BMJ Open

Prevalence and Risk Factors Associated with Prehypertension in Shunde District, Southern China

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2014-006551
Article Type:	Research
Date Submitted by the Author:	04-Sep-2014
Complete List of Authors:	Huang, Yuli; Nanfang Hospital, Southern Medical University, Cardiology Qiu, Wenke; the First People's Hospital of Shunde, Health Management Center Liu, Changhua; Nanfang Hospital, Southern Medical University, Cardiology Zhu, Dingji; Nanfang Hospital, Southern Medical University, Cardiology Hua, Jinghai; Nanfang Hospital, Southern Medical University, Cardiology Cai, Xiaoyan; the First People's Hospital of Shunde, Foshan, Cardiology Wu, Yanxian; the First People's Hospital of Shunde, Foshan, Cardiology Hu, Yunzhao; the First People's Hospital of Shunde, Foshan, Cardiology Xu, Dingli; Nanfang Hospital, Southern Medical University, Cardiology
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Cardiovascular medicine, Global health, Public health
Keywords:	Cardiac Epidemiology < CARDIOLOGY, Hypertension < CARDIOLOGY, EPIDEMIOLOGY

Prevalence and Risk Factors Associated with Prehypertension in Shunde District, Southern China

Running head: Prevalence and Risk Factors of Prehypertension

Yuli Huang,[1,2*] Wenke Qiu,[3*] Changhua Liu,[1] Dingji Zhu,[1] Jinghai Hua,[1] Xiaoyan Cai,[2] Yanxian Wu,[2] Yunzhao Hu,[2] Dingli Xu[1]

[1] Department of Cardiology, Nanfang Hospital, Southern Medical University, Guangzhou, PR China; [2] Department of Cardiology, the First People's Hospital of Shunde, Foshan, PR China; [3] Department of Health Management Center, the First People's Hospital of Shunde, PR China

[*] The authors contributed equally to this work

Corresponding author: Professor Dingli Xu. Department of Cardiology, Nanfang Hospital, Southern Medical University, Guangzhou, PR China. Tel.: + 86 20 61641503 Fax: + 86 20 87705671 E-mail: dinglixu@fimmu.com Or Professor Yunzhao Hu, Department of Cardiology, the First People's Hospital of Shunde, Foshan, PR China. Tel.: + 86 757 22318680 Fax: + 86 757 22223899 E-mail: huyunzhao4406@163.com

ABSTRACT

OBJECTIVE: To explore the incidence and combined cardiovascular risk factors of prehypertension in southern China.

DESIGN: A cross-sectional study; the logistic regression model was use to find the risk factors of prehypertension.

SETTING: The study was conducted in Shunde District, Southern China, using the community-based health checkup information.

PARTICIPANTS: Subjects aged ≥ 35 years with complete health checkup information data between January 2011 and December 2013 were enrolled and divided into hypertension, prehypertension, and optimal blood pressure (BP). Prehypertension was further divided into low-range (BP 120-129/80-84 mmHg) and high-range (BP 130-139/85-89 mmHg) subgroups.

OUTCOME MEASURES: The prevalence of prehypertension and the combined cardiovascular risk factors within the prehypertensive subgroups.

RESULTS: Of the 5,362 initially reviewed cases (aged ≥ 35 years), 651 cases were excluded because of missing data. The proportions of optimal BP, prehypertension, and hypertension were 39.1%, 38.6%, and 22.3%, respectively. The average age, proportion of male sex, overweight, impaired fasting glucose (IFG), dyslipidemia, and hyperuricemia were significantly higher in the prehypertension group than in the optimal BP group (all $P < 0.05$). Compared with low-range prehypertension, the proportions of overweight, dyslipidemia, and IFG were higher in the high-range prehypertension group (all $P < 0.05$). Multivariate logistic regression analysis showed that overweight [odds ratio (*OR*) = 2.89, 95% confidence interval (*CI*) = 1.56–5.35], male sex (*OR* = 2.15, 95% *CI* = 1.37–3.37), and hyperuricemia (*OR* = 1.69, 95% *CI* = 1.18–2.64) were independent risk factors of prehypertension.

CONCLUSIONS: Prehypertension is highly prevalent in southern China. Prehypertensive individuals presented with many other cardiovascular risk factors. There was heterogeneity of combined risk factors within the prehypertensive subgroups.

Keywords: Prehypertension; Prevalence; Risk Factors

Strengths and limitations of this study

■ This study first documented prehypertension is highly prevalent in the Shunde District, southern China.

■ With the economic development and lifestyle changes in China, obesity/overweight has become a very important risk factor for increased blood pressure.

■ This is the first study to show that there was a significant heterogeneity of combined risk factors within the prehypertensive subgroups.

■ Some important confounding factors possibly associated with increased blood pressure were not evaluated in the present study.

Introduction

In 2003, the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) proposed a new blood pressure (BP) category, including 120–139 mmHg systolic blood pressure (SBP) or 80–89 mmHg diastolic blood pressure (DBP), designated as "prehypertension".[1] The incidence of prehypertension is up to 30–50% worldwide, as well as in many districts of China.[2-4] It is known that in China, the incidence of hypertension is significantly higher in the northern than that in the southern area because of the colder climate and high-sodium intake.[5] Such regional factors may also affect the incidence of prehypertension. However, the incidence of prehypertension in Guangdong Province, southern China has been rarely reported.

Prehypertensive individuals are prone to progress into frank hypertension, and most of them present with clustering of other cardiovascular risk factors.[6-8] However, the term of "prehypertension" has been contentious. Most arguments against using this term consist of the possible public anxiety and overtreatment it may cause. Further, there is a high heterogeneity within this category because the risk of progressing to hypertension and developing cardiovascular disease is higher among people with BP 130–139/85–89 mmHg than among those with BP 120–129/80–84 mmHg.[6, 9] Furthermore, whether the concurrent cardiovascular risk factors in subgroups of prehypertension are different remains unanswered.

Given these inconsistent results, we conducted a retrospective analysis to explore the prevalence of prehypertension, and the cardiovascular risk factors in the

sub-groups of prehypertension in Guangdong Province, southern China.

Methods

Study Participants

We performed a retrospective study in Shunde District, a traditional but economically developed district of Guangdong Province, in China, using the community-based health checkup information. Community-based health checkup information was collected in the Health Management Center of the First People's Hospital of Shunde. The centers provided data for participants who enrolled in their health checkup programs conducted between January 2011 and December 2013. Subjects aged ≥ 35 years with complete data for the following characteristics were included in this study: age, sex, smoking/drinking habits, history of chronic diseases and treatment, family history of hypertension, height, weight, BP, fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), low density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), serum creatinine (Scr), blood urea nitrogen (BUN), and serum uric acid (UA). This study was approved by the Ethics Committee of the Affiliated Hospital at Shunde of the Southern Medical University.

Definition of Correlative Risk Factors

Correlative risk factors estimated in our study included the following: (1) BP classification was based on the recommendations from the JNC 7.[1] Normal BP was defined as SBP < 120 mm Hg and DBP < 80 mm Hg. Hypertension was defined as

SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg, or previously diagnosed as hypertension and currently undergoing antihypertensive treatment. Prehypertension was defined if patients were not undergoing antihypertensive treatment and had a SBP of 120–139 mm Hg and/or DBP of 80–89 mm Hg. Prehypertension was further divided into low-range (SBP 120–129 and/or DBP 80–84 mmHg) and high-range (SBP 130–139 mmHg and/or DBP 85–89 mmHg) subgroups. (2) Impaired glucose regulation was diagnosed based on FPG according to the American Diabetes Association criteria,[10] including diabetes (FPG ≥ 7.0 mmol/L) and impaired fasting glucose (IFG, FPG 5.6–6.9 mmol/L). Dyslipidemia was defined as a history of receiving antidyslipidemia agents or as satisfying criteria on admission such as TC ≥ 5.18 mmol/L, LDL-C ≥ 3.37 mmol/L, HDL-C < 1.04 mmol/L, and/or TG ≥ 1.7 mmol/L according to the 2007 Guidelines for Prevention and Treatment of Dyslipidemia in Adults in China.[11] Hyperuricemia was defined as UA ≥ 416 μmol/L in men and 357 mol/L in women. (3) Overweight and obesity were defined as body mass index (BMI) 24–27.9 kg/m^2 and BMI ≥ 28 kg/m^2 according to Chinese criteria.[12] (4) The estimated glomerular filtration rate (eGFR) of each participant was estimated using the modified Modification of Diet in Renal Disease equation adapted for Chinese,[13] as: eGFR = 186 × Scr$^{-1.154}$ × Age$^{-0.203}$ × 0.742 (Female) × 1.233 (Chinese).

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Science software release 16.0 (SPSS Inc., Chicago, IL, USA). Continuous variables are presented as mean ± standard deviation or median (inter-quartile range) as appropriate. Categorical variables are expressed as percentages. After testing for normality using the Kolmogorov–Smirnov test, continuous variables were compared using a *t*-test or the Mann–Whitney *U*-test, categorical variables were compared by chi-square test or Fisher's exact test as appropriate. Multiple logistic regression analysis was performed to evaluate predictive factors for prehypertension. A value of $P < 0.05$ was considered statistically significant.

Ethical clearance

The study was reviewed and approved by the Health Authority Research Ethics Board of the Affiliated Hospital at Shunde (the First People's Hospital of Shunde), Southern Medical University, PR China.

Results

Prevalence of Prehypertension

Of the 5,362 cases (aged ≥ 35 years) initially reviewed, 651 cases were excluded because of missing data. Finally, 4711 cases (2674 men, 2037 women) were analyzed. The proportions of optimal BP, prehypertension, and hypertension were 39.1% (1842 cases), 38.6% (1819 cases), and 22.3% (1050 cases), respectively. The incidence of prehypertension was higher in men than in women (43.5% *vs.* 32.2%, $P < 0.001$). There was an increasing trend of prehypertension prevalence associated with age in men, but in women, the prevalence of prehypertension increased up to the age of 50–64 years and then decreased (Table 1).

Risk Factors Clustering in Different Blood Pressure Statuses

The average age, proportion of male sex, family history of hypertension, overweight, IFG, dyslipidemia, hyperuricemia, levels of FPG, TC, TG, BMI, and UA were significantly higher in prehypertension and hypertension groups than in the optimal BP group (all $P < 0.05$). The proportions of DM, obesity, and levels of LDL-C were also higher in the hypertension groups than in the optimal BP group (all $P < 0.05$); however, the differences were not significant in the prehypertension group (Table 2)

Cardiovascular Risk Factors in Different Sub-ranges of Prehypertension

To explore the heterogeneity within the prehypertension category, patients with prehypertension were further classified into low- and high-range subgroups. The proportions of male sex, overweight, IFG, BMI, and levels of FPG were higher in the low-range prehypertension group than in the optimal BP group (all $P < 0.05$), but there were no significant differences for other cardiovascular risk factors (all $P > 0.05$). The proportions of male sex, overweight, obesity, dyslipidemia, diabetes, IFG, hyperuricemia, BMI, and levels of TC, LDL-C, TG, FPG, and UA were higher in the high-range prehypertension group than in the optimal BP group (all $P < 0.05$). Compared with low-range prehypertension, the proportions of overweight, dyslipidemia, and IFG were higher in the high-range prehypertension (all $P < 0.05$) (Table 3).

