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Title: Fitness attenuates the prevalence of increased coronary artery calcium in individuals with metabolic syndrome.

Authors: Elin Ekblom-Bak[a], Örjan Ekblom[a], Erika Fagman[b], Oskar Angerås[c,d], Caroline Schmidt[d], Annika Rosengren[d], Mats Börjesson[e], Göran Bergström[d].

[a]Åstrand Laboratory of Work Physiology, The Swedish School of Sport and Health Sciences, Stockholm, Sweden.

[b]Department of Radiology, Sahlgrenska Academy, University of Gothenburg and Sahlgrenska University Hospital, Gothenburg, Sweden.

[c]Department of Cardiology, Sahlgrenska University Hospital, Gothenburg, Sweden.

[d]Department of Molecular and Clinical Medicine, Sahlgrenska Academy, University of Gothenburg, and Sahlgrenska University Hospital, Gothenburg, Sweden.

[e]Institute of Neuroscience and Physiology; Department of Food and Nutrition, and Sport Science, University of Gothenburg; Sahlgrenska University Hospital/Östra, Gothenburg, Sweden.

Corresponding author and responsible for requests for reprints:

Elin Ekblom-Bak

Åstrand Laboratory of Work Physiology, The Swedish School of Sport and Health Sciences

Box 5626, 114 86 Stockholm, Sweden.

Telephone number: 0046812053861, E-mail: eline@gih.se

Abstract

Background: The association between cardiorespiratory fitness, physical activity and coronary artery calcium (CAC) are unclear, and whether higher levels of fitness attenuates CAC prevalence in subjects with metabolic syndrome (MetS) is not fully elucidated. The present study aims to a) investigate the independent association of fitness on the prevalence of CAC, after adjustment for moderate-to-vigorous physical activity (MVPA) and sedentary time (SED), and b) study the possible attenuation of increased CAC by a higher fitness, in participants with MetS. *Design:* Cross-sectional.

Methods: In total 678 participants (52% women), 50-65 years, from the SCAPIS pilot study were included. Fitness (VO_2max) was estimated by submaximal cycle ergometer test and MVPA and SED were assessed using hip-worn accelerometers. CAC-score (CACS) was quantified using the Agatston score.

Results: The **odds** of having a significant CACS (≥100) was half in participants with moderate/high fitness compared to their low fit counterparts. Further consideration of MVPA, SED and number of components of the MetS did only slightly alter the effect size. **Those with MetS had 47% higher odds for significant CAC compared to those without MetS. However, moderate/high fitness seems to partially attenuate this risk, as further joint analysis indicated an increased odds for having significant CAC only in the unfit MetS participants.**

Conclusions: Being fit is associated with a reduced risk of having significant CAC in individuals with MetS. While still very much underutilized, fitness should be taken into consideration in everyday clinical risk prediction in addition to the traditional risk factors of the metabolic syndrome.

Introduction

Coronary artery disease (CAD) is a complex process, progressing over many decades, possibly terminating in an acute cardiovascular event. Thus, the detection of CAD, its severity and associated risk prediction are of great clinical importance. Coronary artery calcium (CAC) is a marker that reflects total burden of atherosclerosis in the coronary arteries, and is suggested to be an independent predictor of CAD events and long-time survival.[1, 2] Individuals with clusters of cardiovascular risk factors, such as the metabolic syndrome (MetS), are reported to have an increased progression of CAC over time.[3, 4] CAC is also more prevalent in older age and in men.[5] Clinically, CAC adds predictive power to traditional risk factors, mainly in medium-high risk score patients[6] and is thought to be a marker of a more advanced stage of CAD, compared to carotid intima media thickness.[7]

On the other hand, higher levels of cardiorespiratory fitness (fitness) and physical activity (PA), and low levels of sedentary time (SED), have all been identified as strong correlates to metabolic health the lower risk of CVD morbidity and mortality.[8-11] PA is suggested to act by both improving traditional intermediating CVD risk factors and having an additional effect beyond the traditional risk factors on the burden and progression of atherosclerosis. However, previously reported associations between fitness and/or moderate-to-vigorous PA (MVPA) and CAC are equivocal, with both lower CAC with increasing levels of fitness and PA[12-15], and null-associations or nullified relations after adjusting for conventional CVD risk factors.[16-18] The association between SED and CAC is inconsistent.[15, 19] Also, whether higher levels of fitness attenuates CAC prevalence in subjects with clustering of cardiovascular risk factors is still not fully elucidated.[12]

Accordingly, the present study aim to a) investigate the independent association of fitness with the prevalence of CAC, after taking into consideration objectively assessed

MVPA and SED in a Swedish sample of middle-aged men and women and b) study the possible attenuation of increased CAC, by having a higher fitness, in participants with MetS.

