# RISK FACTORS FOR STROKE IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING

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***Objective:*** **To determine predictors of stroke in patients undergoing first-time coronary bypass grafting, we prospectively collected data on 1631 consecutive patients.** ***Methods:*** **Patients with a history of stroke and/or central nervous system symptoms (*n* = 134) and/or carotid bruits (*n* = 95) underwent carotid Doppler evaluation. Stenosis greater than 70% was considered significant. Patients with symptomatic disease or asymptomatic bilateral disease were referred for combined coronary bypass and carotid endarterectomy (*n* = 21). Patients with neurologic symptoms after the operation were assessed by a neurologist and underwent a computed tomographic scan. Events were classified as reversible transient ischemic attack, reversible ischemic neurologic deficit, or irreversible stroke.** ***Results:*** **There were 19 strokes (1.2%) and 20 deaths (1.2%) in this series. In patients with carotid screening, risk of stroke increased with severity of carotid disease and ranged from 0% in patients without stenosis, to 3.2% (1/31) in those with greater than 70% stenosis, and to 27.3% (6/22) in those with carotid occlusion. By stepwise logistic regression analysis six variables were identified as risk factors for stroke. The most important predictor was carotid occlusion with or without contralateral stenosis (odds ratio = 28, 95% confidence interval (8,105). In this group, four of five strokes occurred on the occluded side. Other risk factors were presence of ascending aortic disease at the time of surgery (odds ratio = 12.8, confidence interval 3,48), perioperative myocardial infarction (odds ratio = 8.2, confidence interval 2,33), poor left ventricular function (odds ratio = 4.6, confidence interval 1,19), peripheral vascular disease (odds ratio = 3.2, confidence interval 1,9), and age >60 years (odds ratio = 2.9, confidence interval 0.8,11).** ***Conclusion:*** **We conclude that risk factors for perioperative stroke in patients undergoing coronary artery bypass grafting are multiple. Carotid scanning in patients with neurologic symptoms or carotid bruits can identify patients at increased risk. Patients with carotid occlusion are at high risk for stroke on the occluded side. (J Thorac Cardiovasc Surg 1996; 112:1250-9)**

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Stroke is an important cause of morbidity and mortality in patients undergoing coronary artery bypass grafting (CABG), occurring in 0.9% to 16% of cases.[1-10] Mechanisms of stroke include embolism from a variety of sources or hypoperfusion caused by hypotension or cerebrovascular disease.[3-12] In previous studies, advanced age,[3, 4, 13-17] peripheral vascular disease,[2, 5, 13, 18] and cerebrovascular disease[2-4, 17-19] have been identified as risk factors for perioperative stroke. The role of preoperative screening to detect significant carotid disease and appropriate treatment of these patients remains unclear.[2, 3, 9, 10] Several studies suggest patients are at high risk if they have symptomatic severe carotid stenosis (>70%) or asymptomatic bilateral disease.[4, 6, 7, 17, 18, 20]

The purposes of this study were to (1) document the prevalence of stroke in patients undergoing CABG, (2) evaluate the relationship of preoperative, intraoperative, and postoperative factors to the prevalence of stroke, and (3) correlate results of preoperative noninvasive carotid testing and combined carotid endarterectomy in selected patients with poor neurologic outcome after CABG.

## Methods

Data were prospectively collected on 1631 consecutive patients undergoing first-time CABG by a single surgeon at The Toronto Hospital between January 1982 and April 1994. Patients with a history of previously documented carotid disease, previous unexplained stroke or unexplained neurologic symptoms, and those with carotid bruits or nonpalpable carotid pulse underwent carotid artery duplex scanning with an Acuson 128 duplex scanner (Acuson Inc., Mountainview, Calif.) or an ATL Ultramark 4 system (Advanced Technology Laboratories, Markham, Ontario, Canada). Significant carotid disease was defined as 70% or greater diameter reduction or occlusion of one or both internal carotid arteries. In patients with symptomatic disease or asymptomatic bilateral disease, carotid endarterectomy was combined with CABG.

Fentanyl citrate was used for induction and maintenance of anesthesia. Carotid and coronary procedures were performed by two teams with the carotid procedure performed before sternotomy. We routinely used a carotid shunt and closed the endarterectomized vessel with a vein patch.

During cardiopulmonary bypass, pump flow was maintained between 2.0 and 2.5 L/min per square meter and mean arterial pressure between 50 and 60 mm Hg in patients without significant carotid disease and between 60 and 70 mm Hg in those with greater than 70% stenosis. Sodium nitroprusside or phenylephrine hydrochloride was used as needed. Before 1987, systemic hypothermia at 25° C was used. In more recent years, temperature has been allowed to drift during the crossclamp period. Proximal vein anastomoses have been performed during a single period of aortic crossclamping.

During the CABG operation the presence of significant ascending aortic calcification or atherosclerotic plaque was assessed by palpation and visual inspection at the site of cannulation and proximal vein anastomoses. Obvious areas of disease were avoided by choosing alternative sites for aortic cannulation (i.e., under surface of arch) and if necessary bringing multiple vein grafts off a single aortic anastomosis. Femoral cannulation was used because of extensive aortic disease in eight patients.

