Stroke Complicating Percutaneous Coronary Intervention in Patients With Acute Myocardial Infarction

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**Background** Stroke associated with percutaneous coronary intervention (PCI) is a tragic complication. Despite advances in the practice of PCI, the incidence of stroke complicating PCI has not changed over the decades. The objective of the present study was to evaluate incidence and correlates of stroke occurring in patients with myocardial infarction (MI) undergoing PCI.

**Methods and Results** Stroke was defined as the presence of any new focal neurological deficit lasting ≥24 h that occurred anytime during or after PCI until discharge. In 2,281 consecutive patients with PCIs for non-ST-elevation MI, or ST-elevation MI (STEMI), 20 strokes were identified (0.88%). Strokes were ischemic in 95%. On multivariate analyses, ejection fraction ≤30% (odds ratio=4.3, p=0.003) was the only independent predictor for stroke. In patients who developed stroke within 24 h of PCI, PCI of vein grafts was more frequent, and use of glycoprotein IIb/IIIa inhibitor was less frequent. Those patients tended to present late in the course of MI. Stroke found more than 24 h after PCI was related to diabetes, higher serum creatinine, lower ejection fraction, anterior wall STEMI and emergency use of intra-aortic balloon pumps.

**Conclusions** Low ejection fraction was the only independent predictor for stroke, but risk factors for periprocedural stroke are different from those of stroke occurring more than 24 h after PCI. Upstream use of glycoprotein IIb/IIIa inhibitor might decrease the risk of periprocedural stroke. (*Circ J* 2007; 71: 1370–1375)

**Key Words:** Catheterization; Cerebral infarction; Complications

Stroke is an infrequent but catastrophic complication of percutaneous coronary intervention (PCI). The rate of stroke in patients undergoing PCI has been reported to be less than 1%.1-8 Despite refinements of devices and techniques in PCI, the incidence of stroke related to PCI has not changed significantly over the decades. Advanced age, diabetes, hypertension, previous cerebrovascular accidents, low creatinine clearance, emergency PCI, vein graft PCI and emergency use of intra-aortic balloon pump have been predictors of periprocedural stroke.6-9 Particularly, stroke in patients with acute coronary syndromes (ACS) has been associated with higher in-hospital mortality.10-13 Registry data has shown that in-hospital stroke was more frequent in patients with ST-elevation myocardial infarction (STEMI) than in patients with non-STEMI (NSTEMI) or unstable angina.11 In the prethrombolytic era, stroke occurred in 1.7% to 2.4% of patients with STEMI, and the mortality rate was as high as 50% to 60%.10,14 Thrombolytic therapy has reduced the occurrence of non-hemorrhagic stroke, but increased the risk of hemorrhagic stroke.15-17 However, the introduction of primary angioplasty has decreased the incidence of hemorrhagic stroke without concomitant increase in ischemic stroke.18 With further improvements of devices, techniques and adjunctive pharmacological therapies, PCI has been more widely used for treatment of ACS. However, data on stroke in patients with ACS undergoing urgent or emergency PCI are limited in published reports. The aim of the present study was to assess the incidence and predictors of stroke in patients with STEMI or NSTEMI undergoing PCI.

**Methods**

**Patient Population** The clinical, angiographic, procedural and in-hospital outcomes of 2,167 consecutive patients who were admitted with myocardial infarction (MI) (STEMI or NSTEMI) and underwent urgent or emergency PCI from January 2001 to June 2005 at the Lahey Clinic Medical Center were analyzed. We excluded 19 patients who underwent urgent or emergency coronary artery bypass grafting during the index hospitalization. None of the excluded patients had a stroke before surgery. The final cohort consisted of 2,148 patients who underwent 2,281 PCI.

