# **Original Paper**



# Prevalence of Comorbidities and Their Influence on Blood Pressure Goal Attainment in Geriatric Patients

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Hypertension in elderly patients is common and is associated with unique challenges. This study examines the prevalence of comorbidities in elderly hypertensive patients and evaluates the association between comorbidities and other covariates with blood pressure goal attainment. Data were collected through retrospective review of medical records and included patient characteristics, comorbidities, treatment-related variables, and blood pressure goal attainment. At least 1 comorbidity was present in 88% of patients, and 61% had multiple comorbidities. The most common comorbidity was isolated systolic hypertension. The presence of diabetes or isolated systolic hypertension at initial visit and treatment with a thiazide diuretic at the final clinic visit were associated with significantly higher odds of patients not achieving blood pressure goal. A diagnosis of heart failure was associated with lower odds of not achieving blood pressure goal. These issues should be given special consideration during the evaluation, treatment selection, and long-term monitoring of this population. (AJGC. 2007;16:24–29) ©2007 Le Jacq

Typertension and its associated chronic com-**▲** plications remain considerable health issues in the United States. Hypertension is defined as systolic blood pressure (SBP) ≥140 mm Hg and diastolic blood pressure (DBP) ≥90 mm Hg.1 According to this definition, approximately 50 million adult Americans have hypertension, and three fourths of these individuals do not have controlled blood pressure (BP) (ie, <140/90 mm Hg).<sup>2,3</sup> Many hypertensive Americans are elderly patients 65 years and older, and this specific population continues to grow. According to the US Census Bureau, there were 35 million Americans 65 years and older in the 2000 census, which represents a 12% increase since 1990.4 Furthermore, data from the National Health and Nutrition

Examination Survey (NHANES)<sup>3</sup> indicate that the prevalence of hypertension increases with age (present in 65.4% of NHANES respondents 60 years and older).

Although the average DBP decreases with advancing age, the average SBP increases, and the prevalence of isolated systolic hypertension, therefore, is increased.<sup>5,6</sup> Burt and associates<sup>7</sup> estimated that only 20% of older people with hypertension are controlled at target BPs (SBP ≤140 mm Hg and DBP ≤90 mm Hg), which is attributed to poor control of SBP.

As a consequence of elevated BP, elderly patients are at higher risk for myocardial infarction (MI) and stroke, among other complications. Elevated BP is a major risk factor that contributes to more than 500,000 strokes and 150,000 stroke deaths yearly in the United States and is also a major



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risk factor in nearly 1 million MIs and 500,000 MI deaths annually.<sup>8</sup> These statistics reflect the magnitude of this health challenge for our elderly patients. Observational studies of more than 1 million people (elderly and nonelderly) have shown that ischemic heart disease and stroke increase linearly as BP increases.<sup>9</sup> BP and the risk of a cardiovascular disease (CVD) event is independent of other risk factors. The higher the BP, the greater the risk of MI and stroke.<sup>1</sup>

The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)<sup>1</sup> guidelines emphasize several key messages. INC 7 guidelines contain updated approaches to the management of hypertension and incorporate findings from large-scale clinical trials published after the publication of the JNC VI guidelines. 10-20 For persons older than 50 years, SBP >140 mm Hg is a more important CVD risk factor than DBP.1 Furthermore, CVD risk factor doubles with each increment of 20/10 mm Hg over 115/75 mm Hg. INC 7 also reports that people who are normotensive at age 55 have a 90% lifetime risk of developing hypertension. An SBP of 120-139 mm Hg or a DBP of 80-89 mm Hg is considered prehypertensive, a new classification in the JNC 7 guidelines, and requires health-promoting lifestyle modifications to prevent CVD.<sup>1</sup>

Although drug treatment with thiazide diuretics, either alone or in combination with drugs from other antihypertensive classes, is recommended as initial therapy for patients with uncomplicated hypertension, JNC 7 states that there are highrisk conditions for which other antihypertensive agents may be needed. In addition, most patients will require 2 or more medications to achieve goal BP, based on the results from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)10 and Controlled Onset Verapamil Investigation of Cardiovascular Endpoints (CONVINCE).<sup>11</sup> INC 7 also emphasizes that if BP is >20/10 mm Hg over goal, then clinicians should consider initiating therapy with 2 agents (one of which should be a thiazide-type diuretic). In addition, the INC 7 guidelines highlight the important role clinicians have in empathizing, building trust, and helping to motivate the hypertensive patient.