**Postoperative care and outcome.** Operative mortality was defined as death within 30 days of the operation or during the hospital stay. The definition for perioperative myocardial infarction has been previously described.[21] Postoperative atrial fibrillation that required drug treatment was recorded. In patients with carotid disease who had an adequate cardiac output but low blood pressure, an oxymetazoline HCl (Neo-Synephrine) drip was used to keep mean arterial pressure greater than 60 mm Hg while in the intensive care unit. Low-output syndrome was defined as need for intraaortic balloon pump or inotropic support to keep cardiac index greater than 2 L/min per square meter. Postoperative neurologic events were evaluated by the attending physician and a consulting neurologist and classified as transient ischemic attack, reversible ischemic neurologic deficit, or stroke. In patients who had a stroke, the defect was located by computed tomography scanning. Stroke severity was assessed at the time of discharge and graded according to the stroke severity scale index proposed by the IC/EC Study Group[22] (Appendix I).

**Statistical analysis.** The SAS (SAS Institute, Inc., Cary, N.C.) and BMDP (BMDP Software, Los Angeles, Calif.) programs were used for statistical analysis. Continuous variables were summarized as mean ± standard deviation. Predictors of stroke were determined by univariate and multivariate techniques. For the univariate analysis, discrete data were analyzed with $\chi^2$ or Fisher's exact test where appropriate. Continuous data were evaluated by Student's $t$ test. Statistical significance was associated with a $p$ value of less than 0.05. Selected variables, including all those with a $p$ value of less than 0.20 by univariate analysis, were entered into multivariate analysis by a stepwise logistic regression technique to determine independent predictors of stroke. Model calibration was assessed by the Hosmer-Lemeshow goodness-of-fit $\chi^2$ test.[23] Predictive accuracy was evaluated by the areas under the receiver-operator characteristic curve or C statistic.[24]

## Results

**Patient population and results of carotid screening.** Of the 1631 patients, 1244 (76%) were male and mean age was 60 ± 9 years (range 31 to 86 years). Most patients had class III or IV angina (1179, 75%). Urgent revascularization from the cardiac care unit or catheterization laboratory was required in 316 (20%). Risk factors for coronary artery disease included diabetes in 350 (22%), hypertension in 720 (44%), hyperlipidemia in 569 (36%), smoking history in 1120 (69%), and a family history of coronary artery disease in 1002 (69%). Twenty-one patients (13%) had peripheral vascular disease. Most patients had double or triple vessel disease (1504, 93%), with left main-stem stenosis in 225 (14%). Sixty-one percent of patients had had a prior myocardial infarction with a preoperative ejection fraction less than 40% in 424 (27%). Carotid screening was carried out in 170 patients. In an additional 20 patients, who by our criteria should have undergone screening, the need for urgent revascularization precluded preoperative testing. When compared with the nonscreened group, screened patients were significantly older (65 ± 8 vs

**Table I.** *Results of carotid screening in relation to incidence of stroke and mortality*

| | *Stroke* | *Mortality* |
|---|---|---|
| Patients not screened (1461) | 12 (0.8%) | 5 (1.2%) |
| Patients screened with no significant stenosis (116) | 0 | 0 |
| Asymptomatic unilateral stenosis* | | |
| CABG (15) | 1 (6.6%) | 0 |
| Symptomatic unilateral carotid stenosis (11) | | |
| CABG + CEA (7) | 0 | 0 |
| CABG (4) | 0 | 0 |
| Unilateral occlusion (12) | | |
| CABG | 2† (16.6%) | 0 |
| Asymptomatic bilateral carotid stenosis* (70%-99%) | 0 | 0 |
| CABG (1) | 0 | 0 |
| CABG + CEA (2) | 0 | 0 |
| Symptomatic bilateral carotid stenosis (70%-99%) | | |
| CABG + CEA (3) | 0 | 0 |
| Occlusion and significant contralateral carotid stenosis (70%-99%) | | |
| CABG + CEA (9) | 3‡ (33%) | 0 |
| Bilateral occlusion (1) | 1 (100%) | 0 |

*CABG,* Coronary artery bypass grafting; *CEA,* coronary endarterectomy.
*Asymptomatic—no prior history of stroke or neurologic symptoms.
†On the occluded side.
‡Two-thirds on the occluded side.

60 ± 9 years, $p < 0.001$), had a higher incidence of hypertension (60% vs 43%, $p < 0.001$) and peripheral vascular disease (42% vs 10%, $p < 0.001$), and were more likely to have triple vessel coronary artery disease (72% vs 60%, $p < 0.001$).

