Hypertension is an independent risk factor for type 2 diabetes: the Korean genome and epidemiology study

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Hypertension and diabetes share common risk factors and frequently co-occur. Although high blood pressure (BP) was reported as a significant predictor of type 2 diabetes, little is known about this association in Korea. This study investigated the relationship of prehypertension and hypertension with type 2 diabetes in 7150 middle-aged Koreans, as well as the effect of BP control on diabetes development over 8 years. At 8 years, 1049 (14.7%) of the 7150 participants had newly developed diabetes, including 11.2, 16.7 and 21.5% of baseline normotensive, prehypertensive and hypertensive subjects, respectively. The overall incidence rate of diabetes was 22.3 events per 1000 person-years. Subjects with baseline prehypertension (hazard ratio (HR), 1.27; 95% confidence interval (CI), 1.09–1.48) and hypertension (HR 1.51; 95% CI, 1.29–1.76) were at higher risk of diabetes than normotensive subjects after controlling for potential confounders (P-value for trend < 0.001). These associations persisted even when subjects were stratified by baseline glucose status, sex and body mass index (BMI). The risk of diabetes was significantly higher in subjects who had normal BP at baseline and progressed to prehypertension or hypertension at 8 years (HR, 1.48; 95% CI, 1.20–1.83) than those with controlled BP, but these associations were not observed in subjects with baseline prehypertension and hypertension. These findings showed that prehypertension and hypertension are significantly associated with the development of diabetes, independent of baseline glucose status, sex and BMI. Active BP control reduced incident diabetes only in normotensive individuals, suggesting the need for early BP management.

Hypertension Research (2015) 38, 783–789; doi:10.1038/hr.2015.72; published online 16 July 2015

Keywords: blood pressure; diabetes; incidence

INTRODUCTION

The worldwide incidence of diabetes has increased significantly, with the number of people of all ages with diabetes expected to approximately double between 2000 and 2030. The prevalence of diabetes increased more among Asians than among whites in 2005. In Korea, the prevalence of diabetes in subjects aged ≥30 years was increased from 8.6% in 2001 to 11.0% in 2013. Diabetes is associated with increased cardiovascular morbidity and mortality, with the risk of vascular diseases being about twofold higher in diabetic patients than without diabetes. Early detection of patients at high risk for diabetes is particularly important in preventing cardiovascular diseases.

Age, ethnicity, obesity, blood pressure (BP), and fasting blood glucose and lipid concentrations were identified as risk factors for diabetes. In particular, hypertension, which is also associated with cardiovascular disease, is emerging as a risk factor for diabetes. A cross-sectional study from China showed that hypertensive subjects with diabetic risk had a greater risk of cardiovascular disease than normoglycemic subjects. Hypertension and diabetes were found to share common risk factors, including obesity, lipid profile and BP; moreover, as both are factors of metabolic syndrome, they commonly occur together in individuals. Although several longitudinal studies indicated that higher BP is a significant predictor of type 2 diabetes, most of these studies have limitations, including self-reporting of diabetes and/or BP, inclusion of a single sex, and lack of information on important baseline characteristics that may confound these relationships.

Glucose surveillance may be important in both hypertensive and prehypertensive individuals. Despite findings showing the association between BP and diabetes, little is known about this association in Koreans or about the relationship between prehypertension and incident type 2 diabetes. Therefore, this study investigated the relationships between prehypertension and hypertension with type 2 diabetes in a prospective community-based epidemiologic cohort that had been followed-up for 8 years. The effect of BP control on development of diabetes was determined by evaluating the risk of incident diabetes relative to change in BP.

MATERIALS AND METHODS

Study participants

The Korean Genome and Epidemiology Study is a population-based prospective cohort study designed to investigate the prevalence of and risk factors for chronic diseases in Korea and supported by the Korean National Institute of...
A1C (HbA1C) concentrations by high-performance liquid chromatography. The approval by the Institutional Review Board of the Korea Centers for Disease follow-up and 217 with incomplete data were excluded. A total of 7150 people diabetes and 451 with incomplete data were excluded. The remaining 8214 the National Institute of Health, Korea. The details of the present cohort have homeostatic model for insulin resistance was calculated as fasting insulin

