AJH 2005; 18:833–838

Predictors of Blood Pressure Control in Patients With Diabetes and Hypertension Seen in Primary Care Clinics

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Background: Blood pressure (BP) is not well controlled in the majority of patients with both diabetes and hypertension. This study was designed to identify predictors of BP control in patients with both diabetes and hypertension who are seen in primary care clinics.

Methods: This retrospective study was conducted by identifying a cohort of patients diagnosed with diabetes before January 1, 2000 (inception) who met predefined criteria for hypertension at inception and who received primary care in the ensuing 3-year study period (January 1, 2000, to February 31, 2002). Using the mean of all BP values between January 1, 2002, and December 31, 2002, subjects were divided into two groups: those with controlled BP and those with uncontrolled BP. The distribution of clinical predictors was compared between the two groups. Independent predictors were identified using multivariate logistic regression.

Results: Predictors of poor BP control were as follows: 1) isolated systolic hypertension at inception (OR = 0.62, CI = 0.47 to 0.82); 2) uncontrolled BP at inception (OR = 0.71, CI = 0.55 to 0.93); 3) use of oral hypoglycemic drugs versus diet and exercise alone or insulin use (OR = 0.73, CI = 0.56 to 0.95); 4) use of three or more antihypertensive drugs (OR = 0.74, CI = 0.56 to 0.97); and 5) older age (OR = 0.98, CI = 0.97 to 0.99). Predictors of better control were 1) use of nitrates (OR = 1.82, CI = 1.26 to 2.64); 2) history of coronary heart disease (OR = 1.47, CI = 1.08 to 2.00); and 3) at least one annual visit to subspecialist physician (OR = 1.43, CI = 1.09 to 1.88).

Conclusions: Patients with both diabetes and hypertension who are older, have isolated systolic hypertension, use oral hypoglycemic drugs, or use three or more antihypertensive drugs should be targeted for better BP control. The roles of nitrate medication and subspecialist physicians in achieving better BP control needs further study. Am J Hypertens 2005;18:833–838 © 2005 American Journal of Hypertension, Ltd.

The overall prevalence of hypertension in diabetic patients is greater than 70%, and elevated blood pressure (BP) significantly increases the risk of complications of diabetes.[1,2] The benefits of adequately controlling the BP in diabetic patients have been documented by numerous studies. The Hypertension Optimal Treatment (HOT) trial assessed the affect of lowering diastolic BP on major cardiovascular events.[3] This study demonstrated a 51% reduction in major cardiovascular events in the study group allocated to a target diastolic BP of ≤80 mm Hg when compared with the group with ≤90 mm Hg. The relation between systolic BP and microvascular or macrovascular complications of type 2 diabetes has also been well demonstrated.[4] In the UK Prospective Study Group 36,[4] each 10–mm Hg decrease in systolic BP from baseline resulted in a 19% decreased risk in deaths related to diabetes, a 13% decreased risk in all-cause mortality, and a 13% decreased risk in myocardial infarction. Blood pressure control in patients with type 2 diabetes without overt albuminuria has also been shown to stabilize kidney function over a 5-year period.[5] Despite the known benefits of lowering BP, recent reports indicate

Received October 15, 2004. First decision December 16, 2004. Accepted December 19, 2004.

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This study was funded in part by the Mayo Foundation and the American Diabetes Association.

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0895-7061/05/$30.00
doi:10.1016/j.amjhyper.2004.12.016

that only 25% of individuals with both diabetes and hypertension have their BP controlled.[6] To improve the BP control rate in the population with both diabetes and hypertension, a more complete understanding of the predictors of BP control is essential. A study by Hyman and Pavlik analyzed patient characteristics associated with uncontrolled hypertension in the general population using the national probability sample from the National Health and Nutrition Examination Survey III (NHANES III).[7] However, no data were available on BP control specific to diabetic subjects who were receiving regular primary care. The current study was designed to identify clinical predictors of BP control in patients with both diabetes and hypertension who were receiving primary care.

