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# Impact of acute cerebral ischemic lesions and their volume on the revascularization outcome of symptomatic carotid stenosis

Rodolfo Pini, MD, Gianluca Faggioli, MD, Matteo Longhi, MD, Liborio Ferrante, MD, Andrea Vacirca, MD, Enrico Gallitto, MD, Mauro Gargiulo, MD, *and* Andrea Stella, MD, *Bologna, Italy*

## ABSTRACT

**Background:** The influence of acute cerebral ischemic lesions (CILs) on the revascularization outcome of symptomatic carotid stenosis has been scarcely investigated in the literature. This study evaluated the effect of CILs and their volume on the results of carotid revascularization in symptomatic patients.

**Methods:** All patients with symptomatic carotid artery stenosis who underwent carotid endarterectomy (CEA) or carotid artery stenting (CAS) between 2005 and 2014 were considered. CILs ipsilateral to the stenosis were identified in the preoperative cerebral computed tomography. The volume was quantified in $mm^3$ and correlated with 30-day rates of stroke and stroke/death by $\chi^2$, multivariate analysis, Pearson correlation, and receiver operating characteristic curves.

**Results:** A total of 489 symptomatic patients were treated by CEA (327 [67%]) or CAS (162 [33%]), 186 (38%) ≤2 weeks and 303 (62%) >2 weeks from symptom onset. CEA and CAS patients had statistically similar rates of stroke (3.3% vs 5.5%; $P = .27$) and stroke/death (3.8% vs 5.9%; $P = .22$). CILs were identified in 251 patients (53%) and were associated with similar stroke and stroke/death rate compared with patients without CIL (12 [4.8%] vs 8 [3.5%], $P = .46$; and 14 [5.6%] vs 8 [3.5%]; $P = .26$, respectively). The median CIL volume was 1000 $mm^3$ (interquartile range [IQR], 7000 $mm^3$). Patients with postoperative stroke and stroke/death had a significantly higher preoperative CIL volume of 5100 $mm^3$ (IQR, 31,000 $mm^3$) vs 1000 $mm^3$ (IQR, 7000 $mm^3$; $P = .01$) and 4500 $mm^3$ (IQR, 17,450 $mm^3$) vs 1000 $mm^3$ (IQR, 7000 $mm^3$; $P = .03$), respectively. The receiver operating characteristic curve analysis showed a volume of 4000 $mm^3$ was predictive of postoperative stroke with 75% sensitivity and 63% specificity. A CIL volume ≥4000 $mm^3$ was an independent risk factor for postoperative stroke, with a stroke rate of 9.3% (n = 9) vs 1.9% (n = 3) for a CIL volume of <4000 $mm^3$ (odds ratio, 4.6; 95% confidence interval, 1.1-19.1; $P = .03$).

**Conclusions:** CIL volume in symptomatic carotid stenosis seems to influence the 30-day outcome independently from the timing of carotid revascularization. A CIL volume of ≥4000 $mm^3$ could be considered a significant predictor for postoperative stroke after carotid revascularization. (J Vasc Surg 2016;■:1-8.)

Recent guidelines and reviews have emphasized the importance of a prompt carotid revascularization for symptomatic stenosis.[1,2] To achieve the greatest benefit for the prevention of neurologic recurrences, the carotid revascularization should be performed ≤2 weeks after the first event.[3] One of the concerns of an expedited carotid revascularization is the potential increase of postoperative complications in some subgroups of patients. The recent review by De Rango et al[4] showed that rather than the timing of revascularization, the type of preoperative symptoms—transient ischemic attack (TIA) vs stroke—could influence the postoperative incidence of complications. Carotid revascularization performed ≤2 weeks after a TIA was associated with a postoperative complication rate as low as 1.6%, whereas patients who underwent revascularization after a stroke encountered a significantly higher risk of major complications (5.0%).

Possible causes for this difference are the presence of an ischemic penumbra or an impaired cerebrovascular reactivity after the stroke, with enlargement of the ischemic area or its hemorrhagic transformation after revascularization.[5,6] However, although the influence of clinical presentation has been well investigated in the literature, data on the effect of the size of the lesions seen at cerebral computed tomography (CT) are sparse. A CT scan is generally performed at the time of symptoms and after 24 to 48 hours in the clinical setting, but current guidelines do not address specifically the correlation among type and size of the acute cerebral ischemic lesion (CIL), timing of revascularization, and outcome.

From the Vascular Surgery, University of Bologna "Alma Mater Studiorum," Policlinico S. Orsola Malpighi.

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Correspondence: Gianluca Faggioli, MD, Vascular Surgery, University of Bologna, Policlinico S. Orsola-Malpighi, via Massarenti 9, Bologna 40138, Italy (e-mail: gianluca.faggioli@unibo.it).

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The aim of present study was therefore to investigate the influence of preoperative CILs and their volume on carotid revascularization outcome.

