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Prior ischemic stroke is not associated with worse clinical outcomes in patients undergoing percutaneous coronary intervention

Abstract

Purpose: Cerebrovascular accidents (CVAs) frequently coexist with coronary artery disease (CAD) and adversely affect prognosis in patients with CAD; however, fewer studies have investigated the role of prior ischemic stroke on the outcomes of percutaneous coronary intervention (PCI). The aim of this study was to determine the safety and effectiveness of PCI in patients with a prior ischemic stroke.

Methods: A review of patients who underwent PCI between June 2003 and September 2005 (n=3893) at the Beijing Anzhen Hospital of Capital University of Medical Science, identified 295 PCI patients with a prior ischemic stroke (≥ 3 months) and 3598 patients without a prior stroke. To investigate whether prior history of an ischemic stroke was independently associated with increased risk of adverse PCI outcomes, prognostic parameters were analyzed using univariate analysis and Cox multivariate regression analysis. Propensity score analysis was then used to match the two subgroups of patients based on multiple factors known to impact cardiac outcome.

Results: Patients with a prior ischemic stroke had more frequent high-risk baseline characteristics (diabetes, hypertension, hyperlipidemia and prior myocardial infarction). No significant differences were found in the major adverse cardiac and cerebrovascular event (MACCEs) rates between the two groups (1.7% in the stroke group *vs.* 1.4% in the non-stroke group; $p=0.06$). Diabetes mellitus, triple vessel CAD, number of diseased vessels, chronic total occlusion and previous myocardial infarction were independent predictors of MACCE in patients with prior stroke undergoing PCI.

Conclusions: This study demonstrates that, in daily clinical practice, PCI can be provided safely and with good results to patients with a prior ischemic stroke (≥ 3 months).

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With improvements in pharmacological and technical aspects, percutaneous coronary intervention (PCI) is increasingly being performed to treat coronary artery disease (CAD) in patients with high-risk baseline characteristics [1, 2]. Recent studies have reported improvements in angiographic and clinical success rates of PCI among high-risk groups [3, 4]; however, the rate of perioperative cardiac complications after cardiac catheterization has remained constant, which is most probably due to the immutability of the majority of risk factors before cardiac procedures. Risk evaluation of the patient before PCI is, therefore, essential to reduce complications and improve prognosis. Cerebrovascular accidents (CVAs) frequently coexist with coronary artery disease (CAD) [5]. In daily clinical practice, clinicians are sometimes faced with the question of safety and prognosis in these patients with a prior ischemic stroke undergoing PCI. Some recent studies have focused on evaluating the impact of prior cerebrovascular disease on the clinical outcomes of patients with acute myocardial infarction (AMI) in the era of drug-eluting stents [6, 7]. More and more, research has focused on the impacts of traditional cardiovascular risks on the safety of patients undergoing PCI [8]. To date, no study has evaluated the effect of a prior stroke on the clinical outcomes in patients undergoing PCI. The aim of this study was to evaluate the effect of a prior stroke on major adverse cardiac and cerebrovascular events (MACCEs) in CAD patients undergoing PCI.

Methods

Study Design

The study retrospectively included 3893 patients who underwent PCI from January 2003 to October 2005 at Beijing Anshan Hospital of the Capital Medical University. Of the 3893 patients, 295 patients were identified as having a prior stroke. The whole cohort was divided into two groups; prior stroke group (n=295) and no prior stroke group (n=3598). All PCIs were performed with standard PCI techniques.

Prior Stroke Definition

Prior stroke was defined as ischemic stroke more than three months before PCI. Clinical notes, discharge summary, neurological consultation notes and CT/MRI reports were collected for all the patients to confirm ischemic stroke. Patients with a hemorrhagic stroke or transient ischemic attack were excluded from the study. Patients with transient ischemia were excluded as there is usually no radiological evidence to confirm the diagnosis.

