Original Article

Attributable risk of all-cause mortality in hypertensive adults based on disease risk prediction model: A Chinese cohort study

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ABSTRACT

Background: The aim of this study was to estimate the attributable risk for all-cause mortality in hypertensive adults living in Beijing, China.

Methods: We conducted a prospective cohort study on the basis of the disease risk prediction model, which included 3006 hypertensive patients aged 50 and over who participated in the annual health examination from thirty-eight community health centers were randomly selected from all 53 community health centers in Dongcheng district of Beijing in China. This cohort study was conducted from January 1, 2013 to June 31, 2018 in these community health centers. Data included age, gender, education level, BMI, smoking and drinking status, renal function, diabetes mellitus (DM), coronary heart disease, levels of blood pressure, use of medications, and blood lipid levels.

Results: the follow-up time was 4.90 ± 0.51 years. There were significant survival differences by gender, renal function (eGFR > 90 vs. 60–90 vs. <60 mL/min per 1.73 m^2), smoking (smoking vs. No smoking), hypertension severity (SBP $\geq$ 140 or DBP $\geq$ r vs. SBP/DBP < 140/90 mmHg), education level (<6 vs. 6–12 vs. >12 years), coronary heart disease (CHD) (CHD vs. NO CHD). In the multivariate Cox proportional hazard analysis, the prognostic factors of all-cause mortality in hypertensive patients were male [HR 1.662, 95% CI 1.110–2.489, p = 0.014], educational level<6 years [HR 2.044, 95% CI 1.164–3.591, p 0.013], age $\geq$65 years [HR 3.092, 95% CI 1.717–5.571, p < 0.001], smoking [HR 1.885, 95% CI 1.170–3.309, p = 0.009], eGFR<60 mL/min per 1.73 m^2 [HR 3.591, 95% CI 2.023–6.371, p < 0.001].

Conclusions: we conclude that decreasing eGFR, increasing age, smoking, low education and gender (male) are significant and independent risk factor for mortality in hypertension for this urban cohort. Recommendations may include protecting renal function, providing patient education, and cessation of smoking. It highlights that early preventive measures are needed to detect kidney impairment and protect renal function. It also suggests that earlier smoking cessation may be important for hypertensive patients.

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Introduction

During 1975–2015, the number of adults around the world with hypertension increased from 594 million to more than 1.1 billion [1]. Hypertension increases the risk of end-organ injury and total mortality. It is a major modifiable risk factor for heart disease, stroke, and kidney failure. In 2010, high blood pressure was the main cause of death and disability-adjusted life years in the worldwide [2,3]. Hypertension is a leading cause for cardiovascular disease and premature death [4]. Recently, the prevalence of hypertension has been increasing, and is reported to be 41.9% among participants aged 35–70 years from the Prospective Urban

Rural Epidemiology (PURE)-China subcohort [5]. Several studies have demonstrated a quantitative association between hypertension and death from cardiovascular disease (CVD) [6,7]. The main goal of this study is to estimate the attributable risks associated with hypertension for all-cause mortality, including renal function, diabetes mellitus (DM), coronary heart disease, smoking, gender, age, education level and the levels of the blood pressure.

Materials and methods

Study population and data collection

Thirty-eight community health centers were randomly selected from all 53 community health centers in Dongcheng District of Beijing in China. Dongcheng District is one of Beijing's 16 districts and its population was 919,000 as of China's 2010 Census. This cohort study was conducted from January 1, 2013 to June 31, 2018 in these community health centers. According to JNC guidelines for the management of hypertension, hypertension was defined as SBP $\geq$ 140 or DBP $\geq$ 90 mmHg or using antihypertensive medication if hypertension was known [8]. Patients with hypertension using this criteria, aged greater than 50 years old, and living in this community for at least 5 years were recruited for the study. Exclude pregnant or lactating women, physical disabilities, and people with mental illness diagnoses. A total of 3006 participants were selected. Follow-up with these cohort members was initiated on January 1, 2013, and individuals were flagged at the occurrence of death from any cause or at the end of the study (31 June 2018). All experiments were performed in accordance with relevant guidelines and regulations. Informed consent was obtained from all patients. The study was approved by the Ethical Committee of Dongzhimen Hospital, Beijing University of Chinese Medicine.