**Definitions** Stroke was defined as any new focal neurological deficit lasting ≥24 h that occurred anytime during or after PCI until discharge. Deficits lasting <24 h were defined as transient ischemic attack (TIA), and were not included in the present study. The diagnosis of stroke was made by experienced neurologists in every case, and confirmed by either computed tomography (CT) or magnetic resonance imaging (MRI). Cardiac ultrasound was performed when appropriate to detect possible embolic sources. Strokes were classified into 3 categories: ischemic, primary hemorrhagic, and ischemic stroke with hemorrhagic conversion. Patients were diagnosed with STEMI when they had new
or presumed-new ST-segment elevation ≥1 mm in 2 or more contiguous leads or new left bundle branch block on the index electrocardiogram (ECG) with positive cardiac biochemical markers. The diagnosis of NSTEMI was made when positive cardiac biochemical markers were noted without new ST-segment elevation on the index ECG. The positive threshold for cardiac biochemical markers in the current study was a cardiac troponin I concentration >0.4 ng/ml.

Cardiogenic shock was defined as a state of hypoperfusion with systolic blood pressure <80 mmHg, or need of intravenous inotropic agents and/or intra-aortic balloon pump to maintain systolic blood pressure >80 mmHg. Angiographic success of PCI was defined as residual diameter stenosis <20% in the presence of grade 3 Thrombolysis In Myocardial Infarction (TIMI) flow.

Statistical Analysis
Quantitative data are presented as mean value ± SD, and qualitative data as frequencies. Continuous variables were compared using unpaired Student’s t-tests or ANOVA. Categorical variables were examined by chi-square test or Fisher’s exact test. To identify independent predictors for stroke, univariate and multivariate analyses by logistic regression were conducted. From the univariate analyses, the following variables were entered into the multivariate model: diabetes, history of stroke, peripheral vascular disease, creatinine clearance <60 ml/min, left ventricular ejection fraction ≤30%, absence of glycoprotein (GP) IIb/IIIa inhibitor use before PCI, and exigent use of intra-aortic balloon pump. All probability values are 2-tailed and a value of p<0.05 was considered statistically significant. Statistical analyses were performed with Stat View (Stat View 5.0, Abacus Concepts Inc, Berkley, CA, USA).

Results
Baseline Characteristics
The average age of the study population was 64 years (range: 27–97). Of the 2,281 procedures, 1,021 were PCI for STEMI (44.8%), and 1,260 were for NSTEMI (55.2%). A stroke was observed in 20 of the 2,281 procedures for a total incidence of 0.88%.

Compared to patients without stroke, history of previous cerebrovascular accident (p=0.048) and chronic renal failure on dialysis (p=0.047) were more prevalent in patients with stroke (Table 1). The stroke group had a trend for more diabetes mellitus (p=0.05) and a history of peripheral vascular disease (p=0.06). Serum creatinine was higher (p=0.01) and left ventricular ejection fraction was substantially lower (p<0.0001) in the stroke group. Although STEMI and NSTEMI were similarly distributed in the 2 groups, anterior wall STEMI was more frequent in the stroke group.

Procedure Characteristics
Procedure characteristics were comparable, except that patients with stroke had less use of GP IIb/IIIa inhibitors before PCI (p=0.01) and more frequent unplanned use of intra-aortic balloon pumps (p=0.02) compared to those without stroke (Table 2). Left heart catheterization and/or left ventriculography were performed at the time of PCI in 60% of patients with stroke, and 67% of patients without stroke (p=0.49). Angiography of the internal mammary artery was performed more frequently in the stroke group, although the trend did not reach statistical significance (15% vs 6%, p=0.1). Activated clotting time was obtained at the end of the procedure in 80% of the patients, and similar between the 2 groups (stroke; 282±80 s, control; 270±56 s, p=0.45).
Angiographic Characteristics

Patients with stroke more often underwent PCI to the left anterior descending coronary artery, although this trend was not statistically significant (50% vs 34%, p=0.09) (Table 3). Other angiographic parameters were similar between the 2 groups.