JNC 7 identifies the following disease states as comorbidities that should prompt the selection of specific antihypertensive therapy: congestive heart failure (CHF), isolated systolic hypertension (ISH), MI, high coronary disease risk, diabetes mellitus (DM), chronic kidney disease (CKD), and recurrent stroke prevention or history of stroke. These guidelines are especially pertinent for elderly patients who are likely to have one or more of these conditions.

Although JNC 7 guidelines identify the elderly as a special population, the goal of antihypertensive therapy for older persons is the same as that for the general younger population of hypertensive patients: decrease BP to <140/90 mm Hg. <sup>1</sup> To prevent unwanted symptoms, JNC 7 recognizes that the initial dose of antihypertensive medication(s) prescribed may need to be reduced compared with the initial dose used in a younger adult; however, standard doses and multiple antihypertensive medications may ultimately be needed to achieve goal BP.1 While BP targets remain unchanged from INC VI for the general hypertensive population (goal BP, <140/90 mm Hg), JNC 7 BP targets for patients with diabetes and CKD have been set lower than those in JNC VI. The current goal for these patients is <130/80 mm Hg.<sup>1</sup>

The purpose of our study was to estimate the prevalence of specific comorbidities in elderly hypertensive patients and to evaluate their association, along with the association of other clinically relevant covariates, with BP goal attainment.

## **METHODS**

Design and Study Participants. This is a secondary analysis of a retrospective, observational study of hypertensive men and women cared for at a geriatric clinic associated with an academic medical center during the period January 1, 1998 to December 31, 1998. Eligible patients were those who had been assigned an International Classification of Diseases, 9th Revision (ICD-9) diagnostic code for hypertension, had attended one or more clinic visits during a 12-month study observation period, were 60 years or older, and had confirmed hypertension based on medical chart review. For chart review, hypertension was defined as SBP ≥140 mm Hg, DBP ≥90 mm Hg, or current use of antihypertensive medication.<sup>21</sup> For patients with diabetes or renal disease, hypertension was defined as SBP/DBP >130/85 mm Hg.<sup>21</sup> Patients with hypertensive emergency or urgency as well as those with pheochromocytoma were excluded from the study. The comorbidities examined in this study were chosen to closely reflect the compelling indications identified in the complete JNC 7 report.<sup>22</sup> The health system's Institutional Review

Table I. Patient Characteristics*							
			BP GOAL				
		BP GOAL	Nот				
	Overall	Achieved	ACHIEVED	P			
No.	388	106 (27)	282 (73)	-			
Sex							
Men	106 (27)	32 (30)	74 (26)	.43			
Women	282 (73)	74 (70)	208 (74)	.40			
Age, y	77.9±7.5 (60–98)	77.2±7.4 (61–98)	78.1±7.5 (60–96)	.25			
No. of visits during study period	5.2±2.2 (2-10)	5.1±2.2 (2–10)	5.2±2.2 (2-10)	.73			
			-				

\*For categoric data, values in parentheses are percentages. Between-group comparisons performed by chi-square analysis. Continuous data are presented as mean ± SD (range). Between-group comparisons performed by 2-sample *t* test. BP indicates blood pressure.

Board for Human Subject Research approved the study protocol.