Risk Factors Associated with Prehypertension

The multivariable-adjusted risk factors associated with prehypertension are presented in Table 4. High BMI (overweight/obesity) was the most important risk factor of prehypertension [odds ratio (*OR*)=2.89, 95% confidence interval (*CI*)=1.56–5.35, $P < 0.001$]. Age (≥ 50 years, *OR*=1.78, 95% *CI*=1.11–2.85, *P*=0.02), male sex (*OR*=2.15, 95% *CI*=1.37–3.37, $P < 0.001$), and hyperuricemia (*OR*=1.69, 95% *CI*=1.18–2.64, *P*=0.02) were also significantly associated with prehypertension.

Discussion

In this study, we found that prehypertension is highly prevalent in the Shunde District, Guangdong Province. Prehypertensive individuals presented with other risk factors associated with cardiovascular disease, such as overweight, dyslipidemia, impaired glucose, and hyperuricemia. Furthermore, combined risk factors were more significant in people with high-range prehypertension. To our knowledge, this is the first study to show that there was a significant heterogeneity of combined risk factors within the prehypertensive subgroups.

Many epidemiological studies have demonstrated that prehypertension is an important public health problem. However, the prevalence of prehypertension in different countries and districts differs significantly, and may be influenced by different regional factors, such as climate and lifestyle, as well as ethnicity. At the beginning of this century (2000–2001), a cross-sectional survey found that the incidence of prehypertension was 21.9% among Chinese subjects aged between 35 and 74 years.[3] However, in other subsequent studies, the incidence of prehypertension was significantly higher than this ratio. In northeast China, the incidence of prehypertension was up to 40%,[2, 4, 14] which may be associated with the cold climate and high-sodium diet. In this study, we found that the prevalence of prehypertension in the Shunde District of Guangdong Province, a traditional but economically developed district of southern China, was up to 38.6%. The incidence was very similar to the prevalence of the northern area, and it was significantly higher than the incidence reported at the beginning of this century for the entire country.[3] Further analysis showed that increased BMI was the most important risk factor of prehypertension in our study. Even among patients with low-range prehypertension, BMI was significantly increased compared with the optimal BP group. Therefore, our study suggests that although sodium intake is relatively low in Guangdong Province in southern China,[15] the prevalence of prehypertension is almost as high as that in the northern area. With the economic development and lifestyle changes, obesity/overweight has become a very important risk factor for increased BP.

Although the proportions of IFG and dyslipidemia were higher in prehypertension than optimal BP groups, in multivariable analysis, the associations of IFG and dyslipidemia with prehypertension were not significant after adjustment for BMI. Many studies have documented that overweight/obesity can cause significant insulin resistance, which may play an important role in impaired glucose metabolism, dyslipidemia, and increased BP.[16, 17] Clinical studies have shown that weight control can significantly lower BP.[18] These results indicated that lifestyle modifications, such as weight loss, are effective in the long-term primary prevention of hypertension. With the economic development and lifestyle changes, lifestyle modifications should be emphasized as a cornerstone in modern China.

Added to traditional risk factors, previous studies have found that serum UA levels were significantly associated with prehypertension.[19, 20] The mechanisms may be associated with inhibition of the nitric oxide pathway and activation of the renin-angiotensin system. Further, UA can cause proliferation of vascular smooth muscle cells and renal microvascular damage because of local inflammation and oxidative stress, finally leading to high BP.[21, 22] In our study, we found that the level of UA tended to increase in the low-range prehypertension group (P = 0.07), and the difference was significant between high-range prehypertension and the optimal BP groups. These results indicate that the effect of UA on BP may be increased throughout the entire prehypertension range.

In a recent randomized controlled trial, prehypertensive obese adolescents aged 11–17 years were enrolled and randomized to urate-lowering therapy (including allopurinol or probenecid) or placebo. Subjects treated with urate-lowering therapy experienced a highly significant reduction in BP (SBP 10.2 mm Hg and DBP 9.0 mm Hg, respectively). Systemic vascular resistance was also reduced in the urate-lowering therapy group.[23] Their findings strongly supported the synergistic pathogenic role of uric acid and obesity in hypertension. Genes and diet are important factors affecting the levels of UA; therefore, we emphasize the importance of lifestyle modification interventions for people with prehypertension.

It was interesting that there was significant ‘heterogeneity’ of combined cardiovascular risk factors within the prehypertensive subgroups in our study. Compared with optimal BP, BMI and FPG were increased in the low-range prehypertension group and were increased even further in the high-range prehypertension group. Furthermore, the proportions of overweight, dyslipidemia, and IFG were higher in the high-range prehypertension than those in the low-range prehypertension groups. These findings confirmed the importance of the definition of prehypertension, as well as the inhomogeneity of the prehypertension subcategories. Thus, we consider that healthcare professionals should recommend lifestyle changes to subjects with prehypertension. Furthermore, high-risk subpopulations with prehypertension, especially those with high-range prehypertension should be selected for future controlled trials to evaluate the effects of pharmacological treatment on this population.

Several limitations of this study must be considered. First, our data were based on community-based health checkup information, and not from a multi-stage stratified clustering sample. This may cause bias of the incidence of prehypertension. Second, some important confounding factors possibly associated with increased BP, such as diet, physical activity, and socioeconomic factors, were not evaluated in the present study. Third, follow up data of individuals with prehypertension were lack and further studies were needed on the matter.

Contributors YulH, YunH, and DX conceptualised the study, designed the protocol. YulH, WQ and XC analysed the data and drafted the manuscript. CL, DZ, JH collected the data. YW, YunH, and DX revised the manuscript. YunH and DX participated in administrative and technical support.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None.

Data Sharing Statement: No additional data available

References:

1. Chobanian AV, Bakris GL, Black HR, *et al.* The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003; 289: 2560-72.

2. Sun Z, Zheng L, Xu C, *et al.* Prevalence of prehypertension, hypertension and, associated risk factors in Mongolian and Han Chinese populations in Northeast China. *Int J Cardiol* 2008; 128: 250-4.

3. Yu D, Huang J, Hu D, *et al.* Prevalence and risk factors of prehypertension among Chinese adults. *J Cardiovasc Pharmacol* 2008; 52: 363-8.

4. Sun Z, Zheng L, Wei Y, *et al.* Prevalence and risk factors of the rural adult people prehypertension status in Liaoning Province of China. *Circ J* 2007; 71: 550-3.

5. Liu LS [2010 Chinese guidelines for the management of hypertension]. *Zhonghua Xin Xue Guan Bing Za Zhi* 2011; 39: 579-615.

6. Elliott WJ, Black HR Prehypertension. *Nat Clin Pract Cardiovasc Med* 2007; 4: 538-48.

7. Egan BM, Lackland DT, Jones DW. Prehypertension: an opportunity for a new public health paradigm. *Cardiol Clin* 2010; 28: 561-9.

8. Pimenta E, Oparil S Prehypertension: epidemiology, consequences and treatment. *Nat Rev Nephrol* 2010; 6: 21-30.

9. Gupta P, Nagaraju SP, Gupta A, Mandya CK. Prehypertension - time to act. *Saudi J Kidney Dis Transpl* 2012; 23: 223-33.

10. Report of the Expert Committee on the Diagnosis and Classification of Diabetes

Mellitus. *Diabetes Care* 2000; 23: S4-19.

11. [Chinese guidelines on prevention and treatment of dyslipidemia in adults]. *Zhonghua Xin Xue Guan Bing Za Zhi* 2007; 35: 390-419.

12. Zhou B. [Predictive values of body mass index and waist circumference to risk factors of related diseases in Chinese adult population]. *Zhonghua Liu Xing Bing Xue Za Zhi* 2002; 23: 5-10.

13. Ma YC, Zuo L, Chen JH, *et al*: Modified glomerular filtration rate estimating equation for Chinese patients with chronic kidney disease. *J Am Soc Nephrol* 2006; 17: 2937-44.

14. Dong GH, Wang D, Liu MM, *et al.* Sex difference of the prevalence and risk factors associated with prehypertension among urban Chinese adults from 33 communities of China: the CHPSNE study. *J Hypertens* 2012; 30: 485-91.

15. Cheng TO. Systolic and diastolic blood pressures and urinary sodium excretion in mainland China. *QJM* 2000; 93: 557-8.

16. Tobias DK, Pan A, Jackson CL, *et al.* Body-mass index and mortality among adults with incident type 2 diabetes. *N Engl J Med* 2014; 370: 233-44.

17. Gillman MW, Ludwig DS. How early should obesity prevention start? *N Engl J Med* 2013; 369: 2173-5.

18. Tyson CC, Appel LJ, Vollmer WM, *et al.* Impact of 5-year weight change on blood pressure: results from the Weight Loss Maintenance trial. *J Clin Hypertens.* 2013;15:458-64.

19. Liang J, Xue Y, Zou C, Zhang T, Song H, Qi L. Serum uric acid and prehypertension among Chinese adults. *J Hypertens* 2009; 27: 1761-5.

20. Kawamoto R, Tabara Y, Kohara K, Kusunoki T, Abe M, Miki T. Interaction between serum uric acid and triglycerides in relation to prehypertension in community-dwelling Japanese adults. *Clin Exp Hypertens* 2014; 36: 64-9.

21. Soltani Z, Rasheed K, Kapusta DR, Reisin E. Potential role of uric acid in metabolic syndrome, hypertension, kidney injury, and cardiovascular diseases: is it time for reappraisal? *Curr Hypertens Rep* 2013; 15: 175-81.

22. Reynolds TM. Serum uric acid and new-onset hypertension: a possible therapeutic avenue? *J Hum Hypertens* 2014;28:519-20.

23. Soletsky B, Feig DI. Uric acid reduction rectifies prehypertension in obese adolescents. *Hypertension* 2012; 60: 1148-56.