Among the screened patients, test results were positive in 54 (32%), or 3.3% of the overall patient population (Table I). Of these 54 patients, 38 (70%) had significant unilateral disease including 12 (22%) with unilateral occlusion. Significant bilateral disease was found in 16 (30%), of whom 10 (19%) had significant stenosis on one side and occlusion on the other. Compared with the 116 screened patients without severe disease, patients with significant stenosis were more likely to have peripheral vascular disease (65% vs 31%, $p < 0.001$) and a carotid bruit (69% vs 41%, $p < 0.001$). Eighteen of the 66 patients (27%) with asymptomatic bruits were found to have significant carotid stenosis.

**Perioperative stroke rate and mortality.** The prevalence of perioperative stroke was 1.2% (19/1631) and operative mortality was 1.2% (20/1631). Operative mortality in the stroke group was 26% (5/19). Table II compares patients with and without a stroke. Patients with a stroke were older and more

**Table II.** *Preoperative, intraoperative, and postoperative variables in patients with and without postoperative stroke*

| | *No stroke* | *Stroke* | *p Value* |
|---|---|---|---|
| Age (yr) | 60.2 ± 9.3 | 64.9 ± 6.7 | 0.032* |
| Age >60 yr | 788 (49%) | 15 (79%) | 0.010* |
| Gender | | | |
| Male | 1231 (76%) | 13 (68%) | |
| Female | 381 (24%) | 6 (32%) | |
| Total | 1612 (99%) | 19 (1%) | 0.419 |
| Obesity (BMI > 27) | 725 (49%) | 12 (67%) | 0.158 |
| Risk factors | | | |
| Diabetes | 345 (22%) | 5 (26%) | 0.579 |
| Hypertension | 708 (44%) | 12 (63%) | 0.108 |
| Hyperlipidemia | 563 (36%) | 6 (33%) | 0.999 |
| Smoking history | 1106 (69%) | 14 (78%) | 0.609 |
| Family history of CAD | 991 (62%) | 11 (61%) | 0.999 |
| Peripheral vascular disease | 201 (13%) | 10 (53%) | 0.000* |
| Prior stroke | 64 (4%) | 5 (26%) | 0.001* |
| Prior neurologic symptoms | 61 (4%) | 4 (21%) | 0.005* |
| Bruit | 89 (6%) | 6 (32%) | 0.000* |
| Clinical presentations | | | |
| Prior MI | 979 (61%) | 13 (68%) | 0.639 |
| Unstable angina | 1180 (73%) | 15 (79%) | 0.795 |
| Functional class | | | |
| I | 118 (8%) | 0 | |
| II | 280 (18%) | 3 (16%) | |
| III | 420 (27%) | 4 (21%) | |
| IV | 743 (47%) | 12 (63%) | 0.141 |
| Congestive heart failure | 72 (5%) | 0 | 0.999 |
| Urgent OR | 310 (19%) | 6 (32%) | 0.237 |
| Preop. IABP | 54 (3%) | 1 (5%) | 0.481 |
| Angiographic and postoperative criteria | | | |
| No. of diseased vessels | | | |
| 1 | 125 (8%) | 1 (5%) | |
| 2 | 497 (31%) | 4 (21%) | |
| 3 | 989 (61%) | 14 (74%) | 0.310 |
| Left main stenosis | 223 (14%) | 2 (11%) | 0.999 |
| LV grade | | | |
| I | 582 (37%) | 4 (21%) | |
| II | 578 (37%) | 7 (37%) | |
| III | 328 (21%) | 5 (26%) | |
| IV | 88 (6%) | 3 (16%) | 0.043* |
| Mean No. of vessels grafted | 3.2 ± 0.9 | 3.3 ± 0.9 | 0.600 |
| Mean pump time | 102 ± 29 | 118 ± 31 | 0.805 |
| Mean crossclamp time | 55 ± 18 | 61 ± 24 | 0.074 |
| Aortic disease | 35 (2%) | 4 (21%) | 0.001* |
| Postoperative atrial fibrillation | 236 (15%) | 5 (26%) | 0.184 |
| Perioperative MI | 58 (4%) | 3 (16%) | 0.031* |
| Postoperative LOS | 176 (11%) | 3 (16%) | 0.458 |
| In-hospital mortality | 15 (1%) | 5 (26%) | 0.000 |

*BMI,* Body mass index; *CAD,* coronary artery disease; *MI,* myocardial infarction; *OR,* operation; *IABP,* intraaortic balloon pumping; *LV,* left ventricular; *LOS,* low-output syndrome.
*$p < 0.05$.