Data Collection and Measurements. Data were collected by review and extraction of information from medical charts at the clinic and recorded on a standardized data collection form. This information was transferred into an electronic format in preparation for further analysis. Hypertension control was defined as BP levels below the thresholds as measured at the final clinic visit during the study period. Comorbidities were defined as an active diagnosis or a documented history of CHF, ISH, MI, high coronary disease risk, DM, CKD, and recurrent stroke prevention or history of stroke.1 Patients were identified as having ISH if SBP was >140 mm Hg and DBP was <90 mm Hg.<sup>21</sup> For the purpose of this analysis, high coronary disease risk was further defined as the presence of 2 risk factors in addition to hypertension including: smoking, DM, dyslipidemia, age (men older than 55 and women older than 65 years), family history of CVD (any CVD in a first-degree female relative at age 65 or younger or first-degree male relative at age 55 or younger), or any prior cardiac event. CKD was identified as a baseline estimated glomerular filtration rate (GFR) <60 mL/min per 1.73 m<sup>2</sup> (corresponding roughly to serum creatinine levels of > 1.5 mg/dL in men or > 1.3 mg/dL in women) in the absence of any acute conditions potentially associated with a decreased GFR or the presence of albuminuria (>300 mg/d or >200 mg albumin per gram of creatinine).

**Statistical Analyses.** To measure the prevalence of comorbidities within a margin of error of 5%, a sample size of 384 patients was required. Descriptive and inferential statistics were prepared using standard spreadsheet (Microsoft Excel 2000; Microsoft Corporation, Redmond, WA) and statistical (SAS 9.1., SAS Institute Inc, Cary, NC) software. Chi-square analysis and 2-sample t testing were used for bivariate analysis of categoric and continuous data, respectively. Binary logistic regression was used to report the adjusted odds ratio [OR] of not achieving BP goal for variables of interest. The following 12 covariates were modeled: age; sex; number of clinic visits during the study period; use of thiazide diuretic at final visit; combination antihypertensive therapy at final visit; and presence of CHF, ISH, MI, high coronary disease risk, DM, CKD, and recurrent stroke prevention or history of stroke. Covariates were chosen based on our desire to control for potential confounding (eg, age, sex, and intensity of care provided), model the effect of relevant comorbid conditions, and evaluate associations between BP goal attainment and medication use.

With respect to medication use, thiazide diuretics and combination therapy were specifically chosen for inclusion in the modeling process to further explore the findings of a recent landmark clinical trial.<sup>10</sup> Backward stepwise logistic regression was used initially to identify variables significantly associated with failure to achieve BP goal. A final regression analysis was then performed that included any significant variables identified from the backward stepwise analysis plus covariates that were deemed clinically relevant. Assessment and selection of the final model was based on standard model fit statistics (percent concordance/discordance, C statistic, Hosmer-Lemeshow goodnessof-fit test, and likelihood ratio test). The ORs of not achieving BP goal along with 95% confidence intervals (CIs) were calculated for each parameter in the final model.

### **RESULTS**

The study population consisted of 388 patients, of whom 282 (73%) patients were not at BP goal at the final clinic visit. The mean age of the study participants was 77.9±7.5 years, and 73% of the subjects were women (Table I). The majority of patients (88.1%) had at least 1 comorbid condition present, and multiple comorbidities were present in 235 (60.6%) patients. ISH was associated with the highest prevalence (67%), followed

by high CAD risk (64.18%), DM (21.39%), stroke (14.69%), CHF (13.14%), MI (9.79%), and CKD (2.32%) (Table II). The most prevalent multiple comorbidity scenario was ISH and DM (15% of patients). Other common profiles were ISH and stroke (10%), ISH and CHF (8%), and ISH and MI (6%). A majority of patients (63%) were receiving combination therapy at their final visit during the study observation period. BP goal attainment was not significantly different in patients who were (25%) and were not (30%) receiving combination antihypertensive therapy from unadjusted, bivariate analysis (P=.13). A thiazide diuretic was utilized in 38% of patients and, of these, it was part of a combination regimen in 91% of cases. Among patients receiving combination therapy, BP goal attainment occurred in 19% and 32% of cases when thiazide diuretics were and were not included, respectively (P=.01).

