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Risk of Early Recurrent Stroke in Symptomatic Carotid Stenosis

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WHAT THIS PAPER ADDS

This large retrospective study looks at the risk of early recurrent ipsilateral stroke in patients with symptomatic carotid artery stenosis. A low risk that seems to coincide with improved medical treatment and is in line with other recent studies was found. This knowledge is important to understand how to best treat patients with symptomatic carotid stenosis and balance the risk of very early carotid endarterectomy.

Objectives: The risk of recurrent stroke in patients with symptomatic carotid artery stenosis is highest in the first weeks after a transient ischemic attack (TIA) or minor stroke and can be reduced with carotid endarterectomy (CEA). The optimal timing of CEA remains a controversial issue since very urgent CEA is associated with an increased procedural risk. The aim of this study was to determine the risk of very early recurrent stroke in a population with symptomatic high grade carotid stenosis.

Methods: Data were analyzed on all patients with ocular TIA, TIA, or minor stroke with >70% carotid stenosis as assessed by carotid ultrasound at Sahlgrenska University Hospital during the periods 2004–2006 and 2010–2012. The two time periods were chosen to minimize selection bias and to analyze changes over time. The risk of recurrent stroke within 30 days of the referring event was assessed.

Results: 397 patients with symptomatic carotid stenosis were identified. The risk of recurrent stroke in the total cohort was 2.0% (CI 95% 0.6–3.4) by day 2, 4.0% (CI 95% 2.0–5.9) by day 7, and 7.5% (CI 95% 4.4–10.6) by day 30. There was no significant difference between the two time periods. Patients with minor stroke had a significantly higher risk of recurrent stroke than patients with TIA or ocular TIA as the referring event.

Conclusions: The data suggest that the early risk of recurrent stroke in symptomatic significant carotid stenosis is not as high as some earlier studies have shown. The risk is similar to several studies in which a modern medical treatment regime could be assumed.

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INTRODUCTION

Stroke is the third most common cause of death in industrialized countries. Transient ischemic attack (TIA) or mild disabling stroke is sometimes a warning sign preceding a severe disabling stroke. Extracranial internal carotid artery stenosis is associated with around 10% of all ischemic strokes.[1] Patients with a high grade symptomatic carotid stenosis have a higher risk of recurrent stroke than patients with other causes of their neurological vascular events.[2,3] A number of studies show that the risk of recurrent stroke is highest in the first weeks after TIA or minor stroke but very few studies have been designed to investigate the risk in patients with carotid stenosis in the very early phase (within 2 days of the referring event).[2,4–10]

The North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST) showed that carotid endarterectomy (CEA) for a symptomatic carotid stenosis can reduce the overall risk of recurrent stroke when performed within 6 months of a neurological ischemic event.[11,12] A pooled analysis from these trials concluded that most of the benefit is seen if surgery is performed within 2 weeks of the referring event.[13] Current guidelines therefore promote early CEA of symptomatic carotid artery stenosis to reduce the risk of recurrent stroke.[14–16] However, the recent analysis of data from the Swedish Vascular Registry (Swedvasc) showed that

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the post-operative complication rate is increased when CEA is performed within 2 days of the referring event, 11.5% on days 0—2 compared with 3.6% on days 3—7, suggesting that adoption of a strategy with very early CEA may not be beneficial.[17]

To optimize the timing of CEA, there is an urgent need for more studies describing the course of symptomatic carotid stenosis with urgent medical treatment alone in the very early phase after the referring event. The aim of the current study was to determine the risk of early recurrent stroke in a large group of patients who had high grade stenosis and were clinically eligible for carotid surgery. Patients were included in the study at the time of their ultrasound examination to minimize bias caused by early recurrent strokes. The study cohort consisted of consecutive patients in everyday clinical practice in a defined geographical area of western Sweden.

