One-Year Progression of Moderate Asymptomatic Carotid Stenosis Predicts the Risk of Vascular Events

Simona Balestrini, MD; Francesca Lupidi, MD; Clotilde Balucani, MD; Claudia Altamura, MD; Fabrizio Vernieri, MD; Leandro Provinciali, MD; Mauro Silvestrini, MD

Background and Purpose—This study aimed at evaluating whether ultrasound monitoring of moderate asymptomatic carotid stenosis may help in identifying subjects at high risk for vascular events.

Methods—We included 523 subjects with unilateral asymptomatic carotid stenosis of 50% to 69%. Follow-up carotid ultrasound was performed within 12 months from inclusion to detect the frequency and degree of stenosis progression. Subjects were prospectively evaluated for a median period of 42 months (interquartile range, 38–45) after a second ultrasound evaluation. Outcome measures were any stroke and transient ischemic attack, myocardial infarction, and death.

Results—Carotid stenosis progression was associated with the occurrence of vascular events (hazard ratio, 21.57; 95% confidence interval, 11.81–39.39; \( P<0.001 \)). During follow-up, 96.7% of subjects without progressive carotid stenosis remained free from vascular events. Among patients with progressive stenosis, 53.7% experienced a vascular event and 27.1% experienced an ipsilateral stroke.

Conclusions—One-year moderate asymptomatic carotid stenosis progression is related to higher risk of vascular events, including ipsilateral stroke. (Stroke. 2013;44:792-794.)

Key Words: carotid stenosis ■ cerebrovascular disease ■ risk factors ■ ultrasound

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a univariate Cox regression model, a multivariable model was used to examine the association between progressive carotid stenosis and occurrence of combined vascular events, adjusting for variables that emerged as significant (\( P < 0.20 \)) in the univariate models. Results of the Cox models are presented as hazard ratio and 95% confidence interval (CI). The proportional hazard assumption of the model was assessed by plotting the scaled Schoenfeld residuals against time for each selected variable in the model. The variable age did not fulfill the assumption; hence, we included the interaction term age and analysis time in the final multivariable model. For accuracy purposes, Cox-Snell residuals were calculated. Finally, we fitted a competing risk model considering only ipsilateral ischemic stroke as the first adverse outcome and all other vascular events as the competing events. Results of this model are presented as the subhazard ratio and 95% CI. Data analysis was performed using Stata/IC 11.1 Statistical package.

**Results**

Of 616 consecutive subjects screened, 93 were excluded: 60 for contralateral ICA stenosis \( \geq 50\% \), 22 for severe medical conditions or embolizing cardiopathies, and 11 for carotid revascularization. Of these 11 patients, in 6 cases the decision to perform revascularization treatment was due to the occurrence of an ipsilateral TIA or minor stroke after the first ultrasound evaluation. We enrolled 523 subjects with moderate ACS. Median time for the second ultrasound evaluation was 9 months (interquartile range, 8–12). Progression of ICA stenosis was detected in 129 subjects (24.7%). The median clinical follow-up period was 42 months (interquartile range, 38–45). Demographics and clinical characteristics of subjects with progressive and nonprogressive ICA stenosis are reported in Table 1.

Eighty-one subjects (15.5%) had clinical events: 42 strokes, 38 ipsilateral to the carotid stenosis, 22 TIAS, 14 MIs, and 3 deaths (related annual incidence rate was 2.35% for overall strokes, 2.12% for ipsilateral strokes, 1.23% for TIAS, 0.78% for MIs, and 0.17% for deaths). Among the 394 subjects without progressive carotid disease, 3 (0.8%) had an ipsilateral stroke, 2 (0.5%) had a contralateral stroke, 6 (1.5%) had MI, and 2 (0.5%) subjects died. Regarding subjects with progressive carotid disease, 35 (27.1%) had an ipsilateral stroke, 22 (17.0%) had TIA, 2 (1.6%) had contralateral stroke, 8 (6.2%) had MI, and 1 (0.8%) died. Progression of carotid stenosis was significantly associated with the occurrence of vascular events. Table 2 presents univariate analyses with all potential predictors of combined vascular events. A further subgroup analysis for different levels of stenosis progression was not performed given the low number of subjects with progression by 2 or 3 categories (5.4% and 0%, respectively).

