Hypertension, Diabetes and the Risk of Cardiac and Cerebrovascular Events: a prospective cohort study

Yao Li

Chinese PLA General Hospital

Junjuan Li

Kailuan General Hospital

Jianli Wang

Kailuan General Hospital

Maoxiang Zhao

Chinese PLA General Hospital

Chi Wang

Chinese PLA General Hospital

Siyu Yao

Chinese PLA General Hospital

Miao Wang

Nankai University School of Medicine

Shouling Wu

Kailuan General Hospital

Hao Xue (✉ xuehaoxh301@163.com)

PLA Army General Hospital <https://orcid.org/0000-0001-5915-4811>

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Abstract

Background Hypertension and diabetes are both risk factors of cardiac and cerebrovascular events (CCVEs), but the combination of those two factors had not been certified the relationships relevant to CCVEs. The objective of this study is to determine the relationships of hypertension, diabetes and CCVEs.

Methods 78380 participants from Kailuan cohort had been analyzed. Baseline information was collected in the health exam and all the participants were regularly followed-up for every two years during 8.96 ± 0.75 years. Participants were divided into six groups according to their hypertension and diabetes status (normal, baseline or follow-up). The incidence of new-onset cerebral ischemic stroke (CI), stroke and CCVEs were respectively calculated. Multiple Cox Regression and Cum Hazard were performed to analyze the hazard ratio for risk of new-onset CI, stroke and CCVEs in each group adjusting for traditional cardiovascular risk markers.

Results In total, 78380 participants (including 61950 men) with a mean age of 56.74 at baseline were enrolled in this study. During about 9 years of follow-up, 3734 CCVEs, 2972 stroke and 2340 CI occurred among all the patients, with the incidence density (Per 1,000 years) of 5.29, 4.07 and 3.32. In patients with baseline hypertension and diabetes, hazard ratios (HRs) and 95% confidence intervals (95% CIs) of new-onset CI (HR = 2.45, 95%CI: 1.93, 3.11), stroke (HR = 2.39, 95%CI: 1.92, 2.98) and CCVEs (HR = 2.08, 95% CI: 1.72, 2.52) were higher than the other groups ($P < 0.001$). Patients with baseline hypertension or diabetes and follow-up diabetes or hypertension had higher risk of CI, stroke and CCVEs than those who with baseline disease only.

Conclusion Hypertension and diabetes alone, especially the combination of these two diseases at baseline and during follow up, contributed significantly to increased risk of new-onset CI, stroke and CCVEs during the 9 years follow up in this cohort.

Background

The incidence of cardiac and cerebrovascular events is usually staying at a high level in many countries especially in developing countries. Currently, in China, 290 million patients are with cardiovascular disease (CVD), 13 million patients are with stroke, 11 million patients are with coronary artery disease, the mortality of CVD remains high as well[1]. Cardiac and cerebrovascular events (CCVEs) are associated with many risk factors including hypertension and diabetes, and constitute most of the mortality in the country and urban China. Previous studies have confirmed the significant contribution of hypertension and diabetes to CCVEs[2].

Hypertension is a vital risk factor of CCVEs. Long-term hypertension will lead to endothelial dysfunction and vascular stiffness and increase the incidence of CVD and stroke[3]. A large-scale cohort study recruited 500223 adults indicated that the prevalence of hypertension was 32.5% in China[4]. Diabetes will also lead to peripheral arterial disease, arteriosclerosis, endothelial dysfunction, and increase the risk of hypertension and stroke[5]. It is well known that hypertension and diabetes are two major manifestations of metabolic syndrome. And there may be a myriad of links between hypertension and diabetes. Previous studies have suggested that antihypertensive therapy can reduce the risk of stroke and the incidence of cardiovascular events[6]. But there is also the risk of new-onset diabetes in the treatment of hypertension due to the side-effect of some antihypertensive drugs[7, 8]. A prospective study indicated that hypertension and diabetes increased the morbidity and mortality of stroke separately, and their combination increased the stroke risk significantly[9].

The purpose of this study is to reveal the relationship between hypertension, diabetes and cardio-cerebral vascular events, to raise the awareness and control rate of hypertension and diabetes and lower the risk of cardiac and cerebrovascular events.

