Optimizing Screening and Management of Asymptomatic Coronary Artery Disease in Patients With Stroke and Patients With Transient Ischemic Attack

Bruce Ovbiagele, MD, MS; David S. Liebeskind, MD; Doojin Kim, MD; Latisha K. Ali, MD; Sandra Pineda, BS; Jeffrey L. Saver, MD

Background and Purpose—The feasibility of implementing an expert consensus guideline recommending use of a stroke patient’s profile to manage undiagnosed coronary artery disease remains unclear.

Methods—Following a guideline-based algorithm, we screened consecutive patients with ischemic stroke and patients with transient ischemic attack for asymptomatic CAD using the Framingham Heart Study Coronary Risk Score (FCRS) cutoff of high risk (≥20%) for experiencing a hard coronary artery disease event over a 10-year period. Patients with high FCRS received dobutamine stress echocardiogram outpatient screening, additional treatment (β-blocker), or further management (cardiologist referral).

Results—From July 2004 to September 2007, among 693 patients, 501 (72%) met study criteria, of which 80 (16%) had high FCRS. Elevated serum glucose, nonhigh-density lipoprotein, triglycerides, homocysteine, and systolic blood pressure measurement 48 to 72 hours after admission or at the time of hospital discharge, whichever came sooner, were averaged. Two separate blood pressure measurements 48 to 72 hours after admission or at the time of hospital discharge, whichever came sooner, were averaged. Among high FCRS patients, 35 (44%) had dobutamine stress echocardiogram performed. Leading reasons for dobutamine stress echocardiogram nonperformance were patient noncompliance (42%) and primary care physician refusal (33%).

Conclusions—Screening for coronary artery disease risk using FCRS is feasible in hospitalized patients with stroke, but outpatient adherence to stress testing is challenging largely due to patient and primary care physician-related factors. (Stroke. 2009;40:3407-3409.)

Key Words: coronary □ Framingham risk score □ myocardial infarction □ risk factors □ screening □ stress testing □ stroke □ TIA

Coronary artery disease (CAD) is the major cause of death in patients with stroke. Recognizing the importance of identifying patients with stroke at high risk for myocardial infarction, the American Heart Association Stroke Council recommends using information from a stroke patient’s profile to screen for asymptomatic CAD and manage appropriately. However, the feasibility of implementing this guideline in routine practice is unknown. Stroke hospitalization provides a window of opportunity to assure initiation of CAD risk management. We assessed the feasibility of asymptomatic CAD management in hospitalized patients with stroke.

Methods

Data were collected prospectively on patients with ischemic stroke or patients with transient ischemic attack aged ≥20 years consecutively admitted to a university teaching hospital from July 1, 2004, to September 30, 2007. Patients with a known history of symptomatic CAD or who experienced an acute myocardial infarction during the index hospitalization were excluded.

We developed a specific program to screen and manage patients based on treatment algorithms derived from the Stroke Council guideline. Our protocol was implemented within a broader stroke quality improvement project and is shown in the Figure. The Framingham Coronary Risk Score (FCRS) is based on age, sex, total blood cholesterol level, high-density lipoprotein cholesterol level, systolic blood pressure measurement, the presence or absence of diabetes, and whether the patient smokes cigarettes. FCRS identifies patients as being at low, average, moderate, or high 10-year risk for experiencing a symptomatic cardiac event and was calculated for each eligible patient. FCRS calculation can readily be performed by inputting variables into a web-based calculator at http://hp2010.nhlbihin.net/atpiii/calculator.asp?usertype=prof. Two separate blood pressure measurements 48 to 72 hours after admission or at the time of hospital discharge, whichever came sooner, were averaged.

We analyzed associations of continuous biomarkers that were not already components of FCRS with dichotomized FCRS as high (≥20%) or low (<20%) using the Wilcoxon rank sum test. Associations of categorical variables and dichotomized FCRS were computed using χ² test. The local Institutional Review Board approved the study.

