Hypertension and diabetes: co-prediction and time trajectories

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Abstract

Type 2 diabetes and hypertension overlap in the population. In many subjects, development of diabetes 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 using data from the Mexico City Diabetes Study (MCDS, a population-based study of diabetes in Hispanic Whites) and in the Framingham Offspring Study (FOS, a community-based study in non-Hispanic Whites) over a 7-year follow-up. Diabetes at baseline was a significant predictor of incident hypertension (in FOS, OR=3.14 [95% CI=2.17–4.54]) independently of gender, age, BMI, and familial diabetes. Conversely, hypertension at baseline was an independent predictor of incident diabetes (in FOS, OR=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 mmHg for systolic BP within 3.5 years (in MCDS). In comparison with the non-converters group, hypertension and diabetes converters shared a metabolic syndrome phenotype (hyperinsulinemia, higher BMI, waist girth, BP, heart rate and pulse pressure, dyslipidemia). Overall, results were similar in the two ethnic groups. We conclude that (1) development of hypertension and diabetes 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 two respective disease states

Keywords

diabetes; hypertension; trajectories; co-prediction; tracking variables; insulin resistance

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Introduction

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 (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 other hand, accumulating evidence suggests that disturbances in carbohydrate metabolism are more common in hypertensive individuals [2, 3], thereby indicating that the etiologic relationship between diabetes and hypertension is actually bidirectional.

The development of hypertension in diabetic individuals not only complicates treatment strategy and increases health care 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 delayed recognition of the presence of hypertension, clinical inertia, poor adherence to the prescribed regimen, but also uncertainty regarding the treatment targets, as well as etiologic correlation.

A previous report from the Mexico City Diabetes Study (MCDS) showed that, in ~2/3 of patients with either normoglycemia or impaired glucose tolerance the development of overt diabetes is characterised by an abrupt (within approximately 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 in MCDS. The second aim was to quantify the longitudinal association of T2D and hypertension in this population-based study over 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 the development of diabetes, hypertension or both. Since the population of MCDS included Hispanic individuals from low-income areas with a high risk for the development of diabetes, we explored the generizability of any results by asking the same questions in the non-Hispanic white population of the Framingham Offspring Study (FOS).

Materials and Methods

The authors declare that all supporting data are available within the article [and its online supplementary files].

Study populations

(a) The Mexico City Diabetes Study (MCDS) is a population-based cohort participating in a longitudinal survey of incident diabetes and cardiovascular risk factors. Low-income neighborhoods in Mexico City were identified, and a complete enumeration of these was carried out from November 1989 to October 1992. Among the 15,532 inhabitants of these

neighborhoods, 2,280 men and women (aged 35 to 64 years) randomly selected from 6 low-income "colonias" examined between 1990–1992 and invited to return for 2 follow-up examinations, the first conducted between 1993–1995 and the second between 1997–1999. Of the 1,770 subjects participating in the first follow up (at 3,25 years), 1,753 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 standardised and included interviews, anthropometry, blood pressure (BP) measurements, a fasting blood draw, and a 75-g oral glucose tolerance test (OGTT). 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.

(b) The Framingham Offspring Study (FOS) is a community-based cohort including 3,754 men and women who attended the fifth clinic examination (1989–1992) of the Framingham Offspring Study. 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 or hypertension were identified as the date of diagnosis; otherwise, follow-up was censored at last follow-up (exam 6 or 7) for participants remaining non-diabetic or non-hypertensive. The protocol was approved by the Ethics Committee of Boston University Medical Canter, and all subjects gave written informed consent.

In both cohorts, hypertension was defined as a systolic BP 140 mmHg or a diastolic BP 90 mmHg or current anti-hypertensive treatment. In both studies, subjects whose BP was <140/90 mmHg at baseline and both follow-up visits were classified as normotensives, those whose BP was <140/90 mmHg at the first visit who became hypertensive at the second or third visit were classified as converters. Type 2 diabetes 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 (OGTT). Subjects who gave a history of diabetes and who at the time of their clinical examination were taking oral antidiabetic agents were also considered to have type 2 diabetes 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 type 2 diabetes. Subjects with type 1 diabetes were excluded. Subjects who developed diabetes at the first or second follow-up were denoted as converters. Subjects who tested normal on the OGTT on all three examinations were considered to be *bona fide* non-converters over the observation period.

