Stroke in Patients With Acute Coronary Syndromes : Incidence and Outcomes in the Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) Trial

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Stroke in Patients With Acute Coronary Syndromes

Incidence and Outcomes in the Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) Trial

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Background—The incidence of stroke in patients with acute coronary syndromes has not been clearly defined because few trials in this patient population have been large enough to provide stable estimates of stroke rates.

Methods and Results—We studied the 10 948 patients with acute coronary syndromes without persistent ST-segment elevation who were randomly assigned to placebo or the platelet glycoprotein IIb/IIIa receptor inhibitor eptifibatide in the Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) trial to determine stroke rates, stroke types, clinical outcomes in patients with stroke, and independent baseline clinical predictors for nonhemorrhagic stroke. Stroke occurred in 79 (0.7%) patients, with 66 (0.6%) nonhemorrhagic, 6 intracranial hemorrhages, 3 cerebral infarctions with hemorrhagic conversion, and 4 of uncertain cause. There were no differences in stroke rates between patients who received placebo and those assigned high-dose eptifibatide (odds ratios and 95% confidence intervals 0.82 [0.59, 1.14] and 0.70 [0.49, 0.99], respectively). Of the 79 patients with stroke, 17 (22%) died within 30 days, and another 26 (32%) were disabled by hospital discharge or 30 days, whichever came first. Higher heart rate was the most important baseline clinical predictor of nonhemorrhagic stroke, followed by older age, prior anterior myocardial infarction, prior stroke or transient ischemic attack, and diabetes mellitus. These factors were used to develop a simple scoring nomogram that can predict the risk of nonhemorrhagic stroke.

Conclusions—Stroke was an uncommon event in patients with acute coronary syndromes in the PURSUIT trial. These strokes are, however, associated with substantial morbidity and mortality rates. The majority of strokes were of nonhemorrhagic causes. Eptifibatide was not associated with an increase in intracranial hemorrhage, and no significant effect on nonhemorrhagic stroke was observed. We developed a useful nomogram for assigning baseline nonhemorrhagic stroke risk in this patient population. **(*Circulation*. 1999;99:2371-2377.)**

Key Words: stroke ■ coronary disease ■ myocardial infarction ■ glycoproteins ■ receptors

The incidence of stroke in patients with acute myocardial infarction treated with and those without thrombolytic therapy has been well established.[1–13] The incidence of stroke in patients with acute coronary syndromes without persistent ST-segment elevation is less clearly defined, as few trials in this patient population have been large enough to provide a stable estimate of stroke rates given the relative infrequency of this adverse event. In the 2 largest trials of this population to date, stroke occurred in 0.8% of patients with acute coronary syndromes not treated with thrombolysis.[14,15] The majority of these strokes were nonhemorrhagic. Risk factors for stroke in this patient population have not been previously analyzed.

The recently completed Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) trial is the largest trial to date of patients with acute coronary syndromes without persistent ST-segment elevation.[16] We prospectively collected information about patients with suspected stroke to determine the incidence of stroke, stroke types, outcomes in patients with stroke, and the independent baseline clinical and demographic risk factors for nonhemorrhagic stroke in this patient population.

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Methods

Study Population

The PURSUIT trial enrolled 10 948 patients in 726 hospitals in 27 countries. Enrollment criteria have been published[16]: In brief, patients with symptoms of ischemic chest pain at rest lasting 10 minutes or longer within the previous 24 hours that was accompanied by either transient ST-segment elevation >0.5 mm, transient or persistent ST-segment depression >0.5 mm, or T-wave inversion >1 mm within 12 hours of the chest pain; or had a creatine kinase myocardial enzymes fraction above the upper limit of normal for that hospital. Exclusion criteria included persistent ST-segment elevation >1 mm; evidence of bleeding; systolic blood pressure >200 mm Hg or diastolic blood pressure >110 mm Hg; major surgery within 6 weeks; a nonhemorrhagic stroke within 30 days or any history of hemorrhagic stroke; renal failure; or treatment with thrombolytic therapy within 24 hours.