Clinical and biochemical measurements

Body weight was measured in the nearest 0.1 kg, and height was measured to

Table 1 Demographic and clinical characteristics of the study subjects at baseline

| Variable | NGT (n = 5593) | Prediabetes (n = 1557) | P-value for trend | NGT (n = 5593) | Prediabetes (n = 1557) | P-value for trend |
|----------|----------------|------------------------|------------------|----------------|------------------------|------------------|
| Age (years) | 49.1 ± 7.8 | 53.4 ± 9.0 | 55.8 ± 8.4 | <0.001 | 50.1 ± 8.3 | 54.3 ± 8.8 | 56.4 ± 8.4 | <0.001 |
| BMI (kg·m²) | 23.8 ± 2.8 | 25.2 ± 3.1 | 25.4 ± 3.1 | <0.001 | 24.5 ± 3.1 | 25.0 ± 3.1 | 25.7 ± 3.4 | <0.001 |
| WC (cm) | 79.8 ± 8.1 | 83.4 ± 8.6 | 85.9 ± 8.2 | <0.001 | 80.7 ± 8.4 | 84.2 ± 8.3 | 86.5 ± 8.6 | <0.001 |
| SBP (mm Hg) | 103.8 (103.5–104.1) | 123.6 (123.2–124.0) | 138.2 (137.2–139.2) | <0.001 | 104.2 (103.5–105.0) | 124.8 (124.1–125.5) | 136.5 (134.9–138.2) | <0.001 |
| DBP (mm Hg) | 67.0 (66.7–67.3) | 79.5 (79.1–79.8) | 87.7 (87.1–88.3) | <0.001 | 67.0 (66.4–67.6) | 79.8 (79.2–80.4) | 86.0 (84.9–87.1) | <0.001 |
| FPG (mg/dl) | 80.4 (80.2–80.6) | 81.6 (81.2–82.0) | 81.8 (81.4–82.3) | <0.001 | 86.5 (85.7–87.2) | 88.3 (87.3–89.4) | 88.0 (87.0–89.0) | 0.013 |
| PP2 glucose (mg/dl) | 99.2 (98.5–100.0) | 99.6 (98.4–100.9) | 102.5 (101.1–104.0) | <0.001 | 151.9 (150.2–153.6) | 152.6 (149.9–155.2) | 153.9 (151.5–156.3) | 0.182 |
| Fasting insulin (μU/ml) | 6.2 (6.0–6.3) | 6.7 (6.3–6.8) | 7.1 (6.8–7.4) | <0.001 | 6.1 (5.9–6.4) | 6.8 (6.4–7.2) | 7.3 (6.9–7.7) | <0.001 |
| PP2 insulin (μU/ml) | 16.4 (15.9–16.9) | 16.3 (15.6–17.2) | 19.9 (18.8–21.1) | <0.001 | 25.4 (23.6–27.3) | 24.4 (22.0–27.0) | 26.7 (24.2–29.4) | <0.001 |
| HOMAIR (%) | 1.2 (1.2–1.3) | 1.3 (1.3–1.4) | 1.4 (1.4–1.6) | <0.001 | 1.3 (1.2–1.4) | 1.5 (1.4–1.6) | 1.6 (1.5–1.7) | <0.001 |
| HbA1C (%) | 5.5 (5.4–5.5) | 5.5 (5.4–5.5) | 5.5 (5.4–5.5) | <0.001 | 5.6 (5.4–5.7) | 5.7 (5.5–5.7) | 5.7 (5.5–5.8) | <0.001 |
| TC (mg/dl) | 182.0 (180.9–183.1) | 185.7 (183.9–187.5) | 189.7 (187.6–198.1) | <0.001 | 189.8 (187.5–192.3) | 199.8 (195.6–202.4) | 196.0 (192.7–199.4) | 0.003 |
| HDL-C (mg/dl) | 44.3 (44.0–44.7) | 44.3 (43.8–44.8) | 43.2 (42.6–43.7) | <0.001 | 44.3 (43.6–45.0) | 44.2 (43.3–45.2) | 43.5 (42.6–44.4) | 0.146 |
| LDL-C (mg/dl) | 109.1 (108.1–110.2) | 108.5 (106.7–110.3) | 111.0 (108.9–112.6) | <0.014 | 114.2 (111.9–116.5) | 117.8 (114.3–121.4) | 113.3 (109.7–117.0) | 0.665 |
| TG (mg/dl) | 120.8 (119.1–122.5) | 136.3 (135.9–139.9) | 149.1 (145.4–153.0) | <0.014 | 132.0 (127.9–136.2) | 154.1 (147.6–160.9) | 163.1 (156.8–169.8) | <0.001 |

Abbreviations: BMI, body mass index; BP, blood pressure; DBP, diastolic BP; FPG, fasting plasma glucose; HbA1C, hemoglobin A1C; HDLC, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model for insulin resistance; LDL-C, low-density lipoprotein cholesterol; NGT, normal glucose tolerance; PP2, postprandial 2 h; SBP, systolic BP; TC, total cholesterol; TG, triglyceride; WC, waist circumference.