Construction method of risk prediction model

The establishment of risk prediction model can better screen high-risk population and predict the incidence of disease. At present, regression statistical methods such as Logistic regression and Cox stepwise regression are mainly used to predict the development of hypertension in pre-hypertension population. Although they have certain predictive ability, these models require variables to be independent and cannot deal with the collinearity between variables.

There are many methods to construct disease risk prediction models, such as Logistic regression, Cox regression, Support Vector Machine (SVM), Neural Network, Markov Model, Decision Tree, Classification Tree, Bayesian Network Model and Time Series Model. At present, it is generally believed that there is no method suitable for any characteristic data. By synthesizing various performance indicators, SVM is the best, followed by Logistic regression, followed by decision tree, Bayesian and neural network. It can be seen that the predictive ability of different models varies with different data types. As long as the type of experimental design and the purpose of research are clearly defined, it is entirely possible to select a better model by reasonably comparing the results of different modeling methods.

Clinical and laboratory measurements

A trained interviewer administered a questionnaire to collect information, which included demographic data, smoking history, symptoms and drug history. These patients were tested for baseline laboratory values at the time of enrolment, as outlined below. They were followed annually.

Weight was recorded to the nearest kilogram while the subjects were minimally clothed and without shoes. Height was measured

in a standing position, without shoes, using a tape measure, while the shoulders were in normal alignment. Body mass index (BMI) was calculated as weight (kg) in kilograms divided by height in meters squared (m^2).

Waist circumference (WC) was measured at the umbilical level, using a measuring tape, without any pressure on the body surface, and was recorded to the nearest 1 cm. Hip circumference was measured at the widest girth of the hip over light clothing and was recorded to the nearest 1 cm. Waist to hip (WHR) was calculated as WC (cm) divided by HC (cm).

After a 10-min rest in the sitting position, systolic and diastolic blood pressures (SBP and DBP) were taken, on the right arm, using a standardized mercury sphygmomanometer.

A blood sample was taken between 7:30 and 10:00 AM from all study participants, after 12 h of overnight fasting. All blood analyses were carried out at the same laboratory on the day of blood collection. Plasma glucose, lipid profile (total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides) and blood uric acid (UA) were measured using standardized procedures. Low-density lipoprotein cholesterol (mmol/L) was calculated using the Friedewald formula [9]. Serum creatinine was measured using the enzymatic method. Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology collaboration (CKD-EPI) formula [10]. All samples were analyzed when internal quality control met the acceptable criteria.

Definition of terms

Education level was classified into 3 categories: (i) those who had studied less than 6 years, (ii) those who had studied for 6–12 years, and (iii) those with more than 12 years of education. Using the definition provided by the American Diabetes Association, participants were considered to have type 2 diabetes if they met at least one of these criteria: FPG $\geq$ 7.0 mmol/L, 2h-PCPG$\geq$11.1 mmol/L or taking anti-diabetic medication. Physician-diagnosed CHD (i.e., history of myocardial infarction, angina, coronary artery bypass) was reported through questionnaires for patients.

Statistical analysis

Mean (SD) values for continuous and categorical variables of baseline characteristics were described. An independent sample t test and a Chi-squared test were performed to compare the significance of discrete variables. Baseline characteristics were compared between three stages of eGFR ($\geq$as, 90–60, <60 mL/min per 1.73 m^2) using ANOVA. Kaplan–Meier and Log Rank tests were performed to time to event analysis. The primary endpoint was all-cause mortality. In the Cox proportional hazard model analysis, hazard ratio (HR) and 95% confidence interval (CI) were calculated after adjusting for age, sex, body mass index (BMI), comorbid conditions (diabetes and CHD), and smoking. The adjustment laboratory variables were normally distributed and were handled as continuous variables. p Value <0.05 was considered statistically significant in all analyses. Statistical analyses were performed using SPSS version 20.0. The Kaplan–Meier analyses were performed with GraphPad Prism 6.0.

