Metabolic Syndrome in Patients With First-ever Ischemic Stroke: Prevalence and Association With Coronary Heart Disease

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Abstract

Background: Most studies of metabolic syndrome (MetS) and coronary heart disease (CHD) have been carried out in the general population, and their association among stroke patients has been rarely explored. We seek to describe the prevalence of MetS among patients with acute ischemic stroke and to assess its association with CHD.

Methods: This hospital-based study included 1851 patients with first-ever acute ischaemic stroke (mean age 61.2 years, 36.5% women) who were hospitalized into two university hospitals in Shandong, China (January 2016-February 2017). Data were collected through interviews, physical examinations, and laboratory tests. MetS was defined following the National Cholesterol Education Program (NCEP) criteria, the International Diabetes Federation (IDF) criteria, and the Chinese Diabetes Society (CDS) criteria. CHD was defined according to clinical and electrocardiogram examinations. Binary logistic regression was performed to determine the associations between MetS and CHD.

Results: The overall prevalence of MetS was 34.0% by NECP criteria, 47.8% by IDF criteria, and 32.9% by CDS criteria. The prevalence of MetS decreased with age and was higher in women than men ($p<0.05$). Abdominal obesity, high blood pressure, high triglycerides, and low HDL-C were significantly associated with CHD (multi-adjusted OR range: 1.27-1.43, $p<0.05$). Compared with those without MetS, the multi-adjusted OR (95% CI) of CHD associated with MetS defined by the NECP criteria, IDF criteria, and CDS criteria was 1.29 (1.04-1.59), 1.46 (1.20-1.78), and 1.29 (1.05-1.59), respectively. In addition, having 1-2 abnormal components (vs. none) was associated with CHD (OR range: 1.63-1.73, $p<0.05$).

Conclusions: MetS affects over one-third of patients with first-ever ischemic stroke. MetS is associated with an increased likelihood of CHD in stroke patients, but treating MetS as a binary entity would underestimate its association with CHD.

Introduction

The metabolic syndrome (MetS), characterized by a constellation of multiple interrelated cardiometabolic risk factors, has become a major concern for public health [1, 2]. Currently, several criteria are proposed to define MetS such as the US National Cholesterol Education Program (NCEP) criteria [3], the International Diabetes Federation (IDF) criteria [4], and the Chinese Diabetes Society (CDS) criteria [5]. Thus, the prevalence of MetS varies across studies and even in the same population, depending on the defining criteria [6].

The associations between MetS and cardiovascular diseases have been well studied in the general population. A systematic review and meta-analysis of 87 population-based prospective studies showed that MetS was associated with an increased risk of cardiovascular diseases, myocardial infarction, stroke, and cardiovascular mortality [7]. We previously reported that MetS was associated with coronary heart disease (CHD), stroke, and cardiovascular multimorbidity among Chinese older adults living in a rural area [6]. So far, evidence is scarce with regard to the relationship between MetS and CHD among patients with ischemic stroke.

Ischemic stroke and CHD are common circulatory disorders among adults and share major common etiological factors (e.g., smoking, hypertension, and high cholesterol) and pathophysiological mechanisms (e.g., atherosclerosis) [8, 9]. However, evidence also suggests that the two entities show differences in risk factors, pathologies, incidence, mortality, and prognosis in the general population [10–12]. As the worldwide leading causes of disability and death, CHD and ischemic stroke together have a great impact on public health [13, 14]. CHD is the leading cause of death following acute ischemic stroke [15]. A large-scale register-based study in Sweden showed that around 50% of the men with both stroke and coronary disease died from coronary heart disease (e.g., myocardial infarction and sudden coronary death) [10]. Thus, dentifying risk factors for CHD among stroke patients is crucial to reduce their risk of coronary events and improve the prognosis.

In this hospital-based study of patients with first-ever acute ischemic stroke, we seek to describe the prevalence of MetS and to assess its association with CHD.

Methods

Study design and population

Data were obtained from the baseline survey of a hospital-based intervention study, the Multimodal Behavioral Intervention Study in Stroke, which is an ongoing randomized controlled multimodal intervention study in two hospitals, i.e., the Shandong Jining No. 1 People's Hospital and the Jining Medical University Affiliated Hospital, Shandong, China [16]. The recruitment and baseline survey of participants was conducted from January 2016 to February 2017. In total, 2205 patients with first-ever acute ischaemic stroke who were hospitalized into the above two hospitals were recruited based on the inclusion criteria similar to those specified in the China National Stroke Registry Protocol [17]: (a) first-ever ischemic stroke or transient ischemic attack (TIA); (b) age ≥ 40 years; (c) patients, family or caregivers can provide consent; (d) others (e.g., direct admission based on physician evaluation or arrival through the emergency department, and confirmed by brain CT or MRI within 14 days after the onset of symptoms). Of the 2205 participants, we excluded 354 patients who had insufficient information to define MetS, leaving 1851 patients (83.9%) for the current analysis.