Methods

The study protocol was approved by the Institutional Review Board at the Mayo Clinic (Rochester, MN). All patients with a diagnosis of diabetes as documented either by International Classification of Diseases, 9th revision (ICD-9) billing code (250) or a physician diagnosis of diabetes in medical records before January 1, 2000 (inception) were identified. The current study was limited to patients that received primary care in the ensuing 3-year study period (January 1, 2000, to December 31, 2002). Primary care was defined as the outpatient medical care delivered in the Division of Primary Care Internal Medicine or in the Department of Family Practice at the Mayo Clinic (Rochester, MN). Before study inclusion, a clinical nurse specialist reviewed the medical records to verify this diagnosis of diabetes. Patients' medical records were reviewed to identify those with hypertension, using the following criteria: 1) documented clinical diagnosis of hypertension in the medical record before inception; or 2) three or more elevated BP readings (systolic BP $\geq$130 mm Hg or diastolic BP $\geq$85 mm Hg) during primary care office visits within 3 years before inception; or 3) use of antihypertensive drugs for the purpose of lowering BP during the study period. Excluded were patients who refused authorization for use of their medical records in research, who were $\leq$18 years of age at inception, who died or were transferred to a nursing home, or who had no documented BP during the study period. The outcome (ie, BP control) was determined by using the mean systolic and diastolic BP recorded during the primary care visits in the last year of the study period (ie, between January 1, 2002, and December 31, 2002). Patients with a mean systolic BP of $<$130 mm Hg and a mean diastolic BP $<$85 mm Hg during this period were considered as having their BP controlled.

Data regarding predictor and outcome variables were abstracted from the medical records. These included the following: patient sex; age at inception; outpatient BP values in the 3 years before inception and for the study period; documentation of diagnosed coronary heart disease (CHD) in the medical record before inception; serum creatinine and HbA_{1C} values for the study period; numbers of office visits to primary care physicians and subspecialist physicians during the study period; medications and diabetes treatment regimen (diet and exercise alone, oral hypoglycemic drugs, use of insulin) at last visit during the study period; last available data during the study period on height and weight; and patients' self-reported alcohol use, smoking status, and exercise status.

The definition of antihypertensive medications was complicated by the fact that although nitrates lower BP, the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High BP (JNC 7) does not list these under oral antihypertensive drugs.[8] The JNC 7, however, recommends adding nitrates under special circumstances, such as when the BP is not controlled on a two-drug regimen (dihydropyridine calcium channel blockers and β-blockers) in patients with ischemic heart disease. For this reason, we chose to analyze nitrate use as a separate variable to assess its effect on BP control. Subspecialist physician visits were defined as out patient visits to a specialist in cardiology or nephrology or endocrine or hypertension. Uncontrolled BP at inception was defined as having a mean systolic BP of $\geq$130 mm Hg or a mean diastolic BP $\geq$85 mm Hg during the 3 years before inception. Isolated systolic hypertension at inception was defined as having a mean systolic BP $\geq$130 mm Hg and a mean diastolic BP $<$85 mm Hg during the 3 years before inception.

Statistical Analysis

The cohort was divided into two groups (those with controlled BP and those with uncontrolled BP) based on BP control in the last year of the study period. Descriptive statistics were used to characterize the distribution of predictor variables in the groups. The distribution of covariates between the groups was compared using a two-sample t test or Wilcoxon rank sum test or χ^2 test as appropriate. A P value of $<$ .05 was considered to be significant. A multivariate analysis using logistic regression was conducted to identify independent predictors of BP control. The risks were reported as odds ratios (OR) with corresponding 95% confidence intervals (CI).