Methods

Study designs and population

We used data from Kailuan study (trial registration number: ChiCTR-TNC-11001489)[10], which was a community-based, prospective cohort study and workforce survey. A total of 88414 participants completed questionnaires and physical examinations from Jun.1st 2006 to Jul.31st 2007. 7837 cases that lacked data of blood pressure or fast blood glucose, 2197 cases which diagnosed cancer or cardiovascular or cerebrovascular disease [including myocardial infarction (MI), cerebral ischemic stroke (CI) and hemorrhage stroke] were excluded. Ultimately, a total of 78380 participants were eligible and informed, and we updated their health status every 2 years according to the follow-up protocol until Dec.31st 2015. The primary endpoint includes myocardial infarction, stroke (cerebral ischemic stroke and hemorrhage stroke) and all-cause mortality. CCVEs include myocardial infarction, cerebral ischemic stroke and hemorrhage stroke (intracranial hemorrhage and subarachnoid hemorrhage).

The protocol of this study was approved by the Ethics Committee of the Kailuan Medical Group, Kailuan Company. All the participants gave their written informed consent. Physical examinations had been conducted for all the workers including retired elders, all participants were permanent residents in Kailuan community, so there was no loss in the follow-up.

Questionnaires assessment

We administered a unified questionnaire in order to obtain demographic and socioeconomic data, previous history, medical history, alcohol consumption, smoking status, physical activity, and some other personal history. Smoking status was classified as “never”, “past smoker” and “current smoker”. Alcohol consumption was defined as a daily drink at least 100ml pure alcohol in recent year. And alcohol consumption was similarity classified as “never”, “past drinker” and “current drinker”. Income was divided into three levels by 600 and 1000 (RMB/month). As for physical activity, we evaluated it from the frequency of physical activity (>20 minutes) and divided it to two levels by 4 times a week. The previous history included previous physician diagnosis of hypertension, coronary atherosclerotic disease, diabetes, stroke, myocardial infarction, tumor, etc.

Clinical measurements

Every participant was measured weight and height using a calibrated RGZ-120 body mass scale with lightly dressed and uncapped, and body mass index (BMI) was calculated as weight (kg)/height² (m²). Height was measured to the nearest 0.1 cm using a tape rule, and weight was measured to the nearest 0.1 kg using calibrated platform scales. Blood pressure was measured by trained medical doctors and nurses with a standardized mercury sphygmomanometer at the subject's left upper arm in the sitting position after at least 5 mins rest. All the participants were instructed to refrain from smoking, alcohol drinking, coffee, tea or avoid intense physical activity before measuring the blood pressure. Two readings SBP and DBP were recorded at a 5-mins interval. The average of the two readings was used for the study. The diagnostic criterion for follow-up hypertension is blood pressure $\geq 140/90$ mmHg or self-reported emerging hypertension. Blood samples were collected from the median cubital vein in the morning after an overnight fast. We used vacuum tubes containing EDTA preserved blood samples. An auto-analyzer (Hitachi 747; Hitachi, Tokyo, Japan) was used to measure biochemical tests including fasting blood glucose (FBG, hexokinase/glucose-6-phosphate dehydrogenates), total cholesterol (TC, endpoint method), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C, direct test method) at Kailuan hospital. The diagnostic criteria for baseline hypertension refer to self-reported history, oral hypotensive agents, or clinical blood pressure. Take blood pressure using a standard measurement method in three different days during the physical examination.[11] The diagnostic criteria for baseline diabetes refer to self-reported history, oral hypoglycemic agents' treatment, or fasting blood glucose level ≥ 7.0 mmol/L.

Statistical analyses

Statistical analyses were performed by SAS software (version 9.3; SAS Institute Inc, Cary, NC), which is a commercially available software program. All the participants were divided into 6 groups: 1). General population (GP); 2). Baseline hypertension (BH); 3). Baseline diabetes (BD); 4). Baseline hypertension and diabetes (BHD); 5). Baseline hypertension and follow-up diabetes (BHFD); 6). Baseline diabetes and follow-up hypertension (BDFH). Baseline hypertension/diabetes means patients have been diagnosed as hypertension/diabetes before they enrolled in this study. Follow-up hypertension/diabetes means participants who had no hypertension and/or diabetes in baseline status, and they had new-onset hypertension and/or diabetes during follow-up. Participants may be diagnosed with hypertension and/or diabetes between the two follow-ups, and the new-onset disease would be recorded at the next examination. Continuous data were expressed as mean $\pm$ standard deviation and categorical data as number (percentage). The incidence of new-onset CI, stroke and CCVEs per 1,000 years were respectively calculated, men and women were statistics separately. Multiple Cox Regression was performed to analyze the hazard ratio for risk of new-onset CI, stroke and CVD in each group. The hazard model was adjusted to calculate hazard ratios (HRs) and 95% confidence intervals (95% CIs). Model 1 was analyzed without adjusting risk factors. Model 2 was performed adjusting for gender and age. Model 3 was further adjusted for gender, age, BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), LDL-C, HDL-C, TG, FBG, uric acid (UA), estimated glomerular filtration rate (eGFR) and smoking status based on the variables in Model 2.

