Does preoperative carotid stenosis screening reduce perioperative stroke in patients undergoing coronary artery bypass grafting?

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ABSTRACT

A number of institutions routinely perform carotid artery ultrasound screening before coronary artery bypass grafting (CABG) to identify carotid artery disease requiring revascularization before or during CABG, with the expectation of reducing perioperative neurologic events. The assumptions are that carotid disease is causally related to perioperative stroke and that prophylactic carotid revascularization decreases the risk of post-CABG neurologic events. Although carotid artery stenosis is a known risk factor for perioperative stroke in patients undergoing CABG, it might be a surrogate marker for diffuse atherosclerotic disease rather than a direct etiologic factor. Moreover, the benefit of prophylactic carotid revascularization in patients with asymptomatic unilateral carotid disease is uncertain. Therefore, we have reviewed the literature for evidence that preoperative carotid artery screening, by identifying patients with significant carotid artery stenosis and altering their management, reduces perioperative neurologic events in those undergoing CABG. (*J Thorac Cardiovasc Surg* 2015;149:1253-60)

Carotid artery duplex ultrasound.

Central Message

A number of institutions routinely perform carotid artery ultrasound screening before coronary artery bypass grafting, with the expectation of decreasing perioperative neurologic events. However, carotid artery stenosis might simply be a surrogate marker for diffuse atherosclerotic disease, and the benefit of prophylactic carotid revascularization in asymptomatic patients with unilateral carotid disease is uncertain.

Author's Perspective

A number of institutions routinely perform carotid artery ultrasound screening before coronary artery bypass grafting (CABG) to identify carotid artery disease that necessitates revascularization before or during CABG, with the expectation of reducing perioperative neurologic events. However, among patients undergoing CABG, clinical variables alone can identify those who have significant carotid artery disease, with as high a degree of sensitivity as ultrasound. Moreover, carotid duplex ultrasound screening, whether selective or nonselective, identifies only a minority of patients who will develop perioperative stroke, and intervening for those with carotid disease might not decrease the risk of these neurologic events.

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Abbreviation and Acronym

CABG = coronary artery bypass grafting

Stroke is a devastating complication of coronary artery bypass grafting (CABG).¹ For this reason, a number of institutions routinely screen patients undergoing CABG (Table 1)²⁻⁷ for severe carotid artery stenosis and potential carotid revascularization, with the expectation of reducing the risk of post-CABG stroke. This practice is contrary to guidelines recommending screening in selected patients only.^{8,9} The underlying assumptions are that carotid disease is causally related to perioperative stroke and that prophylactic carotid revascularization decreases its risk. However, if carotid artery stenosis is not a direct etiologic risk factor for perioperative stroke, routine nonselective screening may not be cost effective.^{4,10} In addition, the benefit of prophylactic carotid revascularization in patients with asymptomatic unilateral carotid disease is controversial.¹¹⁻¹⁵ Therefore, we have reviewed the literature for evidence that preoperative carotid artery screening, by identifying patients with substantial carotid stenosis and altering their management, decreases perioperative neurologic events in patients undergoing CABG.

PERIOPERATIVE STROKE IN PATIENTS UNDERGOING CABG

Stroke is a serious complication of CABG that occurs in 1.3% to 2.0% of patients^{1,16-18} and results in acute mortality of up to 38%.^{19,20} The cause of post-CABG stroke is multifactorial, but because most strokes occur ≥ 24 hours after surgery, embolic events are the most likely culprits.^{15,21-24} Macroembolization of atherothrombotic debris from the severely atherosclerotic aorta is strongly associated with postoperative stroke.^{16,25-27} Shedding of emboli to the brain might be caused by manipulation of the ascending aorta during aortic clamping, cannulation, and proximal graft anastomosis.^{23,28,29} Dislodging of emboli from the heart due to manipulation by the surgeon or atrial fibrillation are other possible causes.³⁰ Intraoperative hemodynamic abnormalities, such as hypotension during cardiopulmonary bypass, and pulmonary diastolic hypertension after cardiopulmonary bypass, are also associated with increased risk of post-CABG stroke.³¹ Microembolization of platelet aggregates and turbulent blood flow during cardiopulmonary bypass are other possible causes.^{28,32} In addition, atherosclerotic disease of the cerebral arteries is an important mechanism of stroke in patients undergoing CABG.⁷