Medications

All patients were treated with 325 mg of daily aspirin prior to the procedure and were advised to continue use of 100 mg aspirin indefinitely post-procedure. Most of the patients were also treated with clopidogrel 300 mg loading dose followed by 75 mg daily for up to 12 months after the procedure (Table 1). In-hospital outcomes included myocardial infarction, emergent PCI or coronary artery bypass graft (CABG), post-PCI stroke and in-hospital all-cause mortality. ST-elevation myocardial infarction (MI) was based on chest pain lasting ≥ 30 min and the presence of new ST-segment elevation >1 mm in at least two leads on the electrocardiogram. Non-ST-elevation MI was defined as elevation of the CK-MB isoenzyme to at least three times the upper limit of normal in at least two blood samples. Post-PCI stroke was defined as abrupt onset of a new non-convulsive, focal, neurologic deficit with residual symptoms lasting more than 24 hours that was confirmed by a neurologist and by CT/MRI findings. Post-PCI strokes occur within 48 hours of PCI and include TIA (neurologic deficits < 24 hours). Strokes included both ischemic and hemorrhagic strokes, based on CT/MRI analysis performed by experienced neuroradiologists.

Statistical Analysis

Patient preoperative demographics, risk factors, and preoperative medications were first compared between the groups by univariate (χ^2) analysis. All significant predictor variables in the univariate analysis were then entered into a multivariate logistical model, and stepwise logistic regression was performed to determine if prior stroke was independently associated with an increase in the risk of adverse postoperative outcomes after PCI. Only those variables that were significant with a 2-tailed nominal $p < 0.05$ were retained within the model. Odds ratios and corresponding 95% CI are reported with associated p values. In order to further adjust for selection bias related to the choice of therapy, propensity scores were also estimated using unconditional logistic regression to determine the predicted probability of inclusion in the "prior stroke" group for each of the 295 patients. All statistical analyses were performed using SPSS statistical software.

Results

Patient preoperative demographics and risk factors are shown in Table 1. Compared with patients without prior stroke, patients with prior stroke were more likely to have a history of myocardial infarction, hyperlipidemia, hypertension and diabetes mellitus (Table 1). Compared with the no prior stroke

TABLE 1. Preoperative demographic variables and risk factors

Demographics and risk factors	No prior stroke (n=3598)	Prior stroke (n=295)	<i>p</i> (χ^2)
Age, years	59±10.8	65±8	NS
Female, %	24.8%	28.5%	NS
Body mass index, kg/m ²	25.79±3.25	25.9±3.12	NS
Triglycerides (mg/dl)	161.43±104.89	156.14±90.26	NS
Total cholesterol (mg/dl)	173.95±34.26	180.60±42.53	<0.05
Low-density lipoprotein (mg/dl)	104.59±32.97	100.32±26.54	<0.05
High-density lipoprotein (mg/dl)	40.92±9.16	40.80±8.88	<0.05
C-Reactive protein (mg/L)	0.953±0.005	1.029±0.021	<0.05
Diabetes mellitus, %	25.2%	34.5%	<0.05
Fasting blood glucose (mg/dl)	108.66±0.67	114.58±40.2	<0.05
Current smoker, %	46.2%	51.4%	NS
Hypertension, %	60.6%	84.4%	<0.05
Systolic blood pressure (mmHg)	128.56±0.33	134.85±1.28	<0.05
Diastolic blood pressure (mmHg)	78.41±0.19	79.21±0.70	NS
Previous myocardial infarction, %	19.0%	19.3%	<0.05
Peripheral vascular disease, %	1.4%	4.1%	NS
Ejection fraction, %	60.93±10.74	60.21±10.58	NS
End diastolic diameter (mm)	49.2±5.8	49.04±5.9	NS
Left main coronary artery disease, %	3.1%	3.4%	NS
Acute coronary syndrome, %	43.2%	40.4%	NS
PCI Access (radial), %	51.6%	49.4%	NS
Number of diseased vessels	1.78±0.79	2.02±0.81	<0.05
Three vessel disease	22.8%	33.6%	<0.05
Chronic total occlusion	12.2%	12.5%	NS
Total number of stents	1.88±1.2	2.06±1.2	<0.05
Statin, %	86.3%	86.8%	NS
ACEI, %	63.1%	69.2%	NS
β-blockers, %	87.2%	88.5%	NS
Aspirin, %	98.8%	98.6%	NS
Clopidogrel, %	99.9%	98.3%	NS
Calcium antagonist, %	28.9%	69.2%	<0.05
Total cost (in Yuan)	76457.69±586.6	83178.3±2080	<0.05