METHODS

Patients and duplex investigation

Data from all patients who received ultrasound examination of the carotid arteries during the periods 2004—2006 ($n = 4632$) and 2010—2012 ($n = 6456$) at Sahlgrenska University Hospital were analyzed retrospectively (Fig. 1). The timing of the duplex investigation in relation to the referring neurological event was set by the clinical practice at that time. The patients were identified through the Western Region INitiative to Gather information on Atherosclerosis (WINGA) registry, which holds information on the clinical results of all carotid ultrasound examinations performed at Sahlgrenska University Hospital from 1 January 2004. Significant carotid stenosis was defined according to local guidelines as ≥70% carotid obstruction due to atherosclerosis on either or both sides according to the ECST criteria using Doppler velocity criteria adapted for duplex ultrasound.[18] A ≥80% carotid stenosis according to ECST equates to a ≥70% carotid stenosis when using NASCET criteria. Similarly, a 60—79% stenosis according to ECST equates to a 50—69% carotid stenosis according to NASCET.

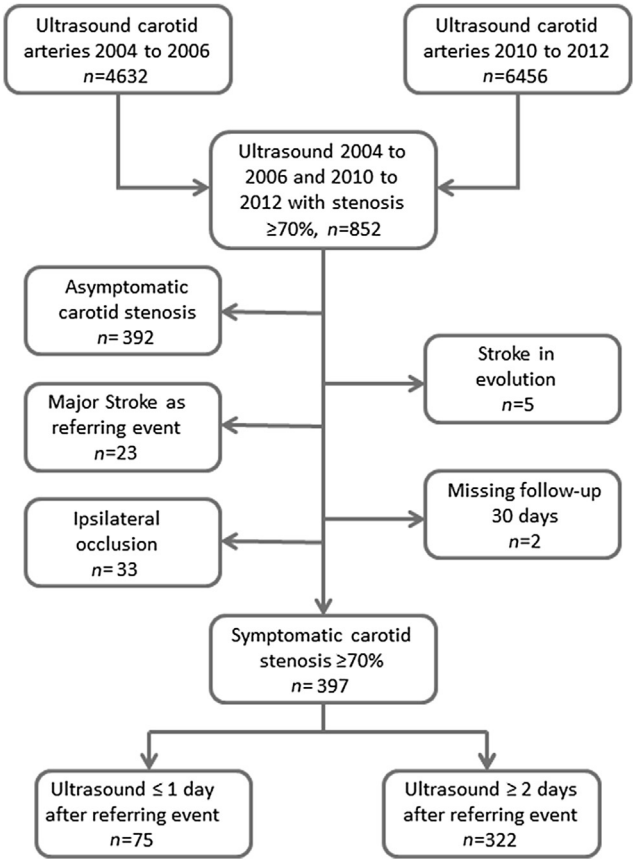

Figure 1. Flow diagram of patients included in the study.

The medical records of each patient identified with significant carotid stenosis were searched manually to identify the referring event (i.e., the neurological event that brought the patient to hospital or general practitioner). Patients who were asymptomatic or had an ipsilateral occlusion of the carotid artery were excluded. Also excluded were patients with a major stroke as the referring event because these patients are not considered suitable for acute CEA, and it is difficult to verify a recurrent event following a recent severely disabling stroke. Also excluded were patients with stroke in evolution with continuous worsening of symptoms, since the potential benefit of CEA in these patients is unknown (Fig. 1).[19,20] The referring event was classified as ocular TIA, TIA, or minor stroke. Patients with crescendo TIA were included in the TIA group. The characteristics of the patients included in the study are thus a cohort that was assessed for potential CEA.

Medical records were searched to determine if and when CEA was performed and to identify all new cerebrovascular strokes ipsilateral to the referring event (either before or after ultrasound) for up to 30 days after the referring event. Patients were censored at the time of recurrent event or CEA. To ensure that no recurrent neurological event had been missed, patients who did not undergo CEA or who suffered a recurrent event during the 30 days after the referring event were only included in the study if a medical record existed confirming that they were free of recurrent cerebrovascular disease beyond the 30 day observation period.

Sahlgrenska University Hospital is the sole supplier of vascular diagnostics in the Gothenburg region, which has approximately 650,000 inhabitants. Ultrasound is the recommended first line investigative tool for carotid arteries in stroke evaluation according to strict local guidelines. The study thus included all patients in this region who were referred for evaluation of carotid atherosclerotic disease, or who were suffering from stroke or TIA. Importantly, inclusion of patients at the time of ultrasound assured that this was done before any decision on CEA was made. Thus, the study cohort includes patients at risk of suffering a recurrent stroke while waiting for the decision on CEA.

Recurrent stroke

Recurrent stroke (the endpoint) was defined as a stroke with neurological symptoms ipsilateral to the referring