Incidence and Clinical Impact of Stroke Complicating Percutaneous Coronary Intervention

Results of the Euro Heart Survey Percutaneous Coronary Interventions Registry

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Background—Stroke is a rare but serious complication of percutaneous coronary interventions (PCIs). So far, scant information is available about the incidence and outcome of patients developing stroke after PCI for stable angina or acute coronary syndrome (ACS) in daily clinical practice in Europe today.

Methods and Results—Between 2005 and 2008, 46,888 patients undergoing PCI were enrolled into the PCI Registry of the Euro Heart Survey Programme (176 centers in 33 European countries) to document patient’s characteristics, PCI details, and hospital complications in different PCI indications. Stroke was observed in 0.4% of the procedures in the total population, in 0.3% of PCIs in elective patients, and in 0.6% in PCIs performed for ACS. The overall in-hospital mortality was 19.2% for patients who developed stroke (elective PCIs, 10.0%; PCI for ACS, 23.2%) compared with 1.3% for those without stroke (elective PCIs, 0.2%; PCI for ACS, 2.3%). In multivariate analysis hemodynamic instability, age ≥75 years, history of stroke, and congestive heart failure were found to be independent predictors for periprocedural stroke in ACS, whereas only PCI of a bypass graft and renal failure could be identified as independent predictors for stroke in elective patients.

Conclusions—Stroke as complication of PCI occurs rarely (0.4%) in clinical practice in Europe today. However, peri-interventional stroke is still associated with an exceedingly high in-hospital mortality rate. Most predictors for periprocedural stroke are not modifiable and cannot be diminished before PCI. Therefore, treatment of patients with stroke after PCI needs further research. (Circ Cardiovasc Interv. 2013;6:362-369.)

Key Words: percutaneous coronary intervention | stroke

Cardiac catheterization and percutaneous coronary interventions (PCIs) have become the standard tool in diagnosis and interventional treatment of coronary artery disease with widespread use in many countries during the past years. With technical and pharmacological improvements, PCI has steadily become safer with improved periprocedural outcomes.1-3 Major adverse cardiac and cerebrovascular events are reported to appear in <1% of all diagnostic cardiac catheterization procedures and in ≈2.5% of all PCIs today.1-5 Nevertheless, PCI is an invasive procedure involving mechanical stress to the arterial vascular system caused by catheter manipulation, which is thought to be the major cause for cerebral embolism during cardiac catheterization.6-9

In a continually aging population, carrying a higher risk for complications during PCI in general, periprocedural complications are still a major concern. When the technique emerged in the 1970s and 1980s, high-risk patients with severe comorbidities had been excluded from cardiac catheterization, whereas these patients are part of the routine population undergoing PCI in clinical practice today. Therefore, periprocedural complications like stroke affect thousands of patients worldwide every year.

Stroke is known to be a rare but serious complication of cardiac catheterization or PCI.10,11 The overall rate of stroke in unselected patients undergoing PCI has been reported to be <1%, ranging from 0.18% to 0.44%10-13 in different registries. Overall complication rates of percutaneous revascularization procedures are known to be higher compared with diagnostic catheterizations.14,15 If PCI is performed in case of an acute coronary syndrome (ACS), the overall risk for complications and cerebrovascular events further increases.11,16 Despite its rare occurrence, stroke still is one of the most dreaded complications during cardiac catheterization with an enormous impact on the patient’s prognosis and on quality of
The protocol of the PCI Registry was approved by the ethical committees responsible for the participating centers as required by local rules. Data were collected using online Internet data capture. The electronic case report form was provided by the Euro Heart Survey Team at the European Heart House and was programmed on the basis of the European Cardiology Audit and Registration Data Standards for PCI.14 All patients gave informed consent for processing their anonymous data. Data were collected on patient’s characteristics, including age, sex, cardiovascular risk factors, concomitant diseases, prior myocardial infarction, prior stroke, prior cardiovascular interventions, chronic medical treatment, indication for PCI, procedural details, adjunctive medical treatment, periprocedural complications, hospital outcome, and the recommendations for long-term medical treatment after PCI. Final editing of the data, as well as the statistical analyses, was performed at the Institut für Herzinfarktforschung Ludwigshafen an der Universität Heidelberg (IHF), Germany.