The data are expressed as mean ± s.d. or as geometric mean (95% confidence interval (CI)). Between group differences were analyzed by one-way analysis of variance.

*Log-transformed values were analyzed, with the geometric means and 95% CIs back-transformed.
Definition of hypertension and diabetes mellitus

BP was classified according to the Seventh Report of the Joint National Committee on High BP categories as normal (<120 mm Hg systolic and <80 mm Hg diastolic); prehypertension (120–139 mm Hg systolic or 80–89 mm Hg diastolic); or hypertension (≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive medication).

Diabetes mellitus was diagnosed according to the 2010 criteria of the American Diabetes Association as an FPG ≥126 mg dl⁻¹, or 2-h PG ≥200 mg dl⁻¹, HbA₁C ≥6.5% or use of an oral hypoglycemic agent, and prediabetes as either impaired fasting glucose (FPG levels 100–125 mg dl⁻¹) and/or impaired glucose tolerance (2-h PG levels 140–199 mg dl⁻¹).

Statistical analysis

Distribution testing for normality was performed using the Shapiro–Wilk test, with the data log-transformed to obtain normalized distributions. The baseline characteristics of subjects were expressed as means ± s.d. or geometric means with 95% confidence intervals (CIs). Differences between groups were compared by one-way analysis of variance for continuous variables and χ² tests for categorical variables. The geometric means of log-transformed variables were back-transformed for ease of interpretation and reported with their 95% CIs. The diabetes incidence rate was calculated per 1000 person-years for each BP category. Cox proportional hazards models were used to analyze time at risk and the association with BP categories, and reported as hazard ratios (HRs) and 95% CIs. Participants with normal BP at baseline were considered the reference.

Table 2 Risk of incident diabetes over 8 years in subjects categorized by baseline BP

| BP groups | Number at risk | Diabetes cases | Unadjusted | Model 1 | Model 2 |
|-----------|---------------|----------------|------------|---------|---------|
|           |               |                | P-value     | P-value | P-value |
|           |               |                | for trend   | for trend | for trend |
| All       |               |                |            |         |         |
| Normal BP | 3930          | 442            | 1 (reference) | <0.001  | 1 (reference) | <0.001  |
| Prehypertension | 1767  | 295            | 1.58 (1.37–1.83)** | <0.001  | 1.44 (1.23–1.67)** | <0.001  |
| Hypertension | 1453 | 312            | 2.12 (1.83–2.45)** | <0.001  | 1.90 (1.63–2.22)** | <0.001  |
| Total     | 7150          | 1049           |             |         |         |
| NGT       |               |                |            |         |         |
| Normal BP | 3198          | 197            | 1 (reference) | <0.001  | 1 (reference) | <0.001  |
| Prehypertension | 1378 | 126            | 1.58 (1.26–1.97)** | <0.001  | 1.43 (1.14–1.80)** | <0.001  |
| Hypertension | 1017 | 125            | 2.12 (1.69–2.65)** | <0.001  | 1.91 (1.51–2.41)** | <0.001  |
| Total     | 5593          | 448            |             |         |         |
| Prediabetes |              |                |            |         |         |
| Normal BP | 732           | 245            | 1 (reference) | 0.001   | 1 (reference) | 0.002   |
| Prehypertension | 389  | 169            | 1.40 (1.15–1.70)** | 0.001   | 1.28 (1.05–1.57)** | 0.002   |
| Hypertension | 436  | 187            | 1.49 (1.24–1.81)** | 0.001   | 1.38 (1.13–1.68)** | 0.001   |
| Total     | 1557          | 601            |             |         |         |

Abbreviations: BP, blood pressure; CI, confidence interval; HR, hazard ratio; NGT, normal glucose tolerance.

By glucose status and BP category at baseline examination.

Model 1: adjusted for age and sex.