Anthropometric measurements—Diabetes in at least one parent or sibling was coded as a positive family history of diabetes. Prior to 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 (PP) was calculated as the difference between systolic and diastolic BP, mean BP as the sum of diastolic BP and one third of PP.

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 follow up.

Statistical analysis—The study design is that of a longitudinal cohort study of incident diabetes as a function of baseline hypertension, or of incident hypertension as a function of baseline diabetes, both with confounder covariate adjustment. We also assessed the rate of change of blood pressure 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 χ^2 test, continuous variables by ANOVA, with Bonferroni-Dunn testing of multiple *post hoc* comparisons. Logistic regression for incident events was carried out by defining response as a diagnosis of hypertension (or diabetes) at either of the two follow-up visits and non-response as no hypertension (or diabetes) 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 predicts hypertension, or vice versa.

Results

Development of hypertension

At the 3 examinations, 16–46% of the study subjects were hypertensive; among them, the prevalence of diabetes (20–39%) was significantly higher than among normotensive subjects (p<0.0001 for all 3 datasets) (Table 1). Among subjects who were normotensive at baseline (n=1,876), 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 over 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 (non-converters), 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 was more prevalent among either group of converters than in non-converters (Table 2). Moreover, among normotensive individuals diabetes 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

(Figure 1). Of note, when the baseline mean blood pressure was included in the model the predictive value of diabetes was attenuated and became non-significant (in the 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 HR for 1SD change in BMI was 1.31 [95% CI 1.12–1.55]; in the same model the corresponding HR for the presence of diabetes at baseline was 1.79 [95% CI 1.14–2.77]). Upon 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] mmHg in subjects converting at examination 2 (n=65) and 19 [17] mmHg in those (n=60) converting at examination 3. Values higher than the 90th percentile of the changes in systolic BP observed in non-converters 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 did not consistently affect the pattern of blood pressure change in patients developing hypertension during the follow-up. Thus, in MCDS patients not receiving antihypertensive medications the increase in SBP in those converting to hypertension at examination 2 was 18 mmHg if nondiabetic and 20 mmHg if diabetic. On the other hand, the corresponding changes in SBP for patients converting at examination 3 were 27 mmHg in diabetic *vs* 17 mmHg in nondiabetic patients ($p<0.05$).

Development of diabetes

Among subjects who were non-diabetic at baseline (n=1,966), 89 had developed diabetes by 3.25 years; another 71 subjects who were non-diabetic at both baseline and 3.25 years were found to be diabetic at 7 years, and 10 other subjects who were non-diabetic at baseline and missed examination 2 were diabetic at examination 3. Thus, a total of 170 subjects converted to diabetes over the 7-year follow up, yielding a crude conversion rate of 1.2% per year. Among nondiabetic individuals, hypertension at baseline was more prevalent among diabetes converters than non-converters (25% *vs* 15%, $p=0.001$), and was a significant predictor of incident diabetes (in FOS, OR = 3.33 [95% CI = 2.50–4.44]) independently of gender, age, BMI, and familial diabetes (Figure 3). Again, the increase in BMI during the observation period was a significant predictor of incident diabetes (in MCDS, the HR for 1SD change in BMI was 1.36 [95% CI 1.16–1.60]; the corresponding HR for presence of hypertension at baseline in the same model was 1.80 [95% CI 1.03–3.04]). Among the 1,656 participants who were normotensive and non-diabetic at baseline, 104 had converted to diabetes at 7 years, 165 to hypertension and 24 to both diabetes and hypertension. In comparison with the non-converters group, hypertension and diabetes 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 3). In addition, in MCDS age was higher in hypertension converters but not in diabetes converters (in FOS age was higher in diabetes converters too), whilst familial diabetes, fasting and 2-hour plasma glucose and serum proinsulin concentrations were higher in diabetes 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 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 type 2 diabetes (Figure 4).