Definitions
Patients were classified in 2 groups: (1) patients undergoing PCI for an ACS (ST-segment–elevation myocardial infarction [STEMI], non–ST-segment–elevation myocardial infarction, and unstable angina) and (2) patients undergoing PCI for an elective indication (stable angina or documented ischemia). The diagnoses of stable or unstable angina were made according to the Canadian Cardiovascular Society grading system.

Myocardial infarction was defined as a typical rise of biochemical markers of myocardial necrosis (troponin or CK-MB) with ≥1 of the following:

1. Ischemic symptoms,
2. Development of pathological Q waves on the ECG, and
3. ECG changes indicative of ischemia (ST-segment–elevation or depression).

In this analysis, stroke was defined as a persistent loss of neurologic function caused by a cerebral ischemic or hemorrhagic event. Intracranial bleeding was defined as bleeding in or around the brain, hemorrhagic conversion of a primary ischemic stroke, subarachnoid hemorrhage, intracerebral hemorrhage, or other like subdural or epidural bleeding.

Diagnosing a stroke was left to the treating physician, who was also responsible for entering the data into the electronic case reports of the PCI Registry of the Euro Heart Survey. Transient ischemic attacks were not evaluated and recorded separately in the registry.

History of chronic renal failure was defined as (1) serum creatinine ≥2.0 mg/dL, or 200 μmol/L, in the past or (2) patients on dialysis or (3) patients having a history of renal transplantation.

Statistical Methods
The patient population is described by absolute numbers and percentages with respect to categorical variables and medians with quartiles for continuous variables and thrombolysis in myocardial infarction flow. The distribution of nominal categorical variables is compared between patient groups by Pearson χ² test that of metrical and ordinal variables by Mann–Whitney test. Odds ratios with 95% confidence intervals were calculated for binary variables. These values were calculated from the available cases.

Patients were separated into 2 groups: (1) stable patients undergoing elective PCI, (2) unstable patients undergoing PCI for ACS. A multivariable logistic regression analysis for independent predictors of in-hospital stroke was performed in every group of patients, including age, sex, prior stroke, valvular heart disease, diabetes mellitus, arterial hypertension, chronic renal failure, congestive heart failure or reduced left ventricular function, and treated bypass graft. For the ACS patients, shock/resuscitation, ongoing STEMI, non–ST-segment–elevation myocardial infarction, prior coronary artery bypass grafting (CABG), and the use of glycoprotein IIb/IIIa antagonists were considered in addition. As prior CABG and treated bypass graft were strongly correlated variables, we paid attention that only 1 of them remained in the final model. In the ACS group, for missing

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**Methods**

**PCI Registry of the Euro Heart Survey Programme**

The PCI Registry was conducted between May 2005 and April 2008 as the first continuous registry within the Euro Heart Survey Programme of the European Society of Cardiology. It was a prospective, multicenter, observational study to document current practice of PCI in consecutive patients in a real-life setting throughout Europe and to evaluate to what extent clinical practice endorses existing European Society of Cardiology practice guidelines in the different settings of PCI. Details of the Euro Heart Survey (EHS) PCI Registry have been published previously in more detail.15 In brief, a total of 176 centers from 33 European Society of Cardiology member countries participated, including university hospitals, tertiary care centers, and community hospitals. The centers were asked to enroll continuously consecutive patients scheduled for emergent, urgent, or elective PCI, independent of age, sex, and any concomitant diseases and independent of the indication for PCI. Those patients who already participated in (eg, randomized) trials or other registries were also eligible for inclusion. If continuous consecutive enrollment was not feasible because of high yearly numbers of PCI, those centers were asked to recruit consecutive patients from days 1 to 7 of every calendar month throughout the study period.

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**WHAT IS KNOWN**

- Stroke is a rare but serious complication of percutaneous coronary interventions (PCIs) and is associated with high morbidity and mortality rates.
- Little data are available about the outcome and therapy of patients developing stroke after PCI in daily clinical practice today.
- Several independent predictors of stroke-complicating PCI such as an advanced age, arterial hypertension, diabetes mellitus, history of stroke or valvular heart disease, cardiogenic shock, or congestive heart failure have previously been reported.

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**WHAT THE STUDY ADDS**

- There is a difference in factors associated with stroke according to the indication for PCI.
- Hemodynamic instability, age ≥75 years, history of stroke, and congestive heart failure were independent predictors for periprocedural stroke in acute coronary syndrome, whereas only PCI of a bypass graft and renal failure were identified as independent predictors for stroke in elective patients.
- These findings are helpful in evaluating patients undergoing PCI.