Results

Among 693 patients, 501 (72%) met study criteria, of which 67 (13%) presented with transient ischemic attack. Summary characteristics are shown in Table 1. Median age was 67 years, 53% were female, and 67% were white. Eighty of the 501 patients (16%) had high FCRS. Comparisons of continuous vascular risk biomarkers in those with low versus high FCRS is shown in Table 2. Serum glucose, nonhigh-density lipoprotein cholesterol, serum triglycerides, homocysteine...
level, and glycosylated hemoglobin were higher in those with high versus low FCRS. Large vessel stroke mechanism was more prevalent in those with high versus low FCRS (30% versus 19.2%, \( P < 0.037 \)) and median FCRS was higher among those with large vessel stroke mechanism compared with all other stroke mechanisms (13% versus 7%, \( P < 0.001 \)).

Among high FCRS patients, 35 (44%) had dobutamine stress echocardiogram (DSE) performed. Median time to DSE performance after hospitalization was 5 weeks. There were no significant differences in demographic and clinical variables between those with DSE screening versus those without. Reasons for DSE nonperformance were patient or caregiver initially agreed to pursue test but did not despite a telephone call reminder (\( n = 19 \)), primary care provider did not approve or resisted test being performed (\( n = 15 \)), patient or caregiver refused test upfront (\( n = 5 \)), denial of test performance by patient’s insurance company (\( n = 2 \)), or patient had died (\( n = 3 \)) or was unreachable (\( n = 1 \)).

Five DSE-screened patients (14%) had abnormal coronary perfusion. These patients with abnormal coronary perfusion were prescribed \( \beta \)-blocker therapy and referred to a cardiologist for further management. Of these 5 patients with abnormal coronary perfusion noted on DSE, within 12 months of their index cerebrovascular event, one person was hospitalized with myocardial infarction and another required urgent coronary revascularization based on results of a coronary angiogram performed after experiencing mild cardiac symptoms. All 5 patients tolerated \( \beta \)-blocker treatment well and remained on the same dose or higher dose of the agent initially prescribed at 1 year. None of the 30 patients without abnormal coronary perfusion experienced an acute coronary syndrome or required coronary revascularization within 12 months of their index cerebrovascular event.

**Discussion**

We found that the FCRS could be readily applied to persons hospitalized with an ischemic cerebrovascular event to identify those individuals who may require further testing or treatment for asymptomatic CAD risk as well as more intensive vascular risk factor control. However, beyond the inpatient use of FCRS to delineate CAD risk, we noted that further testing with DSE in the outpatient setting was challenging due to patient and primary care provider adherence issues.

High FCRS was significantly associated with large vessel atherosclerotic mechanism, several indices of insulin resistance, including higher serum glucose, triglycerides, and glycosylated hemoglobin, as well as higher nonhigh-density lipoprotein and
homocysteine levels. These results are in accord with prior data that independently linked large vessel atherosclerotic disease with FCRS and abnormal results in myocardial imaging studies.5,6 Measures of insulin resistance have also previously been shown to be strongly associated with CAD.7

If CAD risk screening among patients with stroke is to be properly implemented, several issues may need to be addressed. First, patients, healthcare providers, and payors may simply need to be better aware of the guideline itself. More intensive efforts to educate patients, their caregivers, primary care providers, and insurers about the guideline may be warranted. Another option could be to conduct screening for inducible cardiac ischemia while the patients are still in the hospital. Beta-blocker initiation can be done promptly and input from a cardiologist obtained quickly in the event of an abnormal result, and in-hospital management tends to boost adherence in the postdischarge setting. However, the safety of stress echocardiography within days of acute ischemic stroke onset has not been demonstrated and additional inpatient testing may prolong hospitalization and increase acute care costs. A broader issue may be that several care providers are not convinced that such screening is helpful or cost-effective. Indeed, the potential of routine screening to prevent cardiac events in persons without clinically apparent CAD is largely unknown.8 As such, although endorsed by professional organizations,1 screening of persons with no symptoms of CAD remains highly controversial in the absence of prospective outcome studies supporting its usefulness.8

This analysis has limitations. It was a single-center study of modest sample size and results may vary in other hospital types and settings. Nonetheless, systematic in-hospital stroke quality improvement initiatives have been successfully implemented across several different hospital types.2 The low number of individuals who underwent DSE prevents precise inferences from being made about the frequency of abnormal cardiac perfusion and subsequent cardiac events in a cohort of hospitalized stroke and transient ischemic attack with high FCRS. Lastly, it might have been helpful to recalculate FCRS at 1 year to assess consistency and impact of additional risk reduction strategies on the score.

