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Blood pressure and all-cause mortality among patients with type 2 diabetes:

Blood pressure and death risk in diabetic patients

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Abstract

Background—The recommended goal for blood pressure (BP) control has recently been adjusted for people with diabetes, but the optimal BP control range for the diabetic population is still uncertain.

Methods—We performed a prospective cohort study of 35,261 patients with type 2 diabetes. Cox proportional hazards regression models were used to estimate the association of BP with all-cause mortality.

Results—During a mean follow-up period of 8.7 years, 4,199 deaths were identified. The multivariable-adjusted hazard ratios of all-cause mortality associated with different levels of systolic/diastolic BP (<110/65, 110–119/65–69, 120–129/70–80, 130–139/80–90 [reference group], 140–159/90–100, and ≥160/100 mmHg) were 1.70 (95% confidence interval [CI] 1.42–2.04), 1.26 (95% CI 1.07–1.50), 0.99 (95% CI 0.86–1.12), 1.00, 0.92 (95% CI 0.82–1.03), and 1.10 (95% CI 0.98–1.23) using baseline BP measurements, and 2.62 (95% CI 2.00–3.44), 1.77 (95% CI 1.51–2.09), 1.22 (95% CI 1.09–1.36), 1.00, 0.90 (95% CI 0.82–1.00), and 0.98 (95% CI 0.86–1.12) using an updated mean value of BP during follow-up, respectively. The U-shaped associations were confirmed in both African American and white patients, in both men and

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[1]This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

The authors have reported they have no relationships to disclose.

Contributions

W.L. wrote the manuscript and researched data. P.T.K. reviewed and edited the manuscript. R.H. and Y.W. researched data. J.J. reviewed and edited the manuscript. G.H. reviewed, and edited the manuscript and researched data. G.H. 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.

Disclosures

The authors have reported they have no relationships to disclose.

women, in those who were or were not taking antihypertensive drugs; and in patients aged 30–49 years and 50–59 years.

Conclusions—The current study found a U-shaped association between BP at baseline and during follow-up and the risk of all-cause mortality among patients with type 2 diabetes.

Keywords

blood pressure; type 2 diabetes; all-cause mortality; cohort study

1. Introduction

Hypertension and diabetes are two important public health problems in the US, with hypertension affecting approximately 65 million Americans and diabetes affecting approximately 24 million Americans [1–3]. About 70% of patients with diabetes aged >40 years are affected by hypertension [2, 3]. In the past 2 decades, clinical guidelines recommended maintaining blood pressure (BP) levels to below 130/80 mmHg in patients with type 2 diabetes which was more aggressive than in the general population (BP<140/90 mmHg) [4]. This lower treatment target in diabetic patients was mainly based on the results of early randomized clinical trials (RCTs) such as the United Kingdom Prospective Diabetes Study (UKPDS) [5] and Hypertension Optimal Treatment (HOT) trial [6]. These RCTs showed clear benefit with regard to reductions in cardiovascular outcomes in patients with diabetes receiving tight BP control. However, aggressive targets for BP treatment in diabetes guidelines have been questioned recently. The Action to Control Cardiovascular Risk in Diabetes (ACCORD) study did not show further cardiovascular benefits when intensive systolic BP treatment was achieved (Systolic blood pressure [SBP]<120 mmHg) compared with standard therapy (SBP <140 mmHg) [7]. Based on current evidence, targets for BP control for patients with type 2 diabetes have been adjusted to <140/90 mmHg [8, 9] or 140/85 mmHg [10]. Until now, there is still uncertainty about the optimal BP target in people with diabetes. The aim of the present study is to examine the association between different levels of BP and the risk of all-cause mortality among patients with type 2 diabetes in the Louisiana State University Hospital-Based Longitudinal Study (LSUHLS).

2. Materials and Methods

2.1 Study Population

Between 1997 and 2012, LSU Health Care Services Division (LSUHCSD) operated seven public hospitals and affiliated clinics in Louisiana, which provided quality medical care to the residents of Louisiana regardless of their income or insurance coverage [11–14]. Overall, LSUHCSD facilities have served about 1.6 million patients (35% of the Louisiana population) since 1997. Administrative, anthropometric, laboratory, clinical diagnosis, and medication data collected at these facilities are available in electronic form for both inpatients and outpatients from 1997. Using these data, we have established the LSUHLS [11]. A cohort of diabetic patients was established by using the ICD-9 (code 250) between January 1, 1999, and December 31, 2009. Confirmation of diabetes diagnoses was made by applying the American Diabetes Association criteria: a fasting plasma glucose level ≥126 mg/dl (in the absence of unequivocal hyperglycemia, the result should be confirmed by

repeating testing); 2-hour glucose level ≥200 mg/dl after a 75-g 2-hour oral glucose tolerance test; one or more classic symptoms plus a random plasma glucose level ≥200 mg/dl [15]. The first record of diabetes diagnosis was used to establish the baseline for each patient in the present analyses due to the design of the cohort study. Before diagnosis with diabetes, these patients have used our system for an average of 5.0 years. We have validated the diabetes diagnosis in LSUHCSD hospitals. The agreement of diabetes diagnosis was 97%: 20,919 of a sample of 21,566 hospital discharge diagnoses based on ICD codes also had physician-confirmed diabetes by using the ADA diabetes diagnosis criteria [15].