Results

Clinical characteristics

A total of 78380 participants including 61950 men and 16430 women were enrolled in this study and divided into 6 groups according to hypertension and diabetes status as described in Table 1. And the mean age of all the participants is 56.74 at the baseline. In total, 1878 follow-up hypertension and 5446 follow-up diabetes occurred during the mean follow-up of 8.96 ± 0.75 years. In baseline characteristics, the blood pressure of who had baseline hypertension and follow-up diabetes was significantly higher than in other groups. The FBG level of each group was significantly different, participants who had baseline hypertension and diabetes got the highest mean FBG level up to 9.26 mmol/L. The highest LDL-C level was in BHD and BHFD group, but the level in each group was lower than 2.6 mmol/L. Among 78380 participants, 40103 of them suffered from hypertension and 15813 suffered from diabetes (including baseline and follow-up), but only 6322 (15.8%) of hypertensive patients took antihypertensive agents and 2363 (14.9%) of diabetics took hypoglycemic agents.

Table 1
The baseline characteristics in 2006 according to hypertension and diabetes status

		General Population	Baseline Hypertension	Baseline Diabetes	Baseline Hypertension and Diabetes	Baseline Hypertension and Follow-up Diabetes	Baseline Diabetes and Follow-up Hypertension	<i>P value</i>
N		37308	25259	969	7520	5446	1878	
Age, year		53.75 ± 11.70	59.96 ± 10.89	57.30 ± 10.10	60.69 ± 9.91	60.92 ± 9.91	61.07 ± 9.16	< 0.001
Man, %		27564(73.88)	21378(84.64)	746(76.99)	6168(82.02)	4563(83.79)	1531(81.52)	< 0.001
Income level (RMB/month), %	< 600	10492(28.12)	7134(28.24)	284(29.31)	2149(28.58)	1536(28.2)	514(27.37)	< 0.001
	600–1000	22863(61.28)	15927(63.05)	580(59.86)	4592(61.06)	3454(63.42)	1135(60.44)	
	> 1000	2816(7.55)	1295(5.13)	70(7.22)	446(5.93)	234(4.3)	143(7.61)	
	Missing data	1137(3.05)	903(3.57)	35(3.61)	333(4.43)	222(4.08)	86(4.58)	
Physical activity, %	Never	3407(9.13)	2053(8.13)	81(8.36)	616(8.19)	418(7.68)	133(7.08)	< 0.001
(each time more than 20 min)	< 4 times/week	28133(75.41)	18005(71.28)	697(71.93)	5256(69.89)	3898(71.58)	1343(71.51)	
	≥ 4 times/week	4593(12.31)	4247(16.81)	158(16.31)	1304(17.34)	902(16.56)	313(16.67)	
	Missing data	1175(3.15)	954(3.78)	33(3.41)	344(4.57)	228(4.19)	89(4.74)	
Smoking status, %	Never	21782(58.38)	14747(58.38)	569(58.72)	4285(56.98)	3247(59.62)	1057(56.28)	< 0.001
	Past smoker	1586(4.25)	1510(5.98)	45(4.64)	485(6.45)	312(5.73)	130(6.92)	
	Current smoker	13005(34.86)	8299(32.86)	328(33.85)	2496(33.19)	1713(31.45)	633(33.71)	
	Missing data	935(2.51)	703(2.78)	27(2.79)	254(3.38)	174(3.2)	58(3.09)	
Alcohol consumption, %	Never	20740(55.59)	14427(57.12)	578(59.65)	4235(56.32)	3157(57.97)	1073(57.14)	< 0.001
	Past drinker	960(2.57)	942(3.73)	35(3.61)	327(4.35)	184(3.38)	100(5.32)	
	Current drinker	14680(39.35)	9206(36.45)	329(33.95)	2706(35.98)	1932(35.48)	647(34.45)	
	Missing data	928(2.49)	684(2.71)	27(2.79)	252(3.35)	173(3.18)	58(3.09)	
SBP, mmHg		117.13 ± 11.06	147.05 ± 17.15	116.28 ± 10.69	138.87 ± 20.59	149.36 ± 17.54	122.53 ± 9.56	< 0.001
DBP, mmHg		76.43 ± 6.88	92.76 ± 9.94	75.68 ± 7.04	86.72 ± 11.37	93.81 ± 10.61	78.15 ± 6.01	< 0.001
FBG, mmol/L		5.00 ± 0.64	5.03 ± 0.66	5.57 ± 0.76	9.26 ± 3.37	9.21 ± 2.84	9.01 ± 2.80	< 0.001
LDL-C (mmol/L)		2.30 ± 0.84	2.40 ± 0.97	2.37 ± 0.89	2.43 ± 0.98	2.43 ± 1.00	2.41 ± 0.93	< 0.001
HDL-C (mmol/L)		1.54 ± 0.38	1.57 ± 0.41	1.50 ± 0.37	1.54 ± 0.41	1.57 ± 0.42	1.54 ± 0.42	< 0.001
TC, mmol/L		4.85 ± 1.06	5.00 ± 1.20	5.13 ± 1.21	5.18 ± 1.26	5.12 ± 1.22	5.20 ± 1.31	< 0.001
Body Mass index (BMI, Kg/m ²)		24.27 ± 3.27	25.78 ± 3.36	24.76 ± 3.21	26.50 ± 3.44	26.95 ± 3.50	25.72 ± 3.24	< 0.001
Antihypertensive drugs using, %	-	2(0.01)	3761(16.32)	0(0)	1110(16.2)	940(19.08)	509(25.77)	< 0.001
Hypoglycemic drugs using, %	-	51(0.16)	0(0)	277(38.85)	1291(22.44)	177(3.99)	567(40.67)	< 0.001