Data collection

Following the structured questionnaire, data were collected through interviews, clinical and neurological examinations, psychological testing, and laboratory tests by trained nurses, physicians, and technicians from the two hospitals. Epidemiological data were collected via a questionnaire that was developed from the WHO STEPwise approach to Surveillance (STEPS) and the Study on Global Ageing and Adult Health (SAGE) [18, 19].

MetS and its components

Waist circumference was measured at a point midway between the lowest rib and the iliac crest in a horizontal plane using nonelastic tape. After at least a 5-min rest, arterial blood pressure was measured in the sitting position on the right arm using an electronic sphygmomanometer (HEM-7127J, Omron Corporation, Kyoto, Japan) with the cuff maintained at the heart level. Blood pressure was measured three times on one occasion, and the mean of the three readings was used in the analysis. After an overnight fast, peripheral blood samples were taken at the hospital. Fasting plasma glucose (FPG), triglycerides, and high-density lipoprotein cholesterol (HDL-C) were measured using an automatic Biochemical Analyser (Olympus AU-400, Olympus Optical Company, Tokyo, Japan) at the laboratory of the hospitals that is licensed by the local authority.

MetS were defined according to three criteria: the NCEP criteria [3], the IDF criteria [4], and the CDS criteria [5] (Table 1).

Table 1
Three sets of defining criteria for the metabolic syndrome

Traits	NCEP criteria (at least three traits) [3]	IDF criteria (at least three traits) [4]	CDS criteria (at least three traits) [5]
Waist circumference	Men ≥ 102 cm; Women ≥ 88 cm	Chinese men ≥ 85 cm; Chinese women ≥ 80 cm	Chinese men ≥ 90 cm; Chinese women ≥ 85 cm
Blood pressure	≥ 130/85 mmHg or use of antihypertensive drugs	≥ 130/85 mmHg or use of antihypertensive drugs	≥ 130/85 mmHg or use of antihypertensive drugs
Fasting plasma glucose	≥ 6.1 mmol/L or use of antidiabetic drugs	≥ 5.6 mmol/L or use of antidiabetic drugs	≥ 6.1 mmol/L or use of antidiabetic drugs
Triglycerides	≥ 1.7 mmol/L or use of lipid-lowering drugs	≥ 1.7 mmol/L or use of lipid-lowering drugs	≥ 1.7 mmol/L or use of lipid-lowering drugs
High density lipoprotein cholesterol	Men < 1.04 mmol/L, women < 1.29 mmol/L or use of lipid-lowering drugs	Men < 1.04 mmol/L, women < 1.29 mmol/L or use of lipid-lowering drugs	< 1.04 mmol/L or lipid-lowering drugs

NCEP National Cholesterol Education Program, *IDF* International Diabetes Federation, *CDS* Chinese Diabetes Society

Definition of CHD

CHD was defined by senior neurologists via clinical and neurological examinations following the current national guidelines. We ascertained CHD cases via a discharge diagnosis of CHD and a t-wave change on the electrocardiogram.

Covariates

The covariates included age, sex, education, and lifestyles (e.g., smoking, alcohol drinking, physical activity, and dietary). Education was categorized into 4 groups: illiteracy (no education), primary school (1–6 years of education), middle school (7–9 years of education), and high school and above (≥ 10 years of education). Smoking status was categorized as no smoking and ever smoking. Alcohol consumption was defined as drinking alcohol more than once per month during the past year. Physically inactive was defined as selfreported of having not participated in any physical activity during leisure time. Information on dietary habits was collected on the frequency of vegetables or fruits and categorized into daily versus less than daily consumption.

Statistical analysis

The characteristics of study participants were compared between men and women with Student t-test for continuous variables and chi-square test for categorical variables. Due to the skewed distribution, triglycerides were logarithmized before the comparison between men and women. Because around 73.3% of the participants had missing values on waist circumference, a linear regression model ($R^2 = 17\%$, $p < 0.001$) was used to predict and impute the waist circumference based on body mass index and demographic data, as previously reported [20]. The age- and sex-specific prevalence was graphed for MetS and CHD. Binary logistic regression analysis was performed to estimate the odds ratio (OR) and 95% confidence interval (CI) of CHD associated with MetS and its components while adjusting for age, sex, education, smoking, alcohol drinking, physical activity, and dietary habits.

The IBM SPSS Statistics 25 for Windows (IBM SPSS Inc., Chicago, Illinois, USA) was used for all analyses.

Results

The mean age of the 1851 participants was 61.2 (SD 9.7) years and 36.5% women. Compared with men, women were older, less likely to be educated, smoke, drink alcohol, had higher level of waist circumference, systolic blood pressure, blood glucose, triglycerides, and HDL-C, had lower level of diastolic blood pressure (all $p < 0.01$) (Table 2). There was no significant sex difference in the prevalence of physical inactivity and daily eating fruits and vegetables ($p > 0.10$).