Results

The characteristics of hypertension

The study population included a total of 3006 adults with mean (SD) age of 67.05 (8.94) years. The study included 1038 men and 1968 women. All baseline characteristics were significantly different between men and women. Comparison of laboratory characteristics between male and female patients revealed a significant difference. The prevalence of diabetes is 47% (Table 1).

Table 1
Baseline characteristics of hypertension according to gender.

Factors	All patients (N = 3006)	Men (N = 1038)	Women (N = 1968)	p
Age, year	67.05 (8.94)	68.08 (8.83)	66.50 (8.95)	**<0.001**
BMI, kg/m^2	25.57 (3.11)	25.33 (2.87)	25.69 (3.23)	**0.002**
Waist/hip	0.88 (0.06)	0.90 (0.06)	0.88 (0.06)	**<0.001**
SBP, mmHg	125.61(7.09)	126.13 (7.17)	125.33 (7.03)	**0.003**
DBP, mmHg	75.11 (5.84)	75.43 (5.93)	74.95 (5.78)	**0.033**
Diabetes mellitus, n (%)	1408 (46.84)	504 (48.55)	904 (45.03)	0.092
Current smoking, n (%)	391 (13.00)	333 (32.08)	58 (2.95)	**<0.001**
Drinking, n (%)	352 (11.71)	332 (31.98)	27 (1.37)	**<0.001**
Education, n (%)				**<0.001**
<6 years	520 (17.30)	111 (10.69)	409 (20.78)	
6–12 years	1949 (64.83)	678 (65.32)	1271 (64.58)	
≥12 years	537 (17.86)	249 (23.99)	288 (14.63)	
Medication				
Hypotensives (%)	2629 (87.46)	910 (87.66)	1719 (87.35)	
Lipid lowering (%)	1923 (63.97)	641 (61.75)	1282 (65.14)	
Diabetes mellitus (%)	1438 (47.84)	501 (48.27)	937 (47.61)	
Laboratory characteristics				
eGFR (mL/min per 1.73 m^2)	86.57 (15.72)	84.80 (15.69)	87.50 (15.66)	**<0.001**
Serum uric acid (μmol/L)	304.60 (80.53)	334.28 (82.28)	288.95 (75.02)	**<0.001**
Glucose (mmol/L)	5.68 (1.99)	5.84 (2.17)	5.60 (1.88)	**0.002**
Cholesterol (mmol/L)	5.21 (1.04)	4.93 (1.01)	5.35 (1.03)	**<0.001**
Triglyceride (mmol/L)	1.52 (1.03)	1.47 (0.95)	1.55 (1.07)	**0.035**
LDL-C (mmol/L)	3.49 (0.99)	3.37 (0.97)	3.55 (0.99)	**<0.001**
HDL-C (mmol/L)	1.38 (0.34)	1.27 (0.34)	1.43 (0.33)	**<0.001**

Abbreviation: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; LDL-C, low density lipoprotein cholesterin; HDL-C, high density lipoprotein cholesterin.

Table 2
Baseline characteristics of hypertension according to eGFR (mL/min per 1.73 m^2).

