INTRODUCTION

According to the 2016 mental illness survey conducted in Korea, the lifetime prevalence and the annual prevalence of depression were 5.0% and 1.5%, respectively [1]. In a 2018 Statistics Korea survey, 26.6 per 100,000 people died of suicide, more than double the 2016 average for Organization for Economic Cooperation and Development of 11.5 [2]. Depression not only affects daily life and social functions, but is also closely related to suicide [3], so the high suicide rate in Korean society highlights the need for depression assessment and management.

Metabolic syndrome is a multifactorial syndrome composed of risk factors for cardiovascular disease and diabetes, which is defined as abdominal obesity, increased triglycerides, decreased high-density cholesterol, increased fasting blood sugar, and increased blood pressure [4]. Discussions of the relationship between...
metabolic syndrome and depression have been raised. For example, Insulin resistance, Hypercotisolemia, Immunoinflammatory activity, oxidative stress, and autonomic dysregulation are presumed to be pathophysiology shared by metabolic syndrome and depression [5,6]. A meta-analysis of cross-sectional studies confirmed a significant relationship between metabolic syndrome and depression, but the studies included were limited to most of the Americas and European countries [7,8]. However, in a study conducted in China and Taiwan, the relationship between metabolic syndrome and depression was not significant [9,10].

The Patient Health Questionnaire-9 (PHQ-9) is a depression screening tool consisting of 9 major Depression Diagnostic Criteria items in the Diagnosis and Statistics Manual: Mental Disorders, 4th Edition of the Patient Health Questionnaire developed by Kroenke et al. [11]. In the diagnosis of depression, 88% sensitivity and 88% specificity were reported, and Korean studies also reported high levels of reliability and validity with similar levels of sensitivity and specificity [12-14]. In addition, PHQ-9 is likely to be used as a useful tool for screening and evaluating depression because it has fewer questions and easier scoring than other depression assessment tools [14].

Since 2014, the Korean National Health and Nutrition Examination Survey (KNHANES) has adopted PHQ-9 as a screening tool for depression in the mental health area and included it in the 2014, 2016, and 2018 survey items. As a result, it was possible to perform a meaningful analysis in the mental health field compared to the previous survey that only confirmed the presence or absence of depression [15]. In this study, we investigate the relationship between metabolic syndrome and depression in Korean adults using data from the 2016 and 2018 KNHANES. The relationship between each item of PHQ-9 and metabolic syndrome was also examined.

MATERIALS AND METHODS

We utilized raw data from the 7th period 1st year (2016) and the 3rd year (2018) of the KNHANES. KNHANES has been approved by the Institutional Review Board of Korea Centers for Disease Control and Prevention and has been conducted every three years since 1998, and has been conducted annually since 2007. The data consist of health surveys, health examinations and nutrition surveys. Health surveys investigate disease morbidity, medical use, smoking, drinking, and mental health, and health examinations include body measurements, blood pressure and pulse measurements, and blood and urine tests. Of the total 16,142 participants in 2016 and 2018, 10,722 adults were selected. This study was conducted with the approval of Institutional Review Board for Human Research, Haeundae Paik Hospital, Inje University (HPIRB 2020-05-023).

1. Subjects

Among the 2016 and 2018 KNHANES subjects, the inclusion criteria for this study were adults between the ages of 19 and 80 who performed all measures for the diagnosis of metabolic syndrome and responded to all items of PHQ-9. We excluded cases in which any of the tests corresponding to the diagnostic criteria of metabolic syndrome were missing or answered ‘no idea’ to the items in PHQ-9. The total number of study subjects according to the criteria was 10,722.

