# Hypertension and Diabetes Mellitus
## Copredictionand Time Trajectories

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***Abstract***—Type 2 diabetes mellitus and hypertension overlap in the population. In many subjects, development of diabetes mellitus is characterized by a relatively rapid increase in plasma glucose values. Whether a similar phenomenon occurs during the development of hypertension is not known. We analyzed the pattern of blood pressure (BP) changes during the development of hypertension in patients with or without diabetes mellitus using data from the MCDS (Mexico City Diabetes Study; a population-based study of diabetes mellitus in Hispanic whites) and in the FOS (Framingham Offspring Study, a community-based study in non-Hispanic whites) during a 7-year follow-up. Diabetes mellitus at baseline was a significant predictor of incident hypertension (in FOS, odds ratio, 3.14; 95% confidence interval, 2.17–4.54) independently of sex, age, body mass index, and familial diabetes mellitus. Conversely, hypertension at baseline was an independent predictor of incident diabetes mellitus (in FOS, odds ratio, 3.33; 95% CI, 2.50–4.44). In >60% of the converters, progression from normotension to hypertension was characterized by a steep increase in BP values, averaging 20 mm Hg for systolic BP within 3.5 years (in MCDS). In comparison with the nonconverters group, hypertension and diabetes mellitus converters shared a metabolic syndrome phenotype (hyperinsulinemia, higher body mass index, waist girth, BP, heart rate and pulse pressure, and dyslipidemia). Overall, results were similar in the 2 ethnic groups. We conclude that (1) development of hypertension and diabetes mellitus track each other over time, (2) transition from normotension to hypertension is characterized by a sharp increase in BP values, and (3) insulin resistance is one common feature of both prediabetes and prehypertension and an antecedent of progression to 2 respective disease states. **(*Hypertension*. 2018;71:422-428. DOI: 10.1161/HYPERTENSIONAHA.117.10546.)** • **Online Data Supplement**

**Key Words:** blood pressure ■ diabetes mellitus ■ heart rate ■ hypertension ■ insulin resistance



Diabetes mellitus and hypertension are among the most common diseases and cardiovascular risk factors, respectively, worldwide, and their frequency increases with increasing age.[1] Elevated blood pressure (BP) values are a common finding in patients with type 2 diabetes mellitus (T2D) and are thought to reflect, at least in part, the impact of the underlying insulin resistance on the vasculature and kidney.[1] On the contrary, accumulating evidence suggests that disturbances in carbohydrate metabolism are more common in hypertensive individuals,[2,3] thereby indicating that the pathogenic relationship between diabetes mellitus and hypertension is actually bidirectional.

The development of hypertension in diabetic individuals not only complicates treatment strategy and increases healthcare costs but also heightens the risk for macrovascular and microvascular complications considerably.[2,4] Although BP lowering is followed by a significant reduction in cardiovascular and microvascular morbidity and mortality,[5,6] a large proportion of diabetic subjects exhibit poorly controlled hypertension. This observation may reflect not only delayed recognition of the presence of hypertension, clinical inertia, and poor adherence to the prescribed regimen but also uncertainty regarding the treatment targets and pathogenic correlation.

A previous report from the MCDS (Mexico City Diabetes Study) showed that, in ≈2/3 of patients with either normoglycemia or impaired glucose tolerance, the development of overt diabetes mellitus is characterized by an abrupt (within ≈3.5 years) increase in plasma glucose values by ≈50 mg/dL.[7] Whether a similar phenomenon is seen during the development of hypertension is not known. Therefore, the first aim of the present analysis was to determine the pattern of BP changes during the development of hypertension in patients with or without diabetes mellitus in MCDS. The second aim was to quantify the longitudinal association of T2D and hypertension in this population-based study during the follow-up period of 7 years. Within this scope, we tried to identify clinical and laboratory characteristics that may reflect an increased risk for

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the development of diabetes mellitus, hypertension, or both. Because the population of MCDS included Hispanic individuals from low-income areas with a high risk for the development of diabetes mellitus, we explored the generalizability of any results by asking the same questions in the non-Hispanic white population of the FOS (Framingham Offspring Study).

