCD registry during the year of 2013 and examination of outcomes and survival.

Research results

There were 264 asystole episodes in 257 patients and 76% of these events were considered "serious". Overall patient survival after asystole or severe bradycardia events was 42%, and survival after "serious" asystole events was 26%. Among acute survivors, 20% later died during WCD use. Of the 86 living patients at the end of WCD use period, 48 (56%) received ICD/pacemaker and 17 (20%) improved their condition.

Research conclusions

While the current indication for WCDs in high-risk patients is to detect and treat ventricular arrhythmias, patients with reduced LVEF are also at increased risk of having severe bradycardic events. The WCD may improve survival in patients with severe bradycardic/asystolic episodes by alerting bystanders to notify emergency medical services and to perform early cardiopulmonary resuscitation, as well as to detect episodes leading to appropriate permanent device implantation.

Research perspectives

Future large prospective studies examining outcomes of WCD for asystole and severe bradycardia events are necessary to confirm a survival benefit with the device.

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Retrospective Study

Preventive fraction of physical fitness on risk factors in cardiac patients: Retrospective epidemiological study

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Abstract**AIM**

To quantify the preventive fraction of physical fitness on the risk factors in patients with cardiovascular diseases (CVDs).

METHODS

A total of 249 subjects (205 men and 44 women) suffering from CVD were categorized into four groups, according to their percentage of physical fitness. We calculated the odds ratio to obtain the preventive fraction in order to evaluate the impact of the physical fitness level on the risk factors (*i.e.*, abdominal obesity, depression, diabetes, dyslipidemia, hypertension, obesity, overweight and smoking).

RESULTS

It is observed that a normal physical fitness level is sufficient to induce a preventive action on abdominal obesity (38%), diabetes (12%), hypertension (33%), obesity (12%) and overweight (11%). Also, the preventive fraction increases with the level of physical fitness, in particular for hypertension (36%) and overweight (16%). A high physical fitness level does not necessarily induce a preventive action in most risk factors, excluding depression.

CONCLUSION

This is the first study which demonstrates that reaching a normal physical fitness level is enough to induce a protection for some risk factors, despite having a CVD.

Key words: Physical fitness; Cardiovascular diseases; Risk factors; Preventive fraction; Epidemiological study

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Core tip: The effect of physical fitness on the risk factors in patients who have developed a cardiovascular disease remains an open question. This retrospective study aims to measure the preventive fraction of the risk factors observed at different level of the physical fitness. Our work provides new insights on the aggregate role of physical fitness in the development of risk factors in patients with cardiovascular diseases. These results may interest the readership and the journal due to its novelty and of its possible therapeutic use.

Caru M, Kern L, Bousquet M, Curnier D. Preventive fraction of physical fitness on risk factors in cardiac patients: Retrospective epidemiological study. *World J Cardiol* 2018; 10(4): 26-34 Available from: URL: <http://www.wjgnet.com/1949-8462/full/v10/i4/26.htm> DOI: <http://dx.doi.org/10.4330/wjc.v10.i4.26>

INTRODUCTION

Cardiovascular diseases (CVDs) remain the main cause of death in the world with about 17.5 million deaths^[1]. Over the past few years, more and more people in the world develop CVDs; the American Heart Association (AHA) estimated that one in three Americans has a cardiac pathology^[2]. As a matter of fact, in 2014, Nichols *et al*^[3] observe that almost half of the deaths in Europe are attributable to CVDs, touching approximately 1.9 million men and 2.2 million women.

The development of different risk factors^[4] (*i.e.*, abdominal obesity, depression, diabetes, dyslipidemia, hypertension, obesity, overweight, smoking) and physical inactivity promote CVDs. Physical inactivity, which is the fourth cardiovascular risk factor, has deleterious effects on general and cardiovascular health^[5]. It is responsible for 5.3 million deaths^[6] and it may be responsible for 12% of the risk factors

of CVDs^[7]. CVDs are usually associated with a high level of risk factors^[8]. Thus, the practice of physical activities allows to decrease the risk of CVDs^[9] and has a protective role against metabolic risk factors^[10]. In point of fact, non limited to CVDs, physical activity can be considered a non-pharmacologic treatment both in human for other diseases such as musculoskeletal diseases^[11,12] and immunology diseases^[13,14].