Table 1 Prevalence of Prehypertension and Hypertension by Sex and Age Group

Age (years)	n	Optimal BP (%)	Prehypertension (%)	Hypertension (%)
Male				
35~49	970	48.1	34.4	17.4
50~64	996	27.1	48.0	24.9
≥ 65	708	20.6	49.6	29.8
Total	2037	33.0	43.5	23.5
Female				
35~49	758	59.8	26.5	12.9
50~64	797	42.3	36.3	22.2
≥ 65	482	35.1	34.4	30.5
Total	2674	47.1	32.2	20.7
All				
35~49	1728	53.2	31.0	15.5
50~64	1793	33.9	42.8	23.7
≥ 65	1190	26.5	43.4	30.1
Total	4711	39.1	38.6	22.3

BP: blood pressure

Table 2 Cardiovascular Risk Factors in Different Blood Pressure Statuses

	Optimal BP (n=1842)	Prehypertension (n=1819)	Hypertension (n=1050)	*P*
Age (years)	48.8±10.5	52.1±11.3 △	54.3±10.4 △	0.008
Male [n (%)]	829 (45.0)	1163 (63.9)△	628 (59.8)△§	<0.001
Smoking [n (%)]	301 (16.3)	287 (15.8)	186 (17.7)	0.77
Alcoholic [n (%)]	35 (1.9)	42 (2.3)	27 (2.6)	0.464
Family history of Hypertension [n (%)]	274 (14.9)	292 (16.1)△	203 (19.3)△§	0.007
Overweight [n (%)]	236 (12.8)	395(21.7)△	241(23.0)△	<0.001
Obesity [n (%)]	128(6.9)	156(8.6)	98(9.3)△	0.019
BMI (kg/m^2)	21.6±3.2	24.9±3.5 △	25.6±4.8 △	0.001
Dyslipidemia [n (%)]	420(22.8)	488(26.8)△	312(29.7)△§	<0.001
TC (mmol/L)	5.02±1.25	5.39±1.67 △	5.64±1.59 △§	0.01
LDL-C (mmol/L)	3.21±1.15	3.45±1.18	3.68±1.32 △	0.03
HDL-C (mmol/L)	1.18±0.36	1.09±0.38	1.02±0.41	0.75
TG(mmol/L)	1.66±0.42	2.07±0.58 △	2.09±0.63 △	0.001
DM [n (%)]	138(7.5)	168(9.2)	109(10.4)△	0.002
IFG [n (%)]	261(14.2%)	384(21.1%)△	275(26.2)△§	<0.001
FPG (mmol/L)	5.14±1.96	5.79±2.03 △	5.91±2.27 △	0.003
Scr (mmol/L)	72.2±19.7	75.0±25.1	79.2±28.9	0.14
BUN (mmol/L)	5.34±1.71	6.01±1.87	6.25±1.99	0.35
eGFR (ml/min/1.73 m^2)	126.8±27.9	125.2±29.4	118.1±28.6	0.76
Hyperuricemia [n (%)]	233(12.6%)	302(16.6%)△	226(21.5)△§	0.001
UA (mmol/L)	377.5±32.2	402.9±34.6△	428.1±33.8△§	0.007

BP, blood pressure; BMI, body mass index; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; IFG, impaired fasting glucose; Scr, serum creatinine; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; UA, serum uric acid

△ *vs*. Optimal blood pressure $P < 0.05$, § *vs*. prehypertension $P < 0.05$

Table 3 Cardiovascular Risk Factors Different Sub-ranges of Prehypertension

	Low range prehypertension (n=925)	High range prehypertension (n=894)	*P*
Age (years)	50.6±11.2	53.7±12.4[#]	0.08
Male [n (%)]	584 (63.1%)[#]	579 (64.8%)[#]	0.47
Smoking [n (%)]	149 (16.1%)	138 (15.4%)	0.69
Alcoholic [n (%)]	20 (1.9%)	22 (2.7%)	0.29
Family history of Hypertension [n (%)]	153 (16.5%)	139 (15.5%)	0.56
Overweight [n (%)]	183 (19.8%)[#]	212 (23.7%)[#]	0.04
Obesity [n (%)]	75 (8.1%)	81(9.1%)[*]	0.47
BMI (kg/m^2)	23.7±3.3[*]	26.1±3.9[#]	<0.001
Dyslipidemia [n (%)]	227 (24.5%)	261 (29.2%)[#]	0.025
TC (mmol/L)	5.25±1.38	5.53±1.70[#]	0.04
LDL-C (mmol/L)	3.33±1.08	3.58±1.19[*]	0.10
HDL-C (mmol/L)	1.14±0.35	1.03±0.37	0.69
TG(mmol/L)	1.81±0.56	2.34±0.67[*]	0.12
DM [n (%)]	78 (8.4%)	90 (10.1%)[*]	0.23
IFG [n (%)]	171 (18.5%)[#]	213 (23.8%)[#]	0.005
FPG (mmol/L)	5.52±1.91[*]	6.07±2.05[#]	0.002
Scr (mmol/L)	76.1±29.4	73.8±27.0	0.18
BUN (mmol/L)	5.98±2.02	6.04±1.79	0.37
eGFR (ml/min/1.73 m^2)	128.7±30.6	121.6±28.4	0.29
Hyperuricemia [n (%)]	140 (15.1%)	162 (18.1%)[#]	0.09
UA (mmol/L)	392.5±40.2	411.8±37.9[#]	0.08

BMI, body mass index; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; IFG, impaired fasting glucose; Scr, serum creatinine; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; UA, serum uric acid

[*] *vs* optimal blood pressure $P < 0.05$, [#] *vs* Optimal blood pressure $P < 0.01$

Table 4 Multivariate Logistic Regression Analysis for Risk Factors of Prehypertension

Risk Factors	*OR*	95%*CI*	*P* 值
Age (≥ 50 years *vs* < 50 years)	1.78	1.11~2.85	0.02
Sex (Men *vs* Women)	2.15	1.37~3.37	< 0.001
Smoking (Yes *vs* No)	0.97	0.73~1.29	0.83
Alcoholic (Yes *vs* No)	1.09	0.82~1.45	0.55
Family history of Hypertension (Yes *vs* No)	1.24	0.90~1.71	0.19
overweight/obesity (Yes *vs* No)	2.89	1.56~5.35	< 0.001
Dyslipidemia (Yes *vs* No)	1.58	0.92~2.71	0.09
Impaired glucose regulation (Yes *vs* No)	1.63	0.96~2.78	0.07
Hyperuricemia (Yes *vs* No)	1.69	1.18~2.64	0.02

BMJ Open

Prevalence and Risk Factors Associated with Prehypertension in Shunde District, Southern China

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2014-006551.R1
Article Type:	Research
Date Submitted by the Author:	08-Oct-2014
Complete List of Authors:	Xu, Dingli; Nanfang Hospital, Southern Medical University, Cardiology Huang, Yuli; Nanfang Hospital, Southern Medical University, Cardiology Qiu, Wenke; the First People's Hospital of Shunde, Health Management Center Liu, Changhua; Nanfang Hospital, Southern Medical University, Cardiology Zhu, Dingji; Nanfang Hospital, Southern Medical University, Cardiology Hua, Jinghai; Nanfang Hospital, Southern Medical University, Cardiology Cai, Xiaoyan; the First People's Hospital of Shunde, Foshan, Cardiology Wu, Yanxian; the First People's Hospital of Shunde, Foshan, Cardiology Hu, Yunzhao; the First People's Hospital of Shunde, Foshan, Cardiology
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Cardiovascular medicine, Global health, Public health
Keywords:	Cardiac Epidemiology < CARDIOLOGY, Hypertension < CARDIOLOGY, EPIDEMIOLOGY

Prevalence and Risk Factors Associated with Prehypertension in Shunde District, Southern China

Running head: Prevalence and Risk Factors of Prehypertension

Yuli Huang,[1,2*] Wenke Qiu,[3*] Changhua Liu,[1] Dingji Zhu,[1] Jinghai Hua,[1] Xiaoyan Cai,[2] Yanxian Wu,[2] Yunzhao Hu,[2] Dingli Xu[1]

[1] Department of Cardiology, Nanfang Hospital, Southern Medical University, Guangzhou, PR China; [2] Department of Cardiology, the First People's Hospital of Shunde, Foshan, PR China; [3] Department of Health Management Center, the First People's Hospital of Shunde, PR China

* The authors contributed equally to this work

Corresponding author: Professor Dingli Xu. Department of Cardiology, Nanfang Hospital, Southern Medical University, Guangzhou, PR China. Tel.: + 86 20 61641503 Fax: + 86 20 87705671 E-mail: dinglixu@fimmu.com Or Professor Yunzhao Hu, Department of Cardiology, the First People's Hospital of Shunde, Foshan, PR China. Tel.: + 86 757 22318680 Fax: + 86 757 22223899 E-mail: huyunzhao4406@163.com

ABSTRACT

OBJECTIVE: To explore the prevalence and combined cardiovascular risk factors of prehypertension in southern China.

DESIGN: A retrospective study; the logistic regression model was used to find the risk factors of prehypertension.

SETTING: The study was conducted in Shunde District, Southern China, using the community-based health checkup information.

PARTICIPANTS: Subjects aged ≥ 35 years with complete health checkup information data between January 2011 and December 2013 were enrolled and divided into hypertension, prehypertension, and optimal blood pressure (BP). Prehypertension was further divided into low-range (BP 120-129/80-84 mmHg) and high-range (BP 130-139/85-89 mmHg) subgroups.

OUTCOME MEASURES: The prevalence of prehypertension and the combined cardiovascular risk factors within the prehypertensive subgroups.

RESULTS: Of the 5,362 initially reviewed cases (aged ≥ 35 years), 651 cases were excluded because of missing data. The proportions of optimal BP, prehypertension, and hypertension were 39.1%, 38.6%, and 22.3%, respectively. The average age, proportion of male sex, overweight, impaired fasting glucose (IFG), dyslipidemia, and hyperuricemia were significantly higher in the prehypertension group than in the optimal BP group (all $P < 0.05$). Compared with low-range prehypertension, the proportions of overweight, dyslipidemia, and IFG were higher in the high-range prehypertension group (all $P < 0.05$). Multivariate logistic regression analysis showed that overweight [odds ratio (*OR*) = 2.84, 95% confidence interval (*CI*) = 1.55–5.20], male sex (*OR* = 2.19, 95% *CI* = 1.39–3.45), age (per 10 years, *OR*=1.21, 95% *CI*=1.02–1.44, *P*=0.03) and hyperuricemia (*OR* = 1.70, 95% *CI* = 1.14–2.54) were independent risk factors of prehypertension.

CONCLUSIONS: Prehypertension is highly prevalent in southern China. Prehypertensive individuals presented with many other cardiovascular risk factors. There was heterogeneity of combined risk factors within the prehypertensive subgroups.

Keywords: Prehypertension; Prevalence; Risk Factors

Strengths and limitations of this study

■ This study first documented prehypertension is highly prevalent in the Shunde District, southern China.

■ With the economic development and lifestyle changes in China, obesity/overweight has become a very important risk factor for increased blood pressure.

■ This is the first study to show that there was a significant heterogeneity of combined risk factors within the prehypertensive subgroups.

■ Some important confounding factors possibly associated with increased blood pressure were not evaluated in the present study.

Introduction

In 2003, the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) proposed a new blood pressure (BP) category, including 120–139 mmHg systolic blood pressure (SBP) or 80–89 mmHg diastolic blood pressure (DBP), designated as "prehypertension".[1] The prevalence of prehypertension is up to 30–50% worldwide, as well as in many districts of China.[2-4] It is known that in China, the prevalence of hypertension is significantly higher in the northern than that in the southern area because of the colder climate and high-sodium intake.[5] Such regional factors may also affect the prevalence of prehypertension. However, the prevalence of prehypertension in Guangdong Province, southern China has been rarely reported.

Prehypertensive individuals are prone to progress into frank hypertension, and most of them present with clustering of other cardiovascular risk factors.[6-8] However, the term of "prehypertension" has been contentious. Most arguments against using this term consist of the possible public anxiety and overtreatment it may cause. Further, there is a high heterogeneity within this category because the risk of progressing to hypertension and developing cardiovascular disease is higher among people with BP 130–139/85–89 mmHg than among those with BP 120–129/80–84 mmHg.[6, 9] Furthermore, whether the concurrent cardiovascular risk factors in subgroups of prehypertension are different remains unanswered.

