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Original Article

Relationships between Hemoglobin and Each Component of Metabolic Syndrome: A Special Focus on Elderly without Medication☆

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SUMMARY

Background: The relationships between higher hemoglobin (Hb) and the risk of higher metabolic syndrome (MetS) are important. However, most studies did not exclude individuals who were taking medications for MetS components, which would obviously lead to underestimations. At the same time, geriatric medicine is an important issue in our society. The aim of the present study is to determine the relationships between Hb and MetS components in the elderly, after excluding those individuals who were on medication for MetS.
Methods: Individuals aged older than 65 years were randomly selected from a health center between 1999 and 2008. After excluding those with medications for hypertension, hyperlipidemia, and/or diabetes, 3252 individuals were eventually included in the analysis.
Results: The levels of Hb increased with the increasing percentage of MetS. In multivariate analysis, both fasting plasma glucose and high-density lipoprotein cholesterol fail to show significance in both sexes. In addition, in men systolic blood pressure (BP) is not correlated with Hb. The odds ratio is 1.915 in men and 2.088 in women when the highest Hb group is compared with the lowest Hb group ($p < 0.001$ in both sexes).
Conclusion: Higher Hb was associated with increased chances of having MetS in elderly adults. The most important contributors are waist circumference, BP, and low-density lipoprotein cholesterol for both men and women.

1. Introduction

Because of the improvement of the healthcare system in Taiwan as well as in many other countries, human life expectancy has considerably increased; thus, aging has already become a serious challenge. Among these aged people, cardiovascular disease (CVD) is always among the top five causes of death. Metabolic syndrome (MetS) refers to a group of factors that increases an individual's risk of developing CVD. CVD not only causes deterioration in quality of life but also increases the economic burden to society. Therefore, early detection of MetS in elderly individuals is an urgent issue because MetS is manageable and can reduce the risk of developing future CVD without serious complications. As early as 1964, Avagaro et al[1] first reported the phenomenon of clustering of adiposity, hypertension, dyslipidemia, and glucose intolerance. Subsequently, this phenomenon was thought to be related to insulin resistance in 1988[2]. It eventually attracted the attention of the World Health Organization and was termed "MetS".[3] However, more than 40 definitions have been proposed by different societies and used in studies around the world. To resolve this situation, the consensus definition of MetS was finally made in 2009[4]. The factors in the MetS definition were called "traditional factors." In addition, there were many "nontraditional" factors that were shown to be associated with MetS in several studies, including uric acid, fatty liver, and inflammatory markers[5,6].

As noted earlier, the core of MetS is insulin resistance[7]. Other than this, low-grade inflammation is also considered to contribute to the underlying pathophysiology[8]. Among them, for instance, white blood cell count is one of the first inflammatory markers that was proposed to be associated with MetS[9–11]. Other hematogram

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components, such as hemoglobin (Hb) level, has also been found to have this relationship[7,12,13]. Although several reports have shown a positive correlation between Hb and MetS, all of them did not exclude patients who were under treatment for hypertension, hyperglycemia, and/or dyslipidemia. It is important to note that these components are the observational variables. Taking such medications will certainly be a confounding interference for these studies. Therefore, the true relationships between Hb and MetS still remain to be elucidated.

Because of insufficient evidence on the true relationship between Hb and MetS components not affected by medication confounders and, at the same time, considering that geriatric medicine is important, the purpose of the present study was to shed light on the relationships between Hb and MetS components in elderly individuals who were not taking medicines for MetS components at the time of the study.

2. Materials and methods

2.1. Study participants

This cross-sectional study enrolled individuals aged > 65 years who were receiving an annual health examination at the MJ Life Clinic, a large institute that offers routine health examination in north, central, and south Taiwan as well as in China. The Institutional Review Board of MJ Life Clinic approved the study protocol, and all participants provided informed consent.

Initially, a total of 8698 nonrepeated elderly individuals during the period between 1999 and 2008 were randomly selected from the clinic's database. The randomization was by the first 870 elderly individuals in each year (from 1999 to 2008) in the MJ database. Individuals with major diseases such as diabetes and hypertension, or those taking medications for hyperlipidemia, hypertension, or diabetics were all excluded. These stringent exclusion criteria were used in order to determine the true relationships between Hb and each component of MetS. Thus, 5281 individuals were excluded. Another 281 individuals were further excluded owing to missing data on the components of MetS (Figure 1).