Discussion

The first main finding of the present study is that not only does the presence of hypertension predict future diabetes, in agreement with earlier epidemiological observations [2, 3, 8, 9], but also that the incidence of hypertension increases significantly in the presence of diabetes. Over 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 to non-converters, though 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. More strikingly, hypertension and diabetes tracked each other consistently (Figures 1&3), and people at high risk for the development of either hypertension or diabetes share common metabolic abnormalities, *i.e.,* abdominal obesity, hyperinsulinemia, 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 (or both) emerge over time. Importantly, weight gain may be one factor that contributes to the development of both hypertension and diabetes. Parenthetically, the increased incidence of hypertension in patients with diabetes may also reflect the closer surveillance of these individuals (*i.e.,* 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 mmHg for systolic BP within 3.5 years. In more than 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 non-converters. This biphasic BP pattern is similar to that previously described for blood glucose values in MCDS individuals developing diabetes [7]. Finally, both the co-prediction of hypertension and diabetes and this biphasic pattern of progression are not unique to Hispanic individuals since essentially the same findings were observed in the non-Hispanic white population of FOS.

One potential factor responsible for the covariance of diabetes 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 converters. Furthermore, baseline insulin levels co-predicted both hypertension and diabetes 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 two 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 cells 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 that 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 to changes observed in non-converters (or, in the case of patients converting at the 2nd follow up, compared to the changes observed in the same patients between baseline and the 1st 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 following 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 whereas heart rate and pulse pressure, both raw indices of sympathetic nervous system activity, were found to be elevated in patients that converted to hypertension. Finally, obese individuals with or without diabetes have been shown to have reduced concentrations of circulating natriuretic peptides. Since these molecules favorably affect intravascular volume status and vascular tone, this mechanism may be involved in the pathogenesis of hypertension in patients with diabetes [22].

Our findings may have implications in the every-day care of patients with diabetes. 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. Since development of hypertension in patients with diabetes 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 or hypertension are seen two or three times per year. However, the time pattern of BP progression we describe here may still emerge from more frequent follow-up visits. On the other hand, in an era of continuously increasing pressures on health care 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 life style modification several classes of antidiabetic drugs such as SGLT2 inhibitors and GLP-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 endpoint reduction has been unequivocally proven only in individuals with established cardiovascular disease.

Perspectives

The development of hypertension and diabetes predict 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 two respective disease states, especially in individuals who gain weight over time. Since development of hypertension in patients with diabetes 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 blood pressure (such as SGLT2 inhibitors or GLP-1 receptor agonists) in patients with diabetes at high risk for the development of hypertension may be of clinical value.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Novelty and Significance