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Life. Mortality rates for peri-interventional stroke are high and range from 22.7% to 37% in large registries.10–13,16 So far, scant information is available about the incidence and outcome of patients developing stroke after PCI for stable angina or ACS in daily clinical practice in Europe. Therefore, this analysis of data from the Euro Heart Survey PCI Registry was performed to evaluate the current incidence and outcome of patients experiencing periprocedural stroke in Europe today.

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**Statistical Methods**

The patient population is described by absolute numbers and percentages with respect to categorical variables and medians with quartiles for continuous variables and thrombolysis in myocardial infarction flow. The distribution of nominal categorical variables is compared between patient groups by Pearson χ² test that of metrical and ordinal variables by Mann–Whitney test. Odds ratios with 95% confidence intervals were calculated for binary variables. These values were calculated from the available cases.

Patients were separated into 2 groups: (1) stable patients undergoing elective PCI, (2) unstable patients undergoing PCI for ACS. A multivariable logistic regression analysis for independent predictors of in-hospital stroke was performed in every group of patients, including age, sex, prior stroke, valvular heart disease, diabetes mellitus, arterial hypertension, chronic renal failure, congestive heart failure or reduced left ventricular function, and treated bypass graft. For the ACS patients, shock/resuscitation, ongoing STEMI, non–ST-segment–elevation myocardial infarction, prior coronary artery bypass grafting (CABG), and the use of glycoprotein IIb/IIIa antagonists were considered in addition. As prior CABG and treated bypass graft were strongly correlated variables, we paid attention that only 1 of them remained in the final model. In the ACS group, for missing
values of explanatory variables, conditional mean values were imputed, estimated by regression on age, sex, STEMI, and non–ST-segment-elevation myocardial infarction. The variables in the final models were aged ≥75 years and those chosen by a backward selection procedure with a *P* value for removal of >0.15. To reduce bias of the parameter estimates in the situation of rare events, the penalized likelihood confidence intervals were computed. *P* values of <0.05 were considered significant. All *P* values are results of 2-tailed tests. The computations were performed using the SAS system release 9.2 on a personal computer (SAS Institute, Inc, Cary, NC).

### Results

Between 2005 and 2008, a total of 46,888 consecutive patients undergoing PCI at 176 centers in 33 European countries were enrolled into the PCI Registry of the Euro Heart Survey Program. In total, 0.4% of these patients (n=198) developed an in-hospital stroke, 99.6% (n=46,690) did not develop a stroke. We report the following results for PCIs for ACS and for elective PCIs separately. In-hospital stroke was observed in 138 of 24,105 PCIs (0.6%) for ACS and in 60 of 22,783 patients (0.3%) who underwent PCI for stable angina (*P*<0.001; Figure 1).

### PCI for ACS

Patients who developed stroke after PCI for ACS were significantly older, more likely women, and more often had a history of valvular heart disease or stroke. The use of statins was significantly less frequent in patients with stroke after PCI, whereas cardiovascular risk factors like arterial hypertension, diabetes mellitus, and hypercholesterolemia did not differ significantly between both groups (Tables 1 and 2). Patients with stroke significantly more often presented with STEMI and had a significantly worse left ventricular function on admission compared with patients without stroke. In addition, hemodynamic instability, cardiogenic shock, resuscitation at start of PCI, and the use of an intra-aortic balloon pump were all significantly more frequent in patients with periprocedural stroke. Patients with stroke during PCI significantly more often underwent an intervention at the left main stem compared with patients without stroke. During coronary angiography, 3-vessel disease and a lower thrombolysis in myocardial infarction flow before PCI were significantly more prevalent in patients who had stroke. These patients also showed more periprocedural complications like acute segment closure, stent thrombosis, heart block requiring pacing or cardiogenic shock induced by procedure compared with patients without periprocedural stroke (Tables 3 and 4).