## Methods

The authors declare that all supporting data are available within the article (and its online-only Data Supplement).

### Study Populations

The MCDS is a population-based cohort participating in a longitudinal survey of incident diabetes mellitus and cardiovascular risk factors. Low-income neighborhoods in Mexico City were identified, and a complete enumeration of these was performed from November 1989 to October 1992. Among the 15 532 inhabitants of these neighborhoods, 2280 men and women (aged 35–64 years) were randomly selected from 6 low-income colonias examined between 1990 and 1992 and invited to return for 2 follow-up examinations, the first conducted between 1993 and 1995 and the second between 1997 and 1999. Of the 1770 subjects participating in the first follow-up (at 3.25 years), 1753 returned for the second follow-up (at 7 years). The clinical characteristics of the subjects not returning for the second follow-up were essentially superimposable on those of the subjects who did (data not shown).

Examinations were standardized and included interviews, anthropometry, BP measurements, a fasting blood draw, and a 75-g oral glucose tolerance test. Trained interviewers obtained information on medical history, medication use, and smoking status.

The protocol was approved by the Ethics Committee of the Centro de Estudios en Diabetes, Centro de Investigacion en Salud Poblacional, Instituto Nacional de Salud Publica, Mexico City, and all subjects gave informed consent.

The FOS (Framingham Offspring Study) is a community-based cohort including 3754 men and women who attended the fifth clinic examination (1989–1992) of the FHS. Participants were followed up from baseline to the sixth (1995–1998) and seventh (1998–2001) offspring exams, for an average period of 7 years. We used the exam visit date when a new case of diabetes mellitus or hypertension was identified as the date of diagnosis; otherwise, follow-up was censored at last follow-up (examination 6 or 7) for participants remaining nondiabetic or nonhypertensive. The protocol was approved by the Ethics Committee of Boston University Medical Center, and all subjects gave written informed consent.

In both cohorts, hypertension was defined as a systolic BP ≥140 mm Hg or a diastolic BP ≥90 mm Hg or current antihypertensive treatment. In both studies, subjects whose BP was <140/90 mm Hg at baseline and both follow-up visits were classified as normotensives, those whose BP was <140/90 mm Hg at the first visit who became hypertensive at the second or third visit were classified as converters. T2D was classified as a fasting plasma glucose concentration ≥126 mg/dL or a 2-hour plasma glucose concentration ≥200 mg/dL on a standard 75-g oral glucose tolerance test. Subjects who gave a history of diabetes mellitus and who at the time of their clinical examination were taking oral antidiabetic agents were also considered to have T2D regardless of their plasma glucose values. Insulin-taking diabetic subjects whose age of onset was ≥40 years or whose body mass index (BMI) was >30 kg/m$^2$ were also considered to have T2D. Subjects with type 1 diabetes mellitus were excluded. Subjects who developed diabetes mellitus at the first or second follow-up were denoted as converters. Subjects who tested normal on the oral glucose tolerance test on all 3 examinations were considered to be bona fide nonconverters during the observation period.

### Anthropometric Measurements

Diabetes mellitus in at least one parent or sibling was coded as a positive family history of diabetes mellitus. Before examinations, all participants were asked to fast for at least 12 hours. Height, weight, waist and hip circumferences, and systolic and diastolic BP were measured; pulse pressure was calculated as the difference between systolic and diastolic BP and mean BP as the sum of diastolic BP and one third of pulse pressure.

### Biochemical Measurements

Blood samples were obtained in the fasting state and 2 hours after a standard 75-g oral glucose load. Serum samples were centrifuged, divided into aliquots, and stored at −70°C until assayed. Fasting concentrations of serum insulin, proinsulin, plasma glucose, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, and plasma glucose and insulin concentrations 2 hours after an oral glucose load were determined as described elsewhere[7] at baseline and at follow-up.