What Is New

- diabetes and hypertension co-predict 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 predict 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 two respective disease states.
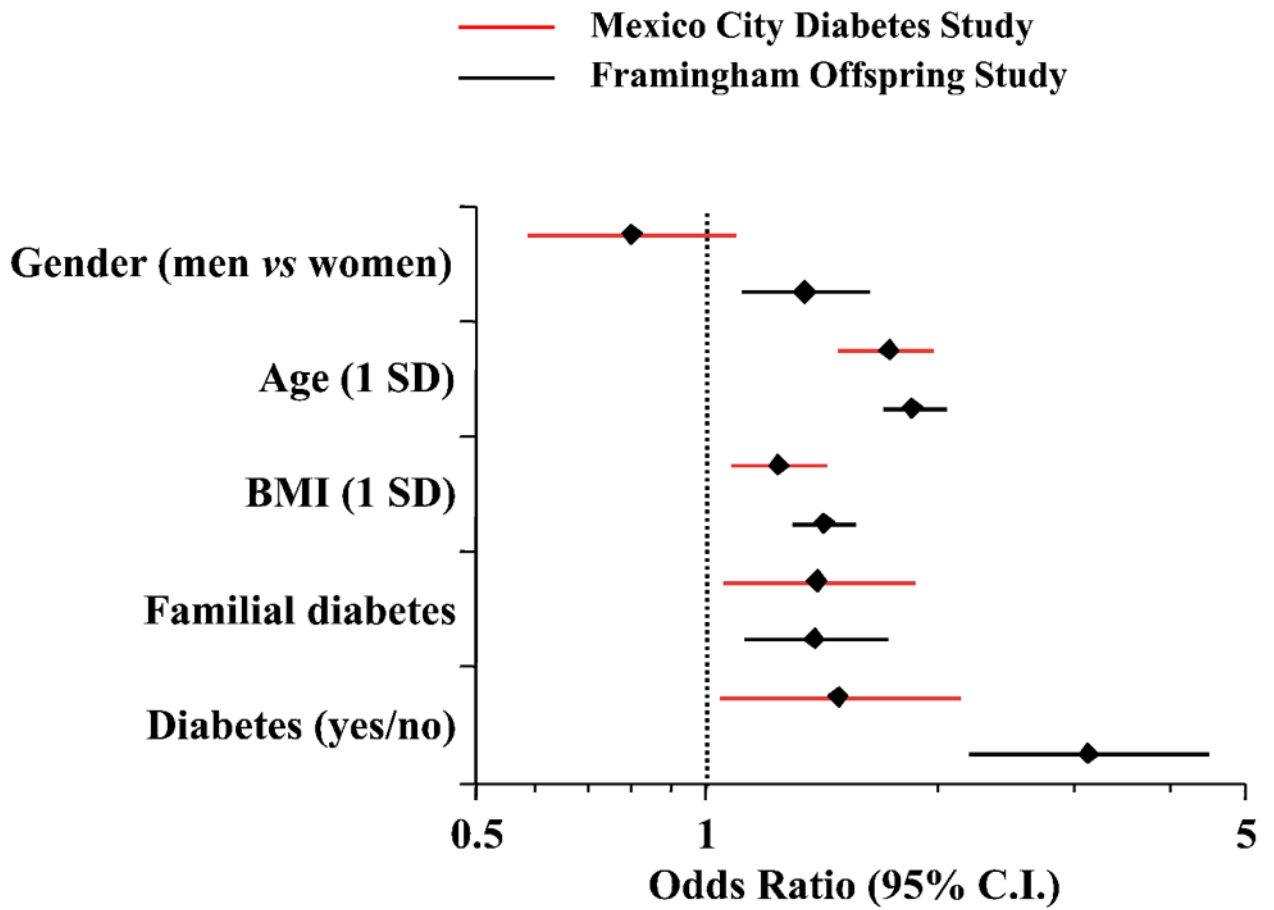
Figure 1.
Multivariate logistic analysis of incident hypertension in normotensive individuals in the Mexico City Diabetes Study (MCDS) and Framingham Offspring Study (FOS). Plots are odds ratios and 95% confidence intervals (calculated for 1 SD of continuous predictor variable).
