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Original Article

Is the Metabolic Syndrome Associated with Cardiovascular Disease, Diabetes Mellitus, and Increased Physical Limitations in an Elderly Population if Multiple Chronic Illnesses are Taken into Consideration?

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SUMMARY

Background: The concept of metabolic syndrome (MetS) was initially designed for long-term outcome prediction in middle aged or younger individuals, but it is unclear whether MetS can be applied in older people. We explored the clinical utility of MetS for prediction of various outcomes in older people. First, we investigated whether MetS is associated with CVD and DM in the short term. Second, we took multiple chronic illnesses into consideration to examine whether MetS is associated with increased physical limitations.
Methods: Participants were selected from the "Social Environment and Biomarkers of Aging Study, 2000" and the "2003 Survey of Health and Living Status of the Middle-Aged and Elderly in Taiwan" aged ≥65 years for whom complete data were available. A total of 543 older Taiwanese were included.
Results: For older people who had MetS compared to those without the syndrome in 2000, the risk of CVD was 1.94 times higher in 2003 ($p < 0.01$) and that of DM was 3.02 times higher in 2003 ($p < 0.01$) after controlling for age, sex, and chronic illnesses. Hierarchical regression models of physical functions showed that MetS did not increase the explained variance in physical functional limitations.
Conclusions: MetS has short-term (3 years) effects on CVD and DM. After taking chronic illnesses into consideration, no association between MetS and physical functioning was obvious. More studies are needed to clarify the relationship among MetS, chronic illnesses, and physical functioning.

1. Introduction

The metabolic syndrome (MetS) is generally characterized as a clustering of abnormal blood lipid levels, impaired fasting glucose, elevated blood pressure, and obesity[1]. The term MetS is used to identify people who are at higher risk of cardiovascular disease (CVD) and diabetes mellitus (DM)[2]. Results from cross-sectional studies have shown that MetS prevalence increases dramatically with age[3]. The prevalence ranges from 5.2% in those aged 20–29 years to 36.5% in those aged 70–79 years in Taiwan[4]. These results imply that MetS is an important issue for older populations. However, the concept of MetS was initially designed for long-term prediction of CVD or DM in middle-aged or younger individuals[5]. If this approach was applied to older people, two problems could occur. First, aging per se is associated with increased incidence and prevalence of CVD, DM, and other chronic illnesses. Approximately 70% of older Taiwanese have one or more chronic illnesses, for whom medications and lifestyle changes are primary treatment approaches. For those who already have CVD or DM, there is no further recommendation for additional MetS diagnosis. Thus, the concept of MetS is only applicable to older people without chronic illnesses. Even for elderly individuals without chronic illnesses, owing to their limited life expectancy, use of long-term predictors might not be suitable for this population.

Some researchers have claimed that, in addition to predicting CVD and DM, MetS is associated with a decline in physical functions. For example, obesity, one of the features of MetS, is independently and directly related to mobility and functional declines[6]. High levels of glucose might cause microvascular impairment in some people with MetS and worsen their physical functions[7]. Empirical studies have shown that MetS is associated with physical functional dependence in elderly populations[8–11]. Blazer et al claimed that MetS might be a risk factor for mobility decline in

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older people[8]. After excluding stroke patients, Roriz-Cruz et al found that MetS was significantly associated with ADL and IADL dependence in older people[9]. Thus, the concept of MetS seems to be suitable for predicting physical functional decline in older people. However, none of these studies took into consideration other chronic illnesses, such as arthritis or hip fracture, that might impair physical functions. Studies with a higher degree of statistical control over chronic illnesses are needed to clarify the association between MetS and functional decline in older populations.

In general, the clinical value of MetS in older populations is unclear[12]. Considering the limited life expectancy of older people, we used short-term follow-up data to investigate the clinical utility of MetS in older people. First, we examined whether MetS is associated with CVD and DM. Second, we examined the correlation between MetS and physical functions. In addition to CVD and DM, we simultaneously considered multiple chronic illnesses related to functional limitations to investigate whether MetS is associated with increased physical limitation in older Taiwanese individuals.

