Original Article

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The association between cardiorespiratory fitness and metabolic syndrome diagnosis: A cross-sectional study in Indonesian middle-aged and older adults

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Abstract

Objectives: The roles of cardiorespiratory fitness (CF) in reducing cardiovascular disease (CVD) and all-cause mortality risks are well established; however, little is known about the role of CF in reducing risk of metabolic syndrome (MetS), a cluster of CVD risk factors, particularly in Asian countries. This research examined associations between CF and MetS diagnosis and its five components in Indonesian middle-aged and older adults. *Methods:* This cross-sectional study included 161 participants (aged 63±8 years; 70% female). CF was assessed with a 6-minute walk test. MetS diagnosis and its components were assessed with the Adult Treatment Panel III. Logistic regression modelling was conducted to examine the relationships between CF and MetS diagnosis and its components, after adjustment for BMI and other confounders. BMI was categorized using cut-points for Asians. *Results:* In adjusted models, participants with low CF had a greater likelihood of being diagnosed with MetS than those with high CF (OR=4.79, 95%CI:2.17-10.62). They were also more likely to have low high-density lipoprotein (OR=2.07, 95%CI:1.02-4.18) or hypertriglyceridemia (OR=2.37, 95%CI:1.15-4.86). There was also borderline significant findings that suggested that participants with low CF had greater likelihood of having abdominal obesity (OR=2.34, 95%CI:0.97-5.65, p=0.06) or hyperglycaemia (OR=2.07 95%CI:0.98-4.41, p=0.06). *Conclusions:* Low CF is associated with increased likelihood of being diagnosed with MetS. The adverse effects of low CF are mainly characterized by dyslipidaemia. Public health messages should emphasise the importance of improving CF for preventing MetS. Assessment of CF could be useful for targeting individuals most likely to benefit from intervention to prevent MetS.

Keywords: abdominal obesity, hyperglycaemia, triglyceride, high density of lipoprotein, hypertension,

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INTRODUCTION

The ageing of populations worldwide is a major contributor to the growing prevalence of metabolic syndrome (MetS) [1], a cluster of interconnected risk factors for cardiovascular diseases (CVD) [2]. MetS is also one of the most prevalent causes of death worldwide [3], particularly among middle-aged and older adult populations. A meta-analyses of studies from Asia, Europe and the US found a 24% increased risk of CVD and 23% increased risk of all-cause mortality among older adults with MetS [1]. In Indonesia, the fourth most populated country in the world, the MetS prevalence is 22% in adults aged ≥40 years [4], who comprise 34% of its population [5]. Based on global trends over the last four decades [1], mortality rates associated with MetS are expected to increase substantially in Indonesia. When combining the adverse consequences associated with MetS with its high prevalence, it appears that MetS will continue to be a serious public health concern in middle-aged and older adults in Indonesia and the world.

The increased prevalence of MetS parallels the global increase in obesity incidence [2,5], which is in line with the growing scientific literature showing that abdominal obesity is the primary trigger for most MetS pathogenesis pathways [6]. Individuals with low cardiorespiratory fitness (CF) are also more likely than those with high CF to develop CVD [7] and are at an increased risk of CVD mortality [8]. Obesity and CF have been recognized as independent risk factors for CVD and all-cause mortality [9]. New evidence, however, indicates a fit-fat paradox [10], in which obese individuals with CF may not present with the expected negative health risk factors associated with CVD usually experienced by individuals with a normal body mass but low CF [11]. Moreover, some research suggests that high CF may be health protective, regardless of obesity status [7], indicating that CF may be a stronger predictor than obesity of health outcomes like MetS.

CF is most accurately assessed using a maximal exercise test, to measure the highest rate of oxygen consumption attainable during maximal or exhaustive exercise (VO2max) [12]. Its application in practice, however, is limited due to the high cost of the equipment required and the need for trained personnel. A simpler approach, the 6-min walk test (6MWT), thus, is often used to assess CF in middle-aged and older adults [13]. The American Thoracic Society released the 6MWT guidelines in 2002 [14]. The test is a submaximal exercise test that involves measurement of the distance walked by individuals over 6 minutes [14], a distance that reflects the physical capacity of individuals to perform routine tasks. The 6MWT is often preferred over direct, maximal exercise tests due to its low cost, safety, and acceptance by participants, including those who are deconditioned, older, or frail [15]. Indeed, this test has been used as a predictor of morbidity and mortality associated with cardio-pulmonary diseases [16-18]. However, use of the 6MWT in predicting metabolic-related diseases such as MetS is limited. The evidence to date suggests that MetS patients perform poorly on the 6MWT [19] and that improvements over time in performance on this test are associated with reductions in the use of the anti-diabetic drug biguanid among MetS patients [20].

