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## Retrospective Study

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

Maxime Caru, Laurence Kern, Marc Bousquet, Daniel Curnier

Maxime Caru, Laurence Kern, Department of Science and Technology of Physical Activities and Sports, University Paris Nanterre, Nanterre 92000, France

Maxime Caru, Daniel Curnier, Department of Kinesiology, University of Montreal, Montreal H2X 0A9, Canada

Marc Bousquet, Clinic of Saint-Orens, Cardiovascular and Pulmonary Rehabilitation Center, Saint-Orens-de-Gameville 31650, France

Daniel Curnier, University of Montreal Hospital Research Center, Montreal H2X 0A9, Canada

ORCID number: Maxime Caru (0000-0003-2904-9185); Laurence Kern (0000-0002-9261-4194); Marc Bousquet (0000-0002-4441-7612); Daniel Curnier (0000-0001-9717-192X).

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**Informed consent statement:** 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<sup>th</sup> 2004). Also, the analysis used clinical data without storage of patient identifiers that were obtained after each patient agreed to treatment by written consent.

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**Correspondence to:** Daniel Curnier, PhD, Professor, Research Scientist, Laboratoire de Physiopathologie de l'EXercice, Department of Kinesiology, University of Montreal, CEPSUM, 2100, boulevard Édouard Montpetit, Montreal H2X 0A9, Canada. [daniel.curnier@umontreal.ca](mailto:daniel.curnier@umontreal.ca)  
Telephone: +1-514-3435942

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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.

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## INTRODUCTION

Cardiovascular diseases (CVDs) remain the main cause of death in the world with about 17.5 million deaths<sup>[1]</sup>. 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<sup>[2]</sup>. As a matter of fact, in 2014, Nichols *et al*<sup>[3]</sup> 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<sup>[4]</sup> (*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<sup>[5]</sup>. It is responsible for 5.3 million deaths<sup>[6]</sup> and it may be responsible for 12% of the risk factors

of CVDs<sup>[7]</sup>. CVDs are usually associated with a high level of risk factors<sup>[8]</sup>. Thus, the practice of physical activities allows to decrease the risk of CVDs<sup>[9]</sup> and has a protective role against metabolic risk factors<sup>[10]</sup>. 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<sup>[11,12]</sup> and immunology diseases<sup>[13,14]</sup>.

Cardiac rehabilitation vs a conventional therapy<sup>[15]</sup> induces a reduction of 20% to 32% of all-cause mortality<sup>[16]</sup>. The goal of cardiac rehabilitation for CVDs is to improve their physical fitness<sup>[17]</sup> and to reduce CVDs in accordance with current guidelines<sup>[18]</sup>. We know that the level of physical fitness has an impact on mortality<sup>[19]</sup> and that the practice of physical activity has benefits on the risk factors after cardiovascular rehabilitation programs<sup>[16]</sup>. 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<sup>[20]</sup>. In order to evaluate the physical fitness of subjects, the maximum oxygen consumption ( $V\cdot O_2\text{peak}$ ) was calculated using equations published by Wasserman and Hansen normalizing  $V\cdot O_2\text{peak}$  depending age, gender, weight and height<sup>[21,22]</sup>. The percentage of physical fitness is the ratio between  $V\cdot O_2\text{peak}$  measured and  $V\cdot O_2\text{peak}$  predicted. It has been calculated using the following

equation: % predicted

$$V \cdot O_2 \text{peak} = \frac{\text{measured } V \cdot O_2 \text{peak (mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1})}{\text{predicted } V \cdot O_2 \text{peak (mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1})} \times 100$$

### Assessment of the risk factors

Cardiovascular risk factors were defined by the following standards<sup>[23,24]</sup> 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  $\geq 102$  cm for the male and  $\geq 88$  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)<sup>[25,26]</sup>. Assuming that the exposure factor (physical activity) is represented by its consequence (physical fitness)<sup>[27]</sup>. 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  $PF = (1-OR)$ . It can then be expressed in percentage with the following equation:  $PF (\%) = (1-OR) \times 100$ . 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<sup>[25]</sup>.

