For decades, carotid endarterectomy (CEA) has been performed to prevent recurrent stroke in patients with symptomatic carotid artery stenosis, but the appropriate timing of surgery remains controversial. Early studies recommended a 4- to 6-week delay from the ischemic event to surgery, but researchers reanalyzed pooled data from the European Carotid Surgery Trial and the North American Symptomatic Carotid Endarterectomy Trial and found that the protective effect against future stroke or death was time dependent. The analysis revealed that surgery within 2 weeks had the most beneficial effect. Subsequently, guidelines from the European Stroke Organization and the American Stroke Association have recommended CEA within 2 weeks of an ischemic event. Subsequent studies demonstrate that the recommendations have been poorly implemented. For example, only 10% to 20% of patients in Denmark, Finland, and the United Kingdom received CEA surgery within the 2-week time frame. Factors contributing to the delay in surgery may include late referrals, the time required for preoperative investigations, and a lack of operating room availability. Furthermore, there is uncertainty about the optimal timing for CEA in patients with medium or large acute infarcts because of fear of perioperative and postoperative complications, in particular the risk of cerebral hyperperfusion syndrome and hemorrhagic transformation.

The aim of this study was to examine the effect of a multidisciplinary nationwide initiative aimed at reducing time to CEA after acute ischemic stroke.

Methods

We examined a historic population-based observational cohort based on individual patient-level records from the Danish Stroke Registry and the Danish Vascular Registry. The implementation of early ultrasound examination of the carotids (within 4 days from admission) in medical departments coupled with fast CEA after referral to a department of vascular surgery were monitored and audited systematically from 2008 and onward.

Results—A total of 813 acute ischemic stroke patients underwent CEA during 2007-2010. The percentage of patients undergoing CEA within 2 weeks increased from 13% in 2007 to 47% in 2010 (adjusted odds ratio, 5.8 [95% CI, 3.4-10.1]). The overall median time decreased from 31 days to 16 days. The percentage of relevant acute ischemic stroke patients receiving early ultrasound examination of the carotids increased from 41% in 2008 to 72% in 2010. The time from referral to operation at a vascular department was reduced by ≈40%.

Conclusions—Establishing time limits of 4 days to ultrasound examination of the carotids and of 2 weeks to CEA from onset of stroke followed by a systematic multidisciplinary monitoring and auditing of processes was associated with a substantial increase in the proportion of acute ischemic stroke patients who undergo CEA within 2 weeks in Denmark. (Stroke. 2013;44:686-690.)

Key Words: carotid endarterectomy ■ carotid stenosis ■ stroke ■ time delay
linkage between the Danish Stroke Registry (formerly the Danish National Indicator Project-Stroke) and the Danish Vascular Registry. The Danish Stroke Registry is a national registry established to monitor and improve the quality of early stroke care among hospitalized patients. Participation is mandatory. In Denmark, 99% of all acute strokes are admitted. Patients with transient ischemic attack (TIA) are not included in the Danish Stroke Registry. The registry captures specific clinical criteria for quality of care and timelines for examinations involving different clinical professions, for example, physicians, nurses, physical therapists, and occupational therapists. In addition, data on lifestyle, medical history, and socioeconomic status are also recorded in the registry. To ensure the completeness of patient data, comparisons with local hospital discharge records are performed regularly. National and regional auditing occurs on an annual basis to evaluate the findings and to ensure quality improvements. Prospective monitoring of early USC was introduced in September 2007, and the first calendar year with complete data was, therefore, 2008.

The Danish Vascular Registry contains information on all of the vascular procedures performed in Denmark since 1996 and is used for surveillance and quality improvement. Reporting is mandatory for all vascular procedures performed in Denmark since 1996 and is used for surveillance and quality improvement. Reporting is mandatory for all vascular surgery departments (n=9), and the registry covers 99.2% of all vascular procedures performed at Danish hospitals (www.karbase.dk, annual report 2009). Data from the registry have been found to be of high validity.15,16

**Initiatives**

After the Rothwell et al22 publication in 2004, the multidisciplinary Danish national clinical guidelines on treatment of patients with stroke issued by the National Board of Health were updated with a recommendation of early CEA (ie, <2 weeks) in relevant AIS patients.23

To reduce the delay from ischemic event to surgery, a national quality initiative was subsequently introduced in September 2007. The initiative systematically monitors whether the departments treating patients with AIS ensure that USC is performed within 4 days of hospitalization. The aim is that ≥90% of all relevant AIS patients (eg, with anterior infarctions) have a USC within 4 days.

