Impact of inhospital stent thrombosis and cerebrovascular accidents on long-term prognosis after percutaneous coronary intervention

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Background Inhospital stent thrombosis (ST) and cerebrovascular accidents (CVA) are rare but serious adverse events after percutaneous coronary intervention (PCI). The association of ST or CVA with long-term outcome after PCI remains poorly investigated.

Methods The study included 18,334 consecutive patients who underwent PCI. Patients were divided into 3 groups: the group with ST, the group with CVA, and the group without these events. The primary outcome was all-cause mortality at 3-year follow-up.

Results Inhospital ST or CVA occurred in 59 patients (0.32%) and in 90 patients (0. 49%), respectively. There were 2,149 deaths (11.7%) during the follow-up: 26 deaths among patients with ST, 32 deaths among patients with CVA, and 2,091 deaths among patients without ST or CVA (Kaplan-Meier estimates of 3-year mortality 45.3%, 38.0%, and 12.9%, odds ratio 6.1, 95% CI 3.6-10.2, $P < .001$ for ST group vs the group without ST or CVA and odds ratio 4.2 [2.7-6.6], $P < .001$ for CVA group vs the group without ST or CVA). There was no significant difference in the 3-year mortality between CVA and ST groups ($P = .29$). The Cox proportional hazards model showed that ST (adjusted hazard ratio 4.97, 95% CI 2.58-9.56, $P < .001$) and CVA (adjusted hazard ratio 2.25 [1.25-4.04], $P = .006$) were independently associated with the increased risk of 3-year mortality.

Conclusion Inhospital ST and CVA after PCI are associated with the increased risk of 3-year mortality. Both events seem to have a similar impact on long-term survival. (Am Heart J 2014;168:862-868.e1.)

Cerebrovascular accidents (CVAs) and stent thrombosis (ST) are rare but serious complications of percutaneous coronary intervention (PCI). Despite significant improvements in the device technology and peri-PCI adjunctive pharmacologic therapy, the incidence of CVA related to PCI appears to have remained relatively constant over the last 20 years, perhaps due to the increased complexity of patients undergoing PCI, which may counterbalance the advantages of improved technology. The incidence of inhospital CVA was reported to be between 0.22% and 1.4%.[1-4] Although hemorrhagic stroke is closely related to the use of anticoagulant and thrombolytic therapy, the mechanisms of ischemic CVA after PCI are poorly understood. Clinical trials and registries have shown that ST is associated with higher rates of morbidity and mortality.[5,6] Although few studies have investigated the impact of inhospital ST on outcome, there is evidence that early (inhospital) ST may have a different impact on prognosis compared with late or very late ST.[6,7] Prior studies have identified a series of demographic and procedural factors that predispose for CVA[2,8] and ST[9] after PCI. Although these studies showed that there is, at least, a partial overlapping of predisposing factors for CVA and ST and most CVA and ST are thrombotic in nature, differences in baseline risk and characteristics of patients across various studies may hamper a comparative analysis of their predisposing factors. So far, a comparative analysis of factors associated with an increased risk of CVA or ST as well as a comparison of their impact on prognosis has not been investigated.

The aim of this study was to assess factors associated with increased risk of inhospital CVA or ST and to investigate and compare the impact of these adverse events on long-term prognosis of patients treated with PCI.

Methods

Study patients

Consecutive patients with symptomatic coronary artery disease admitted in 2 German hospitals for treatment with

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Table I. Baseline characteristics