MetS diagnosis is one measure of CVD and all-cause mortality risks [2]. However, there are reasons for examining individual MetS components as well [1]. First, it has been shown that these components are better predictors of all-cause mortality than a MetS diagnosis [21]. Second, there may be different or opposing effects of obesity and CF with individual components of MetS [22]. However, the associations between these exposures and risks of MetS and its components have not been reported for Asian populations using the recommended body mass index (BMI) cut-points for Asian populations [23]. A lower BMI cut-point for obesity is suggested for Asian populations, as evidence suggests that the risk of CVD is elevated at a substantially lower BMI level than the World Health Organization cut-point for Caucasians [23]. The aim of the current study was, after adjusting for BMI using the Asian cut-points, to examine the associations between CF (measured with the 6MWT) with MetS and its individual components in middle-aged and older adults in Indonesia.

METHODS

Participants and protocol

This study was a cross-sectional study conducted in April 2019. Members of two community services (n=200) that offered health services to middle-aged and older adults in Yogyakarta City, Indonesia were purposively sampled. The inclusion criteria were being aged >45 years and having no mental or physical impairments that hindered participation, assessed subjectively in person. To recruit participants, community leaders announced during a monthly service at their site that members were invited to participate in the research by attending data collection at the next monthly service. Participants provided informed consent prior to their participation. The study protocol was approved by the Institutional Review Board of Human Ethics Committee of Gadjah Mada University (approval number: KE/0142/02/2019).

Measures and data collection

The outcomes were a MetS diagnosis (yes/no) and the presence (yes/no) of MetS component abnormalities (hyperglycemia, hypertriglyceridemia, low high-density lipoprotein (HDL), hypertension, and abdominal obesity). In accordance with criteria of the National Cholesterol Education Program Adult Treatment Panel III [24], abnormalities were defined as: (1) fasting plasma glucose ≥110 mg/dl, for hyperglycemia; (2) triglycerides ≥150 mg/dl, for hypertriglyceridemia; (3) HDL <50 mg/dl for women and <40 mg/dl for men, for low HDL; (4) blood pressure ≥130/85 mmHg, for hypertension; and (5) waist ≥88 cm for women and 102 cm for men, for abdominal obesity [24]. A MetS diagnosis was defined as having three or more abnormalities. Research assistants measured participants' blood pressure using the Nova Presameter Riester sphygmomanometer (Germany) with the auscultatory method in the seated position. Nurse phlebotomists established a place in the community hall for drawing blood samples through venipuncture at the median cubital vein. Blood draws took place in the morning, after participants had fasted for at least 10 hours overnight. The blood samples were then transported to a private laboratory for analysis. Fasting plasma glucose was analyzed using the hexokinase method. High-density lipoprotein level was analyzed using the homogeneous assays, and triglycerides level was analyzed using the enzymatic assay of glycerol-3-phosphate oxidase with spectrophotometry.

Predictors

Body mass index and waist circumference

The research assistants measured weight to the nearest 0.1 kg with the Omron HBF-375 scale (Japan) and height to the nearest 0.1 cm with the portable Seca 213 stadiometer (Estonia). Participants were barefoot and wore light clothing. BMI was calculated by dividing weight (kg) by height (m) squared, and categorized using recommended cut-points for Asians [23]: low to normal body mass (<23.5), overweight (23.5-27.5), and obese (>27.5) [23]. Waist circumference was measured with a multipurpose retractable tape measure (not branded) to the nearest 1.0 cm and at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest. Participants were in a standing position at the end of an expiration phase.

