Intracranial Large Vessel Occlusion as a Predictor of Decline in Functional Status After Transient Ischemic Attack

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Background and Purpose—Clinical scores help predict outcome after transient ischemic attack (TIA), and imaging studies may improve the accuracy of predictions. Intracranial large vessel occlusion (LVO) predicts poor outcome after stroke, but the natural history of symptomatic intracranial LVO in patients with TIA is unknown.

Methods—We studied patients presenting with TIA in the STOP Stroke Study, a prospective imaging-based study of stroke outcomes. All patients underwent brain CTA. If an intracranial vascular occlusion was found in an appropriate territory to account for clinical findings, then it was judged to be a symptomatic LVO. Baseline characteristics, follow-up events, and outcomes were collected. Characteristics of patients with and without LVO were compared using χ² and t tests. Predictors of LVO were analyzed by univariate and multivariate analysis. LVO was assessed as a predictor of asymptomatic outcome (modified Rankin scale [mRS] score, 0), poor outcome (mRS score ≥3), and increase in mRS score over the study period.

Results—Of 97 patients with TIA, 13 (13%) had symptomatic intracranial LVO. Patients with LVO had higher baseline NIHSS on emergency department arrival, which was an independent predictor of LVO (OR, 1.15 per point; 95% CI, 1.02–1.29; P=0.02). Patients with LVO were more likely to have an increase in mRS score during the 90-day follow-up (P=0.03). LVO independently predicted an increase in mRS score (OR, 4.76; 95% CI, 1.23–18.43; P=0.02) and was a borderline predictor of poor outcome (mRS score ≥3; OR, 5.07; 95% CI, 0.92–28.03; P=0.06).

Conclusions—LVO is found in >1 in 10 patients presenting with TIA and predicts a decline in functional status, likely attributable to new brain ischemia. (Stroke. 2011;42:44-47.)

Key Words: intracranial arterial diseases ■ prognosis ■ transient ischemic attack

Patients with transient ischemic attack (TIA) are known to be at high risk for stroke in the days, weeks, and months after their initial event, with frequencies of 10% to 20% within the first 3 months.1–3 Clinical scores predict outcome after TIA with some success,4,5 and imaging studies have shown promise in improving the accuracy of predictions.6–10 Intracranial large vessel occlusions account for a large number of acute ischemic strokes and predict poor outcome after stroke and in combined groups of TIA and minor stroke.7,11 The natural history of symptomatic large vessel occlusion that does not result in stroke, however, has not been well-described.

In this study, we evaluated the frequency of intracranial large vessel occlusion on CT angiogram among patients presenting with TIA to large academic medical centers and its relationship to neurological and functional outcomes. We hypothesized that intracranial large vessel occlusions causing TIA would be predictors of poor outcome.

Materials and Methods

The Screening Technology and Outcomes Project in Stroke (STOP Stroke) Study is a prospective, imaging-based study of stroke outcomes completed at 2 urban, academic medical centers. Consecutive patients with suspected acute stroke or TIA who presented within 24 hours of symptom onset to the institutions’ emergency departments and who underwent multi-modality CT/CTA were approached for consent for 6-month follow-up and collection of clinical data. Both institutions routinely used this technology to image all suspected stroke or TIA during the study period unless contraindications to intravenous contrast existed. Surrogate consent was allowed for patients unable to consent for themselves. Patients consented by surrogate were reconsented for follow-up if they had regained capacity. Patients were excluded if iodinated contrast agent administration was contraindicated (ie, history of allergy, pregnancy, congestive heart failure, increased creatinine) or if there was non-contrast CT evidence of intracranial hemorrhage. The Institutional Review Boards of both institutions approved this clinical study.