In the multivariable Cox model, risk for combined events was predicted by progressive ICA stenosis (hazard ratio, 21.57; 95% CI, 11.81–39.39; \( P < 0.001 \)) after adjusting the model for age, smoking, diabetes mellitus, hypertension, antidiabetics, and the interaction term age and analysis time. Finally, in the competing risks regression analysis, ICA stenosis progression significantly predicted the risk of ipsilateral stroke (subhazard ratio, 31.97; 95% CI, 9.83–103.91; \( P < 0.001 \)) after adjusting the model for the same covariates (Figure).

### Table 1. Demographic and Clinical Characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Progressive Stenosis (n=129)</th>
<th>Nonprogressive Stenosis (n=394)</th>
<th>Difference (Test)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>74 (8)</td>
<td>73 (8)</td>
<td>0.069*</td>
<td></td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>56 (43.4)</td>
<td>185 (47.0)</td>
<td>0.483‡</td>
<td></td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>102 (79.1)</td>
<td>267 (67.8)</td>
<td>0.014†</td>
<td></td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>62 (48.1)</td>
<td>236 (59.9)</td>
<td>0.018†</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>43 (33.3)</td>
<td>93 (23.6)</td>
<td>0.070†</td>
<td></td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>28 (21.7)</td>
<td>104 (26.4)</td>
<td>0.287†</td>
<td></td>
</tr>
<tr>
<td>CAD, n (%)</td>
<td>21 (16.3)</td>
<td>95 (24.1)</td>
<td>0.063†</td>
<td></td>
</tr>
<tr>
<td>Antihypertensives, n (%)</td>
<td>91 (70.5)</td>
<td>246 (62.4)</td>
<td>0.095†</td>
<td></td>
</tr>
<tr>
<td>Antidiabetics, n (%)</td>
<td>40 (31.0)</td>
<td>88 (22.3)</td>
<td>0.047†</td>
<td></td>
</tr>
<tr>
<td>Statins, n (%)</td>
<td>53 (41.1)</td>
<td>163 (41.4)</td>
<td>0.954†</td>
<td></td>
</tr>
<tr>
<td>Antiplatelets, n (%)</td>
<td>75 (58.1)</td>
<td>214 (54.3)</td>
<td>0.448†</td>
<td></td>
</tr>
</tbody>
</table>

*CAD indicates coronary artery disease; and SD, standard deviation.

*Two-sample \( t \) test.

†Pearson \( \chi^2 \) test.
Our study shows that 1-year ultrasound monitoring of moderate ACS can help in identifying subjects at higher vascular risk. Progressive lumen narrowing is significantly associated with the risk of ipsilateral stroke, contralateral stroke, MI, and death. This finding suggests that carotid stenosis should be considered as part of a generalized atherosclerosis process involved in the pathogenesis of vascular accidents at different organic levels. For this reason, the need for more aggressive treatment strategies in these subgroups of subjects with ACS should be stressed. Additional ultrasound follow-up evaluations might have allowed a more comprehensive assessment of carotid plaque characteristics. We attempted to obtain reliable prognostic information without overburdening health service resources; therefore, we performed 2 ultrasound evaluations during a short time interval to avoid patient dropouts. Moreover, among measures potentially able to provide information about plaque-associated risk, we considered the degree of stenosis, which may be evaluated in a relatively simple and reproducible way.

Our results may have implications for disease monitoring and treatment strategies in the clinical practice. Faster rates of progression of moderate ACS as evidenced by a short-term ultrasound monitoring should be considered a marker of increased risk for vascular events.

**Disclosures**

None.

**References**


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