From the Western Vascular Society

The impact of increasing age on anatomic factors affecting carotid angioplasty and stenting

Russell C. Lam, MD, Stephanie C. Lin, MD, Brian DeRubertis, MD, Robert Hynecek, MD, K. Craig Kent, MD, and **Peter L. Faries, MD,** *New York, NY*

Purpose: **Current evaluations of carotid artery angioplasty and stenting (CAS) have suggested equivalency compared with carotid endarterectomy (CEA). However, the incidence of stroke and death with CAS may be higher in elderly patients. We assessed the anatomic characteristics of patients undergoing CAS and compared them based on age older or younger than 80 years. The impact of age on the incidence of postoperative complications was also determined.**

Methods: **From February 2003 to August 2005, 135 CAS procedures were performed in 133 patients. Digital subtraction angiograms for each patient were evaluated by two independent observers blinded to patient identifiers. Anatomic characteristics that impact the performance of CAS were assessed as either favorable or unfavorable. These included aortic arch elongation, arch calcification, arch vessel origin stenosis, common and internal carotid artery tortuosity, and treated lesion stenosis, calcification, and length. Postoperative events were defined as myocardial infarction, stroke, and death. Fisher's exact test and χ^2 tests were used to determine statistical significance ($P < .05$).**

Results: **Of the 133 patients treated, 87 (65%) were men and 46 (35%) were women; and 37 (28%) were ≥80 years of age. The cohort ≥80 years old had an increased incidence of unfavorable arch elongation ($P = .008$), arch calcification ($P = .003$), common carotid or innominate artery origin stenosis ($P = .006$), common carotid artery tortuosity ($P = .0009$), internal carotid artery tortuosity ($P = .019$), and treated lesion stenosis ($P = .007$). No significant difference was found for treated lesion calcification or length. Perioperative cerebral vascular accidents occurred in four patients (3.0%, 3 with no residual deficit, 1 with residual deficit), myocardial infarction in three (2.2%), and one patient (0.8%) died secondary to a hemorrhagic stroke. The combined stroke, myocardial infarction, and death rate for the entire population was 3.7%. The rate was significantly increased in patients aged ≥80 years old (10.8%) compared with those aged <80 years old (1%, $P = .012$).**

Conclusions: **Elderly patients, defined as those aged >80 years, have a higher incidence of anatomy that increases the technical difficulty of performing CAS. This increase in unfavorable anatomy may be associated with complications during CAS. Although the small number of perioperative events does not allow for determination of a direct relationship with specific anatomic characteristics, the presence of unfavorable anatomy does warrant serious consideration during evaluation for CAS in elderly patients. (J Vasc Surg 2007;45:875-80.)**

The treatment of extracranial carotid stenosis is intended to prevent cerebral embolization and resultant cerebrovascular accidents. Past studies have compared carotid endarterectomy (CEA) with best medical therapy for both symptomatic and asymptomatic patients.[1-3] The improved long-term outcomes reported in those studies support the performance of CEA for the prevention of stroke. However, previous studies of the efficacy of CEA excluded patients considered to be at increased risks for surgery, including those aged >80 years.

Carotid angioplasty and stenting (CAS) is a minimally invasive modality with recent support as an equivalent alternative to CEA in the treatment of cerebrovascular occlusive disease in patients with increased risk for surgery.[4-5] With advances in the design of cerebral protection devices and self-expanding stents, fewer technical limitations to CAS exist. Despite this, current data suggest that the incidence of complications is higher when CAS is performed in elderly patients.[6-8] These complications include stroke and non-neurologic events such as myocardial infarction (MI) and death. In contrast, many studies have shown that CEA is safe for octogenarians.[9-14] The incidence of non-neurologic events may be partly explained by the significant medical comorbidities of elderly patients.

In contrast to CEA, CAS necessitates manipulation of arteries other than the carotid bifurcation. The aortic arch and proximal carotid arteries must be traversed to gain access to the carotid stenosis. In addition, the internal carotid artery distal to the stenosis is used to deploy the embolic protection device.

This study examined arterial anatomic features of vessels during the performance of CAS. The incidence of anatomic features that may increase the technical difficulty of the CAS procedure was compared between patients <80 years old and those ≥80 years old.