	General Population	Baseline Hypertension	Baseline Diabetes	Baseline Hypertension and Diabetes	Baseline Hypertension and Follow-up Diabetes	Baseline Diabetes and Follow-up Hypertension	<i>P value</i>
Footnotes: TC, Total cholesterol; LDL-C, low density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.							

In general, the incidence density (per 1000 years) of CI (427 cases, incidence density = 6.31), stroke (501 cases, incidence density = 7.40) and CCVEs (657 cases, incidence density = 9.71) in patients with baseline hypertension and diabetes were significantly higher than those in the other five groups. And excepting the general people group, the lowest incidence density accrued in baseline diabetes group (33 cases of CIs, incidence density = 3.78, 36 cases of stroke, incidence density = 5.15, 48 cases of CCVEs, incidence density = 5.50). (Table 2)

Table 2
The incidence of new-onset CI, stroke and CCVEs among different population according to hypertension and dia

General People			Baseline Hypertension		Baseline Diabetes		Baseline Hypertension and Diabetes		Baseline Hypertension and Follow-up Diabetes	
	Case/n	Incidence density	Case/n	Incidence density	Case/n	Incidence density	Case/n	Incidence density	Case/n	Incidence density
		(Per 1,000 years)		(Per 1,000 years)		(Per 1,000 years)		(Per 1,000 years)		(Per 1,000 years)
CI	472/37308	1.41	1058/25259	4.65	33/969	3.78	427/7520	6.31	245/5445	5.00
stroke	583/37308	1.74	1326/25259	5.83	36/969	5.15	501/7520	7.40	307/5446	6.26
CCVEs	812/37308	2.42	1664/25259	7.32	48/969	5.50	657/7520	9.71	407/5446	8.30

Footnotes: CCVEs: cardiac and cerebrovascular events, CI: cerebral ischemic stroke.

