Prehypertension Among Middle-Aged and Elderly People in Taiwan: A Five-Year Follow-Up

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Aim: To evaluate the prevalence of prehypertension among middle-aged and elderly people in Taiwan and to explore the evolutionary changes of blood pressure in 5-year follow-up period.

Methods: In 2000, people aged over 40 participating in annual health examinations at local health stations in I-Lan County were invited to join the study. Past medical histories were reviewed, physical examinations and serial laboratory tests were performed for participants. All participants were followed in 2005 by a medical record review, telephone survey or personal visit. Subjects with prehypertension were sorted for further analysis.

Results: Overall, 1053 people (mean age 64.4 ± 11.4 years, 44.4% males) were enrolled in the primary cohort. The prevalence of hypertension and prehypertension was 40.4% and 35.8%, respectively. In 2005, 677 subjects (mean age: 68.8 ± 10.4 years, 42.5% males) were successfully followed, which revealed a significant increase of systolic blood pressure (3.7 ± 16.8 mmHg, p < 0.001), but not diastolic blood pressure (0.3 ± 11.5 mmHg, p = 0.758) in prehypertensive subjects; however, both systolic blood pressure (14.3 ± 17.4 mmHg, p < 0.001) and diastolic blood pressure (7.7 ± 13.3 mmHg, p < 0.001) were significantly increased among normotensive subjects. The cumulative incidence of prehypertensive subjects becoming hypertensive was 31.3%, and those who became hypertensive were significantly older (65.3 ± 8.6 vs. 62.2 ± 12.3 years, p = 0.024), having higher pulse pressure in 2000 (49.6 ± 10.6 vs. 45.1 ± 11.6 mmHg, p = 0.001), serum total cholesterol (214.3 ± 31.7 vs. 204.0 ± 37.2 mg/dL, p = 0.020) and low-density lipoprotein-cholesterol (141.7 ± 29.2 vs. 132.7 ± 34.7 mg/dL, p = 0.042).

Conclusions: The prevalence of prehypertension among older Taiwanese was 35.8% and the 5-year cumulative incidence of hypertension from prehypertension was 31.3%. Older prehypertensive subjects with higher pulse pressure, higher serum total cholesterol and higher low-density lipoprotein-cholesterol were more likely to become hypertensive within 5 years.


Key words: Aged, Blood pressure, Cardiovascular disease, Hypertension, Prehypertension

Introduction

High blood pressure has long been recognized as a major risk factor of cardiovascular disease, and main-
in cardiovascular and cerebrovascular disease\cite{4,6}; however, aging alone is associated with a progressive uprising trend of systolic blood pressure\cite{7,9}, so older people are more likely to be prehypertensive or hypertensive. Although the official definition of hypertension remained unchanged, cardiovascular risk was significantly increased in the stage of prehypertension\cite{10}. The prevalence of prehypertension ranges between 31.2–33% in different countries\cite{11,12}. An Israeli study indicated that the prevalence of prehypertension was 23.2% in adults\cite{13}, and would increase up to 56.8% in men and 35.8% in women within 3 years\cite{14}. It has been reported that prehypertension is frequently associated with other CVD risk factors\cite{12}, a higher risk of developing myocardial infarction or coronary artery diseases\cite{15,16}, and higher probabilities of hospitalization and mortality\cite{7}. Although prehypertension has gained extensive research interest, awareness is low and treatment targeted to prehypertension remains unclear\cite{11,12}. Hence, the main purpose of this study was to evaluate the prevalence of prehypertension in Taiwan and to explore the progression of prehypertension to hypertension in a 5-year follow-up period.

Methods

Participants
In 2000, people aged over 40 in Sanhsing, Toucheng and Tongshan Townships of I-Lan County who participated in the health examinations held by community health stations were invited to join the study\cite{18,21}. Subjects were enrolled when they had fully consented. The whole study was approved by the ethical committee of National Yang Ming University.

Demographic and Physical Examinations
Experienced research staff recorded each subject’s age, sex, and we measured each subject’s height and weight. Body mass index (BMI) was calculated accordingly. Obesity was defined by the Recommendations of the International Obesity Task Force\cite{22}. Personal medical history was also recorded in detail. Blood pressure was measured according to the JNC-6\cite{5}. A high blood pressure status was further classified into hypertension, prehypertension and normotension according to JNC-7\cite{25}.

Laboratory Examinations
All subjects underwent blood testing after a 10-h overnight fast to measure serum levels of glucose, total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) using an automatic analyzer (Hitachi Model 736; Tokyo, Japan), and fasting insulin (FI) was measured by radioimmunoassay (Diagnostic Product Corporation, CA, USA).

Diabetes and Insulin Resistance
Diabetes mellitus (DM) was defined according to the criteria proposed by the American Diabetes Association in 2001\cite{23}, and insulin resistance was measured by homeostasis model assessment (HOMA-IR)\cite{24}. The cutoff of HOMA-IR determining insulin resistance for all subjects was defined as the highest quartile of HOMA-IR among lean subjects (BMI < 25 kg/m\(^2\)), and subjects with higher HOMA-IR were considered insulin resistant\cite{25}.