Variable	No ST or CVA (n = 18185)	ST (n = 59)	CVA (n = 90)	P
Age (y)	67.62 (59.20-75.34)	66.47 (56.09-72.62)	71.10* (66.12-77.43)	.003
Women	4683 (25.8)	16 (27.1)	36 (40.0)*	.008
BMI (kg/m^2)	26.67 (24.34-29.40)	26.79 (24.35-29.34)	24.89* (23.34-27.67)	<.001
Diabetes	4702 (25.9)	21 (35.6)	37 (41.1)*	.001
On insulin therapy	1479 (8.1)	8 (13.6)	14 (15.6)*	.012
Arterial hypertension	11655 (64.1)	28 (47.6)*	58 (64.4)	.029
Current smoking	3825 (21.0)	15 (25.4)	21 (23.3)	.62
Hypercholesterolemia	11060 (60.8)	33 (55.9)	46 (51.1)	.13
LVEF (%)	56.0 (42.0-62.0)	48.0* (39.5-55.5)	45.0* (37.25-56.0)	<.001
Atrial fibrillation	2287 (12.6)	2 (3.4)*	18 (20.0)*	.011
Prior cerebrovascular events	576 (3.2)	1 (1.7)	4 (4.4)	.64
Prior myocardial infarction	4387 (24.1)	17 (28.8)	22 (24.4)	.70
Prior CABG surgery	2113 (11.6)	5 (8.5)	12 (13.3)	.66
Clinical presentation				<.001
Stable angina	9546 (52.5)	13 (22.0)*	30 (33.3)*	
NSTE-ACS	4791 (26.3)	15 (25.4)	23 (25.6)	
STEMI	3848 (21.2)	31 (52.6)*	37 (41.1)*	

Data are expressed as median and interquartile range (25th-75th percentiles) or counts (percentages). Abbreviations: *BMI*, body mass index; *CABG*, coronary artery bypass graft; *LVEF*, left ventricular ejection fraction; *NSTE-ACS*, non–ST-segment elevation acute coronary syndrome; *STEMI*, ST-segment elevation myocardial infarction.
* $P < .05$ compared with patients without ST or CVA.

PCI between January 2000 and January 2011 were included. Patients undergoing coronary artery bypass surgery during the index hospitalization were excluded. Clinical and angiographic data were prospectively collected and stored in a dedicated database.

Angiographic examination and PCI

Coronary angiography was performed according to the standard criteria.[10] Off-line analysis of digital angiograms was performed in the core laboratory using an automated edge detection system (CMS; Medis Medical Imaging Systems, Neuen, the Netherlands) by personnel blinded to the clinical data. Angiographic analysis was performed according to the modified American College of Cardiology/American Heart Association Stenosis Morphology Classification.[11] The B2 and C lesions are considered as complex.

Coronary stenting was performed as per standard practice. Before procedure, all patients received 325 to 500 mg of aspirin and a loading dose of 600 mg of clopidogrel. Unfractionated heparin or bivalirudin was used periprocedurally. Post-PCI antithrombotic therapy consisted of aspirin (80-325 mg/d continuously) and clopidogrel (150 mg/d until discharge but for no longer than 3 days followed by 75 mg/d for at least 1 month after bare-metal stent or ≥6 months after drug-eluting stent implantation). Other medications were left at the discretion of the patient's attending physician.

Study definitions

Stent thrombosis. *Inhospital ST* was defined as a new onset of ischemic symptoms or new electrocardiographic changes that suggested acute ischemia or a typical rise and fall in cardiac biomarkers at any time after the PCI during the index hospitalization, associated with angiographic confirmation of ST according to the Academic Research Consortium criteria for definite ST.[12]

Cardiovascular accidents. A *CVA* was defined as the onset of a new neurologic deficit that occurred any time after the PCI, during the index hospitalization. All the neurologic deficits were assessed by an expert neurologist at the time of events. Stroke was diagnosed according to the World Health Organization Criteria, which defines a stroke as focal deficit that lasts for >24 hours.[13] The neurologic deficit lasting <24 hours was classified as a transient ischemic attack (TIA). In addition, brain imaging (computed tomography or magnetic resonance imaging) was obtained in all stroke patients and in most TIA patients, to confirm the diagnosis and establish the origin (ischemic or hemorrhagic) of the neurologic deficit.

Mortality. Deaths occurring during the hospital course (inhospital) and at 30 days and 3 years after PCI were analyzed. Information on deaths was acquired from the hospital records, death certificates, or telephone contact with the referring physician(s), relatives of the patient, insurance companies, or registration of address office.

Patients were visited by their physician or interviewed by telephone at 30 days, 6 months, 1 year, and yearly thereafter after the PCI procedure.

Statistical analysis

Categorical data are presented as count and percentage (%). Continuous data are presented as median with 25th to 75th percentiles or as mean ± SD. The normality of distribution of continuous data was tested with the 1-sample Kolmogorov-Smirnov test. Continuous data are compared with analysis of variance test or with the Kruskal-Wallis rank sum test. For variables that showed a significant difference, intergroup post hoc comparisons were