Model 2: adjusted for the variables in model 1 and fasting plasma glucose, total cholesterol, high-density lipoprotein cholesterol, body mass index, family history of diabetes (yes or no), education (less than high school, high school or equivalent, or college or above), alcohol use (current or non-current) and smoking status (current or non-current).

*P<0.05, **P<0.001.

Figure 2 Effect of baseline glucose status and BP on cumulative incidence rates of diabetes over 8 years.
RESULTS

Baseline characteristics

Table 3 Sex-stratified risk of incident diabetes over 8 years in subjects categorized by baseline BP

| BP groups          | Number at risk | Diabetes cases | Person-years | Diabetes incidence rate per 1000 person-years | OR (95% CI) | P-value for trend | OR (95% CI) | P-value for trend | OR (95% CI) | P-value for trend |
|--------------------|----------------|----------------|--------------|-----------------------------------------------|-------------|-------------------|-------------|-------------------|-------------|-------------------|
|                    |                |                |              |                                               |              |                   |              |                   |              |                   |
| Men                |                |                |              |                                               |              |                   |              |                   |              |                   |
| Normal BP          | 1774           | 229            | 11717.1      | 19.5                                          | 1 (reference) | <0.001            | 1 (reference) | <0.001            | 1 (reference) | <0.001            |
| Prehypertension    | 949            | 168            | 6069.2       | 27.7                                          | 1.43 (1.17–1.75)** | 1.38 (1.13–1.69)* | 1.24 (1.01–1.52)* |                   |                   |
| Hypertension       | 671            | 165            | 4136.8       | 39.9                                          | 2.09 (1.71–2.55)** | 1.98 (1.61–2.42)** | 1.65 (1.34–2.05)** |                   |                   |
| Total              | 3394           | 562            | 21923.1      | 25.6                                          |              |                   |              |                   |              |                   |
| Women              |                |                |              |                                               |              |                   |              |                   |              |                   |
| Normal BP          | 2156           | 216            | 14759.2      | 14.6                                          | 1 (reference) | <0.001            | 1 (reference) | <0.001            | 1 (reference) | 0.018             |
| Prehypertension    | 818            | 127            | 5418.1       | 23.4                                          | 1.69 (1.35–2.10)** | 1.49 (1.19–1.88)* | 1.30 (1.03–1.64)* |                   |                   |
| Hypertension       | 782            | 147            | 5008.6       | 29.3                                          | 2.13 (1.73–2.64)** | 1.79 (1.42–2.25)** | 1.34 (1.05–1.70)* |                   |                   |
| Total              | 3756           | 487            | 25185.9      | 19.3                                          |              |                   |              |                   |              |                   |

Abbreviations: BP, blood pressure; CI, confidence interval; OR, odds ratio. By glucose status and BP category at baseline examination.

Model 1: adjusted for age.
Model 2: adjusted for the variables in model 1 and fasting plasma glucose, total cholesterol, high-density lipoprotein cholesterol, body mass index, family history of diabetes (yes or no), education (less than high school, high school or equivalent, or college or above), alcohol use (current or non-current) and smoking status (current or non-current).

*p<0.05, **p<0.001.

Risk of incident diabetes over 8 years according to baseline BP category

Table 2 shows the risk of incident type 2 diabetes by BP categories. During the 8-year follow-up period, 1049 (14.7%) of the 7150 participants had newly developed diabetes, including 442 (11.2%), 295 (16.7%), and 312 (21.5%) subjects with baseline normal BP, prehypertension and hypertension, respectively. The overall incidence rate for diabetes was 22.3 events per 1000 person-years, which increased from 16.7 per 1000 person-years in baseline normotensive to 34.1 per 1000 person-years in hypertensive subjects (Figure 2). The incidence of diabetes after 8 years was higher in subjects with baseline prediabetes than NGT. Compared with subjects having baseline normal BP, those with baseline prehypertension (HR, 1.27; 95% CI, 1.09–1.48) and hypertension (HR, 1.51; 95% CI, 1.29–1.76) were at higher risk for incident diabetes (P-value for trend <0.001, Table 2); these associations persisted even when subjects were stratified by baseline glucose status. For further analysis, prehypertension category was divided into two groups: those with systolic BP of 120–129 mm Hg or diastolic BP of 85–89 mm Hg. Relative to normotensive subjects, diabetes risk was significantly higher in subjects with BP of 130–139/85–89 mm Hg (HR, 1.48; 95% CI, 1.20–1.82), but not for those with BP of 120–129/80–84 mm Hg (data not shown).