Cardiac rehabilitation vs a conventional therapy^[15] induces a reduction of 20% to 32% of all-cause mortality^[16]. The goal of cardiac rehabilitation for CVDs is to improve their physical fitness^[17] and to reduce CVDs in accordance with current guidelines^[18]. We know that the level of physical fitness has an impact on mortality^[19] and that the practice of physical activity has benefits on the risk factors after cardiovascular rehabilitation programs^[16]. However, we do not know the preventive action of physical fitness on the risk factors in patients who have developed CVDs.

Consequently, the aims of this work are, on the one hand, to observe the distribution of risk factors according to physical fitness and, on the other hand, to study the impact of physical fitness on the preventive fraction of the risk factors in a population of cardiac subjects. We hypothesize that a normal physical fitness level in CVD patients is enough to induce a preventive action on cardiovascular risk factors.

MATERIALS AND METHODS

Study population

In this retrospective epidemiological study, all data were collected in May, 2008 from subjects with CVDs admitted in a cardiac rehabilitation center. Inclusion criteria were participants with coronary, infarct, heart failure or valvulopathy, and the exclusion criteria were participants under 18 years old and with lung disease as primary pathologies. Informed consent was obtained from all participants, and this investigation was conducted in accordance to the World Medical Association Declaration of Helsinki, and depended on country rules (law n°2004-806; August 9, 2004).

Assessment of the physical fitness

At their admission to the cardiac rehabilitation program, all the subject were evaluated for risk factors and physical fitness. Physical fitness of subjects was evaluated from an exercise stress test on ergocycle, conducted by physicians, physiotherapists and exercise physiologist, in accordance with the current recommendations of AHA^[20]. In order to evaluate the physical fitness of subjects, the maximum oxygen consumption ($\dot{V}\text{O}_{2\text{peak}}$) was calculated using equations published by Wasserman and Hansen normalizing $\dot{V}\text{O}_{2\text{peak}}$ depending age, gender, weight and height^[21,22]. The percentage of physical fitness is the ratio between $\dot{V}\text{O}_{2\text{peak}}$ measured and $\dot{V}\text{O}_{2\text{peak}}$ predicted. It has been calculated using the following

equation: % predicted

$$\text{V}\cdot\text{O}_2\text{peak} = \frac{\text{measured V}\cdot\text{O}_2\text{peak (mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1})}{\text{predicted V}\cdot\text{O}_2\text{peak (mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1})} \times 100$$

Assessment of the risk factors

Cardiovascular risk factors were defined by the following standards^[23,24] at the time of the study and were analysed from recent medical records (less than 2 mo) of patients or evaluated at the entrance on the program. Abdominal obesity was defined if the values of the abdominal circumference were ≥ 102 cm for the male and ≥ 88 cm for the female. Diabetes was defined if a subject had a high fasting glucose (> 126 mg/dL or > 7.0 mmol/L), a high non-fasting glucose (> 198 mg/dL or > 11.0 mmol/L), a high glycated hemoglobin (HbA1C $> 7\%$), a diagnosis of diabetes by a physician, a self-reported use of oral hypoglycemic treatment or insulin. Dyslipidemia was defined if a subject had a high total serum cholesterol level (> 250 mg/dL or > 6.5 mmol/L), a high LDL-cholesterol (> 155 mg/dL or > 4.0 mmol/L), a low HDL-cholesterol (for the male: < 40 mg/dL or < 1.0 mmol/L and for the female: < 48 mg/dL or < 1.2 mmol/L), a self-reported use of a treatment for abnormally high levels of cholesterol or a diagnosis of dyslipidemia by the physician. Hypertension was defined if a subject had a high blood pressure ($\geq 140/90$ mmHg at rest), a self-reported use of treatment for hypertension, or a diagnosis of hypertension by the physician. Overweight was defined if the subject had a body mass index (BMI) between 25 and 30 and obesity was defined if the subject had a BMI upper than 30. Depression was defined by a self-reported use of a treatment or diagnosis of depression by a physician. The risk factor associated with smoking was allocated into two categories. Participants classified as "smokers" had the characteristic of being active smokers, having an almost daily consumption or consuming a cigarette for the last time in the six months before the testing procedure. Participants "non-smokers" had the characteristic of never having smoked or the cessation of cigarette smoking more than six months before the testing procedure.

