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Retrospective Cohort Study

A retrospective cohort study of depression in patients with metabolic syndrome

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Abstract

BACKGROUND

Many studies have explored the relationship between depression and metabolic syndrome (MetS), especially in older people. China has entered an aging society. However, there are still few studies on the elderly in Chinese communities.

AIM

To investigate the incidence and risk factors of depression in metabolic syndrome (MetS) patients in mainland China and to construct a predictive model.

METHODS

Data from four waves of the China Health and Retirement Longitudinal Study were selected, and middle-aged and elderly patients with MetS (n = 2533) were included based on the first wave. According to the Center for Epidemiological Survey-Depression Scale (CESD), participants with MetS were divided into depression (n = 938) and non-depression groups (n = 1595), and factors related to depression were screened out. Subsequently, the 2-, 4-, and 7-year follow-up data were analyzed, and a prediction model for depression in MetS patients was constructed.

RESULTS

The prevalence of depression in middle-aged and elderly patients with MetS was 37.02%. The prevalence of depression at the 2-, 4-, and 7-year follow-up was 29.55%, 34.53%, and 38.15%, respectively. The prediction model, constructed using baseline CESD and Physical Self-Maintenance Scale scores, average sleep duration, number of chronic diseases, age, and weight had a good predictive effect on the risk of depression in MetS patients at the 2-year follow-up (AUC=0.775, 95%CI: 0.750–0.800, p<0.001), with a sensitivity of 68% and a specificity of 74%.

CONCLUSION

The prevalence of depression in middle-aged and elderly patients with MetS has increased over time. The early identification of and intervention for depressive symptoms requires greater attention in MetS patients.

Key Words: depression; metabolic syndrome; prevalence; risk factor

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Core Tip: In this study, a 7-year follow-up of middle-aged and elderly people in China Mainland was conducted, and it was found that the incidence of depression increased in the population of metabolic syndrome.

INTRODUCTION

Metabolic syndrome (MetS) is a pathological condition characterized by abdominal obesity, insulin resistance, hypertension, and hyperlipidemia [1]. MetS has become a global problem; although its prevalence varies according to different diagnostic criteria, a high prevalence of MetS is undeniable. A cross-sectional study in China reported a

MetS prevalence of 14.39%, according to diagnostic criteria defined by the Chinese Diabetes Society [2]. Another meta-analysis reported a prevalence of approximately 15.5% in China [3]. MetS is more common in the elderly [4], as it causes diabetes, stroke, and cognitive impairment, posing a serious disease burden to the middle-aged and the elderly populations [5].

MetS is also common in individuals with psychiatric disorders [6], including bipolar disorder [7], schizophrenia [8], depression [9], dementia [10], and other psychiatric disorders [11]. Moreover, MetS is becoming more common in young people with depression [9]. However, this phenomenon has received insufficient attention. This suggests that although MetS is a disease with age-related morbidity, there is still a need to focus on age groups other than the elderly, especially when there is comorbidity with psychiatric disorders.

Depression is also a disease that cannot be ignored in the elderly population. Our previous study, as well as those of others, have reported a high prevalence of depression in middle-aged and older adults [12, 13], leading to significant effects on individual medical expenses [14]. As shown above, both depression and MetS have a high incidence and heavy burden in middle-aged and elderly individuals. Therefore, more attention should be paid to depression and MetS in middle-aged and elderly individuals.

Additionally, a bidirectional relationship seems to exist between depression and MetS [15], and this association is even stronger in older people [16]. On the one hand, elderly patients with MetS have a higher prevalence of depression than the general population [17]. The more MetS components the patients have, the more severe their depressive symptoms are [18]. On the other hand, elderly patients with depression also have a higher prevalence of MetS [19]. Low levels of inflammation, low levels of activity, and antidepressant use in depression patients contribute to the development of MetS [20-22], and may lead to a risk of fatalities [23]. This may be related to the fact that depression and MetS share some pathogenic factors, such as chronic low-grade inflammation [24], and the dysregulation of the hypothalamus-pituitary-adrenal axis, the autonomic

nervous system, the immune system, and platelet and endothelial function [25]. However, other studies have denied a link between depression and MetS [26, 27], or have simply highlighted the association between atypical depression and MetS [28].