### Statistical Analysis

The study design is that of a longitudinal cohort study of incident diabetes mellitus as a function of baseline hypertension or of incident hypertension as a function of baseline diabetes mellitus, both with confounder covariate adjustment. We also assessed the rate of change of BP as hypertension developed. Baseline data are presented as mean±SD; median and (interquartile range) are reported for variables with non-normal distribution, which were log transformed for use in statistical analyses. Categorical variables were compared by the $\chi^2$ test, continuous variables by ANOVA, with Bonferroni–Dunn testing of multiple post hoc comparisons. Logistic regression for incident events was performed by defining response as a diagnosis of hypertension (or diabetes mellitus) at either of the 2 follow-up visits and nonresponse as no hypertension (or diabetes mellitus) at the last visit; results are expressed as the odds ratio (OR) with 95% confidence intervals (95% CI) as a function of baseline exposures. For each continuous variable in a multivariate model, OR was calculated for 1 SD of the population value of that variable. A $P$ value ≤0.05 was considered statistically significant for the test of the hypothesis that diabetes mellitus predicts hypertension or vice versa.

## Results

### Development of Hypertension

At the 3 examinations, 16% to 46% of the study subjects were hypertensive; among them, the prevalence of diabetes mellitus (20%–39%) was significantly higher than that among normotensive subjects ($P$<0.0001 for all 3 data sets; Table 1). Among subjects who were normotensive at baseline (n=1876), 108 became hypertensive at 3.25 years; another 107 subjects who were normotensive at both baseline and 3.25 years were found to be hypertensive at 7 years, and 28 other subjects who were normotensive at baseline and missed examination 2 were hypertensive at examination 3. Thus, a total of 243 subjects converted to hypertension during the 7-year follow-up, yielding a crude conversion rate of ≈2% per year.

In comparison with subjects who were seen and found to be normotensive at all 3 examinations (nonconverters), converters to hypertension were older, heavier with a more central fat distribution, and had higher systolic and diastolic BP values and higher pulse rate at baseline regardless of their time of conversion. Diabetes mellitus was more prevalent among either group of converters than in nonconverters (Table 2). Moreover, among normotensive individuals, diabetes mellitus at baseline was a significant predictor of incident hypertension (in FOS, OR, 3.14; 95% CI, 2.17–4.54) independently of age, BMI, and family history of diabetes mellitus (Figure 1). Of note, when the baseline mean BP was included in the model, the predictive value of diabetes mellitus was

**Table 1. The MCDS (Mexico City Diabetes Study) and the FOS (Framingham Offspring Study)***

| | Baseline | | First Follow-Up | | Second Follow-Up | |
|---|---|---|---|---|---|---|
| Patients | MCDS | FOS | MCDS | FOS | MCDS | FOS |
| n | 2280 | 3754 | 1770 | 3353 | 1753 | 3132 |
| NT, n (%) | 1876 (82) | 2461 (66) | 1487 (84) | 1947 (58) | 1381 (79) | 1678 (54) |
| ND | 1656 (88) | 2321 (94) | 1198 (81) | 1814 (93) | 1102 (80) | 1541 (92) |
| D | 220 (12) | 140 (6) | 289 (19) | 133 (7) | 279 (20) | 137 (8) |
| HT, n (%) | 404 (18) | 1293 (34 | 283 (16) | 1406 (42) | 372 (21) | 1454 (46) |
| ND | 310 (77) | 1040 (80) | 199 (70) | 1406 (80) | 227 (61) | 1097 (75) |
| D | 94 (23) | 253 (20) | 84 (30) | 283 (20) | 145 (39) | 357 (25) |

D indicates diabetic; HT, hypertensive; ND, nondiabetic; and NT, normotensive.

*Number (%) of subjects examined at baseline, first follow-up (3.25 y in MCDS and 4 y in FOS), and second follow-up (7 y in MCDS and 9 y in FOS) by blood pressure (NT and HT) and glucose tolerance status (ND and D).

attenuated and became nonsignificant (in MCDS, OR, 1.44; 95% CI, 0.97–2.14).