Cardiorespiratory fitness

CF was assessed with the 6MWT. The test measures the distance that participants can quickly walk on a flat, hard surface in 6 minutes [14]. The walk was self-paced; thus, it assessed a submaximal level of functional capacity [14]. The test was selected because it may better reflect the functional ability to engage in daily physical activities because most activities of daily living are performed at submaximal levels of exertion, and the time of the test may better reflect activities of daily living compared to other walking tests (i.e., 2- and 12-minute tests) [14,17]. Moreover, the test has been widely used as a predictor of morbidity and mortality [16,18]. The test also has demonstrated good reliability and validity. The test-retest reliability of 6MWT is high (ICC=0.88-0.91) [25], and the test has moderate to high correlations with measures of physical functioning: with functional capacity as assessed by the Duke Activity Status Index (r=0.50, p<0.001), with the Physical Function subscale of the Short Form 36 (r=0.62, p<0.001) [26], and with maximum oxygen uptake (r=0.54, p<0.001) [27].

Prior to conducting the 6MWT, the research assistants prepared six 30-meter flat, hard surface lanes outdoors and used two cones to mark the turnaround points in each lane. Cones were also placed in 10-meter increments in the lanes. Participants wore comfortable, appropriate clothing and footwear for walking and rested for at least 15 minutes before taking the test. In each test batch, the research assistants assigned each of six participants a bib number and a lane, and they instructed participants to walk as far as possible for 6 minutes, to stop when needing to rest (chairs were provided), and to self-pace. For each minute of the test, they yelled out encouragement, using phrasing from the American Thoracic Society guideline [14]. At the end of the test, the research assistants marked each participant's last position and recorded the distance travelled. Each participant completed the test once, and all participants were new to test procedures. Scores on the 6MWT were categorized into high (≥ median) and low (below median) because there are no established methods of classification for Asian populations.

Demographic characteristics

Participants were given a paper-based questionnaire packet to complete on their own. It contained questions about age, sex, marital status, education level, employment status and smoking status.

Data Analysis

Participants with and without MetS were initially compared on all study variables using Pearson's chi-square test. Next, a series of logistic regression models were computed to examine bivariate and multivariable associations between the predictor variables of interest (CF and BMI) and the outcomes (MetS diagnosis and its five components). Multivariable models included these predictor variables and demographic characteristics that were associated with the respective outcome in bivariate models ($p<0.05$). Age and gender were included in all models because previous studies have shown that they are associated with MetS and 6MWT [13,26,28,29]. Data were analyzed using SPSS® v25.0 (SPSS Inc., Chicago, IL, US). A p-value <0.05 represented statistical significance.

RESULTS

In total, 161 participants (mean age=62.7±7.9 years) completed data collection (response rate=81%). Of these, 35% (n=56) were diagnosed with MetS. Table 1 shows that most participants were women, married, lacking tertiary education, non-smokers, and unemployed or retired. No significant differences were found in these characteristics between participants with and without MetS except for a borderline significant difference in the proportion that were male ($p=0.07$). This finding may have reached significance in a larger sample. More participants with MetS than without MetS were obese ($p=0.002$) and had low CF ($p<0.001$).

Figure 1 illustrates the number and the proportion of participants with and without MetS who had each MetS component abnormality. The proportions of participants with abdominal obesity, hyperglycaemia, low HDL, hypertriglyceridemia or hypertension were higher in participants with MetS than in those without MetS ($p<0.001$). Of participants with MetS, 55% had three abnormalities, 34% had four, and 11% had five. Among these participants, hypertension was the most frequent abnormality, followed by elevated triglycerides level. Of participants without MetS, 19% had no abnormalities, 39% had one, and 2% had two.

Table 2 shows the results of modelling the association between CF and BMI with a MetS diagnosis. In multivariable modelling, participants with low CF were more likely than those with high CF to have a MetS diagnosis ($p<0.001$) and to have two of its components, low HDL ($p=0.04$) and hypertriglyceridemia ($p=0.02$). Also, the associations between CF and abdominal obesity ($p=0.06$) and hyperglycemia($p=0.06$) were borderline significant. Notably, in a bivariate model the association between CF and abdominal obesity was significant ($p=0.004$). In multivariable modelling, participants who were obese were more likely than those at a low/normal BMI to be diagnosed with MetS ($p=0.001$) and two of its components, hypertriglyceridemia ($p=0.008$) and hypertension ($p=0.04$). BMI was not used to predict abdominal obesity because, as expected, it was highly correlated with abdominal obesity ($r=0.76$).