Division of Vascular Surgery, New York Presbyterian Hospital, Cornell University, Weill Medical School and Columbia University, College of Physicians and Surgeons.

Competition of interest: none.

Presented at the Western Vascular Society 2006 Annual Meeting, La Jolla, Calif, Sep 16-19, 2006.

Correspondence: Peter L. Faries, MD, FACS, Division of Vascular Surgery, New York Presbyterian Hospital, 525 E 68th St., Room *P*-705, New York, NY 10021 (e-mail: plf2001@med.cornell.edu).

CME article

0741-5214/$32.00

doi:10.1016/j.jvs.2006.12.059

METHODS

Patients. From February 2003 to August 2005, 135 CAS procedures were performed in 133 patients. Data were compiled prospectively in a computerized vascular database and reviewed retrospectively. Preoperative imaging con-

Table I. Patient characteristics by age <80 years old and age ≥80 years old

	<80, n = 96 (%)	*≥80, n = 37 (%)*
Contralateral occlusion	13	14
Previous ipsilateral CEA	18	11
History of neck irradiation	7	0
Goldman class II/III	66	57
Symptomatic	28	37

CEA, Carotid endarterectomy.

sisted of carotid duplex ultrasound or magnetic resonance angiography, or both. No patient was excluded from CAS based on anatomic characteristics noted on preoperative imaging. All but two patients in this cohort underwent successful CAS after initial diagnostic angiography.

Embolic protection devices were used in all but two cases: EPI Filterwire (Boston Scientific, Natick, Mass) in 19%, Guardwire (Medtronic, Minneapolis, Minn) in 19%, Accunet (Guidant, Minneapolis, Minn) in 47%, and Angioguard (Cordis, Sommerville, NJ) in 14%. All patients received a self-expanding stent: Wallstent (Boston Scientific) in 26%, NexStent (Endotex, Santa Rosa, Calif) in 10%, Acculink (Guidant) in 49%, and Precise (Cordis) in 14%. Most of the cases were performed under an investigational protocol. Indications for CAS included prior neck irradiation with or without neck surgery, restenosis after ipsilateral CEA, and significant comorbid medical conditions (Table I).

Anatomic evaluation. Digital subtraction angiograms of all 135 procedures were available for examination. Two vascular surgeons with very limited familiarity with the study population independently evaluated each angiogram blinded to patient identifiers. Because there was nonuniformity in the preoperative imaging, these studies were not used in this postprocedural analysis. Anatomic characteristics assessed were arch elongation, arch calcification, arch vessel origin stenosis, common and internal carotid artery tortuosity, treated lesion stenosis based on the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria, treated lesion calcification, and lesion length. These anatomic characteristics were defined as favorable or unfavorable for CAS. Interpretation of a favorable anatomy was based on anticipated difficulty with vessel cannulation, sheath placement, and passage and positioning of the devices. The criteria used to determine favorable and unfavorable characteristics were defined individually.

The aortic arch elongation classification was defined by the parallel planes perpendicular to the greater (outer) curvature and lesser (inner) curvature of the arch. If the arch vessels arose from the top of the arch or outer curvature, this was described as a type I arch, between the two planes was a type II arch, and proximal or caudal to the lesser curvature of the arch was a type III arch (Fig 1).

Aortic arch calcification was assessed on left anterior oblique views and categorized as favorable if there was no or trace calcium shadowing and unfavorable if there was luminal irregularity or significant calcification.

Fig 1. Type III aortic arch with left common carotid and innominate originate caudal to the lesser curvature of the arch. Also note the significant irregularity visible along both luminal surfaces signifying unfavorable arch calcification.

Arch vessel origin stenosis was divided into <50% stenosis (favorable) and >50% stenosis (unfavorable). Both common and internal carotid tortuosity indices were designed to reflect increasing difficulty for wire and catheter passage. The grading was favorable if there was <30° angulation from the centerline flow of blood and unfavorable if there was >30°.

The internal carotid artery (ICA) was evaluated only for the extracranial portion beyond the carotid bulb, whereas the common carotid artery (CCA) was assessed in its entirety from the arch to the bifurcation (Fig 2 and Fig 3).