**Table III.** *Risk factors for perioperative stroke*

| *Results of multivariate analysis* | *Odds ratio* | *95% CI* | *Hosmer-Lemeshow $\chi^2$ GOF* | *ROC* |
|---|---|---|---|---|
| Model 1: Preop. variables | | | 0.70 | 75% |
| PVD | 17.4 | 2.0-13.7 | | |
| Prior history of stroke | 6.0 | 1.4-13.3 | | |
| Age >60 yr | 4.6 | 1.0-12.0 | | |
| Model 2: Preop. variables plus results of carotid screening | | | 0.21 | 80% |
| Carotid occlusion | 30.0 | 4.3-52.7 | | |
| PVD | 6.7 | 1.1-9.5 | | |
| Age >60 yr | 3.6 | 0.9-11.2 | | |
| Prior history of stroke | 2.7 | 0.9-10.4 | | |
| Model 3: Preop, intraop. and postop. variables | | | 0.75 | 87% |
| Carotid occlusion | 28.0 | 7.5-105.0 | | |
| Ascending aortic disease | 12.8 | 3.4-48.1 | | |
| Periop MI | 8.2 | 2.0-32.6 | | |
| LV IV | 4.6 | 1.1-18.6 | | |
| PVD | 3.2 | 1.1-9.2 | | |
| Age >60 yr | 2.9 | 0.8-10.7 | | |

*CI,* Confidence interval; *GOF,* goodness of fit; *ROC,* receiver operator characteristic; *PVD,* peripheral vascular disease; *MI,* myocardial infarction; *LV IV,* left ventricular ejection fraction less than 20%.

likely to have history of prior stroke, neurologic symptoms, or a carotid bruit. They were more likely to have ascending aortic disease and a perioperative myocardial infarction. They were also more likely to be hypertensive and to have poor left ventricular function (ejection fraction <20%). These differences did not reach statistical significance, however.

Table I shows the relationship between the severity of carotid disease as detected by screening, stroke, and mortality. In patients not screened, the incidence of stroke was 0.8% and mortality was 1.2%. Screened patients had a higher incidence of stroke, 4.1% ($p < 0.001$), and risk of stroke was related to the severity of carotid disease.

Stepwise logistic regression analysis (Table III) of preoperative variables, excluding the results of carotid screening, identified peripheral vascular disease, prior history of stroke, and age greater than 60 years as independent predictors of stroke. Other factors submitted for consideration in the analysis but which were not independent predictors included neurologic symptoms, carotid bruits, sex, triple vessel coronary artery disease, and poor left ventricular function (ejection fraction <20%).

When the severity of carotid disease, as defined by preoperative screening, was included as a variable in constructing the best model, independent predictors of stroke were carotid occlusion (with or without contralateral stenosis), peripheral vascular disease, age greater than 60 years, and prior history of stroke. Additional variables considered in this analysis included significant carotid stenosis and bilateral carotid stenosis.

Intraoperative and postoperative variables were then added to the analysis, and an improved model identified carotid occlusion (with or without contralateral stenosis), ascending aortic disease, perioperative myocardial infarction, poor left ventricular function, peripheral vascular disease, and age greater than 60 years as independent predictors of stroke. Other factors considered in the analysis included pump time, crossclamp time, and postoperative atrial fibrillation.

**Cause and severity of stroke.** There were five transient ischemic attacks, four reversible ischemic neurologic deficits, and 19 permanent neurologic deficits or strokes in this series. After careful review of all available data including computed tomographic scan results, the most likely cause of stroke was determined in each case (Table IV). The severity of stroke at the time of discharge was recorded (Table IV).

## Discussion

Operative morbidity and mortality for CABG has steadily decreased in recent years despite increasing numbers of patients at high risk for complications.[21, 25] The reported incidence of perioperative stroke ranges from 0.9% to 16%.[1-10] In this series the incidence was 1.2%. In these patients, potential causes of stroke are multifactorial. On the basis of available data, stroke was attributed to embolism from ascending aortic disease (four cases), left ventricular thrombus (five cases), atrial fibrillation (three cases) and vertebrobasilar disease (two cases). In the remaining six cases internal carotid

**Table IV.** *Likely cause of stroke and stroke severity*

| Pt. No. | Age (yr) | Sex | CS | CEA | AoD | Other risk factors | TOS | SSS | CT findings |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 71 | M | — | | * | | At OR | 3 | Multiple defects in MCA distribution suggesting shower of emboli |
| 2 | 62 | F | — | | * | PVD | At OR | 3 | No CT (clinical criteria indicate left frontal infarct) |
| 3 | 65 | M | SR | | * | PVD + AFib | At OR | 3 | Bilateral multiple small defects |
| 4 | 54 | M | NA | | * | PVD | At OR | 11† | Old infarct on right, recent infarcts, posterior parietal and occipital lobes on the left (previous right CEA totally occluded, no carotid disease on left) |
| 5 | 81 | F | — | | | POMI | At OR | 4 | Multiple defects in right MCA distribution and right occipital lobe |
| 6 | 65 | F | — | | | POMI | At OR | 7 | Multiple defects, old and new, right MCA distribution and left internal capsule |
| 7 | 59 | M | NA | | * | POMI | At OR | 3† | Small defect left MCA distribution |
| 8 | 61 | M | NA | | | LV IV | At OR | 11† | Massive infarction in MCA distribution |
| 9 | 49 | M | — | | | PVD + LV IV | POD 3 | 3 | Multiple infarcts in right MCA distribution |
| 10 | 63 | F | NA | | | PVD + LV IV | POD 3 | 11† | Old and new defects in the right VBA distribution |
| 11 | 65 | M | NA | | | | At OR | 11† | Huge acute infarct left VBA distribution |
| 12 | 68 | M | OR | | | | At OR | 4 | Multiple old infarcts in right MCA distribution; recent single infarct in the right frontal lobe |
| 13 | 74 | M | OL | | | PVD + LV IV | At OR | 7 | Single huge infarct in the left MCA and anterior cerebral artery distributions with some sparing of midline structures |
| 14 | 64 | M | SROL | R | | | At OR | 3 | No CT (clinical criteria indicate stroke in left cerebral hemisphere) |
| 15 | 64 | M | SROL | R | | PVD | At OR | 4 | Old infarcts in the VBA distribution, old and recent infarct in the left frontoparietalregion |
| 16 | 64 | F | SROL | R | | PVD | POD3 | 6 | Defect in right MCA distribution |
| 17 | 69 | M | OROL | | | PVD + AFib | At OR | 5 | Multiple defects in right and left hemispheres in watershed areas anteriorly and posteriorly |
| 18 | 61 | F | — | | | AFib | POD3 | 4 | Single small defect in right MCA distribution |
| 19 | 62 | M | — | | | PVD + AFib | At OR | 3 | Small infarct in right basal ganglia |