After excluding patients with incomplete data or without at least 2 measurements of any of the required variables for analysis (all variables listed in Table 1), the present study included 35,261 newly diagnosed patients with type 2 diabetes (15,504 white and 19,757 African American) who were 30 to 94 years of age with complete repeated data on all risk factor variables. The study and analysis plan including the procedure of data coding were approved by both the Pennington Biomedical Research Center and LSU Health Sciences Center Institutional Review Boards (IRBs), LSU System. IRBs granted a waiver of informed consent for this perspective study because we used anonymized data compiled from electronic medical records.

2.2 Baseline and follow-up measurements

The patient's characteristics, including age of diabetes diagnosis, sex, race/ethnicity, family income, smoking status, types of health insurance, body mass index (BMI), BP, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, glycosylated hemoglobin (HbA1c), estimated glomerular filtration rate (eGFR), and medication (antihypertensive drug, cholesterol lowing drug and antidiabetic drug) within a half year after the diabetes diagnosis (baseline) and during follow-up after the diabetes diagnosis (follow-up) were extracted from the computerized hospitalization records. In Louisiana State University Health Care Services Division hospitals, eGFR is estimated using Modification of Diet in Renal Disease equation: eGFR= (in ml/mom/1.73 m^2) = 186 × [serum creatinine (in mg/dl) $^{-1.154}$ × Age $^{-0.203}$ × 0.742 (if female) × 1.210 (if black)] [16, 17]. BP was measured from the right arm of the participant after 5 min of sitting using a mercury sphygmomanometer or electronic BP meter in each visit. BP was measured first at baseline and second as an updated mean of annual measurement of systolic BP, calculated for each participant from baseline to each year of follow-up. For example, at 1 year, the updated mean is the average of the baseline and 1-year values, and at 3 years, it is the average of baseline, 1-year, 2-year, and 3-year values. In case of an event during follow-up, the period for estimating updated mean value was from baseline to the year before this event occurred. BP measurements during the follow-up period averaged 14.6 assessments for each patient.

2.3 Prospective follow-up

Follow-up information was obtained from the LSUHLS inpatient and outpatient database by using the unique number assigned to every patient who visits the LSUHCSD hospitals. The diagnosis of all-cause death was the primary endpoint of interest of the study. Mortality outcomes were assessed by linkage with the State Center for Health Statistics at Louisiana's

Office of Public Health (the Louisiana Office of Public Health Vital Records Registry). Follow-up of each cohort member continued until the date of the death, or June 30, 2013.

2.4 Statistical analyses

Cox proportional hazards models were used to assess the association of BP with the risk of all-cause mortality. We categorized BP groups according to guidelines [18–20] and the target of randomized controlled trials (RCTs) [7]. SBP and diastolic blood pressure (DBP) were evaluated as categories (SBP <110, 110–119, 120–129, 130–139 [reference group], 140–159, and ≥160 mmHg; DBP <65, 65–69, 70–79, 80–89 [reference group], 90–100, and ≥100 mmHg; SBP/DBP <110/65, 110–119/65–69, 120–129/70–79, 130–139/80–89 [reference group], 140–159/90–99, and ≥160/100 mmHg). We fitted incremental models, and all analyses were adjusted for age, sex and race; then for smoking, income, type of insurance (multivariable-adjusted model a); and further for BMI, LDL cholesterol, HbA1c, eGFR, use of antihypertensive drugs, glucose-lowering agents, and cholesterol-lowering agents (multivariable-adjusted model b). The proportional hazards assumption in the Cox model was assessed with graphical methods and models including time-by-covariate interactions [21]. In general, all proportionality assumptions were appropriate. To avoid the potential bias due to severe diseases at baseline, additional analyses were carried out excluding the subjects who died during the first two years of follow-up.

To test whether there is a dose-response or non-linear association of BP as a continuous variable with the risk of all-cause mortality, we used restricted cubic splines to develop a hazard ratio (HR) curve to examine full-range association of SBP and DBP with the risk of all-cause mortality. We chose five knots at quintiles 5^{th}, 27.5^{th}, 50^{th}, 75^{th} and 95^{th}. HR between two points of a continuous variable can be estimated by EXP (Y_2-Y_1), where Y_1 and Y_2 are the corresponding spline function values of the two points. If we select a proper point Y_1 as the referent, EXP (Y_2-Y_1) stands for the HR of point 2 versus point 1. Thus, we obtained the HR curves by plotting the HRs of all other points versus the referent point [22]. According to the nadir of the curve, we chose the reference group of categories of BP. Both baseline BP levels and updated mean values of BP during follow-up were used in the analyses. Statistical significance was considered to be $P<0.05$. All statistical analyses were performed with SAS for Windows, version 9.3 (SAS Institute, Cary, NC).