Stroke Characteristics

Head CT scanning or MRI was performed in all patients with stroke, and 95% of the strokes were ischemic. Ischemic stroke with hemorrhagic conversion was found in 15%. There was only 1 (5%) primary hemorrhagic stroke. Ischemic stroke most often involved major cerebral arterial territories: middle cerebral artery in 55%, vertebralbasilar artery in 20%, posterior cerebral artery in 20% and carotid artery in 5%. The most common presentation was hemiparesis (45%), with two-thirds being right-sided. Confusion or decreased alertness was seen in 35%, aphasia 20%, hemianopsia 10%, diplopia 5% and vertigo 5%. Transthoracic or transesophageal echocardiography was performed in 15 out of the 20 patients with stroke at a mean interval of 6 days after the procedure. Left ventricular thrombus was detected in 1 of 7 (14%) patients with anterior wall STEMI in the stroke group. Other echocardiographic findings possibly associated with cardiac source of emboli, such as left atrial thrombus, mobile aortic plaque and patent foramen ovale were not identified in any of those patients.

In-Hospital Outcomes

Patients with stroke had a trend toward higher in-hospital mortality (10.0% vs 3.8%, p=0.18). Death occurred only in 2 patients who developed dramatic alteration of neurological status during PCI and succumbed to ischemic stroke with hemorrhagic conversion. During admission, pulmonary edema occurred more frequently in the stroke group (15% vs 2%, p=0.007). Hospital stay was significantly prolonged in patients with stroke (8.4±7.5 vs 3.9±4.6 days, p<0.001). Of 18 patients who survived the hospitalization, 61% had a persistent neurological deficit at the time of hospital discharge.
Predictors for Stroke

Ejection fraction ≤30% was the only independent predictor for in-hospital stroke (odds ratio (OR) = 4.3, p = 0.003). Although the trend did not reach the statistical significance, pre-procedure use of GP IIb/IIIa inhibitors tended to be a protective factor (OR = 0.3, p = 0.057) (Table 4).

Comparisons of Stroke in Relation to Time From PCI

Of the 20 strokes, 12 (60%) occurred during or within 24 h after PCI, and additional 8 patients developed stroke after 24 h of PCI during the index hospitalization. Of the 12 patients with strokes occurring during or within 24 h after PCI, 9 (75%) developed symptoms during the procedures. In 3 of the 9 patients, changes in mental status were noted immediately after diagnostic angiography but before PCI. In another 2 patients, changes in neurological status were noted during PCI. In the other 4 patients, stroke was suspected at the end of the procedures.

Clinical characteristics were compared among the control group, patients with stroke occurring during or within 24 h after PCI, and those with stroke that occurred more than 24 h after PCI (Table 5). For patients with periprocedural stroke (during or within 24 h after PCI), use of GP IIb/IIIa inhibitors before PCI was less frequent (p = 0.015), and PCI of a saphenous vein graft was more frequent (p = 0.04) than patients without stroke. More patients in the periprocedural stroke group underwent PCI late in the course of MI (more than 24 h after the onset of MI) than patients without stroke (83% vs 48%, p = 0.014). Strokes occurring more than 24 h after PCI were more likely to be related to diabetes, cardiogenic shock at presentation, higher serum creatinine, lower ejection fraction, anterior wall STEMI and emergency use of intra-aortic balloon pumps.

Discussion

The present study shows that incidence of stroke in patients undergoing urgent or emergency PCI for NSTEMI or STEMI was 0.88%. Strokes were ischemic in origin in 95% of the cases. The only independent predictor for stroke was low ejection fraction. Sixty percent of the strokes occurred or were noticed during or within 24 h after PCI. These periprocedural strokes were associated with PCI of a saphenous vein graft, absence of GP IIb/IIIa inhibitors use before PCI and late presentation in the course of MI. However, stroke found more than 24 h after PCI were related to diabetes, anterior wall STEMI and compromised hemodynamic state.

