Plaque morphology (the PLAC Scale) on CT angiography: predicting long-term anatomical success of primary carotid stenting

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OBJECT Carotid angioplasty and stenting has emerged as an alternative to carotid endarterectomy for the treatment of atherosclerotic carotid stenosis. Primary carotid stenting, performed using self-expanding stents alone without deliberate use of embolic protection devices and balloon angioplasty, has been shown to be effective and faster, cheaper, and potentially safer than conventional techniques. However, the long-term morphological results of this technique have not been established. The aim of this study was to determine whether preprocedural carotid plaque imaging at the site of maximal stenosis by using CT angiography (CTA) could predict the long-term morphological outcome of primary carotid stenting.

METHODS One hundred eighty-one patients were treated over an 11-year period. Preprocedural CTA was performed in 102 of these. A morphological scale (the Predicting Long-term outcome with Angioplasty of the Carotid artery [PLAC] Scale), with grades from 0 to 4 and A or B, was used to evaluate the circumferential degree of plaque calcification, and the presence or absence of soft plaque. All patients were followed using duplex carotid ultrasound and plain radiographs. Satisfactory morphological outcome was defined as a peak systolic velocity < 120 cm/s and internal carotid artery/common carotid artery ratio < 1.4.

RESULTS The average follow-up duration was 29.7 months (median 24.5 months, range 0.3–87 months). Univariate logistic regression demonstrated that a low calcification grade (p < 0.001), less thick calcification (p < 0.001), and moderate amounts of soft plaque (p < 0.001) are factors that are highly associated with good long-term outcome. Multivariate analyses confirmed that these factors are independent of each other in predicting outcome.

CONCLUSIONS The long-term morphological outcome of primary carotid stenting was predicted with considerable accuracy by using a straightforward CTA carotid plaque grading scale.

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KEY WORDS carotid stenting; carotid stenosis; CT angiography; plaque morphology; vascular disorders

CAVOTID angioplasty and stenting (CAS) has evolved into an alternative to carotid endarterectomy (CEA) for the treatment of atherosclerotic carotid stenosis, particularly since the publication of the Carotid Revascularization Endarterectomy versus Stent Trial (CREST) in 2010. In the CREST, as in most other randomized controlled trials and large case series, the standard technical protocols include the use of embolic protection devices (EPDs), self-expanding stents (SESs), and balloons pre- and postdilation. It has, however, been shown that EPDs do not catch all debris generated by balloons and that these expensive devices may cause complications themselves.10 Every pass of a device through an atherosclerotic stenosis generates distal emboli.23,31 Balloon angioplasty, both before and after stent insertion, releases significant amounts of embolic debris20,24,26,28,33 and often results in significant hemodynamic instability, defined as bradycardia (< 60 beats/min) and hypotension (systolic blood pressure < 90 mm Hg).27 Some major centers now rarely perform pre-stent balloon angioplasty, deliberately undersize poststent...
angioplasty balloons, or completely omit poststenent angioplasty to decrease the potential for embolic events and hemodynamic depression.\textsuperscript{11,23,27}

In an attempt to lessen the technical complexity, risks, and cost of CAS, several groups have shown that the procedure can be performed safely in the majority of cases without the use of EPDs and balloon angioplasty.\textsuperscript{3,6,17,18} Our group has shown that primary carotid stenting (PCS) performed using SESs alone can be successful in treating more than 80% of patients with severe, symptomatic carotid stenosis who are ineligible for endarterectomy.\textsuperscript{6,18} Potential drawbacks of this balloonless approach include inadequate intraprocedural arterial expansion and early restenosis.

During our review of case material, it became apparent that the morphological appearance of carotid plaque on CT angiography (CTA) was an important predictor of SES expansion and the angiographic success of PCS. It could also help to determine whether the use of balloons and EPDs would be necessary to achieve a satisfactory angiographic result. We found that the amounts of calcification and “soft” or uncalcified plaque at the site of maximal stenosis are important predictors of whether the SES alone can satisfactorily dilate the stenosis in both the short and long term. We therefore undertook a detailed analysis of the CTA morphology of the carotid plaques in our patients undergoing CAS to develop a rating scale (which we have labeled the “PLAC Scale”): Predicting Long-term outcome with Angioplasty of the Carotid artery) to both predict the long-term imaging success of CAS and to help guide the subsequent technical performance of the procedure.