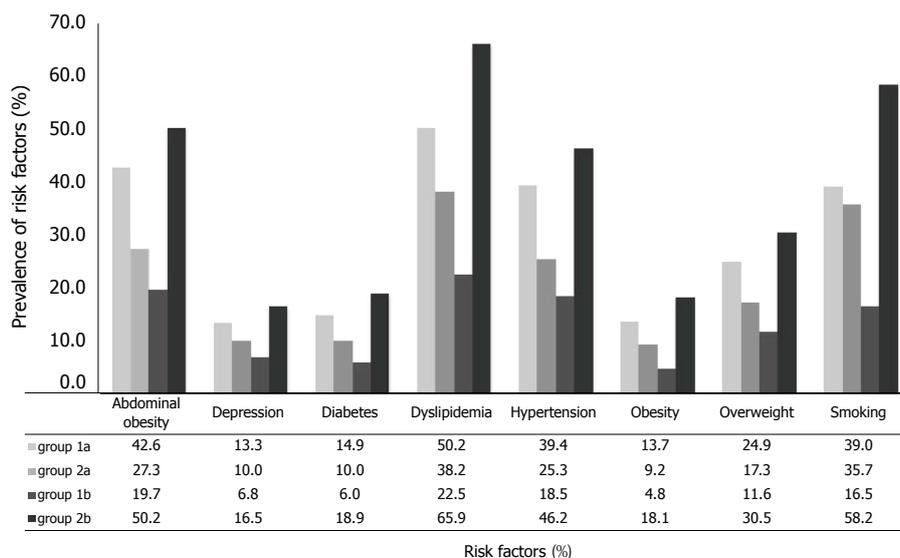
### Statistical analysis

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<sup>[28]</sup>.

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  $\chi^2$  test with a threshold at 5%. The Fisher exact test (performed using univariate analysis) was used when the conditions for applying the  $\chi^2$  test were not met. We carried an analysis of variance (ANOVA) at one factor, for the multiple comparisons of the means. The  $\chi^2$  tests were applied to contingency tables, comparing multiple categorical variables. The  $\alpha$  risk was controlled by Holm method in the analysis of variance and by the Tukey's HSD for the  $\chi^2$  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  $OR < 1$ .

## 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<sup>a</sup>, from group 1 with a normal physical fitness level ( $\geq 80\%$  predicted  $V \cdot O_2 \text{peak}$ ) to group 2 with a poor physical fitness level ( $< 80\%$  predicted  $V \cdot O_2 \text{peak}$ ). In the model<sup>b</sup>, the subjects were assigned to a group 1 with the high physical fitness level ( $\geq 100\%$  predicted  $V \cdot O_2 \text{peak}$ ) to group 2 with the low physical fitness level ( $< 100\%$  predicted  $V \cdot O_2 \text{peak}$ ). 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  $V \cdot O_2 \text{peak}$  during exercise stress test of the subjects, in the model<sup>a</sup> and model<sup>b</sup>, was higher for subjects in group 1 than in group 2. The  $V \cdot O_2 \text{peak}$  in the group 1<sup>b</sup> was higher than the one in the group 1<sup>a</sup> 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<sup>a</sup> (normal physical fitness), the second column (light gray) represents the group 2<sup>a</sup> (poor physical fitness), the third column (dark gray) represents the group 1<sup>b</sup> (highest physical fitness) and the fourth column (black) represents the group 2<sup>b</sup> (lowest physical fitness).

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

Variables	mean $\pm$ SD
Gender (males/females)	205/44
Age, yr	61.8 $\pm$ 11.4
Weight, kg	78.7 $\pm$ 15.7
Height, cm	169.9 $\pm$ 8.5
Body Mass Index, kg.m <sup>-2</sup>	27.2 $\pm$ 4.6
P <sub>max</sub> during exercise stress test, W	108.6 $\pm$ 35.7
P <sub>max</sub> predicted, W	167.5 $\pm$ 48.2
V O <sub>2</sub> peak during exercise stress test, mL/kg min	22.1 $\pm$ 4.8
V O <sub>2</sub> peak predicted	25.2 $\pm$ 5.1
METs peak during exercise stress test, mL/kg min	6.3 $\pm$ 1.4
Physical fitness, % predicted V O <sub>2</sub> peak	89.6 $\pm$ 20.5
<b>Risk factors</b>	<b>Prevalence, n (%)</b>
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<sub>max</sub>: Maximal power; V O<sub>2</sub>: Maximal oxygen consumption; METs: Metabolic equivalents of task.

