Hypertension and the Insulin-related Metabolic Syndrome: Factor Analysis in 17,539 Taiwanese

Shao-Yuan Chuang,1 Chen-Huan Chen2,3,4 and Pesus Chou1

Background: Hypertension is a component of the insulin resistance-related metabolic syndrome. However, the relationship between insulin resistance and hypertension remains unclear. Factor analysis is a statistical technique that extracts several unrelated components from a set of intercorrelated risk variables. Risk variables contributing to the same component may share the same pathophysiological process.

Methods: Risk variables from 17,539 Taiwanese (8516 men and 9023 women, aged 30 years and older) randomly selected from a large physical checkup database were analyzed using exploratory factor analysis with principal components method.

Results: Factor analysis identified two independent factors for men and women, respectively. In men, a cluster of triglycerides, high-density-lipoprotein cholesterol, waist circumference, and body mass index (metabolic syndrome) accounted for 42%, and a cluster of glucose, systolic blood pressure, waist circumference, and body mass index (hyperglycemia plus hypertension plus obesity) accounted for 19% of the total variance in all variables considered. In women, a cluster of glucose, systolic blood pressure, waist circumference, and body mass index (hyperglycemia plus hypertension plus obesity) accounted for 46%, and a cluster of triglycerides, high-density-lipoprotein cholesterol, waist circumference, and body mass index (metabolic syndrome) accounted for 17% of the total variance.

Conclusion: A distinct insulin-resistance-related metabolic syndrome was observed for both men and women in Taiwan. Hypertension was probably linked to the metabolic syndrome through obesity in both Taiwanese men and women.

Key Words: Factor analysis • Metabolic syndrome • Insulin resistance • Hypertension

INTRODUCTION

Central/general obesity, dyslipidemia (high triglyceride concentrations and low high-density-lipoprotein cholesterol), elevated blood pressure, and disturbances in glucose and insulin metabolism are all established risk factors for cardiovascular disease. The clustering of these risk factors has long been recognized as a syndrome with various names,1 and insulin resistance/compensatory hyperinsulinemia may be the unifying underlying pathophysiology.1,2 Recently, the National Cholesterol Education Program Adult Treatment Panel III (ATP III)3 and World Health Organization4 separately proposed diagnostic criteria for the term “metabolic syndrome”. Albeit differences exist, both criteria consider high blood pressure as one of the components of the metabolic syndrome.

Although hyperinsulinemia may directly contribute to elevated blood pressure by enhancing sympathetic nervous system activity and promoting renal sodium retention and insulin resistance may also indirectly increase blood pressure by decreasing the signaling pro-
cesses that are important for vascular relaxation, the relationship between insulin resistance and hypertension remains controversial. In previous studies in Kinmen, we’ve shown that fasting insulin and C-peptide were associated with blood pressure in Chinese with normal glucose tolerance, suggesting a link between insulin resistance and hypertension. Furthermore, by using the technique of exploratory factor analysis, hypertension was linked to the metabolic syndrome in women only.

There appears to be a gender difference in the relationship between insulin resistance and hypertension. It remains to be determined if the observed gender difference is unique to Kinmen islanders. Therefore, in the present study, we applied the same factor analysis technique in a large health check-up population in Taiwan.

MATERIAL AND METHODS

Study population

MJ Health Screening Center is a private membership chain clinic with 4 Health Screening Centers (in Taipei, Taoyuan, Taichung, and Kaohsiung, respectively) around the Taiwan island, which provides periodic health examination to its members. During the period of 2000-2001, about 120,000 members received the health examination in the 4 centers. According to the policy of the MJ incorporation, no more than one-quarter of the records from the database can be open for academic research on request. Therefore, 30,909 records during the period were selected from the database by simple randomization for the purpose of the present study. Subjects in the sampled population were excluded for analysis when they (1) were younger than 30 years old, or (2) had history of diabetes or had a fasting glucose ≥ 126 mg/dL, or (3) were using regular medication for blood pressure control, or (4) when data were incomplete for the present study. Finally, records from a total of 17,539 subjects (8516 men and 9023 women, age range 30-89 years) were eligible for the analysis.

Health screening

The health screening procedures at MJ Health Screening Centers were carried out in a highly efficient way. In 4 hours, every subject attended 18 stations for 28 major examinations. Subjects were advised to fast for at least 8 hours before participating in the health screening. Fasting venous blood samples were collected for a battery of biochemistry analyses. Levels of glucose, triglycerides, and high-density-lipoprotein cholesterol were measured enzymatically on a Hitachi 7150 autoanalyzer (Hitachi, Tokyo, Japan). All subjects were barefoot and wore light indoor clothing to measure body weight and height on an auto-anthropometer (KN-5000A, Nakamura, Tokyo, Japan). Body mass index was calculated by weight divided by the square of height (meters). Waist circumference was measured at the largest waist using a tape measure. Blood pressures over the right arm in a seated position were taken twice using a computerized automatic mercury-sphygmomanometer (CH-5000, Citizen, Tokyo, Japan). The mean of the two readings was used in the current study.