Risk factors for perioperative stroke include older age, prior stroke or transient ischemic attack, peripheral artery disease, hypertension, left ventricular dysfunction, preoperative atrial fibrillation,^{1,25,28,33-36} and carotid artery stenosis.^{11,24,28,34,37} A carotid bruit has been found to be a preoperative predictor of severe aortic arch atheroma.³⁸ Therefore, some consider carotid artery disease to be an epiphenomenon, serving as a marker for diffuse systemic atherosclerotic disease, rather than being a causal factor.^{10,12,39,40} Data from Cleveland Clinic patients undergoing noncardiac surgery demonstrated no association between carotid artery stenosis and stroke (odds ratio 1.0, with a 95% confidence interval of 0.99-1.02) for a 10-unit increase in internal carotid artery peak systolic velocity, the variable used to quantify carotid artery stenosis.⁴¹

POSSIBLE MECHANISMS BY WHICH CAROTID ARTERY STENOSIS COULD LEAD TO PERIOPERATIVE STROKE

It is thought that carotid intraplaque hemorrhage can result in plaque destabilization⁴²⁻⁴⁶ and intimal ulceration, creating a nidus for thromboembolism.⁴⁷⁻⁵² Intraplaque hemorrhage detected by magnetic resonance imaging is associated with increased risk of ipsilateral stroke in symptomatic and asymptomatic nonsurgical patients^{53,54} and is strongly related to onset of symptoms.⁵⁵ We hypothesize that anticoagulating patients during CABG might be responsible for increased intraoperative risk of intraplaque hemorrhage. Mechanical causes can trigger intraplaque hemorrhage as well, such as turbulent blood flow and hypertension, both of which can occur during cardiac surgery.⁵⁵

Impaired cerebral hemodynamic function distal to carotid artery stenosis is another determinant of postoperative stroke.^{22,56} Maximally dilated vessels distal to carotid artery stenosis can no longer vasodilate in response to hemodynamic compromise. Therefore, perioperative reduction in blood pressure or cardiac output in this group of patients is hypothesized to lead to cerebral ischemia.^{40,56} Moreover, reduced cerebral blood flow might result in decreased washout of microemboli in patients undergoing CABG.⁵⁷

DETECTING CAROTID ARTERY DISEASE

Carotid artery duplex ultrasound, which is used to visualize plaque and measure flow velocity to quantify stenosis, is the screening test usually used to identify patients with carotid artery stenosis (see Central Image).⁵⁸ The sensitivity of carotid ultrasound to detect carotid artery stenosis, of $>70\%$ is 86% to 90%, with a specificity of 87% to 94%.⁵⁹ Although ultrasound screening is currently used to determine the degree of carotid artery stenosis, other duplex-determined plaque characteristics are also

TABLE 1. Carotid artery screening in patients undergoing coronary artery bypass grafting

First author and year	No. of screened patients	Population	Routine screening	Screening method	Degree of internal carotid artery stenosis considered significant (%)	Prevalence (%)
Wanamaker ¹⁰⁴ 2012	559	CABG	No	DUS	>50	36
Ansari ⁸¹ 2011	116	CABG with/without valve surgery	No	DUS	>70	6.6
Drohomyrecka ⁸⁰ 2010	682	CABG	No	DUS	≥50	18
Cornily ⁸² 2010	205	CABG	No	DUS	≥70	5.8
Anastasiadis ⁴ 2009	307	Cardiac surgery	Yes	DUS	>70	6.5
Kiernan ⁷⁹ 2009	643	CABG	No	DUS	>70	7.7
Sheiman ⁷⁷ 2007	295	CABG	Yes	DUS	≥50	24
Shirani ⁶ 2006	1045	CABG with/without valve surgery	Yes	DUS	>60	6.9
Durand ⁵ 2004	1138	CABG	Yes	DUS and/or angiography	≥70	13.4
Fukuda ³ 2000	308	CABG	Yes	DUS	>50	14.3
Salasidis ⁷⁸ 1995	387	CABG	No	DUS	>80	8.5