Preventive fraction

The preventive fraction is a ratio used in epidemiological studies to assess the impact of an exposure factor (physical activity) on a disease (risk factors)^[25,26]. Assuming that the exposure factor (physical activity) is represented by its consequence (physical fitness)^[27]. It is an important evaluation tool, which allows knowing the preventive action of the physical fitness levels on the risk factors studied. The PF is derived from odds ratio (OR), indeed, the OR is a measure of association between the physical fitness level and the risk factors. Thus, the preventive fraction can be calculated when OR is under one, as $\text{PF} = (1 - \text{OR})$. It can then be expressed in percentage with the following equation: $\text{PF} (\%) = (1 - \text{OR}) \times 100$. This provides a percentage of

risk factors reduction in the exposed group that can be attributed to the beneficial exposure of physical fitness level of the subjects^[25].

Statistical analysis

The final data analysis has allowed to obtaining, for each subject, a physical fitness levels in the aim to normalize the data and to obtain a classification by physical fitness levels (*i.e.*, high, normal, low and poor). The higher the percentage was, the higher the physical fitness level was, and inversely. We considered the subjects with a normal physical fitness as being physically active before their CVDs and conversely for the subjects with a poor physical fitness^[28].

Statistical analysis was performed using R (R Foundation for Statistical Computing, Vienna, Austria). Quantitative variables were represented by their mean and median and their dispersion was evaluated by the standard deviation. Qualitative variables were represented by their frequency. To compare two means, a two-tailed Student *t*-test was performed with a significance level of 5%. Comparisons of two percentages were performed through a χ^2 test with a threshold at 5%. The Fisher exact test (performed using univariate analysis) was used when the conditions for applying the χ^2 test were not met. We carried an analysis of variance (ANOVA) at one factor, for the multiple comparisons of the means. The χ^2 tests were applied to contingency tables, comparing multiple categorical variables. The α risk was controlled by Holm method in the analysis of variance and by the Tukey's HSD for the χ^2 tests. The OR, related to the risk factors, were obtained using the logistic regression. The selection of logistic regression models was made by minimizing the Akaike criterion. The PF was obtained from the OR when $\text{OR} < 1$.

RESULTS

Characteristics of all participants ($n = 249$) are shown in Table 1. In each model, the subjects were divided into two groups (Table 2) according to their physical fitness level. This distribution allowed to assigning the subjects in the model^a, from group 1 with a normal physical fitness level ($\geq 80\%$ predicted V·O₂peak) to group 2 with a poor physical fitness level ($< 80\%$ predicted V·O₂peak). In the model^b, the subjects were assigned to a group 1 with the high physical fitness level ($\geq 100\%$ predicted V·O₂peak) to group 2 with the low physical fitness level ($< 100\%$ predicted V·O₂peak). We observed in Figure 1 that subjects with a high physical fitness level were less exposed to different risk factors, compared to those with a low physical fitness level. According to our study design we observed (Table 2) that the V·O₂peak during exercise stress test of the subjects, in the model^a and model^b, was higher for subjects in group 1 than in group 2. The V·O₂peak in the group 1^b was higher than the one in the group 1^a during exercise stress test because, only the subjects