All subject groups exhibited weight gain during the observation period independently of the conversion status or the time of conversion. In MCDS, the increase in BMI was a significant independent predictor of incident hypertension (the hazard ratio for 1 SD change in BMI was 1.31; 95% CI, 1.12–1.55 and in the same model, the corresponding hazard ratio for the presence of diabetes mellitus at baseline was 1.79; 95% CI, 1.14–2.77). On conversion, both systolic and diastolic BP values rose markedly and similarly in both groups of hypertension converters (Figure 2). Using only the data of MCDS subjects not receiving antihypertensive treatment, the rise in systolic BP was 19 (14) mm Hg in subjects converting at examination 2 (n=65) and 19 (17) mm Hg in those (n=60) converting at examination 3. Values higher than the 90th percentile of the changes in systolic BP observed in nonconverters were found in 70% of the subjects converting at examination 2 and in 58% of those converting at examination 3. Similar changes were observed in the converters of FOS. The presence of diabetes mellitus did not consistently affect the pattern of BP change in patients developing hypertension during the follow-up. Thus, in MCDS patients not receiving antihypertensive medications, the increase in systolic BP in those converting to hypertension at examination 2 was 18 mm Hg if nondiabetic and 20 mm Hg if diabetic. On the contrary, the corresponding changes in systolic BP for patients converting at examination 3 were 27 mm Hg in diabetic versus 17 mm Hg in nondiabetic patients ($P$<0.05).

## Development of Diabetes Mellitus

Among subjects who were nondiabetic at baseline (n=1966), 89 had developed diabetes mellitus by 3.25 years; another 71 subjects who were nondiabetic at both baseline and 3.25 years were found to be diabetic at 7 years, and 10 other subjects who were nondiabetic at baseline and missed examination 2 were diabetic at examination 3. Thus, a total of 170 subjects converted to diabetes mellitus during the 7-year follow-up, yielding a crude conversion rate of 1.2% per year. Among nondiabetic individuals, hypertension at baseline was more

**Table 2. Clinical Phenotype of Normotensive Subjects Converting to Hypertension at the First or the Second Follow-Up and in Subjects Remaining Normotensive at All 3 Examinations (Nonconverters)**

| | First Follow-Up | | Second Follow-Up | | Nonconverters | | |
|---|---|---|---|---|---|---|---|
| Data Set | MCDS | FOS | MCDS | FOS | MCDS | FOS | *P* Value* |
| N | 108 | 436 | 107 | 235 | 1154 | 1443 | … |
| Sex (M/F) | 39/69 | 218/218* | 38/69 | 113/122 | 479/675 | 606/837 | <0.01 |
| Age, y | 51±8† | 61±9† | 50±8† | 62±9† | 45±8 | 58±9 | <0.0001 |
| BMI, kg/m$^2$ | 29.3±4.4† | 28.3±5.1† | 28.6±4.4† | 28.7±4.9† | 27.6±4.2 | 26.9±4.6 | <0.0001 |
| Waist, cm | 100±11† | 99±13† | 98±11† | 102±13† | 95±12 | 97±13 | <0.0001 |
| Systolic BP, mm Hg | 124±10† | 126±5† | 119±9† | 124±7† | 111±11 | 116±11 | <0.0001 |
| Diastolic BP, mm Hg | 76±7† | 80±10† | 74±9† | 79±10† | 70±8 | 71±8 | <0.0001 |
| Pulse rate, bpm | 76±10† | … | 74±9† | … | 72±9 | … | <0.0001 |
| Diabetes mellitus, % | 50† | 13† | 41† | 16† | 34 | 7 | <0.0001 |

BMI indicates body mass index; BP, blood pressure; FOS, Framingham Offspring Study; and MCDS, Mexico City Diabetes Study.

*ANOVA or $\chi^2$ for the 3 groups for each data set.