Index lesion stenoses were categorized into <85% (favorable) and >85% (unfavorable). Lesion calcification was examined on multiple magnified, oblique views and described as no or minimal calcium seen in the lesion (favorable) and calcium throughout the lesion (unfavorable).

Finally, lesion length was measured using a radiopaque ruler placed externally on the patient's neck at the time of the procedure. The length of >50% diameter reduction that required treatment was divided into 0 to 5 mm (favorable) and >5mm (unfavorable).

Perioperative events. Events occurring ≤30 days of operation were classified as perioperative complications. MI was defined by the presence of elevated cardiac enzymes (troponin) or electrocardiogram (ECG) changes consistent

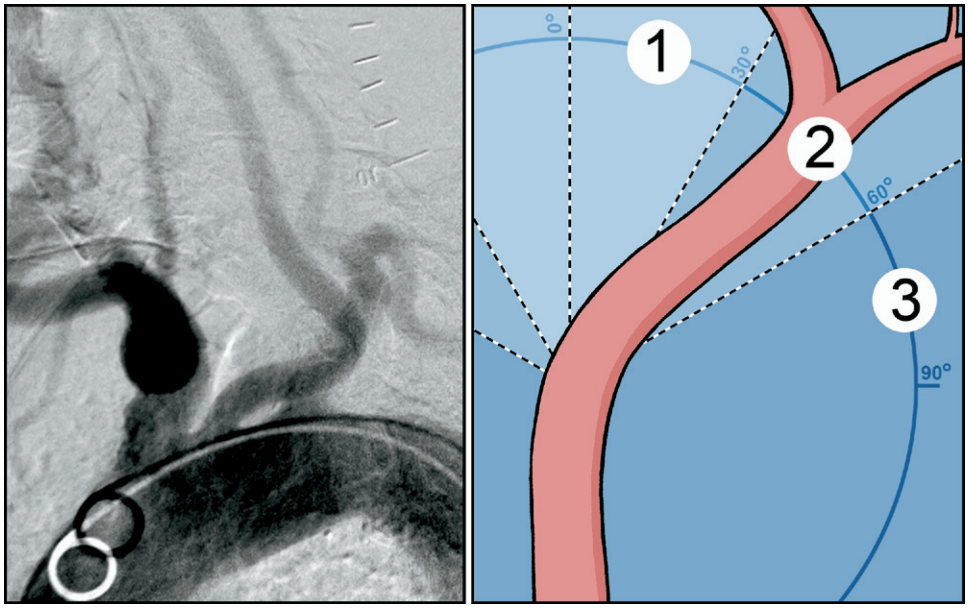

Fig 2. Unfavorable common carotid shows significant tortuosity of bilateral common carotid arteries proximally with nearly 90° turns.

