Strokes After Cardiac Surgery and Relationship to Carotid Stenosis

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Objective: To critically examine the role of significant carotid stenosis in the pathogenesis of postoperative stroke following cardiac operations.

Design: Retrospective cohort study.

Setting: Single tertiary care hospital.

Participants: A total of 4335 patients undergoing coronary artery bypass grafting, aortic valve replacement, or both.

Main Outcome Measures: Incidence, subtype, and arterial distribution of stroke.

Results: Clinically definite stroke was detected in 1.8% of patients undergoing cardiac operations during the same admission. Only 5.3% of these strokes were of the large-vessel type, and most strokes (76.3%) occurred without significant carotid stenosis. In 60.0% of cases, strokes identified via computed tomographic head scans were not confined to a single carotid artery territory. According to clinical data, in 94.7% of patients, stroke occurred without direct correlation to significant carotid stenosis. Undergoing combined carotid and cardiac operations increases the risk of postoperative stroke compared with patients with a similar degree of carotid stenosis but who underwent cardiac surgery alone (15.1% vs 0%; P = .004).

Conclusions: There is no direct causal relationship between significant carotid stenosis and postoperative stroke in patients undergoing cardiac operations. Combining carotid and cardiac procedures is neither necessary nor effective in reducing postoperative stroke in patients with asymptomatic carotid stenosis.

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Cerebrovascular complications following cardiac surgical procedures are a major source of morbidity and mortality. The etiology for postoperative stroke is multifactorial and may include carotid artery stenosis, hypotension, cardiac arrhythmia, aortic atherosclerosis, and transient hypercoagulable state. The presence of multiple coexisting causes makes studying the mechanism of stroke challenging. Significant carotid stenosis has been recognized as a positive predictor of postoperative stroke in patients receiving cardiac surgical procedures. However, studies directly addressing the role of severe carotid stenosis are lacking. To date, no randomized clinical trials have addressed this important topic, and few retrospective trials have investigated the lateralization and territorial distribution of postoperative stroke to determine whether there is a correlation between stroke distribution and carotid stenosis. Therefore, the evidence for carotid stenosis as a cause for postoperative stroke is mostly indirect.

Despite this lack of evidence, combined carotid and cardiac surgical procedures are performed frequently in an effort to reduce the incidence of postoperative stroke. It is estimated that approximately 5000 such procedures were performed in the United States in 2001 alone. More recent analyses, however, have consistently revealed an increased incidence of adverse events, including stroke or death, following combined procedures.

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This retrospective analysis was undertaken to analyze the relationship between stroke and carotid stenosis in patients after cardiac operation. This study aimed to answer 2 simple but critical questions: Does severe carotid stenosis increase the risk of ipsilateral anterior circulation stroke in patients undergoing cardiac surgical procedures? Conversely, does concomitant carotid repair reduce the risk of perioperative stroke?
METHODS

The study was approved by the institutional review board of Lehigh Valley Hospital and Health Network, and individual consent was waived. Two complementary computerized hospital databases were compared and combined. Patients receiving non-urgent coronary artery bypass grafting and/or valve replacement were included. Urgent cardiac surgical procedures (ie, those performed within 24 hours of admission) were excluded because there was insufficient time for carotid evaluation and preoperative consultation by vascular or neurology services. Members of the Division of Cardiothoracic Surgery performed the cardiac procedures for recognized indications. Patients with carotid stenosis of more than 70% in diameter were evaluated by members of the divisions of Vascular Surgery and Neurology to determine the need for prophylactic carotid endarterectomy based on clinical presentation. When combined carotid and cardiac procedures were recommended, members of the Division of Vascular Surgery performed carotid endarterectomy as the initial procedure under the same general anesthesia.

Carotid arteries were initially assessed with high-resolution carotid duplex sonography, mostly performed within the month preceding the surgical date. More than 90% of the studies were performed in our facility, where unified criteria for interpretation have been in place with 96% sensitivity for detecting severe carotid stenosis when compared with percutaneous cerebral arteriography. Significant carotid disease was defined as 50% stenosis or greater, including carotid occlusion. For patients with stenosis of more than 70% on carotid duplex scanning, a second type of imaging such as magnetic resonance angiography, computed tomographic (CT) angiography, or conventional percutaneous angiography was usually performed to verify the degree of stenosis.

Postoperative stroke was defined as persistent (>24 hours) focal or multifocal neurological deficits that were best explained by ischemia involving the brain or retina from the surgical procedure until hospital discharge. All patients with stroke were evaluated by a board-certified neurologist. Patients with nonfocal results from neurological examination, such as encephalopathy, memory deficit, or unsteadiness, were excluded from the study if their examination results continued to be nonfocal and a second CT scan of the brain showed no evidence of ischemia.