Stratification by sex showed that, relative to normotensive men, those with prehypertension (adjusted HR, 1.24; 95% CI, 1.01–1.52) and hypertension (adjusted HR, 1.65; 95% CI, 1.34–2.05) were at higher risk for diabetes (Table 3). Similarly, women with prehypertension (adjusted HR, 1.30; 95% CI, 1.03–1.64) and hypertension (adjusted HR, 1.34; 95% CI, 1.05–1.70) were at higher risk for diabetes than normotensive women.

Stratification by BMI category showed that, of the 7150 subjects, 32.2% had a normal BMI, 26.7% were overweight and 41.4% were obese (Table 4). The effect of BP on risk of diabetes was similar in these three subgroups. For example, the risk of diabetes was ~ 1.5-fold higher among hypertensive than normotensive individuals, regardless of BMI.

BP control and incident diabetes

Table 5 shows the HRs for diabetes according to change in BP over 8 years. Of the 5537 subjects with available BP measurements at baseline and at 8 years, 2768 had controlled BP (normal BP) and 2769 had poorly controlled BP (prehypertension or hypertension). Multivariate analysis Cox proportional hazard models showed that the latter group had a significantly higher risk of diabetes (HR, 1.28; 95% CI, 1.11–1.47) than the former. When the subjects were stratified by BP category at baseline, those who had normal BP at baseline and progressed to prehypertension or hypertension at 8 years had a significantly higher risk of diabetes (HR, 1.48; 95% CI, 1.20–1.83) than subjects with controlled BP. However, no association was observed between BP control and incident diabetes in subjects with prehypertension and hypertension at baseline.

DISCUSSION

The purpose of this study was to examine the relationships of BP and BP progression with type 2 diabetes in a middle-aged Korean population followed-up for 8 years. Prehypertension, as well as hypertension, were strongly and independently associated with type diabetes.
Table 4 BMI-stratified risk of incident diabetes over 8 years in subjects categorized by baseline BP

| BP groups | Number at risk | Diabetes cases | Person-years | Diabetes incidence rate per 1000 person-years | Unadjusted | Model 1 | Model 2 |
|-----------|---------------|----------------|--------------|------------------------------------------------|------------|---------|---------|
|           |               |                |              |                                                | OR (95% CI) | P-value | OR (95% CI) | P-value | OR (95% CI) | P-value |
| BMI ≤ 23 kg m⁻² |               |                |              |                                                |             |         |         |         |             |         |
| Normal BP | 1489          | 134            | 10 067.7     | 13.3                                           | 1 (reference) | <0.001 | 1 (reference) | 0.003 | 1 (reference) | 0.041 |
| Prehypertension | 517          | 58             | 3295.3       | 17.6                                           | 1.37 (1.01-1.87) |         | 1.17 (0.85-1.62) | 0.98 (0.70-1.35) |
| Hypertension | 294           | 47             | 1855.5       | 25.3                                           | 1.98 (1.42-2.76) |         | 1.71 (1.20-2.43) | 1.45 (1.02-2.08) |
| Total      | 2300          | 239            | 15 218.5     | 15.7                                           |             |         |         |         |             |         |
| BMI 23.4-24.9 kg m⁻² |               |                |              |                                                |             |         |         |         |             |         |
| Normal BP | 1108          | 111            | 7434.9       | 14.9                                           | 1 (reference) | <0.001 | 1 (reference) | 0.016 | 1 (reference) | <0.001 |
| Prehypertension | 460          | 85             | 3051.9       | 27.9                                           | 1.91 (1.44-2.53) |         | 1.62 (1.21-2.17) | 1.52 (1.13-2.04) |
| Hypertension | 341           | 60             | 2204.1       | 27.2                                           | 1.85 (1.35-2.54) |         | 1.50 (1.08-2.09) | 1.51 (1.08-2.11) |
| Total      | 1909          | 256            | 12 690.9     | 20.2                                           |             |         |         |         |             |         |
| BMI > 25 kg m⁻² |               |                |              |                                                |             |         |         |         |             |         |
| Normal BP | 1333          | 197            | 8973.7       | 22.0                                           | 1 (reference) | <0.001 | 1 (reference) | <0.001 | 1 (reference) | <0.001 |
| Prehypertension | 790          | 152            | 5140.1       | 29.6                                           | 1.38 (1.11-1.70) |         | 1.28 (1.03-1.59) | 1.29 (1.04-1.60) |
| Hypertension | 818           | 205            | 5085.9       | 40.3                                           | 1.92 (1.58-2.33) |         | 1.74 (1.41-2.13) | 1.52 (1.23-1.88) |
| Total      | 2941          | 554            | 19 199.7     | 28.9                                           |             |         |         |         |             |         |