Table 2
Characteristics of participants by sex

Characteristics*	Total (n = 1851)	Men (n = 1176)	Women (n = 675)	*P*
Age (years), mean (SD)	61.2 (9.7)	60.1 (9.5)	63.1 (9.7)	< 0.001
Education, n (%)				< 0.001
Illiteracy	476 (26.7)	125 (11.1)	351 (53.8)	
Primary School	463 (26.0)	306 (27.1)	157 (24.0)	
Middle School	501 (28.1)	398 (35.2)	103 (15.8)	
High School and Above	343 (19.2)	301 (26.6)	42 (6.4)	
Ever smoking, n (%)	841 (45.4)	795 (67.6)	46 (6.8)	< 0.001
Alcohol drinking, n (%)	611 (35.6)	594 (56.8)	17 (2.5)	< 0.001
Physically inactive, n (%)	533 (28.9)	326 (27.8)	207 (30.8)	0.176
Daily eating fruits and vegetables, n (%)	1659 (90.3)	1049 (89.8)	610 (91.0)	0.391
Waist circumference (cm), mean (SD)	81.7 (6.7)	82.4 (6.6)	80.6 (6.6)	< 0.001
Systolic blood pressure (mmHg), mean (SD)	140.8 (16.6)	139.7 (16.9)	142.9 (16.0)	< 0.001
Diastolic blood pressure (mmHg), mean (SD)	81.7 (11.3)	82.6 (11.5)	80.1 (10.8)	< 0.001
Blood glucose (mmol/l), mean (SD)	6.1 (2.3)	5.9 (2.2)	6.4 (2.5)	< 0.001
Triglycerides (mmol/l), median (IQR)	1.3 (0.9–1.8)	1.2 (0.9–1.8)	1.4 (1.0-1.9)	0.004
HDL-C (mmol/l), mean (SD)	1.2 (0.4)	1.1 (0.4)	1.2 (0.4)	< 0.001

SD standard deviation, *IQR* interquartile range, *HDL-C* high density lipoprotein cholesterol

*The number of missing values was 68 for education, 135 for alcohol drinking, 5 for physical activity, 13 for diet, 51 for waist circumference, 27 for blood pressure, 26 for blood glucose, 34 for triglycerides, 51 for HDL-C.

Figure 1 shows the age- and sex-specific prevalence of MetS defined by three criteria. The overall prevalence of MetS was 34.0% by NECP criteria, 47.8% by IDF criteria, and 32.9% by CDS criteria. For each criteria, women had a higher prevalence than men at each age group, and the sex difference disappeared after the age of 75 years. The prevalence of MetS decreased with age overall and for both men and women.

The overall prevalence of CHD among patients with ischemic stroke was 41.0% (48.0% in women; 37.0% in men, $p < 0.05$). The prevalence increased from 34.0% in those aged 40–54 years old, 39.3% in those aged 55–64 years old, 46.8% in those aged 65–74 years old, to 51.2% in those aged ≥ 75 years old, and the prevalence increased with age for both men and women (Fig. 2). The prevalence of CHD was higher in women than in men across all age groups.

In the total sample, abdominal obesity, high blood pressure, high triglycerides, and low HDL-C were significantly associated with CHD (OR ranged from 1.27 to 1.43), however, there was no significant association between high blood glucose and CHD (Table 3). The MetS defined by three criteria was associated with an increased likelihood of CHD, with the adjusted OR ranging from 1.29 to 1.46 ($P < 0.05$). When the analysis was stratified by sex, abdominal obesity, high blood pressure, high triglycerides, and MetS defined by IDF criteria was significantly associated with an increased likelihood of CHD in men, whereas among women, abdominal obesity, high triglycerides, low HDL-C, and MetS defined by all three criteria were associated with CHD.

Table 3
The associations of metabolic syndrome and its individual components with coronary heart diseases in patients with acute ischemic stroke

Metabolic syndrome	**Total sample (n = 1851)**			**Men (n = 1176)**			**Women (n = 675)**		
and individual components*	No. of patients	No. of CHD cases	OR (95% CI)#	No. of patients	No. of CHD cases	OR (95% CI) #	No. of patients	No. of CHD cases	OR (95% CI) #
Abdominal obesity									
No	1185	455	1.00 (Ref)	861	307	1.00 (Ref)	324	148	1.00 (Ref)
Yes	610	284	1.43 (1.15–1.77)	280	118	1.45 (1.09–1.94)	330	166	1.42 (1.03–1.96)
High blood pressure									
No	413	143	1.00 (Ref)	295	90	1.00 (Ref)	118	53	1.00 (Ref)
Yes	1419	616	1.36 (1.08–1.72)	868	347	1.51 (1.13–2.01)	551	269	1.14 (0.75–1.72)
High blood glucose									
No	993	391	1.00 (Ref)	674	245	1.00 (Ref)	319	146	1.00 (Ref)
Yes	844	366	1.14 (0.94–1.38)	492	190	1.15 (0.90–1.48)	352	176	1.14 (0.83–1.56)
High triglycerides									
No	1221	480	1.00 (Ref)	805	294	1.00 (Ref)	416	186	1.00 (Ref)
Yes	607	277	1.38 (1.12–1.70)	362	143	1.31 (1.00-1.72)	245	134	1.50 (1.08–2.09)