Binary logistic regression analysis of all modeled covariates (full model) demonstrated that the presence of ISH at initial visit (OR, 1.64; 95% CI, 1.01–2.68) and DM (OR, 4.08; 95% CI, 1.87–8.89) were significantly associated with patients not achieving goal BP. In contrast, the presence of CHF was associated with lower odds of not achieving BP goals (OR, 0.36; 95% CI, 0.17–0.76). Statistically significant associations were not found for the following variables: age, sex, high CAD risk, MI, CKD, and patients with a history of stroke (Table III).

Backward stepwise logistic regression identified 3 covariates that were associated with higher odds (DM, ISH at initial visit, and thiazide use at final visit) and 1 covariate associated with lower odds of not achieving BP goal (CHF) at final clinic visit during the study. To adjust for combination antihypertensive therapy at final visit and intensity of follow-up (as measured by number of clinic visits during the study), these variables were added back into the final logistic regression analysis (Table IV). The addition of age and sex did not result in a significant improvement in the final regression model (nonsignificant likelihood ratio test; P=.202) and were not included. Therefore, in our final model, the adjusted odds of not achieving BP goal were higher for patients with DM (OR, 3.33; 95% CI, 1.63–6.81), ISH (OR, 1.67; 95% CI, 1.03–2.69), and who were using a thiazide diuretic at final visit (OR, 1.82; 95% CI, 1.02-3.25). The adjusted odds of patients not achieving BP goals were lower in patients with CHF (OR, 0.37; 95% CI, 0.19-0.74). Regression adequacy statistics suggest a favorable model fit.

**Table II.** Prevalence of Comorbidities (Bivariate Analyses)\*

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		BP GOAL	BP GOAL NOT	
Comorbidity	OVERALL	ACHIEVED		Р
No.	388	106	282	_
Congestive heart failure	51 (13)	22 (43)	29 (57)	.006
Isolated systolic hypertension (initial visit)	260 (67)	60 (23)	200 (77)	.008
Myocardial infarction	38 (10)	15 (39)	23 (61)	.08
High coronary disease risk	249 (64)	72 (29)	177 (71)	.34
Diabetes mellitus	83 (21)	12 (14)	71 (86)	.003
Chronic kid- ney disease	9 (2)	2 (22)	7 (78)	>.05†
Recurrent stroke pre- vention or history of stroke	57 (15)	16 (28)	41 (72)	.89

\*Values in parentheses are percentages. Betweengroup comparisons performed by chi-square analysis unless otherwise indicated. †Fisher exact test. BP indicates blood pressure.

Table III. Full Logistic Regression Model: Odds of Not Achieving Goal Blood Pressure\*

			95% CI
	Odds	95% CI	Upper
Modeled Variable	Ratio	LOWER LIMIT	Limit
Age	1.03	1.00	1.07
Sex	0.96	0.56	1.62
High coronary artery disease risk	0.70	0.40	1.23
Diabetes mellitus	4.08	1.87	8.89
Congestive heart failure	0.36	0.17	0.76
Myocardial infarction	0.67	0.31	1.44
Chronic kidney disease	1.07	0.18	6.31
History of stroke	0.86	0.44	1.71
ISH (at initial visit)	1.64	1.01	2.68
No. of clinic visits	1.03	0.92	1.16
Thiazide (at final visit)	1.66	0.91	3.01
Combination hypertension therapy (at final visit)	1.13	0.63	2.02

\*Model fit statistics: percent concordant, 70.0; percent discordant, 29.5; C statistic, 0.70; Hosmer-Lemeshow chi-square, 8.00; *P*=.43. Cl indicates confidence interval; ISH, isolated systolic hypertension.