Statistical Analysis
Data in the text and tables are expressed as mean values ± standard deviation (mean ± SD). Groups with subjects with and without prehypertension were compared with the Chi square test, Fisher’s Exact test, or Student’s t-test when appropriate (SPSS 13.0, Chicago, IL, USA). One-way ANOVA was used to evaluate differences between variables for each different blood pressure status. For all tests, p values 0.05 (two-tailed) were considered significant.

Results

Demography
In total, 1053 people participated in this study (mean age = 64.4 ± 11.4 years and 44.4% males). The prevalence of normotension, prehypertension and hypertension was 23.8%, 35.8% and 40.4%, respectively. Among all hypertensive subjects, 190 (44.7%) subjects were aware of their hypertension status or currently on anti-hypertensive treatment. Comparisons of demographic data showed that age, prevalence of DM, insulin resistance, BMI, pulse pressure, TC, HDL-C, triglycerides, and HOMA-IR were significantly different between subjects with a different blood pressure status (Table 1).

Five-Year Follow-Up of Subjects with Different Blood Pressure Status
In 2005, 677 subjects (mean age: 68.8 ± 10.4 years, 42.5% males) were successfully followed. Blood pressure and DM status were evaluated again in 2005. Comparisons of subjects with normotension and prehypertension showed a significant increase of systolic blood pressure but not diastolic blood pressure in the prehypertensive group and both systolic and diastolic blood pressure were significantly increased in the normotensive group (Table 2). Overall, the 5-year cumu-
The relative incidence of new onset DM in this study was 9.0%, which was 8.8%, 6.9%, 10.9% in the normotension, prehypertension and hypertension groups, respectively. No statistical significance was found for the incidence of new onset DM between different blood pressure groups (p = 0.289 by Chi square test).

Evolutionary Changes of Subjects with Prehypertension

Among 377 subjects with prehypertension (mean age = 63.9 ± 11.5 years, 45.9% males) in 2000, 316 (mean age = 68.4 ± 11.4 years, 44.6% males) were successfully followed in 2005. Overall, after 5-year follow-up, 19 (6.0%) had returned to normotension, 198 (62.7%) were maintaining prehypertension, and 99 (31.3%) had become hypertensive. The 5-year cumulative incidence of subjects with prehypertension progressing to hypertension was 31.3%. Comparisons between these prehypertensive subjects who maintained prehypertension and progressed to hypertension showed that age, pulse pressure, TC and LDL-C were significantly different between groups (Table 3); however, using a multiple regression model, we found that none of the aforementioned factors could independently predict new-onset hypertension during the follow-up period.

Evolutionary Changes of Subjects with Normotension

Among 251 (mean age = 60.6 ± 12.6 years, 45.4% males) normotensive subjects in 2000, 163 (mean age = 64.1 ± 13.3 years, 45.4% males) were successfully followed in 2005. Among them, 66 (40.5%) remained normotensive, 50 (30.7%) became prehypertensive, and 47 (28.8%) became hypertensive. The 5-year cumulative incidence among normotensive subjects...
was 28.8%. The conversion rate between prehypertensive subjects and normotensive subjects was not significantly different (31.3% vs. 28.8%, \( p = 0.572 \)). Comparisons between normotensive subjects who became prehypertensive and hypertensive showed that only BMI and pulse pressure were significantly different between groups (Table 4).

**Table 3.** Comparisons of prehypertensive subjects becoming hypertensive between 2000–2005

<table>
<thead>
<tr>
<th></th>
<th>Blood pressure status in 2005 of initial prehypertensive subjects ( (n = 316) )</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prehypertension ( (n = 198) )</td>
<td>Hypertension ( (n = 99) )</td>
</tr>
<tr>
<td>Age \footnote{( ^* )}</td>
<td>62.2 ± 12.3</td>
<td>65.3 ± 8.6</td>
</tr>
<tr>
<td>Males (%) \footnote{( ^* )}</td>
<td>47.0</td>
<td>40.4</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>6.0</td>
<td>8.2</td>
</tr>
<tr>
<td>Insulin resistance (%)</td>
<td>33.7</td>
<td>39.0</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2))</td>
<td>24.4 ± 3.5</td>
<td>24.4 ± 3.5</td>
</tr>
<tr>
<td>Pulse pressure (mmHg) \footnote{( ^\dagger )}</td>
<td>45.1 ± 11.6</td>
<td>49.6 ± 10.6</td>
</tr>
<tr>
<td>Fasting glucose (mg/dL) \footnote{( ^* )}</td>
<td>101.9 ± 31.0</td>
<td>111.4 ± 67.8</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL) \footnote{( ^* )}</td>
<td>204.0 ± 37.2</td>
<td>214.3 ± 31.7</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL) \footnote{( ^* )}</td>
<td>47.6 ± 17.8</td>
<td>46.4 ± 17.4</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL) \footnote{( ^\dagger )}</td>
<td>132.7 ± 34.7</td>
<td>141.7 ± 29.2</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>122.6 ± 76.6</td>
<td>139.4 ± 78.8</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.4 ± 1.8</td>
<td>1.7 ± 2.6</td>
</tr>
</tbody>
</table>

