Stroke Complicating Percutaneous Coronary Interventions: Incidence, Predictors, and Prognostic Implications

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Background—Stroke associated with percutaneous coronary intervention (PCI) is an infrequent although devastating complication. We investigated the incidence, predictors, and prognostic impact of periprocedural stroke in unselected patients undergoing PCI.

Methods and Results—A total of 9662 patients who underwent 12,407 PCIs between January 1990 and July 1999 were retrospectively studied. Stroke was diagnosed in 43 patients (0.38% of procedures). Patients with stroke were older (72±11 versus 64±11 years, P<0.001), had lower left ventricular ejection fraction (42±12 versus 46±13%, P=0.04) and more diabetes (39.5% versus 27.2%, P=0.07), and experienced a higher rate of in-hospital major adverse cardiac events (57.1% versus 25%, P=0.037). Multivariate logistic regression analysis identified emergency use of IABP as the strongest predictors for stroke (OR=9.6, CI 3.9 to 23.9, P<0.001), followed by prophylactic use of IABP (OR=5.1, age >80 years (OR=3.2, compared with age <50 years), and vein graft intervention (OR=2.7).

Conclusions—Stroke associated with contemporary PCI is associated with substantial increased mortality. Elderly patients who experience intraprocedural complications necessitating the use of IABP are at particularly high risk. (Circulation. 2002;106:86-91.)

Key Words: stroke ■ angioplasty ■ prognosis

Percutaneous coronary intervention (PCI) is increasingly used to treat patients with diffuse atherosclerosis and high-risk baseline characteristics, such as low ejection fraction and acute coronary syndromes.1–4 Nevertheless, the rates of overall mortality and major cardiac adverse events have decreased.1,3,4 One of the most serious adverse complications is stroke, reported to occur in 0.07% to 0.3% of all PCI procedures.4,6,7 The low incidence makes it difficult to assess predictors and clinical implications of this major PCI-related complication.5 The purpose of this study was to report the incidence, predictors, and prognostic impact of PCI-related stroke in 9662 unselected patients during a 10-year period.

Methods

Study Population

Our database includes 9907 consecutive patients who underwent PCI between January 1, 1991 and July 1, 1999. We excluded 245 patients who underwent urgent or emergent coronary artery bypass grafting (CABG) during the index hospitalization. None of these excluded patients had a stroke before their surgery, but 10 (4%) experienced perioperative stroke. The final study population consisted of 9662 patients who underwent 12,407 PCI procedures, 43 of whom experienced a stroke during or soon after PCI.

Definition of Stroke and Cardiac Source of Emboli

The diagnosis of stroke was made by experienced neurologists and required evidence of sudden or rapid onset of new focal neurological signs considered to be vascular in origin and lasting >24 hours. When the neurological deficits lasted <24 hours, a diagnosis of transient ischemic attack (TIA) was made. The stroke or TIA was considered to be related to the PCI if it occurred within 24 hours after the PCI procedure. Strokes were classified as ischemic or hemorrhagic based on CT analysis performed by experienced neuroradiologists. If no CT was obtained or no autopsy was performed, then the stroke was classified as unknown.

To assess potential cardiac source of emboli in patients with strokes, we analyzed all available echocardiography studies (n=23, all transthoracic) performed within 1 week of the PCI procedure. Presence of aortic root atheroma, left ventricular thrombus, left atrial
thrombus or spontaneous echocardiographic swirling, mechanical valve, patent foramen ovale, and akinetic left ventricular anterior wall and apex were considered potential embolic sources.

Periprocedural and Follow-Up Data
Baseline demographics and in-hospital complications were confirmed by independent hospital chart review. All patients underwent preintervention and postintervention 12-lead ECG. The diagnosis of Q-wave and non-Q-wave myocardial infarction was based on creatine kinase MB fraction (CK-MB) ≥3 times normal with appearance or absence of a new pathologic Q wave in any 2 or more contiguous leads on postintervention surface ECG, respectively. Angiographic success was defined as <50% residual diameter stenosis without compromised antegrade flow. Clinical success was defined as angiographic success without in-hospital cardiac complications (death, Q-wave infarction, or ischemia-driven repeat PCI).