3. Results

General characteristics of the study population are presented in Table 1. During a mean follow-up period of 8.7 years, 4,199 (2,146 white and 2,053 African American) deaths were identified. After adjustment for all confounding factors, a significantly increased risk of all-cause mortality was observed among diabetic patients with SBP <120 mmHg and ≥160 mmHg and DBP <65 mmHg and ≥100 mmHg at baseline (multivariable-adjusted model b, Table 2). When SBP and DBP were considered as continuous variables by using restricted cubic splines, a nadir of the U-shaped association of BP with all-cause mortality risk was observed at 130–150 mmHg for SBP and 80–90 mmHg for DBP (Figure 1).

The multivariable-adjusted HRs of all-cause mortality associated with different levels of joint SBP/DBP at baseline (<110/65, 110–119/65–69, 120–129/70–80, 130–139/80–90

[reference group], 140–159/90–100, and ≥160/100 mmHg) were 1.70 (95% confidence intervals [CIs]1.42–2.04), 1.26 (1.07–1.50), 0.99 (0.86–1.12), 1.00, 0.92 (0.82–1.03), and 1.10 (0.98–1.23), respectively (Table 3).

When we carried out additional analyses by using an updated mean BP during follow-up, we also found a U-shaped association between levels of BP and the risk of all-cause mortality. Lower levels of BP (SBP <130 mmHg or DBP <65 mmHg) were associated with an increased risk of all-cause mortality (Tables 2 and 3).

When stratified by race, sex, and use of antihypertensive drugs, the U-shaped associations of BP with the risk of all-cause mortality were confirmed in both African American and white patients, in both men and women, and also in those who were or were not talking antihypertensive drugs (Table 4 and Online table 1). When stratified by age, the U-shaped association of BP with all-cause mortality risk was more significant in diabetic patients aged 30–49 years and 50–59 years, but weakened and changed to an inverse association in diabetic patients aged ≥60 years (Table 4 and Online table 1). After excluding subjects who died during the first two years of follow-up (n=435), the multivariable-adjusted U-shaped association of BP with the risk of all-cause mortality did not change (Online table 2). After excluding subjects who had coronary heart disease, heart failure, stroke, end stage renal disease, or left ventricular hypertrophy at baseline (n=7,366), the multivariable-adjusted U-shaped association of BP with the risk of all-cause mortality did not change (Online table 3).

4. Discussion

The present study found a U-shaped association between observed BP at baseline and during follow-up and the risk of all-cause mortality among patients with type 2 diabetes. The lowest all-cause mortality risk was observed at 130–150 mmHg for SBP and 80–90 mmHg for DBP. Both lower BP (SBP <120 mmHg or DBP <65 mmHg) and higher BP (SBP ≥160 mmHg or DBP ≥100 mmHg) were associated with an increased risk of all-cause mortality among both African American and white, as well as men and women with type 2 diabetes.

In the past 2 decades, clinical guidelines recommended maintaining BP levels to below 130/80 mmHg [4], which is mainly based on the landmark RCTs like the UKPDS [5] and HOT trial [6]. However, patients assigned to the tight BP group (<150/85 mm Hg) actually achieved a mean BP of 144/82 mmHg in the UKPDS trial [5], and patients assigned to the ≤80 mmHg of DBP actually achieved a mean BP of 140/81 mmHg in the HOT trial [6]. Furthermore, results from several other RCTs continued to question the aggressive targets for BP treatment in diabetes care guidelines, such as the ACCORD RCT [7], the Appropriate Blood Pressure Control in Diabetes (ABCD) trial [23], the Irbesartan Diabetic Nephropathy Trial (IDNT) [24], and the International Verapamil SR-Trandolapril Study (INVEST) [25]. A systematic review pooling 31 RCTs suggested that the risk of stroke decreased progressively with BP reduction, but this association was not significant for myocardial infarction in people with diabetes [26]. Another systematic review of 13 RCTs enrolling 37 736 participants with diabetes or impaired fasting glucose suggested that treatment goal of SBP 130–135 mm Hg is acceptable and more aggressive goals (<130 mmHg) was not associated with the benefit regarding the risk of macrovascular or

microvascular events except stroke [27]. Based on evidence from the above trials, in 2013, targets for BP control for patients with diabetes have been adjusted to <140/80 mmHg [28] or 140/85 mmHg [10]. In 2014 and 2015, the BP guideline of the Eighth Joint National Committee (JNC 8) and American Diabetes Association recommends the goal to be less than 140/90 mmHg among patients with diabetes [8, 9].