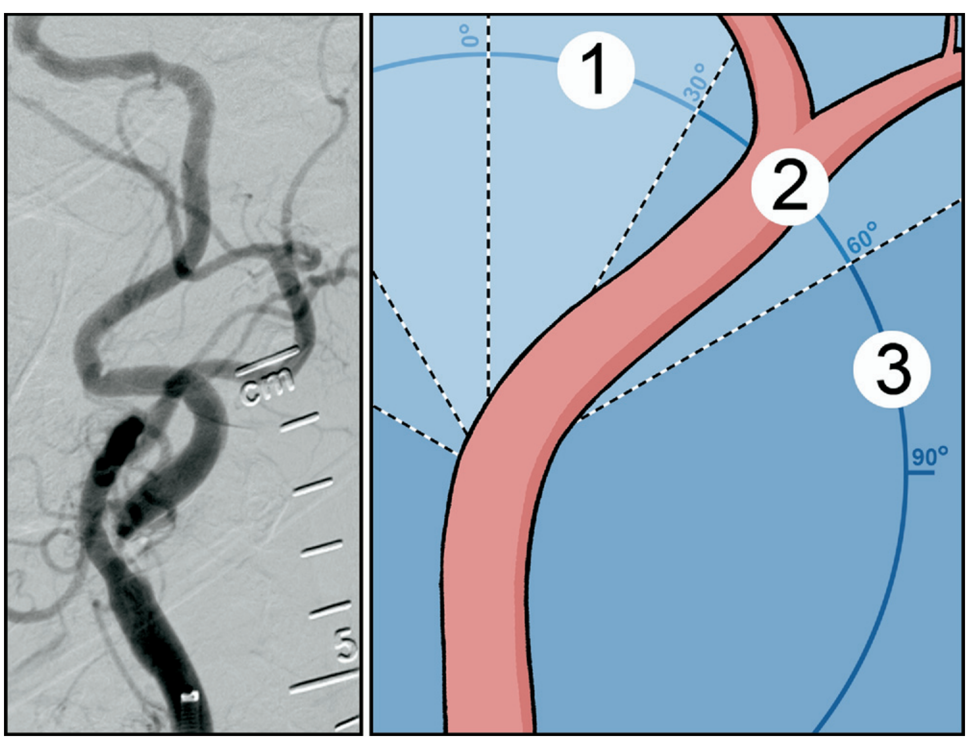

Fig 3. Unfavorable internal carotid shows significant tortuosity of internal carotid artery with sinusoidal turns.

with MI. Cerebral vascular accidents were categorized into those with no residual deficit >72 hours and those with permanent neurologic deficits. These neurologic changes were confirmed by a neurologist and included the use of the National Institutes of Health Stroke Scale.

Statistical analysis. The χ^2 and Fisher exact tests were used to compare each anatomic characteristic for patients grouped by age older or younger than 80 years. The Fisher exact test was used to compare postoperative events for patients grouped by age and also to assess neurologic

Table II. Anatomic evaluations by age <80 years old and age ≥80 years old

	<80, n = 96 (%)	*≥80, n = 37 (%)*	P
Arch elongation	56	82	.008
Arch calcification	30	59	.003
Origin stenosis	22	47	.006
CCA tortuosity	38	70	.0009
Lesion stenosis	56	82	.007

complications for anatomic variables. $P < .05$ was considered statistically significant.

Interobserver agreement was assessed by calculation of the intraclass correlation coefficient (ICC) using a two-way random effects model where both people effects and measures effects are random. An ICC of ≥75% is considered excellent agreement, whereas 40% to 74% is fair-to-good agreement. Interobserver agreement was very good-to-excellent for all anatomic characteristics. For aortic arch calcification, the ICC was 100%, for origin stenosis, 92% (95% confidence interval [CI], 86% to 95%); CCA tortuosity, 84% (95% CI, 74% to 90%); ICA tortuosity, 93% (95% CI, 88% to 96%). Lesion calcification ICC was 70% (95% CI, 53% to 81%); and lesion length was 69% (95% CI, 50% to 81%). Data were analyzed using SPSS statistical software (SPSS, Chicago, Ill).

RESULTS

There were 135 CAS procedures performed in 133 patients, of whom 87 (65%) were men and 46 (35%) were women, 37 (28%) were ≥80 years old (mean, 85 years), and 96 (72%) were <80 years old (mean, 65 years). The technical success rate in completing the CAS procedure was 99% in this study. The two cases in which CAS could not be completed occurred early in our experience. The anatomic factors that precluded completion of these procedures were bovine arch anatomy and ICA tortuosity.

Comparing patients <80 and ≥80 years old, there was an increased incidence of unfavorable anatomic characteristics in patients ≥80 years old for arch elongation (56% vs 82%, $P = .008$), arch calcification (30% vs 59%, $P = .003$), common carotid artery origin stenosis (22% vs 47%, $P = .006$), common carotid artery tortuosity (38% vs 70%, $P = .0009$), internal carotid artery tortuosity (50% vs 74%, $P = .019$), and treated lesion stenosis (56% vs 82%, $P = .007$). No statistically significant difference was found for the treated lesion degree of calcification (51% vs 56%. $P = .62$) or length (56% vs 62%, $P = .59$; Table II).

Perioperative morbidity included three MIs (2.2%): two in the patients <80 years old and one in a patient ≥80 years old (2.1% vs 2.7%, P = NS). All three were detected by enzyme (troponin) elevation only and was not associated with any ECG changes. Comparing the incidence of comorbid medical conditions between patients <80 and ≥80 years old did not revealed any statistical significance for diabetes mellitus, hypertension, coronary artery disease, statin use, or duration of platelet therapy.