*CS,* Carotid screening; *S,* stenosis; *O,* occlusion; *R,* right; *L,* left; *CEA,* carotid endarterectomy; *AoD,* aortic disease; *PVD,* peripheral vascular disease; *AFib,* atrial fibrillation; *POMI,* perioperative myocardial infarction; *LV IV;* left ventricular ejection fraction less than 20%; *TOS,* timing of onset of symptoms; *OR,* operation; *POD,* postoperative day; *SSS,* stroke severity score; *CT;* computed tomography; *MCA,* middle cerebral artery; *VBA,* vertebrobasilar artery; *LV,* left ventricular; *NA,* not available.

*Aortic disease identified at OR.

†Hospital death.

disease appeared to be related to the neurologic event. Although the literature indicates that the existence of simultaneous carotid disease increases stroke risk in patients undergoing CABG, it is not clear whether preoperative carotid screening and a combined procedure in selected patients can decrease the risk of perioperative stroke.

**Noninvasive carotid screening.** Noninvasive carotid screening is expensive and time consuming. Routine screening of all patients undergoing CABG provides a low yield of patients with carotid stenosis. Recent series have reported more than 70% to 80% stenosis in only 2.8% to 6.3% of patients screened.[4, 5, 26, 27]

At the start of this prospective study the approach was to limit the use of carotid screening to patients in whom history and physical examination suggested carotid disease. In the 170 patients screened, 32% were found to have significant disease. One cannot rule out, however, the possibility that severe stenosis or carotid occlusion might have existed in other patients who did not undergo preoperative screening. Because of the relationship demonstrated in this study between peripheral vascular disease and

| *Likely cause of stroke* |
|---|
| Aortic disease |
| Aortic disease |
| Aortic disease or AFib |
| Aortic disease |
| LV thrombus |
| LV thrombus |
| LV thrombus |
| LV thrombus (confirmed on echocardiography) |
| LV tnrombus (confirmed on echocardiography) |
| VBA disease |
| VBA disease |
| Internal carotid occlusion with hypoperfusion via collaterals |
| Internal carotid occlusion with hypoperfusion via collaterals |
| Internal carotid occlusion with hypoperfusion via collaterals |
| Internal carotid occlusion with hypoperfusion via collaterals |
| Embolus from site of carotid endarterectomy which was still patent by angiography |
| Bilateral internal carotid occlusion with hypoperfusion via collaterals |
| AFib |
| AFib |

carotid stenosis, we would in the future broaden our indications for carotid screening to include patients with peripheral vascular disease.

**Relationship between symptoms, severity of carotid disease, and risk of stroke.** In patients undergoing carotid screening (see Table I) the risk of stroke was related to the severity of disease. Risk in patients with negative Doppler studies was 0%. Of 15 asymptomatic patients with significant stenosis (70% to 99%), one patient had a stroke (6.6%) that was attributed to emboli from aortic disease rather than to carotid stenosis. This series corroborates earlier results[6, 8] that risk in patients with asymptomatic carotid stenosis is relatively low. Patients with symptoms and carotid stenosis, but not occlusion, also had excellent results (no strokes) whether they underwent a combined procedure or CABG alone.

In this series, the risk of stroke at the time of CABG was high in patients with carotid occlusion. In 12 patients with unilateral occlusion (eight with prior history of stroke or neurologic symptoms), none had a combined procedure and two had an ipsilateral stroke (16.6%). Of nine patients with unilateral occlusion and significant contralateral disease, all but one had had a prior stroke or neurologic symptoms. All underwent a combined procedure with carotid endarterectomy on the stenosed side. In this group there were three strokes (33%), one on the side of carotid endarterectomy and two on the side of occlusion. One patient with bilateral internal carotid occlusion also had a stroke but survived.

