Is Prehypertension a Risk Factor for the Development of Type 2 Diabetes?

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OBJECTIVE — Prehypertension is associated with cardiovascular disease and insulin resistance. However, whether subjects with prehypertension have more diabetes risk is not known. We examine whether prehypertension is a risk factor for developing type 2 diabetes.

RESEARCH DESIGN AND METHODS — Incident diabetes was examined in nondiabetic normotensive participants in the San Antonio Heart Study (n = 2,767; aged 25–65 years; median follow-up 7.8 years).

RESULTS — Incident diabetes was 12.4% in subjects with prehypertension and 5.6% in subjects with normal blood pressure. The odds of incident diabetes were 2.21 greater for individuals with prehypertension than for those with normal blood pressure (95% CI 1.63–2.98) after adjusting for age, sex, and ethnicity. Prehypertension was not associated with incident diabetes after additional adjustment for BMI, impaired glucose tolerance, insulin resistance and secretion, and family history of diabetes (odds ratio 1.42 [95% CI 0.99–2.02]).

CONCLUSIONS — Subjects with prehypertension are at increased risk of diabetes. Much of this risk is explained by disorders related to the insulin resistance syndrome.

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Hypertension predicts future cardiovascular disease (1,2) and type 2 diabetes (3). Prehypertension (systolic blood pressure [SBP] 120–139 mmHg and/or diastolic blood pressure [DBP] 80–89 mmHg), a novel blood pressure category of "The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report" (4), is also associated with increased cardiovascular risk (5,6) and insulin resistance (7). Furthermore, results from the Framingham Heart Study indicate that cardiovascular risk may be more relevant in individuals with SBP 130–139 mmHg and/or DBP 85–89 mmHg (8). Therefore, we investigated the relationship between prehypertension and incident type 2 diabetes in the San Antonio Heart Study (SAHS).

RESEARCH DESIGN AND METHODS

— The SAHS is a longitudinal epidemiological study on cardiovascular disease and type 2 diabetes in Mexican Americans and non-Hispanic whites living in San Antonio, Texas (aged 25–65 years). Details of the study design, including blood pressure measurement protocols and laboratory details, have been published previously (9,10). Subjects were seen only at the initial encounter and at follow-up.

We used JNC 7 criteria to define normal blood pressure, prehypertension, and hypertension (4). Diabetes was defined as fasting plasma glucose ≥126 mg/dl, 2-h plasma glucose ≥200 mg/dl, and/or use of glucose-lowering agents; impaired fasting glucose (IFG) as fasting glucose 100–25 mg/dl; and impaired glucose tolerance (IGT) as 2-h plasma glucose 140–199 mg/dl (11). The homeostasis model assessment of insulin resistance (HOMA-IR) and β-cell function (HOMA-βC) were used to quantify the level of insulin resistance and secretion (12).

After excluding individuals with baseline hypertension or diabetes (n = 1,171) or individuals who did not present for the follow-up exam (n = 1,220), there were 2,767 (69.4%) subjects eligible for analysis. Median follow-up time was 7.8 years (range 6.3–10.7 years).

The relationship between baseline characteristics and prehypertension was examined using one-way ANCOVA for continuous variables and logistic regression analysis for dichotomous variables. The relation of measures of blood pressure to metabolic variables was assessed by Pearson's partial correlation coefficients. Multivariate logistic regression analysis was used to examine the risk of future diabetes associated with prehypertension.

RESULTS

— The prevalence of prehypertension at baseline was 31.3%. Prehypertension was associated with male sex and Mexican-American ethnic origin as well as with higher BMI, HOMA-IR, HOMA-βC, and levels of fasting glucose, 2-h glucose, fasting insulin, and triglycerides ($P < 0.001$ for all comparisons) (supplemental Table, available in an online appendix at http://care.diabetesjournals.org/cgi/content/full/dc09-0328/DC1).

After adjusting for age, sex, and ethnicity, SBP was positively related to BMI (r = 0.32), waist circumference (r = 0.29), HOMA-IR (r = 0.17), HOMA-βC (r = 0.11), as well as levels of 2-h glucose (r = 0.14), fasting insulin (r = 0.17), and triglycerides (r = 0.18) (all correlations, $P < 0.001$).

There were 213 (7.7%) new cases of diabetes: 12.4% (10.4–14.9) in subjects with prehypertension and 5.6% (4.7–6.8) in those with normal blood pressure. After adjusting for age, sex, and ethnicity, the odds of incident diabetes were 2.21 greater for individuals with prehypertension than for individuals with normal blood pressure (95% CI 1.63–2.98). After the additional adjustment for BMI, IGT, HOMA-IR, HOMA-βC, and family history of diabetes, diabetes risk associated