Disclosures

None.

References


Table 2. Correlations of Dichotomized (≥20% versus <20%) FCRS With Vascular Risk Biomarkers Among Patients Hospitalized With Recent Ischemic Stroke or Transient Ischemic Attack (n=501)

<table>
<thead>
<tr>
<th>Variable</th>
<th>FCRS</th>
<th>Q1 Median</th>
<th>Mean</th>
<th>Q3</th>
<th>SD</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index</td>
<td>&lt;20%</td>
<td>22.30</td>
<td>25.05</td>
<td>25.63</td>
<td>28.71</td>
<td>6.08</td>
</tr>
<tr>
<td></td>
<td>≥20%</td>
<td>23.33</td>
<td>25.73</td>
<td>26.63</td>
<td>29.06</td>
<td>6.34</td>
</tr>
<tr>
<td>Serum glucose, mg/dL</td>
<td>&lt;20%</td>
<td>97.00</td>
<td>108.00</td>
<td>120.10</td>
<td>128.50</td>
<td>44.48</td>
</tr>
<tr>
<td></td>
<td>≥20%</td>
<td>98.00</td>
<td>117.50</td>
<td>147.31</td>
<td>156.50</td>
<td>82.14</td>
</tr>
<tr>
<td>Serum low-density lipoprotein cholesterol, mg/dL</td>
<td>&lt;20%</td>
<td>79.00</td>
<td>98.00</td>
<td>103.46</td>
<td>122.00</td>
<td>33.77</td>
</tr>
<tr>
<td></td>
<td>≥20%</td>
<td>80.00</td>
<td>108.00</td>
<td>108.66</td>
<td>132.00</td>
<td>39.11</td>
</tr>
<tr>
<td>Serum nonhigh-density lipoprotein cholesterol, mg/dL</td>
<td>&lt;20%</td>
<td>102.00</td>
<td>121.00</td>
<td>126.98</td>
<td>149.00</td>
<td>36.17</td>
</tr>
<tr>
<td></td>
<td>≥20%</td>
<td>106.50</td>
<td>133.50</td>
<td>139.35</td>
<td>164.00</td>
<td>46.73</td>
</tr>
<tr>
<td>Serum triglycerides, mg/dL</td>
<td>&lt;20%</td>
<td>70.00</td>
<td>96.00</td>
<td>119.48</td>
<td>141.00</td>
<td>76.86</td>
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<tr>
<td></td>
<td>≥20%</td>
<td>81.00</td>
<td>112.00</td>
<td>155.85</td>
<td>191.00</td>
<td>119.93</td>
</tr>
<tr>
<td>Serum homocysteine level, mg/L</td>
<td>&lt;20%</td>
<td>6.00</td>
<td>8.00</td>
<td>8.33</td>
<td>10.00</td>
<td>3.53</td>
</tr>
<tr>
<td></td>
<td>≥20%</td>
<td>7.00</td>
<td>9.00</td>
<td>9.59</td>
<td>12.00</td>
<td>3.26</td>
</tr>
<tr>
<td>Glycosylated hemoglobin</td>
<td>&lt;20%</td>
<td>0.05</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>≥20%</td>
<td>0.06</td>
<td>0.06</td>
<td>0.14</td>
<td>0.07</td>
<td>0.73</td>
</tr>
<tr>
<td>Serum white blood cell count, 1000 cells(µL)</td>
<td>&lt;20%</td>
<td>6.58</td>
<td>8.12</td>
<td>8.80</td>
<td>10.30</td>
<td>4.28</td>
</tr>
<tr>
<td></td>
<td>≥20%</td>
<td>6.35</td>
<td>8.08</td>
<td>8.51</td>
<td>10.50</td>
<td>2.60</td>
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