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Cardiorespiratory fitness and development of abdominal obesity

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ABSTRACT

Both, cardiorespiratory fitness and abdominal obesity are independently associated with developing cardiovascular disease and its risk factors. However, the relationship between both attributes is unclear. We examine the relationship between cardiorespiratory fitness and the risk of developing abdominal obesity, and secondarily, other adiposity measures.

Retrospective observational study of a cohort of 1284 sedentary patients, who had participated in a clinical trial of physical activity promotion carried out in Spain (2003–2007). At baseline, they were free of cardiovascular disease, hypertension, diabetes, dyslipidemia and/or abdominal obesity, with an indirect VO_2max measurement, were 19–80 years old, 62% women, and had completed the two year follow-up. The exposure factor was cardiorespiratory fitness categorized as high, moderate or low, according to tertiles of VO_2max values. The main outcome measure was the risk of developing abdominal obesity, as defined by waist circumference > 102 (men) and > 88 (women) cm. Secondary outcomes were the risk of developing: general obesity, excess body fat, and their combination ("defined" obesity).

At two years, 10.5% of the participants had developed abdominal obesity: 6.1% in the high cardiorespiratory fitness tertile, 9.7% in the moderate tertile (adjusted odds ratio, 1.20; 95% confidence interval 0.68–2.10), and 15.7% in the low tertile (adjusted odds ratio, 2.29; 95% confidence interval 1.34–3.91). Moreover, 2.2% of participants in the high cardiorespiratory fitness tertile developed "defined" obesity as did 5.4% in the low tertile (adjusted odds ratio, 2.90; 95% confidence interval 1.15–7.29).

Low cardiorespiratory fitness levels are associated with a higher risk of developing abdominal and "defined" obesity.

1. Introduction

A possible explanation as to how a person can evolve from health to cardiovascular disease (CVD) may be as follows: The interaction between genetic factors, environmental factors (toxic habits such as smoking) and behaviors (poor nutrition, but, mainly physical inactivity) combine to cause excessive fat accumulation within the abdominal cavity. Abdominal obesity facilitates the development of hyperinsulinemia (Karter et al., 2005; Ko et al., 2016), which in turn, is a cause of the onset of CVD risk factors that make up the metabolic syndrome (Palaniappan et al., 2004; Utzschneider et al., 2010), such as hypertension, type 2 diabetes and dyslipidemia (Park et al., 2013; Meigs et al., 2007; Robins et al., 2011). These CVD risk factors contribute to the atherosclerotic process (Bertoni et al., 2007; Jeppesen et al., 2007) which will cause coronary heart disease (CHD) or stroke. There is enough evidence to validate each step of this possible evolution toward CVD, except for the first step, i.e., the contribution of physical inactivity to the development of abdominal obesity.

Physical inactivity is fairly well reflected by poor cardiorespiratory fitness (CRF), because CRF is an objective reproducible measure that reflects the functional consequences of recent physical activity habits, health status (mainly oxygen transport system performance), and genetics (Arena et al., 2007).

Poor CRF and/or low physical activity levels have shown to be associated with all of the steps of the above mentioned evolution toward CVD, except with the first. Thus, they are associated with a higher risk of: all-cause (Nocon et al., 2008; Kodama et al., 2009) and CVD (Nocon et al., 2008; Zhang et al., 2017) mortality, incidence of CVD (CHD and

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stroke) (Kodama et al., 2009; Williams, 2001; Wendel-Vos et al., 2004), incidence of metabolic syndrome (Lakka et al., 2003; LaMonte et al., 2005; Schmidt et al., 2016) and its CVD risk factors, hypertension (Chase et al., 2009; Rankinen et al., 2007) type 2 diabetes (Sui et al., 2008; Zaccardi et al., 2015), dyslipidemia (Breneman et al., 2016), and incidence of hyperinsulinemia (Lee et al., 2009; Vella et al., 2016). Nevertheless, the evidence for their association with the incidence of abdominal obesity is lacking.

Therefore, the hypothesis that low CRF is also associated with a higher risk of abdominal obesity, which would be the first step of the evolution from health to CVD, was retrospectively examined. The association of CRF with the risk of developing general obesity, excess body fat and their combination (high body mass index owing to excess body fat which is the definition of obesity), was also examined.