Methods

A sample including 2243 men and women (50-65 years), from low and high socioeconomic status geographical areas, was randomly selected from the census register of the city of Gothenburg, Sweden, for the Swedish CArdioPulmonary bioImage Study (SCAPIS) pilot study. The design and methods of SCAPIS are presented previously.[20] In total 1111 (49.5%) agreed to participate and underwent two days of testing including blood tests, anthropometrics, extensive imaging and functional studies of the heart, lungs and metabolism. The participants performed a submaximal cycle test to estimate cardiorespiratory fitness, completed an extensive questionnaire regarding lifestyle and living conditions and wore an accelerometer for seven days to objectively capture the daily PA pattern. The study was approved by the Umea ethical board (Dnr 2010-228-31M), and all participants provided written informed consent.

Coronary Artery Calcification

CAC was assessed using a state-of-the-art multi-slice computed tomography scanner (Siemens, Somatom Definition Flash, Siemens Medical Solution, Forchheim, Germany). Imaging and analyses were performed using a calcium scoring protocol according to the standardization suggested by McCollough and Agatston.[21, 22] A subset of the subjects (n=84) were imaged using a 100 kV protocol. CAC from these subjects has been recalculated to the standard 120 kV as described in Deprez 2013.[23] The calcium content in each coronary artery was measured and summed and quantified using the Agatston score.[21] An Agatston score ≥ 100 was defined as having significant CAC. This level has previously been demonstrated to

be significantly associated with increased coronary heart disease risk[1] and is considered as a clinically relevant level of CAC. In repeat reading of images from 50 randomly selected subjects, the kappa measure of agreement was 0.91 in identifying subjects with >0 in CACS and 1.00 in identifying subjects with more than 100 in CACS, suggesting an high reproducibility of CAC scoring. CAC score (CACS) was not measured in case of presence of cardiac stent or previous by-pass surgery.

Fitness testing and daily movement pattern

VO_2max (fitness) was obtained by a submaximal cycle ergometer test[24]. The test has high validity as reference to direct measurement (r^2=0.91 SEE: 0.28 $L \cdot min^{-1}$)[24]. To normalize for differences in body size and enable a more correct inter-individual comparison, we used curvilinear, allometric scaling (Y/X^b) over the traditionally used ratio scaling (Y/X) as proposed previously (where Y=VO_2, X=body mass and b=exponent less than 1). The rational for this is that VO_2 increases in proportion to body mass raised to a power less than 1, rather than to in proportion to body mass raised to the power of 1. Several errors arises when using ratio scaling, including penalization of larger subjects and inflation of maximal aerobic capacity scores of lighter subjects.[25] VO_2 scaled to body mass to a power less than 1 seems to minimize these errors, where a body mass exponent of 0.67 have been suggested[26], which is used in the present study. A total of 316 did not perform the fitness test due to a priori exclusion for being diagnosed with heart condition or taking beta-adrenergic blockers, due to the presence of pain complaints (knee, lower back or hip), obesity, perceived inability to perform a test, on-going illnesses or due to malfunction of heart rate monitors or ergometer.

The daily movement pattern was objectively measured by tri-axial ActiGraph accelerometers (model GT3X/GT3X+, ActiGraph LCC, Pensacola, USA) worn during all waking hours for at least 7 consecutive days. ActiLife v.6.10.1 software was used to initialize

the accelerometers (raw data sampling frequency of 30 Hz) and to download and process the collected data (data extracted as 60-s epoch with low frequency extension filter, using the vector magnitude). At least 600 minutes of valid daily monitor wear on at least 4 days was required for inclusion. SED was regarded as intensities between 0 and 199 cpm and MVPA as > 2690 cpm.

The metabolic syndrome

The 2005 AHA/NHLBI MetS criteria was used to classify participants into either having or not having the metabolic syndrome as the presence of three or more of the following[27]: fasting plasma glucose ≥5.5 mmol·l^{-1} or treatment with anti-diabetic drugs or insulin; serum triglycerides≥1.7 mmol·l^{-1} or serum HDL-cholesterol<1.03 mmol·l^{-1} in men and<1.3 mmol·l^{-1} in women or treatment with statins; blood pressure≥130/85 mmHg or antihypertensive drug treatment; or waist circumference≥102 cm in men and≥88 cm in women.