\footnote{\( ^* \)} \( p < 0.05 \) by Fisher’s Exact test or Student’s \( t \)-test

HDL = high-density lipoprotein, LDL = low-density lipoprotein, HOMA-IR = homeostasis model assessment

Insulin resistance was defined as HOMA-IR \( >1.23 \) in this study

**Table 4.** Comparisons of normotensive subjects becoming prehypertension and hypertension between 2000–2005

<table>
<thead>
<tr>
<th></th>
<th>Blood pressure status in 2005 of initial normotensive subjects ( (n = 163) )</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prehypertension ( (n = 50) )</td>
<td>Hypertension ( (n = 47) )</td>
</tr>
<tr>
<td>Age</td>
<td>62.0 ± 9.8</td>
<td>63.4 ± 9.3</td>
</tr>
<tr>
<td>Males (%) \footnote{( ^* )}</td>
<td>46%</td>
<td>38.3%</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>6%</td>
<td>14.9%</td>
</tr>
<tr>
<td>Insulin resistance (%)</td>
<td>27.3%</td>
<td>38.3%</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2))</td>
<td>23.7 ± 3.4</td>
<td>25.2 ± 3.4</td>
</tr>
<tr>
<td>Pulse pressure (mmHg) \footnote{( ^\dagger )}</td>
<td>40.7 ± 8.3</td>
<td>44.6 ± 8.9</td>
</tr>
<tr>
<td>Fasting glucose (mg/dL)</td>
<td>108.9 ± 50.3</td>
<td>106.3 ± 30.2</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>205.6 ± 41.2</td>
<td>208.7 ± 45.5</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>44.9 ± 15.4</td>
<td>46.2 ± 16.9</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>137.6 ± 39.4</td>
<td>139.1 ± 39.3</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>122.6 ± 76.6</td>
<td>139.4 ± 78.8</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.3 ± 1.5</td>
<td>2.2 ± 5.1</td>
</tr>
</tbody>
</table>

\footnote{\( ^* \)} \( p < 0.05 \) by Fisher’s Exact test or Student’s \( t \)-test

HDL = high-density lipoprotein, LDL = low-density lipoprotein, HOMA-IR = homeostasis model assessment

Insulin resistance was defined as HOMA-IR \( >1.23 \) in this study

Discussion

The prevalence of prehypertension was 35.8% in this study, higher than previously reported in an other Taiwanese city\(^{11} \). Results of the Nutrition and Health Survey in Taiwan (NAHSIT) disclosed that the overall prevalence of prehypertension was 34% in Taiwanese adults\(^{26} \), similar to the results from the NHANES III
in the United States (33%)\textsuperscript{12}. In spite of differences in ethnicity and geographic factors, the prevalence of prehypertension is similar in different studies. Comparisons between subjects with different blood pressure status showed significant differences in age, DM, insulin resistance, BMI, pulse pressure, and the lipid profile. The results clearly showed a complex interrelationship between blood pressure and other cardiovascular risk factors, which has been reported previously\textsuperscript{11, 12}.

During the 5-year follow-up period, the cumulative incidence of prehypertension to hypertension was 31.3%; however, evolitional changes of blood pressure among subjects in normotension and prehypertension groups were significantly different. Both systolic and diastolic blood pressure increased in normotensive subjects, but only systolic blood pressure was significantly increased in prehypertensive subjects. This discrepancy may be explained by aging, in which systolic blood pressure kept increasing after middle age but diastolic blood pressure fell after the age of 60\textsuperscript{7-9}. The progression rate of normotension and prehypertension to hypertension was not significantly different in this study. This is an interesting finding because the role of prehypertension as the intermediate state of normotension and hypertension may be questioned. Due to the relatively older age and small study sample, further study is needed to clarify when prehypertension is of the same prognostic value in older people as in the adult and middle-aged population. In addition, it has been reported that DM and impaired glucose tolerance were significantly increased in prehypertensive subjects, and their influences extended into hypertensive subjects\textsuperscript{27, 28}.

There are several limitations in this study. First, all blood pressure measurements were performed by research staff in the community health stations according to the principles of JNC-7; however, the “white-coat” phenomenon may be unavoidable. A 24-hour ambulatory blood pressure measurement may overcome the “white-coat” phenomenon, but it is not practical in a community-based program. Second, not all potentially associative risk factors were collected in this study. For instance, the family history of diseases such as DM or hypertension was not fully obtained because the participants could not recall. Third, the study cohort was generated from a community health screening program in rural Taiwan, which can not be fully extrapolated to the general population; however, through comparisons of the prevalence of prehypertension, we believe that the study results are still applicable to other communities.

In conclusion, the prevalence of prehypertension among middle-aged and elderly people in rural Taiwan was 35.8% and 31.3% of prehypertensive subjects who would become hypertensive in the 5-year follow-up period. Prehypertension clustering with other cardiovascular risk factors was more likely to develop to hypertension. Further study is needed to evaluate the pathological implications of prehypertension and to design appropriate intervention programs to reverse the progression of prehypertension.

References

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