2. Methods

2.1. Study population, design and procedures

The cohort from the PEPAF Study that was established between October 2003 and May 2004 of 4927 sedentary men and women, aged 20 to 80 years without known cardiovascular disease and who visited 56 collaborating general practices at 11 Spanish public primary health care centers, was recruited and distributed into an intervention and a control group to evaluate the effectiveness of the Experimental Program for Physical Activity Promotion; details have been published elsewhere (Grandes et al., 2009). For this study, which is a retrospective observational study of that cohort, participants with hypertension and/or diabetes and/or dyslipidemia (n = 1945) were excluded, as well as, those with missing values for oxygen uptake measurement (n = 220). Also excluded were those men and women (n = 873) with a baseline waist circumference (WC) > 102 cm and 88 cm, respectively, or a missing value at baseline or at the end of follow-up (n = 605), leaving 1284 participants.

With regard to the secondary objectives, instead of those waist circumference measurement exclusions, the following participants were excluded: 1588 men and women with a baseline percent body fat (PBF) > 25% and 30%, respectively, as well as 400 participants with a missing value at the end of follow-up, leaving 774 participants in the final analysis of excess body fat; 449 men and women with a baseline BMI ≥ 30 kg/m^2, as well as 728 participants with a missing value at the end of follow-up, leaving 1585 participants in the final analysis of general obesity; 420 men and women with a baseline PBF > 25% and 30%, respectively, plus BMI ≥ 30 kg/m^2, as well as,736 participants with a missing value at the end of follow-up, leaving 1606 participants in the final analysis of general obesity plus excess body fat.

2.2. Measures

The following measurements and socio-demographic and behavioral variables obtained for the original study from October 2003 to May 2006, at baseline and two years later, were utilized for the purposes of this study: weight, height, WC, 3 skin-folds (thoracic, umbilical and anterior thigh for men, and triceps, suprailiac and anterior thigh for women), maximal oxygen uptake (VO_2max), gender, age, social class, educational level, employment status, smoking habits and physical activity levels.

Standing height and weight (barefoot) were measured by using a standard weighing machine, calibrated before each measurement, and by having the participant wear the minimum amount of clothing and by maintaining the head aligned with the nose and ears. WC was measured level with the umbilicus, with a laminated meter tape. The selected skin-folds were measured by following the Jackson and Pollock's standardized protocols (Jackson and Pollock, 1985; Balady et al., 2000). VO_2max was indirectly estimated by using a sub-maximal cycloergometer (VarioBike 500) exercise test and was standardized by age, sex and resting heart rate, YMCA-ACSM protocol (Balady et al., 2000). Gender, age, social class, educational level, employment status, and smoking habits (never, former, or baseline smoker) were obtained by self-report. Physical activity levels were assessed by using the 7-Day Physical Activity Recall (PAR) semi-structured interview, and the results were shown as minutes per week (minutes/week) and METs × hours per week (MET-h/wk) spent in moderate or vigorous leisure and occupational activity in the week previous to the interview.

All measurements were performed by trained nurses. Data quality was guaranteed by an initial intensive one-week training of research nurses, a pilot study followed by a three-day review training, and double data entry into a centralized Oracle™ database. Quality control was performed daily by online supervision of the study process and data, daily feedback to nurses, monthly progress reports, and regular meetings with the collaborating investigators and nurses every four months.

2.3. Exposure variable

The 1284 subjects of the final sample were categorized into 3 tertiles of CRF (low, moderate and high) according to their estimated VO_2max and gender.

Each group was considered independently, the participants in the low and moderate CRF tertiles as two groups of subjects exposed to the onset of abdominal obesity, and the participants in the high CRF tertile as not exposed subjects.

The CRF tertiles were automatically generated by SAS (ver. 9.2, SAS Institute, Cary, NC, USA, 2009), corresponding to the following VO_2max values: low < 28.47 (men) and < 21.72 (women) ml/kg/min, moderate from 28.47 to 35.01 (men) and 21.72 to 26.04 (women) ml/kg/min, and high > 35.01 (men) and > 26.04 (women) ml/kg/min.

The same procedures were followed for excess body fat, general obesity, and their combination.

