Appropriateness of Indications for Asymptomatic Carotid Endarterectomy and Risk Factors for Perioperative Complications

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Background. Guided by the findings of randomized controlled trials evaluating carotid endarterectomy (CEA), we examined the appropriateness of CEA performed in our hospital for asymptomatic carotid stenosis and determined the incidence and risk factors for postoperative stroke, death and cardiac complications.

Methods. We prospectively reviewed all CEAs performed in Vilnius University Emergency Hospital over 5 years. On the basis of clinical practice guidelines established by the American Heart Association, the appropriateness of CEA for asymptomatic patients was classified into the following categories: acceptable for asymptomatic carotid stenoses ≥75%, uncertain indications <75%–50%, innappropriate < 50%.

Results. Surgical indications were appropriate in 85% of cases (93/110). Stroke and death occurred postoperatively in 5.4% (6/110) of asymptomatic patients. Cardiac complications developed in two patients (1.8%). An independent preoperative risk factor for stroke and death was diabetes mellitus.

Conclusions. Uncertain and inappropriate indications were uncommon. Our high complication rate possibly negate any overall surgical benefit in the group of asymptomatic patients.

Key words: asymptomatic carotid stenosis, carotid endarterectomy, complications, risk factors

INTRODUCTION

The practice of carotid endarterectomy (CEA) for asymptomatic patients is seriously questioned. This is mainly due to its unproven efficacy in stroke prevention, but contributing to these concerns are descriptions of its use for what appeared to be inappropriate indications and high complication rate. Since the results of Asymptomatic Carotid Atherosclerosis Study have been disseminated throughout the medical community in the world, we wanted to reexamine the issues of appropriateness and complications of CEA in asymptomatic patients as currently practiced in our hospital. Using the results of the recently reported randomized trials concidering CEA as guidelines, the goal of this study was to determine the appropriateness and complication rates of all asymptomatic CEAs performed in the Vilnius University Emergency Hospital over 5 years. We also wanted to determine any risk factors in our patients that were significantly predictive of death or postoperative stroke and cardiac complications.

MATERIALS AND METHODS

We performed a perspective study of all CEAs performed in Vilnius University Emergency Hospital from January 1, 1995 through December 31, 1999.The cohort consisted of 259 consecutive cases of CEA performed on 110 asymptomatic patients by seven vascular surgeons. The appropriateness of operative indications was determined on the basis of a review of ACAS and clinical practice guidelines established by the American Heart Association. According to these criteria, the appropriateness of CEA for each patient examined in this study was classified into the following categories: acceptable for asymptomatic carotid stenoses ≥75%, uncertain indications <75%–50%, innapropriate <50% for asymptomatic patients. The angiographic method of measurement used was that of NASCET, *i.e.* comparison of the greatest degree of linear diameter

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stenosis of the internal carotid artery at the carotid bifurcation to the diameter of the distal normal internal carotid artery. Patients with nonhemispheric or nonretinal symptoms, symptom-free and with symptoms of cerebral or retinal ischemia referrable to the contralateral carotid artery were regarded as being asymptomatic from stenotic carotid artery. We excluded patients who were likely to have had embolism from the heart to the brain or eye and patients who had more severe stenosis of the distal than of the proximal carotid artery. The primary outcome was postoperative stroke defined as the onset of a new neurological deficit (unrelated to cranial nerve injury), lasting 24 > hours and causing permanent disability or death during hospital course. Patients were followed for the development of complications during their hospital course. A secondary outcome was the development of cardiac complications, specifically myocardial infarction, congestive heart failure, unstable angina or atrial fibrillation. Measures of association between risk factors and outcome events were expressed as odds ratios with 95% CI. The level of significance was set at $P < 0.05$, and all tests were two-tailed. Associations between risk factors and outcome events were also evaluated with multivariate analyses using logistic regression models. Dependent variables were the dichotomous outcomes of stroke or death and cardiac complications. Independent variables used in these models included those listed in Table 5, as well as the following dichotomous variables: age, sex, current cigarette use, coronary artery disease (angina pectoris, myocardial infarction, congestive heart failure, fibrillatio atriorum, prior CABG/angioplasty), arterial hypertension, diabetes mellitus, claudication, hyperlipidemia, history of stroke, hyperfibrinogenemia, elevated Ht, ipsilateral stenosis 90%≥, contralateral stenosis 70%≥ or occlusion, brain CT, intraoperative shunting, CEA of left internal carotid artery, skill of vascular surgeons.

RESULTS

During the 5-year interval (1995–1999), carotid endarterectomies were performed in 110 asymptomatic patients. The mean age of the patients was 65.5 ± 0.8 years, with a range of 41 to 82 years. There were 85 men (68%) and 35 women (32%). Twelve-percent of the patients were older than 75 years. Patients' characteristics are summarized in Table 1. Hypertension was present in 71, coronary artery disease in 40, tobacco usage in 63 and hyperlipidemia in 46 cases. Of the 110 carotid endarterectomies, 12 (11%) were performed in symptom-free patients, 56 (51%) procedures for nonhemispheric symptoms and 42 (38%) carotid endarterectomies for the contralateral carotid symptoms (Table 2).