2. Measurements

1) Metabolic syndrome

The definition of metabolic syndrome employed in this study was modified in waist circumference from the definition of the American Heart Association/National Heart, Lung and Blood Institute [16] to Korean standards. The following criteria were applied: 1) Elevated waist circumference (>102 cm [>90 cm for Asians] for men, >88 cm [>85 cm for Asians] for women); 2) Elevated triglycerides (≥150 mg/dL, drug treatment for elevated triglycerides is an alternative indicator); 3) Reduced high-density lipoprotein (HDL) cholesterol (<40 mg/dL in men, <50 mg/dL in women, drug treatment for reduced HDL is an alternative indicator); 4) Elevated blood pressure (≥130 mmHg [systolic blood pressure] /≥85 mmHg [diastolic blood pressure], antihypertensive drug treatment in a patient with hypertension is an alternative indicator); 5) Elevated fasting glucose (≥100 mg/dL, drug treatment of elevated glucose is an alternative indicator). When three or more of them were met, metabolic syndrome was diagnosed.

2) Depression

Korean version of the PHQ-9 was used to evaluate depressive symptoms. The primary outcome was the rela-
tionship between the total score of PHQ-9 and metabolic syndrome. In order to confirm the relationship between the severity of depression and the metabolic syndrome, the total score of PHQ-9 was classified as minimal from 0 to 5, mild from 5 to 9, and moderate to severe from 10.

3) Demographic and confounding variables

Age, sex, marital status, employment status, income level, education level, drinking, smoking, and exercise were included in the analysis as demographic characteristics. Income levels were divided into above and below average. Education level was classified based on college or higher education. It was checked whether or not drinking more than one drink per month in the last year and smoking for 5 packs or more for a lifetime. The exercise was checked at least 75 minutes aerobic exercise more than once a week.

In addition to the items involved in the diagnosis of metabolic syndrome, laboratory findings such as hemoglobin, white blood cell (WBC), platelet, aspartate transaminase (AST), alanine transaminase (ALT), blood urea nitrogen (BUN), creatinine, and high-sensitivity C-reactive protein (hsCRP) levels were also analyzed. Underlying diseases such as stroke, myocardial infarction, angina pectoris, thyroid disease, chronic kidney disease, cirrhosis and cancer were included in the analysis.

4) Statistical analyses

Age and laboratory findings were compared using an independent t-test. Sex and underlying disease status were compared through a chi-square test. To analyze the correlation between the severity of depression and metabolic syndrome, a linear by linear association analysis was performed. Variables with statistically significant differences between the group with and without metabolic syndrome were considered as confounding variables, analysis of covariance was performed for the PHQ-9 score and metabolic syndrome. Statistical significance of this study was defined as p<0.05 in both directions, and IBM SPSS Statistics for Windows, Version 23.0 (IBM Co., Armonk, NY, USA) was used for all statistical analysis.

RESULTS

1. Demographic data

In the group with metabolic syndrome, age was older, the proportion of males and married people was higher, and the employment rate was lower. The proportion of high average income of individual and household were lower in group with metabolic syndrome, and the education level was higher. Monthly drinking was lower in the group with metabolic syndrome, but lifelong smoking was higher in group with metabolic syndrome. The exercise rate was lower in the group with metabolic syndrome (Table 1).

2. Laboratory findings

Hemoglobin, WBC, AST, ALT, BUN, and hsCRP were all significantly higher in the group with metabolic syndrome, except platelet (Table 2).

Table 1. Demographic characteristics of the subjects with and without metabolic syndrome

| Demographic characteristics | Total sample (n=10722) | Metabolic syndrome | Statistical |
|----------------------------|-----------------------|--------------------|-------------|
|                            |                       | Yes (n=2742)       | coefficient | p-value     |
| Age (y)                    | 51.13 (16.64)         | 57.57 (14.61)      | t=21.040    | <0.001      |
| Male                       | 4,743 (44.2)          | 1,449 (52.8)       | χ²=110.679  | <0.001      |
| Married                    | 8,965 (83.6)          | 2,557 (93.3)       | χ²=249.874  | <0.001      |
| Employed                   | 6,586 (61.4)          | 1,560 (56.9)       | χ²=31.940   | <0.001      |
| Above average income       | 5,405 (50.4)          | 1,322 (48.2)       | χ²=7.116    | 0.008       |
| Above average income       | 6,125 (57.1)          | 1,277 (46.6)       | χ²=167.541  | <0.001      |
| College or above           | 3,967 (37.0)          | 658 (24.0)         | χ²=267.177  | <0.001      |
| Drinking alcohol           | 5,826 (54.3)          | 1,432 (52.2)       | χ²=6.625    | 0.010       |
| Smoking lifetime           | 4,100 (38.2)          | 1,287 (46.9)       | χ²=118.005  | <0.001      |
| Exercise                   | 4,642 (43.3)          | 983 (35.8)         | χ²=83.166   | <0.001      |