Research coordinators for both sites extracted demographic data and data regarding the acute presentation and hospital course, and performed 6-month phone follow-up for all patients. All clinical data available through the acute hospitalization, including imaging data, were presented to an independent stroke neurologist who then ascribed the final diagnosis for the patient as stroke, TIA or not stroke, or TIA. TIA was defined as a sudden, focal neurological deficit lasting <24 hours, presumed to be of vascular origin, and confined to an area of the brain or eye perfused by a specific artery. Because the diagnoses were ascribed after all information had been...
collected, some patients presenting with a nonzero NIHSS score had resolution of their symptoms within 24 hours and therefore were classified as having TIA. Only cases categorized as TIA were analyzed as part of this study (2 cases of pure transient monocular blindness were not considered as TIA in this analysis). Asymptomatic outcome was defined as a modified Rankin scale (mRS) score of 0 measured at 6 months after the stroke and bad outcome was defined as mRS score of ≥3.

All patients underwent brain CT imaging at 5-mm section thickness, CTA at 2.5-mm increments from the aortic arch through the circle of Willis and after contrast CT imaging. CT angiograms were reconstructed as “thick maximum intensity projection” reconstructions. Both thick maximum intensity projection reconstructions and CT source images were reviewed by 2 neuroradiologists blinded to clinical outcome. Cerebrovascular vessels were divided into segments including supraclinoid internal carotid artery, first division middle cerebral artery (M1), second division middle cerebral artery (M2), first division anterior cerebral artery (A1), second division anterior cerebral artery (A2), basilar artery, intracranial vertebral artery, first division posterior cerebral artery (P1), and second division posterior cerebral artery (P2). A neuroradiologist determined whether any of these vascular segments was occluded. If this analysis showed no vascular occlusion, then the patient was documented as having no large vessel occlusion. If ≥1 vascular segments were occluded, then the case history and NIHSS score were reviewed, and if the vascular occlusion was in the appropriate territory to account for the clinical findings, then the case was classified as having a large vessel occlusion. Otherwise, if the vascular segment occlusion did not explain the clinical symptoms, then the case was classified as not having a large vessel occlusion.

Baseline demographics, medical history, medication history, type of presentation, functional outcomes, recurrent stroke, and functional outcomes were compared between subjects with and without large vessel occlusion (LVO) using χ² tests for nominal variables and t tests for continuous variables. Predictors of LVO were analyzed by univariate and then multivariate modeling using Stata version 10. Multivariate modeling included any variable found to have P < 0.20 in univariate testing with stepwise elimination by highest probability value and variables retained with P < 0.05. LVO was tested as a predictor of asymptomatic outcome (mRS score 0), poor outcome (mRS score ≥3), and increase in mRS over the study period. These models were adjusted for age, gender, ethnicity/race, and presenting NIHSS score. Therapies administered during hospitalization and secondary stroke prophylaxis were not included because the goal of the model was to best-understand prognosis based on initial presenting signs and symptoms.

**Results**

Over a 33-month period, 1626 patients were admitted to the study hospitals with presumed stroke or TIA, and 741 were enrolled in the STOP Stroke study. After review of all clinical and laboratory data, 97 (13%) of these patients were adjudicated as TIA. Of these patients, 43 (19.1%) presented with a NIHSS score of 0.

Thirteen (13%) of the patients with TIA were found to have an intracranial LVO in an appropriate territory to explain their clinical findings. Four patients (4.1%) had an asymptomatic LVO, 1 of whom also had a symptomatic LVO. Demographics, presenting symptoms, TIA etiology, and medical history in the groups with and without LVO are summarized in Table 1. The group with LVO presented with a higher NIHSS score, but there were no significant differences. Of the patients presenting with NIHSS score of 0, 9.3% had LVO whereas 16.7% of those with NIHSS ≥1 had LVO (P = 0.29). Acute NIHSS score was found to be an independent predictor of LVO after controlling for other presenting factors (OR, 1.15; 95% CI, 1.02–1.29; P = 0.02). There were no other independent predictors of LVO.

The mean delay between symptom onset and time of initial CT scan was 360 minutes ±377 minutes. There was a trend toward shorter time to imaging among the group with LVO vs those without LVO (173 vs 390 minutes; P = 0.09). Only 2 patients with TIA were treated with intravenous tissue plasminogen activator.
minogen activator acutely, 1 with LVO and 1 without. Although follow-up imaging was not required as part of STOP Stroke, 26% of patients with TIA in the study did have follow-up studies (21% with MRI, 5% with CT), and follow-up imaging was more frequent among patients presenting with LVO (54% vs 21%; \( P = 0.01 \)). Of those who did have follow-up imaging, 100% of those with LVO and 72% of those without LVO had an infarct (\( P = 0.12 \)).

