

## The National Norwegian Carotid Study: Time from Symptom Onset to Surgery is too Long, Resulting in Additional Neurological Events<sup>☆</sup>

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### WHAT THIS PAPER ADDS

This prospective study covers > 99% of surgical treatment of symptomatic carotid stenosis in a whole nation during 1 year. This constitutes a more solid base than previous observations, even if the numbers are similar, showing that only 61.7% of patients are treated surgically within the national guidelines time limit of 2 weeks. The delays are mainly due to in hospital logistics, and also to patients not seeking medical advice immediately. The study adds to increasing evidence that dual antiplatelet therapy protects against new neurological events in symptomatic patients. The findings constitute a firm platform for implementing coordinated national improvement measures.

**Objective/Background:** The objective was to observe for 1 year all patients in Norway operated on for symptomatic carotid stenosis with respect to (i) the time from the index event to surgery and neurological events during this time; (ii) the level in the healthcare system causing delay of surgical treatment; and (iii) the possible relationship between peri-operative use of platelet inhibitors and neurological events while awaiting surgery.

**Methods:** This was a prospective national multicentre study of a consecutive series of symptomatic patients. Patients were eligible for inclusion when referred for surgery. An index event was defined as the neurological event prompting contact with the healthcare system. All 15 departments in Norway performing carotid endarterectomy (CEA) participated.

**Results:** Three hundred and seventy one patients were eligible for inclusion between 1 April 2014 and 31 March 2015, and 368 patients (99.2%) were included. Fifty-four percent of the patients contacted their general practitioner on the day of the index event. Primary healthcare referred 84.2% of the patients to hospital on the same day as examined. In hospital median time from admission to referral for vascular surgery was 3 days. Median time between referral to the operating unit and actual CEA was 5 days. Overall, 61.7% of the patients were operated on within 2 weeks of the index event. Twelve patients (3.3%) suffered a new neurological event while awaiting surgery. The percentage of patients on dual antiplatelet therapy was lower (25.0%) in this group than among the other patients (62.6%) ( $p = .008$ ). The combined 30 day mortality and stroke rate was 3.8%.

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**Conclusion:** This national study with almost complete inclusion and follow-up shows that the delays occur mainly at patient level and in hospital. The delay is associated with new neurological events. Dual antiplatelet therapy is associated with reduced risk of having a new neurological event before surgery.

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## INTRODUCTION

In patients with ipsilateral carotid stenosis  $\geq 50\%$ , the stroke risk after a minor ischaemic neurological event will exceed 30% during the following 2–3 months,<sup>1</sup> with a peak incidence within the first one or two weeks.<sup>2–5</sup> A large number of studies support urgent surgical treatment of symptomatic carotid stenosis.<sup>6–8</sup> Surgical intervention within a 2 week window is shown to carry an absolute risk reduction of stroke of approximately 20%.<sup>9</sup> Thus, European and US guidelines recommend surgery within 2 weeks.<sup>10,11</sup> In 2007, the UK guideline was to perform surgery within 48 hours. More recent data have shown that very early surgery might be associated with an increased peri-operative risk,<sup>12</sup> and in the fourth set of UK national guidelines (published in 2012), the recommendations have been amended as follows: “as soon as possible and within one week of symptoms”.<sup>13</sup> However, the documented effect of early surgery does not seem to be well implemented in everyday practice. In a Vascunet study only 6.8% of patients operated on by carotid endarterectomy (CEA; 60.1% symptomatic) had been admitted urgently.<sup>14</sup> The percentage varied between participating countries from 2.1% to 24.6%. A retrospective study from Helsinki ( $n = 144$ ; symptomatic patients) demonstrated the same tendency, with 55% of patients admitted urgently and only 37% operated on within 2 weeks of the index event.<sup>15</sup>

Symptoms, degree of stenosis, time from symptoms to surgery, and quality of surgical treatment are the major factors to be taken into account when optimising prophylactic surgery. In addition, platelet inhibitors are shown to reduce the risk of stroke in patients with symptomatic carotid stenosis. Current guidelines advise that all patients should be on low dose aspirin while awaiting CEA, but there is increasing evidence that early commencement of dual antiplatelet therapy (DAPT) might reduce the incidence of early recurrent events.<sup>16–18</sup> Timing of carotid surgery in Norway follows the European and US guidelines. However, it is not well known to what extent these recommendations are implemented in daily practice.

The aim of the study was to cover all carotid surgery for symptomatic disease in Norway for 1 year, to register the timing between the index event and surgery, the healthcare levels for potential delays, and the neurological events occurring during the delay, and, furthermore, to register the use of platelet inhibitors and whether this influenced the risk of such events.

## MATERIAL AND METHODS

This was a prospective, national, multicentre consecutive series of symptomatic patients referred for CEA over 1 year.

Patients were included when referred for surgery if they complied with the inclusion criteria (Table 1). Carotid surgery in Norway is restricted to 15 hospitals and all of them contributed with their operations. Only data related directly to the treatment were registered, that is, no personal identifiable data. The index event was defined as the most recent neurological event leading to contact with the healthcare system. There is a difference between “first event” versus “most recent event that made the patient seek medical support”. Since the focus was on the handling within the healthcare system, the latter definition of the index event was chosen. The index events were divided into four categories; amaurosis fugax, transient ischaemic attacks (TIA), minor stroke (modified Rankin Scale Score [mRSS]  $\leq 2$ ) and major stroke (mRSS  $> 2$ ). In order to identify possible levels of delay, the time spans between (i) the index event; (ii) first medical examination; (iii) first examination by neurologist or vascular surgeon; (iv) referral for surgery; and (v) CEA were analysed. The use of peri-operative platelet inhibitors and anticoagulants were also registered and correlated with the incidence of new neurological events after referral for surgery. Finally, the quality of Norwegian surgical practice regarding peri-operative complications, such as peripheral nerve damage, stroke, myocardial infarction (defined as a state that rendered a classification number of the diagnosis in any of the patient journals covering the time window from the initial consultation by the general practitioner to the 30 day follow-up) and death was evaluated.

**Table 1.** Patient inclusion criteria.

### Inclusion criteria

1. Referred for CEA by neurologist or vascular surgeon after clinical examination and verification of significant carotid stenosis on ipsilateral side by triplex scanning, CTA, and/or MRI.
2. Amaurosis fugax/TIA or stroke during the previous 6 months (index event) confirmed by medical doctor. In the case of multiple neurological events, the last one was registered.
3. Accepted by vascular surgeon for CEA
4. Age  $> 18$  years
5. Able to give informed consent

### Exclusion criteria

1. Haemorrhagic stroke
2. Endovascular treatment (carotid artery stenting)

*Note.* CEA = carotid endarterectomy; CTA = computed tomography angiography; MRI = magnetic resonance imaging; TIA = transient ischaemic attack.

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