Table 1. Characteristics of participants with and without a metabolic syndrome diagnosis

Characteristics	Total (n=161) n (%)	Metabolic Syndrome		p-value
		With (n=56) n (%)	Without (n=105) n (%)	
Sex				
Female	112 (70)	44 (79)	68 (65)	0.07
Male	49 (30)	12 (21)	37 (35)	
Age (years)				
46-65	82 (51)	26 (46)	56 (53)	0.42
65-81	79 (49)	30 (54)	49 (47)	
Marital status				
Married	117 (73)	38 (68)	79 (75)	0.32
Not married/widowed	44 (44)	18 (32)	26 (25)	
Highest education level				
Primary/secondary	92 (57)	34 (61)	58 (55)	0.36
Tertiary	69 (43)	22 (39)	47 (45)	
Employment status				
Employed	17 (11)	7 (13)	10 (10)	0.56
Unemployed/retired	144 (89)	49 (88)	95 (90)	
Smoking status				
Non-smoker	152 (152)	52 (93)	100 (95)	0.53
Smoker	9 (6)	4 (7)	5 (5)	
Body mass index				
<23.5 (low/normal)	47 (29)	10 (18)	37 (35)	0.002
23.5-27.5 (overweight)	69 (43)	21 (45)	48 (46)	
>27.5 (obese)	45 (28)	25 (47)	20 (19)	
Cardiorespiratory fitness				
Low (below median of 475)	79 (49)	41 (73)	38 (36)	<0.001
High (≥475)	82 (51)	15 (27)	67 (64)	

p-value derived from the Pearson Chi-Square test.

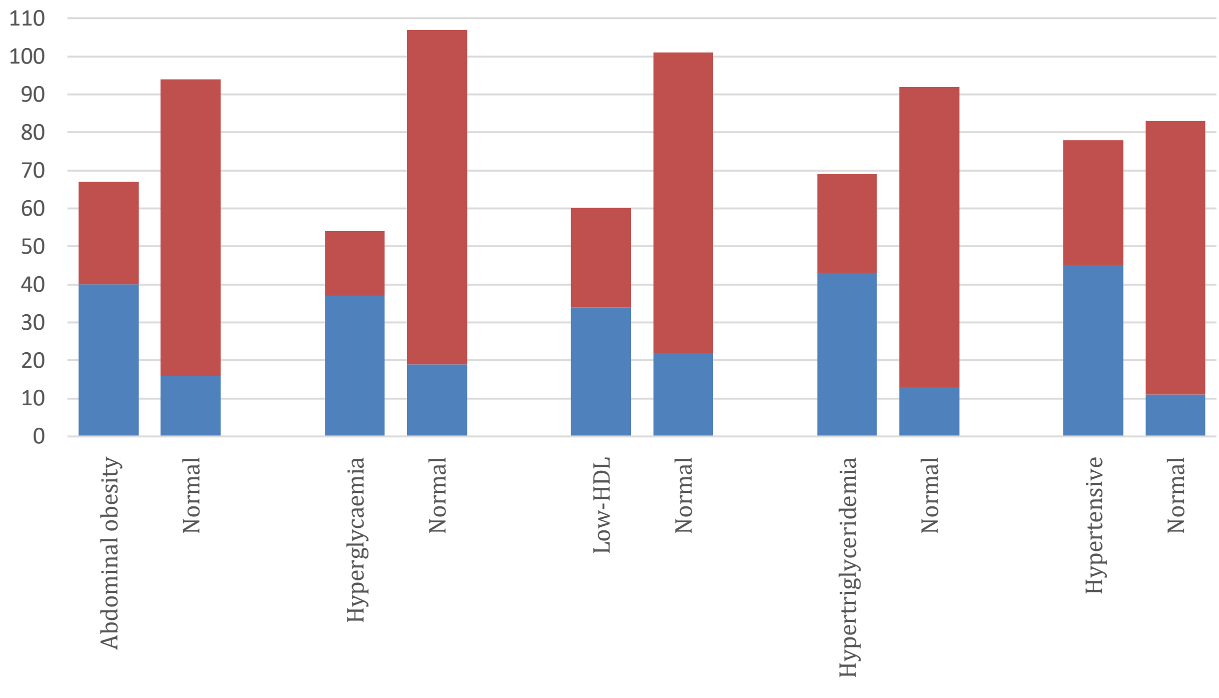

Figure 1. The proportion of participants with abnormalities.