Patients were randomly assigned in double-blind fashion to an intravenous bolus and infusion of placebo, 180 mm/kg bolus plus infusion of 1.3 μg/kg per minute of eptifibatide, or 180 μg/kg bolus plus infusion of 2.0 μg/kg per minute of eptifibatide. Per prespecified plan, after 3218 patients were randomized, an independent Data and Safety Monitoring Committee reviewed the safety data. The committee recommended dropping the lower dose because the high dose had an acceptable safety profile.

A study drug was to be infused until hospital discharge or up to 72 hours, whichever came first (or up to 96 hours in patients undergoing percutaneous intervention at 72 hours). All patients were to receive daily aspirin, and heparin was recommended but not required. Intravenous heparin was to be given as a 5000 U bolus and 1000 U/h infusion with adjustment to maintain activated partial thromboplastin time in the 50 to 70 seconds range. Lower doses were recommended for patients who weighed <70 kg. Other concomitant medications, diagnostic cardiac procedures, or percutaneous or surgical interventions were at the discretion of the treating physician.

Stroke Classification

Stroke was defined as an acute new neurological deficit resulting in death or lasting for >24 hours. A Stroke Adjudication Committee (see Appendix) was established to independently adjudicate and categorize all suspected strokes. Patients with suspected strokes were identified from the Case Report Form.

The evaluation of patients with stroke was prospectively planned. The protocol specified that all patients with a new neurological deficit undergo complete evaluation including brain imaging. Clinical notes, discharge summaries, neurological or neurosurgical consultation notes, autopsy reports, and results of computed tomographic or magnetic resonance imaging (MRI) studies were collected on all patients with suspected stroke. The committee reviewed all available medical records and determined by consensus if a stroke did or did not occur and if so, categorized the type of stroke. The Stroke Adjudication Committee members were blinded to treatment assignment.

Stroke Categories

Strokes were divided into 4 main categories: primary hemorrhagic, nonhemorrhagic, hemorrhagic conversion of infarct, and uncertain. Primary hemorrhagic was diagnosed if a focal collection of intracranial blood was seen on brain imaging or at autopsy and was not believed to represent hemorrhagic conversion. Nonhemorrhagic stroke was categorized if there was a low-density lesion on computed tomography, high-intensity lesion on MRI, or clinical evidence of a stroke and no focal collection of intracranial hemorrhage on brain imaging studies or at autopsy. Hemorrhagic conversion was diagnosed if blood was present within an area of cerebral infarction, but the event was not thought to represent a primary hemorrhagic stroke. The uncertain classification was used if there was clinical evidence of a stroke and no brain imaging or autopsy data were available to determine the type of stroke.

TABLE 1. Incidence of Stroke by 30-Day Follow-Up

	Placebo (n=4739)	Eptifibatide* (n=6209)	Total (n=10 948)
Primary hemorrhagic	2 (<0.1%)	4 (<0.1%)	6 (<0.1%)
Nonhemorrhagic	33 (0.7%)	33 (0.5%)	66 (0.6%)
Cerebral infarction with hemorrhagic conversion	1 (<0.1%)	2 (<0.1%)	3 (<0.1%)
Uncertain	3 (<0.1%)	1 (<0.1%)	4 (<0.1%)
Total	39 (0.8%)	40 (0.6%)	79 (0.7%)

Values are n (%).
*Includes both low-dose and high-dose patients.

Patient Functional Assessment

Functional status was determined for all patients with stroke at hospital discharge or 30 days, whichever came first. Patients were classified by site investigators as not disabled if they had no deficit (no sequelae) or minor deficits (functional status unchanged) and as disabled if they had moderate deficits (significant limitations of activity) or severe deficits (unable to live independently or return to work). The correlation of this classification of disability and direct patient interviews in stroke survivors has been shown to be excellent.[9]

Statistical Analysis

Continuous variables are shown as medians with 25th and 75th percentiles. Discrete variables are shown as frequencies and percentages. Stroke data for all 10 948 patients are included. Analyses that include comparisons between treatment groups only include the 9461 patients assigned placebo or high-dose eptifibatide because the low-dose eptifibatide group was not contemporaneous with the other 2 groups as the result of discontinuation of the low-dose arm after the interim analysis by the Data Safety and Monitoring Board (see Methods). Logistic regression modeling was used to determine the univariable predictors of nonhemorrhagic stroke and the multivariable baseline risk factors for nonhemorrhagic stroke. Predictors were tested with the use of the Wald or likelihood χ^2 test. Results are presented as odds ratios and 95% confidence intervals.