Others have shown increased risk of stroke in patients with increasing severity of carotid disease.[1, 6, 20, 28] In patients undergoing a cardiac procedure, Brenner and associates[6] reported a 6% risk of stroke in those with significant carotid stenosis, which increased to 14% in patients with unilateral occlusion, to 20% in patients with stenosis and contralateral occlusion, and to 33% in those with bilateral occlusion.

**Role of a combined procedure in patients with carotid disease.** Does carotid screening and combined carotid endarterectomy decrease the incidence of stroke, severity of stroke, or mortality at the time of CABG? This series supports the concept that risk of stroke in patients with asymptomatic carotid stenosis is relatively low and in these patients a combined procedure is not likely to decrease risk of stroke at the time of CABG. This approach does not address the ongoing risk of stroke in these patients over time. Clinical data strongly suggest that an unoperated carotid stenosis greater than 70% (symptomatic or asymptomatic) is associated with a 5-year stroke rate of 20% to 30%.[29] Some have argued that a combined procedure in these patients should be undertaken to most efficiently deal with both problems. However, this approach can only be recommended if the combined procedure can be accomplished without added risk. To date, most series of combined procedures, in symptom-free patients, suggest that the risk exceeds that achieved with staged procedures.[6]

It is not clear whether combined endarterectomy and CABG decreases the risk or severity of perioperative stroke in patients with symptomatic carotid stenosis or bilateral disease. Reports in the literature do not answer this question because of small series size, inconsistent degree of stenosis considered to be significant (50% to 80%), unknown prevalence of other risk factors for stroke, and the variable interpretation of what is a significant neurologic event. Ethical concerns may preclude a prospective randomized trial that might answer this question. Reported stroke rates after a combined procedure have varied from 0% to 20% with a mortality of 5.7%.[6, 14, 17, 26, 30] Some authors have advocated performing the carotid endarterectomy during cardiopulmonary bypass at varying degrees of hypothermia to protect the brain.[30, 31]

A combined procedure in this series was performed only in patients with symptomatic or bilateral disease as identified on carotid screening. We will continue to use these indications for a combined procedure. The incidence of stroke in this group was 14.3% (3/21) and all strokes occurred in patients with bilateral disease.

However, the severity of stroke in this group was low (4.3 ± 1.5) and there were no deaths, suggesting that the combined approach may favorably alter these two outcomes.

**Univariate predictors of stroke.** Univariate analysis of preoperative factors demonstrated increased risk of stroke with advanced age, peripheral vascular disease, prior history of stroke, prior neurologic symptoms, and the presence of a carotid bruit. Other series have identified advanced age,[13, 14, 18, 32] peripheral vascular disease,[13, 18, 29] history of stroke,[13, 15-17, 19, 27, 32-34] and presence of a carotid bruit[14, 16-18] as risk factors for stroke. No statistical association was found between stroke and diabetes, a relationship that has been observed in some series[13, 14] but not in others.[1, 4] Because of the small number of strokes in this series, such a potential relationship cannot be ruled out.

A relationship has been previously demonstrated between the presence of mural thrombus and postoperative stroke.[14] In our series, we did not prospectively look for mural thrombus. Although the relationship is not statistically significant, patients having a stroke were more likely to have poor left ventricular function (ejection fraction <20%) ($p = 0.09$). Two patients with poor left ventricular function and a neurologic event were found to have left ventricular clot on echocardiography.

Intraoperative and postoperative variables associated with increased risk of stroke by univariate analysis were aortic atherosclerosis and perioperative myocardial infarction. The incidence of stroke was not related to the number of grafts or pump time, as has been suggested by others.[13, 16, 17, 19, 32]

Postoperative atrial fibrillation has previously been associated with stroke.[19, 35] In our series, patients having a stroke were more likely to have postoperative atrial fibrillation (26% vs 15%, $p = 0.18$), but this difference did not reach statistical significance and in some cases the postoperative arrhythmia was noted only after the neurologic event occurred. Because we did not have continuous Holter monitoring in our patients, we were unable to critically evaluate this potentially important relationship.

**Risk factors for stroke—multivariate analysis.** The power of our analysis was limited by the small number of strokes in this series. Nevertheless, when preoperative variables were entered into a logistic regression analysis and the best model for prediction of perioperative stroke was chosen, the independent predictors demonstrated were peripheral vascular disease, history of stroke, and age older than 60 years.

When the results of carotid screening were included in the analysis, the accuracy of the model predicting stroke improved as evidenced by the ROC statistic. The independent predictors were carotid occlusion (with or without contralateral stenosis), peripheral vascular disease, age older than 60 years, and history of stroke.

The addition of intraoperative and postoperative variables to the analysis provided the most accurate model for predicting a neurologic event. Independent predictors of stroke were carotid occlusion, ascending aortic disease, perioperative myocardial infarction, peripheral vascular disease, poor left ventricular function, and age older than 60 years. It is interesting that when strong predictors of perioperative stroke including carotid occlusion and aortic disease were entered into the model, history of stroke was no longer an independent predictor. Because of the low power of our analysis, we cannot exclude the possibility that other factors related to stroke risk might become obvious if the study were expanded to contain a larger number of patients.

