

Evidence that prehypertension is a risk factor for Type 2 diabetes

Expert Rev. Cardiovasc. Ther. 8(3), 335–337 (2010)

Charles J Everett[†] and Ivar L Frithsen

[†]Author for correspondence
Department of Family Medicine,
Medical University of South
Carolina, 295 Calhoun Street,
MSC 192, Charleston,
SC 29425-1920, USA
Tel.: +1 843 792 3413
Fax: +1 843 792 3598
everettc@muscc.edu

Evaluation of: Mullican DR, Lorenzo C, Haffner SM. Is prehypertension a risk factor for the development of Type 2 diabetes? *Diabetes Care* 32(10), 1870–1872 (2009).

Whether or not blood pressure categories below 140/90 mmHg are associated with incident Type 2 diabetes or cardiovascular disease is subject to debate. Currently, a blood pressure of 120–139/80–89 mmHg is recognized as prehypertension. This article evaluates the association of prehypertension with incident Type 2 diabetes in the San Antonio Heart study. The authors found that prehypertension in the entire cohort was not related to incident Type 2 diabetes in fully adjusted analyses, but that a blood pressure of 130–139/85–89 mmHg was related to incident diabetes. These results, and conclusions of other studies, suggest that the prehypertension category should be divided for diabetes risk assessment.

KEYWORDS: blood pressure • insulin resistance • metabolic syndrome • prehypertension • Type 2 diabetes

This article evaluates the paper by Mullican *et al.* that tests the association of prehypertension and incident Type 2 diabetes [1]. Prehypertension is a category created by the Joint National Commission on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) in 2003 as part of their seventh report (JNC 7) [2]. Prior to JNC 7, the sixth report (JNC 6) recognized blood pressure under 120/80 mmHg as optimal, blood pressure 120–129/80–84 mmHg as normal, and blood pressure 130–139/85–89 mmHg as high-normal [3]. In both JNC 6 and JNC 7, blood pressure was recognized as having a strong, continuous and graded relationship with incident cardiovascular disease [4]. Hence, the problem arises as to how to describe a continuous measure with diagnostic categories. The utility of prehypertension as a category defining elevated risk has been assessed in a limited number of articles. The study reviewed here tests the use of prehypertension as a risk factor for Type 2 diabetes.

Methods & results

The study by Mullican *et al.* was a retrospective analysis to determine if prehypertension is a risk factor for developing Type 2 diabetes. Data were obtained from the San Antonio Heart Study, which is a longitudinal study on cardiovascular

disease and Type 2 diabetes. Study participants were Mexican–Americans and non-Hispanic white individuals, aged 25–65 years who reside in San Antonio (TX, USA). There were 2767 participants with a median follow-up of 7.8 years who were eligible for analysis after excluding those with pre-existing diabetes or hypertension, and those lost in follow-up. JNC 7 criteria were used to classify blood pressure as normal, prehypertension or hypertension, and American Diabetes Association guidelines were used to define plasma glucose levels for diabetes. A multivariate logistic-regression model was used to determine the association of prehypertension with the future development of diabetes.

The baseline prevalence of prehypertension was 31.3%. Prehypertension was associated with male gender, Mexican–American ethnicity, higher BMI, triglycerides and measures indicating impaired glucose tolerance and insulin resistance. Systolic blood pressure was positively associated with BMI, waist circumference, triglycerides and measures indicating impaired glucose tolerance and insulin resistance. A total of 5.6 and 12.4% of subjects who were normal and prehypertensive, respectively, developed diabetes during the study period. The odds ratio for incident diabetes was 2.21 for prehypertensive subjects versus those with normal blood pressure

when controlling for age, gender and ethnicity. However, when BMI and risk factors for diabetes (measures of impaired glucose tolerance, insulin resistance and family history of diabetes) were also adjusted for, the association was not significant. There was a significant relationship for blood pressures ranging from 130–139/85–89 mmHg when the same variables were used in the regression model.