In-hospital mortality of patients with stroke after PCI for ACS was 23.2% in comparison with 2.3% in patients without stroke. These patients also showed more periprocedural complications like acute segment closure, stent thrombosis, heart block requiring pacing or cardiogenic shock induced by procedure compared with patients without periprocedural stroke (Tables 3 and 4). In-hospital mortality of patients with stroke after PCI for ACS was 23.2% in comparison with 2.3% in patients without stroke. These patients also showed more periprocedural complications like acute segment closure, stent thrombosis, heart block requiring

### Table 1. Baseline Characteristics, Medical History, and Medication on Admission of PCIs for ACS

<table>
<thead>
<tr>
<th></th>
<th>Strokes (n=138; 0.6%)</th>
<th>No Strokes (n=23,967; 99.4%)</th>
<th><em>P</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline features</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>71.9 (59.9–78.8)</td>
<td>64.1 (54.8–73.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.7 (24.3–30.1)</td>
<td>27.1 (24.7–29.8)</td>
<td>0.98</td>
</tr>
<tr>
<td>Women</td>
<td>53/138 (38.4%)</td>
<td>6385/23,967 (25.6%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Medical history</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior MI</td>
<td>34/130 (26.2%)</td>
<td>6223/23,419 (26.6%)</td>
<td>0.91</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>18/130 (13.8%)</td>
<td>3980/23,419 (17.0%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Prior CABS</td>
<td>2/130 (1.5%)</td>
<td>1231/23,420 (5.3%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>13/130 (10.0%)</td>
<td>1060/23,418 (4.5%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>History of valvular heart disease</td>
<td>6/127 (4.7%)</td>
<td>469/22,689 (2.1%)</td>
<td>0.04</td>
</tr>
<tr>
<td>History of MI</td>
<td>7/130 (5.4%)</td>
<td>1432/23,419 (6.1%)</td>
<td>0.73</td>
</tr>
<tr>
<td>Stent placement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>6/130 (4.6%)</td>
<td>849/23,418 (3.6%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Current/former smoker</td>
<td>49/122 (40.2%)</td>
<td>12,674/23,058 (55.0%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hypertension</td>
<td>89/125 (71.2%)</td>
<td>15042/23,425 (64.2%)</td>
<td>0.1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>39/129 (30.2%)</td>
<td>5794/23,710 (24.4%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>59/122 (52.7%)</td>
<td>12541/22,131 (56.7%)</td>
<td>0.40</td>
</tr>
</tbody>
</table>

ACS indicates acute coronary syndrome; BMI, body mass index; CABS, coronary artery bypass grafting; MI, myocardial infarction; PAD, peripheral arterial disease; and PCI, percutaneous coronary interventions.

### Table 2. Baseline Characteristics, Medical History, and Medication on Admission of Elective PCIs

<table>
<thead>
<tr>
<th></th>
<th>Strokes (n=60; 0.3%)</th>
<th>No Strokes (n=22,723; 99.7%)</th>
<th><em>P</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline features</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>65.4 (58.1–72.1)</td>
<td>64.1 (56.0–71.6)</td>
<td>0.51</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.8 (26.0–30.3)</td>
<td>27.7 (25.1–30.4)</td>
<td>0.57</td>
</tr>
<tr>
<td>Women</td>
<td>20/60 (33.3%)</td>
<td>5642/22,723 (24.8%)</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>Medical history</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior MI</td>
<td>27/60 (45.0%)</td>
<td>9317/22,610 (41.2%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>18/60 (30.0%)</td>
<td>7113/22,612 (31.5%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Prior CABS</td>
<td>10/60 (16.7%)</td>
<td>1696/22,612 (7.5%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Prior stent</td>
<td>4/60 (6.7%)</td>
<td>814/22,612 (3.6%)</td>
<td>0.20</td>
</tr>
<tr>
<td>History of valvular heart disease</td>
<td>3/55 (5.5%)</td>
<td>502/22,116 (2.3%)</td>
<td>0.11</td>
</tr>
<tr>
<td>History of PAD</td>
<td>6/60 (10.0%)</td>
<td>1348/22,612 (6.0%)</td>
<td>0.19</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>6/60 (10.0%)</td>
<td>731/22,612 (3.2%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Current/former smoker</td>
<td>30/57 (52.6%)</td>
<td>10,998/22,123 (49.7%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Hypertension</td>
<td>47/60 (78.3%)</td>
<td>16787/22,572 (74.4%)</td>
<td>0.48</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>22/60 (36.7%)</td>
<td>5830/22,635 (25.8%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>41/59 (69.5%)</td>
<td>15,590/21,591 (72.2%)</td>
<td>0.64</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; CABS, coronary artery bypass grafting; MI, myocardial infarction; PAD, peripheral arterial disease; and PCI, percutaneous coronary interventions.
stroke. The length of in-hospital stay post procedure of patients discharged alive raised from a median of 3 days (without stroke) to 7 days (with stroke). Postprocedural in-hospital complications like major adverse cardiac events (death, myocardial infarction), myocardial infarction, major bleeding, and renal failure requiring dialysis were all significantly increased in patients developing stroke (Tables 5 and 6).
Predictors for In-Hospital Stroke During PCI for ACS

Multivariate analysis showed the following variables to be independent predictors of periprocedural stroke during PCI for ACS (Figure 2A): hemodynamic instability, age ≥75 years, history of stroke, and congestive heart failure. Prior CABG was significantly associated with a lower risk for stroke in patients undergoing PCI for ACS.