which had the highest physical fitness were assigned to the group 1<sup>b</sup>. In Group 1<sup>a</sup>, the subjects had a V·O<sub>2</sub>peak during exercise stress test (23.6  $\pm$  5.1 mL·kg<sup>-1</sup>·min<sup>-1</sup>) similar to the V·O<sub>2</sub>peak predicted (23.4  $\pm$  4.7 mL·kg<sup>-1</sup>·min<sup>-1</sup>), whereas in group 1<sup>b</sup>, the V·O<sub>2</sub>peak during exercise stress test (25.5  $\pm$  5.5 mL·kg<sup>-1</sup>·min<sup>-1</sup>) is much higher than the V·O<sub>2</sub>peak predicted (22.4  $\pm$  4.6 mL·kg<sup>-1</sup>·min<sup>-1</sup>). In group 2<sup>a</sup> and group 2<sup>b</sup>, V·O<sub>2</sub>peak during exercise stress test (20.0  $\pm$  3.5 mL·kg<sup>-1</sup>·min<sup>-1</sup> and 20.9  $\pm$  4.0 mL·kg<sup>-1</sup>·min<sup>-1</sup>, respectively) were lower than V·O<sub>2</sub>peak predicted (27.8  $\pm$  4.6 mL·kg<sup>-1</sup>·min<sup>-1</sup> and

26.2  $\pm$  4.9 mL·kg<sup>-1</sup>·min<sup>-1</sup>, 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<sup>a</sup>, PF was calculated for age (6%), abdominal obesity (38%), diabetes (12%), hypertension (33%), obesity (12%) and overweight (11%). In the model<sup>b</sup>, 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<sup>[29]</sup> 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<sup>[30]</sup>. 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<sup>[31,32]</sup>. 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 <sup>a</sup>		P value	Model <sup>b</sup>		P value
	Group 1 <sup>a</sup> (n = 143)	Group 2 <sup>a</sup> (n = 106)		Group 1 <sup>b</sup> (n = 64)	Group 2 <sup>b</sup> (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 <sup>2</sup> )	27.8 ± 4.2	27.0 ± 5.0	0.500	27.0 ± 4.3	27.2 ± 4.7	0.700
P <sub>max</sub> 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 <sub>max</sub> predicted (W)	150.8 ± 46.9	190.0 ± 40.3	0.001	139.5 ± 49.9	177.2 ± 43.7	0.001
V O <sub>2</sub> 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 <sub>2</sub> 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 <sub>2</sub> peak)	102.2 ± 17.6	72.6 ± 8.1	0.001	115.2 ± 19.2	80.8 ± 11.7	0.001

Model<sup>a</sup>-group 1<sup>a</sup>: Patients with a normal physical fitness level; Model<sup>a</sup>-group 2<sup>a</sup>: Patients with a poor physical fitness level; Model<sup>b</sup>-group 1<sup>b</sup>: Patients with a high physical fitness level; Model<sup>b</sup>-group 2<sup>b</sup>: Patients with a low physical fitness level. P<sub>max</sub>: Maximal power; V O<sub>2</sub>: 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 <sup>a</sup>						
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 <sup>b</sup>						
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<sup>a</sup>: Patients with a normal physical fitness level; Model<sup>b</sup>: Patients with a high physical fitness level; OR: Odds ratio; PF: Preventive fraction.

prevalence of most CVDs risk factors<sup>[29]</sup>. Our group 2<sup>b</sup>, 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<sup>[33]</sup>. 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<sup>[34]</sup>, our study show that the subjects in the group 1<sup>a</sup> with a normal physical fitness level (20% below the predicted) and in the group 1<sup>b</sup> 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<sup>a</sup>, 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<sup>[33]</sup>. Kodama *et al.*<sup>[35]</sup> 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<sup>b</sup>) are susceptible to get a higher preventive action on hypertension than group 1<sup>a</sup> (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<sup>[36]</sup>. 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<sup>[37]</sup>. 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<sup>a</sup> (PF = 38%), comparatively to the group 1<sup>b</sup> (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<sup>[38]</sup>. Physical activity is known to decrease the risk of cardiovascular mortality in patients with obesity<sup>[39]</sup>. 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<sup>b</sup> 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<sup>[40]</sup> by improving glucose metabolism and insulin sensitivity<sup>[37]</sup>. A moderate exercise program can also reduce the diabetes risk and percentage of body fat<sup>[41]</sup>. It is especially important in the prevention of cardiovascular risk factors because the subjects who suffer overweight have a high risk of developing diabetes<sup>[42]</sup>. 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<sup>b</sup> 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<sup>a</sup>, 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<sup>b</sup> 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<sup>[43]</sup>. The patients with CVDs and with depression are likely to have recurrent heart problems<sup>[44,45]</sup>. According to Gary *et al.*<sup>[46]</sup> 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.*<sup>[47]</sup> 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<sup>[48]</sup>, 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.*<sup>[49]</sup> and O'Connors *et al.*<sup>[50]</sup> and despite the increasing development of new medication, the result of exercise on mortality reduction in CVDs is quite constant<sup>[16]</sup>. The works of Bouchard et Shepard shows that a part of physical fitness can be genetically determined and not related to environment (by physical activity practice)<sup>[51]</sup>. 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<sup>[28]</sup>. 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<sup>[52]</sup> (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<sup>[53]</sup> 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<sup>[19]</sup>.