**Methods**

At our center, CAS is reserved for patients with severe (> 70% by North American Symptomatic Carotid Endarterectomy Trial [NASCET] criteria), symptomatic stenosis who are ineligible for endarterectomy due to medical comorbidities, prior neck radiation therapy, or prior CEA with restenosis. Our current practice is to perform CTA on all potential CAS candidates, although earlier in our experience we treated patients on the basis of duplex carotid ultrasound and MR angiography imaging, without a preoperative CTA. We treated 181 patients between March 2000 and February 2011. Our technical and imaging follow-up protocols for CAS have been published previously.\textsuperscript{6,18}

We use an 8 × 40-mm SES to ensure good plaque coverage and maximal chronic outward force on the stenotic area. Our preference is to avoid the use of EPDs and balloons whenever the plaque morphology appears favorable on preoperative CTA. A calcification scale based on CTA axial source images at the site of maximal stenosis, modified from existing scales of intracranial carotid calcification,\textsuperscript{1} is used to assess the degree of plaque calcification (Table 1). This 5-point scale includes the following grades: Grade 0, indicating absence of calcification; Grade 1, indicating involvement of < 25% of vessel circumference; Grade 2, indicating 25%–50% of vessel circumference; Grade 3, indicating 50%–75% of vessel circumference; and Grade 4, indicating complete circumferential plaque calcification (Fig. 1). Thickness and continuity of calcification are also assessed. “Soft” plaque is defined as non-calcified plaque on CTA source images. The amount of soft plaque is characterized as either moderate (≥ 2 mm) or minimal (< 2 mm). The presence (Grade A) or absence (Grade B) of moderate amounts of soft plaque at the level of maximal stenosis is determined (Fig. 2). The PLAC score is the combination of soft plaque status and calcification grade (i.e., A1).

Prospective and retrospective grading was performed by 2 of the authors (D.M.P. and S.P.L.) on an individual basis, with discrepancies resolved by consensus. Both authors were involved in some of the interventions.

Duplex carotid ultrasound examinations, including peak systolic velocity (PSV) and internal carotid artery/common carotid artery velocity ratio measurements, are performed prior to and immediately following the procedure. These are subsequently repeated at 1 week, 4 months, 1 year, and annually thereafter. Long-term PSV outcome of < 120 cm/s (normal or < 50% residual stenosis by NASCET criteria) and internal carotid artery/common carotid artery ratio < 1.4 are defined as acceptable. A successful outcome is defined as an acceptable long-term PSV and absence of recurrent ipsilateral neurological symptoms. Restenosis is defined as PSV > 230 cm/s (> 70% by NASCET criteria\textsuperscript{15}).

Associations between treatment and prognostic factors and stroke, restenosis, and morphological outcome were evaluated using unpaired t-tests for continuous factors and either chi-square tests or, where appropriate, Fisher’s exact test for categorical variables. Univariate analysis was followed by multivariate analysis of significant variables. Probability values less than 0.05 were considered to be statistically significant. Statistical software (SAS version 9.3) was used to analyze the data. Analysis was performed by an independent biostatistician (L. Stitt).

### Results

One hundred eighty-one consecutive patients who underwent CAS were available for analysis. Of these, CTA was performed prior to CAS in 102 patients and formed the basis for our study of plaque morphology. The mean age was 72 years (range 48–91 years). There were 87 patients (85%) who underwent PCS, whereas 15 patients (15%) underwent CAS with balloons. The latter patients were either enrolled in the CREST trial or had an unsatisfactory intraoperative angiographic result with PCS. An EPD was used in 19 patients (19%).

All patients presented with either ipsilateral stroke or transient ischemic attacks. There were 3 who had received prior neck radiation and 9 who had undergone prior ipsilateral CEA. The remainder had multiple medical comorbidities precluding CEA, including coronary artery and

<table>
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<th>Table 1. The PLAC Scale</th>
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<tr>
<td><strong>Calcification Grade (% vessel circumference affected)</strong></td>
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<tr>
<td></td>
</tr>
<tr>
<td><strong>Grade 0</strong></td>
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chronic respiratory disease, diabetes, hyperlipidemia, and combined hypertension and diabetes.

The mean preprocedural PSV in these patients was 405 cm/s. The average diameter stenosis was 1.3 mm, and the average NASCET stenosis was 78%.

For the PLAC score, intraclass correlation coefficients and weighted kappa coefficients were used to determine the intraobserver reliabilities in 25 cases, assuming random times of assessments. For calcium grade the intraclass correlation coefficient was 83% (95% CI 0.65–0.92), indicating very good reliability. The kappa coefficient was 0.64 (95% CI 0.46–0.82), indicating good reliability. For calcium thickness, and for the presence or absence of moderate soft plaque, kappa coefficients were 0.40 and 0.61, respectively, indicating fair to good reliability.