Values are presented as mean (standard deviation) or number (%).
3. Underlying diseases

The cancer category incorporated the results of liver cancer, colorectal cancer, breast cancer, cervical cancer, lung cancer, thyroid cancer and other cancers. Stroke, myocardial infarction and angina, chronic kidney disease, and cancer showed significantly higher prevalence in the group with metabolic syndrome. The prevalence of Thyroid disease and Liver cirrhosis was not significantly different between the two groups (Table 3).

4. Metabolic syndrome and PHQ-9

Table 4 shows the relationship between the severity of depression and the metabolic syndrome as a linear by linear association. The proportion of moderate to severe depression was 1.4 percentage points higher in the group with metabolic syndrome (6.4% vs. 5.0%), but did not
show a significant difference with a p-value of 0.058. Analysis of covariance was performed to compare PHQ-9 scores according to the presence or absence of metabolic syndrome, and the results are described in Table 5 and Table 6. The following variables, which had significant differences between the two groups, were used as confounding variables. All variables of demographic data, all variables of laboratory findings except platelet, and stroke, myocardial infarction and angina, chronic kidney disease, cancer among underlying diseases. In the group with and without metabolic syndrome, the total score of PHQ-9 was not significantly different when the covariate was corrected (2.56 to 2.48, p=0.406, Table 5). In the group with and without metabolic syndrome, each item of PHQ-9 also showed no significant difference (Table 6).

**DISCUSSION**

In this study, the prevalence of metabolic syndrome in Korean adults was 25.6%, and using 10 points of PHQ-9 as cut-off, the prevalence of depression was 5.3% (Table 4). When the relationship between metabolic syndrome and depression was calculated, the ratio of moderate-to-severe depression was 1.4% higher in metabolic syndrome, but did not show statistical significance when compared with the PHQ total score. The total score of PHQ-9 was also 2.56 points and 2.48 points in the group with and without metabolic syndrome, 0.08 points higher in the group with metabolic syndrome, but this was also not a significant difference.

In the study of the American and European countries, the relationship between metabolic syndrome and depression was continuously reported and confirmed in

| Table 5. PHQ–9 total score of the subjects with and without metabolic syndrome |
|---------------------------------|------------------|------------------|------------------|------------------|
|                                  | Total sample     | Metabolic syndrome | Statistical coefficient | p–value | Adjusted p–value* |
|                                  | (n=10,722)      | Yes (n=2,742) | No (n=7,980) | t=0.883 | 0.377 | 0.406 |
| PHQ–9 total score                | 2.50 (3.64)   | 2.56 (3.94)   | 2.48 (3.53)   | t=0.883 | 0.377 | 0.406 |

Values are presented as mean (standard deviation).
PHQ–9, Patient Health Questionnaire–9.
*Adjusted for the effects of demographic characteristics (age, sex, marriage, employment, income, education, alcohol consumption, smoking, and exercise), laboratory findings (level of hemoglobin, white blood cell, aspartate transaminase, alanine transaminase, blood urea nitrogen, creatinine, and high–sensitivity C–reactive protein), and underlying diseases (stroke, myocardial infarction and angina, chronic kidney disease, cancer).