Overall, the relationship between depression and MetS remains unclear. Large population and cohort studies need to be supplemented to analyze the association between depression and MetS, as well as the complex influencing factors. Therefore, based on a large community-based cohort study conducted in mainland China, we designed this study to address the following: (1) the prevalence of depression in MetS patients; (2) the changing trajectory of the prevalence of MetS during the 7-year follow-up; and (3) the risk factors for the development of depression in MetS patients and the construction of predictive models.

MATERIALS AND METHODS

Study population

The China Health and Retirement Longitudinal Study (CHARLS) is a survey conducted in the Chinese mainland. The survey participants were those in the community who were 45 years old and above. The main contents include demographics, health, function, insurance, work, retirement, and physical examination. CHARLS has been conducting baseline surveys since 2011 and has published data from four surveys. Details such as design and sampling have been covered in previous studies [29,30]. The national baseline survey conducted during 2011–2012 consisted of 17,708 individuals. The second wave was conducted in 2013–2014 for a 2-year follow-up period, and 15,628 individuals were successfully re-interviewed. In 2015–2016, 14,555 individuals enrolled at baseline were re-interviewed for the third wave at the 4-year follow-up. The fourth wave survey—the most recent survey—conducted in 2018–2019, included 19,744 participants who participated in their 7-year follow-up.

Study protocol

Based on the survey data from 2011 as the baseline, participants were selected according to the following inclusion criteria: (1) meeting the diagnostic criteria for MetS,

(2) Center for Epidemiological Survey-Depression Scale (CESD) score, and (3) complete demographic data, health-related data, activities of daily living (ADL), social participation, *etc.* Based on the above criteria, 2,533 patients were selected at baseline. Second, patients' 2-, 4-, and 7-year follow-up information was analyzed. A screening flowchart is shown in Figure 1.

MetS

According to Zhu *et al* [31], the International Diabetes Federation (IDF) definition is more pertinent than the Adult Treatment Panel (ATP) III definition for screening and estimating the risk of cerebrovascular disease and diabetes in Asian American adults. Therefore, in this study, the IDF definition was selected as the diagnostic criteria for MetS, and patients were required to have at least two of the following four conditions on the basis of abdominal obesity: (1) high triglyceride level: ≥ 150 mg/dL (≥1.69 mmol/L); (2) low high-density lipoprotein (HDL) cholesterol level: < 40 mg/dL (<1.03 mmol/L) for men, < 50 mg/dL (<1.29 mmol/L) for women; (3) high blood pressure: ≥ 130 mmHg systolic blood pressure, ≥ 85 mmHg diastolic blood pressure, or receipt of antihypertensive medication; and (4) high fasting glucose (≥100 mg/dL [≥5.56 mmol/L]) or diabetes diagnosis. Abdominal obesity was defined as a waist circumference ≥ 90 cm in men and ≥ 80 cm in women.

Depression status

The CESD is a widely used depression assessment scale used in epidemiological surveys. The CESD comprises 10 items, and each question has a 4-level rating, respectively No, I don't have any difficulty; I have difficulty but can still do it; Yes, I have difficulty and need help; and I cannot do it. Scores of 0–3 are assigned, respectively, two of which are reverse grades. The total score is added to obtain the CESD score. The CESD has been used in a large-scale population survey in mainland China, with certain validity and reliability [32]. In this study, we labeled CESD ≥ 10 symptomatic depression, referred to as depression group, according to the criteria of Andresen *et al* [33]. And participants with CESD < 10 were defined as the non-depressed group.

ADL

The ADL was measure *via* the Physical Self-Maintenance Scale (PSMS) and Instrumental Activity of Daily Living (IADL) [34]. In this study, the PSMS included whether and how difficult it was to jog, walk, climb stairs, bend, and lift heavy objects, while the IADL included housekeeping, preparing meals, shopping, paying, and taking medications. The choices are on a 4-point scale, and they are No, I don't have any difficulty; I have difficulty but can still do it; Yes, I have difficulty and need help; and I cannot do it. A score of 1 to 4 points was assigned. The higher the total score, the more severely affected the individuals' health status.

