Influence of carotid artery stenosis on stroke in patients undergoing off-pump coronary artery bypass grafting

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Abstract

Objective: It is well known that the presence of carotid artery stenosis increases the risk of perioperative stroke in patients undergoing cardiac surgery with cardiopulmonary bypass. Although off-pump coronary artery bypass grafting (CABG) can avoid the adverse effects of cardiopulmonary bypass, the influence of carotid artery stenosis on the incidence of stroke in patients undergoing off-pump CABG has not been well clarified.

Methods: We conducted a retrospective study of 461 patients who underwent elective off-pump CABG after screening for carotid artery stenosis at our institute between September 2004 and May 2007. The incidence and etiologies of stroke were identified. Preoperative screening revealed significant carotid artery stenosis in 49 patients. Clinical results were compared between patients with and without carotid artery stenosis.

Results: Postoperative stroke occurred in two (0.43%) of the 462 study patients, and in-hospital mortality occurred in three (0.65%). Stroke was due to decreased perfusion resulting from hypovolemic shock in one and thrombosis in the other. There was neither stroke nor in-hospital mortality in patients with carotid artery stenosis, although there were two strokes (0.49%) and three in-hospital mortalities (0.73%) in patients without carotid artery stenosis.

Conclusions: The influence of carotid artery stenosis on the incidence of perioperative stroke may be little in off-pump CABG, especially in patients with moderate carotid artery stenosis.

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1. Introduction

Carotid artery stenosis (CAS) is present in 10—20% of patients undergoing coronary artery bypass grafting (CABG) and accounts for 30% of strokes associated with CABG [1]. Current ACC/AHA guidelines recommend prophylactic carotid endarterectomy (CE) to reduce the risk of perioperative stroke in patients with CAS who are scheduled for CABG. This recommendation is based mainly on results of several randomized studies [2—4] of general CAS patients that compared carotid endarterectomy (CE) with medical treatment for stroke prevention. However, in patients with CAS who undergo CABG evidence of a protective effect of prophylactic CE against coronary bypass stroke is lacking, and some researchers have doubted whether there is such an effect on risk reduction [5,6].

The etiology of stroke associated with CABG in patients with CAS may be multifactorial. A recent report by Schoof et al. emphasized the importance of impaired cerebral autoregulation distal to CAS as a main cause of stroke [6]. A typical mechanism is intra-operative hypoperfusion of the brain downstream of significant CAS, which may be due to the adverse effects of extracorporeal circulation. Although off-pump CABG can avoid the adverse effects of extracorporeal circulation, the influence of CAS on stroke in patients undergoing off-pump CABG has not been well clarified. Thus, we conducted a study to evaluate the clinical results of off-pump CABG in patients with unprotected CAS.

2. Materials and methods

The study was a retrospective single institutional analysis of 461 consecutive patients who underwent elective off-pump CABG after screening for CAS between September 2004 and May 2007. No patient who underwent any other associated procedure was included in the analysis. Seventy-three patients who did not undergo screening for CAS before surgery and 71 patients who underwent emergent operation were excluded from this study. During this period, all isolated CABGs were scheduled to be performed off-pump, and six patients in whom the procedure was converted to on-pump CABG were excluded from the study. Our institutional ethics committee waived the need for patient consent for this
study, and approval was provided before publication of the data.

2.1. Screening for CAS

Magnetic resonance angiography (MRA) was performed in all patients who were scheduled for elective CABG. In patients with suspected CAS, carotid artery duplex scanning was conducted to determine the severity of CAS. CAS was classified according to laterality and severity of the stenosis. The severity of CAS was quantified according to the method used in the European Carotid Surgery Trial and was categorized as none/mild (<50%), moderate (50—70%), severe (80—99%), or total occlusion. Significant CAS was found in 49 patients (10.6%). The decision to treat CAS was determined by an attending neurologist. Treatment for CAS before CABG was considered in patients with a symptomatic carotid stenosis or in asymptomatic patients with internal carotid stenosis of 80% or more, if the condition of the patient was stable and surgery on the carotid artery could be performed safely before CABG. In one patient, whose cardiac condition was considered stable, carotid artery stenting proceeded CABG. This patient was excluded from the CAS group.

