Coronary angiography in patients undergoing carotid artery stenting reveals a high incidence of significant coronary artery disease

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Abstract

Objective To assess the incidence, morphology, and associated clinical symptoms of coronary artery disease in patients undergoing elective carotid artery stenting.

Methods In a prospective observational study of a tertiary care centre (university teaching hospital) 444 consecutive patients underwent elective stenting of the carotid artery. Twenty-four patients had to be ruled out because of urgent carotid intervention for severe neurological symptoms, lack of compliance, complications from vascular puncture, or renal failure. In 390 patients, the coronary angiography was performed together with carotid artery stenting in a single session; the remaining 30 patients have had a recent coronary angiography.

Results Single-, two-, three-vessel disease, and left main stenoses were found in 70 (17%), 64 (15%), 93 (22%), and 31 (7%) patients, respectively. Sixty-six (16%) patients had a positive history of coronary artery disease but no current significant stenosis. Only 39% of the patients with significant stenoses (n=258) had clinical cardiac symptoms.

Conclusions For patients, undergoing elective stenting of the carotid, routine coronary angiography reliably disclose morphologically significant coronary artery disease and enables consecutive treatment in 61% and 29%. This safe measure is a useful one, for a majority of patients with a significant stenosis is asymptomatic.

Keywords: carotid artery; coronary angiography; stent
Introduction
The coincidence of stroke in coronary artery patients and, vice versa, myocardial infarction in neurological patients is well known.[1][2][3] These seemingly connected clinical events account for many fatal complications of interventional therapy.[1][3] Knowledge of concomitant coronary artery disease and comprehension of the eventually absence of coronary symptoms in severely diseased patients would probably increase the safety of carotid artery stenting in the patient population becoming increasingly older. It was, therefore, the purpose of our study to analyse systematically the coronary arteries in all, even asymptomatic, patients undergoing routine carotid artery stenting in our institution.

Methods
From July 1998 to January 2004, 444 patients underwent elective stenting of the internal carotid artery in our institution. According to our research protocol, carotid artery stenting was performed in asymptomatic patients with ≥ 80% stenosis of the extracranial carotid artery and symptomatic individuals with ≥ 60% stenosis. Only 10 patients were referred to surgical endarterectomy or treated conservatively because of severe circumferential calcifications or variations of the aortic arch. Patients were referred from our internal and neurological department, from local general practitioners, or from other hospitals. Every patient underwent an independent neurological examination prior to, 24 hours after and 30 days after carotid artery stenting. In addition, a positive history of concomitant coronary artery disease was recorded, and all patients were thoroughly checked and questioned for symptoms of either typical angina pectoris or chest pain. Angina severity at baseline was classified according to the Canadian cardiovascular society classification.[4] A proven history of coronary artery disease was defined either as a previously angiographically documented coronary artery disease according to the criteria used in the present study (see below) or as a history of myocardial infarction treated in a hospital with a discharge letter available to confirm the diagnosis. Exercise stress tests were not performed systematically before the procedures. After the first 40 carotid artery procedures, in all patients without recent coronary angiography (< 3 months), a coronary angiography was attempted in a single session immediately before carotid artery stenting. The following conditions were defined as contraindications and accounted for 24 patients who did not undergo a simultaneous coronary angiography: urgent carotid artery stenting for severe neurological symptoms, lack of compliance, complications from vascular puncture, and renal failure.

The final study population consisted of 420 patients: in 30 patients a recent angiogram was available, in the other 390 patients coronary angiography was performed in a single session immediately before carotid artery stenting. The clinical demographic data are listed in table 1.
All data were collected prospectively. Written, informed consent was obtained from each patient, and the study was approved by our institutional review board.
Table 1. Clinical characteristics of patients with and without coronary artery disease

<table>
<thead>
<tr>
<th></th>
<th>with coronary artery disease</th>
<th>without coronary artery disease</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients, n</td>
<td>324</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>69±9</td>
<td>69±9</td>
<td>NS</td>
</tr>
<tr>
<td>Male sex, n (%</td>
<td>216 (66)</td>
<td>60 (63)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>246 (75)</td>
<td>60 (63)</td>
<td>0.0034</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>94 (29)</td>
<td>24 (25)</td>
<td>NS</td>
</tr>
<tr>
<td>Congestive heart failure, n (%)</td>
<td>42 (13)</td>
<td>2 (2)</td>
<td>0.0022</td>
</tr>
<tr>
<td>Current smoking, n (%)</td>
<td>43 (13)</td>
<td>11 (11)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypercholesterolemia, n (%)</td>
<td>225 (69)</td>
<td>57 (59)</td>
<td>0.049</td>
</tr>
<tr>
<td>Peripheral vascular disease, n (%)</td>
<td>66 (20)</td>
<td>5 (5)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Atrial fibrillation, n (%)</td>
<td>45 (14)</td>
<td>14 (15)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Neurological symptoms

| Stroke, n (%)                        | 21 (6)                      | 14 (15)                         | NS |
| Transitory attack, n (%)             | 102 (31)                    | 27 (28)                         | NS |
| Unspecific symptoms, n (%)           | 57 (18)                     | 12 (13)                         | NS |
| Asymptomatic patients, n (%)         | 144 (45)                    | 43 (44)                         | NS |