Incidence of Stroke Complicating PCI

Stroke is a rare but devastating complication of PCI. Despite of the improvement in techniques and devices, the rate of stroke has increased over the decades.1–8 In the late 1970s to early 1980s, the incidence of stroke was in the range of 0.03 to 0.06%.1,2 From the early 1990s to recent years, the rate has been 0.12 to 0.3%.3–8 A possible explanation for the increased incidence is using PCI for higher-risk patients. The incidence of stroke in the present study was higher than previous reports, which is probably because of different patient characteristics. Emergency or urgent PCI

**Table 4 Predictors for Stroke by Multivariate Analysis**

<table>
<thead>
<tr>
<th>Predictive variables</th>
<th>OR [95%CI]</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection fraction ≤30%</td>
<td>4.3 [1.7–11.1]</td>
<td>0.003</td>
</tr>
<tr>
<td>GP IIb/IIIa inhibitor before PCI</td>
<td>0.3 [0.1–1.0]</td>
<td>0.06</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.4 [0.9–6.3]</td>
<td>0.07</td>
</tr>
<tr>
<td>IABP use, emergency</td>
<td>3.0 [0.8–11.1]</td>
<td>0.10</td>
</tr>
<tr>
<td>History of stroke</td>
<td>2.7 [0.8–9.3]</td>
<td>0.12</td>
</tr>
<tr>
<td>Creatinine clearance &lt;60 ml/min</td>
<td>0.8 [0.3–2.3]</td>
<td>0.69</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>1.0 [0.3–4.0]</td>
<td>0.96</td>
</tr>
</tbody>
</table>

| OR, odds ratio; CI, confidence interval; IABP, intra-aortic balloon pump. Other abbreviations see in Tables 1, 2. |

**Table 5 Characteristics of Early and Late Stroke After PCI**

<table>
<thead>
<tr>
<th>No stroke</th>
<th>Stroke ≤24 h of PCI</th>
<th>Stroke &gt;24 h after PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>64±13</td>
<td>69±10</td>
</tr>
<tr>
<td>Sex, female</td>
<td>66 (29%)</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1,589 (70%)</td>
<td>9 (75%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1,573 (70%)</td>
<td>10 (83%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>581 (27%)</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>418 (18%)</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>Previous bypass graft</td>
<td>218 (10%)</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Periperal vascular disease</td>
<td>243 (11%)</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Previous cerebrovascular accident</td>
<td>157 (7%)</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>95 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Serum creatinine, mg/dl</td>
<td>1.1±0.4</td>
<td>1.1±0.3</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>46.4±12.7</td>
<td>44.6±16.2</td>
</tr>
<tr>
<td>Anterior wall STEMI</td>
<td>376 (17%)</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>Intra-aortic balloon pump</td>
<td>115 (5%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Time from the onset to PCI &gt;24h</td>
<td>1,083 (48%)</td>
<td>10 (83%)</td>
</tr>
<tr>
<td>GP IIb/IIIa before PCI</td>
<td>973 (43%)</td>
<td>4 (8%)*</td>
</tr>
<tr>
<td>LAD PCI</td>
<td>1,058 (34%)</td>
<td>4 (29%)</td>
</tr>
<tr>
<td>Vein graft PCI</td>
<td>176 (6%)</td>
<td>3 (21%)*</td>
</tr>
</tbody>
</table>

| Abbreviations see in Tables 1–3. |
| *p<0.05 vs stroke (−), †p<0.05 vs stroke (−) and stroke <24 h, ‡p<0.05 vs stroke (−) and stroke >24 h. |

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are shown to be associated with higher risk of stroke.6,7 Whereas most previous studies have examined the incidence of stroke in stable patients undergoing elective PCI, our population consisted of patients with MI requiring emergency or urgent PCI. Another possible explanation would be the various definitions of stroke. Some studies investigated only stroke occurring within 24h of the procedure, but our study included all stroke during hospitalization.

