Residual High-Grade Stenosis After Recanalization of Extracranial Carotid Occlusion in Acute Ischemic Stroke

Merel J.A. Luitse, MD; Birgitta K. Velthuis, MD; Meenakshi Dauwan, MD; Jan Willem Dankbaar, MD; Geert Jan Biessels, MD; L. Jaap Kappelle, MD; on behalf of the Dutch Acute Stroke Study Group*

Background and Purpose—Residual stenosis after recanalization of an acute symptomatic extracranial occlusion of the internal carotid artery (ICA) might be an indication for carotid endarterectomy. We evaluated the proportion of residual high-grade stenosis (≥70%, near occlusions not included) on follow-up imaging in a consecutive series of patients with an acute symptomatic occlusion of the extracranial ICA.

Methods—We included patients participating in the Dutch Acute Stroke Study (DUST), who had an acute symptomatic occlusion of the extracranial ICA that was diagnosed on computed tomographic angiography within 9 hours after onset of neurological symptoms. Follow-up imaging of the carotid artery had to be available within 7 days after admission.

Results—Of the 1021 patients participating in DUST between May 2009 and May 2013, an acute symptomatic occlusion of the extracranial ICA was found in 126 (12.3%) patients. Follow-up imaging was available in 86 (68.3%) of these patients. At follow-up, a residual stenosis of <30% was found in 15 (17.4%; 95% confidence interval, 10.8–26.9) patients, a 30% to 49% stenosis in 3 (3.5%; 95% confidence interval, 0.8–10.2) patients, a 50% to 69% stenosis in 2 (2.3%; 95% confidence interval, 0.1–8.6) patients, and a ≥70% stenosis in 14 (16.3%; 95% confidence interval, 9.8–25.6) patients. A near or persistent occlusion was present in the remaining 52 (60.5%) patients.

Conclusions—A residual high-grade stenosis of the extracranial ICA occurs in 1 of 6 patients with a symptomatic occlusion in the acute stage of cerebral ischemia. Because this may have implications for secondary prevention, we recommend follow-up imaging in these patients within a week after the event.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00880113. (Stroke. 2015;46:12-15. DOI: 10.1161/STROKEAHA.114.007169.)

Key Words: angiography, digital subtraction ▼ carotid stenosis ▼ stroke

Acute occlusion of the internal carotid artery (ICA) can lead to a large ischemic stroke with severe disability and poor prognosis in the long term.¹ Recanalization after an occlusion of the ICA in the acute stage may occur more commonly than previously assumed.² If a high-grade stenosis persists after recanalization, this may have important implications for subsequent treatment because the recurrence rate of ischemic stroke in patients with high-grade stenosis within 7 days is ≈8%.³,⁴ Carotid endarterectomy (CEA) has proven to be beneficial in patients with a ≥70% stenosis without near occlusions, and it is recommended within 2 weeks after the first symptoms.⁵-⁷

The combination of noncontrast computed tomography (CT), CT perfusion (CTP), and CT angiography (CTA) is increasingly used to determine the extent and severity of cerebral ischemia and to localize intracranial and extracranial vascular stenosis, occlusion, and recanalization in patients with acute ischemic stroke.⁸

The aim of our study was to determine the frequency of residual high-grade stenosis of ≥70% on follow-up imaging in patients with an acute symptomatic occlusion of the extracranial ICA.

Methods

Study Population

All patients participated in the multicenter prospective Dutch Acute Stroke Study (DUST) between May 2009 and May 2013. Inclusion criteria for the DUST were (1) clinical diagnosis of acute ischemic stroke, (2) noncontrast CT, CTP, and CTA examination performed within 9 hours of symptom onset, and (3) no known history of renal failure or allergy to contrast agents. Follow-up assessment with preferably noncontrast CT, CTA, and CTP was recommended within 3
days after stroke onset. Institutional review boards approved the trial, and written informed consent was obtained for each patient. Detailed information on the DUST has been described earlier.8

For the current study, we included patients with signs or symptoms that originated from an ischemic lesion in the supply territory of the ICA and a symptomatic occlusion of the extracranial ICA on the initial CTA. Furthermore, follow-up imaging of the carotid artery with CTA or alternatively magnetic resonance angiography (MRA), duplex ultrasound (DUS), or digital subtraction angiography (DSA) had to be available within 7 days after admission.