Social participation

The CHARLS investigated the type and frequency of social participation among middle-aged and elderly people. The types of social participation include: (1) interacting with friends; (2) playing Ma-Jong, playing chess, playing cards, or attending a community club; (3) providing help to family, friends, or neighbors who do not live with you and who did not pay you for the help; (4) going to a sport, social, or other kind of club; (5) taking part in a community-related organization; (6) doing voluntary or charity work; (7) caring for a sick or disabled adult who does not live with you and who did not pay you for the help; (8) attending an educational or training course; (9) stock investment; (10) using the Internet; (11) other; (12) none of these. They were then asked, regarding each of the selected activities: "how often have you done these social activities in the past month?" Respondents were asked to select the choice that best suited their situation from "almost every day"; "almost every week"; and "not often". We chose the frequency of activities with the highest participation as the frequency of social participation.

Health information

Physical examinations included height, weight, waist circumference, systolic blood pressure, diastolic blood pressure, sleep, and biomarkers. The sleep aspect included a survey of the average sleep duration and nap time. The collection of blood samples required the respondents to fast for one night, and three tubes of venous blood were

collected from each respondent by medically trained staff from the China Centers for Disease Control and Prevention (CDC), based on a standard protocol. After collection, these fresh venous blood samples were transported at 4℃ to either local CDC laboratories or township-level hospitals near the study sites, or transported to the China CDC in Beijing within 2 wk for further testing. The biomarkers tested included white blood cell count (WBC), HDL, C-reactive protein (CRP), triglycerides (TG), fasting blood glucose (FBG), and uric acid (UA).

Statistical analysis

All the data in this study were imported into SPSS 22.0 (SPSS Inc., Chicago, IL, US) for analysis. First, we described the overall data and divided the patients into a depression group and a non-depression group, according to whether they met the criteria of symptomatic depression at baseline, and compared the overall data of the two groups at baseline. In this part of the results, categorical variables were expressed as N (%), the chi-squared test was used to compare the differences between the two groups, continuous variables were expressed as the mean (95%CI), and the Kolmogorov-Smirnov test was used to compare the two groups.

To determine which factors were associated with depression in MetS patients, we performed regression analyses on baseline data. Variables with p < 0.1 in the comparison of the two groups were screened and included in multivariate regression analysis, with the CESD score as the dependent variable. Subsequently, we performed multiple regression analyses with significant variables obtained from multivariate regression and the CESD score at baseline as independent variables, and the CESD score at follow-up as dependent variables to screen for the factors related to symptomatic depression in MetS patients.

Finally, we used Cox regression to construct a predictive model of depression in MetS patients, with variables with p < 0.1 and the CESD score at baseline as independent variables, and the occurrence of depression as the outcome variable. Two-tailed p < 0.05 was considered statistically significant for all statistical analyses.

RESULTS

1. Descriptive analysis of baseline

In this study, 1,595 cases in the non-depression group and 938 cases in the depression group were included, and the prevalence of depression in MetS patients was 37.02%. The detailed data are shown in Table 1.

1.1 Demographic information

There were significant differences in sex, age, education, and marital status between the two groups (p<0.001). Specifically, women, younger ages, lower levels of education, and single people were overrepresented in the depression group.

1.2 Health information

Compared to the non-depression group, participants in the depression group had lower height and weight, more physical disabilities and chronic diseases, more smoking and drinking, and less average sleep and nap time (p<0.05).

1.3 Physical examination

The depression group had lower serum UA and higher HDL levels (p<0.05). There were no significant differences in WBC, CRP, TG, waist circumference, SBP, DBP, or FBG between the two groups (p>0.05).

1.4 ADL and social participation

The types and frequencies of social participation activities in the depression group were significantly lower than those in the control group, and the scores of PSMS and IADL were significantly higher than those in the control group (p<0.001).