†$P \leq 0.05$ vs nonconverters by Bonferroni–Dunn test for each data set.

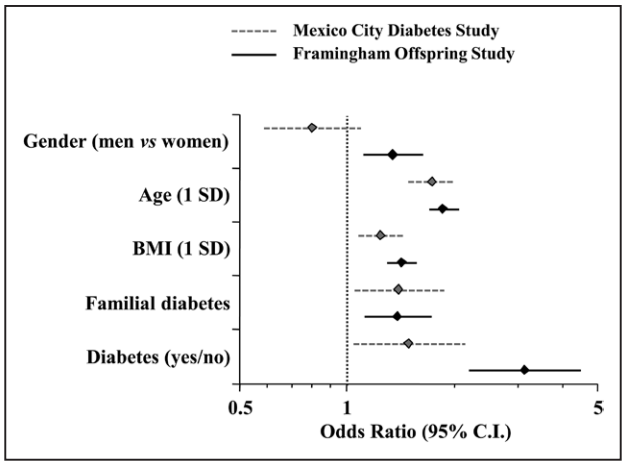


**Figure 1.** Multivariate logistic analysis of incident hypertension in normotensive individuals in the MCDS (Mexico City Diabetes Study) and FOS (Framingham Offspring Study). Plots are odds ratios and 95% confidence intervals (CI; calculated for 1 SD of continuous predictor variable). BMI indicates body mass index.

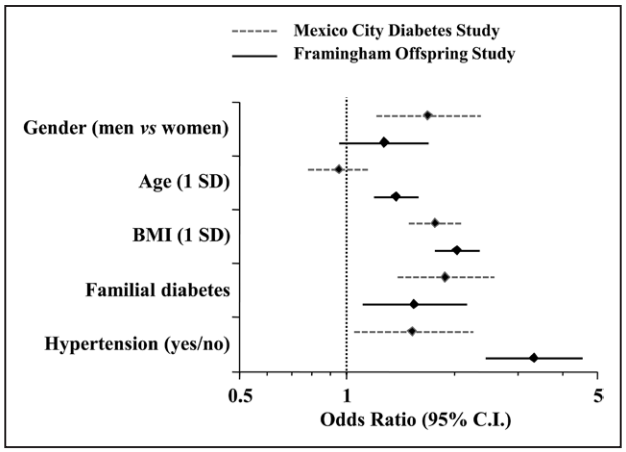


**Figure 3.** Multivariate logistic analysis of incident diabetes mellitus in nondiabetic individuals in the MCDS (Mexico City Diabetes Study) and FOS (Framingham Offspring Study). Plots are odds ratios and 95% confidence intervals (CI; calculated for 1 SD of continuous predictor variable; data are adjusted for smoking categorized as ever or not). BMI indicates body mass index.

prevalent among diabetes mellitus converters than nonconverters (25% versus 15%; $P$=0.001) and was a significant predictor of incident diabetes mellitus (in FOS, OR, 3.33; 95% CI, 2.50–4.44) independently of sex, age, BMI, and familial diabetes mellitus (Figure 3). Again, the increase in BMI during the observation period was a significant predictor of incident diabetes mellitus (in MCDS, the hazard ratio for 1 SD change in BMI was 1.36; 95% CI, 1.16–1.60 and the corresponding hazard ratio for presence of hypertension at baseline in the same model was 1.80; 95% CI, 1.03–3.04). Among the 1656 participants who were normotensive and nondiabetic at baseline, 104 had converted to diabetes mellitus at 7 years, 165 to hypertension, and 24 to both diabetes mellitus and hypertension. In comparison with the nonconverters group, hypertension and diabetes mellitus converters shared most phenotypic traits, namely, higher BMI, waist girth, BP, heart rate and pulse pressure values, serum triglycerides, and plasma insulin concentrations (both fasting and postload; Table S1 in the online-only Data Supplement). In addition, in MCDS, age was higher in hypertension converters but not in diabetes mellitus converters (in FOS, age was higher in diabetes mellitus converters too), whereas familial diabetes mellitus, fasting and 2-hour plasma glucose, and serum proinsulin concentrations were higher in diabetes mellitus converters but not in hypertension converters. All these anthropometric and metabolic differences from the control group were accentuated in the double converters (Table S1 in the online-only Data Supplement). In multivariate analysis, age, BMI, fasting plasma glucose, mean BP, and 2-hour plasma insulin concentrations were independent risk factors for the development of either hypertension or T2D (Figure 4).