2. Methods

The data were taken from The Social Environment and Biomarkers of Aging Study (SEBAS, 2000)[13] and The Survey of Health and Living Status of the Middle-Aged and Elderly in Taiwan (TLSA, 2003)[14]. Both SEBAS and TLSA included face-to-face interviews to gather data on demographics, physical functioning, and history of chronic illnesses. SEBAS also included a medical examination and measurement of biomarkers to supplement the interview data. SEBAS was approved by the institutional review board at the National Institute of Family Planning in Taiwan.

People aged ≥ 65 years with blood sample in 2000, history of chronic diseases, and complete data on mobility, activities of daily living (ADL) and instrumental activities of daily living (IADL) were included in this study. Among the SEBAS participants, 559 were ≥ 65 years and were followed up in TLSA. Of these, 15 were excluded from our study owing to insufficient data (1 for waist circumference in 2000, 7 for mobility in 2000, 1 for ADL in 2000, 5 for IADL in 2000, 2 for mobility in 2003). Thus, 543 older Taiwanese (215 females) were eligible for our study. The average age was 73.9 ± 5.4 years (range 65–98 years).

2.1. Metabolic syndrome

The presence of MetS at baseline was assessed according to NCEP ATP-III with modified criteria on waist circumference for Asians[15]. There are five components in the definition: abdominal obesity (waist circumference ≥ 90 cm in men, ≥ 80 cm in women), elevated triglycerides ($\geq$150 mg/dL), low high-density lipoprotein cholesterol (<40 mg/dL in men, <50 mg/dL in women), elevated blood pressure (systolic blood pressure $\geq$ 130 mmHg or diastolic blood pressure $\geq$ 85 mmHg, or on antihypertensive drug treatment), and elevated fasting glucose ($\geq$ 100 mg/dL or on drug treatment for elevated glucose). A diagnosis of MetS is made if at least three criteria are met.

2.2. Physical functional indexes

Physical functioning was assessed in terms of mobility, ADL, and IADL. All items were rated on a scale from 0 (no problem) to 3 (cannot perform alone). Mobility was assessed in terms of subjective difficulties in various physical tasks using nine items (e.g., squatting, walking 200–300 m). ADL relates to subjective difficulties in meeting various personal care needs and was assessed using six items (e.g., eating, going to the toilet). IADL relates to subjective difficulties in various activities necessary for maintaining a living environment. It was assessed using six items (e.g., buying personal items, traveling by bus). Composite variables were constructed to create a mobility score (range of 0–27), an ADL score, and an IADL score (range of 0–18 for both). Higher scores correspond to greater limitations in physical functioning.

2.3. Self-reported history of chronic illness

Eight out of the 14 conditions listed in the interview questionnaire for history of chronic illnesses were selected from the top 10 leading causes of death in Taiwan: cancer or malignant tumor, stroke (cerebral hemorrhage), CVD, DM, liver or gall bladder disease, kidney disease, and lower respiratory tract disease. The remaining six conditions on the list are likely to cause considerable physical discomfort, including: arthritis or rheumatism, hip fracture, cataracts, gout, and a bone spur.

3. Results

The MetS prevalence was 40.7% in the cohort. Table 1 lists data on sex, age, prevalence of chronic illnesses, and physical functioning for the study participants. On average, each participant had 2.2 chronic diseases before 2000. Only 81 of the participants had no chronic illness in 2000. The prevalence significantly differed between participants with and without MetS for CVD in 2000 ($\chi^2 = 19.88$, $p < 0.001$) and DM in 2000 ($\chi^2 = 70.72$, $p < 0.001$). Most of the participants with MetS also had chronic illnesses. The mean baseline physical functional scores in 2000 were 4.44 ± 5.38 for mobility, 0.17 ± 1.17 for ADL, and 1.66 ± 3.10 for IADL. There

Table 1
Characteristics of the study sample in 2000 and 2003.