CABG, Coronary artery bypass grafting; DUS, duplex ultrasonography.

associated with cerebrovascular symptoms, including hypoechoic lesions (low grayscale median, larger juxtaluminal black area), plaque heterogeneity (presence of noncalcified, discrete white areas without acoustic shadowing), plaque ulceration, and larger plaque area.⁶⁰⁻⁷⁵ Therefore, both carotid artery flow velocity and plaque characterization could be used to identify patients who are at higher risk of developing perioperative neurologic events when undergoing CABG.⁵⁷

Regardless of whether carotid artery stenosis is an etiologic factor for perioperative stroke, carotid artery ultrasound screening detects only a minority of patients who experience perioperative neurologic events. For example, by screening every patient undergoing CABG, Durand and colleagues⁵ found that 13.4% had carotid artery stenosis of ≥70%. Among those who developed postoperative stroke after undergoing CABG, only 19% had carotid artery stenosis of ≥70% ipsilateral to the side of the stroke.

An alternative to routine ultrasound screening is risk profiling. Several groups have identified risk factors associated with significant carotid artery stenosis in patients undergoing CABG (Table 2). Peripheral artery disease, cerebrovascular disease (prior stroke or transient ischemic attack), and old age were the risk factors most consistently identified in these studies.^{2-4,6,37,76-81} Applying carotid disease-screening algorithms to cohorts of ultrasound-screened patients undergoing CABG showed that most who had significant carotid artery stenosis could be detected.^{5,77,82} Thus, Durand and colleagues⁵ found that a risk-profiling algorithm based on a prior stroke or transient ischemic attack, carotid bruit on exam, or age >65 years would have missed significant carotid disease in only 2.3% of patients undergoing CABG (26 of 1138), although

this represented 17% of 152 patients with significant carotid disease, and 582 had a false-positive result.⁵ Thus, their selective screening algorithm had a sensitivity and specificity of 83% and 41%, respectively.

Sheiman and colleagues⁷⁷ used 7 risk factors (history of carotid artery disease, prior cerebrovascular event, hypertension, diabetes, peripheral artery disease, smoking, left main coronary disease, and female gender) to predict which patients have carotid artery disease. The presence of any 1 of these factors was 100% sensitive, but only 30% specific, in detecting patients with ≥50% carotid stenosis. Similarly, Cornily and colleagues⁸² found that risk factors including age >70 years, history of cerebrovascular disease, diabetes mellitus, peripheral artery disease, or carotid bruit on physical examination could have detected 11 of 12 patients with significant carotid artery stenosis. These studies suggest that clinical factors are sensitive in identifying patients with carotid disease, but that specificity is low, requiring more specific screening modalities, such as ultrasound, in more than half of patients.

ROLE OF CAROTID REVASCULARIZATION IN DECREASING THE RISK OF NEUROLOGIC EVENTS

Carotid revascularization by staged or synchronous carotid endarterectomy or carotid artery stenting is considered acceptable in patients with symptomatic carotid disease, bilateral 70% to 99% carotid stenosis, or a unilateral 70% to 99% carotid stenosis with a contralateral occlusion.^{10,83-85} However, most carotid revascularization procedures are performed prophylactically in patients with asymptomatic unilateral carotid artery stenosis,^{11,19,20,24,37} and the value of such interventions is uncertain.