Definitions

The definition of metabolic syndrome was based on the ATP III recommendations with some modification. The clinical components of the metabolic syndrome include abdominal obesity, high triglycerides, low high-density-lipoprotein cholesterol, high blood pressure, and high fasting glucose. According to ATP III, the diagnosis of the metabolic syndrome is made when 3 or more of the following risk determinants are present: abdominal obesity (waist circumference: men > 102 cm; women > 88 cm), high triglycerides (≥1.69 mmol/L [150 mg/dL]), low high-density-lipoprotein cholesterol (men < 1.03 mmol/L [40 mg/dL]; women < 1.29 mmol/L [50 mg/dL]), high blood pressure (systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg), and high fasting glucose (≥ 6.11 mmol/L [110 mg/dL]). Since the ATP III criteria for abdominal obesity might not be appropriate for Chinese, we used the cut-offs of waist circumferences > 90 cm in men and > 80 cm in women instead.

Statistical analysis

All data are expressed as means and standard deviation. Student’s t-test was used for comparisons between men and women. Triglycerides levels were log-transformed. Pearson’s correlation coefficients between risk variables in men and women were provided. Factor analysis was performed in steps of principal component
analysis, rotation of principal components and interpretation of factors. Principal component analysis based on the criteria of eigenvalues > 1.0 was used to extract the initial set of uncorrelated components that were linear combinations of the original variables. The components were orthogonally rotated through processes of maximizing and minimizing factor loadings to obtain the more clearly defined factors. Factor loadings are equivalent to a Pearson’s correlation coefficient between each variable and each factor. Absolute values of factor loadings > 0.4 were considered for factor pattern interpretation.

Because systolic and diastolic blood pressure are highly correlated and they often appear as one factor during factor analysis, the potential association of blood pressure with other risk variables may be obscured. Thus, diastolic blood pressure was not included in the factor analysis. Factor analysis was repeated for subgroups stratified by body mass index (< 25 kg/m² or ≥ 25 kg/m²). All statistical analyses were carried out using SAS statistical package (SAS Inc., Cary, NC, USA).

RESULTS

Table 1 displays the characteristics of study subjects with and without metabolic syndrome. Subjects with metabolic syndrome had worse risk profiles than those without the metabolic syndrome. In subjects without metabolic syndrome, men and women had similar age, while men had significantly higher systolic blood pressure, diastolic blood pressure, body mass index, waist circumference, and levels of fasting glucose, triglycerides, total cholesterol, and low level of high-density-lipoprotein cholesterol than women. In subjects with metabolic syndrome, men were significantly younger than women. Men had lower systolic blood pressure, higher diastolic blood pressure, similar body mass index, greater waist circumference, similar plasma glucose, higher triglycerides, similar total cholesterol, and lower high-density-cholesterol, as compared to women.

Table 2 displays the correlation matrix between the variables for men and women. Each variable was significantly correlated with every other risk variable in both men and women, except for the association between systolic blood pressure and high-density-lipoprotein cholesterol in men.

Table 3 displays the factor-loading patterns after principal component analysis and orthogonal rotation of the correlation matrix for men and women. Two dominant factors were identified underlying the clustering of the risk variables for both men and women (Figure 1). In men, triglycerides, high-density-lipoprotein cholesterol, waist circumference, and body mass index were associated with one factor (metabolic syndrome), which explained 42% of total variance. Systolic blood pressure, fasting glucose, waist circumference, and body mass index were associated a second factor (hyperglycemia plus hypertension plus obesity), which explained 19% of total variance. The explainable cumulative variance was 61% by the two factors in men.

In women, systolic blood pressure, fasting glucose,
waist circumference, and body mass index were associated with one factor (hyperglycemia plus hypertension plus obesity), which explained 46% of total variance. Triglyceride, high-density-lipoprotein cholesterol, waist circumference, and body mass index were associated with a second factor (metabolic syndrome), which explained 17% of total variance. The explainable cumulative variance was 63% by the two factors in women.

Table 4 displays the factor loading patterns for subjects stratified by body mass index. In men and women with body mass index < 25 kg/m², the factor loading patterns were similar to the results derived from the whole population. On the other hand, in men with body mass index ≥ 25 kg/m², three factors were identified. Waist circumference, and body mass index were associated with one factor (hyperglycemia plus hypertension plus obesity), which explained 46% of total variance. Triglyceride, high-density-lipoprotein cholesterol, waist circumference, and body mass index were associated with a second factor (metabolic syndrome), which explained 17% of total variance. The explainable cumulative variance was 63% by the two factors in women.

