Optimizing care for patients with symptomatic carotid disease
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CHAPTER 4
Overestimation of contralateral internal carotid artery stenosis before ipsilateral surgical endarterectomy

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ABSTRACT

Objective. The aim of this study was to investigate a possible overestimation of the degree of contralateral carotid artery stenosis by duplex in patients with significant bilateral carotid stenoses who are to undergo carotid endarterectomy (CEA).

Methods. A retrospective analysis was performed of all patients undergoing CEA in our center over a period of 11 years. Pre- and postoperative duplex ultrasonography measurements of peak systolic velocity (PSV) and end diastolic velocity (EDV) were compared and used to classify the degree of stenosis. Univariate analysis was performed to indicate possible predictors for contralateral stenosis overestimation.

Results. A total of 384 CEA procedures in 357 patients were performed in our hospital. Pre- and postoperative bilateral duplex measurements were available in 135 patients. Forty-four out of 135 patients (33%) were preoperatively identified as having significant stenosis (>60%) of the internal carotid artery on both sides. In these patients, postoperative duplex measurements of the contralateral carotid showed a decrease in mean (SD) PSV from 2.53 (1.11) m s\(^{-1}\) to 1.97 (0.87) m s\(^{-1}\) (P < 0.01) and a decrease in EDV from 0.87 (0.60) m s\(^{-1}\) to 0.60 (0.36) m s\(^{-1}\) (P < 0.01). The absolute changes in contralateral PSV and EDV after CEA were larger among patients with a higher degree of stenosis preoperatively. These changes led to reclassification of stenosis to a lesser degree in 24 (55%) patients. In 16 cases (36%), this resulted in a measured stenosis on the contralateral side of less than 60%.

Conclusions. One-third of the patients with duplex measurements consistent with bilateral significant carotid stenosis did not have a significant contralateral stenosis by duplex after CEA. Therefore, additional postoperative duplex measurement is advisable before planning contralateral CEA.

INTRODUCTION

Stroke-related disability and death are a serious concern in the western world and are responsible for a rising proportion of total health care costs.\(^1\)\(^2\) Patients with a severe carotid artery stenosis are at an increased risk of suffering a disabling or fatal ischemic stroke.\(^3\) The North American Symptomatic Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST) demonstrated that carotid endarterectomy (CEA) is beneficial in symptomatic patients with a severe stenosis of the internal carotid artery (70–99%) with respect to long-term reduction of stroke risk.\(^4\)\(^5\) Also, CEA can decrease the 5-year stroke risk by half in patients with severe carotid stenosis in the absence of neurologic symptoms, especially in male patients up to 75 years of age.\(^6\)

The degree of carotid stenosis can be classified by duplex measurements of the peak systolic velocity (PSV) and end diastolic velocity (EDV) at different levels in the carotid arteries. As a non-invasive investigation, duplex ultrasound (DUS) is becoming increasingly utilized as the sole investigation for assessing the degree of carotid stenosis. Although standardized duplex ultrasound criteria for the grading of internal carotid artery stenosis do not exist, recent meta-analyses showed high sensitivities and specificities (89–90% and 84–94%, respectively) for diagnosing a 70–99% stenosis.\(^7\)\(^8\) However, several studies have described an overestimation with DUS of stenosis contralateral to an artery with significant stenosis or occlusion.\(^9\)\(^10\) In the case of bilateral stenosis, an overestimation of the contralateral stenosis could expose patients to unnecessary morbidity and mortality associated with a second CEA. This is especially true for patients with an asymmetrical contralateral stenosis, as the absolute risk reduction for stroke after CEA is considered to be smaller in these patients. Since the current indication for intervention in patients with carotid artery stenosis is still primarily based on the degree of stenosis, and this is frequently based solely on duplex measurements, it is of great importance to be aware of the fact that contralateral stenosis can influence the measurements on the side to be operated on. Studies on the effect of contralateral degree of stenosis on ipsilateral PSV and EDV all use different criteria. We therefore retrospectively analysed the DUS measurements of all patients who have undergone CEA in our hospital over a recent period of 11 years to investigate the possible overestimation of contralateral stenosis and its clinical impact.