Given these inconsistent results, we conducted a retrospective analysis to explore the prevalence of prehypertension, and the cardiovascular risk factors in the

sub-groups of prehypertension in Guangdong Province, southern China.

Methods

Study Participants

We performed a retrospective study in Shunde District, a traditional but economically developed district of Guangdong Province, in China, using the community-based health checkup information. Community-based health checkup information was collected in the Health Management Center of the First People's Hospital of Shunde. The centers provided data for participants who enrolled in their health checkup programs conducted between January 2011 and December 2013. Subjects aged ≥ 35 years with complete data for the following characteristics were included in this study: age, sex, smoking/drinking habits, history of chronic diseases and treatment, family history of hypertension, height, weight, BP, fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), low density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), serum creatinine (Scr), blood urea nitrogen (BUN), and serum uric acid (UA).

Blood pressure measurement

Although our data were based on retrospective analysis of community-based health checkup information, the protocol of blood pressure measurement in our Health Management Center are carried out consistently since the foundation of the department. Subjects were asked to avoid caffeinated beverages, smoking and exercise for at least 30 minutes, and BP measurements were taken after the subjects were allowed to rest quietly for at least 5 min. Three BP measurements (2 minutes between each) were obtained for each individual by trained nurses, who were part of the Health Management Center, with a mercury sphygmomanometer. The first and fifth Korotkoff sounds were recorded as SBP and DBP respectively. During the measurements, the participants were seated with the arm supported at the level of the heart. The mean of 3 BP measurements was calculated and recorded.

Definition of Correlative Risk Factors

Correlative risk factors estimated in our study included the following: (1) BP classification was based on the recommendations from the JNC 7.[1] Optimal BP was defined as SBP < 120 mm Hg and DBP < 80 mm Hg. Hypertension was defined as SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg, or previously diagnosed as hypertension and currently undergoing antihypertensive treatment. Prehypertension was defined if individuals were not undergoing antihypertensive treatment and had a SBP of 120–139 mm Hg and/or DBP of 80–89 mm Hg. Prehypertension was further divided into low-range (SBP 120–129 and/or DBP 80–84 mmHg) and high-range (SBP 130–139 mmHg and/or DBP 85–89 mmHg) subgroups. (2) Impaired glucose regulation was diagnosed based on FPG according to the American Diabetes Association criteria,[10] including diabetes (FPG ≥ 7.0 mmol/L) and impaired fasting glucose (IFG, FPG 5.6–6.9 mmol/L). Dyslipidemia was defined as with a history of receiving antidyslipidemia agents or TC ≥ 5.18 mmol/L, LDL-C ≥ 3.37 mmol/L, HDL-C < 1.04 mmol/L, and/or TG ≥ 1.7 mmol/L, according to the 2007 Guidelines for Prevention and Treatment of Dyslipidemia in Adults in China.[11] Hyperuricemia was defined as UA ≥ 416 μmol/L in men and 357 μmol/L in women. (3) Overweight and obesity were defined as body mass index (BMI) 24–27.9 kg/m^2 and BMI ≥ 28 kg/m^2 according to Chinese criteria.[12] (4) The estimated glomerular filtration rate (eGFR) of each participant was estimated using the modified Modification of Diet in Renal Disease equation adapted for Chinese,[13] as: eGFR = 186 × Scr$^{-1.154}$ × Age$^{-0.203}$ × 0.742 (Female) × 1.233 (Chinese).

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Science software release 16.0 (SPSS Inc., Chicago, IL, USA). Continuous variables are presented as mean (standard deviation) or median (inter-quartile range) as appropriate. Categorical variables are expressed as percentages. After testing for normality using the Kolmogorov–Smirnov test, continuous variables were compared using a *t*-test or the Mann–Whitney *U*-test, categorical variables were compared by chi-square test or Fisher's exact test as appropriate. Multiple logistic regression analysis was performed to evaluate predictive factors for prehypertension. Individuals with optimal BP were used as reference. Multicollinearity (strong correlations among independent variables) was examined by collinearity diagnostic statistics. Variance inflation factor values >2.5 or tolerance <0.4 may indicate concern for multicollinearity in logistic regression models [14]. A value of $P < 0.05$ was considered statistically significant.

Ethical clearance

The study was reviewed and approved by the Health Authority Research Ethics Board of the First People's Hospital of Shunde, Foshan, PR China.

Results

Prevalence of Prehypertension

Of the 5,362 cases (aged ≥ 35 years) initially reviewed, 651 cases were excluded because of missing data. Finally, 4711 cases (2674 men, 2037 women) were analyzed. The proportions of optimal BP, prehypertension, and hypertension were 39.1% (1842 cases), 38.6% (1819 cases), and 22.3% (1050 cases), respectively. The prevalence of prehypertension was higher in men than in women (43.5% *vs.* 32.2%, $P < 0.001$). There was an increasing trend of prehypertension prevalence associated with age (Table 1).

Risk Factors Clustering in Different Blood Pressure Statuses

The average age, proportion of male sex, family history of hypertension, overweight, IFG, dyslipidemia, hyperuricemia, levels of FPG, TC, TG, BMI, and UA were significantly higher in prehypertension and hypertension groups than in the optimal BP group (all $P < 0.05$). The proportions of DM, obesity, and level of LDL-C were also higher in the hypertension group than in the optimal BP group (all $P < 0.05$); however, the differences were not significant in the prehypertension group compared with that in the optimal BP group (Table 2)

Cardiovascular Risk Factors in Different Sub-ranges of Prehypertension

To explore the heterogeneity within the prehypertension category, patients with prehypertension were further classified into low- and high-range subgroups. The proportions of male sex, overweight, IFG, BMI, and levels of FPG were higher in the low-range prehypertension group than in the optimal BP group (all $P < 0.05$), but there were no significant differences for other cardiovascular risk factors (all $P > 0.05$). The proportions of male sex, overweight, obesity, dyslipidemia, diabetes, IFG, hyperuricemia, BMI, and levels of TC, LDL-C, TG, FPG, and UA were higher in the high-range prehypertension group than in the optimal BP group (all $P < 0.05$). Compared with low-range prehypertension, the proportions of overweight, dyslipidemia, and IFG were higher in the high-range prehypertension (all $P < 0.05$) (Table 3).

Risk Factors Associated with Prehypertension

The multivariable-adjusted risk factors associated with prehypertension are presented in Table 4. High BMI (overweight/obesity) was the most important risk factor of prehypertension [odds ratio (*OR*)=2.84, 95% confidence interval (*CI*)=1.55–5.20, $P < 0.001$]. Age (per 10 years, *OR*=1.21, 95% *CI*=1.02–1.44, *P*=0.03), male sex (*OR*=2.19, 95% *CI*=1.39–3.45, $P < 0.001$), and hyperuricemia (*OR*=1.70, 95% *CI*=1.14–2.54, *P*=0.009) were also significantly associated with prehypertension. Furthermore, collinearity statistics were >0.4 for tolerance and <2.5 for variance inflation factor, suggesting that multicollinearity was not a concern among the independent variables.

Discussion

In this study, we found that prehypertension is highly prevalent in the Shunde District, Guangdong Province. Prehypertensive individuals presented with other risk factors associated with cardiovascular disease, such as overweight, dyslipidemia, impaired glucose, and hyperuricemia. Furthermore, combined cardiovascular risk factors were more significant in people with high-range prehypertension. To our knowledge, this is the first study to show that there was a significant heterogeneity of combined risk factors within the prehypertensive subgroups.

Many epidemiological studies have demonstrated that prehypertension is an important public health problem. However, the prevalence of prehypertension in different countries and districts differs significantly, and may be influenced by different regional factors, such as climate and lifestyle, as well as ethnicity. At the beginning of this century (2000–2001), a cross-sectional survey found that the prevalence of prehypertension was 21.9% among Chinese subjects aged between 35 and 74 years.[3] However, in other subsequent studies, the prevalence of prehypertension was significantly higher than this ratio. In rural northeastern China, the prevalence of prehypertension was 35.1% in men and 32.5% in women,[15] and up to 40% in whole population from urban areas of northeastern China,[16] which may be associated with the cold climate and high-sodium diet. In this study, we found that the prevalence of prehypertension in the Shunde District of Guangdong Province, a traditional but economically developed district of southern China, was up to 38.6%. The prevalence was very similar to that in the urban areas of northeastern China,[16] and significantly higher than the prevalence reported at the beginning of this century for the entire country.[3] Further analysis showed that increased BMI was the most important risk factor of prehypertension in our study. Even among patients with low-range prehypertension, BMI was significantly increased compared with the optimal BP group. Therefore, our study suggests that although sodium intake is relatively low in Guangdong Province in southern China,[17] the prevalence of prehypertension is almost as high as that in the northern area. With the economic development and lifestyle changes, obesity/overweight has become a very important risk factor for increased BP.

Although the proportions of IFG and dyslipidemia were higher in prehypertension than optimal BP groups, in multivariable analysis, the associations of IFG and dyslipidemia with prehypertension were not significant after adjustment for BMI. Many studies have documented that overweight/obesity can cause significant insulin resistance, which may play an important role in impaired glucose metabolism, dyslipidemia, and increased BP.[18, 19] Clinical studies have shown that weight control can significantly lower BP.[20] These results indicated that lifestyle modifications, such as weight loss, are effective in the long-term primary prevention of hypertension. With the economic development and lifestyle changes, lifestyle modifications should be emphasized as a cornerstone in modern China.

Added to traditional risk factors, previous studies have found that serum UA levels were significantly associated with prehypertension.[21, 22] The mechanisms may be associated with inhibition of the nitric oxide pathway and activation of the renin-angiotensin system. Further, UA can cause proliferation of vascular smooth muscle cells and renal microvascular damage because of local inflammation and oxidative stress, finally leading to high BP.[23, 24] In our study, we found that the level of UA tended to increase in the low-range prehypertension group (P = 0.07), and the difference was significant between high-range prehypertension and the optimal BP groups. These results indicate that the effect of UA on BP may be increased throughout the entire prehypertension range.

In a recent randomized controlled trial, prehypertensive obese adolescents aged 11–17 years were enrolled and randomized to urate-lowering therapy (including allopurinol or probenecid) or placebo. Subjects treated with urate-lowering therapy experienced a highly significant reduction in BP (SBP 10.2 mm Hg and DBP 9.0 mm Hg, respectively). Systemic vascular resistance was also reduced in the urate-lowering therapy group.[25] These findings strongly supported the synergistic pathogenic role of UA and obesity in hypertension. Genes and diet are important factors affecting the levels of UA; therefore, we emphasize the importance of lifestyle modification interventions for people with prehypertension.

It was interesting that there was significant ‘heterogeneity’ of combined cardiovascular risk factors within the prehypertensive subgroups in our study. Compared with optimal BP, BMI and FPG were increased in the low-range prehypertension group and were increased even further in the high-range prehypertension group. Furthermore, the proportions of overweight, dyslipidemia, and IFG were higher in the high-range prehypertension than those in the low-range prehypertension groups. These findings confirmed the importance of the definition of prehypertension, as well as the inhomogeneity of the prehypertension subcategories. Our prior meta analysis also found that prehypertension was associated with increased risks of CVD[26] and end-stage renal disease.[27] However, because of limit prospective, randomized trials examining the effects of anti-hypertensive therapy on reducing target organ damage specifically in prehypertension, currently professional societies do not recommend pharmacotherapy for prehypertension, even in individuals with high-range prehypertension.[28,29] This is a great gap to be covered between epidemiological studies and randomized controlled studies in prehypertension. Prehypertensive individuals are at a high risk to progress to sustained hypertension, as well as CVD and renal damage. So periodic screening is important. For therapeutic implications, we consider that healthcare professionals should recommend lifestyle changes to subjects with prehypertension. Furthermore, high-risk subpopulations with prehypertension, especially those with high-range prehypertension should be selected for future controlled trials to evaluate the effects of pharmacological treatment on this population.