PCI for Stable Angina (Elective PCI)

No significant differences in cardiovascular risk factors or medication on admission are found in patients with stroke during elective PCI compared with patients without stroke. In contrast to data from PCI for ACS patients with peri-interventional stroke undergoing elective PCI did not show significant differences in age, sex, history of stroke, or valvular heart disease. History of previous CABG and history of chronic renal failure were significantly more frequent in patients with in-hospital stroke undergoing elective PCI (Tables 1 and 2) in contrast to our data from PCI for ACS.

Patients without in-hospital stroke during elective PCI significantly more often had normal left ventricular function compared with patients with stroke. In accordance with data from patients with ACS, PCI was technically more difficult in patients developing an in-hospital stroke, with a higher prevalence of vessel-occlusion, in-stent restenosis, and a lower thrombolysis in myocardial infarction flow of the target vessel before PCI. Stroke significantly more often occurred in patients undergoing elective PCI if the stenosed vessel was a bypass graft, if more bypass grafts were angiographically documented, and if more bypass grafts were treated with PCI. No significant differences in periprocedural medication could be observed, besides inotropes, which use was significantly increased in patients developing stroke. Periprocedural complications like no-flow/slow-flow phenomenon, shock induced by procedure, cardiac arrest, or acute stent thrombosis significantly more often occurred in patients developing an in-hospital stroke (Tables 3 and 4).

In-hospital mortality of patients with stroke after elective PCI was 10.0% compared with 0.2% in patients without stroke, which means a 50-fold increase in risk of in-hospital death by developing stroke after PCI. The length of in-hospital stay of patients discharged alive increased significantly after developing a stroke during elective PCI. Postprocedural in-hospital complications like major adverse cardiac events (death, myocardial infarction), myocardial infarction, major bleeding, and renal failure requiring dialysis were all significantly increased in patients developing stroke after elective PCI (Tables 5 and 6).

Predictors for In-Hospital Stroke During Elective PCI

All independent predictors, which had been found in PCIs for ACS, were not significantly associated with stroke in elective PCIs for ACS.
PCIs in multivariate analysis (Figure 2B). PCI of a bypass graft and renal failure were found to be the only significant independent predictors of stroke in elective PCIs in this registry. The occurrence of stroke was hardly predictable from the available variables (C=0.599). Most likely for the low number of events in the group of elective PCIs, other variables did not reach statistical significance as predictors for stroke-complicating elective PCI.

Discussion

As a large international database including 46,888 patients, the PCI Registry of the Euro Heart Survey is able to deliver realistic insight into the incidence of severe adverse neurological events and the incidence of in-hospital death complicating real-world PCI in Europe today. The overall rate of periprocedural stroke of 0.4% in an unselected population undergoing PCI is in good accordance with rates reported by other registries during the past 20 years of interventional cardiology.10,19–21 Some authors previously reported slightly lower16 (0.22%), others slightly higher rates of stroke during PCI15 (0.44%). PCI performed under emergency conditions is well-known to increase the risk for stroke.10,13,16