MATERIALS AND METHODS

Design of the study

General inclusion criteria for CEA at our institution are symptomatic patients with a ≥70% stenosis, and asymptomatic patients with a ≥80% stenosis. A retrospective analysis was performed of all patients undergoing CEA between January 1, 1997 and December 31, 2007. All duplex measurements had to be performed in our institution. From patients who eventually received CEA bilaterally, only the measurements before and after the first operation were included. Furthermore, patients with an occluded contralateral internal carotid artery were excluded.

Duplex scan measurements

All patients were investigated by a single experienced vascular laboratory technician. Duplex ultrasound (SONOLINE Antares Ultrasound Imaging system; Siemens Medical solutions, Issaquah, WA, USA) was...
performed with the aid of a VFX9-4 Multi-D linear array transducer (4–8 MHz) within two weeks before the operation and approximately six weeks after the operation. Before obtaining data of the contralateral side, measurements performed up to six months before surgery were used for close comparison. For each investigation, the head of the patient was somewhat turned to the contralateral side so the transducer could be placed laterally from the sternocleidomastoid muscle in a longitudinal direction. By convention, the angle of insonation was 60°. Velocities were obtained from the proximal, middle and distal internal carotid arteries, as well as from the distal common carotid arteries by scanning the vessels from proximal to distal. The highest PSV and EDV values and the presence of an atheromatous plaque were used to indicate the location of the stenosis and its maximum diameter reduction (Fig. 1). Postoperatively, the former site of stenosis at the ipsilateral side could be identified using a digitalized image of the previous duplex measurements. Moreover, turbulences in flow caused by the widened lumen after endarterectomy marked the previous site of stenosis. An ICA/CCA ratio was calculated using the highest PSV of the ICA and the PSV measured in the distal CCA. The degree of stenosis was based on the measured velocities alone and estimated using thresholds derived from the criteria formulated by Bluth et al. (Table 1).

Data collection and further analysis
Data collected included demographics, symptomatology, and side of operation, and duplex measurements as described above. Data were drawn from a database held by our vascular laboratory or, in case of missing data, abstracted from patients’ medical records.

Statistical analysis was performed using the Statistical Package for Social Sciences 14.0 (SPSS Inc., Chicago, IL, USA). To determine if changes in preoperative and postoperative velocities exhibited statistical significance, a two-tailed paired t-test or a Wilcoxon rank test was used, depending on whether a normal distribution was found. Univariate analysis was performed to determine Chi-square test for categorical variables and an independent t-test (normal distribution) or Mann–Whitney test (skewed distribution) for continuous variables. Statistical significance was defined by a P-value of ≤0.05. Results are expressed as the mean ± SD.

Table 1. Criteria for classifying degree of stenosis in percentage based on duplex velocity measurements in ms⁻¹ (PSV, Peak Systolic Velocity; EDV, end diastolic velocity; ICA, internal carotid artery; CCA, common carotid artery).

<table>
<thead>
<tr>
<th>Degree of stenosis (%)</th>
<th>PSV (m s⁻¹)</th>
<th>EDV (m s⁻¹)</th>
<th>ICA/CCA ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–39</td>
<td>&lt;1.10</td>
<td>&lt;0.40</td>
<td>&lt;1.8</td>
</tr>
<tr>
<td>40–59</td>
<td>&lt;1.30</td>
<td>&lt;0.40</td>
<td>&lt;1.8</td>
</tr>
<tr>
<td>60–79</td>
<td>&gt;1.30</td>
<td>&gt;0.40</td>
<td>&gt;1.8</td>
</tr>
<tr>
<td>80–99</td>
<td>&gt;2.50</td>
<td>&gt;1.00</td>
<td>&gt;3.7</td>
</tr>
</tbody>
</table>

Figure 1. Duplex ultrasound of a carotid artery with severe stenosis. (A) Colour flow Doppler image showing the internal carotid artery (and vein) with the exact location of the stenosis. (B) Using pulsed wave spectral Doppler on the narrowest location found by B-mode/colour flow, a velocity (cm s⁻¹, Y-axis) of the blood through the sample region is shown over time (ms, X-axis).
RESULTS

A total of 384 CEA procedures in 357 patients were performed in our hospital between January 1997 and December 2007. Twenty-seven measurements were excluded because the patients had been operated before on the other side. Measurements of 178 patients were incomplete due to the fact that preoperative DUS had already been done in the referring hospital, the degree of stenosis had been assessed by angiography, or patients were lost to follow up as their follow up was performed in the referring hospital. Another 44 patients were excluded because of an occluded contralateral artery. Therefore, measurements of 135 patients were used for analysis.