Thus there is still uncertainty about the optimal BP target in population with type 2 diabetes. In order to design effective interventions that would prevent or delay the onset of CVDs, the validity of BP treatment goals for CVD risk among patients with type 2 diabetes have to be better delineated. However, RCTs may suffer from lower incident events of diabetic complications, short follow-up time, high loss-to-follow-up rates, and strict inclusion and exclusion criteria which limit their applicability to the common diabetic patients in clinical practice. Observational studies, especially from hospital-based cohorts, are needed and important because they may better reflect everyday clinical practice. A retrospective UK cohort study has indicated a U-shaped association of SBP and DBP with the risk of all-cause mortality among patients with type 2 diabetes [29]. Similarly, our study also found a U-shaped association between observed BP and the risk of all-cause mortality among patients with type 2 diabetes. Both lower BP (SBP <120 mmHg or DBP <65 mmHg) and higher BP (SBP ≥160 mmHg or DBP ≥100 mmHg) were associated with an increased risk of all-cause mortality. When we carried out additional analyses by using an updated mean BP during follow-up, we also found a U-shaped association between updated mean levels of BP and the risk of all-cause mortality among patients with type 2 diabetes.

One recent prospective study has found an inverse association between BP and the risk of all-cause mortality in elderly diabetic patients aged >75 years [30]. In the present study, the U-shaped association of BP with all-cause mortality risk was more significant in middle-aged diabetic patients (age 30–49 years and 50–59 years), but in the older group (age ≥60 years) the U-shaped weakened and changed to an inverse association. Some researchers have suggested that lower BP is more common with co-morbidities at older ages and reflects the general frailty of elderly patients [31]. Elderly patients with type 2 diabetes represent a population who are highly enriched with underlying CVD and may be more prone than others to display the inverse association. This observation suggests that lower BP is more harmful than uncontrolled BP for elderly patients.

Because of the observational nature of cohort study, our findings of an increased risk of all-cause mortality associated with low BP did not imply causality. Some studies have suggested tight control of BP might increase cardiovascular risk by the under-perfusion of vital organs [32]. An impaired coronary circulation may be particularly sensitive to decreases in diastolic BP as under-perfusion may push latent or subclinical diastolic dysfunction to clinical all-cause mortality [33]. Some other studies suggested that an increased risk of all-cause mortality associated with lower DBP might be associated with some deterioration of general health, because this relation was also evident in patients treated with placebo [34]. Future studies are needed to clarify the mechanism of association between BP and all-cause mortality among older patients with diabetes.

There are several strengths of our study, including the large sample size, long follow-up time, and the use of administrative databases to avoid differential recall bias. We have used both baseline BP levels and updated mean values of BP during follow-up in the analyses, which can avoid potential bias from a single baseline measurement. In addition, participants in the present study used the same public health care system that minimizes the influence of accessibility to health care. The present study also has limitations. First, more than 45,000 patients with diabetes were excluded in the present study due to missing data on one or more of the required variables, and these patients were younger, and the percentage of African Americans males was smaller compared with those included in the present study. Excluding these patients might have a possible selection bias. Second, we did not have information on cause-specific deaths and could not assess cardiovascular mortality as a separate end-point. Third, even though our analyses adjusted for an extensive set of confounding factors, residual confounding due to the measurement error in the assessment of confounding factors, unmeasured factors such as physical activity, education, and dietary factors, cannot be excluded.

Our study found a U-shaped association between observed BP and the risk of all-cause mortality among patients with type 2 diabetes. We suggested that blood pressure target in diabetic patients might be 130–150 mmHg for SBP and 80–90 mmHg for DBP.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Novelty and Significance

Based on current evidence, targets for BP control for patients with type 2 diabetes have been adjusted to <140/90 mmHg or 140/85 mmHg, but the optimal BP control range for the diabetic population is still uncertain. Our study, based on a hospitalized cohort study of 35,261 patients with type 2 diabetes, suggested a U-shaped association between observed BP and the risk of all-cause mortality among patients with type 2 diabetes. We suggested that the lowest risk of all-cause mortality was observed at 130–150 mmHg for SBP and 80–90 mmHg for DBP.