Factors	eGFR ≥ 90 (N = 1448)	90 > eGFR ≥ 60 (N = 1332)	eGFR < 60 (N = 226)	P
Age, year	61.82 (6.59)	71.60 (7.93)	73.78 (8.54)	**<0.001**
BMI, kg/m^2	25.53 (3.16)	25.61 (3.06)	25.59 (3.17)	0.811
Waist/hip	0.88 (0.06)	0.89 (0.06)	0.89 (0.06)	**0.030**
SBP, mmHg	125.48 (6.78)	125.73 (7.44)	125.68 (6.90)	0.645
DBP, mmHg	75.61 (5.72)	74.66 (5.99)	74.62 (5.40)	**<0.001**
Hyperlipidaemia, n (%)	424 (29.28)	345 (25.90)	59 (26.10)	0.121
Current smoking, n (%)	201 (13.88)	168 (12.61)	23 (10.18)	0.253
Drinking, n (%)	189 (13.05)	150 (11.26)	20 (8.85)	0.114
Education, n (%)		**<0.001**		
<6 years	336 (23.20)	110 (8.26)	74 (32.74)	
6-12 years	1078 (74.44)	760 (52.49)	111 (49.11)	
≥12 years	260 (17.96)	236 (17.72)	41 (18.14)	
Laboratory characteristics				
Serum uric acid (μmol/L)	282.39 (70.87)	316.32 (78.25)	377.86 (93.33)	**<0.001**
Glucose (mmol/L)	5.79 (2.13)	5.52 (1.72)	5.91 (2.41)	**<0.001**
Cholesterol (mmol/L)	5.24 (1.01)	5.16 (1.03)	5.25 (1.20)	0.072
Triglyceride (mmol/L)	1.55 (1.20)	1.48 (0.88)	1.60 (0.78)	0.128
LDL-C (mmol/L)	3.51 (0.97)	3.47 (0.99)	3.46 (1.08)	0.386
HDL-C (mmol/L)	1.40 (0.35)	1.36 (0.34)	1.27 (0.33)	**<0.001**

Abbreviation: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; LDL-C, low density lipoprotein cholesterin; HDL-C, high density lipoprotein cholesterin.

The patients were divided into three major groups by eGFR (≥90, 90–60, <60 mL/min/1.73 m^2). All the baseline characteristics were not significantly different between three groups, except for age, DBP, education. Comparing laboratory characteristics between three groups revealed significant difference, except for glucose, cholesterol, triglyceride (Table 2).

The attributable risk for all-cause mortality in hypertensive adults

Patients were followed up for 4.9 ± 0.5 years. In the Cox proportional hazard analysis, after adjusting for possible confounders, the prognostic factors of all-cause mortality in hypertensive patients were male [HR 1.662, 95% CI 1.110–2.489, p = 0.014], educational level<6 years [HR 2.044, 95% CI 1.164–3.591, p = 0.013], age≥65 years [HR 3.092, 95% CI 1.717–5.571, p < 0.0001], smoking [HR 1.885, 95% CI 1.170–3.309, p = 0.009], and eGFR<60 mL/min per 1.73 m^2 [HR 3.591, 95% CI 2.023–6.371, p < 0.001]. eGFR<60 mL/min

per 1.73 m^2 was independently associated with greater than 3-fold higher risk of eGFR ≥ 90 mL/min per 1.73 m^2 (Table 3).