Several limitations of this study must be considered. First, our data were based on community-based health checkup information, and not from a multi-stage stratified clustering sample. This may cause bias of the prevalence of prehypertension. Second, some important confounding factors possibly associated with increased BP, such as diet, physical activity, and socioeconomic factors, were not evaluated in the present study. Third, follow up data of individuals with prehypertension were lack and further studies were needed on the matter.

Conclusion

This study showed that companied with the economic development and lifestyle changes, prehypertension is highly prevalent in the Shunde District, southern China. Many other cardiovascular risk factors were presented in individuals with prehypertension, especially in those with high-range prehypertension. Periodic screening and lifestyle changes should be recommended to subjects with prehypertension for prevention of hypertension, as well as cardiovascular disease.

Contributors YulH, YunH, and DX conceptualised the study, designed the protocol. YulH, WQ and XC analysed the data and drafted the manuscript. CL, DZ, JH collected the data. YW, YunH, and DX revised the manuscript. YunH and DX participated in administrative and technical support.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None.

Data Sharing Statement: No additional data available

References:

1. Chobanian AV, Bakris GL, Black HR, *et al.* The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003; 289: 2560-72.

2. Sun Z, Zheng L, Xu C, *et al.* Prevalence of prehypertension, hypertension and, associated risk factors in Mongolian and Han Chinese populations in Northeast China. *Int J Cardiol* 2008; 128: 250-4.

3. Yu D, Huang J, Hu D, *et al.* Prevalence and risk factors of prehypertension among Chinese adults. *J Cardiovasc Pharmacol* 2008; 52: 363-8.

4. Sun Z, Zheng L, Wei Y, *et al.* Prevalence and risk factors of the rural adult people prehypertension status in Liaoning Province of China. *Circ J* 2007; 71: 550-3.

5. Liu LS [2010 Chinese guidelines for the management of hypertension]. *Zhonghua Xin Xue Guan Bing Za Zhi* 2011; 39: 579-615.

6. Elliott WJ, Black HR Prehypertension. *Nat Clin Pract Cardiovasc Med* 2007; 4: 538-48.

7. Egan BM, Lackland DT, Jones DW. Prehypertension: an opportunity for a new public health paradigm. *Cardiol Clin* 2010; 28: 561-9.

8. Pimenta E, Oparil S Prehypertension: epidemiology, consequences and treatment. *Nat Rev Nephrol* 2010; 6: 21-30.

9. Gupta P, Nagaraju SP, Gupta A, Mandya CK. Prehypertension - time to act. *Saudi J Kidney Dis Transpl* 2012; 23: 223-33.

10. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus.

Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 2003; 26 Suppl 1: S5-S20.

11. Joint Committee for Developing Chinese guidelines on Prevention and Treatment of Dyslipidemia in Adults. [Chinese guidelines on prevention and treatment of dyslipidemia in adults]. *Zhonghua Xin Xue Guan Bing Za Zhi* 2007; 35: 390-419.

12. Zhou B. [Predictive values of body mass index and waist circumference to risk factors of related diseases in Chinese adult population]. *Zhonghua Liu Xing Bing Xue Za Zhi* 2002; 23: 5-10.

13. Ma YC, Zuo L, Chen JH, *et al*: Modified glomerular filtration rate estimating equation for Chinese patients with chronic kidney disease. *J Am Soc Nephrol* 2006; 17: 2937-44.

14. Pallant J. SPSS survival manual: a step by step guide to data analysis using SPSS for windows (version 10). Open University Press; 2001.

15. Li Z, Guo X, Zheng L, *et al.* Prehypertension in rural northeastern china: results from the northeast china rural cardiovascular health study. *J* Clin Hypertens (Greenwich) 2014;16:664-70.

16. Dong GH, Wang D, Liu MM, *et al.* Sex difference of the prevalence and risk factors associated with prehypertension among urban Chinese adults from 33 communities of China: the CHPSNE study. *J Hypertens* 2012; 30: 485-91.

17. Cheng TO. Systolic and diastolic blood pressures and urinary sodium excretion in mainland China. *QJM* 2000; 93: 557-8.

18. Tobias DK, Pan A, Jackson CL, *et al.* Body-mass index and mortality among adults with incident type 2 diabetes. *N Engl J Med* 2014; 370: 233-44.

19. Gillman MW, Ludwig DS. How early should obesity prevention start? *N Engl J Med* 2013; 369: 2173-5.

20. Tyson CC, Appel LJ, Vollmer WM, *et al.* Impact of 5-year weight change on blood pressure: results from the Weight Loss Maintenance trial. *J Clin Hypertens.* 2013;15:458-64.

21. Liang J, Xue Y, Zou C, Zhang T, Song H, Qi L. Serum uric acid and prehypertension among Chinese adults. *J Hypertens* 2009; 27: 1761-5.

22. Kawamoto R, Tabara Y, Kohara K, Kusunoki T, Abe M, Miki T. Interaction between serum uric acid and triglycerides in relation to prehypertension in community-dwelling Japanese adults. *Clin Exp Hypertens* 2014; 36: 64-9.

23. Soltani Z, Rasheed K, Kapusta DR, Reisin E. Potential role of uric acid in metabolic syndrome, hypertension, kidney injury, and cardiovascular diseases: is it time for reappraisal? *Curr Hypertens Rep* 2013; 15: 175-81.

24. Reynolds TM. Serum uric acid and new-onset hypertension: a possible therapeutic avenue? *J Hum Hypertens* 2014;28:519-20.

25. Soletsky B, Feig DI. Uric acid reduction rectifies prehypertension in obese adolescents. *Hypertension* 2012; 60: 1148-56.

26. Huang Y, Wang S, Cai X, *et al.*. Prehypertension and incidence of cardiovascular disease: a meta analysis. *BMC Med* 2013;11:177.

27. Huang Y, Cai X, Zhang J, *et al.*. Prehypertension and Incidence of ESRD: A Systematic Review and Meta analysis. *Am J Kidney Dis* 2014;63:76-83.

28. James P A, Oparil S, Carter B L, et al. 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)[J]. *JAMA* 2014,311:507-20.

29. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)[J]. *Eur Heart J* 2013,34:2159-219.

Table 1 Prevalence of Prehypertension and Hypertension by Sex and Age Group

Age (years)	n	Optimal BP (%)	Prehypertension (%)	Hypertension (%)
Male				
35~49	970	48.1	34.4	17.4
50~64	996	27.1	48.0	24.9
≥ 65	708	20.6	49.6	29.8
Total	2037	33.0	43.5	23.5
Female				
35~49	758	59.8	26.5	12.9
50~64	797	42.3	36.3	22.2
≥ 65	482	35.1	34.4	30.5
Total	2674	47.1	32.2	20.7
All				
35~49	1728	53.2	31.0	15.5
50~64	1793	33.9	42.8	23.7
≥ 65	1190	26.5	43.4	30.1
Total	4711	39.1	38.6	22.3

BP: blood pressure

Table 2 Cardiovascular Risk Factors in Different Blood Pressure Statuses

	Optimal BP (n=1842)	Prehypertension (n=1819)	Hypertension (n=1050)	*P*
Age (years)	48.8±10.5	52.1±11.3 △	54.3±10.4 △	0.008
Male [n (%)]	829 (45.0)	1163 (63.9)△	628 (59.8)△§	<0.001
Smoking [n (%)]	301 (16.3)	287 (15.8)	186 (17.7)	0.77
Alcoholic [n (%)]	35 (1.9)	42 (2.3)	27 (2.6)	0.464
Family history of Hypertension [n (%)]	274 (14.9)	292 (16.1)△	203 (19.3)△§	0.007
Overweight [n (%)]	236 (12.8)	395(21.7)△	241(23.0)△	<0.001
Obesity [n (%)]	128(6.9)	156(8.6)	98(9.3)△	0.019
BMI (kg/m^2)	21.6±3.2	24.9±3.5 △	25.6±4.8 △	0.001
Dyslipidemia [n (%)]	420(22.8)	488(26.8)△	312(29.7)△§	<0.001
TC (mmol/L)	5.02±1.25	5.39±1.67 △	5.64±1.59 △§	0.01
LDL-C (mmol/L)	3.21±1.15	3.45±1.18	3.68±1.32 △	0.03
HDL-C (mmol/L)	1.18±0.36	1.09±0.38	1.02±0.41	0.75
TG(mmol/L)	1.66±0.42	2.07±0.58 △	2.09±0.63 △	0.001
DM [n (%)]	138(7.5)	168(9.2)	109(10.4)△	0.002
IFG [n (%)]	261(14.2%)	384(21.1%)△	275(26.2)△§	<0.001
FPG (mmol/L)	5.14±1.96	5.79±2.03 △	5.91±2.27 △	0.003
Scr (mmol/L)	72.2±19.7	75.0±25.1	79.2±28.9	0.14
BUN (mmol/L)	5.34±1.71	6.01±1.87	6.25±1.99	0.35
eGFR (ml/min/1.73 m^2)	126.8±27.9	125.2±29.4	118.1±28.6	0.76
Hyperuricemia [n (%)]	233(12.6%)	302(16.6%)△	226(21.5)△§	0.001
UA (mmol/L)	377.5±32.2	402.9±34.6△	428.1±33.8△§	0.007

BP, blood pressure; BMI, body mass index; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; IFG, impaired fasting glucose; Scr, serum creatinine; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; UA, serum uric acid

△ *vs.* Optimal blood pressure $P < 0.05$, § *vs.* prehypertension $P < 0.05$

Table 3 Cardiovascular Risk Factors Different Sub-ranges of Prehypertension

	Low range prehypertension (n=925)	High range prehypertension (n=894)	*P*
Age (years)	50.6±11.2	53.7±12.4 #	0.08
Male [n (%)]	584 (63.1%) #	579 (64.8%) #	0.47
Smoking [n (%)]	149 (16.1%)	138 (15.4%)	0.69
Alcoholic [n (%)]	20 (1.9%)	22 (2.7%)	0.29
Family history of Hypertension [n (%)]	153 (16.5%)	139 (15.5%)	0.56
Overweight [n (%)]	183 (19.8%) #	212 (23.7%) #	0.04
Obesity [n (%)]	75 (8.1%)	81(9.1%) *	0.47
BMI (kg/m^2)	23.7±3.3 *	26.1±3.9 #	<0.001
Dyslipidemia [n (%)]	227 (24.5%)	261 (29.2%) #	0.025
TC (mmol/L)	5.25±1.38	5.53±1.70 #	0.04
LDL-C (mmol/L)	3.33±1.08	3.58±1.19 *	0.10
HDL-C (mmol/L)	1.14±0.35	1.03±0.37	0.69
TG(mmol/L)	1.81±0.56	2.34±0.67 *	0.12
DM [n (%)]	78 (8.4%)	90 (10.1%) *	0.23
IFG [n (%)]	171 (18.5%) #	213 (23.8%) #	0.005
FPG (mmol/L)	5.52±1.91 *	6.07±2.05 #	0.002
Scr (mmol/L)	76.1±29.4	73.8±27.0	0.18
BUN (mmol/L)	5.98±2.02	6.04±1.79	0.37
eGFR (ml/min/1.73 m^2)	128.7±30.6	121.6±28.4	0.29
Hyperuricemia [n (%)]	140 (15.1%)	162 (18.1%) #	0.09
UA (mmol/L)	392.5±40.2	411.8±37.9 #	0.08