**Imaging Protocol**

The admission CT examination included noncontrast CT, CTP of the brain, and cervical and intracranial CTA. Detailed information on the CT imaging and analysis protocol has been described previously.9 The initial CTA and follow-up imaging (CTA, MRA, DUS, and DSA) were evaluated by a radiologist experienced in neurovascular imaging who was blinded for the clinical features. The carotid arteries were evaluated for the presence and degree of stenosis or occlusion on admission and follow-up imaging.

**Clinical Assessment**

Information was collected on the patients’ medical history of ischemic stroke or transient ischemic attack, vascular risk factors, and the use of antithrombotic medication. Stroke severity on admission was assessed by means of the National Institute of Health Stroke Scale and stroke subtype by means of the Trial of Org 10172 in Acute Stroke Treatment classification.10 Treatment categories included intravenous recombinant tissue-type plasminogen activator (r-tPA) and endovascular treatment (intra-arterial thrombolysis with r-tPA, mechanical clot disruption or retrieval, or a combination of these approaches). Clinical outcome at 3 months was assessed by means of the modified Rankin Scale.11 A Rankin score of 0 to 2 was defined as a good outcome and a score of 3 to 6 as a poor outcome.

Finally, information was collected on subsequent treatment as CEA or carotid stenting after the ischemic stroke.

**Outcome Measures**

The primary outcome measure was the proportion of patients with a residual high-grade stenosis on follow-up imaging who might be eligible for CEA or carotid artery stenting. A residual high-grade stenosis was defined as a stenosis of ≥70% excluding near occlusions.6,12 It was determined how many patients had complete or partial recanalization of the extracranial ICA on follow-up imaging and what the degree of residual stenosis was according to the following categories: (1) <30%, (2) 30% to 49%, (3) 50% to 69%, (4) ≥70%, (5) near occlusion, and (6) persistent occlusion.6,12 A near occlusion was defined as a severe stenosis with caliper reduction of the ICA distal to the stenosis.13,14 The categories were labeled for the different treatment types (eg, intravenous r-tPA, endovascular treatment, or conservative treatment).

**Statistical Analysis**

Statistical analyses were performed using IBM SPSS Statistics, version 20. Descriptive analysis was used to determine the frequency of occurrence of categories of residual stenosis with 95% confidence intervals (CIs) on follow-up imaging. Mean values were compared with ANOVA. Differences in proportions were evaluated by the Pearson χ² test. Differences at the level of P<0.05 were considered statistically significant. Finally, for the relationship between residual stenosis and outcome, odds ratios and the corresponding 95% CIs were calculated by means of logistic regression.

**Results**

From May 2009 to May 2013, 1021 patients were included in DUST. A symptomatic occlusion of the extracranial ICA was found in 126 (12.3%) patients. From these 126, 86 (68.3%) patients with adequate follow-up carotid imaging were included in the analysis. There were no differences in baseline characteristics between patients with and without adequate follow-up. The mean age was 63 (SD±12.9) years, and 74% of the patients were men (Table). The mean time between admission and follow-up imaging was 3.2 (SD±1.6) days. Follow-up imaging consisted of CTA in 83.7%, DUS in 9.3%, MRA in 3.5%, and DSA in 3.5% of the patients.

Forty-seven (54.7%) patients were treated with intravenous r-tPA and 11 (12.8%) patients underwent endovascular treatment. The baseline characteristics stratified for the different treatment modalities are presented in Table I in the online-only Data Supplement. The majority of ICA occlusions (76.7%) was considered to be caused by large artery atherosclerosis, whereas 16.3% was attributed to carotid dissection. Cardiac embolism and unknown cause each accounted for 3.5%.