Comparisons of outcomes between the groups with and without LVO are summarized in Table 2. Of the patients with new infarcts during hospitalization, none was in the group with LVO, but this difference was not significant. No patients with LVO had any recorded in-hospital complications, whereas 8 patients without LVO had complications (1 myocardial infarction, 2 urinary tract infections, others unknown; \( P = 0.23 \)). However, patients with LVO were more likely to have an increase in mRS score \( (P = 0.03) \). Asymptomatic outcome was more frequent among patients presenting with LVO than those without \( (P = 0.07) \), whereas 8 patients without LVO had complications (1 myocardial infarction, 2 urinary tract infections, others unknown; \( P = 0.23 \)). Although mRS score before admission was not different between the 2 groups \( (0.23 \text{ vs } 0.44; \ P = 0.40) \), at discharge there was a trend toward poorer mRS score in patients with LVO, but this did not reach significance.

Rehospitalization status was available for 65 patients, of whom 19 (29%) were rehospitalized within the 90-day follow up period, and frequency did not differ between the 2 groups. For 16 of the patients rehospitalized, reasons for hospitalization were falls, infection, patent foramen ovale, stroke, TIA, and other. There were no differences between the groups in reasons for rehospitalizations \( (P = 0.8) \). Two patients without LVO were rehospitalized for stroke and 1 was rehospitalized for TIA, whereas none in the group with LVO was rehospitalized for stroke or TIA. There was no difference in the number of patients using antiplatelet medications, statins, or warfarin at follow-up, and there was no difference in the number of patients who stopped using these medications between discharge and follow-up \( (all \ P > 0.1) \).

Follow-up mRS was available for 82 of the 97 patients \((85\%)\). There were no differences in the presenting symptoms or the medical history between patients who did and did not have follow-up mRS \( (all \ P > 0.10) \). The missing follow-up data were for 13 of the patients in the group without LVO \((15\%\)\) and 2 of the patients with LVO \((15\%; \ P = 0.99)\).

Among the patients with complete follow-up data, patients with LVO were more likely to have an increase in mRS score over the study period than those without LVO \((64\% \text{ vs } 24\%; \ P = 0.01)\). There was no difference in the likelihood of asymptomatic outcome at 90 days between patients with and without LVO, but there was a trend toward higher likelihood of bad outcome \((\text{mRS score } \geq 3)\) for those with LVO. There was no significant difference in the frequency of mRS worsening after discharge \((38.5\% \text{ vs } 30.9\%; \ P = 0.59)\). In addition, of the patients with follow-up imaging, there was no difference in the frequency of mRS score increase during hospitalization \((P = 0.52)\) or over the 90-day follow-up period \((P = 0.31)\).

LVO was an independent predictor of decline in functional status \((\text{increase in mRS score})\) and a borderline significant predictor of poor outcome \((\text{mRS score } \geq 3)\) after adjusting for age, gender, and presenting NIHSS \( (\text{Table 3})\). LVO did not predict rehospitalization \((OR, 1.89; 95\% \text{ CI}, 0.46–7.76; \ P = 0.38)\).

### Discussion

We found intracranial large vessel occlusions in the territory of ischemia in 13% of patients presenting with TIA. Considering the 200 000 to 500 000 TIA diagnosed yearly in the United States,\(^\text{12}\) LVO may be responsible for 26 000 to 65 000 TIA yearly. It appears that LVO predicts a decline in functional status after TIA and a worse overall outcome, and may be a useful addition to clinical tools utilized to predict outcome.