HDL-C high density lipoprotein cholesterol, *CHD* coronary heart disease, OR odds ratio, *CI* confidence interval, *NCEP* National Cholesterol Education Program, *IDF* International Diabetes Federation, *CDS* Chinese Diabetes Society

*The individual components were defined according to the IDF criteria.

#Controlled for age, education, smoking, alcohol drinking, physical activity, and dietary, and if applicable, for sex.

Metabolic syndrome	**Total sample (n = 1851)**			**Men (n = 1176)**			**Women (n = 675)**		
Low HDL-C									
No	855	323	1.00 (Ref)	642	231	1.00 (Ref)	213	92	1.00 (Ref)
Yes	957	427	1.27 (1.04–1.55)	515	202	1.18 (0.92–1.52)	442	225	1.49 (1.06–2.10)
NCEP criteria									
No	1203	467	1.00 (Ref)	845	310	1.00 (Ref)	358	157	1.00 (Ref)
Yes	619	284	1.29 (1.04–1.59)	316	123	1.16 (0.88–1.54)	303	161	1.50 (1.08–2.06)
IDF criteria									
No	957	354	1.00 (Ref)	698	245	1.00 (Ref)	259	109	1.00 (Ref)
Yes	878	406	1.46 (1.20–1.78)	469	192	1.40 (1.08–1.80)	409	214	1.62 (1.16–2.24)
CDS criteria									
No	1228	481	1.00 (Ref)	817	297	1.00 (Ref)	411	184	1.00 (Ref)
Yes	602	273	1.29 (1.05–1.59)	348	137	1.20 (0.92–1.58)	254	136	1.47 (1.06–2.04)

HDL-C high density lipoprotein cholesterol, *CHD* coronary heart disease, OR odds ratio, *CI* confidence interval, *NCEP* National Cholesterol Education Program, *IDF* International Diabetes Federation, *CDS* Chinese Diabetes Society

*The individual components were defined according to the IDF criteria.

#Controlled for age, education, smoking, alcohol drinking, physical activity, and dietary, and if applicable, for sex.

Furthermore, we categorized all participants into three groups according to the number of abnormal MetS components that were defined by each of the three MetS criteria, i.e., 0 (reference), 1–2, and ≥ 3 components. In the total sample, compared to patients without abnormality in any of the five MetS components, having 1–2 and ≥ 3 abnormal MetS components was significantly associated with an increased likelihood of CHD (Table 4). There was no statistical interaction of MetS with sex on CHD. However, when the analysis was stratified by sex, the results showed that for, the for having 1–2 and ≥ 3 abnormal MetS components (vs. none) defined both NCEP and IDF criteria was significantly associated with an elevated likelihood of CHD in men, but not in women. When MetS components were defined by the CDS criteria, having ≥ 3 abnormal components (vs. none) was signifivcantly associated with an increased likelihood of CHD in both men and women (Table 4).

Table 4
The associations between number of metabolic syndrome components and coronary heart diseases in patients with acute ischemic stroke

	Total sample (n = 1851)			Men (n = 1176)			Women (n = 675)		
No. of MetS components	No. of patients	No. of CHD cases	OR (95% CI)*	No. of patients	No. of CHD cases	OR (95% CI)*	No. of patients	No. of CHD cases	OR (95% CI)*
NCEP criteria									
0	150	44	1.00 (Ref)	124	33	1.00 (Ref)	26	11	1.00 (Ref)
1–2	1102	447	1.63 (1.12–2.39)	738	285	1.85 (1.20–2.85)	364	162	1.18 (0.52–2.68)
≥3	599	274	1.97 (1.32–2.94)	314	122	1.97 (1.22–3.17)	285	152	1.70 (0.74–3.89)
IDF criteria									
0	125	34	1.00 (Ref)	106	27	1.00 (Ref)	19	7	1.00 (Ref)
1–2	875	334	1.63 (1.07–2.50)	615	225	1.77 (1.10–2.84)	260	109	1.37 (0.50–3.70)
≥3	851	397	2.37 (1.54–3.65)	455	188	2.39 (1.46–3.90)	396	209	2.29 (0.86–6.11)
CDS criteria									
0	169	48	1.00 (Ref)	122	33	1.00 (Ref)	47	15	1.00 (Ref)
1–2	1108	458	1.73 (1.20–2.48)	716	272	1.76 (1.14–2.72)	392	186	1.78 (0.91–3.49)
≥3	574	259	2.08 (1.41–3.05)	338	135	2.02 (1.26–3.24)	236	124	2.32 (1.16–4.64)

CHD coronary heart disease, *OR* odds ratio, *CI* confidence interval, *NCEP* National Cholesterol Education Program, *IDF* International Diabetes Federation, *CDS* Chinese Diabetes Society

*Controlled for age, sex, education, smoking, alcohol drinking, physical activity, and dietary, and if applicable, for sex.