Carotid artery angiography and stenting:
At least 2 projections of the carotid artery stenosis were obtained for the calculations of the vessel diameter and the degree of the stenosis. Our interventional procedures followed the guidelines of good clinical practice with routine use of protective devices since July 2002.[5]

Coronary angiography:
Coronary angiography could be performed in all projected patients without complications and was routinely performed before carotid artery stenting. For a complete visualization of the left coronary artery system at least 4 different projections were used. For a complete visualization of the right coronary artery at least standard left and right anterior oblique projections were obtained. The degree of a stenosis was initially estimated by the operator in order to facilitate an immediate onsite decision whether or not percutaneous coronary intervention was necessary. For statistical analysis, all visually estimated lesions of ≥ 50% were calculated after the procedure with the use of a semi-automatic device (Hicor®, Siemens®). Only those measurements were taken for analysis in the present study. The criterion for angiographic one-, two-, or three-vessel coronary artery obstruction was either a ≥ 70% reduction of the internal diameter of the right or left anterior descending or left circumflex coronary artery or a ≥ 50% reduction in the internal diameter of the left main coronary artery.[6] In patients with previous coronary artery bypass grafting a graft stenosis, just like a native vessel stenosis, was defined as ≥ 70%.

Coronary artery interventions:
The sequence of interventions was based on clinical symptoms of the patient:[7] Usually a routine coronary angiography was followed by angiography and subsequent intervention of the carotid artery. Percutaneous coronary intervention was carried out last. In patients
presenting in Canadian cardiovascular society class IV, the percutaneous coronary intervention was performed before the stenting of the carotid artery. In 12 cases with stenoses in other extracoronary vessels, angiography and stenting of these lesions were carried out last. All procedures were performed by three experienced cardiologists.

Statistics:
All variables were summarized using frequency distributions for categorical variables and mean ± standard deviation for continuous variables. Comparisons between groups (coronary artery disease or non-coronary artery disease) were performed using the Mann-Whitney U-test for continuous variables and chi-square-test for categorical variables. P values of ≤ 0.05 were considered statistically significant.

Results
Results of carotid artery stenting are shown in table 2.

Table 2. Results and complications of carotid artery stenting

<table>
<thead>
<tr>
<th></th>
<th>with coronary artery disease</th>
<th>without coronary artery disease</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients, n</td>
<td>324</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>Technical success, n (%)</td>
<td>318 (98)</td>
<td>92 (96)</td>
<td>NS</td>
</tr>
<tr>
<td>Neurological complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>2 (0.6)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Major stroke, n (%)</td>
<td>2 (0.6)</td>
<td>2 (2)</td>
<td>NS</td>
</tr>
<tr>
<td>Minor stroke, n (%)</td>
<td>2 (0.6)</td>
<td>2 (2)</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSTEMI, n (%)</td>
<td>1 (0.3)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Inguinal haematoma requiring transfusion</td>
<td>3 (0.9)</td>
<td>1 (1)</td>
<td>NS</td>
</tr>
</tbody>
</table>

NSTEMI: non ST-elevation myocardial infarction

The success rate as well as the neurological complication rate was not statistically different in patients with or without concomitant coronary artery disease. Non ST-elevation myocardial infarction (maximum rise of CK-Mb 29 U/l) occurred in one patient resulting from occlusion of a small side branch during simultaneous percutaneous coronary intervention.

Coronary artery disease was present in 324 (77%) patients of the study population. Sixty-six (16%) patients had a positive history of proven coronary artery disease but no current significant stenosis. Most of these had either had successful percutaneous coronary intervention without restenosis, or coronary artery bypass grafting with open non-stenotic grafts to diseased vessels. In 258 patients with at least one significant stenosis, 93 patients were previously known to have coronary artery disease whereas in 165 individuals coronary artery disease was detected during coronary angiography. The coronary artery morphology is summarized in table 3. Among those with coronary artery
disease, three-vessel disease was most often found. In addition, a significant stenosis of the main stem of the left coronary artery was not uncommon. Hypertension, congestive heart failure, peripheral arterial occlusive disease, and hypercholesterolemia, but not diabetes or current smoking were statistically more often found in patients with concomitant coronary artery disease compared to patients without (table 1).

Clinical cardiac symptoms are listed in table 3. Interestingly enough, 157 of 258 patients (61%) with a significant stenosis as documented during coronary angiography had no clinical symptoms at all regarding coronary artery disease. Clinical symptoms were similar in patients with single vessel, two vessel, and three vessel disease. However, patients with left main coronary artery disease had statistically significant more often CCS III angina (p<0.01).

Location and morphology of the carotid artery stenoses were not statistically different in patients with or without coronary artery disease. The degree (84.4 ± 9.3% vs 85.1 ± 9.6%) and length (11.3 ± 3.8mm vs 11.7 ± 5mm) of carotid artery stenosis was similar in patients with and without concomitant coronary artery disease.