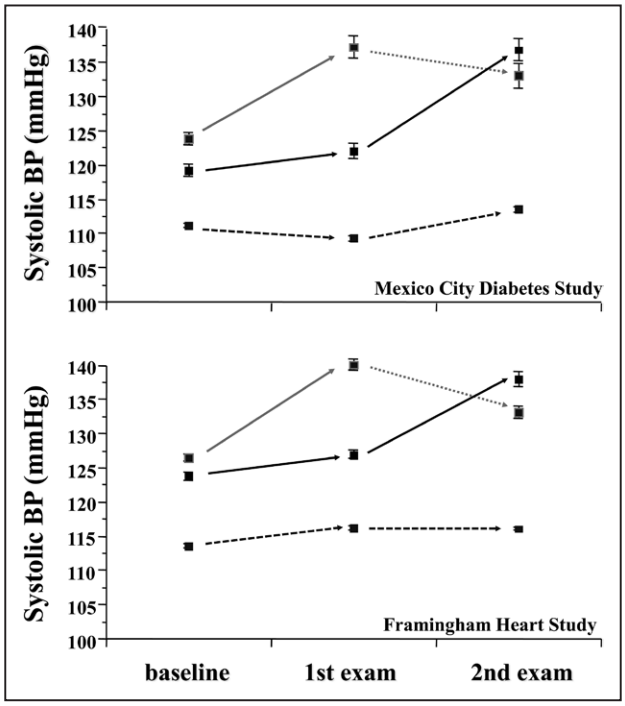


**Figure 2.** Systolic and diastolic blood pressure (BP) values in normotensive subjects who remained normotensive at both follow-up examinations (black dashed lines), became hypertensive at the first examination (gray lines), or became hypertensive at the second examination (black solid lines). Plots are mean±SD. The dotted gray lines indicate that the apparent decline in BP values after diagnosis are likely because of antihypertensive treatment.

## Discussion

The first main finding of the present study is that not only does the presence of hypertension predict future diabetes mellitus, in agreement with earlier epidemiological observations,[2,3,8,9] but also the incidence of hypertension increases significantly in the presence of diabetes mellitus. During the 7 years of follow-up, BP behaved as a tracking variable as individuals who converted to hypertension (at the first or second follow-up visit) had increased baseline BP values compared with nonconverters, although still within the normal range.[10] Indeed, baseline BP was the strongest predictor of incident hypertension, and its inclusion in the statistical model significantly attenuated the predictive value of diabetes mellitus. More strikingly, hypertension and diabetes mellitus tracked each other consistently (Figures 1 and 3), and people

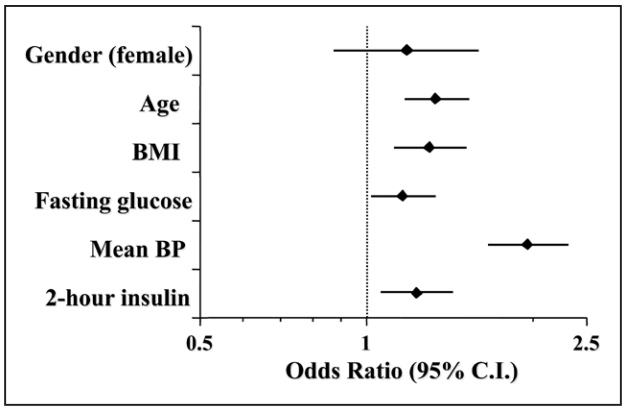


**Figure 4.** Multivariate logistic analysis of incident hypertension or diabetes mellitus in the Mexico City Diabetes Study. Plots are odds ratios and 95% confidence intervals (CI; calculated for 1 SD of continuous predictor variable). BMI indicates body mass index.