	Year 2000			Year 2003		
	MetS	Non-MetS		MetS	Non-MetS	
Participants (n)	221	322				
Female (%)	56.6	28.0**	$\chi^2 = 44.85$			
Age (y)	74.18 ± 5.56	73.73 ± 5.24	$t = -0.97$			
Mobility	5.73 ± 6.22	3.56 ± 4.53**	$t = 4.72$	6.68 ± 6.93	5.58 ± 6.51**	$t = 4.51$
ADL	0.34 ± 1.80	0.05 ± 0.29*	$t = 2.92$	0.85 ± 2.97	0.66 ± 2.67	$t = 1.84$
IADL	2.28 ± 3.75	1.23 ± 2.48**	$t = 3.91$	3.03 ± 4.80	2.37 ± 4.38**	$t = 3.91$
CVD (%)	61.1	41.6**	$\chi^2 = 19.88$	69.2	47.2**	$\chi^2 = 25.83$
DM (%)	31.2	4.6**	$\chi^2 = 70.72$	33.9	6.5**	$\chi^2 = 67.68$
Other chronic illness (%)[a]	72.4	71.4	$\chi^2 = 0.06$	81.4	74.5	$\chi^2 = 3.58$

*$p < 0.01$; **$p < 0.001$.
ADL = activities of daily living; CVD = cardiovascular disease, including high blood pressure, heart disease, and stroke; DM = diabetes mellitus; IADL = instrumental activities of daily living; MetS = metabolic syndrome.
[a] Other chronic illnesses included cancer or malignant tumor, liver or gall bladder disease, kidney disease, lower respiratory tract disease, arthritis or rheumatism, hip fracture, cataracts, gout, and a spinal or vertebral spur.

Table 2
Multivariate-adjusted hazard ratio (95% confidence interval) for the metabolic syndrome in relation to incident CVD, stroke and DM over 3 years of follow-up.

	Incident CVD		Incident DM	
	Model 1	Model 2	Model 1	Model 2
Age	1.04 (1.00–1.09)*	1.04 (1.00–1.09)*	1.01 (0.94–1.07)	1.01 (0.94–1.07)
Sex	1.30 (0.84–2.01)	1.10 (0.70–1.73)	1.22 (0.61–2.45)	0.93 (0.45–1.93)
CVD in 2000	14.72 (9.53–22.73)***	14.10 (9.11–21.83)***	1.13 (0.56–2.26)	0.99 (0.49–2.02)
DM in 2000	1.28 (0.69–2.37)	0.95 (0.50–1.83)	104.78 (49.04–223.83)***	79.58 (36.72–172.47)***
Other chronic illnesses in 2000[a]	1.00 (0.62–1.59)	1.03 (0.64–3.15)	0.67 (0.32–1.42)	0.68 (0.32–1.46)
MetS in 2000		1.94 (1.20–3.15)**		3.02 (1.44–6.36)**

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
CVD = cardiovascular disease, including high blood pressure, heart disease, and stroke; DM = diabetes mellitus; MetS = metabolic syndrome.
[a] Other chronic illnesses included cancer or malignant tumor, liver or gall bladder disease, kidney disease, lower respiratory tract disease, arthritis or rheumatism, hip fracture, cataracts, gout, and a spinal or vertebral spur.

Table 3
Standardized coefficients of hierarchical regression for mobility, ADL, and IADL in 2003.

Dependent variable	Mobility 2003		ADL 2003		IADL 2003	
	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
Sex	0.23***	0.22***	0.01	0.01	0.21***	0.20***
Age	0.23***	0.23***	0.17***	0.17***	0.30***	0.30***
CVD at 2000	−0.01	−0.02	−0.02	−0.02	−0.01	−0.01
DM at 2000	0.22***	0.21***	0.18***	0.17***	0.20***	0.19***
Other chronic illnesses in 2000[a]	0.10*	0.10*	0.01	0.01	0.02	0.02
MetS		0.04		0.01		0.03
Total R square	0.19	0.19	0.05	0.05	0.18	0.18

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
ADL = activities of daily living; CVD = cardiovascular disease, including high blood pressure, heart disease, and stroke; DM = diabetes mellitus; IADL = instrumental activities of daily living; MetS = metabolic syndrome.
[a] Other chronic illnesses included cancer or malignant tumor, liver or gall bladder disease, kidney disease, lower respiratory tract disease, arthritis or rheumatism, hip fracture, cataracts, gout, and a spinal or vertebral spur.

were significant differences between participants with and without MetS for mobility ($p < 0.001$), ADL ($p < 0.05$), and IADL ($p < 0.001$). Participants without MetS had less physical functional limitations at baseline. Only 66 (14.8%) of the participants had no chronic illness in 2003. The mean score for the overall sample was 6.68 ± 6.93 for mobility, 0.85 ± 2.97 for ADL, and 3.03 ± 4.80 for IADL. There were significant differences between participants with and without MetS in the prevalence of chronic illnesses, mobility, and IADL.