Table 2. Correlation matrix of the risk variables

<table>
<thead>
<tr>
<th></th>
<th>Men (n = 8516)</th>
<th>Women (n = 9023)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Systolic blood pressure</td>
<td>Diastolic blood pressure</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>0.697***</td>
<td>0.717***</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>0.213***</td>
<td>0.244***</td>
</tr>
<tr>
<td>Log triglycerides</td>
<td>-0.006</td>
<td>-0.024*</td>
</tr>
<tr>
<td>HDL-cholesterol</td>
<td>0.118***</td>
<td>0.181***</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>0.213***</td>
<td>0.176***</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.245***</td>
<td>0.25***</td>
</tr>
</tbody>
</table>

HDL = high-density-lipoprotein.

* = p < 0.05; ** = p < 0.001; *** = p < 0.0001.

Table 3. Factor loading patterns after orthogonal rotation of principal components in nondiabetic subjects

<table>
<thead>
<tr>
<th></th>
<th>Men (n = 8516)</th>
<th>Women (n = 9023)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Factor 1</td>
<td>Factor 2</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.02</td>
<td>0.76</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>0.07</td>
<td>0.67</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.72</td>
<td>0.01</td>
</tr>
<tr>
<td>HDL-cholesterol</td>
<td>-0.75</td>
<td>0.22</td>
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<tr>
<td>Waist circumference</td>
<td>0.76</td>
<td>0.42</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.77</td>
<td>0.40</td>
</tr>
<tr>
<td>Cumulative % total variance</td>
<td>0.42</td>
<td>0.61</td>
</tr>
</tbody>
</table>

HDL = high-density-lipoprotein.

Bold numbers indicate variables considered for interpretation of the factor.

Figure 1. Clusters of the risk variables in men and women. In both men and women, two clusters interlinked by obesity (waist circumference and body mass index) were identified by factor analysis. BMI = Body mass index; BP = blood pressure; HDL = high-density-lipoprotein; WC = waist circumference.
circumference and body mass index were associated with the first factor, triglyceride and high-density-lipoprotein cholesterol were associated with the second factor, and systolic blood pressure and fasting glucose were associated with the third factor. In contrast, in women with body mass index $\geq 25$ kg/m$^2$, two factors were identified. Systolic blood pressure, waist circumference, and body mass index were associated with the first factor, and fasting glucose, triglyceride, and high-density-lipoprotein cholesterol were associated with the second factor.

**DISCUSSION**

In both Taiwanese men and women who had participated in the health check-up, a factor strongly associated with triglycerides, high-density-lipoprotein cholesterol, waist circumference, and body mass index was identified. Although no fasting insulin levels were available in this study, this factor could be considered as the trait of the insulin resistance-related central metabolic syndrome, similar to the findings from the Kinmen study$^8$ and Framingham study.$^{12}$ On the other hand, systolic blood pressure was associated with another factor, along with fasting glucose, waist circumference, and body mass index, in both men and women. Therefore, the results indicated that, hypertension was linked to the central syndrome through shared correlations with obesity in both men and women, similar to that observed in the Framingham study (Figure 1).$^{12}$ No significant gender difference in the relationship between hypertension and insulin-related metabolic syndrome was observed in the Taiwanese check-up population.

**Association between insulin resistance and hypertension**

The association between insulin resistance and blood pressure may vary, even in the same ethnicities. In Chinese, the relationship is also inconsistent. In Kinmen islanders, we have demonstrated that both insulin and C-peptide were significantly associated with systolic and diastolic blood pressure.$^7$ However, no association between blood pressure and insulin was shown in a Chinese population in Mauritius,$^{13,14}$ and in 2165 Taiwanese older than 35 years in the Chin-Shan community.$^{15}$

**Factor analysis of the metabolic syndrome**

Factor analysis is a multivariate correlation technique that allows extraction of common components among multiple associated variables. Factor analysis accounts for the overlapping variability of interrelated variables by defining a set of new composite independent hypothetical variables (factors).$^{10}$ Risk variables sharing a common pathophysiological mechanism may have greater degrees of overlapping variability than other variables involving different mechanisms, and may cluster to define a composite variable (factor) during factor analysis. On the other hand, component risk variables of different factors generated during factor analysis
may be considered pathophysiologically independent. By factor analysis, a distinct metabolic syndrome characterized by hyperinsulinemia, dyslipidemia, and obesity was identified in the Framingham Offspring Study, in which hypertension was linked to the metabolic syndrome through obesity.