at high risk for the development of either hypertension or diabetes mellitus share common metabolic abnormalities, that is, abdominal obesity, hyperinsulinemia, and hypertriglyceridemia (even more prominent in those destined to develop both abnormalities). Thus, the general population contains a pool of individuals with the phenotype of the metabolic (or insulin resistance) syndrome from which new hypertension or diabetes mellitus (or both) emerge over time. Importantly, weight gain may be one factor that contributes to the development of both hypertension and diabetes mellitus. Parenthetically, the increased incidence of hypertension in patients with diabetes mellitus may also reflect the closer surveillance of these individuals (ie, a small detection bias). The second, and possibly the most important, finding of this study is that the progression from normotension to hypertension in individuals destined to become hypertensive is marked by a steep increase in BP values averaging 20 mm Hg for systolic BP within 3.5 years. In >60% of the converters, the increase in BP values during the period that preceded conversion was greater than the 90th percentile of the changes in systolic BP observed in nonconverters. This biphasic BP pattern is similar to that previously described for blood glucose values in MCDS individuals developing diabetes mellitus.[7] Finally, both the coprediction of hypertension and diabetes mellitus and this biphasic pattern of progression are not unique to Hispanic individuals because essentially the same findings were observed in the non-Hispanic white population of FOS.

One potential factor responsible for the covariance of diabetes mellitus and hypertension is insulin resistance.[1] Of note, in a subcohort of FOS with a shorter follow-up, an inverse association between incident hypertension (or BP progression) and a proxy of insulin resistance was seen principally in younger people.[10] Here, however, both fasting plasma insulin (a typical proxy for insulin resistance in epidemiological studies) and plasma insulin concentrations 2 hours after glucose ingestion were consistently higher at baseline in both hypertension and diabetes mellitus converters. Furthermore, baseline insulin levels copredicted both hypertension and diabetes mellitus after controlling for age and BMI and also for baseline BP and plasma glucose values (Figure 4). This pattern of results lends support to the notion that insulin resistance is one common feature of both prediabetes and prehypertension, and one antecedent of progression to the 2 respective disease states.

Apart from the detrimental effects that disturbed insulin signaling exerts on carbohydrate metabolism, the hyperinsulinemia that characterizes insulin resistance states leads to vascular smooth muscle cell proliferation and increased vascular stiffness, which predispose to the development of hypertension.[11] Additionally, insulin may directly or indirectly impair vasodilation and increase oxidative stress and the inflammatory process in the vascular wall.[12,13] The sum of these effects is the impaired autoregulation of vascular tone, increased vascular resistance, and BP elevation. Finally, the antinatriuretic properties of insulin increase renal retention of sodium and water leading to volume overload, thereby predisposing to the development of hypertension.[14]