Discussion

Summary of findings

MetS affects around one-third to a half of patients with ischemic stroke, depending on the defining criteria for MetS, which ranged from 32.9% by CDS criteria and 34.0% by NECP criteria to 47.8% by IDF criteria. CHD was present in 41.0% of the stroke patients. The prevalence of both MetS and CHD was higher in women than in men, and the prevalence of CHD increased with age but the prevalence of MetS slightly decreased with age. In addition, MetS was associated with increased likelihood of CHD in patients with ischemic stroke. Notably, compared to patients without any of the five MetS components, having even 1–2 abnormal components is associated with a higher likelihood of CHD, especially among male patients.

Compared with other studies

In our study, the prevalence of MetS defined by IDF criteria was 47.8% among patients with ischemic stroke, which was in line with the report from another study of stroke patients in China (51.3%) [21]. However, our prevalence was lower than that in Polish stroke patients (61.2%) based on the same criteria [22]. The difference might be due to the higher proportion of women in Polish study participants than ours (57.6% vs. 36.5%) because women are more likely to have MetS than men. We found that women had a higher prevalence of MetS than men across all age groups. This was consistent with the previous studies [2, 22, 23]. The sex difference might be primarily attributable to the higher levels of MetS components (e.g., waist circumference, systolic blood pressure, blood glucose, and triglycerides) in women than in men. In addition, the prevalence of MetS decreased with age in both men and women. This implies the importance of control MetS and special focus should be paid to young and middle-aged patients and women. This was different from the previous studies, which reported an increasing prevalence with age in young or middle-aged people [24] but a relatively stable prevalence with age in older adults [6, 25]. The decreasing prevalence of MetS with age may be explained by the age-related metabolic and pathophysiological changes, due to which the levels of some components of MetS, e.g., waist circumference, diastolic blood pressure, and serum cholesterol, are not increasing with age, especially in old age [26].

Stroke patients have increased risk of long-term fatal CHD after stroke or transient ischemic attack, and CHD is highly prevalent in patients with ischemic stroke [27]. We found that CHD was present in 41.0% of the patients with ischemic stroke. This is in line with the previous studies, which showed that the prevalence of carotid stenosis of any degree was around 45% in stroke patients [28, 29]. It remains debatable whether MetS is a good predictor of cardiovascular events [30]. The major concern is that defining MetS as a binary entity might have limited prediction of cardiovascular events [31]. In patients with type 2 diabetes, the MetS defined by IDF criteria is unable to identify the patients with the highest risk for CHD [32]. Indeed, our study showed that having even 1–2 abnormal MetS components was associated with CHD. This implies that treating MetS as a binary entity (< 3 abnormal compoments as a reference group) could underestimate the association of MetS with CHD. Our findings of the MetS-CHD associations among patients with ischemic stroke were consistent with those from the general elderly population living in the same area [6]. However, very few studies have investigated the association between MetS and CHD in stroke patients, which limits the comparison of our results with the literature.

Explanation of the associations

The underlying pathways linking MetS with CHD could be that MetS is associated with endothelial dysfunction and inflammation, which are key pathophysiologic features of atherosclerosis [33]. Atherosclerosis plays a key role in CHD through several critical processes in the pathogenesis of atherosclerosis (e.g., lipid accumulation, intimal thickening and fibrosis, vascular inflammation, remodeling, and plaque rupture or erosion) [34]. In addition, the ulceration of atherosclerotic plaques is very important in coronary occlusion [35]. Our analysis showed that having more components was linearly associated with an increased likelihood of CHD. This suggests that multiple individual MetS components may have an accumulative effect on the atherosclerotic process and increase the likelihood of CHD, which is in line with previous studies [36].