Out-of-hospital clinical outcomes were obtained by telephone interviews by experienced research nurses at 6 and 12 months; follow-up was available in 100% and 91% of patients with and without stroke, respectively. All clinical events (cardiac and noncardiac death, Q-wave infarction, and target and nontarget lesion revascularization including PCI and CAGB) were adjudicated by source documentation reviewed by experienced research nurses. The diagnosis of Q-wave infarction during follow-up was based on hospitalization records and documented discharge summaries indicating CK-MB rise ≥3 times normal and appearance of a new pathologic Q-wave in any 2 or more contiguous leads on surface ECG.

Statistics
Continuous variables are presented as mean±1 SD and compared using unpaired Student’s t test. Categorical data are presented as frequencies and compared using χ² statistics or Fisher’s exact tests. Major in-hospital complications and late clinical events were analyzed as hierarchical end points. A multivariate forward, stepwise logistic regression analysis was performed using SAS Logistic Regression Statistics (SAS Institute) to determine independent predictors for periprocedural stroke and overall 1-year mortality. The criterion for entry into the model was a univariate probability value ≤0.1. The discriminatory power of the model was examined using c statistics, whereas c value ranges from 0.5 (the model’s predictions are not better than chance) and 1.0 (the model always assigns higher probabilities to correct cases than to incorrect cases). Wilcoxon statistics were used for survival comparison between groups. P<0.05 was considered statistically significant.

Results
Baseline Demographics
Periprocedural stroke was observed in 43 of 9662 consecutive patients. Subjects who experienced stroke were older (72±11 years), more often women (52.2%), had higher rates of non–insulin-dependent diabetes mellitus (33%), lower left ventricular ejection fraction (42±12%), and lower body weight (74±14 kg), and less often underwent prior PCI (27.9%) (Table 1). The proportion of women who experienced stroke (22 of 2857 [0.77%]) was 2.5 times higher compared with the proportion of men (21 of 6762 [0.31%]).

Angiographic and Procedural Results
Patients with stroke more often underwent interventions to a saphenous vein grafts (38.8% versus 15.4%) and less often to the left circumflex artery (7.5% versus 23.5%) (Table 2). Target lesion location and characteristics were otherwise similar between groups, and angiographic results were comparable.

Procedure type was similar between groups (Table 3). The duration of the PCI procedure was longer and the frequency of angiographic complications higher in patients with stroke, including dissections (16.4% versus 7.4%), abrupt closure (4.9% versus 0.8%), and no reflow (3.3% versus 0.8%). Despite similar angiographic success, patients with strokes more often had periprocedural Q-wave infarction (4.7% versus 0.3%) and non–Q-wave infarction (41.5% versus 19.3%) and overall higher postprocedural peak CK-MB levels (50±82 versus 15±52 ng/mL, P=0.01). Use of abcix-
imab (mostly as a rescue measure, 11.6% versus 4.7%) and intra-aortic balloon pump (IABP) (34.9% versus 7.4%) was more common in patients with stroke.

**Stroke Characteristics**

CT scanning was performed in 41 patients. Two patients had clinical diagnosis of stroke but CT scan was not obtained (unknown stroke, 4.7%). Hemorrhagic stroke was documented in 20 (46.5%) and ischemic stroke in 21 (48.8%) patients. Hemorrhagic stroke most often presented as intraparenchymal bleeding (30%) and parenchymal hematoma (20%), and intraventricular (25%), subarachnoid (20%), and subdural hypotension (20%). Ischemic stroke most often involved the major cerebral-arterial territories (middle cerebral artery, 47.6%; posterior cerebral artery, 23.8%; and anterior cerebral artery, 9.6%). Lacunar stroke was diagnosed in 19% of the cases.