Other measurements

Weight, height and waist circumference were measured.[20] Through self-administrated questionnaire responses, education level was dichotomized into university degree or not and perceived psychosocial stress was divided into four levels. Life exposure to smoking was reported **as pack-year, defined as number of average pack smoked per day multiplied by years of smoking** (10 subjects had missing data, of which two were never smokers and eight ex-smokers, where zero packages per/year were imputed for never smokers and lowest possible package, one per/year, imputed for the ex-smokers). Familiar history of cardiovascular events was defined as having a parent suffering from myocardial infarction or stroke prior to 65 years of age.

Statistical analysis

All continuous variables displayed non-normality using the Shapiro-Wilk test, and presented as proportions or median and 25th-75th percentile (Q1-Q3). Fitness tertiles were computed gender-specific as followed; Women<109.4; 109.4-130.4; >130.4 Men<144.0; 144.0-162.6; >162.6 $ml \cdot min^{-1} \cdot kg^{-0.67}$. Binomial logistic regression modelling was used to assess odds ratios (ORs) with 95% confidence interval (95% CI) for having an Agatston score≥100 in relation to fitness (per fitness tertile and increment in metabolic equivalent=15 $ml \cdot min^{-1} \cdot kg^{-0.67}$) and MetS (prevalence and increment in number of MetS risk factors), respectively (Table 2). The associations were adjusted for age and sex (model 1) and for familiar history of cardiovascular events, educational level, life exposure to smoking, and perceived psychological stress (model 2). In further models, %SED of daily wear time (model 3), %MVPA of daily wear time (model 4) and number of MetS components (model 5) were entered, respectively. To test for possible biological interaction between MetS prevalence and low fitness on significant CACS, an additive model was used to calculated the relative excess risk of interaction (RERI).[28] No gender-specific analyses were performed due to low prevalence of CACS≥100 in women. **Also, no interactions were seen between men-only and gender-combined results in table 2 and figure 1, p≥0.72 for all interaction analyses.** The RERI 95% CI was estimated using modified regression models, revealing evidence of excess risk of interaction if excluding zero. **No apriori sample size calculations have been performed since this is a pilot study**. All analyses were cross-sectional and performed using IBM SPSS (24.0, 2016, SPSS Inc, Chicago, IL).

Results

A total of 795 participants provided valid estimated fitness value. Out of these, 4 had previous history of myocardial infarction or stroke, 10 had no valid CAC score, 88 did not provide

valid accelerometer data, 10 had missing data of one or more of the components of the MetS and 5 had missing data for other covariates. Hence, 678 individuals (52% women) provided data for full sample analyses (table 1).

[Insert table 1]

An inverse linear association between the proportion of men having a CACS≥100 and fitness level was seen with a prevalence of 29.0%, 20.0% and 11.1% of CACS≥100 in the lowest, medium and highest fitness tertile, respectively. Similar relations were seen for women with increasing fitness tertiles, albeit at lower prevalence; 6.9%, 1.7% and 2.5% in the lowest, medium and highest fitness tertile.

Table 2 lists the OR (95%CI) for CACS≥100 with higher tertiles of fitness (upper part of Table) and for individuals with MetS compared to those without (lower part of Table). The **odds** was reduced by half in the high fitness tertile compared to the low, even after adjusting for age, gender, familiar history of cardiovascular events, educational level, life exposure to smoking and perceived stress. MetS prevalence associated with a 72% increase in OR after adjustment for the same variables. In model 3 and 4, introducing continuous variable of % SED of daily wear time did not alter the association neither for fitness nor MetS, but with some reduced associations, and the MetS association becoming non-significant, after adjustment for continuous %MVPA of daily wear time. Introducing numbers of MetS components in the model slightly affected the effect size for fitness, however, still with 43% lower **odds** for CACS≥100 for those in the highest compared to the lowest tertile (non-significant). On the other hand, those having the MetS had 47% increased odds after adjusting for fitness (non-significant).