2.4. Outcome variables

The primary outcome was the cumulative incidence of abdominal obesity, defined as the transition from a WC of 102 cm or less in men or 88 cm or less in women, at the study baseline, to a WC of > 102 or 88 cm in men and women (Kushner, 2012), respectively, two years later.

Secondary outcomes were: the cumulative incidence of excess body fat, defined as the transition from a PBF of ≤25% in men or ≤30% in women, at the study baseline, to a PBF of > 25% or > 30% in men and women (Jackson and Pollock, 1985), respectively, two year later; the cumulative incidence of general obesity, defined as the transition from a BMI lesser than 30 kg/m^2, at the study baseline, to a BMI of 30 or more, two years later; and the cumulative incidence of “defined” obesity, that was defined as the transition from, either, a PBF of ≤25% in men or ≤30% in women, or a BMI < 30 kg/m^2, at the study baseline, to a PBF of > 25% or > 30% in men and women, respectively, plus a BMI of 30 or more two years later.

PBF was calculated by the Siri's formula (Jackson and Pollock, 1985; Balady et al., 2000), after introducing the body density obtained from Jackson and Pollock's formulas for the 3 measured skin-folds.

BMI was calculated as weight in kilograms divided by the square of height in meters.

The following variables that may influence CRF (Arena et al., 2007) and/or body fat were considered as potential confounders: gender, age, social class, educational level, employment status, smoking habits and physical activity levels.

2.5. Statistical analysis

All analyses were conducted using SAS (ver. 9.2, SAS Institute, Cary, NC, USA, 2009) in April 2010. Means (SDs) were calculated for all

continuous variables and the percentage of participants in each category was determined for all categorical variables. Their values were shown distributed by CRF tertiles. The groups were compared using a chi-square test for the proportions of categorical variables and analysis of variance for the means of continuous variables. The two year cumulative incidence of abdominal obesity, excess body fat, general obesity and "defined" obesity were calculated by dividing the number of new cases by the number of exposed participants in each of the tertiles. The relative risks of developing abdominal obesity, excess body fat, general obesity and "defined" obesity were computed as the ORs of the two year cumulative incidence in the low and moderate CRF tertiles, divided by the cumulative incidence in the high CRF tertile, as a point of reference. Multivariate mixed logistic regression models were used to adjust for potential confounding variables, and baseline WC, PBF and BMI measures centered by gender, taking into account the hierarchical structure of the data, with patients clustered in centers.

3. Results

Overall, the mean age of the 1284 participants was 42.5 (SD, 13.5) years, of which 62% were women. The participants' baseline characteristics, by CRF tertiles, are summarized in Table 1, which shows that all tests for linear trends throughout the CRF tertiles were significant ($p < 0.05$), except for body weight, gender, social class and minutes/week of physical activity.

Table 1
Baseline characteristics of sample individuals according to cardiorespiratory fitness tertiles for the primary outcome (abdominal obesity).

Variable	High (N = 428)	Moderate (N = 424)	Low (N = 432)
Age, mean (SD) y	34.8 (9.7)*	40.2 (11.1)*	52.3 (12.9)*
Weight, mean (SD) kg	64.9 (12.1)	66.4 (11.9)	64.8 (10.6)
WC, mean (SD) cm	81.0 (9.3)*†	83.4 (9.4)*	84.6 (9.2)†
PBF, mean (SD) %	24.6 (6.3)*	27.3 (6.4)*	28.8 (6.2)*
BMI, mean (SD) kg/m^2	23.4 (3.1)*	24.3 (3.1)*	24.9 (3.1)*
VO_2max, mean (SD) ml/kg/min	35.0 (7.3)*	26.8 (4.2)*	20.1 (4.2)*
Gender, no (%)			
Female	264 (61.7)	261 (61.6)	265 (61.3)
Male	164 (38.3)	163 (38.4)	167 (38.7)
Social class, no. (%)			
Manual worker	199 (46.5)	186 (43.9)	220 (50.9)
Intermediate employee	131 (30.6)	136 (32.2)	126 (29.2)
Manager small enterprise	57 (13.3)	56 (13.2)	42 (9.7)
Manager large enterprise	41 (9.6)	46 (10.7)	44 (10.2)
Educational level, no. (%)*			
None	2 (0.5)	7 (1.7)	16 (3.7)
Elementary school	24 (5.6)	51 (12.0)	128 (29.6)
Middle or high school	257 (60.0)	243 (57.3)	215 (49.8)
University studies	145 (33.8)	123 (29.0)	73 (16.9)
Employment status, no. (%)*			
Works outside of home	311 (72.6)	294 (69.3)	211 (48.8)
Homemaker	33 (7.7)	50 (11.8)	90 (20.8)
Retired	5 (1.2)	22 (5.2)	94 (21.8)
Student	34 (8.0)	15 (3.5)	7 (1.6)
Unemployed	32 (7.5)	35 (8.2)	19 (4.4)
Other	13 (3.0)	8 (1.9)	11 (2.6)
Smoking status no.° (%)*			
Never	175 (40.9)	162 (38.2)	227 (52.5)
Current	198 (46.2)	166 (39.1)	122 (28.3)
Former	55 (12.9)	96 (22.7)	83 (19.2)
Physical activity levels, mean (SD)			
METs-h/week	1.04 (2.56)*	0.64 (1.55)*	0.95 (2.0)
Minutes/week	93.0 (206.3)	75.7 (208.1)	101.6 (209.4)