There was a significant survival difference between men and women (p < 0.0001) (Fig. 1A). The all-cause mortality rate was 5.59% in men and 3.05% in women. The incidence rate of death was 11.1/1000 person-years in men and 6.1/1000 person-years in women. We also found a significant survival difference between eGFR ≥ 90, 90–60 and <60 mL/min per 1.73 m^2 (p < 0.0001) (Fig. 1B). The all-cause mortality rates of the three groups were 1.80%, 4.80% and 12.39%, respectively. The incidence rates of death were 3.6/1000 person-years, 9.6/1000 person-years and 25.9/1000 person-years, respectively. There were significant survival differences between smokers vs. non-smokers (p = 0.007) (Fig. 1C), coronary heart disease (CHD vs. NO CHD) (p 0.0174) (Fig. 2A), hypertension severity (SBP ≥ 140 or DBP ≥ r vs. SBP/DBP < 140/90 mmHg) (p 0.029) (Fig. 2B), education level (<6 vs. 6–12 vs. > 12 years)
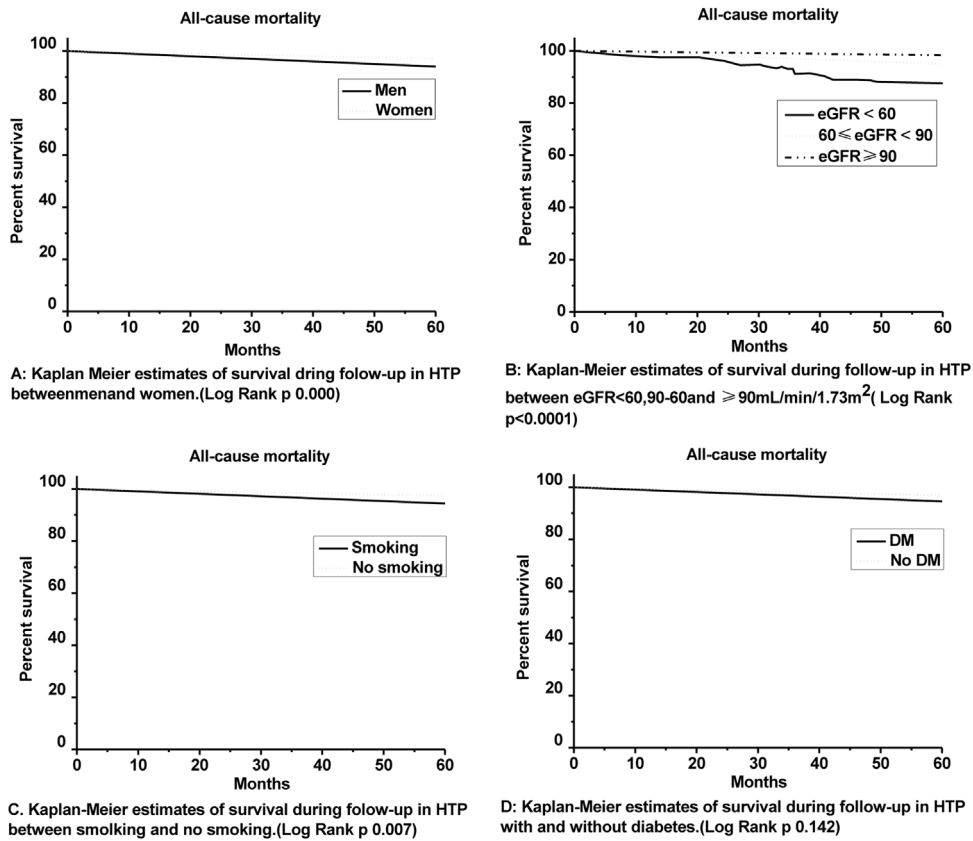
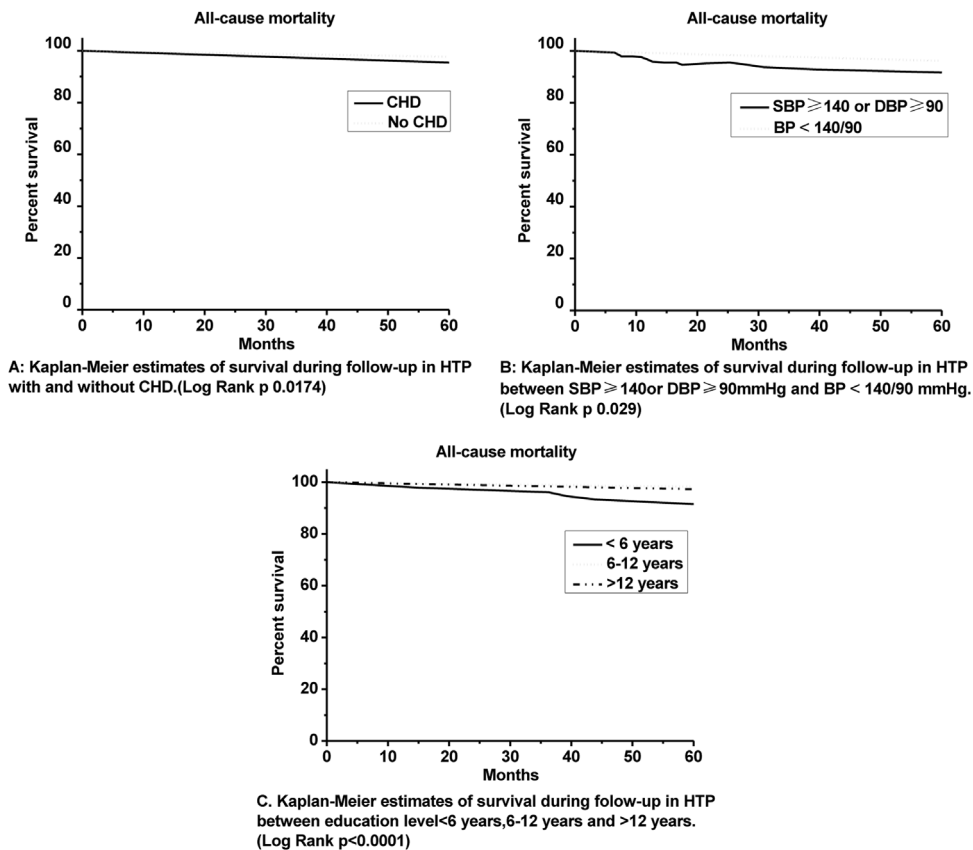**Fig. 1.** Kaplan–Meier estimates of survival during follow-up in HTP.