One or more echocardiographic findings potentially associated with cardiac source of emboli were identified in 8 patients (4 with ischemic and 4 with hemorrhagic stroke) and included akinetic apex (n=6), akinetic left ventricular anterior wall (n=4), aortic root atheroma (n=2), mechanical valve (n=1), patent foramen ovale (n=1), left ventricle thrombus (n=1), and left atrial thrombus (n=1). The latter 2, however, were identified only in patients with ischemic stroke.

**Ischemic Versus Hemorrhagic Stroke**

Patients with hemorrhagic versus ischemic stroke had similar baseline demographic, procedure, and postprocedure laboratory variables except for more frequent history of previous CABG and more saphenous vein graft interventions (data not shown).

Patients with ischemic stroke had a trend for higher in-hospital mortality and significantly higher rate of overall major complications (Table 4). Patients with hemorrhagic stroke, however, experienced a larger drop in hematocrit (postprocedural nadir compared with preprocedure levels), although no differences in clinical bleeding or transfusion rates were noted (Table 4). Also, there were no differences in activating clotting time, platelet count, or use of glycoprotein IIb/IIIa antagonists comparing patients with hemorrhagic versus ischemic stroke.

**Stroke Versus Transient Ischemic Attack**

TIA was diagnosed in 15 patients (0.12% of the procedures). CT scan or magnetic resonance imaging was available in 8 patients, revealing no acute changes in 5 patients and small ischemic infarcts in the remaining. None had evidence of intracranial hemorrhage.

Patients with TIA had similar baseline demographic and procedure characteristics compared with stroke patients, except for a less frequent diagnosis of unstable angina and no emergent use of IABP (data not shown). Patients with TIA had no in-hospital mortality, and only 1 patient died during 1-year follow-up.

**Predictors for Stroke**

Annual stroke rate (per PCI procedure) was 0.38±0.20% and remained rather constant over a 10-year period (P=0.2). Forward, stepwise logistic regression analysis was used to identify independent predictors for major periprocedural stroke. Variables included in the model were age by category (50 to 59, 60 to 69, 70 to 79, and ≥80 years of age compared with patients <50 year of age), sex, history of diabetes, history of hypertension, admission diagnosis of unstable angina, body weight, use of abximab, use of IABP, procedural hypotension, and saphenous vein graft intervention. Age ≥80 years, use of IABP, and an intervention to a saphenous vein graft were found as independent predictors of stroke (Table 5). C statistic was 0.81, suggesting a well-discriminatory power of the model.
TABLE 5. Independent Predictors for In-Hospital Stroke and One-Year Mortality

<table>
<thead>
<tr>
<th>Predictive Variables</th>
<th>OR</th>
<th>95% Confidence Interval</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>9.6</td>
<td>3.9–23.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IABP, emergency use</td>
<td>5.1</td>
<td>1.8–14.0</td>
<td>0.002</td>
</tr>
<tr>
<td>Age &gt;80 years*</td>
<td>3.2</td>
<td>1.4–7.7</td>
<td>0.008</td>
</tr>
<tr>
<td>Intervention to SVG</td>
<td>2.7</td>
<td>1.3–5.8</td>
<td>0.01</td>
</tr>
</tbody>
</table>

1-year mortality

| Stroke                             | 9.8  | 4.6–21                  | <0.001 |
| IABP, emergent use                 | 4.4  | 3.3–6.0                 | <0.001 |
| IABP, prophylactic use             | 2.9  | 2.2–3.9                 | 0.002  |
| Age*                               | 1.8  | 1.3–2.3                 | <0.001 |
| 61–70 y                            | 3.1  | 2.4–4.0                 | <0.001 |
| >80 y                              | 5.1  | 3.6–7.0                 | <0.001 |
| Chronic renal failure              | 3.4  | 2.7–4.2                 | <0.001 |
| Diabetes                           | 1.9  | 1.5–2.3                 | <0.001 |
| Intervention to SVG                | 1.6  | 1.3–2.0                 | <0.001 |
| CK-MB >5 times, periprocedure      | 1.6  | 1.3–1.9                 | <0.001 |
| Female sex                         | 1.3  | 1.1–1.5                 | 0.003  |
| Prior myocardial infarction        | 1.3  | 1.1–1.6                 | 0.004  |
| Unstable angina                    | 1.3  | 1.0–1.5                 | 0.019  |
| Hypertension                       | 1.2  | 1.0–1.5                 | 0.034  |

*Odds ratio presents estimated risk compared with patients <50 years of age.