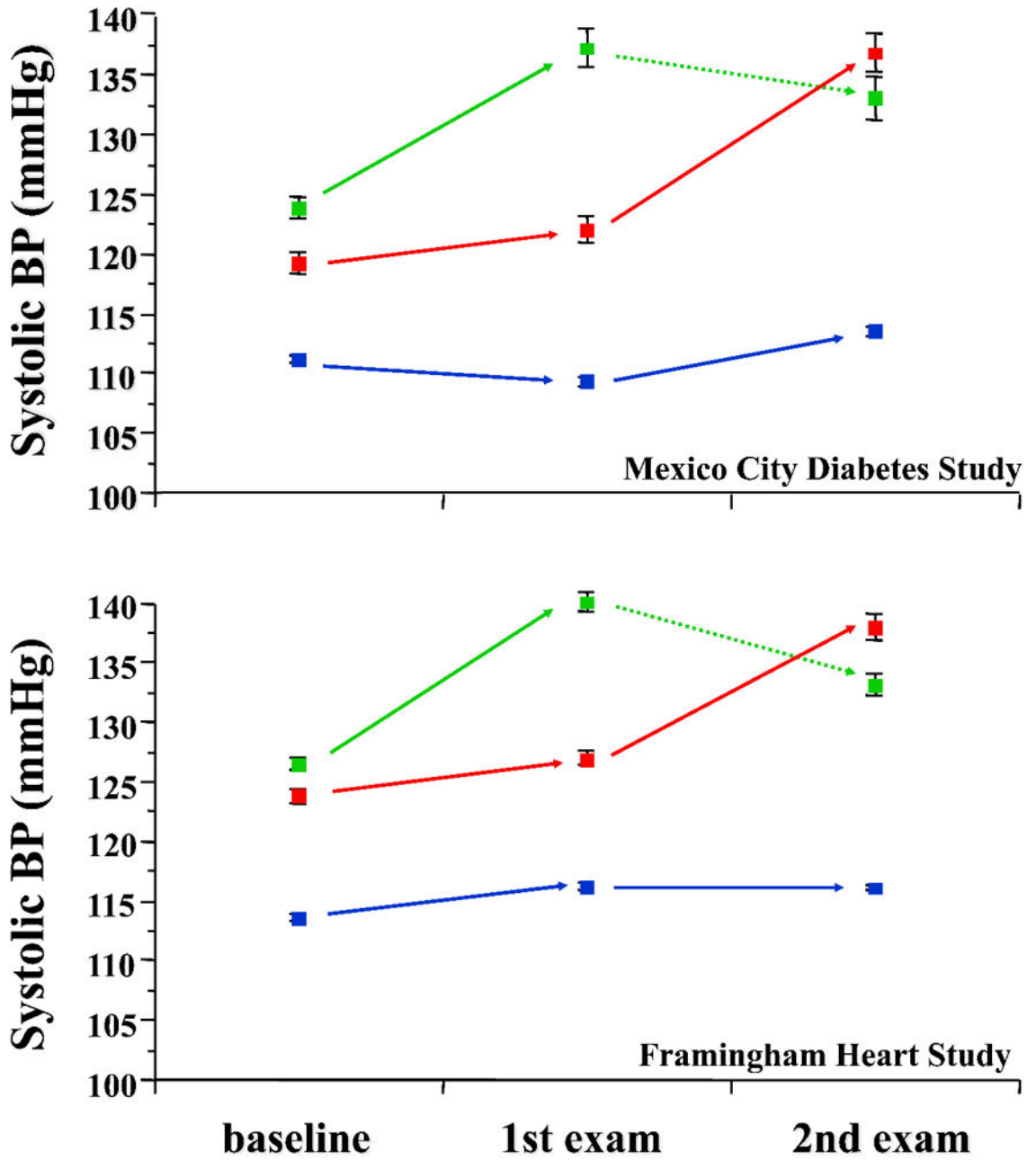
Figure 2.
Systolic and diastolic blood pressure values in normotensive subjects who remained normotensive at both follow-up examinations (*blue lines*), became hypertensive at the first examination (*green lines*) or at the second examination (*red lines*). Plots are mean±SD. The dotted green lines indicate that the apparent decline in BP values after diagnosis are likely due to anthypertensive treatment.
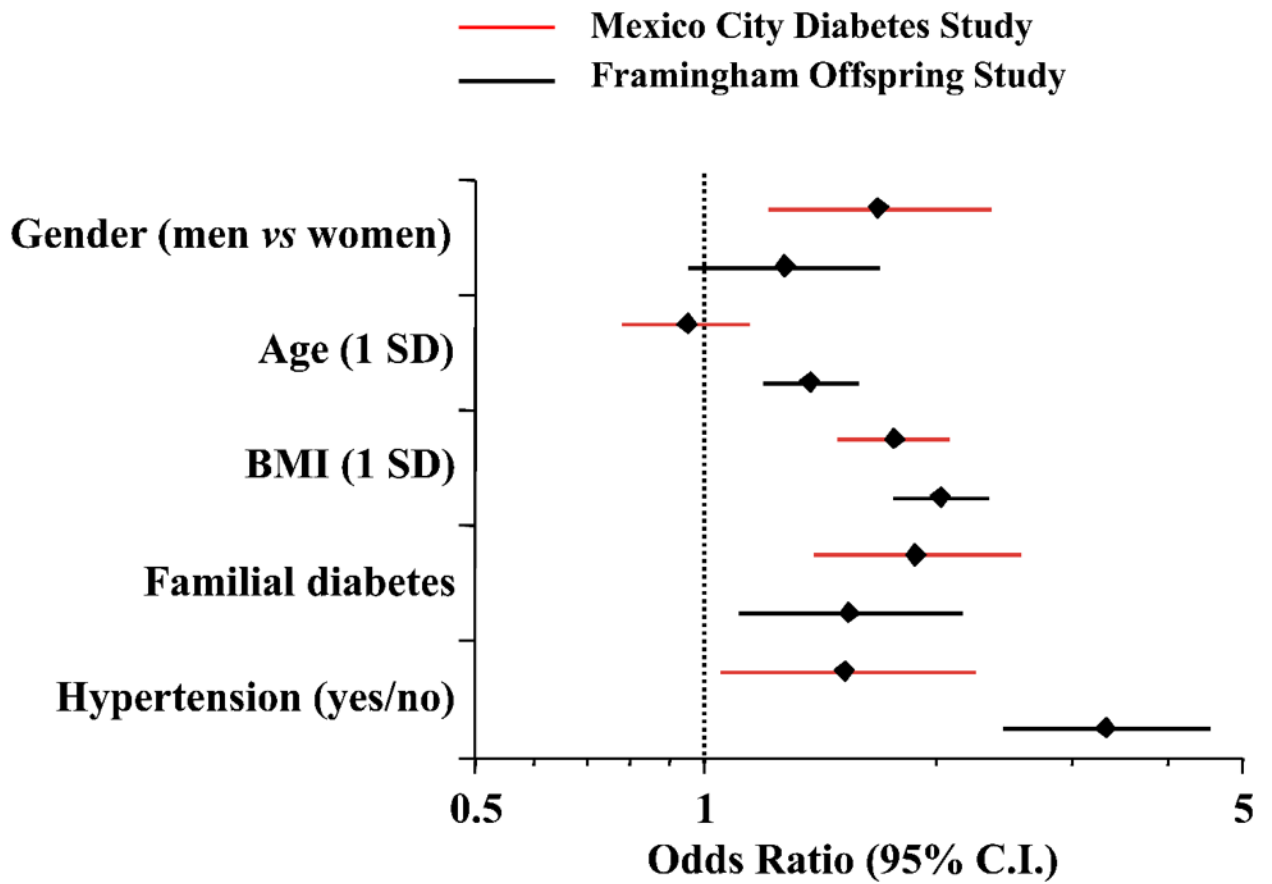
Figure 3.