## METHODS

This study was performed according to the rules of the University of Bologna Ethical Review Board.

**Study design and setting.** Data for consecutive symptomatic patients who underwent carotid revascularization by endarterectomy (CEA) or carotid artery stenting (CAS) from January 2005 to December 2014 in a single academic center were prospectively entered into a dedicated database and reviewed. All patients gave their informed consent for the procedure.

The study end point was to compare the perioperative (30-day) stroke and death rates in patients with and without CIL who underwent carotid revascularization, according to type (CEA vs CAS) and timing (≤2 weeks and >2 weeks) of revascularization and to evaluate the effect of CIL volume on the postoperative outcome.

**Patients.** Carotid revascularization was performed for symptomatic carotid artery stenosis >50% (according to the North American Symptomatic Carotid Endarterectomy Trial Collaborators criteria) fulfilling the requirements of Society for Vascular Surgery guidelines.[1,7] Clinical characteristics, technical aspects, and perioperative (30-day) outcome were entered into a dedicated database. The clinical characteristics included age, sex, hypertension (systolic blood pressure >140 mm Hg or diastolic >90 mm Hg, or specific therapy), dyslipidemia (total cholesterol >200 mg/dL or low-density lipoprotein >120 mg/dL, or specific therapy), diabetes mellitus (prediagnosed in therapy with oral hypoglycemic drugs or with insulin), current smoking, coronary artery disease (defined as a history of angina pectoris, myocardial infarction or coronary revascularization), chronic obstructive pulmonary disease (defined as chronic bronchitis or emphysema), chronic renal failure (glomerular filtration rate <60 mL/min), contralateral carotid occlusion, and atrial fibrillation (paroxysmal or permanent). Perioperative medical therapy was also considered: specifically, therapy with one or two antiplatelet medications, statins, and oral anticoagulant therapy.

All patients had a preoperative cerebral CT scan evaluation at the time of the neurologic event and after 24 to 48 hours before carotid revascularization. A neurologic evaluation was performed before and after the carotid revascularization by an in-hospital neurologist. TIA was defined as temporary focal neurologic deficit with complete resolution ≤24 hours, and stroke was a focal neurologic deficit maintained for >24 hours.[7] The time elapsed from symptoms and carotid revascularization was determined by logistic issues and the presence of stable neurologic status (crescendo TIA and stroke in evolution were not considered in the present analysis), considering for an expedited revascularization patients with National Institutes of Health Stroke Scale[8] values <15 and stable cardiologic and respiratory clinical condition. In case of a hemorrhagic cerebral infarction, patients were monitored by cerebral CT evaluation, and the carotid revascularization was performed in case of hemorrhagic resolution and neurologic stability.

As previously described, all CEA procedures were performed by trained vascular surgeons, with the patient under general anesthesia, and with routine shunting and Dacron (DuPont, Wilmington, Del) patching.[9,10] CAS was selected, as previously reported, in patients at high cardiologic or respiratory risk or with a hostile neck if the preoperative CT angiography showed a normal arch anatomy.[11] The 30-day outcome considered was stroke (clinically evaluated by the neurologist) and death.

**Cerebral CT evaluation.** A cerebral CT scan was routinely performed at the time of symptoms and after 24 to 48 hours before carotid revascularization (multislice, 16-slice, GE Light Speed scanner; General Electric, Milwaukee, Wisc). Acute CIL was defined as an embolic lesion ipsilateral to the carotid target lesion by expert neuroradiologists.[12,13] The CIL volume was obtained retrospectively through multiplanar reconstructions, considering the three longer axes in the axial, coronal, and sagittal planes (example in Fig 1) and calculating the volume of the corresponding ellipsoid expressed in $mm^3$.

**Statistical analysis.** Continuous variables are expressed as means ± standard deviations and frequencies by percentages. Analyses of the differences between two groups were performed using $\chi^2$ or Fisher test, when appropriate, for categoric variables. The comparison of the CIL volume between patients with and without postoperative complication was performed by the Mann-Whitney *U* test, with data expressed as the median with the interquartile range (IQR). The investigation of CIL volume cutoff was performed by the evaluation of sensitivity and specificity of the receiver operating characteristic (ROC) curve by the Youden *J* statistic ($J$ = sensitivity + specificity − 1) to determine the optimal threshold. Multivariable analysis was performed to identify independent risk factors for stroke and stroke/death considering the significant ($P < .05$) or nearly significant ($P < .20$) risk factor for stroke and stroke/death at the univariable analysis (data not shown) and reported as the odds ratio (OR) and 95% confidence interval (CI) or with the evaluation of preselected characteristics (age, sex, type of revascularization, timing of revascularization, contralateral carotid occlusion, and selected volume of CIL). A $P \leq .05$ (two-tailed) was considered to be significant. The statistical tests were performed using SPSS 21.0 for Windows (IBM Corp, Armonk, NY).