*† = Significant differences between tertiles, $p < 0.05$;
Notes: (1) Abbreviations: BMI, body mass index; PBF, percent body fat; SD, standard deviation; WC, waist circumference. (2) Cardiorespiratory Function (CRF) corresponded to the following VO_2max values: low < 28.47 (men) and < 21.72 (women) ml/kg/min, moderate from 28.47 to 35.01 (men) and 21.72 to 26.04 (women) ml/kg/min, and high > 35.01 (men) and > 26.04 (women) ml/kg/min.

Table 2
Factors associated with development of abdominal obesity: Multivariate adjusted odds ratios.

	AOR (95%CI)	p
CRF		0.003
Low vs high	2.29 (1.34–3.91)	
Moderate vs high	1.20 (0.68–2.10)	
Gender		0.004
Women vs. men	1.95 (1.24–3.08)	
Baseline smoking status		0.015
Former vs never	1.28 (0.73–2.25)	
Current vs never	1.96 (1.24–3.11)	
Baseline waist circumference	1.30 (1.23–1.37)	< 0.001
Between centre variability (logit scale)	$\sigma^2 = 0.152$	< 0.001

Notes: (1) Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; CRF, cardiorespiratory fitness; (2) Numbers are based on 68 subjects with abdominal obesity from those with Low CRF, 41 subjects with abdominal obesity from those with Moderate CRF and 26 subjects with abdominal obesity from those with High CRF; Abdominal obesity was develop in 101 women and 34 men; lastly, 50 former smokers, 59 current smokers and 26 non-smokers developed abdominal obesity, respectively.

At the end of the follow-up, there were 135 new cases of abdominal obesity. Cumulative incidence rates across high, moderate and low CRF, respectively, were 6.07%, 9.67% and 15.74% for abdominal obesity ($p < 0.001$ for linear trend).

Table 2 summarizes the results of the adjusted ORs of the factors associated with developing abdominal obesity after adjusting for gender, smoking habits, physical activity levels and baseline WC values centered by gender. It can be seen that, compared to high CRF, low CRF is associated with a higher risk (OR = 2.29; 95%CI, 1.34–3.91) of developing abdominal obesity. It can be also seen that the risk of developing abdominal obesity is higher in women (OR = 1.95; 95%CI, 1.24–3.08) than in men, and in baseline smokers (OR = 1.96; 95%CI, 1.24–3.11) than in those that had never smoked. An increase in baseline waist circumference is associated with an OR = 1.30 (95%CI, 1.23–1.37) of developing abdominal obesity.

The mean ages of the study cohorts for general obesity, excess body fat and "defined" obesity were 43.9 (SD, 13.5), 40.1 (SD, 13.4) and 43.9 (SD, 13.5) years, respectively, of which 69%, 56% and 68% were women.

At the end of the follow-up, there were 63 new cases of general obesity, 136 new cases of excess body fat and 59 new cases of "defined" obesity. Cumulative incidence rates across high, moderate and low CRF, respectively, were: 3.03%, 3.41% and 5.48% for general obesity (chi-square test p = 0.090); 12.02%, 19.84% and 20.85% for excess body fat (chi-square test p = 0.015); and 2.24%, 3.36% and 5.42% for "defined" obesity (chi-square test p = 0.019). In the multivariate analysis (see Table 3), low CRF was associated only with a higher risk (OR = 2.90; 95%CI, 1.15–7.29) of developing "defined" obesity compared to high CRF after adjusting for gender, age, smoking habit and baseline BMI values (p-value = 0.038).