SVG indicates saphenous vein graft.

Clinical Outcomes

Patients with stroke had higher in-hospital and 1-year cumulative mortality, and higher in-hospital Q- and non–Q-wave myocardial infarction rates (Table 6). Out-of-hospital mortality rate was also increased in stroke patients (22.2% versus 3.9%, P=0.006). In-hospital death occurred 8.0±10.9 and 6.4±10.0 days after the procedure in patients with and without periprocedural stroke, respectively (P=0.52). Post-procedure in-hospital stay was significantly prolonged in patients with stroke (15.2±16.5 versus 3.7±4.3 days, P<0.001), as was the intensive care unit stay (4.3±6.9 versus 0.5±1.8 days, P<0.001).

Seven baseline characteristics, 2 intraprocedural parameters, and 2 periprocedural complications were identified as independent predictors for 1-year mortality (Table 5). The most important were periprocedural stroke, older age, emergent use of IABP, and history of chronic renal failure.

Discussion

The present study showed that the rate of periprocedural stroke in an unselected group of patients undergoing PCI from 1991 to 1999 was 0.38%. Strokes occurred in a distinct group of patients: older, female, with non–insulin-dependent diabetes mellitus and evidence of advanced atherosclerosis; patients undergoing vein graft intervention; and patients with periprocedural complications (dissections, abrupt closure, and no reflow) often necessitating IABP use. In the present study, periprocedural stroke was associated with substantially increased in-hospital and 1-year mortality. Independent predictors for periprocedural stroke were advanced age, use of IABP, and intervention to a saphenous vein graft. Ischemic, compared with hemorrhagic, stroke was associated with a higher rate of major in-hospital adverse cardiac events. Periprocedural TIA was not associated with increased mortality.

Our stroke event rate of 0.38% is in accord with the reports from Emory University (0.05% to 0.38%) and Cleveland Clinic (0.3%) and national Canadian reports (0.25%). A similar 30-day stroke rate of 0.36% was also observed in trials assessing the efficacy of abciximab among patients who underwent PCI. Lower rates, however, were reported by the National Heart Lung and Blood registry (0.07%). Potentially explained by lower patient risk profiles, including younger age, stable angina, single-vessel disease, and good LV function. Finally, the higher rate we observed in patients >80 years of age agrees with the increased rate (2.5 times) observed among octogenarians compared with younger patients.

Stroke carries substantial morbidity and mortality rates. The case fatality rate among middle-age adults with out-of-hospital stroke is 10.3% at 30 days, and the 1-year mortality among 1-month stroke survivors is 9.8%. Strokes among patients with acute coronary syndromes enrolled in the Organization to Assess Strategies for Ischemic Syndromes (OASIS) I and II studies were associated with 6-month mortality rates of 27%. In these studies, most of the strokes occurred after CABG that was performed within the first month of the index hospitalization. Our study included only patients who experienced stroke within 24 hours after PCI and excluded patients who eventually underwent in-hospital urgent or emergent CABG surgery. Therefore, we directly assessed patients sustaining peri-PCI stroke. The outcome of this patient cohort was poor, and despite being a relatively rare complication (0.38% of procedures), it accounted for 10.6% of the total PCI-related in-hospital deaths. These
results are in accord with previous observation of 4 deaths out of 9 PCI-related strokes, which accounted for 7% of all procedural-related mortality. In comparison, among large cohorts of patients who underwent CABG in our institution, strokes occurred in 2% and accounted for 9.7% of the overall in-hospital case fatality rate.