Discussion & significance

Two previous studies of risk factors for incident diabetes have used the National Cholesterol Education Program (NCEP) Adult Treatment Panel III definition of metabolic syndrome [5] as a starting point. The metabolic syndrome includes a blood pressure of 130/85 mmHg or more or use of antihypertensive medication as a risk factor, along with waist circumference (women: >88 cm; men: >102 cm), low high-density lipoprotein (HDL) cholesterol (men: <1.03 mmol/l; women: <1.29 mmol/l), high triglycerides (>1.7 mmol/l) and hyperglycemia (fasting glucose: ≥ 6.1 mmol/l or ≥ 5.6 mmol/l). In the NCEP (augmented) diabetes risk score, Schmidt *et al.* assigned 1 point for each element of the metabolic syndrome, except for fasting glucose (2 points when fasting glucose ≥ 5.6 mmol/l, or 5 points when fasting glucose ≥ 6.1 mmol/l) [6]. In addition, 1 point was added for a BMI of 30 kg/m² or more. Using these rules, Schmidt *et al.* were able to predict incident diabetes with an area under the receiver operating characteristic (ROC) curve of 0.78 in the Atherosclerosis Risk in Communities (ARIC) study [6]. A score of 4 or more had a sensitivity of 68% and specificity of 75% in the ARIC cohort.

Mainous *et al.* used the same diabetes risk score in the Coronary Artery Risk Development in Young Adults (CARDIA) study [7]. In the CARDIA study, participants were 18–30 years of age at baseline, whereas participants in the ARIC study were 45–64 years of age at baseline. The ARIC diabetes risk score had an area under the ROC curve of 0.70 when applied to the CARDIA study, which was not significantly different from BMI (area under the ROC curve: 0.67). These results suggest that a blood pressure of 130/85 mmHg or more is more important in middle-aged adults. However, in Mullican *et al.*, prehypertension was significantly related to incident diabetes in adults 25–49 years of age, but not in those aged 50–65 years [1]. Overall, a blood pressure of 130–139/85–89 mmHg was significantly associated with incident diabetes in the San Antonio Heart Study, indicating this blood pressure category should be recognized in diabetes risk assessment. For further evidence supporting the use of blood pressure 130–139/85–89 mmHg as a category predicting incident diabetes, see Conen *et al.* [8].

The relationship between prehypertension and cardiovascular disease has been studied more than the association of prehypertension and diabetes, but the results are mixed. Two studies have found a relationship with prehypertension (120–139/80–89 mmHg), three studies found an association with blood a pressure of 130–139/85–89 mmHg but not a blood pressure of 120–129/80–84 mmHg, and one study found no relationship. Analyzing the Framingham Heart

Study, Qureshi *et al.* found prehypertension related to myocardial infarction and coronary artery disease, but not stroke [9]. Hsia *et al.* found prehypertension to be associated with cardiovascular disease mortality, and cardiovascular disease events in the Women's Health Initiative [10]. Vasan *et al.* found a blood pressure of 130–139/85–89 mmHg related to cardiovascular disease events in the Framingham Heart Study [11]. Working with the National Health and Nutrition Examination Survey (NHANES) I and Follow-up, Liszka *et al.* found a blood pressure of 130–139/85–89 mmHg associated with cardiovascular disease events [12]. More recently, Lorenzo *et al.* found a blood pressure of 30–139/85–89 mmHg related to all-cause mortality and cardiovascular disease mortality in the San Antonio Heart Study, the same study that is the subject of this article [13]. Finally, Mainous *et al.* found no relationship between prehypertension and cardiovascular disease mortality in the NHANES II mortality follow-up [14]. The results of these studies suggest that the prehypertension category should be divided as it was in JNC 6 with a blood pressure of 130–139/85–89 mmHg as a separate category from a blood pressure of 120–129/80–84 mmHg for the determination of diabetes risk.

Expert commentary & conclusion

Mullican *et al.* showed that a blood pressure of 130–139/85–89 mmHg was associated with incident diabetes in the San Antonio Heart Study [1]. Along with three out of six studies of cardiovascular disease, this study points to the difficulty of using the prehypertension category as defined in the JNC 7 in determining diabetes risk, and suggests the JNC 6 categories illuminate important differences in patient populations. This recommendation also needs to be viewed from the stand point of the treatment of individuals having diabetes and prehypertension [15,16]. Should these individuals be treated as though they have hypertension even if their blood pressure is 120/80 mmHg? Would the JNC 6 categories be more useful? The evidence appears to be firmly mixed with respect to incident diabetes and cardiovascular disease events.