4. Discussion

In this retrospective cohort of patients without a history of CVD, hypertension, diabetes or dyslipidemia, and who had consulted their family physician, data indicate that low CRF is a risk factor for subsequent development of abdominal obesity. Particularly, a CRF < 8.13 METs in men and 6.21 in women was associated with a 129% increase in the risk of abdominal obesity when compared with a CRF > 10.00 METs in men and 7.44 in women, at two years. Moreover, the risk of developing abdominal obesity is greater in women vs. men, and is greater in current smokers vs. non-smokers, respectively.

Low CRF is also a risk factor for the subsequent development of "defined" obesity (BMI ≥ 30 kg/m^2 due to excess body fat). Specifically,

Table 3
Factors associated with development of defined obesity: Multivariate adjusted odds ratios.

	AOR (95%CI)	p
CRF		0.038
Low vs high	2.90 (1.15–7.29)	
Moderate vs high	1.22 (0.53–2.87)	
Gender		0.215
Women vs. men	1.52 (0.78–3.00)	
Baseline smoking status		0.007
Former vs never	2.84 (1.25–6.48)	
Current vs never	2.97 (1.44–6.17)	
Age	0.95 (0.93–0.99)	0.005
Baseline body mass index	2.63 (2.13–3.26)	< 0.001

Notes: (1) Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; CRF, cardiorespiratory fitness; (2) No center variability was estimated by the model; (3) Numbers are based on 29 subjects with defined obesity from those with low CRF, 18 subjects with defined obesity from those with Moderate CRF and 12 subjects with defined obesity from those with High CRF; defined obesity was developed in 43 women and 16 men; lastly, 14 former smokers, 26 current smokers and 19 non-smokers developed defined obesity, respectively.

at two years, a CRF < 8.03 METs in men and < 5.99 in women was associated with a 190% increase in the risk of "defined" obesity in comparison with a CRF > 9.97 METs in men and > 7.20 in women.

Research indicates that CRF levels are, at least in part, a result of genetic heritability (Arena et al., 2007) and are poorly correlated with physical activity levels (Williams, 2001) because of the difficulty of accurately measuring physical activity. However, they are undoubtedly the main consequence (attribute) of physical activity levels (behavior) and CRF either increases or decreases as a result of physical training or detraining (Arena et al., 2007). It is probable that the lower the CRF of a person, the less the ability to perform aerobic activities in daily living because of a lesser oxygen supply to muscles. Given that fat is the metabolic substrate for only that kind of physical effort, fat has less probability of being oxidized and more probability of accumulating in all areas of the body, thereby increasing PBF and, in passing, body weight and BMI. Since the abdominal cavity seems to have more capacity for fat accumulation than the limbs, most fat coming from foods and excessive carbohydrates that the body does not utilize, will be converted into fat, will accumulate in the abdomen, and will increase WC. In this study, those who developed abdominal obesity increased their body weight, PBF and BMI, a 4.9%, 5.5% and 5.0%, respectively, in comparison with those who do not.

On the other hand, the lack of association of CRF with the subsequent development of general obesity may be due to the particular manner of measuring obesity. BMI demonstrates a relationship between body weight (fat mass + muscle mass + residual mass) and height, which contributes to the far from negligible proportion of individuals with increased muscle mass and normal fat mass in the range of BMI values of 25–35 kg/m^2. In this study, the proportion of individuals with normal PBF in that range of BMI values was 13.8% in the 1606 participants of "defined" obesity. Those individuals, of possible athletic morphology, also have a higher CRF (In this study, their VO_2max was the highest of all groups with 30.57 ml/kg/min). And this would be the reason why people with overweight had the lowest risk of mortality in a meta-analysis (Flegal et al., 2013).