Table 2. Associations between cardiovascular fitness and body mass index with metabolic syndrome diagnosis and abnormalities

Indicator	Category	Bivariate models		Multivariable models[1]	
		OR	95%CI	OR	95%CI
Metabolic Syndrome					
Cardiorespiratory fitness	High (ref)	1.00		1.00	
	Low	**4.82**	**2.36-9.83**	**4.79**	**2.17-10.62**
Body mass index	<23.5 (ref)	1.00		1.00	
	23.5-27.5	1.62	0.68-3.85	1.66	0.66-4.21
	>27.5	**4.62**	**1.86-11.53**	**5.26**	**1.94-14.30**
Abdominal obesity					
Cardiorespiratory fitness	High (ref)	1.00		1.00	
	Low	**2.59**	**1.36-4.93**	2.34	0.97-5.65
Hyperglycemia [2]					
Cardiorespiratory fitness	High (ref)	1.00		1.00	
	Low	1.66	0.86-3.21	2.07	0.98-4.41
Body mass index	<23.5 (ref)	1.00		1.00	
	23.5-27.5	0.96	0.43-2.17	0.87	0.38-1.99
	>27.5	1.89	0.80-4.45	1.85	0.77-4.45
Low high-density lipoprotein					
Cardiorespiratory fitness	High (ref)	1.00		1.00	
	Low	**2.02**	**1.06-3.88**	**2.07**	**1.02-4.18**
Body mass index	<23.5 (ref)	1.00		1.00	
	23.5-27.5	0.80	0.37-1.69	0.73	0.33-1.61
	>27.5	0.90	0.39-2.07	0.76	0.32-1.82
Hypertriglyceridemia					
Cardiorespiratory fitness	High (ref)	1.00		1.00	
	Low	1.87	1.00-3.53	**2.37**	**1.15-4.86**
Body mass index	<23.5 (ref)	1.00		1.00	
	23.5-27.5	2.13	0.96-4.73	2.06	0.92-4.60
	>27.5	3.27	1.37-7.79	**3.30**	**1.37-7.95**
Hypertension					
Cardiorespiratory fitness	High (ref)	1.00		1.00	
	Low	1.77	0.95-3.31	1.42	0.71-2.84
Body mass index	<23.5 (ref)	1.00		1.00	
	23.5-27.5	0.90	0.42-1.90	1.03	0.47-2.24
	>27.5	2.04	0.89-4.69	**2.56**	**1.05-6.20**

[1] All multivariate models adjusted for age and sex. [2] Multivariable model also adjusted for smoking status. bold - denotes significant difference to reference group (p<0.05).

DISCUSSION

Our findings suggest that CF is associated with a MetS diagnosis and with some of its components in middle-aged and older Indonesians, after adjusting for BMI. The BMI cut-points were those recommended for Asian populations [23]. The study was in response to findings suggesting that the association between CF and MetS is influenced by ethnicity [1,2], whilst studies conducted in Asia are lacking.

The most notable findings were that after adjusting for age and sex, participants with low CF were almost five times more likely than those with high CF to have a MetS diagnosis, and those who were obese were five times more likely than those who had a low or normal body mass to have this diagnosis. These findings are consistent with significant inverse associations between both CF and BMI with a MetS diagnosis reported in previous studies [11,28,30]. Findings from a recent US study showed that the most fit participants were over 20 times less likely to have MetS compared with the least fit, in modeling not adjusted for BMI [30]. Similarly, findings from a Korean study showed that men and women in the highest tertile of BMI but lowest tertile of CF were 19 times and 8 times, respectively, more likely to be diagnosed with MetS than the respective men and women in the lowest tertile of BMI and highest tertile of CF [28]. A study of older adults in Finland showed that men and women with the lowest CF were 10 and 11 times, respectively, more likely of having MetS compared to their counterparts with the highest CF. Differences in estimates among studies could be attributed to differences in CF and BMI cut-points used, sample sizes, and measures of CF [30,31]. Regardless, the current study's findings contribute to the literature showing strong associations between CF and a MetS diagnosis and add that strong associations are also found in an Asian country after Asian-specific cut-points for BMI are used.