[Insert table 2]

In joint analysis (Figure 1), participants with moderate/high fitness level and having MetS demonstrated similar OR of CACS≥100 as the reference group with moderate/high fit participants without MetS (1.22; 95%CI 0.53-2.82). However, participants with low fitness having MetS were 2.49 (95%CI 1.23-5.05) times more likely to have a CACS≥100 compared to moderate/high fit without MetS, and did also have a higher odds compared to their unfit counterparts without MetS (1.38; 0.67-2.82). To study if the observed effect of fitness in MetS participants may be mediated by variation in conventional risk factors, the joint analysis was further adjusted for the components of MetS and LDL cholesterol (continuous variables). The effect sizes was only slightly modified with somewhat larger confidence intervals due to the increased number of variables introduced in the model and hence lowered power; No MetS and Moderate/High fitness 1.00 (ref), MetS and Moderate/High fitness OR=1.17 (0.45-3.06), No MetS/Low fitness OR=1.26 (0.59-2.68), MetS/Low fitness OR=2.21 (0.83-5.89). Moreover, a Kruska Wallis ANOVA with pairwise comparisons of continuous variables between the groups revealed borderline significant differences (p=0.043) only in age (median; 56.5 years vs. 59.5 years) and systolic blood pressure (median; 132 vs. 139 mmHg) between participants with MetS and Moderate/High fitness and participants MetS and low fitness. RERI was 0.89 (95% CI -0.91 to 2.70) for the interaction between having both MetS and low fitness.

[Insert figure 1]

Discussion

In a sample of middle-aged men and women, the **odds** of having a significant CACS (≥100) was found to be almost half in participants with moderate/high fitness compared to their low

fit counterparts, even after adjustment for familiar history of cardiovascular events, education level, perceived stress and life exposure to smoking. Further consideration of objectively assessed sedentary time and MVPA as well as adjustment for number of components of the MetS did only slightly alter the effect size. Similar to previous studies[3, 12], those with MetS had 47% increased **odds** for significant CAC. Though, moderate/high fitness seems to **partially** attenuate this risk, as further joint analysis **indicated** an increased **odds** for having significant CAC only in the unfit participants having MetS.

We found a strong association of fitness with the prevalence of increased CAC, even after taking into consideration objectively assessed sedentary time and MVPA. Increased %MVPA was associated with lower OR for having a CACS≥100, while no association was seen for %SED. This suggests that although fitness depends largely on long-term PA habits, fitness contains other aspects and may act through other pathways than MVPA, and that these two measures should be evaluated and considered separately in future analyses. Only in one previous study has self-reported PA been introduced as a confounder when analyzing the importance of high fitness for advanced CAC.[14] Interestingly, in contrast to the present findings, Sung and co-workers found that those engaging in regular exercise ≥3 times per week had a 54% increased risk for advanced CAC score (>75th percentile according to age group) compared to those exercising less than 3 times a week. They suggested that this was due to subjects with known risk factors or coronary prone disease consciously had changed their lifestyle and had become more active, as subjects with diabetes and hypertension in their study were more likely to exercise. The association between fitness and CAC may be complex, and possibly not linear. Indeed, exercise training leading to higher fitness level has previously been proposed to actually increase CAC[17, 29], but that acceleration of CAC induced by exercise training may lead to denser or/and more stable plaques and a subsequent lower CVD risk. This was supported by findings in a study on male marathon runners, where

coronary atherosclerosis was detected in almost 50% of the runners older than 45 years, but where only a minority of those had obstructive CAD and elevated CVD risk.[30] These disparate findings highlight that fitness and exercise habits, as well as comprehensive imaging including calcium content and plaque morphology, should be evaluated in future studies, to further elucidate the relationship between exercise, CAC and subsequent CAD.

This is, to our knowledge, the first study in a European population evaluating the possible attenuation of the presence of significant CAC, by higher fitness level among participants with MetS. Similar to the present findings, Jae and co-workers demonstrated in middle-aged and older South Korean men that having the MetS increased the risk of having a CACS>0, but that higher fitness appeared to offset this risk.[12] In a prospective analysis of a larger sample of the same study cohort (median follow-up 3.6 years), the authors concluded that fitness had a protective effect on the progression of CAC even after adjustment for conventional risk factors at baseline.[31] Also, vigorous PA is shown to reduce incident CAC (going from CACS=0 at baseline to CACS>0 at follow-up) after adjusting for traditional risk factors. Conversely, in a large sample of women (40-90 years) detectable CAC and CACS≥100 were both higher in low fit participants but the relationship was diminished after adjustment for traditional risk factors.[16] Moreover, in young adults (18-30 years) each additional minute of baseline exercise test was associated with a lower hazard of CVD and death after full adjustment at follow-up (26.9 years), however no association with CAC was seen.[17]