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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## REFERENCES

- 1 **World Health Organization.** Global status report on noncommunicable diseases 2014. Geneva: World Health Organization, 2014
- 2 **Roger VL,** Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, Carnethon MR, Dai S, de Simone G, Ford ES, Fox CS, Fullerton HJ, Gillespie C, Greenlund KJ, Hailpern SM, Heit JA, Ho PM, Howard VJ, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Makuc DM, Marcus GM, Marelli A, Matchar DB, McDermott MM, Meigs JB, Moy CS, Mozaffarian D, Mussolino ME, Nichol G, Paynter NP, Rosamond WD, Sorlie PD, Stafford RS, Turan TN, Turner MB, Wong ND, Wylie-Rosett J; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2011 update: a report from the American Heart Association. *Circulation* 2011; **123**: e18-e209 [PMID: 21160056 DOI: 10.1161/CIR.0b013e3182009701]
- 3 **Nichols M,** Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe 2014: epidemiological update. *Eur Heart J* 2014; **35**: 2929 [PMID: 25381246 DOI: 10.1093/eurheartj/ehu378]
- 4 **World Health Organization.** Cardiovascular diseases (CVDs). World health organization, 2015
- 5 **Chomistek AK,** Manson JE, Stefanick ML, Lu B, Sands-Lincoln M, Goings SB, Garcia L, Allison MA, Sims ST, LaMonte MJ, Johnson KC, Eaton CB. Relationship of sedentary behavior and physical activity to incident cardiovascular disease: results from the Women's Health Initiative. *J Am Coll Cardiol* 2013; **61**: 2346-2354 [PMID: 23583242 DOI: 10.1016/j.jacc.2013.03.031]
- 6 **Wen CP,** Wu X. Stressing harms of physical inactivity to promote exercise. *Lancet* 2012; **380**: 192-193 [PMID: 22818933 DOI: 10.1016/s0140-6736(12)60954-4]
- 7 **Yusuf S,** Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, McQueen M, Budaj A, Pais P, Varigos J, Lisheng L; INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004; **364**: 937-952 [PMID: 15364185 DOI: 10.1016/s0140-6736(04)17018-9]
- 8 **Kim C,** Beckles GL. Cardiovascular disease risk reduction in the Behavioral Risk Factor Surveillance System. *Am J Prev Med* 2004; **27**: 1-7 [PMID: 15212768 DOI: 10.1016/j.amepre.2004.03.008]
- 9 **Li J,** Siegrist J. Physical activity and risk of cardiovascular disease—a meta-analysis of prospective cohort studies. *Int J Environ Res Public Health* 2012; **9**: 391-407 [PMID: 22470299 DOI: 10.3390/