Abbreviations: BMI, body mass index; BP, blood pressure; CI, confidence interval; OR, odds ratio. By BMI and BP category at baseline examination.
Model 1: adjusted for age and sex.
Model 2: adjusted for the variables in model 1 and fasting plasma glucose, total cholesterol, high-density lipoprotein cholesterol, body mass index, family history of diabetes (yes or no), education (less than high school, high school or equivalent, or college or above), alcohol use (current or non-current) and smoking status (current or non-current).

Table 5 Risk of incident diabetes according to change in BP over 8 years in subjects categorized by baseline BP

| BP change after 8 years | Number at risk | Diabetes cases (%) | HR (95% CI) | P-value | HR (95% CI) | P-value | HR (95% CI) | P-value |
|-------------------------|---------------|-------------------|-------------|---------|-------------|---------|-------------|---------|
| All                     | 5557          | 884 (16.0)        | 1 (reference) |         | 1 (reference) |         | 1 (reference) |         |
| Controlled BP¹          | 2768          | 346 (12.5)        | 1.60 (1.40-1.83) | <0.001 | 1.45 (1.26-1.66) | <0.001 | 1.28 (1.11-1.47) | <0.001 |
| Poorly controlled BP²    | 2769          | 538 (19.4)        |             |         |             |         |             |         |
| Normal at baseline       | 3100          | 372 (12.0)        |             |         |             |         |             |         |
| Controlled BP³           | 2032          | 195 (9.6)         | 1 (reference) |         |             |         |             |         |
| Poorly controlled BP²    | 1068          | 177 (16.6)        | 1.78 (1.45-2.18) | <0.001 | 1.65 (1.34-2.03) | <0.001 | 1.48 (1.20-1.83) | <0.001 |
| Prehypertension at baseline | 1343        | 238 (17.7)        |             |         |             |         |             |         |
| Controlled BP³           | 446           | 73 (16.4)         | 1 (reference) |         |             |         |             |         |
| Poorly controlled BP²    | 897           | 165 (18.4)        | 1.10 (0.84-1.45) | 0.486 | 1.11 (0.84-1.46) | 0.470 | 1.05 (0.80-1.39) | 0.717 |
| Hypertension at baseline | 1094          | 274 (25.0)        |             |         |             |         |             |         |
| Controlled BP³           | 290           | 78 (26.9)         | 1 (reference) |         |             |         |             |         |
| Poorly controlled BP²    | 804           | 196 (24.4)        | 0.89 (0.68-1.15) | 0.361 | 0.88 (0.68-1.14) | 0.339 | 0.93 (0.71-1.22) | 0.607 |

Abbreviations: BP, blood pressure; CI, confidence interval; HR, hazard ratio. By glucose status at baseline examination and BP change after 8 years.
Model 1: adjusted for age and sex.
Model 2: adjusted for the variables in model 1 and fasting plasma glucose, total cholesterol, high-density lipoprotein cholesterol, body mass index, family history of diabetes (yes or no), education (less than high school, high school or equivalent, or college or above), alcohol use (current or non-current) and smoking status (current or non-current).

2 diabetes, even after controlling for potential confounders. Moreover, the risk of incident diabetes was significantly greater when BP was poorly controlled than well-controlled, with this association observed only in subjects with normal BP at baseline.

During the 8-year follow-up period, about 14.7% of all participants developed type 2 diabetes, with incidence rates in baseline normotensive, prehypertensive and hypertensive subjects of 16.7, 25.7 and 34.1 per 1000 person-years, respectively. These results indicated that participants with normal BP had the lowest risk of type 2 diabetes, with the risk steadily increasing as BP increased. In addition, these associations persisted after stratification by glucose status, sex and BMI.

