Original Article

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

Li-Kuo Liu^{1,2,3}, Li-Ning Peng^{1,2,3}, Liang-Kung Chen^{1,2,3}, Shinn-Jang Hwang^{1,2,3}, and Shu-Ti Chiou⁴

¹Division of Geriatric Medicine, Department of Family Medicine, Taipei Veterans General Hospital, Taipei, Taiwan

²Center for Geriatrics and Gerontology, Taipei Veterans General Hospital, Taipei, Taiwan

³Department of Family Medicine, National Yang Ming University, School of Medicine, Taipei, Taiwan

⁴Institute of Public Health and Department of Social Medicine, National Yang Ming University, School of Medicine, Taipei, Taiwan

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.

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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-

taining optimal blood pressure control is of great benefits to reduce cardiovascular disease¹). The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) has introduced a new classification of high blood pressure²), replacing "high normal pressure" in JNC-6 with "prehypertension"³). After the introduction of prehypertension, a great number of studies started to explore the pathological implications, prognosis, and nature course of prehypertension

Address for correspondence: Liang-Kung Chen, Division of Geriatric Medicine, Department of Family Medicine, Taipei Veterans General Hospital, Taipei 11217, Taiwan

E-mail: lkchen2@vghtpe.gov.tw

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in cardiovascular and cerebrovascular disease⁴⁻⁶; however, aging alone is associated with a progressive upris- ing trend of systolic blood pressure⁷⁻⁹, so older people are more likely to be prehypertensive or hyperten- sive. Although the official definition of hypertension remained unchanged, cardiovascular risk was signifi- cantly increased in the stage of prehypertension¹⁰.

The prevalence of prehypertension ranges between 31.2–33% in different countries^{11, 12}. An Israeli study indicated that the prevalence of prehyper- tension was 23.2% in adults¹³, and would increase up to 56.8% in men and 35.8% in women within 3 years¹⁴. It has been reported that prehypertension is frequently associated with other CVD risk factors¹², a higher risk of developing myocardial infarction or cor- onary artery diseases^{15, 16}, and higher probabilities of hospitalization and mortality¹⁷. Although prehyper- tension has gained extensive research interest, aware- ness is low and treatment targeted to prehypertension remains unclear^{11, 12}. Hence, the main purpose of this study was to evaluate the prevalence of prehyperten- sion in Taiwan and to explore the progression of pre- hypertension 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 study¹⁸⁻²¹. Subjects were enrolled when they had fully consented. The whole study was approved by the ethi- cal 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 accord- ingly. Obesity was defined by the Recommendations of the International Obesity Task Force²². Personal medical history was also recorded in detail. Blood pressure was measured according to the JNC-6³. A high blood pressure status was further classified into hypertension, prehypertension and normotension according to JNC-7².

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 lipo- protein cholesterol (HDL-C) using an automatic ana-

lyzer (Hitachi Model 736; Tokyo, Japan), and fasting insulin (FI) was measured by radioimmunoassay (Diag- nostic Product Corporation, CA, USA).

Diabetes and Insulin Resistance

Diabetes mellitus (DM) was defined according to the criteria proposed by the American Diabetes Association in 2001²³, and insulin resistance was mea- sured by homeostasis model assessment (HOMA-IR)²⁴. The cutoff of HOMA-IR determining insulin resis- tance for all subjects was defined as the highest quar- tile of HOMA-IR among lean subjects (BMI < 25 kg/ m²), and subjects with higher HOMA-IR were con- sidered insulin resistant²⁵.

Statistical Analysis

Data in the text and tables are expressed as mean values $\pm$ standard deviation (mean $\pm$ SD). Groups with subjects with and without prehypertension were com- pared with the Chi square test, Fisher's Exact test, or Student's *t*-test when appropriate (SPSS 13.0, Chi- cago, IL, USA). One-way ANOVA was used to evalu- ate 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 $\pm$ 11.4 years and 44.4% males). The prevalence of normotension, prehypertension and hypertension was 23.8%, 35.8% and 40.4%, respec- tively. Among all hypertensive subjects, 190 (44.7%) subjects were aware of their hypertension status or currently on anti-hypertensive treatment. Compari- sons of demographic data showed that age, prevalence of DM, insulin resistance, BMI, pulse pressure, TC, HDL-C, triglycerides, and HOMA-IR were signifi- cantly 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 $\pm$ 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 pre- hypertension 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 nor- motensive group (Table 2). Overall, the 5-year cumu-

Table 1. Comparison of demographic data between subjects with different blood pressure status