**Association between ascending aortic disease and perioperative stroke.** In this series, on the basis of intraoperative palpation and inspection, aortic disease was documented in 39 of 1631 patients (2.4%). Those with aortic disease were more likely to have peripheral vascular disease (31% vs 13%, $p < 0.002$). They were also more likely to be hypertensive (59% vs 44%) and to have carotid bruits (13% vs 6%), but these differences did not reach statistical significance ($p = 0.07$).

Stroke occurred in 10% of patients with versus 0.9% of patients without aortic disease ($p < 0.001$). No strokes occurred in the eight patients in whom femoral cannulation was used. An association between ascending aortic disease and increased risk of stroke has been previously demonstrated.[14, 15, 28, 36] Gardner and associates[16] reported severe atherosclerosis in 56 of 3279 (4.7%) patients undergoing CABG. Stroke occurred in 14% of patients with aortic disease versus 3% in those without. Wareing and colleagues[37] used ultrasonography to detect aortic disease in patients older than 50 years of age undergoing cardiac surgery and found significant disease in 19.3% of patients. However, in 35% of their patients, procedures other than CABG were performed. They replaced the ascending aorta in 27 patients with moderate or severe disease, with no strokes and only one death (mortality 3.7%). Whether intraoperative ultrasonography and an aggressive approach to aortic replacement might reduce risk of stroke without increasing morbidity and mortality requires further study.

This series demonstrates that when preoperative carotid screening was performed in selected patients and combined carotid endarterectomy was carried out in those at high risk, the incidence of stroke at the time of CABG was low (1.2%). Patients who were referred for CABG without a history of stroke or other neurologic symptoms and without a carotid bruit were at very low risk for stroke (0.6%). Cause of stroke in these patients was multifactorial. Although carotid screening in all of these patients might identify some with significant carotid disease, the potential risk/benefit ratio for combined procedures in these patients would appear to be small. With respect to ascending aortic disease and its contribution to the likelihood of stroke, further studies are needed to evaluate aggressive operative strategies that might further reduce stroke risk.

In those with coronary artery disease in whom history or presence of a carotid bruit suggested coexisting carotid disease, noninvasive testing allowed us to stratify with respect to stroke risk and to select those in whom a combined procedure should be considered (those with symptomatic stenosis or bilateral severe disease). Patients with asymptomatic stenosis (70% to 99%) were at relatively low risk for perioperative stroke. These patients should probably undergo carotid endarterectomy as a staged procedure to decrease the risk of stroke during follow-up.

Patients with unilateral occlusion were at increased risk for stroke (16.6%), but in this group carotid endarterectomy has little to offer. Special efforts to increase perfusion pressure during the pump run and to avoid postoperative hypotension should be investigated as a possible means of decreasing the risk of stroke or severity of stroke in these patients.

In patients with occlusion on one side and stenosis on the other, the risk of stroke at the time of CABG was high even when a carotid endarterectomy of the stenosed side was carried out (stroke rate 33%). When a combined procedure was undertaken, strokes occurring on the occluded side tended to be minor and mortality in this group was low. Further refinement of operative technique and potential modifications of other stroke risk factors, including atrial arrhythmias, perioperative myocardial infarction, poor left ventricular function, and vertebrobasilar disease need to be addressed and should be the topic of future studies.

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## Discussion

**Dr. Cary M. Akins** *(Boston, Mass.).* Dr. Mickleborough and her colleagues have drawn our attention to the most devastating complication of myocardial revascularization, namely, perioperative stroke, clearly a multifactorial problem. The identical mortality and stroke rates of 1.2% are very admirable, even in light of the fact that the mean patient age was only 60 years and that more than 80% of the operations were nonemergency.

Several observations in this study warrant comment. Although there were more than 1600 patients in this study, only 58 had asymptomatic carotid bruits, and only 18 of the 58 had significant carotid stenosis by noninvasive testing, a number too small to fully justify the conclusion that such patients can be managed safely by CABG alone. Does the broader total Toronto hospital experience substantiate the authors' results?

Recent randomized trials, namely, the North American and European studies of symptomatic carotid stenosis and the Veterans Administration and ACAS studies of asymptomatic carotid disease, have established the efficacy of carotid endarterectomy. However, before one can advocate the routine use of combined carotid and coronary surgery, as we at the Massachusetts General Hospital do, the perioperative stroke rate must be acceptably low. Of the 21 patients in this study who had concomitant carotid and coronary surgery, 14% had a perioperative stroke. Dr. Mickleborough, why did you not enter concomitant carotid and coronary operation as a variable in your multivariate model for predicting stroke?