This indicates that the group of individuals who develop general obesity, is made up of people with excess body weight for their height owing to, either, increased muscle mass, and thus a higher CRF, or excess body fat, and thus a lower CRF. In this study, among the 63 new cases of general obesity, at 2 years, 12.7% had normal body fat and a VO_2max of 29.83 ml/kg/min versus 23.39 ml/kg/min among those with excess body fat. Likewise, the association of low CRF with the risk of developing general obesity plus excess body fat corroborates all of the above.

In the evidence found, there is no longitudinal study which has assessed the risk of developing abdominal obesity entailed by a low CRF. Existing studies, similar to this one, have studied the protection of higher CRF against abdominal or general obesity and have searched for the association of higher CRF with lower risk of abdominal obesity or excess body fat. Two cross-sectional studies (Ross and Katzmarzyk, 2003; Wedell-Neergaard et al., 2018) analyzed the association of CRF with abdominal obesity or excess body fat for a given BMI value, and found an inverse relationship between a higher CRF and a lower WC or PBF. Another cross-sectional study (Wong et al., 2004) analyzed the association of CRF with abdominal obesity for a given BMI value, and found an inverse relationship between a higher CRF and a lower WC or total, subcutaneous and visceral fat. In another study of participants in the HERITAGE Family Study (Janssen et al., 2004), individuals with a moderate CRF level had lower levels of total body fat and subcutaneous and visceral abdominal fat than individuals with a lower CRF level; moreover, a 20-week aerobic exercise program was associated with significant reductions in total adiposity and abdominal fat.

The limitations of this study may include methods of measuring CRF, WC and PBF.

The exposure variable, that is CRF, has been measured by an indirect method and a sub-maximal exercise test, which are valid and feasible measuring ways for Primary Care and have been used in numerous studies, although the most accurate measuring way is a direct method and a maximal exercise test (Arena et al., 2007).

Outcome variables, that is abdominal obesity and excess body fat, have been measured by waist circumference and percent body fat, instead of computerized tomography and hydrostatic weighing techniques, because they are also valid and more feasible methods of measurement for Primary Care, and have been used in numerous studies. Waist circumference has been validated against other ways of measuring abdominal fat, such as computerized tomography, and correlations of 0.84, 0.71 and 0.73, with total, subcutaneous and visceral abdominal fat, respectively, have been found (Sampaio et al., 2007). Percent body fat has also been validated against hydrostatic weighing techniques, and correlations of 0.84, for men, and 0.91, for women, with the three skin-folds used in this study, have been found (Jackson and Pollock, 1985).

On the other hand, correlations among exposure and outcome variables in the original cohort (Grandes et al., 2009) (0.82 for WC and BMI, 0.45 for WC and PBF, 0.56 for BMI and PBF, and −0.11, −0.54, and −0.18 for VO_2max and, respectively, WC, PBF and BMI) were similar to those found in another study (Sui et al., 2007) among individuals 60 year or older, which may indicate consistency in the measuring techniques.

Finally, a sedentary lifestyle, reflected by a low cardiorespiratory fitness, does not generate an increase in body fat on its own, but it does generate a low energy expenditure. The increase in fat mass is produced by an energy imbalance between the calories that are consumed with food and drinks in a certain period of time and those that are spent with all the activities that the body performs in that same period of time, especially physical activity. In this regard, physical activity and diet are two inseparable factors when evaluating the causes of obesity. Food is what provides fat to the body and physical activity is what makes the body to use this fat (negative energy balance = calories spent in activity greater than ingested with food) or stored causing obesity (positive energy balance = calories spent in activity less than ingested with food).

Therefore, it is necessary to take into account the eating patterns, but not so much the type of food as the total number of calories consumed. In this study it is not necessary to calculate the calories of the diet because when we are speaking about a balance between two factors, if one of them decreases (energy expenditure) it is clear that the other has stayed the same, increased or decreased less (energy intake).

5. Conclusions

This study shows that abdominal obesity evolving from poor CRF may be the first missing step in the hypothesis for the evolution from health toward CVD proposed in the introduction. The present data provide evidence that low CRF is a risk factor for developing abdominal obesity. Given that CRF can be increased, either by exercise training or higher lifestyle physical activity levels (Duncan et al., 2005; Dunn et al., 1999), all men and women with a CRF equivalent to a VO_2max < 28.47 and 21.72 ml/kg/min, respectively, might reduce their risk of abdominal obesity and prevent all of its subsequent consequences by increasing the above values through those stated activities.

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