The cardioprotective effect of fitness probably acts via multiple mechanistic pathways. Conventional risk factors enhance calcification of the coronary arteries[32], but they may decrease with higher levels of fitness and vigorous PA[16, 17]. As reported, adjustment for traditional risk factors may therefore attenuate or nullify an initial association between fitness and CAC. However, such results are often improperly interpreted and it is commonly stated

that fitness level has no effect on the level of CAC. A more correct interpretation would be that fitness does have an effect, but it is mainly mediated through the conventional risk factors. However, as demonstrated in the present joint analysis and other studies, risk factors or MetS prevalence may not fully explain the distribution of CAC. Hence, other suggested possible cardioprotective mechanisms of fitness include reduction of vascular inflammation, increased shear-stress and enhanced endothelial function, protective effects on the coagulation cascade and a number of mechanisms on cellular and molecular level[33-35], which all may contribute to lower CAC.

Strengths of the present study include the inclusion of a broad population-based sample of men and women from both high and low socioeconomic areas. The use of accelerometers enables for the first time analyses of CAC prevalence in relation to both fitness and objectively assessed SED and MVPA time. Moreover, the separate analyses of fitness and moderate CAC prevalence conducted in participants with and without the MetS provides a more clinically relevant interpretation of the results compared to only adjustment for conventional risk factors. Limitations of the study includes the exclusion of participants not able to perform the fitness test. Moreover, the results of the current study in middle-aged subjects may not be applicable to younger or older age groups. The cross-sectional design of the study limits any conclusions of causality.

In summary, risk stratification for CVD in clinical practice typically involves standard risk scoring based on the presence of traditional risk factors. In addition, CAC has been shown to add to the predictive power of traditional risk factors. **CAC scoring is not recommended for population screening of low risk individuals but has shown promising results in reclassification of intermediate risk individuals.[20]** Fitness is also associated with CVD morbidity and mortality, but is not included in any of the present risk score charts. Therefore the findings of the present study, showing that higher fitness may attenuate the

association between MetS and CAC, is important. From a clinical point of view, it is of value to recognize/identify patients in the lowest-level fitness group, which are thus possible targets for intervention. The results of the present study needs to be confirmed in other age and fitness-groups. While still very much underutilized, fitness should be taken into consideration in everyday clinical risk prediction, in addition to using the traditional risk factors of the MetS.

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Conflict of Interest

The Authors declare that there is no conflict of interest.

Author contributions

EEB, ÖE, AR, MB, GB contributed to the conception or design of the work. EEB, ÖE, EF, OA, CS, MB, GB contributed to the acquisition, analysis, or interpretation of data for the work. EEB and ÖE drafted the manuscript. All authors critically revised the manuscript, gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

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Figure legend

Figure 1. Odds ratio (95% CI) for CACS ≥100 in relation to cross-tabulation of fitness and MetS prevalence. Adjustment made for age, sex, familiar history of cardiovascular events, educational level, life exposure to smoking, perceived psychological stress, % SED of daily wear time and % MVPA of daily wear time.

Table 1. Characteristics of the study population in relation to gender-specific tertiles of fitness (n=678)