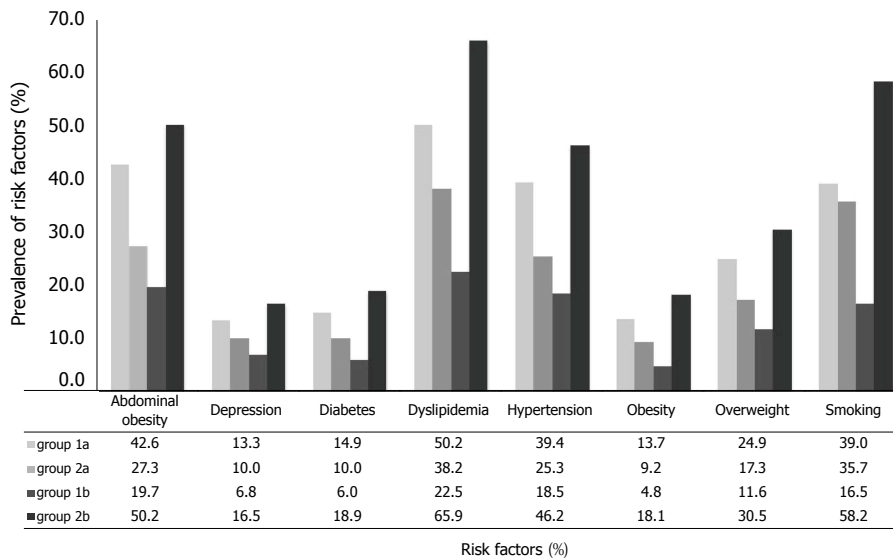


Figure 1 Distribution of the risk factors by the physical fitness level. From left to right for each risk factor: the first column (very clear gray) represents the group 1^a (normal physical fitness), the second column (light gray) represents the group 2^a (poor physical fitness), the third column (dark gray) represents the group 1^b (highest physical fitness) and the fourth column (black) represents the group 2^b (lowest physical fitness).

Table 1 Characteristics of the included subjects (*n* = 249) in this studies *n*%

Variables	mean ± SD
Gender (males/females)	205/44
Age, yr	61.8 ± 11.4
Weight, kg	78.7 ± 15.7
Height, cm	169.9 ± 8.5
Body Mass Index, kg.m ⁻²	27.2 ± 4.6
P _{max} during exercise stress test, W	108.6 ± 35.7
P _{max} predicted, W	167.5 ± 48.2
V O ₂ peak during exercise stress test, mL/kg min	22.1 ± 4.8
V O ₂ peak predicted	25.2 ± 5.1
METs peak during exercise stress test, mL/kg min	6.3 ± 1.4
Physical fitness, % predicted V O ₂ peak	89.6 ± 20.5
Risk factors	Prevalence, <i>n</i> (%)
Abdominal obesity	174 (69.9)
Depression	58 (23.3)
Diabetes	62 (24.9)
Dyslipidemia	220 (88.4)
Hypertension	161 (64.7)
Obesity	57 (22.9)
Overweight	105 (42.2)
Smoking	186 (74.7)

P_{max}: Maximal power; V O₂: Maximal oxygen consumption; METs: Metabolic equivalents of task.

which had the highest physical fitness were assigned to the group 1^b. In Group 1^a, the subjects had a V·O₂peak during exercise stress test (23.6 ± 5.1 mL·kg⁻¹·min⁻¹) similar to the V·O₂peak predicted (23.4 ± 4.7 mL·kg⁻¹·min⁻¹), whereas in group 1^b, the V·O₂peak during exercise stress test (25.5 ± 5.5 mL·kg⁻¹·min⁻¹) is much higher than the V·O₂peak predicted (22.4 ± 4.6 mL·kg⁻¹·min⁻¹). In group 2^a and group 2^b, V·O₂peak during exercise stress test (20.0 ± 3.5 mL·kg⁻¹·min⁻¹ and 20.9 ± 4.0 mL·kg⁻¹·min⁻¹, respectively) were lower than V·O₂peak predicted (27.8 ± 4.6 mL·kg⁻¹·min⁻¹ and

26.2 ± 4.9 mL·kg⁻¹·min⁻¹, respectively).