A scoring nomogram was created from the coefficients from the baseline multivariable regression modeling. Each independent predictor was assigned a score according to its predictive value. The sum of the scores indicates the probability of a nonhemorrhagic stroke, based on baseline predictors for individual patients.[17]

Results

A total of 79 (0.7%) strokes occurred within 30 days in the 10 948 patients enrolled in the PURSUIT trial. Table 1 shows the type of strokes by treatment assignment. Nonhemorrhagic stroke was the most common stroke type. Specifically, nonhemorrhagic stroke was observed in 28 (0.6%) high-dose eptifibatide patients and in 33 (0.7%) placebo patients. The median (25th, 75th) time to onset of nonhemorrhagic stroke symptoms was 6.5 (3, 12) days (Figure 1). The clinical outcomes for patients with stroke are shown in Table 2. Overall, 54% of patients with stroke died or were disabled at the time of hospital discharge or 30-day follow-up, whichever came first.

Table 3 shows the baseline clinical characteristics for patients with and those without stroke and for patients with nonhemorrhagic stroke. Patients with stroke were older and more often female, had lower body weight and higher heart rate, and more frequently had prior myocardial infarction, diabetes mellitus, history of hypertension, hypercholesterolemia, coronary artery bypass surgery, and history of stroke or

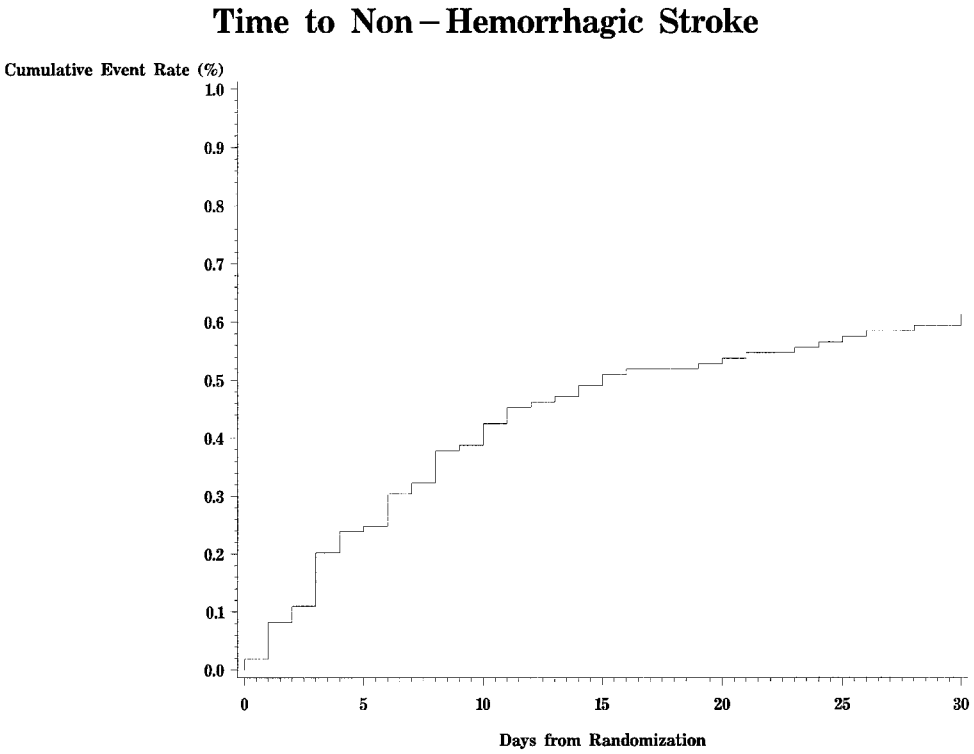

Figure 1. Cumulative frequency distribution of days from enrollment to nonhemorrhagic stroke in PURSUIT trial.

transient ischemic attack. Patients with stroke more commonly experienced adverse in-hospital events including hypotension, atrial fibrillation, congestive heart failure, cardiogenic shock, and coronary artery bypass surgery (Table 4).