BMI, body mass index; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; IFG, impaired fasting glucose; Scr, serum creatinine; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; UA, serum uric acid

* *vs* optimal blood pressure $P < 0.05$, # *vs* Optimal blood pressure $P < 0.01$

Table 4 Multivariate Logistic Regression Analysis for Risk Factors of Prehypertension

Risk Factors	*OR*	95%*CI*	*P* 值
Age (per 10 years)	1.21	1.02~1.44	0.03
Sex (Men *vs* Women)	2.19	1.39~3.45	< 0.001
Smoking (Yes *vs* No)	0.97	0.70~1.34	0.85
Alcoholic (Yes *vs* No)	1.12	0.89~1.41	0.33
Family history of Hypertension (Yes *vs* No)	1.29	0.88~1.89	0.19
overweight/obesity (Yes *vs* No)	2.84	1.55~5.20	< 0.001
Dyslipidemia (Yes *vs* No)	1.58	0.92~2.71	0.09
Impaired glucose regulation (Yes *vs* No)	1.64	0.96~2.81	0.07
Hyperuricemia (Yes *vs* No)	1.70	1.14~2.54	0.009

Prehypertension was defined if individuals were not undergoing antihypertensive treatment and had a SBP of 120–139 mm Hg and/or DBP of 80–89 mm Hg. Individuals with optimal blood pressure (SBP < 120 mm Hg and DBP < 80 mm Hg) were used as reference.

Prevalence and Risk Factors Associated with Prehypertension in Shunde District, Southern China

Running head: Prevalence and Risk Factors of Prehypertension

Yuli Huang,[1,2*] Wenke Qiu,[3*] Changhua Liu, [1] Dingji Zhu, [1] Jinghai Hua, [1] Xiaoyan Cai,[2] Yanxian Wu, [2] Yunzhao Hu, [2] Dingli Xu[1]

[1] Department of Cardiology, Nanfang Hospital, Southern Medical University, Guangzhou, PR China; [2] Department of Cardiology, the First People's Hospital of Shunde, Foshan, PR China; [3] Department of Health Management Center, the First People's Hospital of Shunde, PR China

* The authors contributed equally to this work

Corresponding author: Professor Dingli Xu. Department of Cardiology, Nanfang Hospital, Southern Medical University, Guangzhou, PR China. Tel.: + 86 20 61641503 Fax: + 86 20 87705671 E-mail: dinglixu@fimmu.com Or Professor Yunzhao Hu, Department of Cardiology, the First People's Hospital of Shunde, Foshan, PR China. Tel.: + 86 757 22318680 Fax: + 86 757 22223899 E-mail: huyunzhao4406@163.com

ABSTRACT

OBJECTIVE: To explore the incidenceprevalence and combined cardiovascular risk factors of prehypertension in southern China.

DESIGN: A retrospective cross-sectional study; the logistic regression model was used to find the risk factors of prehypertension.

SETTING: The study was conducted in Shunde District, Southern China, using the community-based health checkup information.

PARTICIPANTS: Subjects aged ≥ 35 years with complete health checkup information data between January 2011 and December 2013 were enrolled and divided into hypertension, prehypertension, and optimal blood pressure (BP). Prehypertension was further divided into low-range (BP 120-129/80-84 mmHg) and high-range (BP 130-139/85-89 mmHg) subgroups.

OUTCOME MEASURES: The prevalence of prehypertension and the combined cardiovascular risk factors within the prehypertensive subgroups.

RESULTS: Of the 5,362 initially reviewed cases (aged ≥ 35 years), 651 cases were excluded because of missing data. The proportions of optimal BP, prehypertension, and hypertension were 39.1%, 38.6%, and 22.3%, respectively. The average age, proportion of male sex, overweight, impaired fasting glucose (IFG), dyslipidemia, and hyperuricemia were significantly higher in the prehypertension group than in the optimal BP group (all $P < 0.05$). Compared with low-range prehypertension, the proportions of overweight, dyslipidemia, and IFG were higher in the high-range prehypertension group (all $P < 0.05$). Multivariate logistic regression analysis showed that overweight [odds ratio (*OR*) = 2.8984, 95% confidence interval (*CI*) = 1.5655–5.3520], male sex (*OR* = 2.1519, 95% *CI* = 1.3739–3.3745), age (per 10 years, *OR*=1.21, 95% *CI*=1.02–1.44, *P*=0.03) and hyperuricemia (*OR* = 1.6970, 95% *CI* =

1.~~18~~14–2.~~64~~54) were independent risk factors of prehypertension.

CONCLUSIONS: Prehypertension is highly prevalent in southern China. Prehypertensive individuals presented with many other cardiovascular risk factors. There was heterogeneity of combined risk factors within the prehypertensive subgroups.

Keywords: Prehypertension; Prevalence; Risk Factors

Strengths and limitations of this study

▪ This study first documented prehypertension is highly prevalent in the Shunde District, southern China.

▪ With the economic development and lifestyle changes in China, obesity/overweight has become a very important risk factor for increased blood pressure.

▪ This is the first study to show that there was a significant heterogeneity of combined risk factors within the prehypertensive subgroups.

▪ Some important confounding factors possibly associated with increased blood pressure were not evaluated in the present study.

Introduction

In 2003, the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) proposed a new blood pressure (BP) category, including 120–139 mmHg systolic blood pressure (SBP) or 80–89 mmHg diastolic blood pressure (DBP), designated as "prehypertension".[1] The prevalenceincidence of prehypertension is up to 30–50% worldwide, as well as in many districts of China.[2-4] It is known that in China, the prevalence incidence of hypertension is significantly higher in the northern than that in the southern area because of the colder climate and high-sodium intake.[5] Such regional factors may also affect the prevalenceincidence of prehypertension. However, the prevalenceincidence of prehypertension in Guangdong Province, southern China has been rarely reported.

Prehypertensive individuals are prone to progress into frank hypertension, and most of them present with clustering of other cardiovascular risk factors.[6-8] However, the term of "prehypertension" has been contentious. Most arguments against using this term consist of the possible public anxiety and overtreatment it may cause. Further, there is a high heterogeneity within this category because the risk of progressing to hypertension and developing cardiovascular disease is higher among people with BP 130–139/85–89 mmHg than among those with BP 120–129/80–84 mmHg.[6, 9] Furthermore, whether the concurrent cardiovascular risk factors in subgroups of prehypertension are different remains unanswered.

Given these inconsistent results, we conducted a retrospective analysis to explore the prevalence of prehypertension, and the cardiovascular risk factors in the

sub-groups of prehypertension in Guangdong Province, southern China.

Methods

Study Participants

We performed a retrospective study in Shunde District, a traditional but economically developed district of Guangdong Province, in China, using the community-based health checkup information. Community-based health checkup information was collected in the Health Management Center of the First People's Hospital of Shunde. The centers provided data for participants who enrolled in their health checkup programs conducted between January 2011 and December 2013. Subjects aged ≥ 35 years with complete data for the following characteristics were included in this study: age, sex, smoking/drinking habits, history of chronic diseases and treatment, family history of hypertension, height, weight, BP, fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), low density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), serum creatinine (Scr), blood urea nitrogen (BUN), and serum uric acid (UA). ~~This study was approved by the Ethics Committee of the Affiliated Hospital at Shunde of the Southern Medical University.~~

Blood pressure measurement

Although our data were based on retrospective analysis of community-based health checkup information, the protocol of blood pressure measurement in our Health

Management Center are carried out consistently since the foundation of the department. Subjects were asked to avoid caffeinated beverages, smoking and exercise for at least 30 minutes, and BP measurements were taken after the subjects were allowed to rest quietly for at least 5 min. Three BP measurements (2 minutes between each) were obtained for each individual by trained nurses, who were part of the Health Management Center, with a mercury sphygmomanometer. The first and fifth Korotkoff sounds were recorded as SBP and DBP respectively. During the measurements, the participants were seated with the arm supported at the level of the heart. The mean of 3 BP measurements was calculated and recorded.

Definition of Correlative Risk Factors

Correlative risk factors estimated in our study included the following: (1) BP classification was based on the recommendations from the JNC 7.[1] ~~Normal~~ Optimal BP was defined as SBP < 120 mm Hg and DBP < 80 mm Hg. Hypertension was defined as SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg, or previously diagnosed as hypertension and currently undergoing antihypertensive treatment. Prehypertension was defined if ~~patients~~ individuals were not undergoing antihypertensive treatment and had a SBP of 120–139 mm Hg and/or DBP of 80–89 mm Hg. Prehypertension was further divided into low-range (SBP 120–129 and/or DBP 80–84 mmHg) and high-range (SBP 130–139 mmHg and/or DBP 85–89 mmHg) subgroups. (2) Impaired glucose regulation was diagnosed based on FPG according to the American Diabetes Association criteria,[10] including diabetes (FPG ≥ 7.0 mmol/L) and impaired fasting glucose (IFG, FPG 5.6–6.9 mmol/L). Dyslipidemia was defined as with a history of receiving antidyslipidemia agents or TC ≥ 5.18 mmol/L, LDL-C ≥ 3.37 mmol/L, HDL-C < 1.04 mmol/L, and/or TG ≥ 1.7 mmol/La history of receiving antidyslipidemia agents or as satisfying criteria on admission such as TC ≥ 5.18 mmol/L, LDL-C ≥ 3.37 mmol/L, HDL-C < 1.04 mmol/L, and/or TG ≥ 1.7 mmol/L, according to the 2007 Guidelines for Prevention and Treatment of Dyslipidemia in Adults in China.[11] Hyperuricemia was defined as UA ≥ 416 μmol/L in men and 357 μmol/L in women. (3) Overweight and obesity were defined as body mass index (BMI) 24–27.9 kg/m^2 and BMI ≥ 28 kg/m^2 according to Chinese criteria.[12] (4) The estimated glomerular filtration rate (eGFR) of each participant was estimated using the modified Modification of Diet in Renal Disease equation adapted for Chinese,[13] as: eGFR = 186 × Scr$^{-1.154}$ × Age$^{-0.203}$ × 0.742 (Female) × 1.233 (Chinese).