We built hazard models according to hypertension and diabetes status and taking the GP group as reference. The hazard ratios and 95% confidence intervals of new-onset CI, stroke and CCVEs were calculated separately. And age, gender, income level (< 600 RMB/month, 600–1000 RMB/month, > 1000 RMB/month), physical activity (never, < 4 times/week, ≥ 4 times/week), smoking status (never, past smoker, current smoker), alcohol consumption (never, past drinker, current drinker), antihypertensive drugs using (no, yes), hypoglycemic drugs using (no, yes), SBP (mmHg), DBP (mmHg), BMI, TC (mmol/L), LDL-C (mmol/L), and HDL-C (mmol/L) were adjusted for model 3. Patients with baseline hypertension and diabetes were associated with the highest risk of CI, stroke and CCVEs ($HR_{CI}=2.45$, 95% CI: 1.93, 3.11; $HR_{stroke}=2.39$, 95% CI: 1.92, 2.98; $HR_{CCVEs}=2.08$, 95% CI: 1.72, 2.52), and followed by BHFD group ($HR_{CI}=2.13$, 95% CI: 1.65, 2.75; $HR_{stroke}=2.28$, 95% CI: 1.81, 2.86; $HR_{CCVEs}=2.03$, 95% CI: 1.66, 2.48), and the next was BH group ($HR_{CI}=2.10$, 95% CI: 1.75, 2.51; $HR_{stroke}=2.09$, 95% CI: 1.77, 2.46; $HR_{CCVEs}=1.94$, 95% CI: 1.68, 2.23). Dramatically, the HRs of CI, stroke and CCVEs in patients with baseline diabetes were closed to those in the general population which is the reference of the other group ($HR_{CI}=1.04$, 95% CI: 0.46, 2.38; $HR_{stroke}=1.04$, 95% CI: 0.49, 2.23; $HR_{CCVEs}=1.27$, 95% CI: 0.70, 2.28). (Table 3) These results meant that hypertension combined with diabetes was more vital for the risk of CI, stroke and CCVEs instead of single-disease, and hypertension may make more contribution to those risks than diabetes.

Table 3

The hazard ratios (HRs) and 95% confidence intervals (95%CI) of new-onset CI, stroke and CCVEs, according to hypertension and diabetes status.

Baseline/follow-up hypertension and diabetes status	General Population	Baseline Hypertension	Baseline Diabetes	Baseline Hypertension and Diabetes	Baseline Hypertension and Follow-up Diabetes	Baseline Diabetes and Follow-up Hypertension	<i>P-trend</i>
CI							
Model 1	Ref	3.33(2.99–3.72)	2.65(1.85–3.79)	4.57(4.01–5.22)	3.58(3.07–4.18)	4.51(3.65–5.57)	< 0.001
Model 2	Ref	2.45(2.12–2.85)	2.00(1.12–3.56)	3.26(2.71–3.91)	2.83(2.31–3.46)	3.15(2.31–4.29)	< 0.001
Model 3	Ref	2.10(1.75–2.51)	1.04(0.46–2.38)	2.45(1.93–3.11)	2.13(1.65–2.75)	1.95(1.29–2.94)	< 0.001
stroke							
Model 1	Ref	3.43(3.11–3.78)	2.42(1.73–3.39)	4.39(3.89–4.94)	3.67(3.2–4.22)	4.17(3.42–5.08)	< 0.001
Model 2	Ref	2.47(2.16–2.82)	1.77(1.02–3.07)	3.06(2.58–3.62)	2.96(2.47–3.55)	3(2.25–4)	
Model 3	Ref	2.09(1.77–2.46)	1.04(0.49–2.23)	2.39(1.92–2.98)	2.28(1.81–2.86)	2.04(1.40–2.98)	< 0.001
CCVEs							
Model 1	Ref	3.11(2.86–3.39)	2.31(1.72–3.1)	4.16(3.75–4.62)	3.55(3.15–4)	3.61(3.02–4.31)	< 0.001
Model 2	Ref	2.25(2.01–2.52)	1.73(1.08–2.77)	2.75(2.38–3.18)	2.75(2.35–3.21)	2.48(1.91–3.22)	< 0.001
Model 3	Ref	1.94(1.68–2.23)	1.27(0.70–2.28)	2.08(1.72–2.52)	2.03(1.66–2.48)	1.64(1.16–2.32)	< 0.001
Footnotes: CI: cerebral ischemic stroke; CCVEs: cardiac and cerebrovascular events; Model 1, single factor analysis; model 2 adjusted for model 1 and age, sex; model 3 adjusted for model 2 and income level (< 600RMB/month, 600–1000 RMB/month, > 1000 RMB/month), physical activity (never, < 4 times/week, ≥ 4 times/week), smoking status(never, past smoker, current smoker), alcohol consumption (never, past drinker, current drinker), antihypertensive drugs using (no, yes), hypoglycemic drugs using(no, yes),SBP (mmHg), DBP (mmHg), BMI (body mass index), TC (total cholesterol, mmol/L), LDL-C (low density lipoprotein, mmol/L), and HDL-C (high-density lipoprotein, mmol/L).							