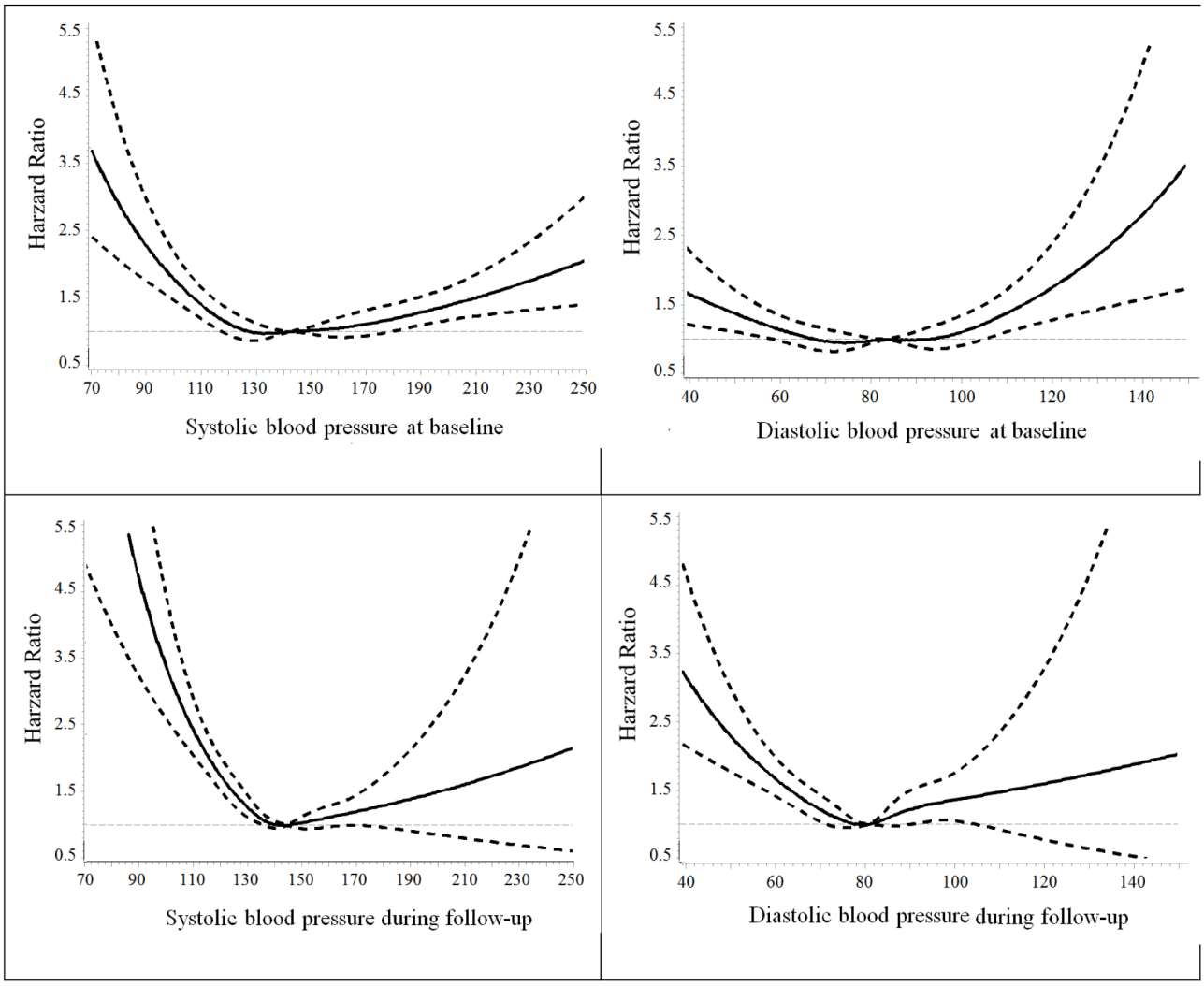

Figure 1.

Hazard ratios for all-cause mortality by systolic blood pressure and diastolic blood pressure at baseline and during follow-up. Adjusted for age, sex and race, smoking, income, type of insurance, BMI, LDL cholesterol, HbA1c, eGFR, use of antihypertensive drugs, glucose-lowering agents, and cholesterol-lowering agents.

Table 1

Baseline characteristics of African American and white patients with diabetes

	African American	White	P value
No. of participants	19757	15504	
Male, %	35.5	40.8	<0.001
Age, mean (SD), yr	51.1 (0.1)	53.7 (0.1)	<0.001
Income, mean (SD), $/family	18963 (192)	19741 (218)	0.008
Body mass index, mean (SD)	33.6 (0.1)	35.0 (0.1)	<0.001
Baseline Blood pressure, mean (SD), mm Hg			
Systolic	146 (0.2)	141 (0.2)	<0.001
Diastolic	82 (0.1)	78 (0.1)	<0.001
HbA1c, mean (SD), %	7.94 (0.02)	7.35 (0.02)	<0.001
LDL cholesterol, mean (SD), mg/dL	113 (0.3)	110 (0.3)	<0.001
Glomerular filtration rate (mL/min/1.73 m2), %			<0.001
≥90	53.8	35.9	
60–89	35.2	47.0	
30–59	9.3	15.6	
15–29	1.1	1.1	
<15	0.6	0.4	
Smoking status, %			<0.001
Never smoking	67.8	63.3	
Past smoking	7.0	7.6	
Current smoking	25.3	29.1	
Type of insurance, %			<0.001
Free	78.3	76.1	
Self-pay	5.8	3.8	
Medicaid	6.1	4.0	
Medicare	8.2	13.2	
Commercial	1.7	2.9	
Uses of medications, %			
Glucose-lowering medication			<0.001
Oral hypoglycemic agents	33.4	34.5	
Insulin	32.8	26.6	
Lipid-lowering medication	55.1	58.2	<0.001
Antihypertensive medication	75.4	69.6	