We are unable to clearly define the reason for poor outcome in patients with LVO presenting with TIA. Patients with LVO do appear to present earlier than those without LVO, possibly indicating that the occlusion may resolve over time and early imaging increases the chance of its detection. They are also more likely to follow-up imaging performed, but it is difficult to interpret the results based on our limited sample size. The differences in timing of initial imaging and likelihood of follow-up imaging do not explain the difference in functional status at follow-up. It appears that these patients have similar functional status before their event as those without LVO, but there is a trend toward a worsening of functional status during their hospitalization. Based on our data, this in-hospital worsening is not clearly justified by recurrent stroke or other hospital complications. Disparities in secondary stroke prophylaxis treatment or medication compliance could explain the difference in outcomes, but this does not appear to be the case in our study population. We are also unable to explain the differences in outcome based on rehospitalizations after discharge, although our follow-up data are somewhat limited.

Other studies evaluating the prognostic significance of intracranial LVO have focused mainly on its significance in patients presenting with stroke or have combined the outcomes in TIA and stroke.\(^\text{7,11,13}\) LVO is present in 28% to 46% of patients presenting with stroke and is a predictor of poor neurological outcome at hospital discharge and poor outcome and mortality at...
In addition, in a group of patients presenting with TIA and minor stroke, intracranial LVO on MRA predicted recurrent stroke as well as functional impairment at 90 days. There is little other evidence for the natural history of intracranial LVO, specifically in patients with clinical TIA.

From a pathophysiological standpoint, it is somewhat surprising that patients with LVO can present with TIA, because the resolution of symptoms implies that little to no infarct has occurred. Some of the patients identified in this study with TIA and LVO may have had pre-existing LVO with flow-related TIA, but presumably some of these were de novo LVO. This study is one of the first to show this occurrence.

Because no neurological deficit persists, LVO associated with TIA may represent a different process than LVO associated with stroke. Inadequate collateral recruitment is associated with decline in neurological status among patients presenting with middle cerebral artery occlusion and acute ischemia. The presence of good collateral circulation is also associated with low risk of infarct expansion and better prognosis after stroke. Similarly, one could postulate that patients with intracranial LVO presenting with TIA are more likely than those with stroke to have adequate collateral circulation, accounting for their ability to regain all function.

Despite their likely better collateral circulation, however, it does appear that LVO is a marker of poorer outcomes after TIA. It is not clear from this study whether the poorer outcomes among patients found to have LVO are related to recurrent strokes in the territory of the vessel occlusion. In fact, none of the patients with LVO had strokes during the initial hospital admission, and there was no difference in rehospitalization rate among those with and without LVO. LVO in these cases therefore may be a marker of more diffuse vascular disease.

This study has several limitations. The goal of the STOP Stroke study was to evaluate CTA findings in patients with acute ischemic stroke and, therefore, patients with TIA were a small part of the study. In addition, follow-up data are missing for 15% of the patients. It may be somewhat controversial that NIHSS score was not 0 in all of the patients with TIA diagnosed and, in fact, this was a predictor of LVO. However, all patients presenting with TIA or stroke were enrolled in the study, and clinical data were later reviewed by a neurologist who adjudicated the final diagnosis. Some of the patients with TIA diagnosed presented with continuing symptoms that subsequently resolved during the first 24 hours. This finding suggests that patients with LVO present with more severe symptoms than those without LVO. In addition, follow-up data are missing for 13% of our subjects, also reflecting the small role of patients with TIA in this study. The follow-up data that we do have are limited, and we have to rely on functional scores rather than other clinical outcomes. We do have information regarding rehospitalizations and reasons for rehospitalization, but other than this information we do not have data regarding recurrent strokes among our population.

Despite the shortcomings of this study, it offers a first look at the significance of LVO in patients presenting with TIA, which has not been well-described previously. We chose to include variables in our models that reflect a patient’s status at the time of presentation (demographics, NIHSS score, symptoms, and CTA findings) because this is the most crucial time for a prediction tool to help in counseling patients and making treatment decisions. Therefore, we did not analyze the effect of other secondary stroke-preventative treatments. Ideally, we would have liked to add intracranial LVO to a clinical predictor model, such as the ABCD² score, to assess its additive effect on prognostication. Because STOP Stroke was not designed specifically to evaluate patients with TIA, all of the information for this analysis was not available and another study is required.

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### Disclosures

None.

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