	Women			Men		
	Low fitness	Moderate fitness	High fitness	Low fitness	Moderate fitness	High fitness
n	116	119	118	107	110	108
Age (years)	59.3 (54.9-62.5)	57.4 (54.1-61.0)	55.1 (52.4-58.2)	59.5 (55.1-62.7)	57.1 (54.9-61.6)	55.1 (51.8-58.5)
University degree	35%	43%	62%	26%	34%	49%
Life exposure to smoking (pack-year[#])	0.0 (0.0-15.0)	2.0 (0.0-18.9)	0.2 (0.0-7.4)	6.0 (0.0-20.0)	5.0 (0.0-19.1)	0.0 (0.0-5.0)
High perceived stress*	27%	29%	25%	12%	12%	14%
Menopause	72%	77%	64%			
Waist circumference (cm)	97 (89-103)	88 (80-97)	81 (77-86)	102 (98-109)	99 (93-105)	94 (89-99)
Systolic BP (mmHg)	126 (116-135)	119 (110-128)	112 (104-122)	134 (121-145)	126 (118-135)	116 (110-125)
Diastolic BP (mmHg)	73 (69-79)	72 (65-77)	67 (63-75)	79 (74-85)	76 (72-83)	72 (68-77)
Triglycerides (mmol/L)	1.1 (0.8-1.5)	1.0 (0.8-1.4)	0.8 (0.6-1.0)	1.3 (1.0-2.0)	1.1 (0.9-1.7)	1.0 (0.8-1.4)
HDL cholesterol (mmol/L)	1.8 (1.5-2.0)	1.9 (1.6-2.2)	2.2 (1.8-2.4)	1.4 (1.2-1.6)	1.4 (1.2-1.6)	1.6 (1.3-1.8)
LDL cholesterol (mmol/L)	4.0 (3.4-4.5)	3.8 (3.2-4.6)	3.5 (2.9-4.2)	3.9 (3.2-4.6)	3.9 (3.2-4.3)	3.8 (3.2-4.4)

Glucose (mmol/L)	5.5 (5.2-5.8)	5.5 (5.1-5.8)	5.2 (5.0-5.6)	6.0 (5.6-6.6)	5.7 (5.4-6.1)	5.6 (5.3-6.0)
Metabolic syndrome	41%	26%	3%	48%	34%	9%
CACS≥100	7%	2%	3%	29%	20%	11%
Antidiabetics drug treatment	2%	0%	0%	3%	3%	0%
Antihypertensive drug treatment	14%	11%	5%	11%	8%	4%
Statin treatment	8%	3%	1%	6%	8%	4%
% SED of daily weartime	51 (45-60)	50 (45-57)	49 (43-54)	57 (51-63)	55 (49-61)	55 (50-61)
% MVPA of daily weartime	4.8 (3.2-6.6)	5.4 (3.6-7.2)	6.7 (5.3-9.0)	5.1 (2.9-7.5)	5.6 (3.8-7.7)	6.3 (4.8-8.1)
VO_2max (L $O_2 \cdot min^{-1}$)	1.84 (1.67-2.00)	2.10 (1.95-2.22)	2.32 (2.16-2.45)	2.63 (2.44-2.83)	2.99 (2.83-3.22)	3.33 (3.17-3.57)
VO_2max (ml $O_2 \cdot min^{-1} \cdot kg^{-2/3}$)	101 (95-104)	122 (116-125)	141 (136-150)	132 (125-138)	155 (149-159)	176 (168-184)

BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SED, sedentary; MVPA, moderate-to-vigorous physical activity; VO_2max, maximal oxygen uptake

Data presented as proportions or median (Q1-Q3)

[#]Number of average pack smoked per day multiplied by years of smoking; *Constant during last year or longer