Fig. 2. Kaplan–Meier estimates of survival during follow-up in HTP.

Table 3
Hazard ratios for association between five-year mortality and gender, education level, age, smoking, eGFR in hypertensive patients.

Characteristic	Univariable		Multivariable model[a]	
	Hazard ratio (95% CI)	*p* value	Hazard ratio (95% CI)	*p* value
Gender				
Female	1		1	
Male	1.854 (1.293–2.660)	**0.001**	1.662 (1.110–2.489)	**0.014**
Educational level				
≥12 years	1		1	
<6 years	2.568 (1.505–4.383)	**0.001**	2.044 (1.164–3.591)	**0.013**
6–12 years	0.764 (0.452–1.290)	0.314	0.905 (0.905–0.534)	0.712
Age				
<65 years	1		1	
≥65 years	4.983 (2.941–8.440)	**<0.001**	3.092 (1.717–5.571)	**<0.001**
Smoking				
No	1		1	
Yes	1.821 (1.171–2.832)	**0.008**	1.885 (1.170–3.309)	**0.009**
eGFR (mL/min per 1.73 m^2)				
≥90	1		1	
<60	7.299 (4.280–12.448)	**<0.001**	3.591 (2.023–6.371)	**<0.001**
60–90	2.719 (1.724–4.289)	**<0.001**	1.425 (0.869–2.335)	0.160

[a] Each risk factor (gender, educational level, age, smoking, eGFR) has been adjusted for the other factors.

($p < 0.0001$) (Fig. 2C). There were no significant survival differences from DM (DM vs. No DM) ($p = 0.142$) (Fig. 1D).

Discussion

It is particularly important to identify the high-risk pre-hypertension population that may develop into hypertension and predict the risk of developing into hypertension in the future. By establishing a mathematical model, we can analyze and infer the possible risk state, influencing factors and changing trend in the future, that is, risk prediction. The mathematical model is called risk prediction model. In recent years, risk prediction has been used to study the quantitative dependence and regularity between risk factors and morbidity and mortality of chronic diseases. It has transformed factors such as lifestyle, physical and chemical indicators into measurable indicators for predicting the risk of disease or death in the future.