* Values represent mean or percentage. Body mass index was calculated as the weight in kilograms divided by the square of the height in meters.

Table 2

Hazard ratio of all-cause mortality according to different levels of systolic blood pressure and diastolic blood pressure at baseline and during follow-up among patients with type 2 diabetes

	Systolic blood pressure (mmHg)					
	<110	**110–119**	**120–129**	**130–139**	**140–159**	**≥160**
Baseline						
No. of Patients	1,840	3,035	4,908	6,235	11,132	8,111
No. of deaths	355	424	520	638	1,189	1,073
Person-years	14,727	25,158	41,652	53,765	97,681	72,899
Age, gender and race adjustment HR (95% CI)	2.03 (1.78–2.31)	1.48 (1.31–1.67)	1.08 (0.96–1.21)	1.00	1.01 (0.91–1.11)	1.23 (1.11–1.36)
Multivariable adjustment HR (95% CI)[a]	1.89 (1.60–2.22)	1.43 (1.23–1.67)	1.10 (0.95–1.26)	1.00	1.02 (0.90–1.14)	1.24 (1.10–1.40)
Multivariable adjustment HR (95% CI)[b]	1.70 (1.45–2.01)	1.39 (1.20–1.62)	1.04 (0.91–1.20)	1.00	1.01 (0.89–1.13)	1.20 (1.06–1.35)
Follow-up						
No. of Patients	574	2,144	6,073	9,354	12,860	4,256
No. of deaths	186	410	722	904	1,336	641
Person-years	4,226	16,687	49,937	80,039	116,067	38,926
Age, gender and race adjustment HR (95% CI)	3.46 (2.95–4.05)	2.30 (2.04–2.58)	1.28 (1.16–1.41)	1.00	0.96 (0.88–1.05)	1.43 (1.29–1.58)
Multivariable adjustment HR (95% CI)[a]	3.12 (2.50–3.90)	2.05 (1.77–2.37)	1.27 (1.13–1.43)	1.00	0.97 (0.88–1.07)	1.25 (1.10–1.42)
Multivariable adjustment HR (95% CI)[b]	2.47 (1.97–3.09)	1.82 (1.58–2.11)	1.24 (1.11–1.40)	1.00	0.94 (0.85–1.04)	1.03 (0.91–1.18)
	Diastolic blood pressure (mmHg)					
	<65	65–69	70–79	80–89	90–99	≥100
Baseline						
No. of Patients	4,114	3,287	9,933	10,005	5,308	2,614
No. of deaths	808	482	1,078	994	527	310
Person-years	36,363	28,848	87,546	85,865	45,468	21,791
Age, gender and race adjustment HR (95% CI)	1.41 (1.28–1.55)	1.17 (1.05–1.31)	0.95 (0.87–1.03)	1.00	1.09 (0.99–1.22)	1.44 (1.26–1.63)
Multivariable adjustment HR (95% CI)[a]	1.26 (1.12–1.41)	1.13 (0.99–1.29)	0.91 (0.82–1.01)	1.00	1.04 (0.92–1.19)	1.34 (1.14–1.56)
Multivariable adjustment HR (95% CI)[b]	1.18 (1.05–1.32)	1.12 (0.98–1.28)	0.91 (0.82–1.01)	1.00	1.03 (0.91–1.17)	1.28 (1.09–1.49)

	Systolic blood pressure (mmHg)					
	<110	**110–119**	**120–129**	**130–139**	**140–159**	**≥160**
Follow-up						
No. of Patients	2,579	4,329	15,005	9,970	2,682	696
No. of deaths	699	658	1,554	869	309	110
Person-years	23,149	39,548	131,187	84,140	22,110	5,748
Age, gender and race adjustment HR (95% CI)	1.64 (1.47–1.82)	1.06 (0.96–1.18)	0.94 (0.86–1.02)	1.00	1.49 (1.31–1.70)	2.10 (1.72–2.56)
Multivariable adjustment HR (95% CI)[a]	1.50 (1.32–1.72)	0.94 (0.82–1.06)	0.92 (0.83–1.01)	1.00	1.35 (1.15–1.60)	1.65 (1.23–2.21)
Multivariable adjustment HR (95% CI)[b]	1.37 (1.20–1.57)	0.95 (0.83–1.08)	0.95 (0.85–1.05)	1.00	1.25 (1.06–1.47)	1.30 (0.97–1.75)

Abbreviations: HR, hazard ratio; CI, confidence interval.