In order to evaluate and define the relationships more clearly, only those with normal levels of Hb were included (12.5–16.5 g/dL in men and 11.5–14.5 g/dL according to MJ Life Clinic's normal references). Finally, 3252 individuals were included for analysis.

2.2. Anthropometric measurements and general data

The participants presented at the clinic at 8:00 AM after at least 10 hours of fasting. Senior nursing staff obtained information on medical history, lifestyle, alcohol intake, smoking, and physical exercise. Physicians performed complete physical examinations and measured the waist circumference (WC). Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice after at least 5 minutes of rest using standard sphygmomanometers. Blood samples for biochemistry study were drawn from the antecubital vein.

2.3. Laboratory measurements

Plasma was separated from blood within 1 hour after extraction and then stored at $-70^{\circ}C$ until analysis. The samples are analyzed for plasma glucose and lipid levels. Fasting plasma glucose (FPG) was examined using the glucose oxidase method (YSI 203 glucose analyzer; Scientific Division, Yellow Spring Instrument Company, Yellow Spring, OH, USA). Triglyceride (TG) and total cholesterol were measured with the dry, multilayer analytical slide method in the Fuji Dri-Chem 3000 analyzer (Fuji Photo Film, Minato-Ku, Tokyo, Japan). Serum high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) concentrations were measured using enzymatic cholesterol assay following dextran sulfate precipitation, whereas Hb was measured using an Abbott Cell Dyn 3000 hematology analyzer (Abbott Laboratories, Abbott Park, IL, USA).

2.4. Definition of MetS

The latest harmonized criteria of MetS in 2009[4] were used, with one modification—wherein the criterion for WC was set to ≥ 90 cm and 80 cm for Taiwanese men and women, respectively[14]. The other four criteria were the same: SBP ≥ 130 mmHg or DBP ≥ 85 mmHg, TG ≥ 150 mg/dL, FPG ≥ 100 mg/dL, and HDL ≤ 40 mg/dL and 50 mg/dL in men and women, respectively. Individuals must meet at least three criteria to be diagnosed with MetS.

2.5. Statistical analysis

The data were analyzed using the SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). All data were tested for normal distribution using Kolmogorov–Smirnov test and for homogeneity of variances by Levene's test. Continuous variables were expressed as mean ± standard deviation. The *t* test was used to evaluate differences between the two groups. According to the levels of Hb, the participants were classified into quartiles. When comparing the differences among these four groups, one-way analysis of variance was used. For *post hoc* comparison, the Bonferroni test was applied. To observe correlations among different parameters, simple correlation and multivariate linear regression were used. Odds ratio (OR) was calculated by logistic regression model to compare the possibility of having MetS in different groups. All statistical tests were two-sided. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Demographic data of study population

A total of 3252 elderly individuals were enrolled in the current study, comprising 1799 men and 1453 women. The mean age is 70.1 years for men and 69.7 years for women. Table 1 shows the demographic data of the study population with and without MetS. Not surprisingly, all MetS components are higher in individuals with MetS. Moreover, the age in both sexes shows no significant differences. However, LDL-C shows significant differences only in elderly women. In addition, Hb is significantly higher in the group with MetS regardless of sex with $p < 0.001$.

3.2. Hb and components of MetS

We divided the study participants into quartiles according to the Hb level. Among the four quartiles (from the lowest to highest Hb, Hb1 to Hb4), the trends of almost all MetS components are found to be correlated with Hb. Higher Hb level had higher levels of WC, SBP, DBP, FPG, total cholesterol, and LDL-C (Table 2). Although the trend seems to have a positive relationship with SBP and Hb in males, it still did not reach significance. HDL-C decreases as Hb increases in men, with statistical significance, but this effect was not observed in women. Another interesting finding is age. As men get older, their Hb level falls. An inverse correlation is seen, but not in women.

Subsequently, we further analyzed the correlation between MetS components and Hb in the linear regression model. After univariate and multivariate analyses (Table 3), SBP remained