In our study, the prevalence of diabetes is 47%, and there was no significant between DM and no DM. Hypertension (HTN) is present in more than 50% of patients with diabetes mellitus (DM) [11]. An analysis of the Framingham data showed that the population with HTN at the time of DM diagnosis had higher rates of mortality for all causes (32 versus 20 per 1000 person-years; p < 0.001) [12]. But the incidence rate of death was 11.1/1000 person-years in men and 6.1/1000 person-years in women in our study. The mortality rate was lower than in the Framingham data. The reason may be that the medical conditions in Dongcheng district of Beijing are relatively good in China. According to the analysis report on residents' health and related factors released annually by Beijing's Dongcheng district, the average life expectancy in 2016 was 84.31 years, ranking first in China. The reason for the no difference in mortality between diabetic and non-diabetic patients with hypertension may be that the follow-up time was not long enough.

Among 3006 patients with hypertension. The study included 1038 men and 1968 women. The ratio of men to women in our study was 1:2. In China, hierarchical medical system has not been completely implemented. Patients can choose to go to the community health center or directly go to a larger hospital, which may result in the fact that patients registered in the community center are relatively sicker or more women than men.

We have identified lower eGFR and older age as very important prognostic factors for the all-cause mortality. In addition, educational level (<6 years) is a secondary prognostic factor for the all-cause mortality. Hypertensive patients with abnormal renal function and smoke appear to have a particularly poor prognosis. In our patient group, diabetes mellitus, serum blood lipid level and serum urine acid did not influence the progression to death.

Hypertension (HTN) is a major contributor to morbidity and mortality. Studies show that, in 80% of stroke events that can be prevented by controlling blood pressure, controlling blood pressure can reduce the incidence by 54% [13]. Hypertension increases risk of kidney injury, CVD morality risk, and was associated with increased risk of CVD mortality when comparing to blood pressure less than 120/80 mmHg [14]. It is reported that about one-third of Chinese adults have hypertension, and the levels of diagnosis, treatment, and control were lower than in Western population [15]. It has been shown that diastolic blood pressure provides relatively little independent mortality risk information in adults over 50, but is an important predictor of mortality in younger adults [16].

High blood pressure is the second leading assigned cause of ESRD in the United States behind diabetes mellitus [17]. On the one hand, systemic hypertension may cause renal disease and accelerate renal function deterioration. On the other hand, even subtle renal dysfunction may cause elevation in blood pressure. In our study, a mild-to-moderate reduction in renal function is very common, and there were only four patients with eGFR < 30 mL/min/1.73 m^2. We observed an increase in mortality risk at eGFR < 60 mL/min/1.73 m^2. The global scale meta-analysis shows that the risk of all-cause and cardiovascular mortality is increased in patients with eGFR < 60 mL/min/1.73 m^2 [18]. It has been shown that middle aged and elderly patients with mild-to-moderate CKD are more likely to die from CKD than to progress to ESRD [19]. Impaired kidney function and increased concentrations of albumin in urine increase the risk of cardiovascular disease two to four fold [20]. Cardiovascular mortality was about twice as high in patients with stage 3 CKD (eGFR 30–59 mL/min per 1.73 m^2) and three times higher at stage 4 (15–29 mL/min per 1.73 m^2) when compared to individuals with normal kidney function [21]. Patients in these studies were sampled from a hypertensive population that did not include severe, significantly advanced kidney failure. Furthermore, the mean age of the study population was less than 65 years; therefore, these findings may not be reflective of an elderly group. In our study, the mean age of the population is 67 years. Overall, assessment of eGFR level is required to identify individuals at high risk of mortality and to establish appropriate measures of prevention.