[a] Adjusted for age, gender, race, type of insurance, income, and smoking.

[b] Adjusted for age, gender, race, type of insurance, income, smoking, body mass index, low-density lipoprotein cholesterol, HbA1c, glomerular filtration rate, use of antihypertensive drugs, glucose-lowering agents, and cholesterol-lowering agents.

Table 3

Hazard ratio of all-cause mortality according to different levels of systolic/diastolic blood pressure at baseline and during follow-up among patients with type 2 diabetes

	Systolic blood pressure/diastolic blood pressure (mmHg)					
	<110/65	**110–119/65–69**	**120–129/70–79**	**130–139/80–89**	**140–159/90–99**	**≥160/100**
Baseline						
No. of Patients	1,022	1,790	5,116	7,228	11,478	8,627
No. of deaths	234	302	576	747	1,216	1,124
Person-years	8,333	14,960	43,438	61,739	100,480	76,933
Age, gender and race adjustment HR (95% CI)	2.03 (1.75–2.35)	1.50 (1.32–1.72)	1.09 (0.98–1.22)	1.00	0.96 (0.88–1.05)	1.18 (1.08–1.30)
Multivariable adjustment HR (95% CI)[a]	1.88 (1.57–2.26)	1.29 (1.09–1.52)	1.05 (0.92–1.20)	1.00	0.93 (0.84–1.04)	1.14 (1.02–1.27)
Multivariable adjustment HR (95% CI)[b]	1.70 (1.42–2.04)	1.26 (1.07–1.50)	0.99 (0.86–1.12)	1.00	0.92 (0.82–1.03)	1.10 (0.98–1.23)
Follow-up						
No. of Patients	113	316	783	986	1,347	654
No. of deaths	185	996	5,455	9,076	11,634	3,716
Person-years	849	2,477	6,464	8,340	12,130	5,965
Age, gender and race adjustment HR (95% CI)	3.20 (2.63–3.89)	2.34 (2.06–2.65)	1.29 (1.18–1.42)	1.00	0.92 (0.85–1.00)	1.37 (1.24–1.51)
Multivariable adjustment HR (95% CI)[a]	3.35 (2.56–4.39)	1.97 (1.67–2.31)	1.26 (1.12–1.41)	1.00	0.93 (0.85–1.03)	1.18 (1.04–1.35)
Multivariable adjustment HR (95% CI)[b]	2.62 (2.00–3.44)	1.77 (1.51–2.09)	1.22 (1.09–1.36)	1.00	0.90 (0.82–1.00)	0.98 (0.86–1.12)

Abbreviations: HR, hazard ratio; CI, confidence interval.

[a] Adjusted for age, gender, race, type of insurance, income, and smoking.

[b] Adjusted for age, gender, race, type of insurance, income, smoking, body mass index, low-density lipoprotein cholesterol, HbA1c, glomerular filtration rate, use of antihypertensive drugs, glucose-lowering agents, and cholesterol-lowering agents.

Table 4

Hazard ratio (95% confidence interval) of all-cause mortality according to different levels of blood pressure at baseline among patients with type 2 diabetes of various subpopulations