| Table 6. PHQ–9 sub–item scores of the subjects with and without metabolic syndrome |
|----------------------------------|------------------|------------------|------------------|------------------|
|                                  | Total sample     | Metabolic syndrome | Difference between means | Adjusted p–value* |
|                                  | (n=10,722)      | Yes (n=2,742) | No (n=7,980) |                     |                   |
| Sub–item 1. Loss of interest    | 0.34 (0.73)   | 0.31 (0.74)   | 0.35 (0.73)   | –0.04 | 0.895 |
| Sub–item 2. Depressive mood     | 0.25 (0.62)   | 0.25 (0.67)   | 0.25 (0.60)   | 0.00  | 0.676 |
| Sub–item 3. Change of sleep     | 0.55 (0.96)   | 0.60 (1.00)   | 0.54 (0.89)   | 0.06  | 0.058 |
| Sub–item 4. Decreased energy    | 0.63 (0.91)   | 0.60 (0.96)   | 0.65 (0.89)   | –0.05 | 0.952 |
| Sub–item 5. Change of appetite  | 0.28 (0.68)   | 0.28 (0.71)   | 0.28 (0.67)   | 0.00  | 0.106 |
| Sub–item 6. Self–blame          | 0.17 (0.54)   | 0.18 (0.58)   | 0.17 (0.52)   | 0.01  | 0.997 |
| Sub–item 7. Decreased concentration | 0.12 (0.48) | 0.13 (0.57)   | 0.12 (0.46)   | 0.01  | 0.978 |
| Sub–item 8. Psychomotor change  | 0.07 (0.36)   | 0.09 (0.43)   | 0.06 (0.34)   | 0.03  | 0.396 |
| Sub–item 9. Suicide or self–harm| 0.09 (0.39)   | 0.12 (0.48)   | 0.08 (0.36)   | 0.04  | 0.416 |
|                                  | 0.34 (0.73)   | 0.31 (0.74)   | 0.35 (0.73)   | –0.04 | 0.895 |

Values are presented as mean (standard deviation).
PHQ–9, Patient Health Questionnaire–9.
*Adjusted for the effects of demographic characteristics (age, sex, marriage, employment, income, education, alcohol consumption, smoking, and exercise), laboratory (level of hemoglobin, white blood cell, aspartate transaminase, alanine transaminase, blood urea nitrogen, creatinine, and high–sensitivity C–reactive protein), and underlying diseases (stroke, myocardial infarction and angina, chronic kidney disease, cancer).
the meta-analysis [7,8]. Significant results were also reported in two prospective cohort studies conducted in Japan [18,19] and a cross-sectional study based on KNHANES in 2014 and 2016 in Korea [20]. However, in cross-sectional studies in Asia such as China and Taiwan, insignificant results were reported [9,10]. As there are not many studies conducted on Asians about the relationship between metabolic syndrome and depression, it is thought that there will still be limitations to establish a clear correlation as in Western studies. In addition, the discrepancy between the reports raises the need to consider socio-cultural backgrounds such as races, genetic effects or life styles of different cultures in the study of metabolic syndrome and depression.

The study also has limitations. Since this study was conducted based on a large-scale epidemiological survey of general adults in Korea, it has the advantage of having a large number of samples and analyzing various demographic factors. However, this study is a retrospective cross-sectional study based on epidemiological investigations already conducted, so it is difficult to identify the causal relationship between metabolic syndrome and depression. In addition, because the epidemiological investigation (KNHANES) was not designed for the study of metabolic syndrome and depression, it is difficult to completely exclude bias even though various confounding factors are controlled. Because, among the studies conducted in Asia, two cohort studies conducted in Japan showed a significant correlation between metabolic syndrome and depression, but no significant results were reported in cross-sectional studies conducted in China and Taiwan. Therefore, in order to clearly identify the relationship between metabolic syndrome and depression in the adult population of Korea in the future, it is believed that additional prospective studies will be helpful as well as continuously tracking epidemiological findings.

CONCLUSION

Most studies have shown that metabolic syndrome is associated with depression, but there are also reports that there are no significant differences among races or cultures. In this study, we tried to investigate the relationship between metabolic syndrome and depression in Korean adults using epidemiological surveys in 2016 and 2018, but could not find any significant correlation between them. However, considering the limitations of the study mentioned above, future research on the relationship between metabolic syndrome and depression in Korean adults is expected to require a prospective study that considers racial and genetic trends, life style, as well as demographic variables.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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