Results

There were 1231 diabetic hypertensive patients identified, of whom 92 (7.5%) declined research authorization and 49 (4%) patients had no data on outpatient BP during the study period. Data on the remaining 1090 who met study criteria were analyzed. The majority of these patients (N = 838; 77%) were receiving care at this institution 3 years before inception. Approximately 10% of all diabetic hypertensive patients did not receive any antihypertensive drugs. The proportion of patients receiving angiotensin-converting enzyme inhibitors was 58%; 41% were treated with β-blockers, 24% calcium channel blockers, and 12%

Table 1. Baseline characteristics of 1090 diabetic patients with hypertension

Characteristic	Controlled Blood Pressure (431)	Uncontrolled Blood Pressure (659)	*P* Value
Age (y)*	64 ± 12	67 ± 11	.0001
Gender (% women)	43	51	.02
Body mass index*	29.2 ± 6.3	29.5 ± 6.6	.66
Systolic blood pressure at inception*	126 ± 9	142 ± 11	<.0001
Diastolic blood pressure at inception*	70 ± 7	73 ± 8	<.0001
Isolated systolic hypertension (%)	51	67	.0001
History of coronary heart disease (%)	39	29	.0006
Use of nitrates (%)	23	13	<.0001
Use of ≥3 antihypertensive drugs (%)	32	39	.02
Use of statin drugs (%)	59	56	.30
HbA1c*	7.2 ± 1.2	7.0 ± 1.1	.02
Serum creatinine*	1.2 ± 0.3	1.2 ± 0.3	.08
Number of visits to primary care physicians per year*	3.7 ± 2.7	3.5 ± 2.5	.70
At least one annual visit to primary care physicians (%)	94	94	.90
Number of visits to subspecialist physicians per year*†	1 ± 1.3	0.8 ± 1.23	.005
At least one annual visit to subspecialist physicians† (%)	39	29	.0003
Diabetes treatment regimen (%)			
Diet and exercise alone	15	13	.41
Oral hypoglycemic drugs	41	50	
Any insulin use	44	37	
Alcohol use (%)			
Current	32	31	.32
Previous	20	15	
Never	46	50	
Unknown	3	4	
Smoking (%)			
Current	11	9	.06
Previous	40	35	
Never	47	55	
Unknown	2	1	
Exercise (%)			
<3 h/week	44	48	.32
≥3 h/week	15	13	
None	13	13	
Unknown	28	26	

* Mean ± SD.
† Specialist in cardiology or nephrology or endocrine or hypertension.

with angiotensin receptor blockers. Blood pressure was controlled in 431 patients (40%). The baseline characteristics stratified by BP control are shown in Table 1. Compared with diabetic patients whose BP was controlled, those with uncontrolled BP were significantly older ($P = .0001$) and more likely to be female ($P = .02$). They were also more likely to have had isolated systolic hypertension at inception ($P = .0001$). Both the mean systolic and diastolic pressures in 3 years before inception were higher in the patients with uncontrolled BP. In addition, patients with uncontrolled hypertension were significantly less likely to have a history of diagnosed CHD ($P = .0006$) and to be using nitrate medications ($P < .0001$) when compared with those with controlled BP.

A high proportion (94%) of patients in both groups made at least one office visit per year to primary care physicians, and the average number of visits per year was similar between the two groups. However, when compared with patients with controlled BP, the group with uncontrolled BP made significantly fewer office visits to subspecialist physicians per year. Similarly, a significantly lower proportion of patients with uncontrolled BP made at least one annual visit to subspecialist physicians. No significant differences between the groups were noted in body mass index, serum creatinine level, diabetes treatment regimens, self-reported history of alcohol use, or smoking and exercise status.

In the multivariate analysis, a number of factors were found to be associated with BP control in diabetic patients (Table 2). The predictors that were associated with poor

Table 2. Predictors associated with blood pressure control in multivariate analysis

Covariate	OR	95% CI	*P* Value
Age	0.98	0.97–0.99	.0021
Female sex	0.88	0.68–1.14	.34*
Use of ≥3 antihypertensive drugs	0.74	0.56–0.97	.0321
Use of oral hypoglycemic drugs	0.73	0.56–0.95	.0204
Uncontrolled blood pressure at inception	0.71	0.55–0.93	.0114
Isolated systolic hypertension at inception	0.62	0.47–0.82	.0009
At least one annual visit to subspecialist	1.43	1.09–1.88	.0104
History of coronary heart disease at inception	1.47	1.08–2.00	.0142
Use of nitrates	1.82	1.26–2.64	.0015

CI = confidence interval; OR = odds ratio.
* Not significant.