The mean age of these patients at the time of operation was 67 (7.65) years (range 43–83 years). Ninety-nine (72%) were males and 36 were females (28%). A total of 122 (88%) were treated for symptomatic disease. The measurements were performed at a mean of 9.0 (17.8) weeks before and 7.7 (7.0) weeks after surgery.

Forty-four out of 135 patients were preoperatively identified as having significant stenosis (>60%) of the internal carotid artery on both sides. In these patients, postoperative duplex measurements showed a decrease in PSV from 2.54 (1.11) m s\(^{-1}\) to 1.97 (0.87) m s\(^{-1}\) \((P < 0.01); \text{Fig. 2}\) and a decrease in EDV from 0.87 (0.60) m s\(^{-1}\) to 0.60 (0.36) m s\(^{-1}\) \((P < 0.01); \text{Fig. 3}\). No significant difference was found between pre- and postoperative ICA/CCA ratios, which showed a decrease from 3.73 (2.05) to 3.20 (1.80) \((P = 0.077); \text{Fig. 4}\). The absolute changes in contralateral PSV and EDV were higher among patients with a preoperative higher degree of stenosis in the non-operated artery. The mean decrease in contralateral postoperative PSV was 1.24 (1.13) m s\(^{-1}\) in patients with a preoperative contralateral stenosis of 80–99% compared to 0.29 (0.71) m s\(^{-1}\) in patients with a preoperative contralateral stenosis of 60–79% \((P < 0.01); \text{Fig. 5}\). Similarly, the mean decrease in EDV was 0.66 (0.59) m s\(^{-1}\) in patients with a preoperative contralateral stenosis of 80–99% compared to 0.13 (0.22) m s\(^{-1}\) in patients with a stenosis of 60–70% \((P < 0.01)\). When the Bluth-criteria were applied on the postoperative measurements, a drop in the degree of stenosis on the contralateral side was seen in 24 (55%) of the patients with a preoperative contralateral stenosis of more than 60%. In 16 cases (36%), this resulted in a newly measured stenosis on the contralateral side of less than 60%. The higher the preoperative contralateral stenosis, the higher the percentage of patients with postoperative downgrading in degree of contralateral stenosis (Table 2). Univariate analysis did not identify age, sex, side of procedure or symptomatology as predictors for a contralateral drop to a lower degree of stenosis. However, univariate subgroup analysis for patients with a preoperative contralateral stenosis of more than 60% indicated a significantly larger decrease in PSV and EDV among women and patients less than 70 years.
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Figure 5. Mean change in contralateral PSV classified according to pre-procedural degree of stenosis (error bars ± 1 SEM).

Table 2. Effect of carotid endarterectomy on contralateral postoperative degree of stenosis. The rows show the number of patients distinguished by their preoperative degree of contralateral stenosis; the columns distinguish the patients by their postoperative degree of contralateral stenosis.

<table>
<thead>
<tr>
<th>Preoperative degree of stenosis (%)</th>
<th>Postoperative degree of stenosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;40</td>
</tr>
<tr>
<td>&lt;40</td>
<td>58</td>
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<tr>
<td>40–59</td>
<td>14</td>
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<td>60–79</td>
<td>6</td>
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<tr>
<td>80–99</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>79</td>
</tr>
</tbody>
</table>

DISCUSSION

Our results show that the degree of carotid stenosis can be overestimated in patients with significant bilateral carotid disease when using duplex measurements of peak velocities. This phenomenon is more distinct in those patients with a higher preoperative degree of stenosis.

The decreases we found in PSV and EDV and the concomitant drop in duplex category are similar to those found by other investigators. In our study, a drop in degree of stenosis on the contralateral side was seen in 24 (55%) of the patients with a preoperative contralateral stenosis of more than 60%. Bussutil et al. found a decrease in at least one duplex category in 52% of 128 non-operated contralateral stenoses. Also, in the study published by Ray et al., 42% of the patients with contralateral carotid disease of more than 50% were downgraded to a less severe category of stenosis. Our findings that patients with a preoperative higher degree of contralateral stenosis show a larger decrease in PSV and EDV postoperatively were also consistent with results published by others. However, in interpreting this last finding, one must take the statistical phenomenon of regression to the mean into account.