The calcification grade was distributed as follows: 17% were Grade 0; 15% were Grade 1; 19% were Grade 2; 33% were Grade 3; and 16% were Grade 4. Approximately half of the plaques were therefore Grade 3 or 4. Thirty percent had thick plaque calcification. Soft plaque in any amount was observed in 86%, while in 74% soft plaque was present to a moderate degree.

Overall incidence of any periprocedural 30-day stroke or death was 5.9%. The 30-day major stroke or death rate was 2%. In terms of plaque characteristics and incidence of stroke, there was no relationship to plaque calcification, although there was a trend toward an association with Grade 2, 3, or 4 versus Grade 0 or 1 plaques (p = 0.076). There was no association with the severity of stenosis (p = 0.885) or the use of balloons (p = 0.470).

The average ultrasound follow-up was 29.7 months (range 0.3–87 months). Results showed PSV under 200 cm/s in 80 of 102 patients (78%). Of these, 52% were less than 110 cm/s, 5% were between 110 and 120 cm/s, and 26% were between 120 and 199 cm/s.

Significantly fewer patients with Grade 3 or 4 calcification attained a PSV < 120 cm/s versus those with Grade 0, 1, or 2 plaques (19 of 50 [38%] vs 39 of 52 [75%], p < 0.001, Table 2). The same was true of thick calcification: only 25% (8 of 31) of thickly calcified plaques improved to PSV < 120 cm/s versus 70% (50 of 71) of thinly calcified ones (p < 0.001). With respect to soft plaque, the presence of any soft plaque, but particularly to a moderate or high degree, was significantly greater in patients who attained a PSV < 120 cm/s than in those who did not (50 of 74 [68%] vs 8 of 28 [29%], p < 0.001). Multivariate logistic regression confirmed calcium grade, calcium thickness, and the presence of moderate to large amounts of soft plaque as independent significant variables. However, neither the presence of soft plaque (minimal or moderate in amount), nor the degree of continuity of the calcification surrounding the lumen entered the regression equation.

FIG. 1. Axial source images from CTA of carotid bifurcation stenosis. Examples of calcium grade. A: Grade 0 on the left (arrow). B: Grade 1 on the right (arrow). C: Grade 2 on the left (arrow). D: Grade 3 on the right (arrow). E: Grade 4 on the right (arrow).
When the 15 patients who underwent balloon angioplasty were excluded from the analysis, the results were the same as in the entire CAS cohort. Calcification Grade 3 or 4 (p = 0.003) and calcification thickness (p < 0.001) were both significant predictors of unsatisfactory morphological outcome. The presence of soft plaque and lower grades of calcification were positively predictive of a satisfactory morphological outcome.

The restenosis rate at 2 years was 11.8% (Table 3). Plaque calcification was found to have an association: 10 of 50 (20%) of highly calcified Grade 3 or 4 plaques developed restenosis, whereas only 4% of less calcified or noncalcified plaques restenosed.

The predictive value of individual PLAC scores for satisfactory morphological outcome of PSV < 120 cm/s is shown in Table 4. The presence of soft plaque and lower grades of calcification were positively predictive of a satisfactory morphological outcome.

**Discussion**

Diagnostic evaluation of cervical carotid atherosclerosis has evolved from catheter-based angiography to less invasive modalities such as ultrasound, CT, and MRI. Not only can stenosis be measured, but carotid plaque can also be characterized. Plaque morphology on CTA has been correlated with histopathological findings in postendarterectomy surgical specimens to identify “vulnerable” or unstable plaque, which is most likely to cause symptoms. Only 1 paper classified calcification into definite shapes and thicknesses and posited a relationship to expansion of intravascular balloons and stents. Recent investigations have used MRI to more accurately detect lipid content, plaque hemorrhage, necrosis, ulceration, and thin fibrous cap to identify unstable plaque. The CTA modality with modern, multislice scanners is excellent for localization and quantification of calcification, and the relationship to internal architecture, ulceration, and prediction of “vulnerability” is becoming clear. Although the CT calcification grade is known to predict the expansion of coronary stents and has been suggested to be a relative contraindication to CAS, few investigators use plaque morphology to help guide the choice of treatment or to predict the immediate or long-term morphological success of CAS procedures.

This study has shown that high-grade plaque calcification (Grade 3 or 4) is a very significant factor determining the long-term morphological outcome of CAS (p < 0.001) when either PCS or standard balloon techniques are used. The presence of moderate amounts of soft plaque (p < 0.001) and the presence of thick calcification (p < 0.001) are also significant factors. High-grade calcification...
calcification is a significant predictor of subsequent restenosis (p = 0.011).