	Systolic blood pressure (mmHg)					
	<110	**110–119**	**120–129**	**130–139**	**140–159**	**≥160**
Race						
African American	1.89 (1.48–2.41)	1.35 (1.07–1.70)	0.98 (0.79–1.22)	1.00	1.02 (0.86–1.21)	1.20 (1.01–1.42)
White	1.57 (1.26–1.96)	1.43 (1.17–1.75)	1.09 (0.91–1.32)	1.00	1.00 (0.85–1.17)	1.20 (1.01–1.42)
Age group, years						
<50	1.90 (1.41–2.55)	1.18 (0.88–1.57)	0.96 (0.73–1.26)	1.00	1.02 (0.81–1.28)	1.42 (1.12–1.79)
50–59	1.85 (1.40–2.45)	1.46 (1.12–1.91)	1.08 (0.84–1.38)	1.00	1.02 (0.83–1.25)	1.30 (1.06–1.60)
60–94	1.34 (1.01–1.77)	1.47 (1.16–1.86)	1.04 (0.83–1.31)	1.00	1.02 (0.84–1.22)	1.05 (0.86–1.27)
Sex						
Men	1.80 (1.44–2.25)	1.49 (1.21–1.83)	1.22 (1.01–1.47)	1.00	1.06 (0.89–1.25)	1.16 (0.98–1.39)
Women	1.56 (1.23–2.00)	1.28 (1.03–1.60)	0.85 (0.69–1.06)	1.00	0.95 (0.80–1.12)	1.19 (1.01–1.41)
Using antihypertensive drugs						
No	2.09 (1.60–2.74)	1.39 (1.06–1.82)	1.03 (0.80–1.33)	1.00	1.08 (0.87–1.34)	1.24 (1.00–1.56)
Yes	1.49 (1.20–1.84)	1.40 (1.16–1.67)	1.05 (0.89–1.25)	1.00	0.98 (0.85–1.12)	1.17 (1.01–1.34)
	Diastolic blood pressure (mmHg)					
	<65	65–69	70–79	80–89	90–99	≥100
Race						
African American	1.15 (0.96–1.39)	1.28 (1.06–1.56)	0.94 (0.81–1.09)	1.00	1.11 (0.94–1.32)	1.31 (1.07–1.59)
White	1.15 (0.99–1.34)	0.99 (0.82–1.19)	0.88 (0.76–1.01)	1.00	0.93 (0.77–1.14)	1.22 (0.93–1.60)
Age group, years						
<50	1.53 (1.19–1.97)	1.08 (0.81–1.45)	0.95 (0.78–1.15)	1.00	0.96 (0.77–1.20)	1.39 (1.08–1.78)
50–59	1.06 (0.86–1.32)	1.15 (0.92–1.44)	0.90 (0.76–1.07)	1.00	1.11 (0.90–1.37)	1.24 (0.95–1.61)
60–94	1.18 (0.99–1.41)	1.17 (0.95–1.43)	0.90 (0.76–1.07)	1.00	0.98 (0.77–1.25)	1.05 (0.75–1.46)
Sex						
Men	1.19 (1.00–1.40)	1.06 (0.88–1.28)	0.93 (0.81–1.07)	1.00	0.88 (0.73–1.05)	1.07 (0.86–1.34)

	Systolic blood pressure (mmHg)					
	<110	**110–119**	**120–129**	**130–139**	**140–159**	**≥160**
Women	1.19 (1.01–1.40)	1.20 (1.00–1.45)	0.90 (0.77–1.05)	1.00	1.24 (1.03–1.48)	1.56 (1.24–1.95)
Using antihypertensive drugs						
No	1.19 (0.97–1.45)	1.02 (0.80–1.29)	0.88 (0.73–1.06)	1.00	0.96 (0.75–1.22)	1.12 (0.82–1.54)
Yes	1.17 (1.01–1.35)	1.17 (1.00–1.37)	0.92 (0.81–1.04)	1.00	1.07 (0.92–1.25)	1.33 (1.11–1.60)
	Systolic blood pressure/Diastolic blood pressure (mmHg)					
	<110/65	110–119/65–69	120–129/70–79	130–139/80–89	140–159/90–99	≥160/100
Race						
African American	1.99 (1.51–2.63)	1.24 (0.95–1.62)	0.91 (0.74–1.12)	1.00	0.95 (0.81–1.11)	1.10 (0.94–1.29)
White	1.52 (1.19–1.94)	1.28 (1.02–1.59)	1.05 (0.88–1.24)	1.00	0.90 (0.78–1.05)	1.10 (0.93–1.29)
Age group, years						
<50	2.39 (1.73–3.31)	1.06 (0.75–1.52)	0.93 (0.72–1.19)	1.00	0.92 (0.74–1.13)	1.27 (1.02–1.57)
50–59	1.87 (1.36–2.58)	1.35 (0.99–1.82)	1.07 (0.85–1.34)	1.00	0.96 (0.79–1.16)	1.23 (1.02–1.49)
60–94	1.23 (0.90–1.67)	1.33 (1.03–1.71)	0.95 (0.77–1.18)	1.00	0.94 (0.79–1.12)	0.96 (0.79–1.15)
Sex						
Men	1.79 (1.40–2.28)	1.17 (0.93–1.49)	1.10 (0.92–1.31)	1.00	0.91 (0.78–1.06)	1.02 (0.87–1.20)
Women	1.57 (1.19–2.07)	1.34 (1.05–1.71)	0.85 (0.70–1.05)	1.00	0.93 (0.79–1.09)	1.15 (0.98–1.35)
Using antihypertensive drugs						
No	2.22 (1.66–2.96)	1.22 (0.91–1.64)	0.93 (0.74–1.17)	1.00	0.93 (0.76–1.13)	1.08 (0.87–1.33)
Yes	1.43 (1.12–1.82)	1.28 (1.04–1.57)	1.02 (0.87–1.20)	1.00	0.92 (0.81–1.05)	1.10 (0.96–1.25)

Adjusted for age, gender, race, type of insurance, income, smoking, body mass index, low-density lipoprotein cholesterol, HbA1c, glomerular filtration rate, use of antihypertensive drugs, glucose-lowering agents, and cholesterol-lowering agents other than the variable for stratification.