The OR was calculated to obtain the PF of the cardiovascular risk factors in order to assess the effect of the exposure factor. Upon univariate analysis (Table 3), in the model^a, PF was calculated for age (6%), abdominal obesity (38%), diabetes (12%), hypertension (33%), obesity (12%) and overweight (11%). In the model^b, PF was calculated for the age (5%), abdominal obesity (37%), depression (22%), hypertension (36%) and overweight (16%). In both models, PF was not calculated for dyslipidemia and smoking because OR > 1.

DISCUSSION

Our main results validate the hypothesis whereby a normal physical fitness level provides a preventive action on cardiovascular risk factors despite people having already developed a CVD. The findings add new insights with previously published reports^[29] and allow the identification of a prophylactic effect of the physical fitness on cardiovascular risk factors studied despite presenting the diagnosis of heart disease.

The presence of risk factors for the patient does not necessarily imply a direct relationship between cause and effect because some people could have a CVD inheritance. Moreover, it is not necessary to have risk factors to develop a CVD, the genetic heritage of the person might be the cause^[30]. The overall percentage of the risk factors prevalence seems to be higher in our population compared to previous studies, nevertheless, it follows the trend according to the exposure of patients to different cardiovascular risk factors^[31,32]. Several epidemiological studies demonstrated that low physical activity levels are associated with a higher

Table 2 Characteristics of subjects for each of models

Variables (units)	Model ^a		P value	Model ^b		P value
	Group 1 ^a (n = 143)	Group 2 ^a (n = 106)		Group 1 ^b (n = 64)	Group 2 ^b (n = 185)	
Gender (males/females)	101/42	104/2	-	39 / 25	166 / 19	-
Age (yr)	64.7 ± 11.0	58.0 ± 10.8	0.001	66.2 ± 11.7	60.3 ± 10.9	0.001
Weight (kg)	77.2 ± 14.8	80.7 ± 16.6	0.090	75.0 ± 15.1	80.0 ± 15.7	0.030
Height (cm)	167.8 ± 9.1	172.7 ± 6.8	0.001	166.3 ± 8.1	171.2 ± 8.3	0.001
Body Mass Index (kg/m ²)	27.8 ± 4.2	27.0 ± 5.0	0.500	27.0 ± 4.3	27.2 ± 4.7	0.700
P _{max} during exercise stress test (W)	118.0 ± 39.1	95.8 ± 25.7	0.001	128.3 ± 45.0	101.7 ± 29.1	0.001
P _{max} predicted (W)	150.8 ± 46.9	190.0 ± 40.3	0.001	139.5 ± 49.9	177.2 ± 43.7	0.001
V O ₂ peak during exercise stress test (mL/kg/min)	23.6 ± 5.1	20.0 ± 3.5	0.001	25.5 ± 5.5	20.9 ± 4.0	0.001
V O ₂ peak predicted (mL/kg/min)	23.4 ± 4.7	27.8 ± 4.6	0.001	22.4 ± 4.6	26.2 ± 4.9	0.001
METs peak during exercise stress test	6.8 ± 1.5	5.7 ± 1.0	0.001	7.3 ± 1.6	6.0 ± 1.1	0.001
Physical fitness (% predicted V O ₂ peak)	102.2 ± 17.6	72.6 ± 8.1	0.001	115.2 ± 19.2	80.8 ± 11.7	0.001

Model^a-group 1^a: Patients with a normal physical fitness level; Model^a-group 2^a: Patients with a poor physical fitness level; Model^b-group 1^b: Patients with a high physical fitness level; Model^b-group 2^b: Patients with a low physical fitness level. P_{max}: Maximal power; V O₂: Maximal oxygen consumption; METs: Metabolic equivalents of task.