Our findings are consistent with previous studies of the association between BP and the risk of type 2 diabetes. The Osaka Health Survey reported that high normal BP and hypertension were associated with an increased risk of diabetes. Moreover, the Women’s Health Initiative Study found that subjects with high normal BP and hypertension were at about 1.5- and 2.0-fold higher risk of...
developing diabetes than normotensive subjects. A recent study from Sweden showed that hypertension and high normal systolic BP at midlife was a significant predictor of type 2 diabetes. In the present study, Cox proportional hazards models indicated that prehypertensive and hypertensive participants were at 1.3- and 1.5-fold higher risk of type 2 diabetes than normotensive subjects, indicating that the increased risk of diabetes starts at near-normal BP. These associations remained significant after stratification by baseline glucose status and sex. Stratification by BMI showed that prehypertension and hypertension were associated with increased risk of diabetes among overweight (BMI, 23–24.9 kg m\(^{-2}\)) and obese (BMI, \(\geq 25\) kg m\(^{-2}\)) individuals, emphasizing the importance of BP control in prehypertensive subjects with BMI \(\geq 23\) kg m\(^{-2}\).

Prehypertension is associated with increased cardiovascular risk and insulin resistance. For example, results from the San Antonio Heart Study indicated that subjects with prehypertension are at greater risk of diabetes than those with normal BP. In particular, a BP of 130–139/85–89 mm Hg was associated with incident type 2 diabetes, indicating that prehypertension subcategories may differ in diabetes risk. Our study also found that type 2 diabetes development was associated with a BP of 130–139/85–89 mm Hg (HR, 1.33; 95% CI, 1.20–1.82) but not a BP of 120–129/80–84 mm Hg. Although the clinical impact of these BP categories requires further analysis, active BP control in the former subcategory should be considered to reduce the development of diabetes. These findings indicate the importance of glucose surveillance in prehypertensive, as well as in hypertensive subjects.

This study also found that subjects with poorly controlled BP were more likely to develop type 2 diabetes than those with controlled BP. The risk of incident diabetes was significantly higher among subjects with poorly controlled than well-controlled baseline BP, in agreement with results showing that women with BP progression over 48 months had a higher risk of developing type 2 diabetes than women without BP progression. The United Kingdom Prospective Diabetes Study trial showed that strict BP control significantly reduced the risk of diabetes-related end points compared with less-tight control. By contrast, we found no significant associations between BP control and incident diabetes in baseline prehypertensive and hypertensive subjects, suggesting that the relative risk-reductions observed in subjects with controlled BP are lost once the BP is higher than the normal range. Continuous monitoring of BP levels during follow-up may elucidate the mechanisms underlying these results.

The pathophysiological mechanisms explaining the association between BP and incident type 2 diabetes are not clear, but several hypotheses were proposed. High BP was shown to induce microvascular dysfunction, which may contribute to the pathophysiology of diabetes development. Endothelial dysfunction which is related to insulin resistance is also closely associated with hypertension, and biomarkers of endothelial dysfunction were found to be independent predictors of type 2 diabetes. Insulin resistance constitutes a common soil for BP, type 2 diabetes and cardiovascular disease. Thus it could be other potential links between BP and type 2 diabetes. In addition, inflammatory markers, especially C-reactive protein, are related to both incident type 2 diabetes and increased BP levels.

The strengths of this study include its assessment of a prospectively enrolled community-based cohort study from the general populations followed-up for 8 years. However, this study also had several limitations. First, the study population consisted only of those aged 40–69 years. Nevertheless, our results may be representative of the general population in Korea because the data were from a community-based prospective cohort study, which may have minimized the sampling-bias effect. Second, BP control was based on measured BP values at baseline and at 8 years, and not at intermediate time points. This may have led to a misclassification of BP, with under- or overestimations of the prevalence of controlled and poorly controlled BP. Because of the limitations inherent in observational studies, further intervention trials will be needed to confirm these findings. Third, some antihypertensive drugs may increase the risk of type 2 diabetes. This should be further examined. Finally, the follow-up time examining the relationship between BP and diabetes was <10 years. Longitudinal studies with longer follow-up are needed to confirm these findings.

In conclusion, prehypertension, as well as hypertension, was a significant risk factor for incident diabetes, independent of baseline glucose status, sex and BMI. These results indicate that active BP control, including early BP management, is needed to prevent incident diabetes.

**CONFLICT OF INTEREST**

The authors declare no conflict interest.

**ACKNOWLEDGEMENTS**

This work was supported by the Korea National Institute of Health intramural research grant, 4800-4845-302(2011-NG63002-00).

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