**Table IV.** Final Logistic Regression Model: Odds of Not Achieving Goal Blood Pressure\*

	Odds	95% CI	95% CI		
Variable	Ratio	Lower Limit	Upper Limit		
Diabetes mellitus	3.33	1.68	7.11		
Congestive heart failure	0.37	0.19	0.74		
Isolated systolic hypertension (at initial visit)	1.67	1.03	2.69		
No. of clinic visits during study period	1.02	0.92	1.15		
Use of thiazide (at final visit)	1.82	1.02	3.28		
Combination thera- py (at final visit)	1.04	0.59	1.82		

\*Model fit statistics: percent concordant, 67.1; percent discordant, 31.1; C statistic, 0.68; Hosmer-Lemeshow chi-square, 7.88; *P*=.45. Cl indicates confidence interval.

### **DISCUSSION**

Our findings demonstrate that comorbidities are present in the majority of geriatric hypertensive patients and that approximately two thirds of these patients have multiple comorbidities. As expected, ISH was quite common, present in two thirds of these patients, and 1 in 5 had diabetes. Further, ISH occurs regularly in patients with DM (15% of cases). Other combinations of comorbidities were also present. An important challenge for health care providers while managing patients with hypertension is selecting the appropriate antihypertensive agent or combination of agents to optimize the use of evidence-based therapies across multiple chronic disease states.

Of highest clinical relevance is the fact that patients with either ISH or DM had increased adjusted odds of not reaching their BP goals. With respect to ISH, this may reflect a general underappreciation for the associated cardiovascular risk and the importance of optimal control. The presence of CHF was associated with a greater likelihood of a patient being at or below their BP goal during the final clinic visit during our study period. These statistical findings correlate well with the known hemodynamic consequences of heart failure.

As confirmed by multiple clinical trials, thiazide diuretics remain an important initial treatment option for patients with hypertension; however, our findings suggest that the use of these agents was associated with a higher chance of patients not achieving their BP goal as defined by INC 7

even when they are used as part of a combination regimen. Our study design does not allow us to make conclusions regarding causes for this relationship. Previous work suggests that adherence or persistence with diuretics is often lower than with other classes of antihypertensive agents. This may provide a partial explanation for our findings. 23,24 When ISH is a primary concern, previous treatment guidelines (JNC VI)21 and controlled trial evidence (Systolic Hypertension in Europe [Syst-EUR] study)<sup>25</sup> suggest that a long-acting dihydropyridine calcium channel blocker (eg, amlodipine or felodipine) is an appropriate option for geriatric patients. In patients with multiple risk factors or those with diabetes or renal insufficiency, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers are good, evidencebased options.1

An important point to consider with respect to our study methods is that creatinine alone does not reflect true GFR in the same way that JNC 7 defines renal insufficiency (GFR <60 mL/min). Therefore, it is possible that even more people in our study have renal insufficiency than we estimate. If this is the case, more patients in our cohort would require even more aggressive BP treatment, likely with careful inhibition of the renin–angiotensin system with close attention to serum potassium and GFR.

Treatment of geriatric patients, especially those who have multiple comorbidities, should be guided by current evidence-based recommendations (eg, JNC 7). These findings identify specific patient variables that are most likely to influence BP goal attainment in the geriatric population. Importantly, this population has a high short-term risk for CVD and relatively low rates of strict BP control.<sup>26</sup> Additional work is needed to assist clinicians in selecting the best strategies to overcome these comorbidity- and medication-related challenges.