Table 3 Measures-univariate and multivariate on subjects with cardiovascular risk factors

Variables	Univariate analysis			Multivariate analysis		
	OR (95%CI)	P value	PF (95%CI)	OR (95%CI)	P value	PF (95%CI)
Model ^a						
Age	0.94 (0.92; 0.96)	< 0.001	0.06 (0.04; 0.08)	0.93 (0.90; 0.96)	< 0.001	0.07 (0.04; 0.10)
Abdominal obesity	0.62 (0.36; 1.07)	0.09	0.38 (-0.07; 0.64)	-		
Depression	1.02 (0.56; 1.85)	0.92	-	-		
Diabetes	0.88 (0.48; 1.57)	0.68	0.12 (-0.57; 0.52)	-		
Dyslipidemia	1.24 (0.56; 2.83)	0.59	-	-		
Hypertension	0.67 (0.39; 1.13)	0.13	0.33 (-0.13; 0.61)	-		
Obesity	0.88 (0.48; 1.61)	0.70	0.12 (-0.60; 0.52)	-		
Overweight	0.89 (0.53; 1.48)	0.65	0.11 (-0.48; 0.47)	0.64 (0.35; 1.14)	0.130	0.36 (-0.14; 0.65)
Smoking	2.48 (1.34; 4.74)	< 0.010	-	-		
Model ^b						
Age	0.95 (0.92; 0.97)	< 0.001	0.05 (0.03; 0.08)	0.95 (0.92; 0.98)	0.001	0.05 (0.02; 0.08)
Abdominal obesity	0.63 (0.32; 1.20)	0.17	0.37 (-0.20; 0.68)	-		
Depression	0.78 (0.41; 1.54)	0.47	0.22 (-0.54; 0.59)	-		
Diabetes	1.11 (0.58; 2.22)	0.75	-	-		
Dyslipidemia	1.11 (0.44; 2.57)	0.80	-	-		
Hypertension	0.64 (0.33; 1.18)	0.16	0.36 (-0.18; 0.67)	-		
Obesity	1.39 (0.70; 2.94)	0.36	-	3.40 (1.06; 11.83)	0.040	-2.4 (-10.83; -0.06)
Overweight	0.84 (0.47; 1.49)	0.55	0.16 (-0.49; 0.53)	-		
Smoking	2.03 (1.08; 3.76)	0.02	-	-		

-: This variable was eliminated from the selection of logistic regression models in minimizing the Akaike criterion. Model^a: Patients with a normal physical fitness level; Model^b: Patients with a high physical fitness level; OR: Odds ratio; PF: Preventive fraction.

prevalence of most CVDs risk factors^[29]. Our group 2^b, composed of patients with the lowest physical fitness level, confirms this observation. It is shown that a low physical fitness level is associated with an important risk factor and with increased mortality for both men and women^[33]. The physical fitness level declines with the age, even more, if a regular physical activity is not preserved. Contrary to what is observed in the literature^[34], our study show that the subjects in the group 1^a with a normal physical fitness level (20% below the predicted) and in the group 1^b with a high physical fitness level were the oldest (64.7 ± 11.0 years old and 66.2 ± 11.7 years old, respectively).

The subjects physically or professionally active before their cardiac events, no matter their age,

will be able to have a better physical fitness level than those who were physically inactive. Within this context, our study observed positive results for the patients admitted into a cardiac rehabilitation center. Indeed, getting a physical fitness level close to the baseline level (even 20% below the predicted fitness) induces a preventive action on the cardiovascular risk factors. In the group 1^a, we observed a positive action of the physical fitness level on five of our eight risk factors studied (*i.e.*, abdominal obesity, diabetes, hypertension, obesity and overweight). A correlation between physical activity and physical fitness level demonstrates that it is the practice of physical activity that could reduce many risk factors^[33]. Kodama *et al.*^[35] have confirmed that the physical fitness level is associated