- ijerph9020391]
- 10 **Glazer NL**, Lyass A, Eslinger DW, Blease SJ, Freedson PS, Massaro JM, Murabito JM, Vasan RS. Sustained and shorter bouts of physical activity are related to cardiovascular health. *Med Sci Sports Exerc* 2013; **45**: 109-115 [PMID: 22895372 DOI: 10.1249/MSS.0b013e31826beae5]
  - 11 **Musumeci G**. Effects of exercise on physical limitations and fatigue in rheumatic diseases. *World J Orthop* 2015; **6**: 762-769 [PMID: 26601057 DOI: 10.5312/wjo.v6.i10.762]
  - 12 **Musumeci G**, Loreto C, Imbesi R, Trovato FM, Di Giunta A, Lombardo C, Castorina S, Castrogiovanni P. Advantages of exercise in rehabilitation, treatment and prevention of altered morphological features in knee osteoarthritis. A narrative review. *Histol Histopathol* 2014; **29**: 707-719 [PMID: 24452819 DOI: 10.14670/hh-29.707]
  - 13 **Fairey AS**, Courneya KS, Field CJ, Mackey JR. Physical exercise and immune system function in cancer survivors: a comprehensive review and future directions. *Cancer* 2002; **94**: 539-551 [PMID: 11900239 DOI: 10.1002/cncr.10244]
  - 14 **O'Brien K**, Nixon S, Tynan AM, Glazier R. Aerobic exercise interventions for adults living with HIV/AIDS. *Cochrane Database Syst Rev* 2010: CD001796 [PMID: 20687068 DOI: 10.1002/14651858.CD001796.pub3]
  - 15 **Anderson L**, Taylor RS. Cardiac rehabilitation for people with heart disease: an overview of Cochrane systematic reviews. *Cochrane Database Syst Rev* 2014: CD011273 [PMID: 25503364 DOI: 10.1002/14651858.CD011273.pub2]
  - 16 **Taylor RS**, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K, Skidmore B, Stone JA, Thompson DR, Oldridge N. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am J Med* 2004; **116**: 682-692 [PMID: 15121495 DOI: 10.1016/j.amjmed.2004.01.009]
  - 17 **Simons-Morton DG**, Calfas KJ, Oldenburg B, Burton NW. Effects of interventions in health care settings on physical activity or cardiorespiratory fitness. *Am J Prev Med* 1998; **15**: 413-430 [PMID: 9838981]
  - 18 **Piepoli MF**, Corrà U, Benzer W, Bjarnason-Wehrens B, Dendale P, Gaita D, McGee H, Mendes M, Niebauer J, Zwisler AD, Schmid JP; Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. Secondary prevention through cardiac rehabilitation: from knowledge to implementation. A position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. *Eur J Cardiovasc Prev Rehabil* 2010; **17**: 1-17 [PMID: 19952757 DOI: 10.1097/HJR.0b013e3283313592]
  - 19 **Kokkinos P**. Physical activity, health benefits, and mortality risk. *ISRN Cardiol* 2012; **2012**: 718789 [PMID: 23198160 DOI: 10.5402/2012/718789]
  - 20 **Guazzi M**, Adams V, Conraads V, Halle M, Mezzani A, Vanhees L, Arena R, Fletcher GF, Forman DE, Kitzman DW, Lavie CJ, Myers J; European Association for Cardiovascular Prevention & Rehabilitation; American Heart Association. EACPR/AHA Scientific Statement. Clinical recommendations for cardiopulmonary exercise testing data assessment in specific patient populations. *Circulation* 2012; **126**: 2261-2274 [PMID: 22952317 DOI: 10.1161/CIR.0b013e31826fb946]
  - 21 **Hansen JE**, Sue DY, Wasserman K. Predicted values for clinical exercise testing. *Am Rev Respir Dis* 1984; **129**: S49-S55 [PMID: 6421218 DOI: 10.1164/arrd.1984.129.2P2.S49]
  - 22 **Wasserman K**, Hansen JE, Sue DY, Stringer W, Whipp BJ. Principles of Exercise Testing and Interpretation. In: Weinberg R, editor. Normal Values. Philadelphia, PA: Lippincott Williams and Wilkins; 2005, 160-182
  - 23 **European Society of Hypertension-European Society of Cardiology Guidelines Committee**. 2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. *J Hypertens* 2003; **21**: 1011-1053 [PMID: 12777938 DOI: 10.1097/01.hjh.0000059051.65882.32]
  - 24 **Smith SC Jr**, Blair SN, Bonow RO, Brass LM, Cerqueira MD, Dracup K, Fuster V, Gotto A, Grundy SM, Miller NH, Jacobs A, Jones D, Krauss RM, Mosca L, Ockene I, Pasternak RC, Pearson T, Pfeffer MA, Starke RD, Taubert KA. AHA/ACC Scientific Statement: AHA/ACC guidelines for preventing heart attack and death in patients with atherosclerotic cardiovascular disease: 2001 update: A statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation* 2001; **104**: 1577-1579 [PMID: 11571256]