Table 5 shows the univariable baseline factors associated with nonhemorrhagic stroke. Five independent baseline clinical and demographic predictors of stroke occurring by 30-day follow-up were identified (Table 6). Higher heart rate was the most important independent baseline clinical predictor; older age, previous anterior myocardial infarction, prior stroke or transient ischemic attack, and history of diabetes mellitus were the other statistically significant predictors. Other possible but not statistically significant predictors were prior percutaneous intervention ($P=0.09$), history of aspirin use ($P=0.06$), and history of hypercholesterolemia ($P=0.09$). The predicted probability in individual patients for nonhemorrhagic stroke within 30-day follow-up can be calculated by using the nomogram in Figure 2.

Discussion

In the PURSUIT trial of almost 11 000 patients, the overall stroke rate through 30-day follow-up was 0.7%. The majority of these strokes were not hemorrhagic. We identified 5 easily determined independent baseline clinical and demographic risk factors for nonhemorrhagic stroke in the PURSUIT population (higher heart rate, older age, prior anterior myocardial infarction, prior stroke or transient ischemic attack, and diabetes mellitus).

In patients with ST-segment elevation, acute myocardial infarction, the incidence of stroke in the era before the routine use of thrombolytic therapy was 1.7% to 3.2%.[1–5] In the thrombolytic era, the incidence of stroke has decreased, but

TABLE 2. Clinical Outcomes in Stroke Patients by Stroke Type

Outcome	Primary Hemorrhagic (n=6)	Nonhemorrhagic (n=66)	Infarct With Hemorrhagic Conversion (n=3)	Uncertain (n=4)	Total (n=79)
Death	4 (67%)	11 (17%)	1 (33%)	1 (25%)	17 (22%)
Severe deficit	0 (0%)	10 (15%)	1 (33%)	0 (0%)	11 (14%)
Moderate deficit	1 (17%)	14 (21%)	0 (0%)	0 (0%)	15 (19%)
Mild deficit	0 (0%)	14 (21%)	0 (0%)	1 (25%)	15 (19%)
No deficit	0 (0%)	6 (9%)	0 (0%)	1 (25%)	7 (9%)
Unknown	1 (17%)	11 (17%)	1 (33%)	1 (25%)	14 (18%)
Death or disabled	5 (83%)	35 (53%)	2 (67%)	1 (25%)	43 (54%)

Values are n (%).

TABLE 3. Baseline Characteristics of Stroke Patients

	Nonhemorrhagic Stroke (n=66)	All Stroke (n=79)	No Stroke (n=10 869)	Overall (n=10 948)
Age	69 (61, 75)	70 (61, 75)	64 (55, 71)	64 (55, 71)
Female sex	30 (45%)	35 (44%)	3822 (35%)	3857 (35%)
Systolic blood pressure	130 (115, 149)	130 (115, 146)	130 (116, 145)	130 (116, 145)
Diastolic blood pressure	72 (65, 81)	72 (65, 80)	75 (67, 83)	75 (67, 83)
Heart rate	75 (65, 88)	76 (65, 90)	72 (62, 80)	72 (62, 80)
Prior anterior MI	12 (18%)	14 (18%)	958 (9%)	972 (9%)
Prior MI	27 (41%)	30 (38%)	3519 (32%)	3549 (33%)
Height, cm	169 (160, 175)	169 (161, 175)	170 (163, 176)	170 (163, 176)
Time to treatment, min	35 (20, 90)	32 (16, 83)	30 (15, 57)	30 (15, 57)
History of smoking	21 (32%)	24 (30%)	3556 (33%)	3580 (33%)
Current smoker	19 (29%)	22 (28%)	3077 (28%)	3099 (28%)
Diabetes mellitus	25 (38%)	28 (35%)	2453 (23%)	2481 (23%)
Weight, kg	72 (65, 90)	73 (65, 89)	78 (69, 88)	78 (69, 88)
Previous CABG	12 (18%)	13 (16%)	1282 (12%)	1295 (12%)
Previous PTCA	4 (6%)	4 (5%)	1425 (13%)	1429 (13%)
Previous angina	53 (80%)	64 (81%)	8801 (81%)	8865 (81%)
History of hypertension	44 (67%)	50 (63%)	5980 (55%)	6030 (55%)
History of hypercholesterolemia	33 (50%)	37 (47%)	4490 (42%)	4527 (42%)
Family history of CAD	27 (41%)	30 (39%)	3808 (35%)	3838 (35%)
Prior stroke/TIA	10 (15%)	12 (15%)	647 (6%)	659 (6%)