BP control were as follows: 1) isolated systolic hypertension at inception (OR = 0.62, CI = 0.47 to 0.82); 2) uncontrolled BP at inception (OR = 0.71, CI = 0.55 to 0.93); 3) use of oral hypoglycemic drugs (versus diet and exercise alone or use of insulin) (OR = 0.73, CI = 0.56 to 0.95); 4) taking three or more antihypertensive drugs (OR = 0.74, CI = 0.56 to 0.97); and 5) older age (OR = 0.98, CI = 0.97 to 0.99). Predictors that were associated with better control were the following: 1) use of nitrates (OR = 1.82, CI = 1.26 to 2.64); 2) history of diagnosed CHD (OR = 1.47, CI = 1.08 to 2.00); and 3) at least one annual visit to subspecialist physician (OR = 1.43, CI = 1.09 to 1.88).

Discussion

This large retrospective cohort study has identified several important clinical predictors of BP control in subjects with both diabetes and hypertension who were receiving primary care. These patients were seen on average nearly four times per year, indicating good access to primary care. The overall BP control rate in this cohort with both diabetes and hypertension was 40%, which is higher than the NHANES III (1991 to 1994) rate of 17.2% or the most recent NHANES (1999 to 2000) rate of 25.4%.[6,9] Between-study differences such as the definition of BP control, regular medical care, and demographics could have contributed to a better BP control rate in our cohort. The BP control rate in our diabetic and hypertensive cohort was closer to the target of 50% recommended by the US Department of Health and Human Services (Healthy People 2010).[10,11]

Prior research has suggested gender differences in BP control, indicating less favorable control in diabetic women compared with men.[12] However, in the current study, female gender was not an independent predictor of BP control. The current study suggests an association between older age and poorer BP control in diabetic patients, similar to findings for the general population in study by Hyman and Pavlik.[7] In fact, our study indicates that with every 10-year increment in age, patients with both diabetes and hypertension were 0.83 (95% CI = 0.74 to 0.94) times less likely to have their BP controlled. Regular follow-up of diabetic patients in primary health care clinics was previously shown to improve BP to a significant extent over time.[13] Nevertheless, the current study indicates that having uncontrolled BP at inception is a significant predictor of poor BP control, even after a follow-up of more than 2 years in primary care clinics.

Decreased glomerular filtration rate (GFR) from kidney disease can cause volume retention and this can influence BP response to therapy.[8] Using the Cockcroft-Gault formula, we estimated the GFR for the study population. This was lower in the group with uncontrolled BP compared with the group with controlled BP (74 *v* 77, $P = .20$). Similarly, the proportion of patients with chronic kidney disease (CKD), defined as GFR <60 mL/min, was higher in the group with uncontrolled BP compared with the group whose BP was controlled (36% *v* 33%, $P = .28$). This lack of statistical significance was likely due to insufficient power to detect a small difference between the groups. In fact, the study had only 17% power to detect a CKD proportion difference of 3% between the groups.

Several studies have shown that control of systolic BP affords cardiovascular protection.[14–16] The results of this study indicate that systolic BP is not well controlled, and the presence of isolated systolic hypertension was a significant predictor of uncontrolled BP. In fact, BP in diabetic patients with isolated systolic hypertension was nearly two times less likely to be controlled compared with BP in diabetic patients without isolated systolic hypertension. Thus, an important target group to focus aggressive efforts to achieve better BP control would be elderly diabetic patients with isolated systolic hypertension.

Treatment with different oral hypoglycemic drugs is known to have variable effect on BP. Thiazolidinediones were shown to decrease BP, whereas treatment with sulfonylureas might increase BP.[17–19] Although we did not distinguish between the types of oral agents, patients taking any oral hypoglycemic drugs had significantly poorer BP control compared with those being treated with insulin or with diet and exercise alone. Similarly, patients receiv-

ing three or more antihypertensive drugs had poorer BP control compared with those receiving two or less. The JNC 7 defines resistant hypertension as failure to achieve goal BP in patients who are adhering to full doses of an appropriate three-drug regimen that includes a diuretic.[8] Our study did not have data on whether these patients were receiving full doses of three-drug regimen that included a diuretic. It is possible that a proportion of this subgroup may have had resistant hypertension requiring more drugs or may even have had underlying secondary hypertension. A careful review of the medical regimen, medication adherence, and assessment for secondary causes of hypertension is indicated in this subgroup of patients with both diabetes and hypertension.