All brain CT and magnetic resonance imaging scans were reviewed by a neuroradiologist (Q.L.) who was blind to all clinical information except the date of symptom onset. After review of the scans, the neuroradiologist (Q.L.) provided an interpretation, including the presence, size, and arterial distribution of infarction.

Stroke subtypes were classified with modified TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria. Cardioembolism was defined based on the following criteria: (1) cortical or cerebellar lesions, subcortical or brainstem lesions of more than 1.5 cm; (2) lack of large-vessel disease in the corresponding territory (carotid or basilar artery); and (3) lesions in multiple vessel territories (bilateral anterior and posterior circulation) or at least 1 of the following: atrial fibrillation, acute myocardial infarction, or dilated cardiomyopathy. Large-artery atherosclerosis was defined based on the following criteria: (1) cortical or cerebellar lesions, subcortical or brainstem lesions of more than 1.5 cm; and (2) 50% stenosis or greater or occlusion in the internal carotid or basilar artery. Small-vessel occlusion was defined as the following: (1) no symptoms suggestive of cortical dysfunction, such as visual loss or aphasia; (2) isolated subcortical or brainstem lesion of less than 1.5 cm or normal results on a CT scan; and (3) clinical mani-festation of pure motor, pure sensory, ataxic hemiparesis, clumsy-hand, or sensorimotor syndrome.

Analyses were completed using the Pearson χ² or Fisher exact test for categorical variables and the t test for continuous variables. Significance was set at α < .05.

RESULTS

DEMOGRAPHIC AND OPERATIVE CHARACTERISTICS

From July 1, 2001, to December 31, 2006, 4924 patients underwent cardiac procedures at our institution; 589 patients were excluded because of urgent operational status or the rarity of the procedure performed, such as aortic dissection repair or myxoma removal. A cohort of 4335 patients was identified for this retrospective analysis. Of this cohort, 3196 patients had coronary artery bypass grafting, 557 had aortic valve replacement, and 582 had both. The mean (SD) age of the patients studied was 67.5 (11.0) years. The study included 2930 men and 4232 white participants. A total of 3942 patients (90.9%) underwent preoperative carotid evaluation with noninvasive ultrasonography. In addition, 133 patients (3.1%) underwent magnetic resonance angiography, CT angiography, or conventional percutaneous angiography.

POSTOPERATIVE EVENTS

A total of 76 patients (1.8%) developed postoperative stroke (n = 75) or retinal ischemia (n = 1) (the single patient with retinal ischemia was considered to have a stroke in subsequent analysis). Among these, 55 cases of strokes (72.4%) were detected within 24 hours of operation and 68 (89.5%) within the first 72 hours. The time period for initial recognition of stroke ranged from postoperative day 1 through day 9. All strokes were ischemic, and 1 was associated with hemorrhagic transformation. A total of 65 patients died, among whom 8 deaths were believed to be secondary to stroke.

Applying modified TOAST criteria, 57 patients (75.0%) were classified as having cardioembolic stroke (new onset atrial fibrillation, n = 20; previously existent and persistent atrial fibrillation, n = 14; acute myocardial infarction, n = 11; stroke in multiple artery territories, n = 20; multiorgan embolism, n = 4), 4 patients (5.3%) had large-vessel stroke (carotid artery, n = 1; basilar artery, n = 3), and 10 patients (13.2%) had small-vessel stroke. In 5 patients, stroke could not be categorized owing to multiple coexisting etiologies.

DISTRIBUTION OF INFARCTS ON IMAGING

Of 76 patients with stroke, 75 patients underwent noncontrast CT scanning of the head; 70 patients had a second brain CT scan after 24 hours, and 2 patients also underwent magnetic resonance imaging. A total of 60 patients had evidence of acute infarction, whereas 15 patients had normal results on scanning. Table 1 describes the distribution of stroke on imaging. Of 60 patients with abnormal imaging results, 22 had stroke in
unilateral carotid distribution, 1 had a watershed pattern, and 36 had infarctions in the bilateral anterior distribution or posterior circulation that were not confined to 1 carotid artery. The remaining patient had a basal ganglia stroke, the territory of which could not be precisely determined.

### INFARCTS AND SIGNIFICANT CAROTID DISEASE

All 76 patients with stroke had preoperative carotid evaluation. Of these, 18 patients (23.7%) had significant carotid stenosis. Two patients had bilateral significant carotid stenosis, and both had an infarction in the posterior circulation. Table 2 shows the incidence and distribution of stroke in these patients based on clinical and radiographic data. In 14 of 18 patients (77.8%), stroke occurred outside the territory of diseased carotid artery. Of 4 patients with infarcts found exclusively within the diseased carotid artery, 3 had ipsilateral occlusion and 1 patient had an ipsilateral 60% stenosis.