Smoking was also significantly associated with mortality. Cigarette smoking is a major modifiable cause of morbidity and

mortality worldwide [22]. Sekai et al. followed up 1000 patients with hypertension for 30 years, and found that smoking had synergistic effect on the risk of coronary heart disease, cerebral apoplexy, and all-cause death, and the risk of coronary heart disease, cerebral apoplexy and all-cause death was the highest in those who smoked the most [23]. According to the meta-analysis of Shiying et al., family history, overweight, smoking, alcoholism, and impatience were the main risk factors of hypertension in Chinese residents [24]. Ruihan et al. showed that drinking and smoking were the risk factors of hypertension in China [25]. Akinbodewa et al. reported that single cardiovascular risk factor contributed 50% of the risk of cardiovascular and cerebrovascular diseases, while three or more risk factors contributed 70% of the risk of these diseases and deaths [26]. Hadii et al. also showed that the 10-year risk of hypertension increased with the increase of risk factors [27]. Older male smokers had higher systolic BP adjusted for age, BMI, social class, and alcohol intake than did non-smoking men [28]. This is much higher than seen worldwide, where men are estimated to smoke five times more than women [29]. In high-income countries, women smoke at nearly the same rate as men, however, in many low- and middle-income countries, women smoke less than men [30]. In our study, men smoked nearly ten times more than women. It has been reported that current cigarette smoking is independently associated with rapid renal function decline in a dose-dependent manner [31]. However, smoking may not be physiologically related to impaired kidney function; smoking status may be merely a surrogate for other health behaviors that may badly affect renal function. Perry et al. observed 11,912 male retired officers over at least 13.9 years and found no relationship between smoking and ESRD incidence [32]. Similarly, our study provides evidence that the prevalence of smoking was similar in the eGFR < mL/min per 1.73 m^2 and eGFR$\geq$60 mL/min per 1.73 m^2 groups. This suggests that smoking may not be related to impaired kidney function.

In this study, lower educational levels were associated with mortality in hypertensive patients. It has been shown that patient literacy mediated the relationship between education and hypertension knowledge, and that literacy was a significant independent predictor of blood pressure control [33]. It has been shown that inadequate health literacy, as measured by reading fluency, was an independent predictor of all-cause mortality and cardiovascular death among community-dwelling elderly persons [34]. A survey shows that the mortality rate of hypertension patients with education level of primary school and below is significantly higher than that of the rest [35]. However, one study found that socioeconomic differences in health-related behavior were small, especially for nutritional behavior and physical activity [36]. The results of our study indicate that hypertensive patients with lower education levels have a higher risk of the mortality. There are several mechanisms that explain the association between lower education and all-cause mortality in hypertension. Education may be associated with greater health and awareness in hypertension [37,38] Patients with higher education may obtain more health-related information that develops health promoting behaviors and attitudes. Low levels of health literacy are also related to low income, which is a major cause of mortality. Lack of high school education accounts for the income level effect and is a powerful predictor of mortality variation among US states [39]. Therefore, it is necessary to provide extra care with these patients, including improvement of health knowledge and exercises program.

It should be noted that our study has several limitations. Inherent in any prospective study, the level of risk factors at the baseline examination and test might can change during the follow up. Also, this was sampled from a specific urban, thus the presented results are not directly representative of patients in suburban. Dongcheng district can only represent Beijing and other developed areas, but not other poor areas. Moreover, the length of follow-up was only 5

years. However, we had reasonable number of events in the total population, which allowed us to evaluate the attributable risk for all-cause mortality in older, hypertensive adults. To the best of our knowledge, our study is unique, as it reports on a large China urban cohort.

In summary, we conclude that decreasing eGFR, increasing age, smoking, low education and gender (male) are each highly significant and independent risk factor for mortality in hypertension. It highlights that early preventive measures are needed to detect kidney impairment and protect renal function. It also suggests that earlier smoking cessation may be important for hypertensive patients.

Funding

Competing interests

None declared.

Ethical approval

Not required.

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