2. Descriptive analysis of follow-up

2.1 Two-year follow-up

During the 2-year follow-up, 929 patients were lost to follow-up or died, and the remaining 1,604 patients were followed up. Their average CESD score was 7.59 (95%CI: 7.30–7.88). Among this group, 474 patients (29.55%) had depression. Compared with the baseline, the CESD score did not significantly increase or decrease (P = 0.132, Figure 2), and 181 cases (17.01%, 181/1,064) newly developed depression.

2.2 Four-year follow-up

During the 4-year follow-up, compared with the baseline, 998 cases were lost to follow-up or died, 1,535 cases remained with an average CESD score of 8.16 (95%CI: 7.71–8.30), and 530 cases had depression, accounting for 34.53% of the cohort. There were no significant differences in CESD scores from the baseline (P = 0.163, Figure 2), and 239 cases (23.62%, 239/1,012) had newly developed depression.

2.3 Seven-year follow-up

During the 7-year follow-up, compared with the baseline period, 1,196 patients were lost to follow-up or died, and the remaining 1,337 patients had an average CESD score of 8.67 (95%CI: 8.31–9.02). Compared with baseline, the CESD score was significantly increased (P = 0.004, Figure 2). A total of 510 patients (38.15%) had depression. There were 243 new cases of depression, accounting for 26.85% of the cohort (243/905).

During the overall follow-up, 1,186 patients completed the follow-up. Among them, 462 patients (38.95%) were newly diagnosed with depression, and the average time required for depression to manifest was (4.000 ± 1.978) years.

3. Regression analysis

3.1 Factors associated with CESD at baseline

Multivariable logistic regression analysis with baseline CESD score as the dependent variable showed that CESD at baseline was associated with PSMS, IADL, average sleep duration, marital status, number of chronic diseases, age, and weight (Table 2, p<0.05).

3.2 Factors associated with CESD at follow-up

The multivariable logistic regression analysis with CESD score in the follow-up period as the dependent variable found that CESD score at the 2-year follow-up was associated with baseline CESD score, PSMS, average sleep duration, number of chronic diseases, age, and weight. CESD score at the 4-year follow-up was associated with baseline CESD, ADL, and weight, while CESD score at the 7-year follow-up was associated with baseline CESD, ADL, average sleep duration, age, and weight. The detailed data are shown in Table 2.

These factors were used as independent variables to construct the CESD prediction model during the follow-up period. The results showed that the CESD prediction model

constructed during the 2-year follow-up period had a better predictive ability than other follow-up periods (AUC =0.775, 95%CI: 0.750–0.800, p<0.001), with a sensitivity of 68% and a specificity of 74% (Figure 3).

3.3 Factors associated with new onset depression

Cox regression analysis showed that age (OR=0.986, 95%CI: 0.978–0.993), weight (OR=0.487, 95%CI: 0.421–0.564), average sleep duration (OR=0.926, 95%CI: 0.894–0.959), and ADL (OR=1.042, 95%CI: 1.026–1.058) were associated with symptomatic depression in MetS patients within 7 years of follow-up (all p<0.001).

DISCUSSION

The bidirectional relationship between depression and MetS remains questionable, especially in middle-aged and older adults, who have high rates of both conditions. This study focused on middle-aged and elderly patients with MetS in mainland China and followed them for 7 years to screen for risk factors associated with depression in MetS patients. We compared the information of people with depression and those without depression among MetS patients at baseline and found many differences, such as that those with MetS and depression included more women, lower education level, more single people, lower height and weight, more physical disabilities, more chronic diseases, more smoking and drinking, less average sleep and nap time, less frequency of social participation, impaired ability of daily living, etc [13,35-38]. These are all features of depression that have been reported in previous studies. However, we found that people with depression and MetS were younger than those without depression, which is related to the younger age of the current depressed population. On the one hand, the onset of depression tends to be younger, and on the other hand, a meta-analysis of observational studies found that depressive participants under 50 years of age were more likely to develop MetS than those over 50 years [34], and concluded that the odds of MetS in depressive patients decreased with age. These results suggest that the mutual worsening of MetS and depression is more significant in younger adults.