Four cerebrovascular accidents (CVAs) occurred, one in a patient <80 years old age and three in patients ≥80 years old (1.0% vs 8.1%, P = NS). Two of the three patients ≥80 years of age who experienced CVAs had unfavorable arch calcification and ICA tortuosity, and the remaining patient had only unfavorable ICA tortuosity. Three patients who experienced CVAs had no residual deficit >72 hours, and one had a persistent focal deficit. One patient ≥80 years old experienced both MI and CVA. The single death occurred in a 93-year-old man who sustained a hemorrhagic stroke after receiving periprocedural abciximab (0.8% overall, 2.7% in ≥80 group, P = NS). The composite complication rate consisting of stroke, MI, or death for the entire population was 3.7% (1.0% for patients <80 years old vs 10.8% for patients ≥80 years old, $P = .012$).

DISCUSSION

This study sought to examine the possibility that unfavorable arterial anatomic characteristics are associated with the reported increased incidence of perioperative complications when CAS is performed in elderly patients. Investigators in the Carotid Revascularization Endarterectomy vs Stent Trial (CREST) trial reported a 30-day stroke and death rate of 12% for octogenarians compared with 3.23% among nonoctogenarians.[6] Kastrup et al[7] also reported a combined stroke and death rate of 10% for symptomatic and 13% for asymptomatic patients >75 years old. This is compared with a rate of <3% stroke and death in patients <75 years old .[7]

Our hypothesis was that the higher rate of stroke associated with CAS in elderly patients was related to the more unfavorable anatomy that must be navigated in the course of performing the procedure. This includes not only ICA tortuosity as Hobson et al[6] suggest but also aortic calcification, arch vessel origin stenosis, and aortic arch elongation and distortion.[15,16] Both aortic atherosclerosis and arch vessel tortuosity are associated with increased age.[7-18]

It is also likely that these factors make a CAS procedure technically more difficult and may contribute to an increase in technical errors leading to a higher risk of thromboembolic complications. Not only can emboli be dislodged during device manipulation within heavily calcified or angulated arch vessels, but dissections can occur and thrombus can form when significant force and repeated endothelial trauma is generated in crossing these lesions with the various catheters and wires required in complex CAS procedures.

There is a well-documented risk of neurologic events associated with cerebral angiography (<1%) as well as coronary angiography (0.3%).[19-21] Coronary artery bypass grafting (CABG) is also associated with an estimated stroke risk of 2%.[22] All of these complications have been attributed to emboli of atheromatous debris, thrombus, and even air bubbles.[23,24] It has also been shown that silent emboli are produced during these procedures and radiographically detected infarcts also occur.[25,26] Although not stratified for age, these data reflect the inherent risk of vascular procedures in patients with advanced atherosclerosis. In all of

Table III. Anatomic evaluation of favorable and unfavorable arterial characteristics

	Favorable	*Unfavorable*
Arch elongation	Vessel origins off top of the arch (type I)	Origin from ascending or between greater and lesser curvatures (type II and III)
Arch calcification	No or trace shadowing	Luminal irregularity or diffuse calcification
Origin stenosis	<50%	>50%
CCA or ICA tortuosity	<30° angularity	>30° angularity
Lesion stenosis	<85%	>85%
Lesion calcification	No or trace shadowing	Calcium in portions or throughout
Lesion length	0-5 mm	>5 mm

CCA, Common carotid artery; *ICA,* internal carotid artery.

these studies, however, neither the volume of emboli nor the presence of defects on MRI has correlated directly with clinical neurologic changes.

As the demand for and comfort with CAS grows, it will be valuable to delineate those factors that may create a difficult, hazardous procedure and therefore warrant reconsideration of the use of this procedure. It is also likely that the additive effects of emboli, hypoperfusion, and susceptibility of elderly neuronal parenchyma produce the higher risk for a neurologic event in elderly patients undergoing CAS.[27] The relatively small number of elderly patients and neurologic events limits our ability to determine how severe a particular anatomic factor must be to preclude CAS. However, the results do suggest that when there is a constellation of unfavorable anatomic characteristics are present, consideration of CEA or medical management alone should be considered, particularly in patients >80 years old (Table III).