Multivariate logistic analysis of incident diabetes in nondiabetic individuals in the Mexico City Diabetes Study (MCDS) and Framingham Offspring Study (FOS). Plots are odds ratios and 95% confidence intervals (calculated for 1 SD of continuous predictor variable; data are adjusted for smoking categorized as ever or not).
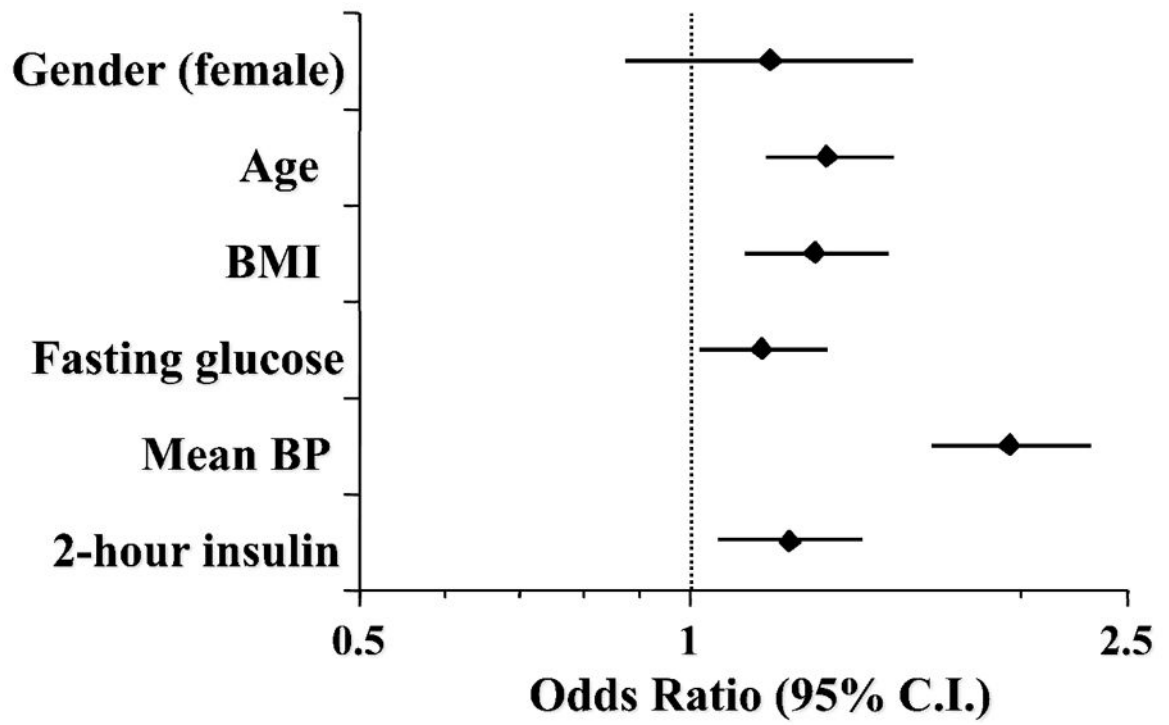
Figure 4.
Multivariate logistic analysis of incident hypertension or diabetes in the Mexico City Diabetes Study. Plots are odds ratios and 95% confidence intervals (calculated for 1 SD of continuous predictor variable).