Our findings also showed that after adjusting for BMI, age and sex, participants with low CF were twice as likely to have a low HDL level or an elevated triglycerides level, compared with those who had high CF. This increased likelihood of dyslipidemia supports findings reported previously [32,33]. A study of healthy men, aged 25-74 years, in the US and Canada showed that high CF was associated with lower triglycerides levels and higher HDL levels, after adjustment for age, visceral and subcutaneous fat [32]. Likewise, a study in Finland of men and women aged 25-64 years showed that high CF was associated with these MetS abnormalities after adjusting for abdominal obesity [33]. Our study contributes to this research by demonstrating that the adverse effect of low CF on MetS is mainly due to dyslipidemia in a general population of Indonesian middle-aged and older adults.

In bivariate modeling, we found a significant association between low CF and having abdominal obesity, but only a borderline significant association after adjustment for age and sex. Our findings support that of a Canadian study of adults aged 25-59 years [34]. In that study participants with high CF had lower levels of abdominal obesity than those with low CF, at any given level of BMI, after adjusting for sex. Our findings also support those of a study in post-menopausal South Asian women in which women with high CF had significantly lower waist circumference and total abdominal tissue compared to women with low CF [35]. In post-hoc bivariate regression modeling, being female increased the likelihood of having abdominal obesity [OR=4.77, 95%CI 2.12-10.76, $p<0.001$]. Since women have higher percentages of body fat than men for any given BMI level, women are more susceptible to abdominal obesity, with postmenopausal women, the majority of our participants, are at highest risk of experiencing the abnormality [36]. This could also explain why we had more women than men with abdominal obesity (54% vs 18%). Further study is needed to clarify whether sex modifies the association between CF and abdominal obesity.

We also found a borderline significant association between low CF and having hyperglycemia, after adjustment for age and sex. For our study we followed the criteria of the National Cholesterol Education Program Adult Treatment Panel III [24] for designation of hyperglycemia. As a result, cases of hyperglycemia included both diabetics and pre-diabetics, with pre-diabetics not usually having any signs or symptoms [37], including deterioration in CF. Approximately one fourth of participants (28%) were pre-diabetics with hyperglycemia, and their inclusion as cases of hyperglycemia could have attenuated the association between CF and hyperglycemia. To test whether their inclusion was attenuating the findings, post-hoc we reclassified hyperglycemia cases as only including diabetics, and in this new analysis, participants with low CF were significantly more likely to have hyperglycemia than were participants with high CF ($p<0.01$). This finding supports the finding from a US study of adults aged 20-90 years of a significant inverse association between CF and fasting plasma glucose in men [38].

The increased likelihood of MetS in participants with low CF in this study supports findings from studies that used maximal exercise testing [30,31], studies of younger population [39] and with longitudinal studies [7]. Notably, we report lower overall 6MWT scores compared to those reported in studies conducted in South and North America [29] and the published reference norms for Western populations [40]. Because no norms have been published for Asian populations, we are unable to compare our results to the norms of comparable populations. Also noteworthy is that we conducted the 6MWT once, due to time and resource limitations, not twice, as recommended [14]. It is possible that this protocol contributed to low 6MWT performance because a learning effect increases 6MWT performance [14]. Due to this limitation, future research for identifying the 6MWT performance threshold for MetS prevention and risk identification is needed.

Our results must be interpreted in light of other limitations as well. First, our study was a cross-sectional study; thus, causation could not be inferred from our findings. Second, although participants displayed a variety of demographic characteristics, they were all healthy, communitydwelling middle-aged, and predominantly female and older adults, which limits the generalizability of the results to other populations, most notably younger populations and the growing nursing-home population. Third, our modest sample size did not enable us to examine dose-response relationships and interactions between CF and BMI, nor stratify our analyses by sex.

In conclusion, our study shows that low CF, characterized by poor 6MWT performance, increases the likelihood of being diagnosed with MetS or dyslipidemia conditions related to MetS (i.e., low HDL and elevated triglycerides). The overall findings, thus, emphasize the importance of improving CF for preventing MetS in middle-aged and older adults. Furthermore, in clinical practice, the 6MWT may be a feasible measure for identifying patients who would likely benefit from lifestyle interventions to prevent MetS, which is particularly important in developing countries such as Indonesia, where health care resources are limited.

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COMPETING INTERESTS

The authors declare no competing interests.

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