Antihypertensive Medications Prescribed at Discharge After an Acute Ischemic Cerebrovascular Event

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Background and Purpose—Hypertension is poorly controlled in stroke survivors, thereby placing them at increased risk for recurrent events. Clinical trial evidence suggests that antihypertensive treatment may be beneficial for stroke prevention in hypertensive and normotensive stroke patients. We aimed to evaluate the discharge antihypertensive prescription patterns in patients hospitalized for an ischemic cerebrovascular event and to determine factors associated with treatment utilization.

Methods—We analyzed patients diagnosed with ischemic stroke or transient ischemic attack (TIA) in the California Acute Stroke Prototype Registry (CASPR). We used generalized estimating equations to identify factors independently associated with receiving antihypertensives at the time of hospital discharge.

Results—Data were collected on 764 consecutive patients with ischemic stroke or TIA encountered at 11 hospitals representative of facilities in the state of California. Overall, the rate of discharge with a prescription for any antihypertensive in the CASPR cohort was 69.4%. Hospital-specific rates were heterogeneous (P=0.04), varying from 55% to 100%. In multivariate analysis, independent predictors of prescription for antihypertensive medication at discharge were a history of hypertension (P<0.0001), diabetes (P=0.0009), and older age.

Conclusions—About two-thirds of patients hospitalized with acute ischemic cerebrovascular events are discharged from the hospital on ≥1 antihypertensive medication. However, there is great variability in prescription rates between hospitals and considerable room for improvement. (Stroke. 2005;36:1944-1947.)

Key Words: hypertension ■ secondary prevention ■ stroke

Hypertension is a potent yet modifiable risk factor for recurrent stroke, and the use of antihypertensive treatment has been shown to reduce this risk substantially. Nonetheless, blood pressure is poorly controlled among individuals who have experienced a previous stroke. Indeed, with recent community-based data revealing a high early risk of secondary stroke and evidence indicating the presence of hypertension at the time of hospital discharge as a predictor of such risk, there is a need to improve antihypertensive treatment rates in stroke survivors, including those who are normotensive.

A potential bridge for the antihypertensive knowledge—treatment divide could be the systematic and appropriate prescription of antihypertensives before the patient leaves the hospital or after admission for an acute ischemic stroke or transient ischemic attack (TIA). This strategy is attractive because it can be safe, and evidence suggests that in-hospital behavior strongly influences postdischarge community practice, and moderate reductions in blood pressure during the first week after hospital admission have been associated with improved short-term functional outcome in patients with acute ischemic stroke. However, no previous study has analyzed the frequency and patterns of discharge prescription for antihypertensives in patients with ischemic stroke or TIA.

In a cohort study derived from representative Californian hospitals, we evaluated the frequency and patterns of discharge antihypertensive utilization in a large, multicenter cohort of hospitalized stroke and TIA patients and assessed the impact of recent national hypertensive guidelines and clinical trial evidence on discharge prescription behavior.

Patients and Methods

Data from the California Acute Stroke Prototype Registry (CASPR) were analyzed. CASPR collected data prospectively on acute stroke care in individuals with a diagnosis of suspected stroke or TIA in 11 hospitals in 5 major population regions of California from November 1, 2002, through January 31, 2003, and from November 1, 2003, through January 31, 2004. The CASPR study methods have been described previously. Human subject review boards at each participating center approved CASPR.

For these analyses, we included all patients with a discharge diagnosis of ischemic stroke or TIA who were admitted during either time period. We first examined rates of antihypertensive use among hospitals to determine whether intrahospital variability existed at a
significant level. We identified the rates of use of different classes of medication categorizing antihypertensives into the following groups: angiotensin-converting enzyme inhibitors (ACEIs), \(\beta\)-adrenergic blocking agents, calcium channel blockers, angiotensin receptor blockers, diuretics, and “other” antihypertensives, including centrally acting adrenergics, peripherally acting antiadrenergics, and vasodilators. We then examined characteristics potentially associated with receipt of any antihypertensive medication at discharge in the overall cohort. Because this analysis could potentially reflect risk factors for hypertension as well as predictors of treatment with antihypertensive medications, we also analyzed patients with and without a history of hypertension separately.

**Statistical Analysis**

The \(\chi^2\) test for homogeneity was used to evaluate whether or not the hospitals were homogeneous with respect to the proportion of patients treated with antihypertensive medications. Because a significant difference in treatment rates was observed, generalized estimating equations were used for univariate and multivariate analyses to account for within-hospital and between-hospital variances. Variables significant at the \(\alpha=0.05\) level in univariate analysis were included in multivariate analysis. SAS (version 8e; SAS Institute) was used for all statistical analysis.

**Results**

Overall, 764 patients were diagnosed with either ischemic stroke or TIA at the 11 CASPR hospitals. Subjects in the overall cohort were 53.4\% women, 55.4\% white, 9.9\% black, with an average age of 70.4 (\(\pm 15.4\)) years.