MI indicates myocardial infarction; CAD, coronary artery disease; TIA, transient ischemic attack.
Values are n (%) or median (25th, 75th) where appropriate.

there is a higher proportion of intracranial hemorrhage (0.07% to 1.5%) and a lower rate of nonhemorrhagic stroke (0.1% to 1.3%).[6–12] The rates observed for nonhemorrhagic stroke in the current study were similar to those for patients with acute myocardial infarction treated with thrombolysis and, as would be expected, the incidence of intracranial hemorrhage was lower. The observed rate of intracranial hemorrhage was 0.05% (6/10948) without evidence of an increase in the eptifibatide groups compared with placebo (4 patients vs 2 patients). These data support the safety of eptifibatide regarding intracranial hemorrhage.

The Global Use of Strategies to Open Occluded Arteries in acute coronary syndromes (GUSTO IIb) trial[14] was the largest trial of patients with acute coronary syndromes prior to PURSUIT. In GUSTO IIb, 8011 patients with acute coronary syndromes without persistent ST-segment elevation were randomly assigned to intravenous heparin or the novel antithrombin, hirudin. All patients were to be treated with aspirin. The overall incidence of stroke was 0.8%. Nonhemorrhagic stroke occurred in 0.5% of patients and 0.09% of patients had a primary hemorrhagic stroke.[14] No difference in stroke rates was observed by treatment assignment. These data are similar to the stroke rates in PURSUIT, in which patients were to be treated with heparin and aspirin and randomly assigned to the glycoprotein IIb/IIIa receptor inhibitor eptifibatide or to placebo. The patients in PURSUIT were more often female (35% vs 33%), younger (64 vs 66 years), heavier (78 vs 76 kg), and had lower enrollment systolic blood pressure (130 vs 139 mm Hg), lower heart rate (72 vs 74 bpm) and were more likely to have a history of diabetes (23% vs 19%), hypertension (55% vs 48), or previous coronary intervention (13% vs 12%) compared with the GUSTO IIb population. However, the impact of these factors on stroke rates in the 2 trials is unknown.

No previous studies have determined the risk factors for stroke in the unstable angina population to use for comparison with our results. In the GUSTO I trial of >41 000 patients treated with thrombolysis for acute myocardial infarction, the baseline independent risk factors for nonhemorrhagic stroke were similar to those identified for the PURSUIT population.[13] In GUSTO I, as in PURSUIT, older age, higher heart rate, history of stroke or transient ischemic attack, and diabetes mellitus were independent baseline predictors of stroke.[18] Prior anterior myocardial infarction was not a risk factor in the GUSTO I stroke prediction model, but prior angina was an independent predictor. A history of hypertension was also an independent predictor in the GUSTO I population, but it was not in the PURSUIT nonhemorrhagic stroke model, although it did achieve borderline statistical significance in univariable analysis. The reason higher heart rate is an independent predictor for nonhemorrhagic stroke is not clear from these data, but heart rate may correlate with larger infarctions that predispose patients to a higher likelihood of atrial arrhythmia and left ventricular thrombi.

The clinical outcomes of stroke patients with unstable angina/non–Q-wave myocardial infarction have not been previously reported. In PURSUIT, stroke was associated with substantial morbidity and mortality rates. In GUSTO I, the percentage of nonhemorrhagic stroke patients who died or