### INCIDENCE OF SIGNIFICANT CAROTID STENOSIS

Of 3942 patients who received preoperative carotid evaluation, 239 (6.1%) had significant carotid stenosis (Table 3). Based on North American Symptomatic Carotid Endarterectomy Trial criteria, 5 were symptomatic and 234 asymptomatic.10

A randomized trial to explore the relationship between carotid stenosis and postoperative stroke following cardiac operations was proposed many years ago but has never been attempted because of the extraordinarily large number of patients needed for statistical power and the prohibitively high cost of completing such a study.11 Using carotid duplex and CT scanning as the major detection methods, this retrospective study provided a detailed analysis of the distribution of stroke and its relationship
with significant carotid disease at the bifurcation in patients undergoing routine cardiac procedures.10,12 Only clinically significant strokes were considered, and patients who had transient ischemic attacks were excluded. This study did not enroll patients at multiple centers, and therefore bias toward the surgical, anesthetic, and medical practices specific to a single center could not be minimized.

In this cohort, the incidence of postoperative stroke (1.8%) corresponds well with most of the previously published large trials, which report stroke risks from 0.9% to 3.2%.1,2,13-24 The incidence appeared to be slightly higher among patients undergoing combined valve replacement and coronary artery bypass grafting, but it did not alter our analysis of carotid stenosis in the pathogenesis of postoperative stroke (data not shown). It was observed that the incidence of stroke after cardiac procedures could be as much as 4 times higher among patients with significant carotid stenosis vs those without.3 Comparably, our analysis suggested a 4-fold increased relative risk (7.5% vs 1.8%).

However, this study strongly suggests there is no direct causal relationship between postoperative stroke and severe carotid stenosis. First, only 5.3% of postoperative strokes were in the large-vessel category, based on TOAST criteria. Second, 76.3% of postoperative strokes occurred in the absence of significant carotid disease at the bifurcation. Third, 60.0% of strokes on CT scanning had a distribution that was not confined to a single carotid artery (Table 1). Most strokes occurred in the vertebrobasilar artery, contralateral carotid artery, or multivessel territory. Only 4 patients with significant carotid stenosis developed stroke in the diseased carotid territory (Table 2). Of 76 strokes, 72 are not related to significant carotid stenosis at the bifurcation. Therefore, most of these postoperative strokes had alternate causes.

The failure to establish carotid stenosis as a cause of perioperative stroke in patients undergoing cardiac operations has been observed by others. Barbut et al25 reported the presence of infarction in multiple arterial territories and the preponderance of infarction in the posterior circulation in their cohort. Infarction was attributed to high-grade carotid stenosis in only 1 of 24 patients. In an extensive review, Naylor et al5 noted that primary carotid disease alone was only responsible for up to approximately 40% of postoperative strokes. In addition, Libman et al1 determined that 7 of 44 postoperative strokes (16%) in their series fit the criteria for classical lacunar syndromes.

Multiple causes other than carotid stenosis could account for postoperative stroke in patients undergoing cardiac procedures. For example, coexistence of aortic atherosclerosis has been demonstrated to be a significant determinant of postoperative stroke.26 In some studies, clamping and manipulation of the aorta or heart could account for more than 60% of emboli.27 Van der Linden and Casimir-Ahn28 reported that cerebral emboli are most likely to occur during the redistribution of blood from the heart-lung machine to the patient, which supports the idea that release of particles from the cardiopulmo-

| Table 5. Risk Factor Comparison in Patients With Severe Carotid Stenosis Undergoing Combined Carotid and Cardiac vs Cardiac Operations Alone* |
|---------------------------------|-----------------|-------|
| Risk Factor                     | Cardiac Operation Alone (n=51) | Combined Operations (n=53) | P Value |
| Female sex                      | 17 (33)          | 18 (34) | .95   |
| Age, mean (SD), y               | 72.0 (8.8)       | 71.8 (9.1) | .92   |
| Hypertension                    | 43 (84)          | 48 (91) | .34   |
| Hyperlipidemia                  | 46 (90)          | 44 (83) | .28   |
| Peripheral vascular disease     | 23 (45)          | 19 (36) | .34   |
| Diabetes mellitus               | 18 (35)          | 19 (38) | .95   |
| Smoking                         |                  |       |       |
| Previous                        | 27 (53)          | 34 (64) | .25   |
| Active                          | 7 (14)           | 10 (19) | .48   |
| History of preoperative stroke or TIA | 12 (24)     | 8 (15) | .28   |
| Cardiomyopathy                  | 12 (24)          | 9 (17) | .41   |
| Atrial fibrillation             |                  |       |       |
| Chronic                         | 6 (12)           | 4 (8)  | .47   |
| Postoperative                   | 21 (41)          | 16 (30) | .24   |
| Aortic sclerosis                | 23 (45)          | 21 (40) | .57   |
| Bilateral carotid stenosis >=50% | 8 (16)           | 13 (25) | .26   |
| Preoperative renal failure      | 4 (8)            | 1 (2)  | .16   |
| CABG/VR combined                | 10 (20)          | 6 (11) | .09   |
| Second CABG                     | 3 (6)            | 1 (2)  | .29   |
| Bypass time, mean (SD), min     | 125 (63)         | 122 (48) | .82   |
| Clamp time, mean (SD), min      | 97 (52)          | 94 (43) | .72   |
| Postoperative ventricular arrhythmia | 14 (28)      | 9 (17) | .20   |
| Use of intra-aortic balloon pump | 5 (10)          | 2 (4)  | .22   |
| Severe hypotension during surgery | 1 (2)           | 2 (4)  | .58   |
| Use of inotropic agent          | 20 (39)          | 16 (30) | .33   |
| Postoperative stroke            | 0                | 8 (15) | .004  |