Table 1

The Mexico City Diabetes Study (MCDS) and the Framingham Offspring Study (FOS) [*]

Patients	Baseline		1st follow up		2nd follow up	
	MCDS	FOS	MCDS	FOS	MCDS	FOS
n	2280	3754	1770	3353	1753	3132
NT	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	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%)

[*] Number (percentage) of subjects examined at baseline, 1st follow up (3.25 years in MCDS and 4 years in FOS), and 2nd follow up (7 years in MCDS and 9 years in FOS) by blood pressure (NT=normotensive, HT=hypertensive) and glucose tolerance status (ND=non-diabetic, D=diabetic).

Table 2

Clinical phenotype of normotensive subjects converting to hypertension at the 1st or the 2nd follow-up and in subjects remaining normotensive at all 3 examinations (non-converters).

Dataset	1st follow-up		2nd follow up		Non-converters		p[•]
	MCDS	FOS	MCDS	FOS	MCDS	FOS	
n	108	436	107	235	1154	1443	
Sex (M/F)	39/69	218/218[o]	38/69	113/122	479/675	606/837	<0.01
Age (years)	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 (mmHg)	124 ± 10[*]	126 ± 5[*]	119 ± 9[*]	124 ± 7[*]	111 ± 11	116 ± 11	<0.0001
Diastolic BP (mmHg)	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 (%)	50[o]	13[o]	41[o]	16[o]	34	7	<0.0001

[o] ANOVA or χ^2 for the 3 groups for each dataset

[*] p 0.05 vs non-converters by Bonferroni-Dunn test for each dataset