The Asymptomatic Carotid Atherosclerosis Study (ACAS) and the Asymptomatic Carotid Surgery Trial (ACST) demonstrated an absolute risk reduction of more than 5% with asymptomatic stenosis of 80–99%. The morbidity rate associated with CEA in our hospital is less than 3%, thus, patients with an asymptomatic carotid stenosis of 80–99% are considered for surgical treatment in our center. The results of this study are of significant relevance for this group of patients, as postoperative contralateral duplex showed a drop in at least one duplex category in 61% of these patients. These patients could inappropriately undergo a second carotid endarterectomy and be exposed to an unnecessary operative risk when indication for bilateral intervention is solely based on preoperative DUS before the first CEA. Therefore, in patients with bilateral carotid stenosis, other diagnostic methods such as CTA or MRA should be considered, or a repeat duplex should be obtained before proceeding with the second CEA.

The overestimation of contralateral carotid stenosis is likely to be related to changes in distribution of blood flow to the brain. Using MRA, van Everdingen et al. showed that increased volume flow is frequently found in ICAs with a <70% stenosis that are contralateral to an occlusion or an ICA with a >70% stenosis. They also found a significant correlation between volume flow and PSV, indicating that changes in PSV are mainly due to changes in volume flow. Thus, in case of bilateral stenosis, shunting of blood flow through the least stenotic artery leads to higher velocities at duplex measurement. In addition to shunting of blood flow, a decreased compliance of the vessel wall in atherosclerotic disease might have an effect on increase in postoperative velocities. A lower compliance results in a reduction of flow-induced vascular dilatation and a consequent increase in flow velocities in diseased vessels.

Diminished autoregulation of intracerebral vascular tone has also been described to be a contributing factor of postoperative overestimation of contralateral velocities. In patients with significant bilateral stenosis, loss of autoregulatory mechanisms due to persistent low-flow states in cerebral vasculature can result in chronically dilated intracerebral vessels. This ultimately leads to a lower intracranial perfusion pressure with a concomitant larger pressure gradient across the stenosis. With increasing stenosis, the velocity will increase proportionally.

Although a lowering in postoperative contralateral velocities with concomitant drop in duplex category was seen in many of the patients with significant bilateral carotid stenosis, this was not seen in all of them. A considerable number of the patients showed no change in duplex category and a few patients were noted to have an increase in postoperative estimated stenosis. This may be explained by collateralization of the external carotid artery to the internal carotid artery via the ophthalmic artery and other collateral sites in patients with high grade stenosis. An extensive collateral network reduces the degree of earlier explained shunting to the opposite side. For this reason, these patients are not expected to show a decrease in contralateral velocities after ipsilateral CEA. Furthermore, in patients with bilateral stenosis, the degree of stenosis on the operated side might be influenced by the presence...
of the contralateral stenosis as well. Grajo et al. found that in patients with a contralateral stenosis of 40% or more, ultrasound Doppler velocities are a less accurate method of determining the degree of stenosis. Therefore, it is understandable that the operated symptomatic stenosis might be less severe than the asymptomatic stenosis on the contralateral side. In that case, postoperative shunting to the contralateral side is unlikely and the decrease in contralateral postoperative velocities probably less evident.

The retrospective nature of this study leads to a few important limitations. First, the degree of contralateral carotid stenosis has not been determined by macroscopic measurement of the cross-sectional stenotic area after CEA, which would have provided the true overestimation of contralateral stenosis. Second, we were not able to withdraw any information about blood pressure during the measurements from the available data, which may cause a confounding bias for flow measurements. Furthermore, the number of patients with bilateral significant stenosis on first duplex is small, but the patient numbers and our results were comparable with previous studies. Finally, when focusing on bilateral significant stenosis, only those patients with high velocity measurements are taken into account. Hence, in our study, the statistical phenomenon of regression towards the mean might be an additional confounding factor.

In conclusion, in patients with bilateral significant carotid stenosis, DUS tends to overestimate the degree of stenosis on the contralateral side. After unilateral CEA, a considerable number of patients with significant contralateral carotid stenosis are downgraded by at least one duplex stenosis category. This phenomenon is more pronounced in patients with a higher postoperative estimated degree of stenosis. Therefore, when DUS is used as sole investigation for determining degree of carotid stenosis, it is advisable to repeat the examination after unilateral CEA in patients with bilateral significant carotid stenosis or to consider other diagnostic methods such as CTA or MRA.

REFERENCES