In addition, the Danish Vascular Society and the vascular surgery departments introduced initiatives to reduce the delay from referral to CEA. Several vascular surgery departments began to schedule at least twice weekly CEA operations to avoid a lack of operating room availability, whereas others reclassified CEA as a more urgent, subacute procedure. In 2010, the Danish Vascular Society also released its own new guidelines for the treatment of carotid stenosis, recommending that patients be examined on the day of referral or the following work day, and, when surgery is indicated, the surgery should be performed within 48 hours. However, most departments had instituted these changes 1 or 2 years before the official written guidelines were issued.

**Patients**

From the Danish Stroke Registry, we identified 39 752 AIS patients admitted between January 1, 2007, and December 31, 2010, of whom 813 patients subsequently underwent CEA.

**Outcomes**

The outcomes included early USC (within 4 days from admission) and early CEA (within 2 weeks from admission). Furthermore, we determined the times from admission to referral to a vascular department and from referral to CEA.

**Covariates**

The following covariates were obtained from the Danish Stroke Registry: age, sex, living status (cohabiting versus living alone), previous stroke, diabetes mellitus, atrial fibrillation, hypertension, smoking, and Scandinavian Stroke Scale score. The Scandinavian Stroke Scale score at the time of admission reflects the severity of the neurological injury. The scale is a validated and widely used neurological stroke scale in Scandinavia. It evaluates level of consciousness; eye movement; power in the arm, hand, and leg; orientation; aphasia; facial paresis; and gait as a total score ranging from 0 to 58.19,20 We classified stroke severity as moderate-severe (≤44 points) versus mild (>45 points).

**Statistical Analysis**

We first computed the proportion of patients who underwent CEA among all of the patients admitted with ischemic stroke. Secondly, we computed the proportion of patients who underwent CEA within 2 weeks after hospital admission with acute stroke, as well as the proportion of relevant patients who received USC within 4 days after admission, both overall for the entire study period and according to calendar year (2008–2010). Changes in the median time to CEA, the median time from admission to CEA referral (delay in the neurology departments), and the median time from referral to CEA (delay in the vascular surgery departments) were also calculated.

Comparisons across calendar years of the chance of undergoing CEA within 2 weeks after admission with stroke were made by using multivariable logistic regression to determine the odds ratio with 95% CI using 2007 as reference. We controlled for the covariates listed above in the analyses.

We used multiple imputation to overcome potential problems with missing data on the covariates assuming that the missing values were missing at random (stata command: ice).20–22 We created 5 data sets based on the covariates listed above.

Separate analyses were made for patients with minor and moderate-severe stroke, respectively. The analyses were repeated including only patients with available information on all of the covariates (complete case analysis). All of the analyses were made using Stata 10.0 (StataCorp LP, College Station, TX). Finally, we repeated the multivariable analyses of comparisons over time and only included patients where information was available on all of the covariates (complete case analysis). They resulted in virtually no differences compared with the primary analyses based on multiple imputation (data not shown).