The risk of CI, stroke and CCVEs increased with age. Among patients with baseline hypertension and diabetes, the risk of stroke and CCVEs increased the most pronounced, and followed by patients with baseline diabetes and follow-up hypertension. (Figs. 2 and 3) For the risk of CI, it was closed between patients with baseline hypertension and diabetes and patients with baseline diabetes and follow-up hypertension, much higher than that in patients with baseline diabetes only. (Fig. 1) These results demonstrated that patients would be more likely to suffer from stroke and CCVEs when they had both hypertension and diabetes. Individuals with diabetes would have increased risk of CI, stroke and CCVEs, if they incident new-onset hypertension.

Discussion

Our primary finding was that both hypertension and diabetes would impact the risk of CI, stroke and CCVEs and there was a synergistic interaction of hypertension and diabetes. Patients with baseline hypertension or baseline diabetes were more likely to suffer from CI, stroke and CCVEs if they incident new-onset another complication (diabetes or hypertension) during follow-up. Major conventional risk factors of cardiac and cerebral vascular disease including hypertension, diabetes, dyslipidemia, cigarette smoking, obesity, physical activity et al., which are considered to contribute significantly to CCVEs, result in a load of healthcare expenditure and mortality[12].

Hypertension is becoming more and more common in China even across Asia. We hold it to be self-evident that hypertension is an important risk factor of MI, stroke, CCVEs, heart failure, et al. It was reported that the prevalence of hypertension with acute MI was 35% in men, and 53% in women[13]. Hypertension almost causes half of the cardiovascular death[4]. In 2010, a study suggested that a reduction of systolic blood pressure could decrease 20.4% of mortality risk of coronary heart diseases, following treatments for coronary heart diseases and cholesterol[14]. And a recent study indicated that the presence of resistant hypertension in individuals with diabetes implied an increased risk of cardiovascular and mortality outcomes[15]. In our study, patients with baseline hypertension had a much higher risk of CI, stroke and CCVEs than patients with baseline diabetes or with follow-up hypertension. This suggested that hypertension and diabetes both make a contribution to cardiac and cerebrovascular disease, there was a synergy between hypertension and diabetes, and hypertension may contribute more than diabetes does. But the precise mechanisms remain controversial. We speculate that the magnitude of diabetes cases was much lower compared to the hypertensive patients in the current study (969 diabetes in baseline and 5445 in follow-up vs. 25259 hypertension in baseline and 1878 in follow-up), observational associations might be overestimated.

Lots of studies had consistent results. In the Framingham Offspring Study, participants had intermediate or ideal cardiovascular health score in 5-year duration, they were less likely to develop adverse outcomes including CCVEs (HR = 0.73, 95%CI: 0.63–0.85, $P < 0.001$) and mortality (HR = 0.86, 95%CI: 0.76–0.97, $P = 0.02$).[16] A large-scale study in Thailand indicated that the combined effect of hypertension and diabetes had the most significant impact on stroke (HR_{male}=10.48, 95%CI: 4.54–24.20; HR_{female}=9.29, 95%CI: 3.81–22.68)[17]. Another study conducted in Taiwan also showed that there is a synergy between

hypertension and diabetes[18]. The north Manhattan study presented that a combination of hypertension and diabetes were closely related to stroke, especially in Hispanics [19]. And a recent study indicated that patients with diabetes had higher cardiovascular risks over the whole BP range[20].