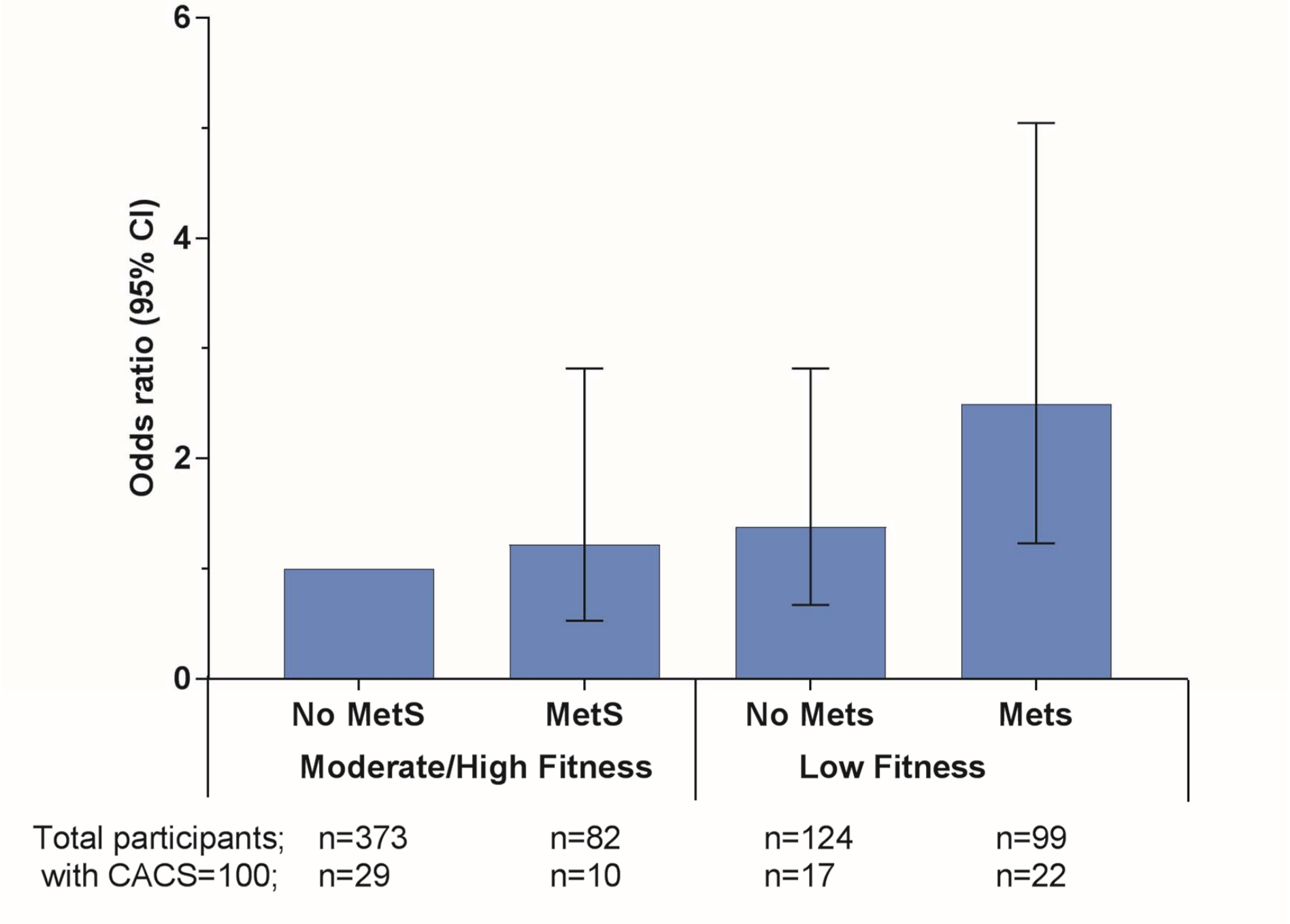
Table 2. Odds ratio (95% CI) for CACS ≥100 in relation to fitness and MetS prevalence

		Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**
	% CACS≥100	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Low Fitness	18% (39/223)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Moderate Fitness	11% (24/229)	0.60 (0.34-1.08)	0.60 (0.33-1.09)	0.60 (0.33-1.10)	0.62 (0.34-1.14)	0.65 (0.35-1.20)
High Fitness	7% (15/226)	0.47 (0.24-0.92)	0.47 (0.23-0.96)	0.47 (0.23-0.98)	0.50 (0.24-1.04)	0.57 (0.26-1.26)
per METs increase		0.82 (0.68-0.99)	0.81 (0.66-1.00)	0.81 (0.66-1.00)	0.83 (0.67-1.02)	0.86 (0.69-1.08)
No MetS	9% (46/497)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
MetS	17% (32/181)	1.82 (1.08-3.07)	1.72 (1.00-2.94)	1.70 (0.99-2.96)	1.67 (0.96-2.89)	1.47 (0.82-2.64)
per MetS component (range 0-5)		1.25 (1.03-1.50)	1.19 (0.98-1.45)	1.19 (0.97-1.45)	1.18 (0.97-1.44)	1.12 (0.91-1.39)

CACS, coronary artery calcium score; MetS, Metabolic syndrome; METs, Metabolic equivalent (1 MET=15 $ml \cdot min^{-1} \cdot kg^{-2/3}$); SED, sedentary; MVPA, moderate-to-vigorous physical activity.

Model 1, Adjusted for age and sex; Model 2, + familiar history of cardiovascular events, educational level, life exposure to smoking, perceived psychological stress; Model 3, + % SED of daily wear time; Model 4, + % MVPA of daily wear time; Model 5, + MetS components or fitness.

Figure 1


6
4
2
0
Odds ratio (95% CI)
No MetS
MetS
No Mets
Mets
Moderate/High Fitness
Low Fitness
Total participants; n=373 n=82 n=124 n=99
with CACS=100; n=29 n=10 n=17 n=22