TABLE 2. Risk factors for significant carotid artery stenosis

First author and year	Older age (y)	Female	Bruit	Smoking	DM	Htn	LMCA	History of CVD	PAD	Others
Wanamaker ¹⁰⁴ 2012	Yes	Yes	NS	No	No	Yes	Yes	Yes	Yes	Renal failure (dialysis)
Ansari ⁸¹ 2011	Yes	NS	NS	No	No	No	NS	Yes	Yes	Hypercholesterolemia/abnormal renal function
Cornily ⁸² 2010	NS	No	Yes	No	Yes	No	NS	No	Yes	
Drohomirecka ⁸⁰ 2010	Yes	No	NS	NS	No	No	No	Yes	Yes	Unstable angina
Anastasiadis ⁴ 2009	No	No	Yes	No	No	No	No	Yes	NS	
Kiernan ⁷⁹ 2009	NS	NS	Yes	NS	NS	NS	Yes	Yes	Yes	
Sheiman ⁷⁷ 2007	NS	No	NS	Yes	Yes	Yes	Yes	Yes	Yes	History of carotid disease
Shirani ⁶ 2006	>50	Yes	NS	No	Yes	NS	NS	NS	NS	Cholesterol >240 Triglycerides >240
Durand ⁵ 2004	>65	Yes	Yes	NS	No	Yes	Yes	Yes	Yes	
Fukuda ³ 2000	No	NS	NS	No	No	No	No	Yes	Yes	Atherosclerosis of ascending aorta
D'Agostino ³⁷ 1996	Yes	Yes	NS	Yes	Yes	NS	Yes	Yes	Yes	Prior vascular operation
Salasidis ⁷⁸ 1995	Yes	NS	NS	No	No	No	NS	Yes	Yes	Prior carotid endarterectomy
Berens ⁷⁶ 1992	NS	Yes	NS	Yes	NS	No	Yes	Yes	Yes	

Bruit, Carotid bruit; *DM*, diabetes mellitus; *Htn*, hypertension; *LMCA*, left main coronary artery; *CVD*, cerebrovascular disease; *PAD*, peripheral artery disease; *NS*, not studied.

The assumed benefit of treating asymptomatic patients is extrapolated from the Asymptomatic Carotid Atherosclerosis Study and Asymptomatic Carotid Surgery Trial, which concluded that carotid endarterectomy decreases the 5-year risk of ipsilateral stroke in patients with asymptomatic isolated carotid disease.^{86,87} However, the purpose of prophylactic carotid revascularization in patients undergoing CABG is to reduce perioperative neurologic events. Thus, long-term risk reduction of stroke should not be used as a justification to perform carotid revascularization in these patients, especially if operative morbidity from the combined procedures is higher than the added risks of the procedures performed separately.¹² Results of the ongoing Coronary Artery Bypass graft surgery in patients with Asymptomatic Carotid Stenosis (CABACS) randomized clinical trial comparing the safety and efficacy of isolated CABG versus synchronous CABG and carotid endarterectomy in patients with asymptomatic high-grade carotid artery stenosis will elucidate whether surgical carotid revascularization helps to reduce the risk of perioperative stroke in patients undergoing CABG.⁸⁸ However, the trial does not have a staged carotid artery stenting arm, so the best approach to managing these patients might remain unclear.⁸⁹

Currently, several findings argue against the usefulness of carotid revascularization in patients undergoing CABG. First, no direct causal relationship has been found between carotid artery stenosis and postoperative ipsilateral stroke,¹² and most strokes occur outside the territory supplied by the carotid artery.⁹⁰ Second, the risk of perioperative stroke in patients with carotid disease is low.^{12,13,91-93} In a meta-analysis by Naylor and Bown,⁹⁴ the risk of ipsilateral

stroke in patients with a unilateral, asymptomatic 50% to 99% stenosis was found to be only 2%.