# REFERENCES

- 1 The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA. 2003;289:2560–2572.
- 2 Burt VL, Whelton P, Roccella EJ, et al. Prevalence of hypertension in the US adult population. Results from the Third National Health and Nutrition Examination Survey. 1988–1991. *Hypertension*. 1995;25:305–313.
- **3** Hajjar I, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988–2000. *JAMA*. 2003;290:199–206.
- 4 US Census Bureau. *The 65 Years and Older Population: 2000*. Washington, DC: US Census Bureau; 2001.
- 5 Implications of the systolic hypertension in the elderly program. The Systolic Hypertension in the Elderly Program

- Cooperative Research Group. Hypertension. 1993;21:335–343.
- **6** Franklin SS, Jacobs MJ, Wong ND, et al. Predominance of isolated systolic hypertension among middle-aged and elderly US hypertensives: analysis based on National Health and Nutrition Examination Survey (NHANES) III. *Hypertension*. 2001;37:869–874.
- 7 Burt VL, Cutler JA, Higgins M, et al. Trends in the prevalence, awareness, treatment, and control of hypertension in the adult US population: data from the health examination surveys, 1960 to 1991. *Hypertension*. 1995;26:60–69.
- 8 National Center for Health Statistics. *Health Promotion* and Disease Prevention United States, 1990. Hyattsville, MD: Public Health Service; 1993:33. Dept of Health and Human Services publication 93–1513.
- **9** Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Prospective Studies Collaboration. *Lancet.* 2002;360:1903–1913.
- 10 The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in highrisk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) [published corrections appear in JAMA. 2003;289:178 and JAMA. 2004;291:2196]. JAMA. 2002;288:2981–2997.
- 11 Black HR, Elliott WJ, Neaton JN, et al, for the CONVINCE Research Group. Baseline characteristics and early blood pressure control in the CONVINCE Trial. *Hypertension*. 2001;37:12–18.
- 12 Vasan RS, Beiser A, Seshadri S, et al. Residual lifetime risk for developing hypertension in middle-aged women and men: the Framingham Heart Study. *JAMA*. 2002;287;1003–1010.
- 13 Neal B, MacMahon S, Chapman N. Effects of ACE inhibitors, calcium antagonists, and other blood pressure-lowering drugs: results of prospectively designed overviews of randomised trials. *Lancet.* 2000;356:1955–1964.
- 14 National Kidney Foundation Guideline. K/DOQI clinical practice guidelines for chronic kidney disease. Kidney Disease Outcome Quality Initiative. *Am J Kidney Dis.* 2002;39(suppl 2):S1–S246.
- 15 Black HR, Elliott WJ, Grandits G, et al. Principal results of the Controlled Onset Verapamil Investigation of

- Cardiovascular End Points (CONVINCE) trial. JAMA. 2003;289:2073–2082.
- 16 Yusuf S, Sleight P, Poque J, et al, for the Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. N Engl J Med. 2000;342:145–153.
- 17 Pitt B, Remme W, Zannad F, et al, for the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study Investigators. Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med.* 2003;348:1309–1321.
- 18 UK Prospective Diabetes Study Group. Efficacy of atenolol and captoril in reducing risk of marcrovascular and microvascular complications in type 2 diabetes: UKPDS 39. BMJ. 1998;317:713–720.
- 19 Wright JT Jr, Agodoa L, Contreras G, et al. Successful blood pressure control in the African American Study of Kidney Disease and Hypertension. Arch Intern Med. 2002;162:1636–1643.
- 20 Dahlöf B, Devereux RB, Kjeldsen SE, et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomized trial against atenolol. *Lancet*. 2002;359:995–1003.
- **21** The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Arch Intern Med.* 1997;157:2413–2446.
- **22** Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42:1206–1252.
- 23 Wannemacher AJ, Schepers GP, Townsend KA. Antihypertensive medication compliance in a Veterans Affairs Healthcare System. Ann Pharmacother. 2002;36:986–991.
- 24 Degli Esposti ED, Sturani A, Di Martino M, et al. Long-term persistence with antihypertensive drugs in new patients. J Hum Hypertens. 2002;16:439–444.
- 25 Staessen JA, Fagard R, Thijs L, et al, on behalf of the Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. *Lancet*. 1997;350:757–764.
- **26** Lloyd-Jones DM, Evans JC, Levy D. Hypertension in adults across the age spectrum: current outcomes and control in the community. *JAMA*. 2005;294:466–472.