with a weakening in CVDs. The subjects who are exposed to a high physical fitness level (group 1^b) are susceptible to get a higher preventive action on hypertension than group 1^a (PF = 36% and PF = 33%, respectively). It is argued that improving physical fitness, through the physical activity, has an effect on hypertension by reducing blood pressure^[36]. Physical activity is also important in the fight against the weight gain and the development of fat and abdominal obesity which are favorable to the appearance of hypertension^[37]. Thus, our results show a preventive action of the normal and high physical fitness level groups on the abdominal obesity. This preventive action is in favor of the group 1^a (PF = 38%), comparatively to the group 1^b (PF = 37%). In a recent study, it has been shown that the excess of abdominal fat would be associated with a higher risk of cardiovascular mortality than overweight or obesity^[38]. Physical activity is known to decrease the risk of cardiovascular mortality in patients with obesity^[39]. In our study, it is clearly identified that a normal physical fitness level induces a preventive action on the obesity (PF = 12%) since the group 1^b has not observed a benefit action of the exposure factor on this risk factor. We observe the same result for diabetes risk factor. Indeed, the group with a normal physical fitness level induces a preventive action for diabetes (PF = 12%), which was not observed for the subjects with a high physical fitness level. Reaching moderate or high physical activity levels reduce the risk of CVDs mortality in type 2 diabetics patients^[40] by improving glucose metabolism and insulin sensitivity^[37]. A moderate exercise program can also reduce the diabetes risk and percentage of body fat^[41]. It is especially important in the prevention of cardiovascular risk factors because the subjects who suffer overweight have a high risk of developing diabetes^[42]. Our results demonstrate that the subjects who have a normal physical fitness level induce a preventive action of 11% on the overweight risk factor. A 5% difference, in favor of group 1^b with a high physical fitness level (PF = 16%), was observed for overweight. The logistic regression models in the multivariate analysis have shown that the group 1^a, composed of subjects with a normal physical fitness level, induced a preventive action of 36% on the overweight. These findings strengthen our hypothesis and highlight the importance of having a normal physical fitness level, without necessarily being a patient with a high physical fitness level.

Yet, only the group 1^b with a high physical fitness level induce a preventive action on the depression risk factor (PF = 22%). We have not observed a preventive action on the depression in the patients with a normal physical fitness level. The subjects with a low self-reported physical activity levels are associated with an increased prevalence of depressive symptoms^[43]. The patients with CVDs and with depression are likely to have recurrent heart problems^[44,45]. According to Gary *et al*^[46] the patients who are facing a cardiac

complication recognize a depressive episode afterward. Furthermore, our results demonstrate the importance of having a high physical fitness level, before and after a cardiac event, to induce a preventive action on the depression. Finally, our findings have not observed a preventive action for smoking, this is consistent with the statement of Marín Armero *et al*^[47] who suggest that the best way to stop smoking is to combine smoking cessation with a psychological program. Smoking may induce changes in the serum lipoprotein profiles causing an increase in total cholesterol^[48], which might explain that no positive effect of the physical fitness levels were observed for dyslipidemia.

This study is based in retrospective data, which may represent some limitations. Retrospective studies have disadvantages because peoples who were responsible for the data collections might have made classification errors or information bias. This is why we have worked closely with the cardiologist of the cardiac rehabilitation center whose data were from. Also, as pharmacological treatments could have been optimized since the data collection it could be argued that results would have been different and that the positive impact of physical training would be attenuated. Over a long period (from 1988 until now), since the firsts meta-analysis by Oldridge *et al*^[49] and O'Connors *et al*^[50] and despite the increasing development of new medication, the result of exercise on mortality reduction in CVDs is quite constant^[16]. The works of Bouchard *et al* shows that a part of physical fitness can be genetically determined and not related to environment (by physical activity practice)^[51]. Finally, treatments were not introduced in the study as recruitment were made from University hospital with patients arriving with optimized treatment so inducing a low deviation between subject, furthermore due to the small number of the subjects for such a study we did not separate the different pathologies in the analysis and consider CVD's as a whole group.