ACEI, angiotensin converting enzyme inhibitor; NS, not significant; PCI, percutaneous coronary intervention

TABLE 2. Preoperative demographic variables and risk factors in propensity-matched cohorts

Demographics and risk factors	No prior stroke (n=295)	Prior stroke (n=295)	<i>p</i> (χ^2)
Age, years	60	63	NS
Female, %	23%	24%	NS
Body mass index, kg/m ²	26	27	NS
Triglycerides (mg/dl)	160	157	NS
Total cholesterol (mg/dl)	180	178	NS
Low-density lipoprotein (mg/dl)	110	108	NS
High-density lipoprotein (mg/dl)	41	42	NS
C-reactive protein (mg/L)	0.9	1.0	NS
Diabetes mellitus, %	24%	25%	NS
Fasting blood glucose (mg/dl)	110	114	NS
Current smoker, %	45%	48%	NS
Hypertension, %	61%	63%	NS
Systolic blood pressure (mmHg)	130	132	NS
Diastolic blood pressure (mmHg)	78	79	NS
Previous myocardial infarction, %	19.0%	19.3%	NS
Peripheral vascular disease, %	1.4%	4.1%	NS
Ejection fraction, %	55%	56%	NS
End diastolic diameter (mm)	49	50	NS
Left main coronary artery disease, %	3.0%	2.9%	NS
Acute coronary syndrome, %	34.2%	30.4%	NS
PCI access (radial), %	24.6%	20.4%	NS
Number of diseased vessels	1.8	2.0	NS
Three vessel disease, %	23%	26%	NS
Chronic total occlusion, %	12%	13%	NS
Statin, %	86%	87%	NS
ACEI, %	60%	61%	NS
β -blockers, %	87%	88%	NS
Aspirin, %	98%	99%	NS
Clopidogrel, %	99 %	100%	NS
Calcium antagonist, %	68%	68%	NS
Total number of stents	1.9	2.0	NS
Total cost (in Yuan)	81085	82178	NS

ACEI, angiotensin converting enzyme inhibitors; NS, non-significant; PCI, percutaneous coronary intervention

TABLE 3. Incidence of MACCE in patients undergoing PCI

Outcome	Entire sample			Propensity-matched group		
	No prior stroke (n=3598)	Prior stroke (n=295)	<i>p</i>	No prior stroke (n=290)	Prior stroke (n=290)	<i>p</i>
In-hospital mortality	0.4% (15/3598)	0.0% (1/295)	NS	0	0	NS
Myocardial infarction	0.7% (25/3598)	1.4% (4/295)	NS	0.34% (2/290)	0.68% (2/290)	NS
Stroke	0.2% (7/3598)	0.3% (1/295)	NS	0.34% (1/290)	0.34% (1/290)	NS
Revascularization	0.1% (5/3598)	0.0% (0/295)	NS	0% (0/290)	0.34 (1/290)	NS
Overall MACCE	1.4%	1.7%	NS	0.68%	1.36%	NS

MACCE, major adverse cerebrovascular and cardiovascular events; NS, not significant; PCI, percutaneous coronary intervention

group, patients in the prior stroke group had significantly higher levels of fasting plasma glucose, total cholesterol, C-reactive protein and higher systolic blood pressure. Angiograms of patients with previous history of stroke often revealed multivessel CAD and needed more stents per treatment. On the other hand, the prior stroke group was also associated with more cost of hospitalization from longer length of hospital stay. The rest of the baseline characteristics were similar between the two groups, including use of preoperative β -blockers, number of diseased vessels and gender. The MACCE data during in-hospital stay are presented in Table 3. Univariate analysis revealed that the risk of overall MACCE rate did not increase in patients with prior stroke (1.7% *vs.* 1.4%; respectively, $p>0.05$).