Third, if carotid disease is truly an important risk factor for post-CABG stroke, then patients with bilateral, severe carotid disease undergoing unilateral carotid revascularization should have a high rate of stroke ipsilateral to the “nonrevascularized” artery. However, studies show that the risk of perioperative neurologic events ipsilateral to the nonrevascularized artery is low.^{94,95} Fourth, combined CABG and carotid revascularization is associated with higher risk than isolated CABG. Thus, Ghosh and colleagues¹³ found that occurrence of death, cerebrovascular events, and myocardial infarction within 30 days of CABG without prophylactic revascularization in asymptomatic patients with carotid artery stenosis of $\geq 70\%$ was 4%, but Naylor¹⁰ reported that the composite risk of death, stroke, or myocardial infarction within 30 days of combined CABG and carotid revascularization was 9% to 11%.

Surgeons can consider several other strategies to reduce the risk of perioperative neurologic events. First, monitoring of blood pressure throughout the procedure and postoperatively; avoiding extremes of blood pressure during surgery is important, because both hypertension, when it leads to carotid artery plaque rupture, and hypotension, when it leads to cerebral ischemia, can initiate neurologic damage. Second, postoperative antiplatelet therapy should be considered,^{8,96} because most strokes result from thromboembolic events.

Third, because these patients are likely to have aortic arch atheroma as part of their diffuse atherosclerotic disease, intraoperative assessment of the aorta should be done before clamping, and strategies should be used to

decrease the shedding of emboli from the aorta during surgery, such as off-pump CABG without a partial occlusion clamp, or on-pump CABG with continuous perfusion without aortic clamping. Monitoring brain oxygen saturation during CABG through cerebral oximetry, to avoid profound cerebral desaturation, is also associated with better outcomes.⁹⁷ Moreover, dynamic bubble trap and arterial line filters may be considered to reduce the occurrence of stroke in patients undergoing CABG.^{98,99}

VALUE OF ROUTINE CAROTID SCREENING

The Society of Thoracic Surgeons and the American College of Cardiology/American Heart Association recommend ultrasound screening for carotid artery stenosis in selected patients only (class IIa recommendation, level of evidence C).^{8,9,100} The guidelines document¹¹ “2012 Appropriate Use Criteria for Peripheral Vascular Ultrasound and Physiological Testing” rated all clinical scenarios for cerebrovascular duplex scanning before cardiac surgery as uncertain (or “may be appropriate”).¹⁰¹ The Society of Vascular and Interventional Neurology recommends screening of selected patients undergoing CABG (grade B), but screening of all patients was considered a grade D recommendation.¹⁰²

Because carotid artery stenosis is common in patients with coronary artery disease and is a marker of increased risk of cardiovascular events, detecting it is thought by some to be important for preoperative risk stratification.¹⁰³ However, the cost effectiveness of such nonselective screening in patients undergoing cardiac surgery is unknown. Indeed, the first research priority identified by the writing committee of the “2012 Appropriate Use Criteria for Peripheral Vascular Ultrasound and Physiologic Testing” document was to determine the clinical and cost effectiveness of carotid screening in patients undergoing cardiac surgery.¹⁰¹

CONCLUSIONS

Among patients undergoing CABG, clinical variables alone can identify those who have significant carotid artery disease with as high a degree of sensitivity as ultrasound. However, low specificity would seem to dictate ultrasound screening, and possibly additional confirmatory testing⁴ of a large proportion of these patients, to alleviate a false-positive diagnosis. On the other hand, carotid duplex ultrasound screening, whether selective or nonselective, identifies only a minority of patients who will develop perioperative stroke, and intervening for those with carotid disease might not decrease the risk of these neurologic events. Absence of a direct causal relationship between carotid artery stenosis and ipsilateral stroke, and the increased morbidity associated with carotid revascularization, support the argument that prophylactic carotid

revascularization might be of no benefit in asymptomatic patients undergoing CABG. This area, then, is clearly in great need of further research.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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