**Table 1. Patient Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%) (N=813)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, y</td>
<td>69</td>
</tr>
<tr>
<td>Male/female ratio</td>
<td>63:37</td>
</tr>
<tr>
<td>Factors of lifestyle</td>
<td></td>
</tr>
<tr>
<td>&lt;14/21 alcohol units/w</td>
<td>684 (84)</td>
</tr>
<tr>
<td>&gt;14/21 alcohol units/w</td>
<td>73 (9)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>384 (47)</td>
</tr>
<tr>
<td>Previous smoker</td>
<td>212 (26)</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>144 (18)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>510 (63)</td>
</tr>
<tr>
<td>Previous AMI</td>
<td>101 (12)</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>181 (22)</td>
</tr>
<tr>
<td>Present stroke</td>
<td></td>
</tr>
<tr>
<td>Moderate stroke</td>
<td>140 (17)</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>594 (73)</td>
</tr>
<tr>
<td>Stroke severity unknown</td>
<td>72 (8)</td>
</tr>
<tr>
<td>Median SSS (range, 0–58)</td>
<td>54</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>71 (9)</td>
</tr>
<tr>
<td>Living</td>
<td></td>
</tr>
<tr>
<td>Cohabitant</td>
<td>542 (67)</td>
</tr>
<tr>
<td>Private home</td>
<td>766 (94)</td>
</tr>
<tr>
<td>Nursing home</td>
<td>6 (1)</td>
</tr>
</tbody>
</table>

AMI indicates acute myocardial infarction; and SSS, Scandinavian Stroke Scale.
Results

During the observation period, 813 AIS patients underwent CEA. Table 1 illustrates the patient characteristics. Stroke severity was classified as minor in 594 patients (73%), moderate to severe in 140 patients (17%), and unknown in 71 patients (9%).

In 2007, 161 of 10,052 AIS patients received CEA, equaling 1.6 CEA operations per 100 AIS. This number increased to 215 to 220 CEA operations among 9,549 to 10,095 AIS patients in the years 2008-2010, equaling 2.1 to 2.3 CEA operations per 100 AIS. Thus, we found an increase in the proportion of operations from 2007 to 2008 of 30% but no further increase thereafter.

In total, 275 patients (34%) were operated within 2 weeks from admission during 2007-2010. The delay from admission to surgery decreased significantly during the 4 years with 21 patients (13%) undergoing CEA within 2 weeks in 2007, 72 (33%) in 2008, 81 (37%) in 2009, and 101 (47%) in 2010 (adjusted odds ratio, 5.8 [95% CI, 4.3–10.1] when comparing 2010 with 2007).

In 2008 (the first year with data on USC available for an entire year), 2,390 patients (41%) underwent USC within 4 days. This proportion increased to 52% in 2009 and further to 72% in 2010. Figure 1 shows the increase in the proportion of patients having USC within 4 days after AIS and the increase in the proportion of CEA performed within 2 weeks.

The overall median time for CEA decreased from 31 days in 2007 to 18 days in 2008 and 2009 and 16 days in 2010. The median time from admission to referral to a vascular department decreased by ≈50% from 19 days in 2007 to 9 days in 2010. The median time from referral to CEA operation decreased from 12 days in 2007 to 7 days in 2010 and was thus reduced by 40%. Figure 2 shows the median waiting times.

The time to CEA was reduced among both patients with minor strokes and those with moderate strokes. The number of patients with minor stroke receiving CEA within 2 weeks was 14 (13%) in 2007, 53 (32%) in 2008, 59 (37%) in 2009, and 52 (37%) in 2010 (adjusted odds ratio, 5.2 [95% CI, 2.6–10.2] when comparing 2010 with 2007). Among patients with moderate stroke, 3 patients (11%) received CEA within 2 weeks in 2007, 14 (38%) in 2008, 12 (33%) in 2009, and 23 (59%) in 2010 (adjusted odds ratio, 14.9 [95% CI, 2.9–75.0]; Table 2).

Discussion

This study found that the introduction of a national quality standard of USC within 4 days of admission for acute carotid distribution ischemic stroke in combination with several vascular surgery initiatives reduced the interval between AIS and CEA in Denmark. Almost half of the patients were treated according to guideline recommendations and were operated within 2 weeks by the end of the study period. Reductions in time from admission to CEA were seen for both minor and moderate-severe strokes. This was achieved by reducing delays in both medical and vascular surgery departments. A 30% increase in the number of CEA operations was also achieved.