In our study, 66.0% of patients with baseline diabetes incident new-onset hypertension, and 17.7% of patients with baseline hypertension incident new-onset diabetes during follow-up for 9 years, accompanying much increased risk of CI, stroke and CCVEs. However, the precise mechanisms for our findings are complicated. Some medications, including antihypertensive drugs and statins, have the risk of developing new-onset diabetes. Aikens et al. reported that elevation of systolic blood pressure levels by 1 mmHg was associated with a 2% increased risk of diabetes (odds ratio: 1.02, 95%CI: 1.01, 1.03, $P=9.05\cdot10^{-5}$) due to genetic score[21]. And, the causality for patients with baseline diabetes incident new-onset hypertension was biologically plausible. Sun et al. gave a genetic possible explanation for the causal relationship of diabetes with hypertension risk, and diabetes was associated with higher systolic blood pressure[22]. Apparently, diabetes shared broad cardiometabolic disorders proposed in the initiation of hypertension, including obesity, insulin resistance inflammation, β -cell dysfunction, sodium retention and renin-angiotensin-aldosterone system activation[23].

In this study, patients with hypertension and follow-up diabetes have not been given enough attention to the therapy, the reason could be little impact of their symptoms on their lives. There may be something to do with the way of lifestyles and habits. Smoking, high salt and fat diet, less physical exercise and stress are all risk factors for cardiac and cerebrovascular diseases. In addition, compliance was not ideal, while multiple medications need to be taken daily to treat hypertension and diabetes simultaneously. And economic or some other external factors also can result in a low therapy rate. In our study, patients with hypertension controlled their blood pressure better in baseline hypertension group than that in baseline hypertension and follow-up diabetes group, though patients in both groups didn't control their blood pressure under 140/90 mmHg. Insufficient blood pressure controlling may be related to new-onset CI, stroke and CCVEs.

The advantages of this study include the following points. The total number of patients enrolled in the study reached 73780, and the results were convincing. We divided groups meticulous including hypertension and diabetes status at baseline and follow-up. Previous studies divided groups based on hypertension and diabetes status, and it was easy to miss diagnosis during follow-up. This study demonstrated the condition of new-onset hypertension and diabetes, and the risk of CI, stroke and CCVEs were calculated respectively. However, there were also existing limitations. Firstly, males accounted for more than 80% of the enrolled patients, which had to do with the work of the community, tending to force work. The population in this study could not represent the general population. Secondly, it was a pity that the study did not investigate the control rate of blood pressure and blood glucose to access the contribution of hypertension and diabetes for CI, stroke and CCVEs for the level of blood pressure and glucose also played an important role in the occurrence of them. And the effect of the duration of follow-up hypertension or diabetes on endpoint events has not been analyzed.

Conclusion

Hypertension and diabetes alone, especially the combination of these two diseases at baseline and during follow up, contributed significantly to increased risk of new-onset CVD, CI and stroke during the 9 years follow up in this cohort.

Abbreviations

CVD: cardiovascular disease; CCVEs: cardiac and cerebrovascular events; CI: cerebral ischemic stroke; MI: myocardial infarction; BMI: body mass index; FBG: fasting blood glucose; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; HRs: hazard ratios; 95%CIs: 95% confidence intervals; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; UA: uric acid; eGFR: estimated glomerular filtration rate;

Declarations

Ethics approval and consent to participate

The Kailuan study is a prospective cohort study based on Kailuan community in Tangshan city in northern China (trial registration number: ChiCTR-TNC-11001489). Our study complied with the Declaration of Helsinki and was approved by the hospital's ethical review board (Kailuan General Hospital, TangShan, China). Informed written consent was obtained from all patients enrolled in this study.

Availability of data and materials

The raw data and materials used and/or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Competing interest

None declared.

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Authors' contributions

Y.L.: study conception and design, analysis of data, drafting of the manuscript and critical revision; J.L., J.W.: study conception and design, acquisition, interpretation and analysis of data; M.Z., C.W.: drafting of the manuscript, analysis of data; S.Y., M.W.: study conception and design; S.W. and H.X.: study conception and design, drafting of the manuscript and critical revision. H.X. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved the final manuscript.

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Consent for publication

Not applicable

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Figures

Figure 1. Cum Hazard of new-onset cerebral ischemic stroke among different population according to hypertension and diabetes status.

Figure 1

Cum Hazard of new-onset cerebral ischemic stroke among different population according to hypertension and diabetes status.

Figure 2. Cum Hazard of stroke among different population according to hypertension and diabetes status.

Figure 2

Cum Hazard of stroke among different population according to hypertension and diabetes status.

Figure 3. Cum Hazard of Cardiac and Cerebrovascular events among different population according to hypertension and diabetes status.

Figure 3

Cum Hazard of Cardiac and Cerebrovascular events among different population according to hypertension and diabetes status.