  - 25 **Gargiulo PM**, Rothenberg RB, Wilson HG. Confidence intervals, hypothesis tests, and sample sizes for the prevented fraction in cross-sectional studies. *Stat Med* 1995; **14**: 51-72 [PMID: 7701158]
  - 26 **Miettinen OS**. Proportion of disease caused or prevented by a given exposure, trait or intervention. *Am J Epidemiol* 1974; **99**: 325-332 [PMID: 4825599]
  - 27 **Blair SN**, Cheng Y, Holder JS. Is physical activity or physical fitness more important in defining health benefits? *Med Sci Sports Exerc* 2001; **33**: S379-99; discussion S419-20 [PMID: 11427763]
  - 28 **Myers J**, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med* 2002; **346**: 793-801 [PMID: 11893790 DOI: 10.1056/NEJMoa011858]
  - 29 **Lavie CJ**, Arena R, Swift DL, Johannsen NM, Sui X, Lee DC, Earnest CP, Church TS, O'Keefe JH, Milani RV, Blair SN. Exercise and the cardiovascular system: clinical science and cardiovascular outcomes. *Circ Res* 2015; **117**: 207-219 [PMID: 26139859 DOI: 10.1161/circresaha.117.305205]
  - 30 **McCusker ME**, Yoon PW, Gwinn M, Malarcher AM, Neff L, Khoury MJ. Family history of heart disease and cardiovascular disease risk-reducing behaviors. *Genet Med* 2004; **6**: 153-158 [PMID: 15354334 DOI: 10.109701.gim.0000127271.60548.89]
  - 31 **Bernardo AFB**, Rossi RC, Souza NMD, Pastre CM, Vanderlei LCM. Association between physical activity and cardiovascular risk factors in individuals undergoing cardiac rehabilitation program. *Revista Brasileira de Medicina do Esporte*. 2013; 231
  - 32 **Koltuniuk A**, Rosińczuk J. The prevalence of risk factors for cardiovascular diseases among Polish surgical patients over 65 years. *Clin Interv Aging* 2016; **11**: 631-639 [PMID: 27257376 DOI: 10.2147/CIA.S105201]
  - 33 **Sandvik L**, Erikssen J, Thaulow E, Erikssen G, Mundal R, Rodahl K. Physical fitness as a predictor of mortality among healthy, middle-aged Norwegian men. *N Engl J Med* 1993; **328**: 533-537 [PMID: 8426620 DOI: 10.1056/nejm199302253280803]
  - 34 **Fleg JL**, Morrell CH, Bos AG, Brant LJ, Talbot LA, Wright JG, Lakatta EG. Accelerated longitudinal decline of aerobic capacity in healthy older adults. *Circulation* 2005; **112**: 674-682 [PMID: 16043637 DOI: 10.1161/circulationaha.105.545459]
  - 35 **Kodama S**, Saito K, Tanaka S, Maki M, Yachi Y, Asumi M, Sugawara A, Totsuka K, Shimano H, Ohashi Y, Yamada N, Sone H. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. *JAMA* 2009; **301**: 2024-2035 [PMID: 19454641 DOI: 10.1001/jama.2009.681]
  - 36 **Pescatello LS**, Franklin BA, Fagard R, Farquhar WB, Kelley GA, Ray CA; American College of Sports Medicine. American College of Sports Medicine position stand. Exercise and hypertension. *Med Sci Sports Exerc* 2004; **36**: 533-553 [PMID: 15076798]
  - 37 **Lee DC**, Sui X, Church TS, Lavie CJ, Jackson AS, Blair SN. Changes in fitness and fatness on the development of cardiovascular disease risk factors hypertension, metabolic syndrome, and hypercholesterolemia. *J Am Coll Cardiol* 2012; **59**: 665-672 [PMID: 22322083 DOI: 10.1016/j.jacc.2011.11.013]
  - 38 **Sahakyan KR**, Somers VK, Rodriguez-Escudero JP, Hodge DO, Carter RE, Sochor O, Coutinho T, Jensen MD, Roger VL, Singh P, Lopez-Jimenez F. Normal-Weight Central Obesity: Implications for Total and Cardiovascular Mortality. *Ann Intern Med* 2015; **163**: 827-835 [PMID: 26551006 DOI: 10.7326/m14-2525]
  - 39 **Lavie CJ**, McAuley PA, Church TS, Milani RV, Blair SN. Obesity and cardiovascular diseases: implications regarding fitness, fatness, and severity in the obesity paradox. *J Am Coll Cardiol* 2014; **63**: 1345-1354 [PMID: 24530666 DOI: 10.1016/j.jacc.2014.01.022]
  - 40 **Hu G**, Eriksson J, Barengo NC, Lakka TA, Valle TT, Nissinen A,