Abbreviations: CABG, coronary artery bypass grafting; TIA, transient ischemic attack; VR, valve replacement.

*Data are given as number (percentage) of patients unless otherwise indicated.
nary bypass pump is a major contributor to stroke. Postoperative atrial fibrillation is seen in 30% to 50% of patients. There is also evidence that the fibrinolytic shutdown activates postoperatively, which may account for the occurrence of embolic and lacunar infarctions. A recent multivariate analysis by Filsoufi et al suggested that older age, female sex, and presence of diabetes mellitus, cardiomyopathy, longer bypass time, and aortic calcifications are independent predictors of postoperative stroke. The apparent paradox that carotid stenosis is associated with an increased incidence of stroke but is not a direct cause of postoperative stroke may suggest that it is an epiphenomena indicating an increased underlying cardiovascular risk.

The lack of a causal relationship between carotid stenosis and postoperative stroke raises serious doubts about hypoperfusion as a major mechanism. This finding is in line with data from the Northern New England Cardiovascular Disease Study Group suggesting that fewer than 10% of postoperative strokes were caused by hypoperfusion. In our study, the incidences of stroke for patient subgroups with 50% to 79% stenosis, 80% to 99% stenosis, and occlusion were 4.9%, 7.0%, and 15.6%, respectively (Table 3). Although higher incidence of stroke was associated with more severe stenosis, this trend did not reach statistical significance. The most plausible explanation for such a trend might simply be the cardiovascular risk burden, as reflected by the degree of carotid stenosis. The observation that more postoperative strokes occur outside rather than within the territory of diseased carotid arteries was consistent among these subgroups.

The increased incidence of stroke among patients with carotid stenosis has led to the proposal for combining carotid and cardiac procedures in selected patients. However, recent analyses suggest that simultaneous repair of carotid lesions is associated with a higher risk of postoperative stroke and death in patients undergoing cardiac operations. In this sample of 239 patients with significant carotid stenosis, 4 patients had strokes found to be caused by carotid disease, but only the patient with 60% unilateral carotid stenosis would have been considered a candidate for endarterectomy based on results of the Asymptomatic Carotid Atherosclerosis Study. Therefore, there is virtually no compelling evidence to suggest that repairing the diseased carotid artery prevents postoperative stroke after cardiac procedures. Could the effect of carotid stenosis be falsely low because a significant portion of patients underwent carotid revascularization procedures before cardiac operations? We do not believe this is the explanation. Instead, the incidence of stroke (15.1%) was significantly higher in the subgroup of patients undergoing combined carotid and cardiac procedures than among patients with similar degrees of carotid stenosis but who underwent cardiac procedures alone (Table 4). Further risk analysis failed to identify any factors that could account for the difference in the incidence of postoperative stroke between the 2 groups (Table 5). Also, the operative risk for combined procedures is higher than the added stroke risks from separate cardiac procedures (1.8%) and carotid endarterectomy (<1% of the 30-day risk of postoperative stroke in our institution; data not shown). Therefore, the occurrence of postoperative stroke in this subgroup is likely related to the combined procedure itself, with a possible correlation to the duration of the operation. As such, our findings strongly support the idea that combined carotid and cardiac procedures are neither necessary nor effective in reducing the risk of postoperative stroke in this population. Assuming that 5000 combined carotid endarterectomies and cardiac operations are performed annually in the United States, avoidance of such procedures alone could prevent nearly 500 postoperative strokes per year.

In conclusion, we examined the relationship between postoperative stroke and carotid stenosis in a large group of patients undergoing common, nonurgent cardiac procedures at a single medical center. We confirmed a higher incidence of stroke in the subgroup of patients with significant carotid stenosis. However, most strokes have no direct causal relationship with the diseased carotid artery. Combined carotid and cardiac procedures result in a significantly higher incidence of postoperative stroke and should be avoided. Preoperative studies such as echocardiography or CT or magnetic resonance imaging of the heart and aorta could identify disease-free areas for manipulation and clamping to prevent postoperative strokes.

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