TABLE 4. In-Hospital Cardiac Events, Medications, and Procedures

	Nonhemorrhagic Stroke (n=66)	All Stroke (n=79)	No Stroke (n=10 869)	Overall (n=10 948)
Ejection fraction, %	50.5 (40, 60)	50 (40, 60)	55 (45, 65)	55 (45, 65)
Hypotension requiring treatment	14 (21%)	16 (20%)	714 (7%)	730 (7%)
Atrial fibrillation/flutter*	18 (27%)	20 (26%)	713 (7%)	733 (7%)
Aspirin during infusion	57 (86%)	69 (87%)	10 092 (93%)	10 161 (93%)
Heparin during infusion	62 (94%)	72 (91%)	9730 (90%)	9802 (90%)
Cardiac catheterization				
Total	51 (77%)	58 (73%)	6842 (63%)	6900 (63%)
Before stroke onset†	48 (73%)	55 (70%)		
PCI				
Total	8 (12%)	11 (14%)	2803 (26%)	2814 (26%)
Before stroke onset†	7 (11%)	10 (13%)		
CABG				
Total	33 (50%)	35 (44%)	1676 (15%)	1711 (16%)
Before stroke onset†	33 (50%)	35 (44%)		
IABP				
Total	11 (17%)	11 (14%)	282 (3%)	293 (3%)
Before stroke onset†	11 (17%)	11 (14%)		
Congestive heart failure				
Total	7 (11%)	8 (10%)	592 (5%)	600 (5%)
Before stroke onset†	4 (6%)	5 (6%)		
Cardiogenic shock				
Total	7 (11%)	8 (10%)	266 (2%)	274 (3%)
Before stroke onset†	5 (8%)	6 (8%)		

PCI indicates percutaneous coronary intervention; IABP, intra-aortic balloon pump.
Values are n (%).
*After enrollment.
†Occurring on same day as or before stroke onset.

were disabled was comparable with that in the PURSUIT population (57% vs 54%).[9]

The incidence of nonhemorrhagic stroke in patients assigned high-dose eptifibatide compared with placebo was similar (0.6% vs 0.7%, respectively; $P=0.53$). Treatment assignment was not a statistically significant predictor of nonhemorrhagic stroke in the univariable or multivariable analyses. The overall number of strokes was small; therefore definitive conclusions cannot be made about the potential risks or benefits of glycoprotein IIb/IIIa receptor blockade on the incidence of nonhemorrhagic stroke from these data. A lower incidence of nonhemorrhagic stroke in the eptifibatide group would have been consistent with the known benefits of antiplatelet therapy in decreasing the incidence of stroke in patients with acute myocardial infarction or prior stroke as well as in other high-risk patient groups including unstable angina.[19] Ongoing studies of prolonged oral glycoprotein

TABLE 5. Univariable Baseline Predictors of Nonhemorrhagic Stroke

	Likelihood Ratio χ^2	*P*	Odds Ratio
Age (per 10 years)	11.3	<0.001	1.48
Higher heart rate (per 10 bpm)	10.7	0.001	1.29
Diabetes mellitus	7.8	0.005	2.10
Prior stroke or TIA	7.1	0.008	2.81
Prior aspirin use	5.8	0.016	1.95
Prior CHF	5.6	0.018	2.16
Prior anterior MI	5.6	0.018	2.30
History of hypertension	3.7	0.055	1.64
Female sex	2.9	0.087	1.53

TIA indicates transient ischemic attack; CHF, congestive heart failure; and MI, myocardial infarction.

TABLE 6. Independent Baseline Clinical and Demographic Predictors of Nonhemorrhagic Stroke

	Wald χ^2	*P*	Odds Ratio (95% CI)
Higher heart rate (per 10 bpm)	8.5	0.004	1.25 (1.08–1.45)
Older age (per 10 years)	6.6	0.01	1.38 (1.08–1.77)
Prior anterior MI	6.6	0.01	2.30 (1.22–4.34)
Prior stroke or TIA	5.4	0.02	2.27 (1.14–4.54)
Diabetes mellitus	4.4	0.03	1.73 (1.03–2.89)

MI indicates myocardial infarction; TIA, transient ischemic attack.
Model $\chi^2=31.512$; 10 812 patients were included in model, with 64 nonhemorrhagic strokes (2 of the 66 nonhemorrhagic stroke patients excluded because of missing key variables). C-index=0.685.