Attendance in a hypertension clinic has been shown to improve BP to a significant extent.[20] One study found that patients who were seen in a specialist hypertension clinic that used a goal-oriented management approach achieved better control rates than those reported in clinical trials.[21] However, the impact of office visits to subspecialists (in cardiology, endocrinology, nephrology, and hypertension) on BP control in diabetic patients has previously not been known. The current study indicates that diabetic patients with an annual visit to these subspecialist physicians were nearly 1.5 times more likely to have BP controlled, even after adjusting for a history of diagnosed CHD and use of nitrates. This important finding deserves further study to understand why, among diabetic hypertensive patients, those with one annual visit to a subspecialist physicians achieve better BP control than those with no such visit.

In the current study, patients with a history of diagnosed CHD had better control of BP compared with those without. This subgroup of patients are more likely to be treated with drugs such as β-blockers, angiotensin-converting enzyme inhibitors, and nitrates for their heart disease. However, their BP control was significantly better even after adjusting for number of antihypertensive drugs and use of nitrates. Results of prior studies have similarly suggested coronary heart disease is an independent predictor of better BP control.[22] It is possible that patients with CHD may have been managed more aggressively compared with those who did not have this diagnosis.

One interesting finding was that the patients treated with nitrates had better control of BP compared with patients who were not taking nitrates, even after adjusting for history of CHD and heart failure. Patients taking nitrates for CHD are more likely to be treated with β-blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers. To determine whether this potential confounder has biased the results, we performed an additional analysis. A new variable was created that included all patients treated with β-blockers, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers. Admission of this into the multivariate regression model did not have any significant effect on our final results, and there were no interaction terms. Analyzing the data by admitting each of the above medications separately into the multivariate model also did not make any difference. This suggests that a better control of BP seen with nitrates was not confounded by the concurrent use of β-blockers, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers.

Insulin resistance is known to be associated with hypertension, and one proposed mechanism is endothelial dysfunction resulting in decreased production of a potent vasodilator nitric oxide.[23] Nitric oxide donors such as isosorbide mononitrate have been shown to lower BP and are considered suitable treatment especially for isolated systolic hypertension.[24] The high prevalence of isolated systolic hypertension and insulin resistance in the study population might explain the favorable effect of nitrates on BP seen in the study. Some investigators have recommended adding isosorbide mononitrate for patients with suboptimally controlled isolated systolic hypertension who are receiving conventional treatment.[25] Further studies are needed to determine the role of nitrate medications in the treatment of patients with diabetes and hypertension for lowering BP.

We acknowledge several important limitations of the study. The retrospective design implies that this study can only suggest possible associations. Although the study cohort included only primary care patients, a potential for referral bias exists because Mayo Clinic is a tertiary care referral institution. One important limitation to our study was a lack of ethnic diversity (90% white, 3% all others combined, 7% ethnicity data not available). Similarly, exclusion of nursing home residents and those who died within the study period may have implications in regard to the generalizability of the study results. Nonetheless, the results are likely generalizable to patients who are being followed in similar settings. The study did not provide data on duration of diabetes, duration of hypertension, dosages of antihypertensive drugs, or compliance with medical regimens. The differences between the study groups may be explained by other factors such as differences in diet, salt intake, nonsteroidal anti-inflammatory drugs, white coat hypertension, and secondary hypertension.

This study suggests some important predictive factors of poor BP control, such as advanced age, isolated systolic hypertension, and treatment with oral hypoglycemic drugs. Patients with these characteristics may represent important subgroups to target for better control in primary care practice. Further studies are needed to determine the role of nitrates in the treatment of BP in diabetic patients and to find out why patients seen by subspecialists annually achieve better BP control. Primary care physicians need to be more aggressive in controlling BP in diabetic patients, as these physicians are the principal caregivers of the growing diabetic population.

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