Strengths and limitations

This hospital-based study includes a relatively large sample of patients with first-ever ischemic stroke who were mostly from the rural areas (26.7% illiteracy) of the southwest of Shandong province, a less developed region compared to the eastern coastal areas. In addition, trained staff and clinicians performed comprehensive assessments on a range of health-related factors and health conditions, which allowed us to make a more valid definition of MetS and CHD. However, this study also has limitations. First, because the study participants were recruited from local two university hospitals (tertiary hospitals), the patient sample might not be representative of the patient population. This should be kept in mind when generalizing our study findings. Second, a considerable proportion (73.3%) of participants had missing data on waist circumference, and an imputed waist circumference based on age, sex, and body mass index was used instead. However, this approach has previously been validated in terms of correct classification of abdominal obesity (88.4%) and cardiometablic risk (91.5% in men and 99.5% in women) [20], thus, any bias from the missing waist circumference is likely to be minimal. Finally, the cross-sectional nature of the study design does not allow us to determine the causal relationship between MetS and CHD, and the cross-sectional association might be subject to survival bias that usually leads to underestimation of the true associations.

Conclusions

Our study suggested that MetS affects around one-third to a half of patients with acute ischemic stroke, depending on the defining criteria for MetS, and that CHD was present in over 40% of the stroke patients. MetS is associated with an increased likelihood of CHD, but treating MetS as a binary entity may underestimate its association with CHD.

Abbreviations

MetS: Metabolic syndrome; NCEP: National Cholesterol Education Program; IDF: International Diabetes Federation; CDS: Chinese Diabetes Society; CHD: Coronary heart disease; TIA: Transient ischemic attack; STEPS: WHO STEPwise approach to Surveillance; SAGE: Study on Global Ageing and Adult Health; FPG: Fasting plasma glucose; HDL-C: High-density lipoprotein cholesterol; OR: Odds ratio; CI: Confidence interval.

Declarations

Ethics approval and consent to participate

The study protocols were approved by the Ethics Committee at Jining Medical University, Shandong, China (No. 2015B006). Written informed consent was obtained from all participants, or in case of cognitively impaired persons, from informants, usually the next-of-kin (spouse or children). Research within this project had been conducted according to the principles expressed in the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available from the corresponding authors upon reasonable request and approval.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Concept and design of the study: YL, ZY, YH, ZZ, YD, JD, BB, and CQ. Execution: ZY, YH, PW, ZZ, and BB. Statistical analysis: YL and QW; Writing of the manuscript: YL and CQ. Critical revision of the manuscript and approval of the final versions for submission: all authors.

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References

1. Church TS, Thompson AM, Katzmarzyk PT, et al. Metabolic syndrome and diabetes, alone and in combination, as predictors of cardiovascular disease mortality among men. Diabetes Care. 2009;32:1289–94.
2. Gu D, Reynolds K, Wu X, et al. Prevalence of the metabolic syndrome and overweight among adults in China. Lancet. 2005;365:1398–405.
3. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP). Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA. 2001;285:2486–97.
4. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009;120:1640-5.
5. Chinese Diabetes Society. Guideline for Prevention and Treatment of Type 2 Diabetes in China. Chin J Diabetes Mellitus. 2018;10:4–67.
6. Liang Y, Yan Z, Song A, et al. Metabolic syndrome and cardiovascular disease in elderly people in rural china: a population-based study. J Am Geriatr Soc. 2013;61:1036–8.
7. Mottillo S, Filion KB, Genest J, et al. The metabolic syndrome and cardiovascular risk a systematic review and meta-analysis. J Am Coll Cardiol. 2010;56:1113–32.
8. Puddu P, Puddu GM, Bastagli L, et al. Coronary and cerebrovascular atherosclerosis: two aspects of the same disease or two different pathologies? Arch Gerontol Geriatr. 1995;20:15–22.
9. Soler EP, Ruiz VC. Epidemiology and risk factors of cerebral ischemia and ischemic heart diseases: similarities and differences. Curr Cardiol Rev. 2010;6:138–49.
10. Wilhelmsen L, Köster M, Harmsen P, et al. Differences between coronary disease and stroke in incidence, case fatality, and risk factors, but few differences in risk factors for fatal and non-fatal events. Eur Heart J. 2005;26:1916–22.
11. Agmon Y, Khandheria BK, Meissner I, et al. Relation of coronary artery disease and cerebrovascular disease with atherosclerosis of the thoracic aorta in the general population. Am J Cardiol. 2002;89:262–7.
12. Leening MJG, Cook NR, Franco OH, et al. Comparison of Cardiovascular Risk Factors for Coronary Heart Disease and Stroke Type in Women. J Am Heart Assoc. 2018;7:e007514.
13. GBD Compare Data Visualization. Seattle WA: Institute for Health Metrics and Evaluation (IHME), University of Washington; 2016.
14. Ervasti J, Virtanen M, Lallukka T, et al. Permanent work disability before and after ischaemic heart disease or stroke event: a nationwide population-based cohort study in Sweden. BMJ Open. 2017;7:e017910.
15. Gunnoo T, Hasan N, Khan MS, et al. Quantifying the risk of heart disease following acute ischaemic stroke: a meta-analysis of over 50,000 participants. BMJ Open. 2016;6:e009535.
16. Bai B, Yan Z, Hao Y, et al. A randomised controlled multimodal intervention trial in patients with ischaemic stroke in Shandong, China: design and rationale. Lancet. 2017;390:13.