	Normotension (<i>n</i> = 251)	Prehypertension (<i>n</i> = 377)	Hypertension (<i>n</i> = 425)	<i>p</i> value
Age (year)	61.0 ± 12.3	63.8 ± 11.7	67.0 ± 9.8	< 0.001
Males (%)	47.4	44.6	42.6	0.475*
Diabetes mellitus (%)	11.2	10.1	21.2	< 0.001*
Insulin resistance (%)	28.4	34.3	43.3	0.001*
Body mass index (kg/m ²)	23.5 ± 3.6	24.2 ± 3.4	25.5 ± 3.8	< 0.001
Pulse pressure (mmHg)	41.6 ± 9.3	48.1 ± 11.4	61.5 ± 18.4	< 0.001
Fasting glucose (mg/dL)	104.1 ± 34.1	104.5 ± 43.4	110.0 ± 36.6	0.069
Total cholesterol (mg/dL)	202.8 ± 44.2	206.9 ± 35.4	212.4 ± 42.0	0.009
HDL-cholesterol (mg/dL)	47.5 ± 16.9	47.4 ± 17.6	44.4 ± 17.7	0.034
LDL-cholesterol (mg/dL)	133.6 ± 42.4	135.2 ± 32.9	137.5 ± 37.9	0.445
Triglycerides (mg/dL)	117.9 ± 76.6	126.5 ± 76.4	148.7 ± 143.5	0.001
HOMA-IR	1.5 ± 2.9	1.5 ± 2.1	2.0 ± 2.8	0.018

*by Chi square test

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

Table 2. Evolutionary changes of blood pressure among subjects with prehypertension and normotension

		Prehypertension	Normotension
Year 2000	SBP (mmHg)	127.5 ± 8.1	107.6 ± 8.2
	DBP (mmHg)	78.7 ± 7.8	67.0 ± 7.7
Year 2005	SBP (mmHg)	132.1 ± 17.4	122.7 ± 17.9
	DBP (mmHg)	78.9 ± 11.1	76.3 ± 11.0
Change of SBP (mmHg)*		4 (− 41, 66) mmHg	12 (− 29, 73) mmHg
Change of DBP (mmHg)*		0 (− 31, 35) mmHg	7 (− 38, 43) mmHg

SBP=systolic blood pressure; DBP=diastolic blood pressure.

Changes in SBP (DBP) were identified by SBP (DBP) in 2005 minus SBP (DBP) in 2000 for each subject and expressed as the median (range).

**p* < 0.001 by paired *t*-test within group

lative 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

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

	Blood pressure status in 2005 of initial prehypertensive subjects (<i>n</i> = 316)		<i>p</i> value
	Prehypertension (<i>n</i> = 198)	Hypertension (<i>n</i> = 99)	
Age*	62.2 ± 12.3	65.3 ± 8.6	0.024
Males (%)*	47.0	40.4	0.285
Diabetes mellitus (%)	6.0	8.2	0.374
Insulin resistance (%)	33.7	39.0	0.428
Body mass index (kg/m ²)	24.4 ± 3.5	24.4 ± 3.5	0.983
Pulse pressure (mmHg)*	45.1 ± 11.6	49.6 ± 10.6	0.001
Fasting glucose (mg/dL)	101.9 ± 31.0	111.4 ± 67.8	0.097
Total cholesterol (mg/dL)*	204.0 ± 37.2	214.3 ± 31.7	0.020
HDL cholesterol (mg/dL)	47.6 ± 17.8	46.4 ± 17.4	0.609
LDL cholesterol (mg/dL)*	132.7 ± 34.7	141.7 ± 29.2	0.042
Triglycerides (mg/dL)	122.6 ± 76.6	139.4 ± 78.8	0.077
HOMA-IR	1.4 ± 1.8	1.7 ± 2.6	0.350

**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

	Blood pressure status in 2005 of initial normotensive subjects (<i>n</i> = 163)		<i>p</i> value
	Prehypertension (<i>n</i> = 50)	Hypertension (<i>n</i> = 47)	
Age	62.0 ± 9.8	63.4 ± 9.3	0.473
Males (%)*	46%	38.3%	0.538
Diabetes mellitus (%)	6%	14.9%	0.191
Insulin resistance (%)	27.3%	38.3%	0.336
Body mass index (kg/m ²)*	23.7 ± 3.4	25.2 ± 3.4	0.032
Pulse pressure (mmHg)*	40.7 ± 8.3	44.6 ± 8.9	0.031
Fasting glucose (mg/dL)	108.9 ± 50.3	106.3 ± 30.2	0.764
Total cholesterol (mg/dL)	205.6 ± 41.2	208.7 ± 45.5	0.725
HDL cholesterol (mg/dL)	44.9 ± 15.4	46.2 ± 16.9	0.720
LDL cholesterol (mg/dL)	137.6 ± 39.4	139.1 ± 39.3	0.861
Triglycerides (mg/dL)	122.6 ± 76.6	139.4 ± 78.8	0.077
HOMA-IR	1.3 ± 1.5	2.2 ± 5.1	0.297

**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

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**).

Discussion

The prevalence of prehypertension was 35.8% in this study, higher than previously reported in an other Taiwanese city¹¹. Results of the Nutrition and Health Survey in Taiwan (NAHSIT) disclosed that the overall prevalence of prehypertension was 34% in Taiwanese adults²⁶, similar to the results from the NHANES III

in the United States (33%)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^{11, 12)}.

During the 5-year follow-up period, the cumulative incidence of prehypertension to hypertension was 31.3%; however, evolutionary 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 60⁷⁻⁹⁾. 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^{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.

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