Five-year view

At present, the successor to JNC 7 is being crafted and it is important that interested parties publish their views. Additional studies are needed to clarify the logic behind blood pressure categories. The fundamental problem is that blood pressure is a continuous measure, whereas guidelines require categories. Epidemiology of large cohorts will advance knowledge and provide illumination on the question of how to delineate blood pressure categories in the prehypertension range.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Key issues

- Prehypertension is presently recognized as a risk factor for cardiovascular disease.
- Prehypertension was not found to be related to incident Type 2 diabetes in fully adjusted analyses of the San Antonio Heart study.
- A blood pressure of 130–139/85–89 mmHg was found to be associated with incident diabetes, and may be a more meaningful category for diabetes risk assessment.

References

Papers of special note have been highlighted as:

- of considerable interest

- Mullican DR, Lorenzo C, Haffner SM. Is prehypertension a risk factor for the development of Type 2 diabetes? *Diabetes Care* 32(10), 1870–1872 (2009).
- Chobanian AV, Bakris GL, Black HR *et al.*; National High Blood Pressure Education Program Coordinating committee. The seventh report of the Joint National committee on prevention, detection, evaluation, and treatment of high blood pressure. *JAMA* 289, 2560–2572 (2003).
- Joint National committee. The sixth report of the Joint National committee on prevention, detection, evaluation, and treatment of high blood pressure. *Arch. Intern. Med.* 157, 2413–2446 (1997).
- Stamler J, Stamler R, Neaton JD. Blood pressure, systolic and diastolic, and cardiovascular risks: US population data. *Arch. Intern. Med.* 153, 598–615 (1993).
- Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 285, 2486–2497 (2001).
- Schmidt MI, Duncan BB, Bang H *et al.* Identifying individuals at high risk for diabetes: the Atherosclerosis Risk in Communities study. *Diabetes Care* 28, 2013–2018 (2005).
- Mainous AG III, Diaz VA, Everett CJ. Assessing risk for development of diabetes in young adults. *Ann. Fam. Med.* 5, 425–429 (2007).
- Conen D, Ridker PM, Mora S, Buring JE, Glynn RJ. Blood pressure and risk of developing Type 2 diabetes mellitus: the Women's Health Study. *Eur. Heart J.* 28, 2937–2943 (2007).
- Qureshi AI, Suri MFK, Kirmani JF *et al.* Is prehypertension a risk factor for cardiovascular diseases? *Stroke* 36, 1859–1863 (2005).
- Hsia J, Margolis KL, Eaton CB *et al.* Prehypertension and cardiovascular disease risk in the Women's Health Initiative. *Circulation* 115, 855–860 (2007).
- Vasan RS, Larson MG, Leip EP *et al.* Impact of high-normal blood pressure on the risk of cardiovascular disease. *N. Engl. J. Med.* 345, 1291–1297 (2001).
- Liszka HA, Mainous AG III, King DE, Everett CJ, Egan BM. Prehypertension and cardiovascular morbidity. *Ann. Fam. Med.* 3, 294–299 (2005).
- Lorenzo C, Aung K, Stern MP, Haffner SM. Pulse pressure, prehypertension, and mortality: the San Antonio Heart study. *Am. J. Hypertens.* 22, 1219–1226 (2009).
- Tests the association of prehypertension with cardiovascular disease mortality in the San Antonio Heart Study.
- Mainous AG III, Everett CJ, Liszka H, King DE, Egan BM. Prehypertension and mortality in a nationally representative cohort. *Am. J. Cardiol.* 94, 1496–1500 (2004).
- Sequra J, Ruilope LM. Treatment of prehypertension in diabetes and metabolic syndrome: what are the pros? *Diabetes Care* 32(Suppl. 2), S284–S289 (2009).
- Nilsson PM. Hypertension and diabetes: should we treat early surrogates? What are the cons? *Diabetes Care* 32(Suppl. 2), 290–293 (2009).

Affiliations

- Charles J Everett, PhD
Department of Family Medicine,
Medical University of South Carolina,
295 Calhoun Street, MSC 192, Charleston,
SC 29425-1920, USA
Tel.: +1 843 792 3413
Fax: +1 843 792 3598
everettc@musc.edu
- Ivar L Frithsen, MD, MS
Department of Family Medicine,
Medical University of South Carolina,
295 Calhoun Street, MSC 192, Charleston,
SC 29425-1920, USA
Tel.: +1 843 792 7183
Fax: +1 843 792 3598
frithse@musc.edu