The finding of increased lesion stenosis in patients ≥80 years of age was unexpected. One explanation may be that the decision to operate was deferred in these elderly patients until the stenoses became severe. Moreover, atherosclerosis is generally a disease of advancing age, and it has been reported that the rate of plaque formation accelerates with age.[28] Conversely, the lesions in the elderly were not necessarily more heavily calcified or of greater length, and to date, no known association has been found between plaque calcification and age.

Limitations of this study include the relatively small number of patients treated and the infrequency of neurologic events. This limits the ability to demonstrate statistically significant associations between unfavorable anatomic characteristics and neurologic complications. Additional limitations include the qualitative assessment of the arterial anatomic features and that patient selection for CAS was not randomized.

CONCLUSION

This study aims to provide key decision points in assessing the suitability of patients for CAS. Arch elongation and calcification, origin and lesion stenosis, and vessel tortuosity are all features that increase the difficulty of CAS and may make it a high-risk procedure. Although more prevalent in the elderly, these characteristics may be found in patients of any age and may be considered as risk factors for perioperative stroke with CAS. In determining whether a patient should undergo CAS or CEA, evaluation of the relevant anatomy is important to minimize operative risk.

AUTHOR CONTRIBUTIONS

Conception and design: SL, RL, BD, RH, KK, PF
Analysis and interpretation: SL, RL, BD, PF
Data collection: SL, RL, BD,
Writing the article: SL, RL, BD, PF
Critical revision of the article: SL, RL, RH, KK, PF
Final approval of the article: SL, RL, BD, RH, KK, PF
Statistical analysis: RL, BD,
Obtained funding: RH, KK,
Overall responsibility: PF

REFERENCES

1. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med 1991;325:445-53.
2. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. JAMA 1995;273:1421-8.
3. Mayberg MR, Wilson SE, Yatsu F, Weiss DG, Messina L, Hershey LA, et al. Carotid endarterectomy and prevention of cerebral ischemia in symptomatic carotid stenosis. Veterans Affairs Cooperative Studies Program 309 Trialist Group. JAMA 1991;266:3289-94.
4. Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med 2004;351:1493-501.
5. Carotid Revascularization Using Endarterectomy or Stenting Systems (CaRESS) phase I clinical trial: 1-year results. J Vasc Surg 2005;42:213-9.
6. Hobson RW 2nd, Howard VJ, Roubin GS, Brott TG, Furguson RD, Popma JJ, et al. Carotid artery stenting is associated with increased complications in octogenarians: 30-day stroke and death rates in the CREST lead-in phase. J Vasc Surg 2004;40:1106-11.
7. Kastrup A, Schulz JB, Raygrotzki S, Groschel K, Ernemann U. Comparison of angioplasty and stenting with cerebral protection versus endarterectomy for treatment of internal carotid artery stenosis in elderly patients. J Vasc Surg 2004;40:945-51.
8. Roubin GS, New G, Iyer SS, Vitek JJ, Al-Mubarak N, Liu MW, et al. Immediate and late clinical outcomes of carotid artery stenting in patients with symptomatic and asymptomatic carotid artery stenosis: a 5-year prospective analysis. Circulation 2001;103:532-7.
9. Ballotta E, Renon L, Da Giau G, Barbon B, Terranova O, Baracchini C. Octogenarians with contralateral carotid artery occlusion: a cohort at higher risk for carotid endarterectomy? J Vasc Surg 2004;39:1003-8.
10. Mozes G, Sullivan TM, Torres-Russotto DR, Bower TC, Hoskin TL, Sampaio SM, et al. Carotid endarterectomy in SAPPHIRE-eligible high-risk patients: implications for selecting patients for carotid angioplasty and stenting. J Vasc Surg 2004;39:958-65; discussion 965-6.