Kouchoukos and associates have emphasized the importance of ascending atherosclerosis, which they found in

19% of their patients with intraoperative echocardiography. Using only an inspection and palpation, the authors here report only a 2% incidence of ascending aortic disease, which did, however, turn out to be a significant predictor of stroke. Dr. Mickleborough, do you think that there is an increasing role for intraoperative echocardiographic evaluation of the ascending aorta?

Recently published results confirm the contention that cerebral blood flow during bypass is dependent on perfusion pressure, not pump flow rates. The authors sought a mean arterial pressure of 60 to 70 mm Hg in patients with known carotid disease. Dr. Mickleborough, in light of your watershed strokes with carotid occlusion, have you increased your target level of arterial perfusion on bypass?

Finally, the majority of the strokes in this series actually occurred in the patients who were not preoperatively screened for carotid disease. Did you perform noninvasive carotid testing in patients with postoperative strokes who had not been tested preoperatively and did any of them have significant disease?

**Dr. Mickleborough.** Thank you Dr. Akins. For clarification, 20% of patients in this series underwent surgery on an urgent basis, which means they came from the catheterization laboratory or the cardiac care unit in an acutely unstable condition. An additional 20% were operated on semielectively. Only 60% of patients in this series had truly elective operations.

You asked why I did not review the total experience at The Toronto Hospital. I would have done so had the information regarding carotid disease been available and had the approach to these patients been uniform among other surgeons' practices. Unfortunately, it was impossible to get a uniform policy with regard to recording of prior neurologic history or careful preoperative assessment for carotid bruits. In many cases, auscultation for possible bruits was not carried out as part of the staff surgeon's preoperative assessment. Also, it was not possible to gain agreement on a uniform approach to preoperative carotid screening. Even in screened patients, there was often disagreement as to whether a combined procedure should be recommended. For these reasons, this series is based on a single surgeon's approach, which remained uniform over the 12-year period.

You pointed out that the mean age in this series was 60 years, which is less than the mean age in most current CABG series. The average age of patients undergoing revascularization in our institution has steadily increased in the past decade and the mean of 60 years reflects the 12-year duration of the study. In 1982, the average age was significantly lower than it is now.

You asked why I did not use the "combined procedure" as a variable in the multivariate analysis. This is a very good question. If it had been used, it would certainly have come out as a predictor of stroke. The question is whether these patients had a stroke because of the combined procedure or in spite of it. Only three patients in this group had strokes. All of these patients had bilateral disease with total occlusion on one side. Two of the strokes occurred on the occluded side (2/9, 22%). The other stroke occurred on the side of the carotid endarterectomy on the third postoperative day, presumably because of an embolus, because the endarterectomy site was subsequently proved to be patent. In this series, patients who had total occlusion on one side and no significant stenosis on the other and who did not undergo a combined procedure had a similar risk of stroke on the occluded side (2/12, 17%). Therefore, we believe that the occlusion was the important issue with respect to stroke risk rather than the fact that the patient underwent a combined procedure.

With respect to the role of intraoperative echocardiography in evaluating ascending aortic disease, in our series without echocardiographic evaluation, the incidence of significant ascending aortic disease based on palpation and inspection at the time of the operation was low (3.2%). However, aortic disease was the second most important factor associated with perioperative stroke. Whether use of intraoperative Doppler echocardiography would have allowed us to modify our operative approach and avoid stroke in some of our patients remains unknown. I do agree with you that this is a very important issue that deserves further investigation.

With respect to perfusion pressures during pump support, which was maintained at 60 to 70 mm Hg in patients with carotid disease, whether maintaining pressure at a higher level would have decreased the severity or the incidence of stroke in patients with total internal carotid occlusion cannot be determined.

Finally, whenever possible we did noninvasive carotid testing in patients with a stroke who had not been tested before the operation. Testing was not possible in the four patients who had a severe stroke and never left the intensive care unit. In one patient postoperative testing showed bilateral occlusion of both internal carotid arteries. This patient had had no prior symptoms and no carotid bruits. He had a relatively minor stroke despite his severe carotid disease and made a good recovery. In the other patients having a stroke, postoperative carotid testing failed to show significant carotid stenosis.

**Appendix Table 1.** *Stroke severity scale*

| *Severity grade* | *Impairment** | *Neurologic symptoms* | *Neurologic signs* |
|---|---|---|---|
| 1 | None | Present | Absent |
| 2 | None | Absent | Present |
| 3 | None | Present | Present |
| 4 | Minor, in one or more domains | Present | Present |
| 5 | Major, in only one domain | NA† | NA |
| 6 | Major, in any two domains | NA | NA |
| 7 | Major, in any three domains | NA | NA |
| 8 | Major, in any four domains | NA | NA |
| 9 | Major, in all five domains | NA | NA |
| 10 | Reduced level of consciousness | NA | NA |
| 11 | Death | NA | NA |

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*Impairment in the domains of swallowing, self-care, ambulation, communication, and comprehension. If independence is maintained despite the impairment, it is classified as minor; if independence is lost, it is classified as major.

†Neurologic signs and symptoms are integrated into the higher grades of impairment.