Risk Factors for Stroke Complicating PCI

With regard to the predictors for stroke complicating PCI, Fuchs et al showed that use of an intra-aortic balloon pump, advanced age and vein graft intervention were independent predictors for stroke occurring within 24h of PCI.8 Dukkipati et al showed that independent predictors for TIA and stroke were diabetes, hypertension, previous cerebrovascular events, creatinine clearance ≤40ml/min, urgent or emergency procedures, use of thrombolytics or heparin before PCI and exigent use of intra-aortic balloon pumps.9 Furthermore, Wong et al revealed age, GP IIb/IIIa inhibitor use, acute MI, congestive heart failure on admission, history of carotid disease and chronic renal disease, as independent predictors.10 However, the majority of patients in those studies underwent elective PCI with limited use of stent and GP IIb/IIIa inhibitors. As for the ACS population with or without PCI, the GRACE registry has shown that the incidence of in-hospital stroke was significantly higher in patients with STEMI than NSTEMI or unstable angina (1.3%, 0.9%, 0.5%, respectively).11,12 Previous studies have shown that anterior wall STEMI has higher risk of in-hospital stroke.14,19,20 Patients with anterior wall STEMI are more likely to have low ejection fractions11 and the incidence of left ventricular mural thrombus is higher22 which might account for the higher risk of stroke in those populations. The results of our study are generally in line with those previous reports, except for the absence of upstream use of GP IIb/IIIa inhibitors as a risk factor. In Wong and colleagues’ study, the use of GP IIb/IIIa inhibitors increased risk of stroke.8 However, patients with MI in the study were less than 10% of the population.

The cause of PCI-related strokes is mostly embolic in origin. Potential embolic sources are air injection, atherosclerotic plaque of the ascending aorta, thrombi formed on catheters or guide wires, left ventricular mural thrombi, thrombi in the left atrium and paradoxical embolism through a patent foramen ovale. However, the observation that upfront use of GP IIb/IIIa inhibitors tended to be associated with lower risk of periprocedural stroke in the present study suggests that platelet reactivity and vascular inflammation might play a role. Serum inflammatory markers such as C-reactive protein, interleukin-6 and soluble CD40 ligand are shown to predict clinical outcomes in patients with ACS, as well as in those with stroke.23–27 Use of GP IIb/IIIa inhibitors has been shown to suppress serum concentrations of these markers and contribute to better outcomes in patients with ACS undergoing PCI.27,28 A meta-analysis suggested small excess of ischemic strokes in patients treated with lower doses of abciximab, which might be related to insufficient levels of anti-inflammatory and antiplatelet efficacy.29 In patients with ACS, vascular inflammation is a systemic condition, which might not be confined to coronary arteries, but extended to carotid arteries.30 Reducing inflammation and platelet reactivity with those agents might lead to a lower thrombus burden in the vasculature, and a lower probability of thrombus formation on PCI devices, which could decrease the risk of stroke related to the procedure.

Study Limitations

There are several limitations to the current study. First, the sample size was relatively small. A larger cohort would be required to clarify predictors for stroke because of the small event rate and multifactorial nature of the complication. Second, the actual incidence of neurological events after PCI could be even higher because we included only those cases with clinically and radiographically documented strokes. Third, our study consisted of the mixed population of NSTEMI and STEMI. Although both share similar pathophysiologies in the coronary artery, the causes of stroke might be different. Lastly, data on serum inflammatory markers were not available. Information on C-reactive protein and other specific cytokines will be required to further elucidate the role of inflammation in stroke complicating acute PCI.

Conclusions

Stroke complicating PCI remains a vexing challenge, especially in patients undergoing urgent or emergency procedures for acute MI. In addition to the traditional risk factors, absence of upstream use of GP IIb/IIIa inhibitors and late presentation in the course of MI are associated with the risk of periprocedural stroke. Although the cause of stroke during acute PCI is multifactorial, systemic inflammation might play an important role. Vigilance in these factors can lead to earlier diagnosis, treatment and improved outcome of stroke occurring in patients with acute MI undergoing PCI.

References

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