It is established that the exercise capacity is an important prognostic factor in patients with CVD^[28]. There is evidence of an inverse relationship between the physical activity and CVDs; our study reinforces these statements. Regular physical activity is a practice accessible to all patients with CVDs, but it may be difficult to adhere to an aerobic-based exercise program, due to external constraints. Our study suggests that even if the recommendations of ACSM^[52] (allowing to reach 100% of the theoretical physical fitness) are not met, a normal physical fitness level, even 20% below the predicted fitness, is enough to reduce some of the risk factors studied. This is in concordance with the recommendations of European Society of Cardiology^[53] which supports that the subjects with a physical fitness level, even 25% below the predicted fitness, will face long-term health issues. The practice of physical activity should be maintained throughout life to preserve these training effects^[19].

In summary, this study demonstrated that a normal

physical fitness level induces a preventive action for most risk factors studied and that a high level of physical fitness does not necessarily lead to a better preventive fraction. Our work provides new insights on the aggregate role of physical fitness in the development of cardiovascular risk factors.

ARTICLE HIGHLIGHTS

Research background

Cardiovascular diseases (CVDs) remain the main cause of death in the world with about 17.5 million deaths. CVDs are usually associated with a high level of risk factors. The practice of physical activity has benefits on the risk factors, however, we do not know the preventive action of physical fitness on the risk factors in patients who have developed CVDs. Thus, this study aims to quantify the preventive fraction of physical fitness on the risk factors in patients with CVDs.

Research motivation

The effect of physical fitness on the risk factors in patients who have developed a cardiovascular disease remains an open question. Regular physical activity is a practice accessible to all patients with CVDs, but it may be difficult to adhere to an aerobic-based exercise program, due to external constraints.

Research objectives

Quantifying the preventive fraction of physical fitness on the risk factors in patients with CVDs is very important. The aggregate role of physical fitness in the development of cardiovascular risk factors needs to be better documented. Our work provides new insights on this research field.

Research methods

A total of 249 subjects (205 men and 44 women) suffering from a CVD were categorized into four groups, according to their percentage of physical fitness. The physical fitness of subjects was evaluated from an exercise stress test on an ergocycle. We calculated the odds ratio to obtain the preventive fraction in order to evaluate the impact of the physical fitness level on the risk factors (*i.e.*, abdominal obesity, depression, diabetes, dyslipidemia, hypertension, obesity, overweight and smoking). The preventive fraction is a ratio used in epidemiological studies to assess the impact of an exposure factor (physical fitness) on a disease (risk factors). It is an important evaluation tool that allows knowing the preventive action of the physical fitness levels on the risk factors studied.

Research results

It is observed that a normal physical fitness level is sufficient to induce a preventive action on abdominal obesity (38%), diabetes (12%), hypertension (33%), obesity (12%) and overweight (11%). Also, the preventive fraction increases with the level of physical fitness, in particular for hypertension (36%) and overweight (16%). A high physical fitness level does not necessarily induce a preventive action in most risk factors, excluding depression. Our study suggests that even if the recommendations of ACSM (allowing to reach 100% of the theoretical physical fitness) are not met, a normal physical fitness level, even 20% below the predicted fitness, is enough to reduce some of the risk factors studied.

Research conclusions

This study demonstrates that a normal physical fitness level induces a preventive action for most risk factors studied. A high level of physical fitness does not necessarily lead to a better preventive fraction. CVDs remain the main cause of death in the world with about 17.5 million deaths. It is observed that almost half of the deaths in Europe are attributable to CVDs, touching approximately 1.9 million men and 2.2 million women. The development of different risk factors (*i.e.*, abdominal obesity, depression, diabetes, dyslipidemia, hypertension, obesity, overweight, smoking) and physical inactivity promote CVDs. The practice of physical activities allows to decrease the risk of CVDs and has a protective role against metabolic risk factors.

Research perspectives

There is evidence of an inverse relationship between the physical activity and CVDs; our study reinforces these statements. However, it may be difficult to adhere to an aerobic-based exercise program, due to external constraints. Our study suggests that a normal physical fitness level, even 20% below the predicted fitness, is enough to reduce some of the risk factors studied. The practice of physical activity should be maintained throughout life to preserve these training effects. The future research should include the pharmacological treatments.

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