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Science software release 16.0 (SPSS Inc., Chicago, IL, USA). Continuous variables are presented as mean ± (standard deviation) or median (inter-quartile range) as appropriate. Categorical variables are expressed as percentages. After testing for normality using the Kolmogorov–Smirnov test, continuous variables were compared using a *t*-test or the Mann–Whitney *U*-test, categorical variables were compared by chi-square test or Fisher's exact test as appropriate. Multiple logistic regression analysis was performed to evaluate predictive factors for prehypertension. Individuals with optimal BP were used as reference. Multicollinearity (strong correlations among independent variables) was examined by collinearity diagnostic statistics. Variance inflation factor values >2.5 or tolerance <0.4 may indicate concern for multicollinearity in logistic regression models [14]. A value of $P < 0.05$ was considered statistically significant.

Ethical clearance

The study was reviewed and approved by the Health Authority Research Ethics Board of the Affiliated Hospital at Shunde (the First People's Hospital of Shunde), Southern Medical UniversityFoshan, PR China.

Results

Prevalence of Prehypertension

Of the 5,362 cases (aged ≥ 35 years) initially reviewed, 651 cases were excluded because of missing data. Finally, 4711 cases (2674 men, 2037 women) were analyzed. The proportions of optimal BP, prehypertension, and hypertension were 39.1% (1842 cases), 38.6% (1819 cases), and 22.3% (1050 cases), respectively. The prevalenceincidence of prehypertension was higher in men than in women (43.5% *vs.* 32.2%, $P < 0.001$). There was an increasing trend of prehypertension prevalence associated with age in men, but in women, the prevalence of prehypertension increased up to the age of 50–64 years and then decreased (Table 1).

Risk Factors Clustering in Different Blood Pressure Statuses

The average age, proportion of male sex, family history of hypertension, overweight, IFG, dyslipidemia, hyperuricemia, levels of FPG, TC, TG, BMI, and UA were significantly higher in prehypertension and hypertension groups than in the optimal BP group (all $P < 0.05$). The proportions of DM, obesity, and levels of LDL-C were also higher in the hypertension groups than in the optimal BP group (all $P < 0.05$); however, the differences were not significant in the prehypertension group compared with that in the optimal BP group (Table 2)

Cardiovascular Risk Factors in Different Sub-ranges of Prehypertension

To explore the heterogeneity within the prehypertension category, patients with prehypertension were further classified into low- and high-range subgroups. The proportions of male sex, overweight, IFG, BMI, and levels of FPG were higher in the low-range prehypertension group than in the optimal BP group (all $P < 0.05$), but there were no significant differences for other cardiovascular risk factors (all $P > 0.05$). The proportions of male sex, overweight, obesity, dyslipidemia, diabetes, IFG, hyperuricemia, BMI, and levels of TC, LDL-C, TG, FPG, and UA were higher in the high-range prehypertension group than in the optimal BP group (all $P < 0.05$). Compared with low-range prehypertension, the proportions of overweight, dyslipidemia, and IFG were higher in the high-range prehypertension (all $P < 0.05$) (Table 3).

Risk Factors Associated with Prehypertension

The multivariable-adjusted risk factors associated with prehypertension are presented in Table 4. High BMI (overweight/obesity) was the most important risk factor of prehypertension [odds ratio (*OR*)=2.~~89~~84, 95% confidence interval (*CI*)=1.~~56~~55–5.~~35~~20, *P* < 0.001]. Age (~~≥ 50~~per 10 years, *OR*=1.~~78~~21, 95% *CI*=1.~~11~~02–~~2.85~~1.44, *P*=0.~~02~~03), male sex (*OR*=2.~~15~~19, 95% *CI*=1.~~37~~39–3.~~37~~45, *P* < 0.001), and hyperuricemia (*OR*=1.~~69~~70, 95% *CI*=1.~~18~~14–2.~~64~~54, *P*=0.~~02~~009) were also significantly associated with prehypertension. Furthermore, collinearity statistics were >0.4 for tolerance and <2.5 for variance inflation factor, suggesting that multicollinearity was not a concern among the independent variables.

Discussion

In this study, we found that prehypertension is highly prevalent in the Shunde District, Guangdong Province. Prehypertensive individuals presented with other risk factors associated with cardiovascular disease, such as overweight, dyslipidemia, impaired glucose, and hyperuricemia. Furthermore, combined cardiovascular risk factors were more significant in people with high-range prehypertension. To our knowledge, this is the first study to show that there was a significant heterogeneity of combined risk factors within the prehypertensive subgroups.

Many epidemiological studies have demonstrated that prehypertension is an important public health problem. However, the prevalence of prehypertension in different countries and districts differs significantly, and may be influenced by different regional factors, such as climate and lifestyle, as well as ethnicity. At the beginning of this century (2000–2001), a cross-sectional survey found that the prevalence~~incidence~~ of prehypertension was 21.9% among Chinese subjects aged between 35 and 74 years.[3] However, in other subsequent studies, the prevalence~~incidence~~ of prehypertension was significantly higher than this ratio. In rural northeastern China, the prevalence~~incidence~~ of prehypertension was 35.1% in men and 32.5% in women,[15] and up to 40% in whole population from urban areas of northeastern China,~~up to 40%,~~[~~2, 4, 14~~–16] which may be associated with the cold climate and high-sodium diet. In this study, we found that the prevalence of prehypertension in the Shunde District of Guangdong Province, a traditional but economically developed district of southern China, was up to 38.6%. The prevalence~~incidence~~ was very similar to th~~e prevalence of~~at in the urban areas of northeastern China~~northern area~~,[16] and ~~it was~~ significantly higher than the ~~incidence~~prevalence reported at the beginning of this century for the entire country.[3] Further analysis showed that increased BMI was the most important risk factor of prehypertension in our study. Even among patients with low-range prehypertension, BMI was significantly increased compared with the optimal BP group. Therefore, our study suggests that although sodium intake is relatively low in Guangdong Province in southern China,[~~15~~ 17] the prevalence of prehypertension is almost as high as that in the northern area. With the economic development and lifestyle changes, obesity/overweight has become a very important risk factor for increased BP.

Although the proportions of IFG and dyslipidemia were higher in prehypertension than optimal BP groups, in multivariable analysis, the associations of IFG and dyslipidemia with prehypertension were not significant after adjustment for BMI. Many studies have documented that overweight/obesity can cause significant insulin resistance, which may play an important role in impaired glucose metabolism, dyslipidemia, and increased BP.[~~16~~18, ~~17~~–19] Clinical studies have shown that weight control can significantly lower BP.[~~18~~20] These results indicated that lifestyle modifications, such as weight loss, are effective in the long-term primary prevention of hypertension. With the economic development and lifestyle changes, lifestyle modifications should be emphasized as a cornerstone in modern China.

Added to traditional risk factors, previous studies have found that serum UA levels were significantly associated with prehypertension.[~~19~~21, ~~20~~–22] The mechanisms may be associated with inhibition of the nitric oxide pathway and activation of the renin-angiotensin system. Further, UA can cause proliferation of vascular smooth muscle cells and renal microvascular damage because of local inflammation and oxidative stress, finally leading to high BP.[~~21~~23, ~~22~~–24] In our study, we found that the level of UA tended to increase in the low-range prehypertension group (P = 0.07), and the difference was significant between high-range prehypertension and the optimal BP groups. These results indicate that the effect of UA on BP may be increased throughout the entire prehypertension range.

In a recent randomized controlled trial, prehypertensive obese adolescents aged 11–17 years were enrolled and randomized to urate-lowering therapy (including allopurinol or probenecid) or placebo. Subjects treated with urate-lowering therapy experienced a highly significant reduction in BP (SBP 10.2 mm Hg and DBP 9.0 mm Hg, respectively). Systemic vascular resistance was also reduced in the urate-lowering therapy group.[~~23~~ 25] The~~ir~~se findings strongly supported the synergistic pathogenic role of ~~uric acid~~UA and obesity in hypertension. Genes and diet are important factors affecting the levels of UA; therefore, we emphasize the importance of lifestyle modification interventions for people with prehypertension.

It was interesting that there was significant 'heterogeneity' of combined cardiovascular risk factors within the prehypertensive subgroups in our study. Compared with optimal BP, BMI and FPG were increased in the low-range prehypertension group and were increased even further in the high-range prehypertension group. Furthermore, the proportions of overweight, dyslipidemia, and IFG were higher in the high-range prehypertension than those in the low-range prehypertension groups. These findings confirmed the importance of the definition of prehypertension, as well as the inhomogeneity of the prehypertension subcategories. Our prior meta analysis also found that prehypertension was associated with increased risks of CVD[26] and end-stage renal disease.[27] However, because of limit prospective, randomized trials examining the effects of anti-hypertensive therapy on reducing target organ damage specifically in prehypertension, currently professional societies do not recommend pharmacotherapy for prehypertension, even in individuals with high-range prehypertension.[28,29] This is a great gap to be covered between epidemiological studies and randomized controlled studies in prehypertension. Prehypertensive individuals are at a high risk to progress to sustained hypertension, as well as CVD and renal damage. So periodic screening is important. For therapeutic implications, ~~Thus,~~ we consider that healthcare professionals should recommend lifestyle changes to subjects with prehypertension. Furthermore, high-risk subpopulations with prehypertension, especially those with high-range prehypertension should be selected for future controlled trials to evaluate the effects of pharmacological treatment on this population.

Several limitations of this study must be considered. First, our data were based on community-based health checkup information, and not from a multi-stage stratified clustering sample. This may cause bias of the ~~incidence~~prevalence of prehypertension. Second, some important confounding factors possibly associated with increased BP, such as diet, physical activity, and socioeconomic factors, were not evaluated in the present study. Third, follow up data of individuals with prehypertension were lack and further studies were needed on the matter.

Conclusion

This study showed that companied with the economic development and lifestyle changes, prehypertension is highly prevalent in the Shunde District, southern China. Many other cardiovascular risk factors were presented in individuals with prehypertension, especially in those with high-range prehypertension. Periodic screening and lifestyle changes should be recommended to subjects with prehypertension for prevention of hypertension, as well as cardiovascular disease.

Contributors YulH, YunH, and DX conceptualised the study, designed the protocol. YulH, WQ and XC analysed the data and drafted the manuscript. CL, DZ, JH collected the data. YW, YunH, and DX revised the manuscript. YunH and DX participated in administrative and technical support.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None.

References:

1. Chobanian AV, Bakris GL, Black HR, *et al.* The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003; 289: 2560-72.

2. Sun Z, Zheng L, Xu C, *et al.* Prevalence of prehypertension, hypertension and, associated risk factors in Mongolian and Han Chinese populations in Northeast China. *Int J Cardiol 2*008; 128: 250-4.

3. Yu D, Huang J, Hu D, *et al.* Prevalence and risk factors of prehypertension among Chinese adults. *J Cardiovasc Pharmacol* 2008; 52: 363-8.

4. Sun Z, Zheng L, Wei Y, *et al.* Prevalence and risk factors of the rural adult people prehypertension status in Liaoning Province of China. *Circ J* 2007; 71: 550-3.

5. Liu LS [2010 Chinese guidelines for the management of hypertension]. *Zhonghua Xin Xue Guan Bing Za Zhi* 2011; 39: 579-615.

6. Elliott WJ, Black HR Prehypertension. *Nat Clin Pract Cardiovasc Med* 2007; 4: 538-48.

7. Egan BM, Lackland DT, Jones DW. Prehypertension: an opportunity for a new public health paradigm. *Cardiol Clin* 2010; 28: 561-9.