2.2. Operative techniques

Heparin (3.0 mg/kg) was administered intravenously after sternotomy to maintain an activated clotting time of more than 400 s, and it was neutralized at the end of the procedure with the use of protamine sulfate (3.0 mg/kg). In patients who underwent CABG with a saphenous vein graft, continuous heparin infusion was started after hemostasis was achieved to maintain an activated clotting time of 160—180 s until warfarin control was achieved. In patients who suffered new atrial fibrillation postoperatively, continuous heparin infusion was also started in the same manner. Aspirin was given to all patients.

In patients with a proximal anastomosis, epiaortic ultrasonography was performed to identify any atherosclerotic lesion of the ascending aorta. In patients with a diseased ascending aorta, a heartstring anastomotic device (Guidant, Indianapolis, IN) was used. During manipulation of the heart systolic arterial pressure was maintained above 80 mmHg.

2.3. Diagnosis of brain infarction

Stroke was suspected from any new global or focal neurological deficit and was confirmed by computed tomography or magnetic resonance imaging. Stroke was diagnosed definitively by an attending neurologist. Reversible cerebral ischemic events were not included. Stroke etiologies were identified and divided into two categories: thromboembolism and hypoperfusion. Thromboembolism was further divided into three types: embolic, lacunar, and thrombotic.

2.4. Statistical analysis

Continuous variables are reported as mean ± SD. Fisher’s exact test was used to analyze between group differences in categorical variables. The Mann–Whitney test was used to analyze differences in continuous variables. Statistical significance was accepted at \( p < 0.05 \). Statistical analysis was performed with SPSS statistical software (SPSS version 11.0; SPSS Japan, Tokyo, Japan).

3. Results

3.1. Stroke associated with off-pump CABG

Patient characteristics and clinical outcomes are shown in Table 1. The incidence of perioperative stroke was 0.43% (2/461), and operative mortality was 0.65% (3/461). Character-
Characteristics of the stroke patients are listed in Table 2. All strokes occurred during the postoperative period, and there was no intraoperative stroke. Stroke was due to thrombosis in one, and decreased perfusion resulting from hypovolemic shock in the other.

### 3.2. CAS

Results of carotid artery screening are shown in Table 3. CAS was found in 49 patients (10.6%). Unilateral stenosis was found in 39 patients with moderate stenosis in 26, severe stenosis in 6, and total occlusion in 7. Bilateral stenosis was found in 10 patients with moderate bilateral stenosis in 8, and severe bilateral stenosis in 2. All patients were asymptomatic.

Patients in the CAS group were significantly older than patients in the non-CAS group and the prevalence of peripheral vascular disease was significantly higher in the CAS group than in the non-CAS group. Among patients with CAS there was no mortality (0%) or stroke (0%). Among patients without CAS, there were 2 strokes (2/412, 0.49%) and 3 in-hospital mortalities (3/412, 0.65%).

### 4. Discussion

The incidence of stroke associated with conventional on-pump CABG with cardiopulmonary bypass is around 0.8% and 5.2% [7]. Whether off-pump CABG reduces the incidence of stroke remains controversial. According to two meta-analyses, the benefit of off-pump coronary bypass surgery in reducing the incidence of stroke is marginal [8,9]. However, according to a large retrospective analysis (n = 16,184), the incidence of stroke is significantly lower with off-pump CABG (2.5%) than with conventional CABG (3.9%) [10].

The characteristics of stroke may differ between on- and off-pump CABG. With regard to the timing of stroke, less than half of the strokes (35—46%) occurred intraoperatively in patients undergoing conventional on-pump CABG [11—14]. In our patients undergoing off-pump CABG no stroke occurred intraoperatively. Our results are in agreement with results of the Peel et al. study in which on-pump surgery was associated with early stroke (2 days), whereas off-pump surgery was associated with later stroke (4 days) [15]. With regard to the reported etiology of stroke, most strokes in patients undergoing conventional on-pump CABG were of two major causes: embolism (40.9—54.3%) and hypoperfusion (35.6—45.7%) [11,13,14,16]. In off-pump CABG, the number of strokes due to low perfusion has decreased dramatically, which suggests an advantage of off-pump CABG in eliminating the adverse effects of cardiopulmonary bypass.