We then analyzed the follow-up data and selected the follow-up time points of 2, 4, and 7 years. It was found that the depression score at the 7-year follow-up was significantly higher than that of the baseline period, the prevalence of depression reached 38.15%, and the incidence of depression reached 26.85%, while there was no significant difference between the depression scores of the 2-year and 4-year follow-up periods and the baseline period. Akbaraly *et al* [39] proposed that the presence of MetS is associated with an increased risk of future depressive symptoms, and the results of this study further suggest that the longer the patients have MetS, the higher the risk of depression. Mulvahill *et al* [19] reported that the presence of MetS in elderly patients with depression is associated with the symptom severity of depression, and that poor antidepressant responses are observed in MetS patients. This indicates that the changes brought about by MetS not only increase the risk of depression but also affect the treatment efficacy. Therefore, patients must be identified and managed as early as possible to improve their outcomes.

Although the prevalence of depression in MetS patients was the highest after 7 years of follow-up, the predictive effect of the model established with the screened baseline information on the risk of depression in MetS patients after 7 years is limited. We found that the prediction model constructed by baseline CESD, PSMS, average sleep duration, number of chronic diseases, age, and weight had a good predictive effect on the risk of depression at the 2-year follow-up (AUC=0.775, 95%CI: 0.750–0.800), with a sensitivity of 68% and a specificity of 74%. It is worth noting that there are also complex interactions between these factors, such as depression and sleep duration, depression and chronic disease, chronic disease and ADL, and depression and ADL [40-41]. This suggests that paying attention to individuals who already have depressive symptoms, especially those with sleep problems and chronic diseases, is important for reducing the development of depression in MetS patients.

This study had some limitations. First, the patients in this study were from a community population, and the assessment of depressive symptoms was carried out with the self-rating scale used in a large epidemiological survey; therefore, the selected

depression could not completely replace a diagnosis of depression. In addition, in the follow-up, to avoid too many influencing factors, we started from the data at 2 years, 4 years, and 7 years, instead of continuous analysis of the same group of patients. However, the prediction efficiency of the model constructed by this analysis method worsened with a longer follow-up time, indicating that the influencing factors within the follow-up years play a certain role. Finally, antidepressants may affect metabolism, but the use of antidepressants was not analyzed in this study; therefore, the results regarding the association between MetS and depression may have been affected.

CONCLUSION

In conclusion, this study described changes in the prevalence of depression in MetS patients over a 7-year period, screened out factors associated with the development of depression in MetS patients, and constructed a 2-year model to predict the risk of depression. The early identification of depression and the provision of interventions can improve patient outcomes.

ARTICLE HIGHLIGHTS

Research background

MetS is also common in individuals with psychiatric disorders and becoming more common in young people with depression. However, the relationship between depression and MetS remains unclear.

Research motivation

Many studies have explored the relationship between depression and metabolic syndrome (MetS), especially in older people. China has entered an aging society. However, there are still few studies on the elderly in Chinese communities.

Research objectives

To investigate the incidence and risk factors of depression in metabolic syndrome (MetS) patients in mainland China and to construct a predictive model.

Research methods

Based on a large community-based cohort study conducted in mainland China, we designed this study to address the following: (1) the prevalence of depression in MetS patients; (2) the changing trajectory of the prevalence of MetS during the 7-year follow-up; and (3) the risk factors for the development of depression in MetS patients and the construction of predictive models.

Research results

We found the prevalence of depression in middle-aged and elderly patients with MetS was 37.02%. The prevalence of depression at 2-, 4-, and 7-year follow-up were 29.55%, 34.53%, and 38.15%, respectively. The prediction model constructed by baseline CESD, PSMS, average sleep duration, number of chronic diseases, age, and weight had a good predictive effect on the risk of depression in patients with MetS at 2-year follow-up (AUC=0.775, 95%CI: 0.750-0.800, p<0.001), with a sensitivity of 68% and a specificity of 74%.

Research conclusions

All in all, this study shows the prevalence of depression in middle-aged and elderly patients with MetS increases over time. More attention should be paid to early identification and intervention of depressive symptoms in MetS patients.

Research perspectives

Mechanisms of depression in patients with metabolic syndrome, early predictors and intervention modalities.

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