8. Pimenta E, Oparil S Prehypertension: epidemiology, consequences and treatment. *Nat Rev Nephrol* 2010; 6: 21-30.

9. Gupta P, Nagaraju SP, Gupta A, Mandya CK. Prehypertension - time to act. *Saudi J Kidney Dis Transpl* 2012; 23: 223-33.

10. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus.

Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* ~~2000~~2003; 26 Suppl 1: S5-S20.~~23: S4-19.~~

11. Joint Committee for Developing Chinese guidelines on Prevention and Treatment of Dyslipidemia in Adults. [Chinese guidelines on prevention and treatment of dyslipidemia in adults]. *Zhonghua Xin Xue Guan Bing Za Zhi* 2007; 35: 390-419.

12. Zhou B. [Predictive values of body mass index and waist circumference to risk factors of related diseases in Chinese adult population]. *Zhonghua Liu Xing Bing Xue Za Zhi* 2002; 23: 5-10.

13. Ma YC, Zuo L, Chen JH, *et al*: Modified glomerular filtration rate estimating equation for Chinese patients with chronic kidney disease. *J Am Soc Nephrol* 2006; 17: 2937-44.

14. Pallant J. SPSS survival manual: a step by step guide to data analysis using SPSS for windows (version 10). Open University Press; 2001.

15. Li Z, Guo X, Zheng L, *et al.* Prehypertension in rural northeastern china: results from the northeast china rural cardiovascular health study. *J Clin Hypertens (Greenwich)* 2014;16:664-70.

1~~4~~6. Dong GH, Wang D, Liu MM, *et al.* Sex difference of the prevalence and risk factors associated with prehypertension among urban Chinese adults from 33 communities of China: the CHPSNE study. *J Hypertens* 2012; 30: 485-91.

1~~5~~7. Cheng TO. Systolic and diastolic blood pressures and urinary sodium excretion in mainland China. *QJM* 2000; 93: 557-8.

1~~6~~8. Tobias DK, Pan A, Jackson CL, *et al.* Body-mass index and mortality among adults with incident type 2 diabetes. *N Engl J Med* 2014; 370: 233-44.

179. Gillman MW, Ludwig DS. How early should obesity prevention start? *N Engl J Med* 2013; 369: 2173-5.

1820. Tyson CC, Appel LJ, Vollmer WM, *et al.* Impact of 5-year weight change on blood pressure: results from the Weight Loss Maintenance trial. *J Clin Hypertens.* 2013;15:458-64.

1921. Liang J, Xue Y, Zou C, Zhang T, Song H, Qi L. Serum uric acid and prehypertension among Chinese adults. *J Hypertens* 2009; 27: 1761-5.

2022. Kawamoto R, Tabara Y, Kohara K, Kusunoki T, Abe M, Miki T. Interaction between serum uric acid and triglycerides in relation to prehypertension in community-dwelling Japanese adults. *Clin Exp Hypertens* 2014; 36: 64-9.

2123. Soltani Z, Rasheed K, Kapusta DR, Reisin E. Potential role of uric acid in metabolic syndrome, hypertension, kidney injury, and cardiovascular diseases: is it time for reappraisal? *Curr Hypertens Rep* 2013; 15: 175-81.

2224. Reynolds TM. Serum uric acid and new-onset hypertension: a possible therapeutic avenue? *J Hum Hypertens* 2014;28:519-20.

2325. Soletsky B, Feig DI. Uric acid reduction rectifies prehypertension in obese adolescents. *Hypertension* 2012; 60: 1148-56.

26. Huang Y, Wang S, Cai X, *et al.*. Prehypertension and incidence of cardiovascular disease: a meta analysis. *BMC Med* 2013;11:177.

27. Huang Y, Cai X, Zhang J, *et al.*. Prehypertension and Incidence of ESRD: A Systematic Review and Meta analysis. *Am J Kidney Dis* 2014;63:76-83.

Formatted: French (France)

Formatted: French (France)

Formatted: Danish

28. James P A, Oparil S, Carter B L, et al. 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)[J]. *JAMA* 2014,311:507-20.

29. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)[J]. *Eur Heart J* 2013,34:2159-219.

Table 1 Prevalence of Prehypertension and Hypertension by Sex and Age Group

Age (years)	n	Optimal BP (%)	Prehypertension (%)	Hypertension (%)
Male				
35~49	970	48.1	34.4	17.4
50~64	996	27.1	48.0	24.9
≥ 65	708	20.6	49.6	29.8
Total	2037	33.0	43.5	23.5
Female				
35~49	758	59.8	26.5	12.9
50~64	797	42.3	36.3	22.2
≥ 65	482	35.1	34.4	30.5
Total	2674	47.1	32.2	20.7
All				
35~49	1728	53.2	31.0	15.5
50~64	1793	33.9	42.8	23.7
≥ 65	1190	26.5	43.4	30.1
Total	4711	39.1	38.6	22.3

BP: blood pressure

Table 2 Cardiovascular Risk Factors in Different Blood Pressure Statuses

	Optimal BP (n=1842)	Prehypertension (n=1819)	Hypertension (n=1050)	*P*
Age (years)	48.8±10.5	52.1±11.3 △	54.3±10.4 △	0.008
Male [n (%)]	829 (45.0)	1163 (63.9)△	628 (59.8)△§	<0.001
Smoking [n (%)]	301 (16.3)	287 (15.8)	186 (17.7)	0.77
Alcoholic [n (%)]	35 (1.9)	42 (2.3)	27 (2.6)	0.464
Family history of Hypertension [n (%)]	274 (14.9)	292 (16.1)△	203 (19.3)△§	0.007
Overweight [n (%)]	236 (12.8)	395(21.7)△	241(23.0)△	<0.001
Obesity [n (%)]	128(6.9)	156(8.6)	98(9.3)△	0.019
BMI (kg/m^2)	21.6±3.2	24.9±3.5 △	25.6±4.8 △	0.001
Dyslipidemia [n (%)]	420(22.8)	488(26.8)△	312(29.7)△§	<0.001
TC (mmol/L)	5.02±1.25	5.39±1.67 △	5.64±1.59 △§	0.01
LDL-C (mmol/L)	3.21±1.15	3.45±1.18	3.68±1.32 △	0.03
HDL-C (mmol/L)	1.18±0.36	1.09±0.38	1.02±0.41	0.75
TG(mmol/L)	1.66±0.42	2.07±0.58 △	2.09±0.63 △	0.001
DM [n (%)]	138(7.5)	168(9.2)	109(10.4)△	0.002
IFG [n (%)]	261(14.2%)	384(21.1%)△	275(26.2)△§	<0.001
FPG (mmol/L)	5.14±1.96	5.79±2.03 △	5.91±2.27 △	0.003
Scr (mmol/L)	72.2±19.7	75.0±25.1	79.2±28.9	0.14
BUN (mmol/L)	5.34±1.71	6.01±1.87	6.25±1.99	0.35
eGFR (ml/min/1.73 m^2)	126.8±27.9	125.2±29.4	118.1±28.6	0.76
Hyperuricemia [n (%)]	233(12.6%)	302(16.6%)△	226(21.5)△§	0.001
UA (mmol/L)	377.5±32.2	402.9±34.6△	428.1±33.8△§	0.007

BP, blood pressure; BMI, body mass index; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; IFG, impaired fasting glucose; Scr, serum creatinine; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; UA, serum uric acid

△ *vs.* Optimal blood pressure $P < 0.05$, § *vs.* prehypertension $P < 0.05$

Table 3 Cardiovascular Risk Factors Different Sub-ranges of Prehypertension

	Low range prehypertension (n=925)	High range prehypertension (n=894)	*P*
Age (years)	50.6±11.2	53.7±12.4[#]	0.08
Male [n (%)]	584 (63.1%)[#]	579 (64.8%)[#]	0.47
Smoking [n (%)]	149 (16.1%)	138 (15.4%)	0.69
Alcoholic [n (%)]	20 (1.9%)	22 (2.7%)	0.29
Family history of Hypertension [n (%)]	153 (16.5%)	139 (15.5%)	0.56
Overweight [n (%)]	183 (19.8%)[#]	212 (23.7%)[#]	0.04
Obesity [n (%)]	75 (8.1%)	81(9.1%)[*]	0.47
BMI (kg/m^2)	23.7±3.3[*]	26.1±3.9[#]	<0.001
Dyslipidemia [n (%)]	227 (24.5%)	261 (29.2%)[#]	0.025
TC (mmol/L)	5.25±1.38	5.53±1.70[#]	0.04
LDL-C (mmol/L)	3.33±1.08	3.58±1.19[*]	0.10
HDL-C (mmol/L)	1.14±0.35	1.03±0.37	0.69
TG(mmol/L)	1.81±0.56	2.34±0.67[*]	0.12
DM [n (%)]	78 (8.4%)	90 (10.1%)[*]	0.23
IFG [n (%)]	171 (18.5%)[#]	213 (23.8%)[#]	0.005
FPG (mmol/L)	5.52±1.91[*]	6.07±2.05[#]	0.002
Scr (mmol/L)	76.1±29.4	73.8±27.0	0.18
BUN (mmol/L)	5.98±2.02	6.04±1.79	0.37
eGFR (ml/min/1.73 m^2)	128.7±30.6	121.6±28.4	0.29
Hyperuricemia [n (%)]	140 (15.1%)	162 (18.1%)[#]	0.09
UA (mmol/L)	392.5±40.2	411.8±37.9[#]	0.08

BMI, body mass index; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; IFG, impaired fasting glucose; Scr, serum creatinine; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; UA, serum uric acid

[*] *vs* optimal blood pressure $P < 0.05$, [#] *vs* Optimal blood pressure $P < 0.01$

Table 4 Multivariate Logistic Regression Analysis for Risk Factors of Prehypertension

Risk Factors	*OR*	95%*CI*	*P* 值
Age (per 10 years ~~≥ 50 years *vs* < 50 years~~)	1.~~78~~21	1.~~11~~02~~~2~~1.~~85~~44	0.~~02~~03
Sex (Men *vs* Women)	2.~~15~~19	1.~~37~~39~3.~~37~~45	< 0.001
Smoking (Yes *vs* No)	0.97	0.~~73~~70~1.~~29~~34	0.~~83~~85
Alcoholic (Yes *vs* No)	1.~~09~~12	0.~~82~~89~1.~~45~~41	0.~~55~~33
Family history of Hypertension (Yes *vs* No)	1.~~24~~29	0.~~90~~88~1.~~71~~89	0.19
overweight/obesity (Yes *vs* No)	2.~~89~~84	1.~~56~~55~5.~~35~~20	< 0.001
Dyslipidemia (Yes *vs* No)	1.58	0.92~2.71	0.09
Impaired glucose regulation (Yes *vs* No)	1.~~63~~64	0.96~2.~~78~~81	0.07
Hyperuricemia (Yes *vs* No)	1.~~69~~70	1.~~18~~14~2.~~64~~54	0.~~02~~009

Prehypertension was defined if individuals were not undergoing antihypertensive treatment and had a SBP of 120–139 mm Hg and/or DBP of 80–89 mm Hg. Individuals with optimal blood pressure (SBP < 120 mm Hg and DBP < 80 mm Hg) were used as reference.