One factor that likely contributed to these successful results was the annual systematic audits of the Danish Stroke Registry and the Danish Vascular Registry. The audit results are made publicly available, which in our experience represents an important incentive for hospital departments to strive for improvements.
A range of concrete steps was taken locally to fulfill the demands for a shorter delay to CEA. The individual institutions were free to make whatever arrangements they found useful to improve the results. Typically steps included a higher priority of USC in relevant acute stroke patients at the departments of neuroradiology, larger capacity of subacute USC through training of neurologists to perform USC, simplified logistical procedures (eg, referring patients to surgery by telephone or e-mail instead of filling out and mailing paper forms), and redefining CEA in symptomatic patients as a semurgent procedure thereby ensuring a higher priority in the departments of vascular surgery.

The driver of these concrete steps was the strict time limits on USC and CEA, which forced the hospitals to reconsider their previous practice and to systematically evaluate all of the steps from the time of admission to surgery to identify procedures that could be become more effective. The local experiences were shared between the hospitals during the annual national and regional multidisciplinary audits.

In accordance with our findings, large reductions in time to CEA among patients with AIS or TIA have been reported in Sweden with a decrease in the median delay to CEA from 2004 (11.7 weeks) to 2006 (6.9 weeks). This was mainly explained by the awareness of the importance of rapid investigation. Initiatives of public awareness and education to general practitioners were made on a national level, and the national median time from symptom onset to surgery was reduced from 12 days in 2009 to 9 days in 2010. Furthermore, a New Zealand project from 2008 found that by considering CEA as an urgent vascular procedure instead of an elective procedure, median waiting time from symptom to surgery was reduced from 83 to 32 days. The reduction was exclusively achieved within the time window from referral to a vascular surgery department to CEA.

In addition to our report, these 2 studies exemplify initiatives aimed at reducing the time from carotid distribution ischemic stroke to CEA. The process can be divided into 3 stages: (1) from ischemic event to admission; (2) from admission to referral to a vascular department; and (3) from referral to operation. Different initiatives affect each stage and not necessarily the other stages, as demonstrated in the New Zealand study. Therefore, to accommodate the guideline recommendation of a maximum 2 weeks from ischemic event to CEA, it is important that all of the departments in this process participate actively to reduce the waiting time.

Our study has some limitations, because it only concerned stroke patients and not patients with TIA or amaurosis fugax. Time to CEA after TIA may differ, especially if most TIA patients are seen in outpatient clinics, where patient delay defined as time from TIA onset to medical attention, as well as waiting time for examinations, may be longer. Therefore, the results are not directly comparable to former studies on delay of CEA that include all patients irrespective of the indication.

Furthermore, we did not have data on the exact time of stroke onset but only the admission time. However, 80% to 90% of all strokes in Denmark are admitted within 24 hours. We, therefore, consider admission time (date) as a reasonable proxy for time of stroke onset.

In conclusion, this study found that introducing time limits of 4 days to USC and of 2 weeks to CEA from stroke onset followed by systematic multidisciplinary monitoring and auditing of processes was associated with a substantial increase in the proportion of AIS patients who undergo CEA within 2 weeks in Denmark. The introduction of early USC (within 4 days from admission) as an indicator of quality of care seems to play a key role in reducing the delay to CEA. The intervention resulted in a substantial immediate increase in the number of patients being operated. A reduction in time from vascular department referral to CEA prompted by new guidelines combined with individual initiatives during the period furthermore resulted in a reduction of the total waiting time from stroke to CEA, and operation within 2 weeks was achieved in approximately half of all patients in 2010.

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Disclosures

None.

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5. Goldstein LB, Bushnell CD, Adams RJ, Appel LJ, Brain LT, Chaturvedi S, et al.; American Heart Association Stroke Council; Council on Cardiovascular Nursing; Council on Epidemiology and Prevention; Council for High Blood Pressure Research, Council on Peripheral Vascular...


Reducing Delay of Carotid Endarterectomy in Acute Ischemic Stroke Patients: A Nationwide Initiative

Agnes Hauschultz Witt, Soren Paaske Johnsen, Leif Panduro Jensen, Allan Kornmaaler Hansen, Heidi Holmager Hundborg and Grethe Andersen

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