11. Norman PE, Semmens JB, Laurvick CL, Lawrence-Brown M. Long-term relative survival in elderly patients after carotid endarterectomy: a population-based study. Stroke 2003;34:e95-8.
12. Rockman CB, Jacobowitz GR, Adelman MA, Lamparello PJ, Gagne PJ, Landis R, et al. The benefits of carotid endarterectomy in the octogenarian: a challenge to the results of carotid angioplasty and stenting. Ann Vasc Surg 2003;17:9-14.
13. Schneider JR, Droste JS, Schindler N, Golan JR. Carotid endarterectomy in octogenarians: comparison with patient characteristics and outcomes in younger patients. J Vasc Surg 2000;31:927-35.
14. Alamowitch S, Eliasziw M, Algra A, Meldrum H, Barnett HJ; North American Symptomatic Carotid Endarterectomy Trial (NASCET) Group. Risk, causes, and prevention of ischaemic stroke in elderly patients with symptomatic internal-carotid-artery stenosis. Lancet 2001;357:1154-60.
15. Amarenco P, Cohen A, Tzourio C, Bertrand B, Hommel M, Besson G, et al. Atherosclerotic disease of the aortic arch and the risk of ischemic stroke. N Engl J Med 1994;331:1474-9.
16. Davila-Roman VG, Barzailai B, Wareing TH, Murphy SF, Schechtman KB, Kouchoukos NT. Atherosclerosis of the ascending aorta. Prevalence and role as an independent predictor of cerebrovascular events in cardiac patients. Stroke 1994;25:2010-6.
17. Tuman KJ, McCarthy RJ, Najafi H, Ivankovich AD. Differential effects of advanced age on neurologic and cardiac risks of coronary artery operations. J Thorac Cardiovasc Surg 1992;104:1510-7.
18. Salomon NW, Page US, Bigelow JC, Krause AH, Okies JE, Metzdorff MJ. Coronary artery bypass grafting in elderly patients. Comparative results in a consecutive series of 469 patients older than 75 years. J Thorac Cardiovasc Surg 1991;101:209-17; discussion 217-8.
19. Low AS, Lim WE, Chan LL, Tan HM, Tan KP. Audit of diagnostic and interventional craniocervical catheter angiographic procedures at the Singapore General Hospital. Ann Acad Med Singapore 2004;33:607-13.
20. Gerraty RP, Bowser DN, Infeld B, Mitchell PJ, Davis SM. Microemboli during carotid angiography. Association with stroke risk factors or subsequent magnetic resonance imaging changes? Stroke 1996;27:1543-7.
21. Brown DL, Topol EJ. Stroke complicating percutaneous coronary revascularization. Am J Cardiol 1993;72:1207-9.
22. Acinapura AJ, Rose DM, Cunningham JN Jr, Jacobowitz IJ, Kramer MD, Zisbrod Z. Coronary artery bypass in septuagenarians. Analysis of mortality and morbidity. Circulation 1988;78:I179-84.
23. Davila-Roman VG, Murphy SF, Nickerson NJ, Kouchoukos NJ, Schechtman KB, Barzilai B. Atherosclerosis of the ascending aorta is an independent predictor of long-term neurologic events and mortality. J Am Coll Cardiol 1999;33:1308-16.
24. Van der Linden J, Hadjinikolaou L, Bergman P, Lindblom D. Postoperative stroke in cardiac surgery is related to the location and extent of atherosclerotic disease in the ascending aorta. J Am Coll Cardiol 2001; 38:131-5.
25. Bendszus M, Koltzenburg M, Burger R, Warmuth-Metz M, Hofmann E, Salymosi L. Silent embolism in diagnostic cerebral angiography and neurointerventional procedures: a prospective study. Lancet 1999;354: 1594-7.
26. Knipp SC, Matatko N, Wilhelm H, Schlamann M, Massoudy P, Forsting M, et al. Evaluation of brain injury after coronary artery bypass grafting. A prospective study using neuropsychological assessment and diffusion-weighted magnetic resonance imaging. Eur J Cardiothorac Surg 2004;25:791-800.
27. Orlandi G, Fanucchi S, Gallerini S, Sonnoli C, Cosottini M, Puglioli M, et al. Impaired clearance of microemboli and cerebrovascular symptoms during carotid stenting procedures. Arch Neurol 2005;62:1208-11.
28. Van Oostrom O, Velema E, Schoneveld AH, de Vries JP, de Bruin P, Seldenrijk CA, et al. Age-related changes in plaque composition: a study in patients suffering from carotid artery stenosis. Cardiovasc Pathol 2005;14:126-34.

Submitted Jul 5, 2006; accepted Dec 21, 2006.