Factor analysis of the components of the metabolic syndrome has been examined in nondiabetic white American men and women, southern Indians, Javanese-American men, nondiabetic Chinese, and nondiabetic Koreans. These studies consistently identified two or more independent factors for both men and women, implying that insulin resistance alone does not explain completely the clustering of cardiovascular risk factors. Although frequently a factor representing the central metabolic syndrome (presumably related to insulin resistance) can be identified, obesity (body mass index, body weight, waist circumference) appears to be the link between the independent factors. In the present study, the factor loading patterns for subjects with body mass index < 25 kg/m² were similar to those for the whole population. This might imply that, in addition to insulin resistance, obesity also plays an important role in the manifestation of the metabolic syndrome.

Because systolic and diastolic blood pressure are highly correlated, the inclusion of the two highly correlated variables may amplify the representative percentage of the total variance of all variables and may inevitably force the emergence of a separate blood pressure factor in the factor analysis and obscure the potential linking of blood pressure with other risk variables. By removing diastolic blood pressure from the factor analysis or by applying structural equation modeling or confirmatory factor analysis, insulin resistance could be shown to be associated with systolic blood pressure in Hong Kong Chinese, Kinmen women, and nondiabetic white American men and women.

Comparison between Kinmen and Taiwan

In the Kinmen study, a cluster of systolic blood pressure and fasting glucose was identified in men that was independent of the factor representing the central metabolic syndrome. In contrast, systolic blood pressure was a component of the factor representing the central metabolic syndrome. Thus, in the Kinmen study, hypertension was linked to the metabolic syndrome in women only. The gender difference was not observed in the present study involving Taiwanese check-up population. The different observations may reflect the different lifestyles between the two populations. In Kinmen, before the termination of the military mission in 1992, men received regular military physical training every year while women married and bore children in their twenties and remained as housewives for most of their lives. Women usually gained significant weight after their thirties. The high levels of physical activity in men might partly explain their lower prevalence of the metabolic syndrome as compared to women in Kinmen. In contrast, in Taiwan, many women worked as hard as men and the lifestyle difference between men and women (as far as the levels of physical activity were concerned) was not as great as that in Kinmen.

Implication of the present study

Previous study in Kinmen provided implications about the sympathetic activation and insulin resistance as the potential pathophysiological factors in hypertension. In the present study, the results implied that insulin resistance alone did not appear to underlie all features of the insulin resistance syndrome. Hypertension was linked to the central metabolic syndrome through obesity, especial central obesity, in both men and women. The results are in concert with the recent recognition of the importance of obesity in the pathogenesis of hypertension and metabolic syndrome.

Limitations of present study

The study subjects of the present study were members of the private health check-up clinics and were not representative of the general population. Different lifestyles and psychosocial stress may affect several aspects of the metabolic syndrome.

In conclusion, similar to Kinmen islanders, a distinct insulin resistance-related metabolic syndrome was observed for both men and women in Taiwanese. Dissimilar to Kinmen islanders, hypertension was linked to the metabolic syndrome through obesity in both Taiwanese men and women. No significant gender difference was observed. The causal relationship between insulin resistance and
and the development of hypertension should be confirmed in longitudinal studies.

ACKNOWLEDGEMENT

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REFERENCES

高血壓與胰島素阻抗相關代謝異常症侯群：17539 名台灣人之因素分析結果

莊紹源 1  陈震寰 2,3,4  周碧瑟 1
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背景  高血壓是胰島素阻抗相關之代謝異常症侯群的成份之一，然而胰島素阻抗與高血壓之間的關係仍然未有定論。因素分析法是一種統計方法，可以從一組相關的危險因子變項中，抽取出數個不相關的因素。對相同的因素有貢獻的數個危險因子變項之間，可能具有相同的致病機轉。

方法  隨機抽樣所得之 17539 位 (男性 8516 位；女性 9023 位) 30 歲以上成人健診資料，利用主成分分析法就其心血管疾病危險因子變項進行探索式因素分析。

結果  因素分析分別於男女各區辨出 2 個獨立因素。男性的第一個因素包括三酸甘油酯、高密度脂蛋白膽固醇、腰圍及身體質量指數 (命名為代謝異常症侯群)，可以解釋 42% 的總變異量；第二個因素包括收縮血壓、空腹血糖、腰圍與身體質量指數 (命名為高血糖加高血壓加肥胖)，可以解釋 19% 的總變異量。女性的第一個因素包括血糖、收縮血壓、腰圍與身體質量指數 (命名為高血糖加高血壓加肥胖)，可以解釋 46% 的總變異量；第二個因素包括三酸甘油酯、高密度脂蛋白膽固醇、腰圍及身體質量指數 (命名為代謝異常症侯群)，可以解釋 17% 的總變異量。

結論  台灣地區的成年男女，均呈現明顯之胰島素阻抗相關代謝異常症侯群特質。無論男女，高血壓與代謝異常症侯群的關係均透過肥胖而連結。

關鍵詞：因素分析、代謝異常症侯群、胰島素阻抗、高血壓。