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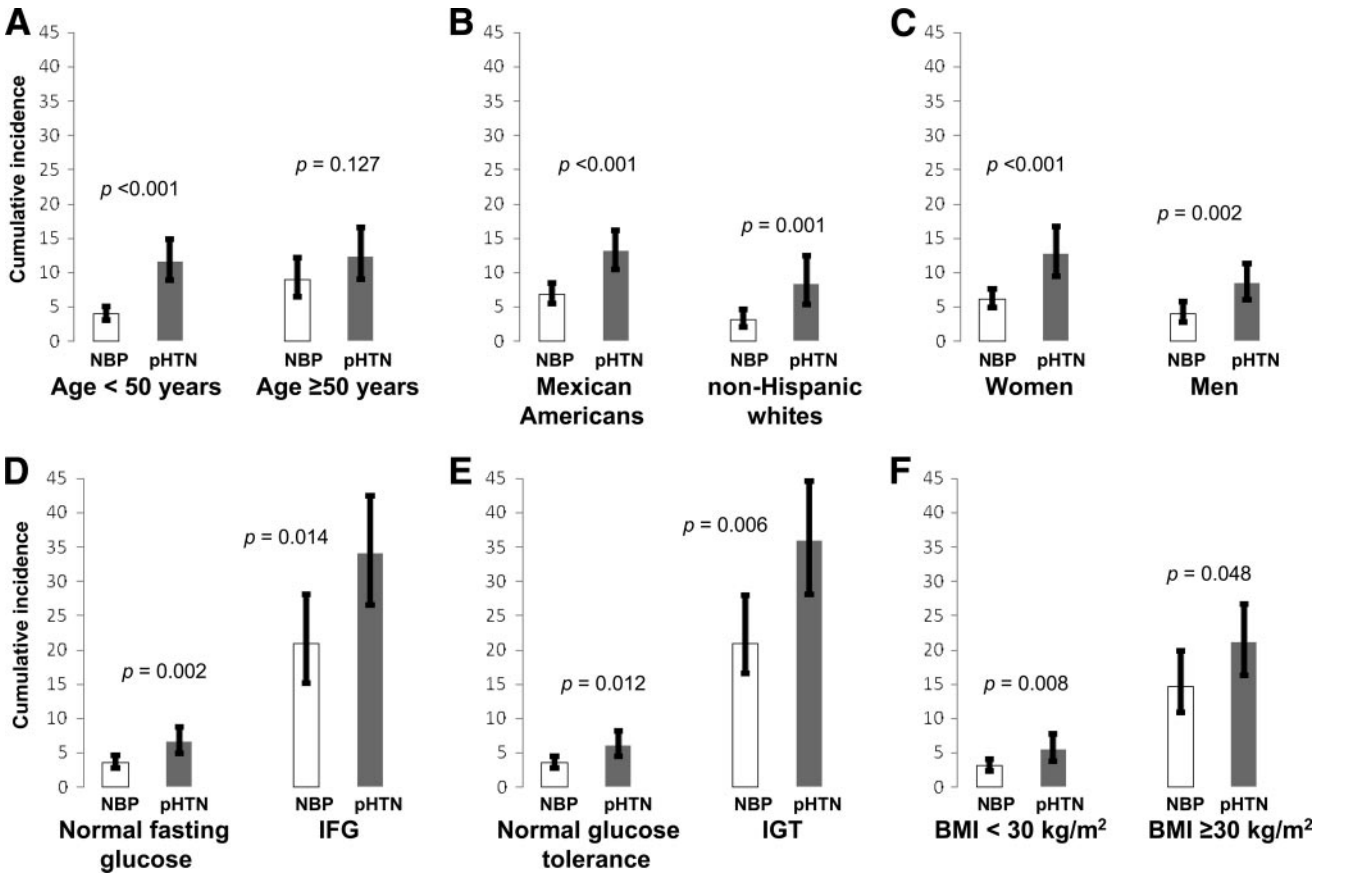

Figure 1—*Shown is the 7.8-year cumulative incidence of diabetes by prehypertension status and categories of age, ethnicity, sex, fasting glucose, glucose tolerance, and BMI. A: Age, adjusted for sex and ethnicity*. B: *Ethnicity, adjusted for age and sex. C: Sex, adjusted for age and ethnicity*. D–F: *Fasting glucose* (D), *glucose tolerance* (E), *and BMI* (F), *adjusted for age, sex, and ethnicity*. P *values for test of difference in incident diabetes between subjects with prehypertension and subjects with normal blood pressure. White bars = NBP, normal blood pressure; gray bars = pHTN, prehypertension.*

with prehypertension was not statistically significant (odds ratio 1.42 [95% CI 0.99–2.02]; $P = 0.052$). The risk remained significant for SBP 130–139 mmHg and/or DBP 85–89 mmHg (1.69 [1.03–2.77]) but did not remain significant for SBP 120–129 mmHg and DBP 80–84 mmHg (1.31 [0.88–1.94]).

Subjects with prehypertension had more diabetes risk than those with normal blood pressure regardless of sex, ethnic origin, and categories of obesity and glucose tolerance (Fig. 1). Prehypertension was also associated with increased diabetes risk in individuals aged 25–49 years but not in those aged 50–65 years ($n = 752$; $P = 0.127$).

CONCLUSIONS — Our study confirms previous reports on the relation of prehypertension to obesity (13) and insulin resistance (7) and demonstrates that individuals with prehypertension have higher rates of conversion to diabetes than those with normal blood pressure. Much of the diabetes risk associated with prehypertension is explained by disorders related to the insulin resistance syndrome.

Subjects with prehypertension have more diabetes risk than those with normal blood pressure regardless of sex, ethnicity, and categories of obesity and glucose tolerance. However, prehypertension is not associated with incident diabetes in subjects aged ≥50 years. Potential explanations may be a lack of statistical power ($n = 752$) or a lesser relationship between blood pressure and insulin resistance in individuals aged ≥50 years.

A significant limitation in our study is the lack of information on waist circumference, chronic inflammation, and physical activity for all participants. These confounders could be relevant for explaining the relationship between prehypertension and incident diabetes.

In summary, our study shows that subjects with prehypertension had greater risk of converting to diabetes than those with normal blood pressure. Further study is needed regarding mechanisms of this phenomenon and treatment options for participants with prehypertension.

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No potential conflicts of interest relevant to this article were reported.

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