1. Find Points For Each Risk Factor

Age (years)		Heart Rate (beats/min)		Diabetes		Prior MI Location	
Age	Points	Rate	Points		Points		Points
20	0	20	0	Yes	14	Anterior	21
30	8	40	12	No	0	Other	0
40	16	60	25				
50	24	80	37				
60	32	100	50				
70	40	120	63				
80	48	140	75				
90	56	160	87	Previous CVD			
100	64	180	100		Points		
				Yes	21		
				No	0		

2. Sum Points For All Risk Factors

Age	+	Heart rate	+	Diabetes	+	Prior MI	+	Previous CVD	=	Point Total
_____		_____		_____		_____		_____		_____

3. Look Up Risk Corresponding to Point Total

Points	Risk	Points	Risk
75	0.5%	129	4%
93	1%	135	5%
111	2%	154	10%
121	3%		

Figure 2. Nomogram for predicting nonhemorrhagic stroke with the use of baseline clinical and demographic characteristics. In panel 1, find the value most closely matching the patient's risk factors and circle the corresponding point assignment. In panel 2, sum the points for all predictive factors. In panel 3, determine probability of in-hospital nonhemorrhagic stroke. Example: A 71-year-old nondiabetic patient with a heart rate of 101 bpm, prior anterior myocardial infarction, and no history of prior stroke or transient ischemic attack would have a total score of [40+50+0+21+0]=111. This score corresponds to a predicted probability of nonhemorrhagic stroke within 30-day follow-up of 2%. MI indicates myocardial infarction; CVD, cardiovascular disease.

IIb/IIIa receptor antagonists in patients with acute coronary syndromes and cerebrovascular disease will provide more definitive data about treatment benefits with such agents in these patient populations.

Study Limitations

Our study has several limitations. The baseline predictors of stroke may not account for all the risk for stroke in this patient population. Fifty percent of nonhemorrhagic strokes occurred >6.5 days after enrollment, and we were not able to account for in-hospital procedures or events that may be associated with stroke, primarily because of the relatively small sample size and limited regression modeling that could be performed. There was no systematic assessment of the cardiac rhythm at the time of study enrollment; therefore atrial fibrillation was not included in the prediction model. However, only 159 (1.5%) patients had atrial fibrillation reported on the Case Report Form before or within 4 hours of study enrollment, and only 2 of these patients had nonhemorrhagic stroke.

The mechanism of the strokes, particularly the nonhemorrhagic strokes, was not assessed. However, systematic review of all suspected strokes by the Stroke Adjudication Committee, which included analysis of computed axial tomographic data, MRI data, or autopsy results in 80% of patients, allowed determination of stroke types in a majority of cases, and the number of "unknowns" was small.

The logistic regression model and associated scoring nomogram were developed with the use of only 64 nonhemorrhagic strokes and therefore require validation in a larger patient population. However, the similarity to the prediction model from the GUSTO-I trial is supportive. Finally, these results are only applicable to patients with acute coronary syndromes without persistent ST-segment elevation treated with heparin and aspirin and should not be generalized to all patients with acute coronary syndromes.

Conclusions

Stroke was an uncommon event in patients with acute coronary syndromes without persistent ST-segment elevation treated with antiplatelet and antithrombin therapy in the PURSUIT trial. The majority of strokes were of nonhemorrhagic causes. Despite the low incidence of stroke, its prevalence is substantial because more than 1 million patients present each year with non–ST-segment elevation acute coronary syndromes to hospitals in the United States, with similar numbers in Western Europe. Therefore >7000 patients with acute coronary syndromes in the United States alone have a stroke, and these strokes are associated with significant morbidity and mortality rates. The use of eptifibatide, a glycoprotein IIb/IIIa receptor antagonist, was not associated with an increased incidence of intracranial hemorrhage, and we observed no significant effect on the occurrence of nonhemorrhagic stroke. Higher heart rate, older age, prior stroke or transient ischemic attack, prior anterior myocardial infarction, and diabetes mellitus were independent baseline predictors of nonhemorrhagic stroke. Physicians can use these factors to determine the probability of nonhemorrhagic stroke with a simple scoring nomogram (Figure 2). The impact of stroke risk assessment on patient management requires further study.

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Appendix

Stroke Adjudication Committee

Cardiologists were Brian S. Crenshaw, Christopher B. Granger, Robert A. Harrington, Kenneth W. Mahaffey, and Julie M. Miller. Neurologists were Mark J. Alberts, Carmelo Graffagnino, and Daniel Laskowitz.

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