CAS is considered to play an important role in the mechanism of stroke associated with coronary bypass. In the general CABG population, the prevalence of significant CAS is relatively high. The reported prevalence of moderate CAS (more than 50% stenosis) is 22% [17] and results in a 3.8% stroke rate [18], and the prevalence of severe CAS (more than 80% stenosis) is 8.5% [17], which results in a 14% stroke rate [19]. Therefore, CAS is considered to account for 30% of strokes associated with coronary bypass [1]. The typical characteristic of stroke caused by CAS is intraoperative hypoperfusion ipsilateral to the location of the CAS [6,20]. Stamou et al. reported that among 21 CAS patients who suffered stroke, 16 strokes were ipsilateral [21]. Mickleborough et al. reported that among 7 CAS patients who suffered strokes, 4 strokes were ipsilateral and 6 strokes occurred intraoperatively [20]. Recently, Schoof et al. reported that typical strokes in CAS patients undergoing on-pump CABG were caused by decreased cerebral perfusion pressure and impaired cerebral autoregulation to compensate for the additional blood pressure decrease [6]. Our result is very interesting because there were no strokes in the 49 CAS patients who underwent elective off-pump CABG. This suggests that such low perfusion status might have a detrimental effect on the brain only under extracorporeal circulation. Unfortunately, one patient with CAS who underwent emergent CABG suffered a stroke in this study period. This patient was excluded from this study because the operation was emergent. The stroke occurred in a female patient who had suffered a transient ischemic attack and was diagnosed with unilateral carotid artery occlusion (symptomatic CAS) before the onset of ischemic heart disease. She suffered unstable angina due to severe stenosis of the left main trunk and emergent CABG was performed immediately after diagnosis. The stroke occurred on postoperative day 2 after she had recovered from anesthesia without any neurologic deficit. Computed tomography revealed multiple small strokes in both hemispheres, which suggested an embolic cause.

### Table 2
Profile of stroke patients

<table>
<thead>
<tr>
<th>No.</th>
<th>Age/sex</th>
<th>Cause of stroke</th>
<th>Timing of onset</th>
<th>Location of stroke</th>
<th>Carotid lesion</th>
<th>Stroke history</th>
<th>Aortic clamp</th>
<th>AF</th>
<th>Anti-coagulant</th>
<th>Coronary risk factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>80/male</td>
<td>Thrombotic</td>
<td>6</td>
<td>Multiple</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>HT, HLP</td>
</tr>
<tr>
<td>2</td>
<td>76/female</td>
<td>Hypoperfusion due to shock</td>
<td>1</td>
<td>Right corona radiata</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>HT, DM, HD</td>
</tr>
</tbody>
</table>

AF: atrial fibrillation; HT: hypertension; HLP: hyperlipidemia; DM: diabetes mellitus.

### Table 3
Results of carotid artery screening

<table>
<thead>
<tr>
<th>Laterality</th>
<th>Severity</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral</td>
<td>Moderate</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Occluded</td>
<td>7</td>
</tr>
<tr>
<td>Bilateral</td>
<td>Moderate and moderate</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Moderate and severe</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Severe and severe</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Both occluded</td>
<td>0</td>
</tr>
</tbody>
</table>
The current ACC/AHA guidelines recommend prophylactic CE to reduce the incidence of perioperative stroke in patients with moderate symptomatic CAS or severe asymptomatic CAS. However, some authors have doubted the effectiveness of prophylactic endarterectomy for reducing coronary bypass stroke [22]. Gaudino et al. reported similar in-hospital results between patients with and without prophylactic CAS treatment, although a significant difference was observed in cerebral events at mid-term follow-up [5]. Schoof et al. reported that among 113 patients with severe CAS who were candidates for prophylactic CAS treatment, stroke occurred in only two patients (1.8% stroke incidence). Thus, it seems prophylactic CAS treatment would not have been beneficial because the incidence of stroke, even with prophylactic treatment, was similar [6] (2–3% stroke incidence). The findings of our study were similar; the only stroke occurred in a patient with an occluded carotid artery.

4.1. Study limitations

Limitations of the present study include those inherent to retrospective, nonrandomized data collection. The number of study patients is relatively small which does not allow discussion of the effect of an off-pump procedure on rare complications like stroke. Our results would not override the need for carotid artery screening in patients undergoing off-pump CABG because our study did not include the highest risk group, patients with an occluded artery and severe contralateral stenosis. In addition, the possibility of intraoperative conversion to on-pump CABG cannot be avoided.

5. Conclusion

There may be little influence of carotid artery stenosis on the incidence of perioperative stroke in off-pump CABG especially in patients with moderate carotid artery stenosis.

References