- Jousilahti P, Tuomilehto J. Occupational, commuting, and leisure-time physical activity in relation to total and cardiovascular mortality among Finnish subjects with type 2 diabetes. *Circulation* 2004; **110**: 666-673 [PMID: 15277321 DOI: 10.1161/01.cir.0000138102.23783.94]
- 41 **Nicklas BJ**, Katzel LI, Bunyard LB, Dennis KE, Goldberg AP. Effects of an American Heart Association diet and weight loss on lipoprotein lipids in obese, postmenopausal women. *Am J Clin Nutr* 1997; **66**: 853-859 [PMID: 9322560]
- 42 **Resnick HE**, Valsania P, Halter JB, Lin X. Relation of weight gain and weight loss on subsequent diabetes risk in overweight adults. *J Epidemiol Community Health* 2000; **54**: 596-602 [PMID: 10890871]
- 43 **Suija K**, Timonen M, Suviola M, Jokelainen J, Järvelin MR, Tammelin T. The association between physical fitness and depressive symptoms among young adults: results of the Northern Finland 1966 birth cohort study. *BMC Public Health* 2013; **13**: 535 [PMID: 23731782 DOI: 10.1186/1471-2458-13-535]
- 44 **Barth J**, Schumacher M, Herrmann-Lingen C. Depression as a risk factor for mortality in patients with coronary heart disease: a meta-analysis. *Psychosom Med* 2004; **66**: 802-813 [PMID: 15564343 DOI: 10.1097/01.psy.0000146332.53619.b2]
- 45 **Bounhoure JP**, Galinier M, Curnier D, Bousquet M, Bes A. [Influence of depression on the prognosis of cardiovascular diseases]. *Bull Acad Natl Med* 2006; **190**: 1723-1731; discussion 1731-1732 [PMID: 17650755]
- 46 **Gary RA**, Dunbar SB, Higgins MK, Musselman DL, Smith AL. Combined exercise and cognitive behavioral therapy improves outcomes in patients with heart failure. *J Psychosom Res* 2010; **69**: 119-131 [PMID: 20624510 DOI: 10.1016/j.jpsychores.2010.01.013]
- 47 **Marín Armero A**, Calleja Hernandez MA, Perez-Vicente S, Martinez-Martinez F. Pharmaceutical care in smoking cessation. *Patient Prefer Adherence* 2015; **9**: 209-215 [PMID: 25678779 DOI: 10.2147/ppa.s67707]
- 48 **Mouhamed DH**, Ezzaher A, Neffati F, Gaha L, Douki W, Najjar M. Association between cigarette smoking and dyslipidemia. *Immunanalyse Biologie Spécialisée*. 2013: 195
- 49 **Oldridge NB**, Guyatt GH, Fischer ME, Rimm AA. Cardiac rehabilitation after myocardial infarction. Combined experience of randomized clinical trials. *JAMA* 1988; **260**: 945-950 [PMID: 3398199]
- 50 **O'Connor GT**, Buring JE, Yusuf S, Goldhaber SZ, Olmstead EM, Paffenbarger RS Jr, Hennekens CH. An overview of randomized trials of rehabilitation with exercise after myocardial infarction. *Circulation* 1989; **80**: 234-244 [PMID: 2665973]
- 51 **Bouchard C**, Shepard T. Physical activity, fitness and health the model and key concepts In C Bouchard, R Shephard T Stephens (Eds.), *Physical activity, fitness and health—consensus statement*, 11-23. Champaign, Illinois: Human Kinetics Publishers. 1993
- 52 **Thompson PD**, Arena R, Riebe D, Pescatello LS; American College of Sports Medicine. ACSM's new preparticipation health screening recommendations from ACSM's guidelines for exercise testing and prescription, ninth edition. *Curr Sports Med Rep* 2013; **12**: 215-217 [PMID: 23851406 DOI: 10.1249/JSR.0b013e31829a68cf]
- 53 **Guazzi M**, Arena R, Halle M, Piepoli MF, Myers J, Lavie CJ. 2016 Focused Update: Clinical Recommendations for Cardiopulmonary Exercise Testing Data Assessment in Specific Patient Populations. *Circulation* 2016; **133**: e694-e711 [PMID: 27143685 DOI: 10.1161/cir.0000000000000406]

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