Table 2 shows the multivariate-adjusted hazard ratio for MetS in relation to CVD and DM in 2003. Age is strongly associated with CVD, but is weakly or not associated with DM. After controlling for age, sex, and chronic illnesses in 2000, the risk of developing CVD in 2003 was 1.94 times higher in participants with MetS compared to those without MetS in 2000 ($p < 0.01$). The result for DM was similar. The DM hazard ratio in 2003 was 3.02 in participants who had MetS in 2000 ($p < 0.01$).

Hierarchical regression models of physical functioning are presented in Table 3. The models show that age and DM in 2000 can significantly predict mobility, ADL, and IADL in 2003 (all $p < 0.001$). Other chronic illnesses in 2000 can significantly predict mobility in 2003 ($p < 0.05$), but not ADL and IADL. After controlling for age, sex, and chronic illnesses in 2000, MetS did not increase the explained variance in mobility, ADL, and IADL in 2003.

4. Conclusions

According to our results, MetS cannot be used to predict the incidence of CVD or DM in the short term. The utility of MetS should be more feasible in predicting physical functional decline. However, our results show that MetS was associated with CVD and DM three years after the identification. After considering function-impairing chronic illnesses, we did not find any significant association between MetS and physical functional limitations. Most studies of MetS predicting CVD and DM looked at an interval of more than 10 years. To the best of our knowledge, only one study explored the relationship between MetS and the incidence of CVD and other chronic diseases in the short term, and no correlation between MetS and CVD was found in non-diabetic older people[16]. Since older people without diabetes have relatively healthier lifestyle, the study sample might not be a good representation of the entire older population. The external validity of the study is limited. We used a nationally representative sample and statistically controlled for the presence of chronic illnesses. The results show that MetS is associated with CVD and DM in older Taiwanese individuals. Therefore, MetS in older people is still worthy of attention.

Some previous studies have shown an association between MetS and physical functional dependence in older people. However, none of these studies took other function-impairing chronic illnesses into consideration. According to our results, DM has salient effects on physical functioning. Older people with diabetes not only have more limited mobility, but also have more difficulties in self-care. Other chronic illnesses limit only mobility and not self-care abilities. After controlling for chronic illnesses, we found hardly any association between MetS and physical functional limitations. Therefore, in terms of preventing disabilities, the effects of chronic illnesses should be considered more seriously.

Ideally, the use of older people without CVD or DM as a study population could produce more powerful evidence to clarify the association between MetS and CVD or DM. However, only a small proportion of the elderly do not have CVD or DM. In the present study, only 246 (45.3%) participants were without CVD and DM, and among them, only 63 (25.6%) met the MetS criteria. The low sample number and uneven distribution might diminish the power of the findings in this study. Furthermore, older people without CVD or DM might have different lifestyles from those who have CVD or DM. A rigorous sampling strategy would lower the external validity and there would be more limitations in applying the study results. We controlled for the presence of CVD and DM to maintain the representativeness of the sample statistically. The results show that MetS is associated with CVD and DM over a period of 3 years. In other words, if older people meet the MetS criteria, they have a significantly higher chance of developing CVD or DM within 3 years. Therefore, active intervention to prevent CVD and DM is warranted for older people with MetS.

According to our results, MetS has a weak or no association with physical functional limitations after controlling for chronic illnesses. The results do not support a direct correlation between MetS and functional decline in older people. The findings seem to imply that a complex relationship exists among MetS, chronic illnesses, and physical functioning. More research is needed to clarify the association between MetS, chronic illnesses, and functional decline, and to explore the underlying mechanisms.

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