In our analysis, we found a 2-fold increase in peri-interventional stroke rate if PCI was performed urgently or in an emergency situation (0.6%) compared with an elective procedure (0.3%). Explanations could be a more severe vascular calcification in patients presenting with an ACS and a longer duration of the catheterization procedure during urgent or even emergency situations with possibly less careful advancement of catheters through the aorta under pressure of time, which is associated with an increased risk of cerebral embolization by scraping at aortic plaques.9,22 Differences in plaque composition in ACS versus stable patients leading to an increased chance to cause embolism could also be an explanation for the findings. The possibility for hemodynamic compromise is also higher in patients with an ACS, which is known to increase the risk for intracardial thrombus formation and the risk for stroke. The Global registry of Acute Coronary Events (GRACE) registry, evaluating the outcome of patients with an ACS, has shown an even higher incidence of in-hospital stroke compared with our data (STEMI, 1.3%; non–ST-segment–elevation myocardial infarction, 0.9%; and unstable angina, 0.5%).23 The present results show cerebrovascular accidents mainly to occur in a distinct group of patients undergoing PCI. The higher the patient’s atherosclerotic and vascular risk, the higher the patients’ risk for periprocedural stroke, in general. In our results of PCIs for ACS, variables like an advanced age, a history of stroke or valvular heart disease, and congestive heart failure were significantly more present in patients with a cerebrovascular accident complicating PCI (Tables 1 and 2). This is in agreement with risk factors for cerebrovascular accidents during PCI, which have previously been found in other large registries.10,11,13,16 Strokes significantly more often occurred in PCI procedures, which were technically more challenging with a higher incidence of 3-vessel disease, lower thrombolysis in myocardial infarction flow before PCI, and increased complication rates such as acute segment closure or shock induced by procedure.

In our analysis, in which we examined elective PCIs and PCIs for ACS separately, we found a remarkable difference in independent predictors for peri-interventional strokes between the 2 groups, which—to the best of our knowledge—had not been reported previously. In elective PCIs, well-known risk factors for periprocedural stroke such as advanced age, history of stroke, or valvular heart disease did not show to be significantly associated with an increased risk for periprocedural strokes compared with PCIs for ACS. Furthermore, other variables, which previously had not played a major role in PCIs for ACS, seem to gain an importance in elective cases. Interventions at bypass grafts and renal failure were significantly more often associated with the occurrence of periprocedural cerebrovascular events during elective procedures.

This shift to different risk factors in elective cases compared with PCIs performed for ACS is difficult to explain out of the available data in the PCI Registry of the Euro Heart Survey. One likely explanation is the severity of vascular calcification, which could be lower in patients undergoing PCI under elective procedures by trend. As chronic renal failure is known to be a cardiovascular risk factor and CABG is usually performed for severe coronary artery disease, both variables indicate a more severe vascular calcification status in this subgroup of patients undergoing PCI under elective circumstances. Because of difficulty in control of anticoagulation therapy for many substances like heparin, renal failure is a generally known risk factor for intracranial or major bleeding, as well.13,16,24 In our data we found a higher rate of intracranial...
bleeding in elective PCIs compared with PCIs for ACS (21/59 [35%] patients versus 33/136 [24%] patients). Therefore, an increase in intracranial bleeding because of renal failure is another explanation for a higher rate of periprocedural cerebrovascular events in patients undergoing an elective PCI.

However, there are procedural and anatomic reasons possibly leading to a higher stroke rate in patients being intervened at a bypass graft. Interventions at bypass grafts are usually technically more challenging, showing longer fluoroscopy times and, therefore, potentially leading to a higher risk of cerebral microembolism.22

Especially in PCIs of internal mammary artery bypass grafts, which need to be intubated via the subclavian artery lying close to the internal carotid or vertebral artery, the risk of scratching at atherosclerotic plaques increases, potentially leading to a higher rate of cerebral embolism.

Periprocedural cerebrovascular accidents are well-known to be associated with high in-hospital mortality.10,11,13,16,21 However, neurological deficits, which often lead to disability, persist in the vast majority of patients, who survive this devastating complication.10

Our analysis of data from PCIs performed in an unselected European population from 2005 until 2008 showed a 15-fold increase in the overall mortality rate of patients who developed a peri-interventional stroke compared with patients who did not develop a stroke (19.2% versus 1.3%; P<0.001). Other registries previously reported a 16- to 55-fold increase in mortality rates if a patient experiences peri-interventional stroke.10,11,13,16 We found a 10-fold increase (23.2% versus 2.3%) in the overall in-hospital mortality rate if a patient developed a stroke during PCI for ACS, in contrast to a 50-fold increase (10.0% versus 0.2%) in the in-hospital mortality rate of patients developing stroke during an elective PCI compared with patients without this complication. PCI is generally known to be associated with higher mortality rates if performed under urgent or emergency situations. Therefore, the difference in mortality rates between patients undergoing elective PCI and PCI performed for ACS must be carefully interpreted and is because of a generally higher mortality rate of patients with an ACS compared with patients with stable angina. Thus, we saw a >10-fold increased mortality rate itself in patients with an ACS not having stroke compared with stable patients. Especially in elective procedures with usually low periprocedural mortality rates today, the enormous impact of this complication on the patient’s prognosis can be seen.