17. Wang Y, Cui L, Ji X, et al, China National Stroke Registry Investigators. The China National Stroke Registry for patients with acute cerebrovascular events: design, rationale, and baseline patient characteristics. Int J Stroke. 2011;6:355–61.
18. World Health Organization. The STEPS Instrument and Support Materials. Available at: https://www.who.int/ncds/surveillance/steps/instrument/en/. Accessed 5 Dec 2020.
19. Kowal P, Chatterji S, Naidoo N, et al. Data resource profile: the World Health Organization Study on global AGEing and adult health (SAGE). Int J Epidemiol. 2012;41:1639–49.
20. Bozeman SR, Hoaglin DC, Burton TM, et al. Predicting waist circumference from body mass index. BMC Med Res Methodol. 2012;12:115.
21. Mi D, Jia Q, Zheng H, et al. Investigators for the Survey on Abnormal Glucose Regulation in Patients with Acute Stroke Across China ACROSS-China. Metabolic syndrome and stroke recurrence in Chinese ischemic stroke patients–the ACROSS-China study. PLoS One. 2012;7:e51406.
22. Brola W, Sobolewski P, Fudala M, et al. Metabolic Syndrome in Polish Ischemic Stroke Patients. J Stroke Cerebrovasc Dis. 2015;24:2167–72.
23. Mabry RM, Reeves MM, Eakin EG, et al. Gender differences in prevalence of the metabolic syndrome in Gulf Cooperation Council Countries: a systematic review. Diabet Med. 2010;27:593–7.
24. Villegas R, Xiang YB, Yang G, et al. Prevalence and determinants of metabolic syndrome according to three definitions in middle-aged Chinese men. Metab Syndr Relat Disord. 2009;7:37–45.
25. He Y, Jiang B, Wang J, et al. Prevalence of the metabolic syndrome and its relation to cardiovascular disease in an elderly Chinese population. J Am Coll Cardiol. 2006;47:1588–94.
26. Qiu C. Preventing Alzheimer's disease by targeting vascular risk factors: hope and gap. J Alzheimers Dis. 2012;32:721–31.
27. Amarenco P, Steg PG. Stroke is a coronary heart disease risk equivalent: implications for future clinical trials in secondary stroke prevention. Eur Heart J. 2008;29:1605–7.
28. Touboul PJ, Elbaz A, Koller C, et al. on behalf of the GE´NIC investigators. Common carotid artery intima-media thickness and ischemic stroke: the GE´NIC case-control study. Circulation. 2000;102:313–8.
29. Gongora-Rivera F, Labreuche J, Jaramilo A, et al. The prevalence of coronary atherosclerosis in patients with stroke. Stroke. 2007;38:1203–10.
30. Kahn R. Metabolic syndrome–what is the clinical usefulness? Lancet. 2008;371:1892–3.
31. Sone H, Mizuno S, Fujii H, et al, Japan Diabetes Complications Study. Is the diagnosis of metabolic syndrome useful for predicting cardiovascular disease in asian diabetic patients? Analysis from the Japan Diabetes Complications Study. Diabetes Care. 2005;28:1463–71.
32. Tong PC, Kong AP, So WY, et al. The usefulness of the International Diabetes Federation and the National Cholesterol Education Program's Adult Treatment Panel III definitions of the metabolic syndrome in predicting coronary heart disease in subjects with type 2 diabetes. Diabetes Care. 2007;30:1206–11.
33. Kressel G, Trunz B, Bub A, et al. Systemic and vascular markers of inflammation in relation to metabolic syndrome and insulin resistance in adults with elevated atherosclerosis risk. Atherosclerosis. 2009;202:263–71.

34. Fairweather D. Sex differences in inflammation during atherosclerosis. Clin Med Insights Cardiol. 2015;8:49–59.
35. Falk E. Plaque rupture with severe pre-existing stenosis precipitating coronary thrombosis: characteristics of coronary atherosclerotic plaques underlying fatal occlusive thrombi. Br Heart J. 1983;50:127–34.
36. Scuteri A, Najjar SS, Muller DC, et al. Metabolic syndrome amplifies the age-associated increases in vascular thickness and stiffness. J Am Coll Cardiol. 2004;43:1388–95.