In 34 (39.5%; 95% CI, 29.9–50.1) of the 86 patients, the occluded extracranial ICA was completely or partially recanalized at follow-up. Near occlusions were not included in this group. Characteristics of patients with a near or persistent occlusion (n=52) and patients with an open extracranial ICA at follow-up (n=34) are shown in Table. In the group with CTA follow-up only, the occluded carotid artery recanalized in 40.3%. For the remaining follow-up imaging modalities together, this was 35.7% (P=0.75).

The Figure shows the proportion of the residual stenosis according to the different categories. A residual stenosis of <30% occurred in 15 (17.4%; 95% CI, 10.8–26.9) patients; a 30% to 49% stenosis in 3 (3.5%; 95% CI, 0.8–10.2) patients; a 50% to 69% stenosis in 2 (2.3%; 95% CI, 0.1–8.6) patients;
a residual high-grade stenosis of ≥70% in 14 (16.3%; 95% CI, 9.8–25.6) patients; a near occlusion was found in 3 (3.5%; 95% CI, 0.8–10.2) patients, and a persistent occlusion in 49 (57.0%; 95% CI, 46.4–66.9) patients.

With regard to acute treatment, a residual high-grade stenosis of the extracranial ICA was found in 2 (7.1%; 95% CI, 0.9–23.7) of the 28 untreated patients and in 11 (23.4%; 95% CI, 13.5–37.4) of the 47 patients treated with intravenous r-tPA. In 1 (9.1%; 95% CI, −0.6 to 40.0) of the 11 patients with endovascular treatment, a residual high-grade stenosis was present, but this patient also underwent stenting of the occluded extracranial ICA during endovascular treatment.

Of the 14 patients with a residual high-grade stenosis, 8 were later treated with CEA. Two patients were diagnosed with carotid artery dissection and, therefore, they were not eligible for CEA. The 2 patients with a residual stenosis of 50% to 69% did not undergo CEA.

Good clinical outcome (modified Rankin Scale, ≤2) 3 months after stroke did not differ significantly in patients with either a residual high-grade stenosis (odds ratio, 2.1; 95% CI, 0.6–7.1; P=0.23) or patients with a residual stenosis <70% (odds ratio, 1.3; 95% CI, 0.5–3.7; P=0.64) compared with patients with a near or persistent occlusion.

Discussion

In 1 of 6 patients with an occlusion of the extracranial ICA in the acute stage of ischemic stroke, a residual high-grade stenosis remains after recanalization. Our findings have implications for secondary prevention because CEA or stenting might be indicated in a selected group of these patients.

The proportion of patients with ischemic stroke and acute carotid occlusion in our study concurs with findings in previous studies in which rates between 6% and 15% have been reported.12,15 Our recanalization rate of acute carotid occlusion (39.5%) also falls within the range (15.8%–62.5%) described in other studies.2,16–18 The rate of recanalization is dependent on several factors, such as the type of acute treatment and the segment affected.17,19

This is the first study with a prospective design on the occurrence of a residual high-grade stenosis after recanalization of an extracranial ICA occlusion in the acute stage of cerebral ischemia. One previous retrospective study showed that a high-grade stenosis remained in 13 (25%) of 52 patients with an acute occlusion.18 Two smaller studies reported a residual high-grade stenosis in 1 of 12 (8.3%) patients and 2 of 20 (10.0%) patients, respectively.2,16 More than half of the patients with a residual high-grade stenosis in our study population underwent CEA or carotid stenting. In addition, CEA could also be considered in patients with a residual stenosis of 50% to 69%.6 This emphasizes the importance of follow-up imaging of a carotid artery that is found to be occluded in the acute phase.