In the very beginning of cardiac catheterization in the 1970s and 1980s, the incidence of periprocedural stroke was reported to be in the range of 0.03% to 0.06%.25,26 During the following years, an increase in the incidence of stroke-complicating PCI could be seen (0.18%–0.44%), which is most likely because of an extended use of coronary angiography and PCI also in high-risk patients with severe vascular calcification and comorbidities, who previously had been excluded.11,13,16,19,20 However, increasing rates in periprocedural stroke over time could also relate to the introduction of more sensitive diagnostic tools in clinical practice, such as high-resolution cerebral computed tomography scan or MRI. Despite all technical and pharmacological improvement in cardiac catheterization, the rate of periprocedural stroke has reached a plateau and has not changed significantly during the past years of interventional cardiology.20 This is most likely because of the fact that most of the risk factors associated with periprocedural stroke are not modifiable before PCI (for instance, advanced age, sex, history of stroke, ACS, and valvular heart disease). Therefore, an improvement of the prognosis of patients undergoing this complication will only be possible by improving therapeutic options of cerebrovascular accidents. Only a few reports—most often from case series—suggesting a therapeutic management of peri-interventional stroke are available today15,27–29 and no randomized controlled trials on this topic have been performed so far.

Because of its low incidence, embolic stroke during PCI has not been covered in practice guidelines and only few recommendations on therapeutic options for this serious complication exist today. Therefore, treatment of patients with stroke after PCI still is not evidence-based and needs further research. It will be of paramount importance to develop studies evaluating best medical and interventional treatment after this complication occurred to being able to reduce the high mortality and morbidity associated with this complication in the future.

Limitations

Despite its prospective recording of all data according to prespecified definitions, this study carries all limitations of a retrospective analysis and should, therefore, be interpreted cautiously. In the EHS PCI Registry, the treatment was completely left to the discretion of the physician. This possibly may lead to a bias in the estimation of treatment effects, which cannot be fully eliminated even by using a multivariable analysis. Because periprocedural complications such as stroke depend on a self-initiated reporting by the operator, an under-reporting of complications cannot be excluded, as well.

Furthermore, we have to report on an incomplete ascertainment on the dataset with diversifying proportions of patients missing in the subgroup analyses. Incomplete data are a problem in many large registries and finally we cannot exclude an impact on some of our conclusions by this. Nevertheless, we think the remaining large number of patients in this registry of the EHS program to be a relatively solid basis for our analysis.

There was no routine use of cerebral computed tomography scan or cerebral MRI after every PCI and no differentiation between the pathogenesis of a stroke (ischemic or hemorrhagic) or the anatomic localization was recorded routinely in the PCI Registry. Nevertheless, in case of stroke a cerebral computed tomographic scan was performed in almost every elective or ACS patient. Furthermore, the diagnosis of stroke was predominantly a clinical one made by the treating physician.

The PCI Registry of the Euro Heart Survey did only evaluate the in-hospital outcome of patients undergoing PCI in clinical practice. No follow-up data are available and the long-term clinical outcome of patients remains unknown. For the lack of a routine neurological examination by a neurologist of all patients after PCI and the lack of routine cerebral imaging especially strokes with mild neurological symptoms might have been missed in the registry, which possibly have influenced the long-term outcome of patients undergoing PCI, on which we are not able to report in our analysis. Variables
regarding long term disability and quality of life were not recorded in the PCI Registry of the EHS, therefore we cannot report on them.

Furthermore, the low number of strokes associated with elective PCI in this registry possibly makes our multivariate analysis error-prone, which is another limiting factor of this analysis. Some of the observed differences rely on few cases, and statistically significant results in the multivariable analyses may be because of multiple testing. Especially, our results on independent predictors for stroke in the setting of elective PCI need to be interpreted with caution and need further validation by other large registries.

The presence of atrial fibrillation, as an important and frequent cause for stroke, was not recorded in this registry. Therefore, differences in the incidence of atrial fibrillation between the 2 groups possibly leading to a higher stroke rate in 1 group cannot be excluded.

Disclosures

None.

References

Incidence and Clinical Impact of Stroke Complicating Percutaneous Coronary Intervention: Results of the Euro Heart Survey Percutaneous Coronary Interventions Registry

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