Primary carotid stenting has in our experience proven to be a safe, efficient, and less complicated method to treat the majority of symptomatic patients with severe carotid stenosis.6,18 This procedure is particularly effective for the treatment of postendarterectomy restenosis,7 and, due to the avoidance of balloon angioplasty, it results in less hemodynamic instability.5 Although progressive SES expansion can be seen up to 6 months postprocedure,9 our results show that PCS is less likely to give a satisfactory long-term result in the presence of significant plaque calcification and the absence of soft plaque (PLAC score of B3 or 4). We believe that abundant calcification and the absence of soft, compressible plaque opposes the outward force of the SES and prevents satisfactory short- and long-term stent expansion.34 In our experience, this phenomenon was also observed when balloon angioplasty was used.

Our current practice is to assess the degree of calcification and soft plaque status on axial CTA source images in all patients who may undergo CAS. If the calcification grade is low (0–2) and soft plaque is present (Grade A; i.e., a PLAC score of A0, A1, or A2), we will proceed with the intent to perform PCS. If the calcification grade is high (3–4) and soft plaque is absent (Grade B; i.e., a PLAC score of B3 or B4), we will perform CAS with the intent to perform PCS. If the calcification grade is low (0–2) and soft plaque is present (Grade A; i.e., a PLAC score of A0, A1, or A2), we will proceed

<table>
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<th>Characteristic</th>
<th>Restenosis: PSV &gt;230 cm/s</th>
<th>p Value</th>
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<tbody>
<tr>
<td>No. of patients</td>
<td>90</td>
<td>12</td>
</tr>
<tr>
<td>Preop PSV in cm/s</td>
<td>402</td>
<td>430</td>
</tr>
<tr>
<td>Mean stenosis in mm</td>
<td>1.31</td>
<td>1.22</td>
</tr>
<tr>
<td>Stent used alone</td>
<td>86.7%</td>
<td>75%</td>
</tr>
<tr>
<td>Balloon used prestent</td>
<td>8.9%</td>
<td>16.7%</td>
</tr>
<tr>
<td>Balloon used poststent</td>
<td>5.6%</td>
<td>8.3%</td>
</tr>
<tr>
<td>Calcification Grade 3 or 4</td>
<td>44.4%</td>
<td>83.3%</td>
</tr>
<tr>
<td>Moderate amount of soft plaque</td>
<td>76.1%</td>
<td>58.3%</td>
</tr>
</tbody>
</table>

* Log-transformed to improve normality.

Conclusions

Long-term morphological outcome of PCS may be predicted with considerable accuracy by using the PLAC Scale, a simple assessment tool involving calcium grading and the observation of soft plaque on diagnostic, preprocedural CTA imaging. Use of this scale can also help to determine whether PCS is a feasible alternative to traditional CAS techniques in which EPDs and balloon angioplasty are used.

Acknowledgments

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References


<table>
<thead>
<tr>
<th>PLAC Scale</th>
<th>PSV &lt;120 cm/s</th>
<th>PSV ≥120 cm/s</th>
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<tbody>
<tr>
<td>A0</td>
<td>14 (93%)</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>B0</td>
<td>1 (50%)</td>
<td>1 (50%)</td>
</tr>
<tr>
<td>A1</td>
<td>10 (67%)</td>
<td>5 (33%)</td>
</tr>
<tr>
<td>B1</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>A2</td>
<td>14 (70%)</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>B2</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>A3</td>
<td>14 (48%)</td>
<td>15 (52%)</td>
</tr>
<tr>
<td>B3</td>
<td>1 (20%)</td>
<td>4 (80%)</td>
</tr>
<tr>
<td>A4</td>
<td>3 (33%)</td>
<td>6 (66%)</td>
</tr>
<tr>
<td>B4</td>
<td>1 (14%)</td>
<td>6 (86%)</td>
</tr>
<tr>
<td>Total no. of patients</td>
<td>58</td>
<td>44</td>
</tr>
<tr>
<td>Composite A3 &amp; A4</td>
<td>17 (45%)</td>
<td>21 (55%)</td>
</tr>
<tr>
<td>Composite B3 &amp; B4</td>
<td>2 (17%)</td>
<td>10 (83%)</td>
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* Except for the total patients, values are expressed as the frequency (%).
22. Niwa Y, Katano H, Yamada K: Calcification in carotid ath-
39. Niwa Y, Katano H, Yamada K: Calcification in carotid ath-
40. The PLAC Scale
41. Author Contributions
Conception and design: Pelz, Lownie. Acquisition of data: Pelz, Lownie, Lee. Analysis and interpretation of data: Pelz, Lownie. Drafting the article: Pelz, Lownie. Critically revising the article: Lee, Boullon.
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