Figures

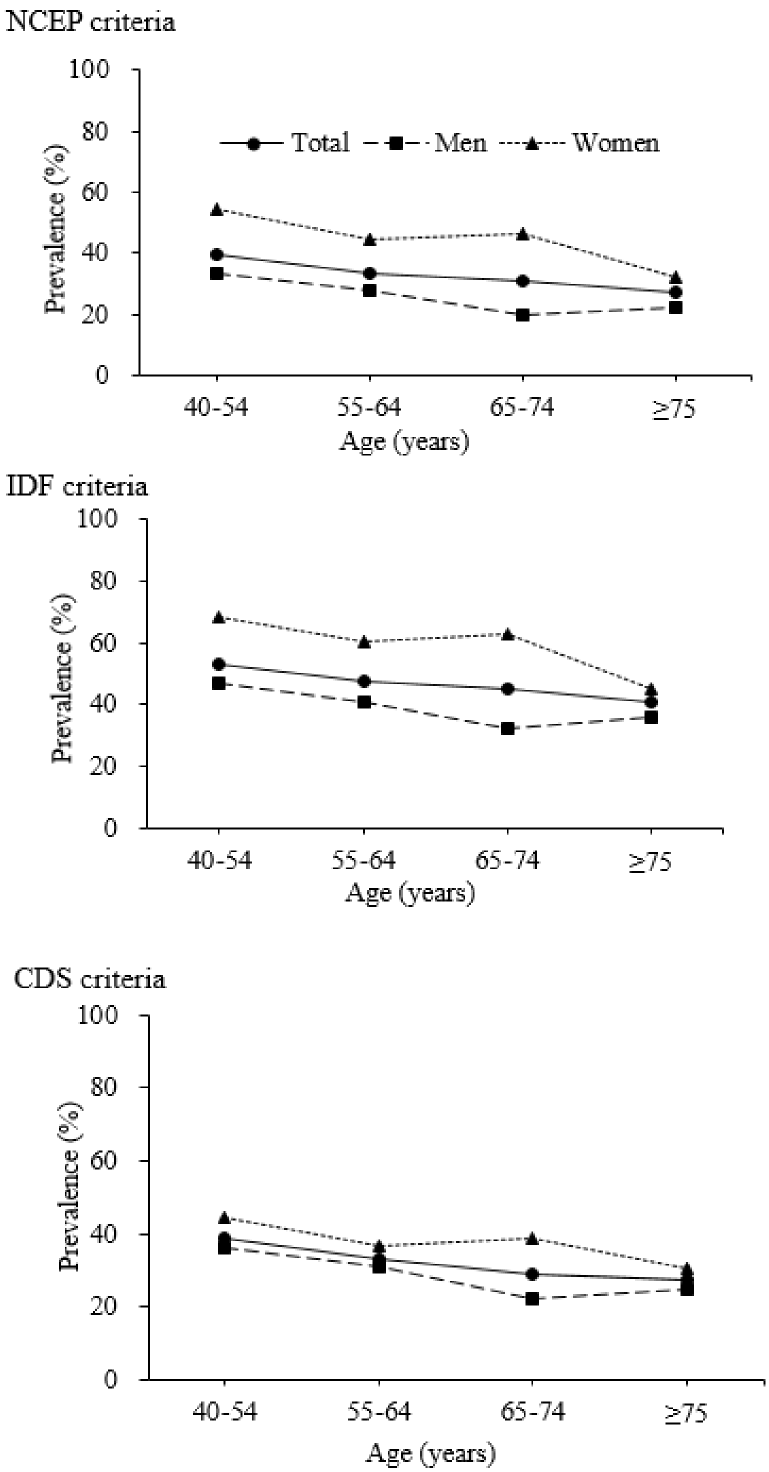

Figure 1

The age- and sex-specific prevalence (per 100 patients) of metabolic syndrome defined by three criteria in patients with acute ischemic stroke NCEP National Cholesterol Education Program, IDF International Diabetes Federation, CDS Chinese Diabetes Society

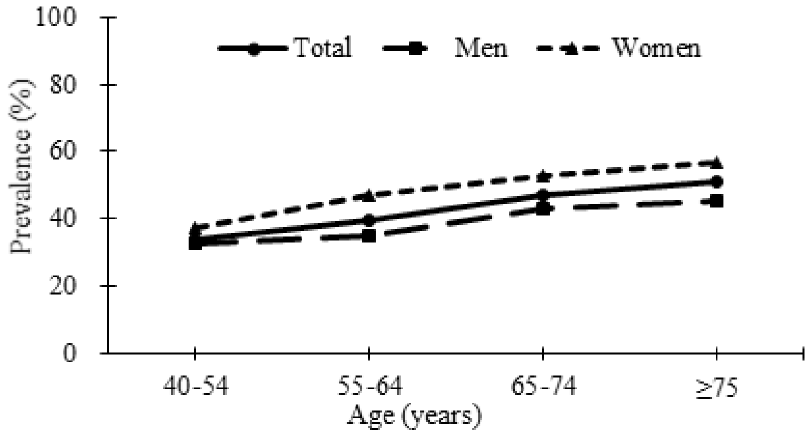

Figure 2

The age- and sex-specific prevalence (per 100 patients) of coronary heart disease in patients with acute ischemic stroke