Potential association between IABP use and stroke was suggested by Stone at al, who observed a 2.4% stroke rate in patients with acute myocardial infarction randomized to 36 to 48 hours of IABP (compared with 0% in the control group). Studies assessing risk factors for stroke after CABG, however, found no such association. Given the fact that patients who experienced periprocedural stroke were older with more risk factors for atherosclerosis, these patients may have had more extensive carotid and cerebral vascular disease. Cerebral hemodynamic impairment in these patients would increase the risk of ischemic stroke secondary to reduced flow, which may be additionally compromised by systemic hypoperfusion. Hemodynamic instability has been shown to facilitate ischemic injury secondary to embolic events in an animal model. In addition, delayed subdural hematoma may follow recovery from peripheral vascular collapse. Hence, the risk associated with use of IABP in our patients may merely reflect periprocedural hemodynamic impairment and not be causative. Additional possible mechanisms include increased risk of hemorrhagic stroke secondary to more intense and prolonged anticoagulation in patients necessitating IABP. This potential deleterious effect of heparin was suggested by Akkerhuis et al, who observed increased 30-day hemorrhagic stroke rates only among patients who received standard but not low-dose heparin as an adjunctive to abciximab. Ischemic events, however, may be facilitated by IABP use because of activation of the coagulation system. Other predictors for periprocedural stroke, such as vein graft intervention, may reflect increased risk of catheter-induced embolization of complex aortic atheroma frequently located at the ascending aorta and proximal aortic arch, locations of the aortosaphenous anastomotic sites. This location of atherosclerotic disease is mostly seen in the elderly population, especially those >80 years of age. Alternatively, the need for saphenous vein graft intervention may merely be a marker for more advanced atherosclerosis. Echocardiographic findings, although available in only a subset of patients, suggest many different pathophysiologic etiologies, the common denominator of which is more advanced atherosclerotic disease. Finally, patients who experienced stroke had excessive rates of postprocedural complications reflecting high-risk baseline characteristics and high iniprocedural complication rates. Among these, non-Q-wave myocardial infarction, pulmonary edema, and major bleeding could facilitate hemodynamic instability, aggravating cerebral underperfusion.

Differences in predictors for stroke after PCI compared with CABG may be clinically noteworthy. For example, a history of a previous stroke was identified as a major predictor for stroke after CABG, whereas we noticed no such association in relation to stroke after PCI. Thus, to minimize procedural risks, one may favor PCI over CABG in patients with a history of previous stroke.

Strokes after PCI have not been fully characterized. We observed similar incidences of hemorrhagic and ischemic etiologies. Hemorrhagic strokes were less frequently reported by the Cleveland Clinic (22% of strokes) and by the combined analysis of 4 abciximab trials (39% of strokes). This dissimilarity may be explained in part by differences in patients characteristics, including older age and more frequent need for IABP among our stroke patients. We also observed a higher complication rate and a trend for increased mortality in patients with ischemic compared with hemorrhagic stroke, which is in discordance with the 4-fold increased mortality rate noted in out-of-hospital hemorrhagic compared with ischemic stroke. Excluding history of CABG and more frequent vein graft intervention, we found no differences between patients who experienced hemorrhagic compared with ischemic stroke. Moreover, hemorrhagic stroke was not associated with systemic bleeding events and was not related to iniprocedural intensity of anticoagulation or IIb/IIIa antagonist use. Compared with stroke, TIA occurred less frequently and was associated with low mortality rate.

Study Limitations
The present study carried the inherent limitations of a retrospective analysis. However, all data information was prospectively recorded according to prespecified definitions. Because of the overall low incidence of periprocedure stroke events, we were able to identify a relatively small number of patients with strokes. This may have limited the power of the study to detect smaller differences between groups as well as the identification of other predictors for stroke. Finally, the present study was not designed to identify echocardiographic parameters associated with increased risk of stroke.

Conclusions
Stroke after PCI is an uncommon but devastating event associated with substantial short- and long-term mortality. Stroke after PCI affects mainly elderly and high-risk patients with iniprocedural complications. The rate of periprocedure stroke has remained constant over the last 10 years. A large registry might be able to identify potentially modifiable factors.

References


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