Among these, 530 patients (69.4\%) received a discharge prescription for any antihypertensive. However, rates among hospitals were heterogeneous (\(P=0.04\)), ranging from a low of 55\% to a high of 100\%. Across the entire cohort, 17 (2.2\%) were discharged on \(\geq 4\) antihypertensive agents, 60 (7.9\%) on 3, 177 (23.2\%) on 2, and 276 (36.1\%) on 1.

Factors associated in univariate analysis with receipt of antihypertensives at discharge included older age, diagnosis of ischemic stroke (versus TIA), history of coronary artery disease, history of congestive heart failure, history of hypertension, history of diabetes, and history of atrial fibrillation (Table). Patients who received tissue plasminogen activator who were ambulatory at discharge or who were discharged home were less likely to receive antihypertensives (Table). In multivariate analysis, history of hypertension, history of diabetes, and older age (those who were 73 years of age compared with those who were \(\leq 60\) years of age) remained significantly associated with receiving antihypertensives at discharge (Table).

In separate analyses of patients without a history of hypertension (\(n=242\)), 39\% received antihypertensive medication at discharge. Older age and a history of atrial fibrillation were significantly associated with higher rates of antihypertensive usage at discharge among those with no previous history of hypertension, whereas those patients with independent ambulation were less likely to receive treatment. Patients with a documented history of hypertension were more likely to receive antihypertensives at discharge if they had a history of dyslipidemia or diabetes (multivariate analysis; results not shown).

ACEIs were the most prescribed class of antihypertensives in 303 patients (39.7\% of the cohort), as seen in the Figure. Among the 254 patients in the entire cohort taking 2 or more antihypertensives, the most common combination regimen was ACEI and a \(\beta\)-blocker, which was used in 59 patients (23\%).

**Discussion**

This study shows that at representative hospitals in California, a substantial majority of individuals discharged from the hospital after an ischemic stroke or TIA are prescribed \(\geq 1\) antihypertensive agents, but 1 of every 3 patients is discharged on no antihypertensive therapy. Strengths of our study are the inclusion of multiple hospitals in different healthcare settings and the examination of characteristics associated with receipt of antihypertensive treatment at discharge. We found that older individuals and those with a history of hypertension or diabetes were more likely to receive a prescription for an antihypertensive at the time of hospital discharge.

At first glance, the fact that a majority of hospitalized ischemic stroke and TIA patients are discharged on \(\geq 1\) antihypertensive drug may seem encouraging. However, the evidence that large numbers of stroke survivors with hypertension remain poorly controlled suggests there is either ineffective implementation or suboptimal long-term maintenance of these therapies. Studies have shown that strategies such as low-dose combination therapy, for instance, increase antihypertensive treatment efficacy and reduce adverse effects, and current national guidelines specifically call for combination therapy in stroke survivors. However, only 33.2\% of patients in our study were discharged on combination antihypertensive regimens. It should also be noted that in our study, a history of a previous stroke or TIA was not independently associated with antihypertensive prescription. This is despite current guidelines and a large secondary stroke prevention trial, indicating the benefit of antihypertensive treatment for secondary stroke prevention among those with relatively normal blood pressures. Such omission after \(\geq 2\) cerebrovascular events is cause for concern because it is inappropriate to assume that therapy will be initiated in a timely fashion, if at all, after hospitalization for a vascular event. Another finding from our study, was that although national guidelines recommend that thiazide-type diuretics be used in drug treatment for most hypertensive patients either alone or combined with drugs from other classes, we found a lower prescription of these medications compared with ACEIs and \(\beta\)-blockers among our patients.

A wide variation in discharge antihypertensive treatment rates existed among CASPR hospitals. This is perhaps not surprising given the paucity of data and guidelines pertaining to the appropriate timing for systematic, safe, and appropriate antihypertensive drug initiation after an ischemic stroke or TIA. Supporting an early rather than delayed approach to antihypertensive agent initiation, a recent study showed that systematic in-hospital initiation of antihypertensives before hospital discharge after an ischemic stroke or TIA was associated with high treatment adherence rates 3 months after hospitalization. The results of the ACCESS trial, in which improved outcomes were observed in patients receiving an antihypertensive agent early after stroke onset, lends further credence to the potential safety and effectiveness of this strategy. The first few weeks and months after initial TIA or
ischemic stroke is the period of highest risk for recurrence, making early implementation of optimal secondary prevention therapies highly desirable. Interestingly, we observed that a substantial proportion of individuals with no history of hypertension were discharged on antihypertensive agents. However, this finding may reflect the influence of clinical trial results that suggest stroke survivors with normal blood pressures may reap benefit from antihypertensive treatment, or these agents may have been prescribed for other therapeutic reasons such as β-blocker use for cardiac rate control or ACEIs for heart failure.