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>1 VD</th>
<th>2 VD</th>
<th>3 VD</th>
<th>LM</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients, n</td>
<td>258</td>
<td>70</td>
<td>64</td>
<td>93</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>No clinical symptoms, n (%)</td>
<td>157 (61)</td>
<td>43</td>
<td>42</td>
<td>58</td>
<td>14</td>
<td>NS</td>
</tr>
<tr>
<td>CCS II, n (%)</td>
<td>58 (22)</td>
<td>16</td>
<td>16</td>
<td>21</td>
<td>5</td>
<td>NS</td>
</tr>
<tr>
<td>CCS III, n (%)</td>
<td>30 (12)</td>
<td>7</td>
<td>5</td>
<td>7</td>
<td>11</td>
<td>NS</td>
</tr>
<tr>
<td>CCS IV, n (%)</td>
<td>13 (5)</td>
<td>4</td>
<td>1</td>
<td>7</td>
<td>1</td>
<td>NS</td>
</tr>
</tbody>
</table>

VD: vessel disease
LM: left main coronary artery
CCS: Canadian Cardiovascular Society classification

Treatment of coronary artery disease:
In summary, 123 (48%) out of 258 patients got interventional (41%) or surgical (7%) therapy and the rest was treated conservatively. In 78% (82 of 105 patients) undergoing percutaneous coronary intervention the procedure was performed in a single session with carotid artery stenting.

Discussion
This is the first report depicting prospectively the presence and extension of coronary artery disease in patients undergoing carotid artery stenting. In 420 consecutive patients undergoing stenting for clinical significant stenosis of the carotid artery coronary arteries were investigated angiographically. The incidence of significant stenoses was surprisingly high. With respect to good clinical practice, 29 % of all consecutively examined patients had an indication for interventional therapy. The high number of coronary artery disease
seems reasonable in the light of the advanced age and the frequent co-morbidity of our patient population. In the past, some authors have reported on neurological complications occurring in connection with coronary artery bypass grafting or myocardial infarctions complicating the endarterectomy of carotid artery stenoses.\cite{8}\cite{9}\cite{10} Doppler flow investigations of the carotid artery rather than invasive data were used in most of the studies. Angiographic data regarding the coincidence of carotid and coronary artery disease are limited to non-prospective observational data with a limited number of patients. Consequently, there have been discussions about the best method or sequence of the surgical treatment of carotid artery stenoses and coronary artery disease.\cite{11}\cite{12}\cite{13}\cite{14}\cite{15} As stenting of the carotid artery is replacing surgery more and more the number of publications concerning carotid artery stenting in the presence of coronary artery disease is on the increase as well.\cite{16} A few authors reported on simultaneous stenting of the carotid artery and coronary arteries.\cite{7}\cite{17}\cite{18}\cite{19}\cite{20} Patients undergoing carotid artery stenting seem to be older and more often affected by a clinically significant co-morbidity than patients undergoing surgical endarterectomy. This clinical observation is confirmed by the considerable high number of NASCET ineligible patients undergoing carotid artery stenting in several studies.\cite{18}\cite{21} Thus, information about the coronary artery pathology seems to be of clinical importance, especially for this patient population. The search for specific risk factors or co-morbidities that could help to speculate about concomitant coronary artery disease in carotid artery stenting patients without typical symptoms of coronary artery disease does not seem to be clinically accurate: Consistent with findings of other authors, most of the common risk factors were associated with a higher incidence of concomitant coronary artery disease,\cite{22}\cite{23} but only symptomatic peripheral artery occlusive disease turned out to occur much more often in coronary artery disease patients (table 1). Several years ago, Vigneswaran et al did a small study that suggested a higher incidence of left main disease compared to 3-vessel disease not involving the left main stem in patients with significant carotid artery stenoses.\cite{24} However, this observation cannot be supported by our own data. More strikingly, in the present patient population exercise angina and even the presence of severe coronary symptoms did not correlate with a more extensive coronary pathology. In other words, in this specific patient cohort it seems impossible to judge the extent of the coronary artery disease just by the clinical presentation of a patient. To a certain extent, these specific findings may be explained by the morbidity and lack of physical activity in our patient cohort, as physically active patients might experience symptoms before inactive patients do. The clinical importance of our findings is obvious: patients undergoing elective stenting of the carotid artery have a high incidence of concomitant coronary artery disease. Consistently performed routine coronary angiography has been proved to be a safe method with high diagnostic efficiency and promises to be a useful tool to avoid unexpected cardiac complications during stenting of the carotid artery. Limitations: Patients scheduled for carotid artery stenting tend to be older than patients referred for surgical endarterectomy. Thus, the percentage of patients with concomitant coronary artery disease in the present cohort could be higher than in the overall carotid artery stenosis patient population. The number could also be affected by the cardiology nature of our department, which does not only treat patients referred from the outside but also recruits them from our own specific patient population.
References


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