Our study has several strengths, including the prospective design, the use of a standardized CTA imaging protocol, and review of the imaging data, blinded to clinical findings. A possible limitation might be that the baseline and follow-up imaging were not performed in all patients with a carotid occlusion. This was because of a contraindication for iodinated contrast administration at the baseline of follow-up, early discharge of the patients, or no permission to perform a follow-up CTA. However, baseline characteristics did not differ between patients with and without follow-up imaging. Furthermore, DUST was designed as a diagnostic and prognostic observational study on the value of CTA and CTP in acute ischemic stroke. There was no standardized collection of recurrent strokes, additional therapeutic strategies, or outcome other than the modified Rankin Score. In addition, follow-up examinations consisted of 4 different modalities (CTA, MRA, DUS, and DSA). Although standardization of the follow-up imaging would have increased the validity of our study, previous
studies have shown that the accuracy of CTA is comparable with MRA, DSA, and DUS in grading carotid stenosis.\textsuperscript{20} In our study, we found no differences in recanalization of the occluded carotid artery between the group with CTA follow-up only and the other imaging modalities. Furthermore, follow-up imaging was not performed at standardized time-intervals, but mostly performed within 3 days. Therefore, we were not able to assess at what time recanalization occurred and whether recanalization was temporary or persistent. Although 3 days may be considered a fairly tight time window, this time window may be relatively short for the subgroup with a near occlusion at follow-up. In this subgroup, it is possible that the recanalization process may still be ongoing and repeated follow-up imaging at later time-intervals might be indicated.

In conclusion, follow-up carotid imaging of patients with an acute asymptomatic ICA occlusion on admission identifies a potentially treatable residual high-grade stenosis in 1 of 6 patients. We, therefore, recommend follow-up imaging within a week after the event in all patients with an acute symptomatic ICA occlusion.

Appendix

The DUST investigators are: Academic Medical Center, Amsterdam, The Netherlands (C.B. Majoie, Y.B. Roos); Catharina Hospital, Eindhoven, The Netherlands (L.E. Duijnm, K. Keizer); Erasmus University Medical Center, Rotterdam, The Netherlands (A. van der Lugt, D.W. Dippel); Gelse Hospitals, Apeldoorn, The Netherlands (K.E. Droogh-de Greve, H.P. Bienfait); Leiden University Medical Center, Leiden, The Netherlands (M.A. van Walderveen, M.J. Wermer); Medical Center Haaglanden, The Hague, The Netherlands (G.J. Lycklama à Nijeholt, J. Boiten); Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands (D.A. Duynndam, V.I. Kwa); Radboud University Medical Center, Nijmegen, The Netherlands (F.J. Meijer, E.J. van Dijk); Rijnstate Hospital, Arnhem, The Netherlands (F.O. Kesseling, J. Hofmeijer); St. Antonius Hospital, Nieuwegein, The Netherlands (J.A. Vos, W.J. Schonewille); St. Elisabeth Hospital, Tilburg, The Netherlands (W.J. van Rooij, P.L. de Kort); St. Franciscus Hospital, Rotterdam, The Netherlands (C.C. Pleiter, S.L. Bakker); VU University Medical Center, Amsterdam, The Netherlands (J.C. Bot, M.C. Visser); University Medical Center Utrecht, Utrecht, The Netherlands (B.K. Velthuis, I.C. van der Schaaf, J.W. Dankbaar, W.P. Mali, T. van Seeters, A.D. Horsch, J.M. Niesten, G.J. Biessels, L.J. Kappelle, M.J. Luitse, Y. van der Graaf).

Sources of Funding

DUST was supported by the Dutch Heart Foundation (grant number 2008T034) and the Nuts Ohra foundation (grant number 0903-012).

Disclosures

None.

References


Residual High-Grade Stenosis After Recanalization of Extracranial Carotid Occlusion in Acute Ischemic Stroke
Merel J.A. Luitse, Birgitta K. Velthuis, Meenakshi Dauwan, Jan Willem Dankbaar, Geert Jan Biessels and L. Jaap Kappelle on behalf of the Dutch Acute Stroke Study Group

Stroke. 2015;46:12-15; originally published online December 9, 2014; doi: 10.1161/STROKEAHA.114.007169

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/46/1/12

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/