Although we collected data on history of hypertension among CASPR subjects, we did not collect data on the premorbid use of antihypertensive agents. We are also limited by a paucity of information on the potential contraindications or adverse reactions that might have prevented the use of certain antihypertensive medications. CASPR investigators also did not collect information on stroke/TIA mechanisms, which could have influenced the decision to initiate antihypertensive therapies, particularly in patients with nonatherosclerotic mechanisms such as hypercoagulable states, vasculitis, etc, for their event. Finally, we have no information on actual blood pressure measurements during hospitalization; and although these may have impacted treatment decisions, it has been shown that blood pressures in the majority of acute stroke patients may not return fully to baseline levels for several days to weeks after the index event, and so stroke hospitalization blood pressures may not be the best parameter by which to judge the treatment needs of an individual stroke patient. Furthermore, the approach of using blood pressure measurement as the sole determinant in the decision whether to initiate antihypertensives for the majority of ischemic

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Antihypertensive at Discharge (n = 522)</th>
<th>Univariate†</th>
<th>Adjusted†</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>No (%)</td>
<td>OR (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Age in quartiles</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>&lt;60 years</td>
<td>183</td>
<td>102 (55.7)</td>
<td>Reference</td>
<td>Reference</td>
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<tr>
<td>60–73 years</td>
<td>180</td>
<td>128 (71.1)</td>
<td>2.17 (1.25, 3.77)</td>
<td>&lt;0.006</td>
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<tr>
<td>73–82 years</td>
<td>188</td>
<td>144 (76.6)</td>
<td>2.98 (2.13, 4.16)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&gt;82 years</td>
<td>213</td>
<td>156 (73.2)</td>
<td>2.45 (1.72, 3.48)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Gender</td>
<td></td>
<td></td>
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<tr>
<td>Female</td>
<td>408</td>
<td>290 (71.1)</td>
<td>Reference</td>
<td>Reference</td>
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<tr>
<td>Male</td>
<td>356</td>
<td>240 (67.4)</td>
<td>0.83 (0.62, 1.09)</td>
<td>0.18</td>
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<tr>
<td>Ethnicity</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>76</td>
<td>54 (71.1)</td>
<td>Reference</td>
<td>Reference</td>
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<tr>
<td>Other</td>
<td>688</td>
<td>476 (69.2)</td>
<td>1.09 (0.58, 2.04)</td>
<td>0.79</td>
</tr>
<tr>
<td>Event type</td>
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<td></td>
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<tr>
<td>TIA</td>
<td>172</td>
<td>108 (63)</td>
<td>Reference</td>
<td>Reference</td>
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<tr>
<td>Ischemic stroke</td>
<td>592</td>
<td>422 (71)</td>
<td>1.45 (1.05, 2.00)</td>
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<td>Treatment year</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Year 1</td>
<td>516</td>
<td>355 (68.8)</td>
<td>Reference</td>
<td>Reference</td>
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<tr>
<td>Year 2</td>
<td>248</td>
<td>175 (70.6)</td>
<td>1.16 (0.70, 1.92)</td>
<td>0.57</td>
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<tr>
<td>History of*</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Hypertension</td>
<td>516</td>
<td>431 (83.5)</td>
<td>8.03 (6.08, 10.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>277</td>
<td>203 (73.3)</td>
<td>1.36 (0.97, 1.90)</td>
<td>0.07</td>
</tr>
<tr>
<td>Myocardial infarction or coronary artery disease</td>
<td>160</td>
<td>126 (78.8)</td>
<td>1.84 (1.31, 2.57)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Heart failure</td>
<td>83</td>
<td>67 (80.7)</td>
<td>2.00 (1.24, 3.23)</td>
<td>0.005</td>
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<tr>
<td>Diabetes</td>
<td>199</td>
<td>160 (80.4)</td>
<td>2.17 (1.70, 2.77)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Dyslipidemia</td>
<td>243</td>
<td>188 (77.4)</td>
<td>1.80 (1.40, 2.30)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>125</td>
<td>102 (81.6)</td>
<td>2.19 (1.30, 3.69)</td>
<td>0.003</td>
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<tr>
<td>Received tissue plasminogen activator</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>748</td>
<td>523 (69.9)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Yes</td>
<td>16</td>
<td>7 (43.8)</td>
<td>0.35 (0.17, 0.72)</td>
<td>0.005</td>
</tr>
<tr>
<td>Ambulation status**</td>
<td>400</td>
<td>257 (64.3)</td>
<td>0.60 (0.50, 0.71)</td>
<td>&lt;0.0001</td>
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<td>Discharged home</td>
<td>501</td>
<td>333 (66.5)</td>
<td>0.67 (0.50, 0.91)</td>
<td>0.009</td>
</tr>
</tbody>
</table>

†All analyses performed using generalized estimating equations; *reference category consists of all patients without a history of the given characteristic; †at discharge.
stroke/TIA patients may not be as relevant as thought previously because the key to the efficacy of antihypertensive treatment in stroke prevention may lie in blood pressure reduction and perhaps additional mechanisms, not just treatment of diagnosed hypertension.

Acknowledgments
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References
19. Carlberg B, Asplund K, Hagg E. The prognostic value of admission blood cation at discharge. Percentages for each group do not total to 100% because some patients received >1 antihypertensive medication.

Percentage of total patients with ischemic stroke or TIA who were treated with each specific class of antihypertensive medication.

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