To determine whether prior stroke was independently associated with a significant increase in the risk of MACCE during in-hospital stay after PCI, Cox multivariate analysis of MACCE was performed, controlling for patient demographics. Our analysis showed that patients with prior stroke were not independently associated with a significant reduction in the risk of MACCE in hospital. Compared with patients without prior stroke, the hazard ratio for MACCE during the hospital stay was 1.389 (95% CI, 0.254-1.610, $p=0.743$), the independent prognostic parameters for MACCE were triple

vessel CAD, DM, number of diseased vessels, CTO, previous MI. In order to further control for selection bias related to the choice of therapy, stepwise logistic regression was also performed on a propensity score-matched cohort of 290 patients. Table 2 lists the variables used to determine each subject's propensity score, and demonstrates that no significant differences existed between the prior stroke group and the without prior stroke group in the propensity-matched cohort. Even after controlling for propensity score, prior stroke group was not found to be independently associated with a significant increase in the risk the rates of MACCE undergoing PCI (1.34% *vs.* 0.68%; $p>0.05$) (Table 3).

Discussion

Our analysis demonstrated significant differences in baseline characteristics between patients with or without a prior stroke. Patients with prior stroke clearly represented a high-risk PCI cohort, with a higher prevalence of cardiovascular risk factors and higher-risk coronary anatomy. Our study showed that these patients with a prior stroke were more likely to have prior history of myocardial infarction and risk factors including hyperlipidemia, hypertension and diabetes mellitus. Also, this

TABLE 4. Cox Multivariate analyses of MACCE in patients undergoing PCI.

Independent predictors	Hazard ratio	95% CI	<i>p</i>
Prior stroke	1.389	0.254-1.610	0.743
Triple vessel coronary artery disease	1.622	1.096-2.4	0.016
Diabetes mellitus	2.699	1.413-5.157	0.003
Number of diseased vessels	1.052	1.018-1.087	0.003
Chronic total occlusion	1.104	1.003-1.215	0.04
Previous myocardial infarction	1.030	1.008-1.120	0.02

CI, confidence interval

group was observed to be associated with higher healthcare costs from a prolonged hospital stay.

Our data did not show that patients with prior stroke had significantly higher risk of MACCE during PCI, even after controlling for propensity score. The current study demonstrated that prior stroke does not increase the mortality (0% *vs.* 0.4%; $p>0.05$) and overall MACCE (1.7% *vs.* 1.4%; $p>0.05$). Compared with patients with no prior stroke, the adjusted odds ratio for overall MACCE in patients with no prior stroke was 1.389 (95% CI, 0.254-1.610).

Cerebrovascular event (CVE) is one of the most daunting complications of cardiac catheterization [9]. The incidence of stroke following percutaneous coronary intervention (PCI) has been variably reported between 0.3% and 0.4% [10, 11]. Patients with an in-hospital stroke had higher rates of death, MI, emergent CABG and higher triple composite endpoints, all of which have an enormous impact on the patient's prognosis and on quality of life [10]. Our stroke rate (0.3%) in this study population was same as reports from the Cleveland Clinic (0.3%) [12] and the national Canadian Stroke Network (0.25%) [13]. Similarly, Fuchs *et al.* showed that the rate of peri-procedural stroke in an unselected group of patients undergoing PCI was 0.38% [14]. Although some studies suggest that a prior stroke in patients undergoing PCI is associated with more risks, such as cerebral hemorrhage, reinfarction and prolonged hospital stay [15, 16], our study suggests that PCI is feasible and probably safe, if adequate standardized treatment were given before PCI, even for patients with a prior stroke. On the other hand, in our study, patients with prior recent stroke (ischemic stroke within 3 months) and hemorrhagic stroke were excluded from enrollment, which might have some effects on the clinical outcomes in patients undergoing PCI suggesting an inherent selection bias.

Several limitations are apparent in our current analyses. Our study is a retrospective analysis. Confounding variables were minimized using propensity score and multivariate regression analyses, but there still could be unmeasured confounders, such as the quality of preoperative care and patients' medical knowledge. Further large-scale prospective randomized clinical trials are necessary to confirm these observations. Despite statistical limitations, our study is large enough to answer the question of whether a prior stroke is associated with a higher incidence of MACCE undergoing PCI.

In conclusion, this study demonstrates that PCI can be provided safely and with good results in patients with a prior ischemic stroke (≥ 3 months). Patients with a prior stroke were more likely to have diabetes mellitus, hyperlipidemia and hypertension than patients without a prior stroke. History of a

prior stroke was not associated with increased incidence of MACCE in patients undergoing PCI.

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