A novel finding from both study cohorts is that, in individuals who ultimately develop T2D, hypertension, or both, the time trajectory of plasma glucose[7] and BP values is not a progressive slow increase but—in the majority of cases—a steep elevation several-fold larger compared with changes observed in nonconverters (or, in the case of patients converting at the second follow-up, compared with the changes observed in the same patients between baseline and the first follow-up visit). Although the pathophysiological basis of this relatively acute decompensation remains indeterminate, it could be hypothesized that it may be related to sympathetic excitation. The sequence of events that lead to activation of the sympathetic nervous system is unknown. However, in healthy volunteers, insulin dose dependently stimulates norepinephrine release, particularly in skeletal muscle, and enhances sympathetic neuronal discharge.[15] In subjects with uncomplicated obesity monitored for 24 hours, there is episodic sympathetic dominance in phase with postprandial hyperinsulinemia, which abates after weight loss.[16] The autonomic contribution to BP is greater in obesity, and ganglionic blockade of the autonomic nervous system results in BP decrease that is more pronounced in obese individuals.[17] Obese subjects with hypertension display increased sympathetic nerve activity, an abnormality that is partially corrected after diet-induced weight loss.[18] Leptin, an adipokine that has been found to circulate in increased concentrations in obese and insulin resistant subjects, can act centrally to activate the sympathetic nervous system[19]; not all studies have confirmed this hypothesis.[20] In addition, experimental models suggest that leptin may also contribute to the pathogenesis of hypertension via aldosterone-dependent mechanisms.[21] In line with these suggestions, in our population, BMI values at baseline and weight gain during the observation period were significant predictors of both incident hypertension and diabetes mellitus, whereas heart rate and pulse pressure, both raw indices of sympathetic nervous system activity, were found to be elevated in patients who converted to hypertension. Finally, obese individuals with or without diabetes mellitus have been shown to have reduced concentrations of circulating natriuretic peptides. Because these molecules favorably affect intravascular volume status and vascular tone, this mechanism may be involved in the pathogenesis of hypertension in patients with diabetes mellitus.[22]

Our findings may have implications in the everyday care of patients with diabetes mellitus. Thus, diabetic patients with BP values near the upper limit of normal should be monitored for the development of hypertension, especially if they have a positive family history of hypertension and the phenotypic features of the metabolic syndrome. Because development of hypertension in patients with diabetes mellitus is marked by a significant increase in macrovascular and microvascular risk,[2,23] efforts should be made to delay or ideally prevent the increase in BP. Obviously, the follow-up scheme of both MCDS and FOS does not reflect everyday clinical practice, as is generally true of observational population-based studies. Under ideal conditions, patients with diabetes mellitus or hypertension are seen 2 or 3 times per year. However, the time pattern of BP progression we describe here may still emerge from more frequent follow-up visits. On the contrary, in an era of continuously increasing pressures on healthcare systems, understanding the factors that predispose to, or precipitate, the development of an outcome should increase clinicians' awareness and may facilitate the timely diagnosis of conditions that might otherwise go unnoticed.

Apart from lifestyle modification, several classes of antidiabetic drugs such as SGLT2 (sodium-glucose cotransporter 2) inhibitors and GLP-1 (glucagon-like peptide 1) receptor agonists have been shown to lower BP[24,25] (although the data for liraglutide is less convincing[26]) and reduce cardiovascular events in secondary prevention.[25,27] Thus, use of these drugs might be prioritized in diabetic patients at high risk for the development of hypertension, although the clinical value of this strategy in terms of hard end point reduction has been unequivocally proven only in individuals with established cardiovascular disease.

## Perspectives

The development of hypertension and diabetes mellitus predicts each other over time. The transition from normotension to hypertension is characterized by a sharp increase in BP values. Insulin resistance is one common feature of both prediabetes and prehypertension, and an antecedent of progression to 2 respective disease states, especially in individuals who gain weight over time. Because development of hypertension in patients with diabetes mellitus is marked by a significant increase in macrovascular and microvascular risk, efforts should be made to delay or ideally prevent the increase in BP. In this context, the prioritization of antidiabetic drugs that reduce BP (such as SGLT2 inhibitors or GLP-1 receptor agonists) in patients with diabetes mellitus at high risk for the development of hypertension may be of clinical value.

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## Disclosures

None.

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## Novelty and Significance

### What Is New?

- Diabetes mellitus and hypertension copredict each other.
- The progression to hypertension is marked by a steep increase in blood pressure values.

### What Is Relevant?

- Diabetic patients with blood pressure values near the upper limit of normal should be monitored for the development of hypertension.
- Antidiabetic drugs that reduce blood pressure should be prioritized in diabetic patients at high risk for the development of hypertension.

### Summary

The development of hypertension and diabetes mellitus predict each other over time. The transition from normotension to hypertension is characterized by a sharp increase in blood pressure values. Insulin resistance is one common feature of both prediabetes and prehypertension and an antecedent of progression to 2 respective disease states.