Overall, there were four deaths (3.6%) and two (1.8%) strokes (Table 2). The combined stroke or death rate in this series was 5.4%. Of the four deaths that occurred in this series, three deaths were due to major ischemic stroke in the territory of the operated carotid artery and one to intracerebral hemorrhage. Perioperative cardiac complications were also documented in the entire patient group. One patient suffered non Q-wave myocardial infarct and one patient developed congestive heart failure. The incidence of cardiac complications was 1.8%.

The data on the appropriateness of CEA are summarized in Table 3. Acceptable indications for CEA were found in 85% of patients (93/110), whereas 7% had indications considered uncertain (8/110),

Table 1. **Selected characteristics of patients**

	Characteristic	Cases (n = 110)	
		N %	%
1.	Age 75>y	13	12
2.	History of hypertension	71	65
3.	History of angina pectoris	40	36
4.	History of myocardial infarction	32	29
5.	Cardiac dysrhythmia	4	4
6.	History of CHF	3	3
7.	Prior CABG/angioplasty	12	11
8.	Current cigarette use	63	57
9.	Diabetes mellitus	14	13
10.	Claudication	20	18
11.	Hyperlipidemia	46	42
12.	Obesity	25	23

CABG – coronary artery bypass grafting, CHF – coronary heart failure.

Table 2. **Mortality and complication rates according to operative indication**

Indication		Mortality	Non fatal stroke	Cardiac complications	Total	
		No.	No.	No.	No.	%
Symptom free	n = 12	0	0	0	0	0
TIA in v/b	n = 36	0	0	0	0	0
Stroke in v/b	n = 20	1	1	0	2	10
Contralateral carotid stroke	n = 42	3	1	2	6	14

v/b – vertebrobasilar system.

Table 3. **Appriopriateness of carotid endarterectomy**

Level of appropriateness	Stenoses, %	No. of cases	Total %	Complications	
				No.	%
Appropriate	≥75	93	85	6	5.4
Uncertain	50–74	8	7	0	0
Inappropriate	<50	9	8	0	0
	110	100	6	5.4	

and inappropriate surgical indications were found in 8% of patients (9/110).

Operative experience was analyzed with respect to each surgeon's overall and average annual operative experience. The number of CEAs performed by surgeons varied from 7 to 27 annually. Surgeons were separated into two groups according to whether or not they performed an average of one CEA per month during the time they were practising in the hospital (Table 4). Only 3 of the 7 surgeons performed not less than 10 CEAs annually. Stroke and death rates among different surgeons varied from 0% to 12.5 %, although both extremes were from surgeons performing <10 CEAs each during the study period. There was no statistically significant correlation (p = 0.059) between the number of CEAs performed by each individual surgeon and the combined stroke-mortality rates, witch varied from 0% to 25% (for one surgeon who performed eight CEAs). The operative stroke rates of two groups did not differ significantly. Overall, combined stroke-mortality rates were better for the more active surgeons, but the difference did not reach statistical difference.

Significant risk factors for stroke or death were determined by univariate analysis, and data of multiple logistic regression are summarized in Table 5. Independent preoperative risk factors for stroke or death by multivariate analysis was diabetes mellitus, for cardiac complications – history of myocardial infarction.

DISCUSSION

A literature review of the studies that examined the results of CEA performed for asymptomatic carotid stenosis revealed the perioperative mortality and stroke of 0% to 3.2% (1). The 5.4% postoperative stroke or death rate in our asymptomatic patients (5.4%) was higher than the rate found in a review of asymptomatic studies and significantly higher than the corresponding (12%) rate found in ACAS (2, 3). The comparatively greater complication rate for our asymptomatic patients probably negated any overall benefit from CEA for this group of patients.

Table 4. **Operative complications *versus* annual surgical experience (1995 to 1999)**

Group	No. CEA/yr.	No. CEA	Death		Stroke		Combined stroke and death	
			No.	%	No.	%	No.	%
I	≥10	75	1	1.3	1	1.3	2	2.6
II	<10	35	3	8.5	1	2.8	4	11.4
		110	4	3.6	2	1.8	6	5.4

Table 5. **Significant risk factors for postoperative complications by multivariate analysis**

Risk factor	Adjusted risk % *vs* %	OR (95% CI)	P
1. Age >75 *versus* ≤75 years	0 100		
2. Hypertension *versus* none	88 12	3.7 (0.3–43.7)	0.29
3. Angina pectoris *versus* none	50 50	0.8 (0.1–6.3)	0.91
4. Diabetes *versus* none	38 62	11.5 (1.5–86.7)	0.01*
5. Stroke *versus* nonhemispheric or asymptomatic	67 33	3.8 (0.3–38.5)	0.25
6. Hyperfibrinogenemia *versus* none	50 50	1.1 (0.1–7.2)	0.91
7. Claudication *versus* none	33 67	0.6 (0.05–9.3)	0.78
8. ACIS *versus* ACID	50 50	1.8 (0.2–13.7)	0.54
9. Shunt used *versus* none	50 50	1.7 (0.2–13.1)	0.57
10. Surgeons 10≥ CEA *versus* <10 per year	38 62	0.1 (0.01–1.1)	0.06
11. Ipsilateral stenosis ≥90 *versus* <90	67 33	1.7 (0.2–13.3)	0.57
12. Contralateral stenosis ≥70 or occlusion *versus* <70	38 62	0.6 (0.06–7.1)	0.74

* Statistically significant.

This higher frequency of complications is unexplained, but it possibly may be related with technical performance or patient selection or may simply be a realistic overall portrayal of CEA as it is practiced in a community-based studies. Higher complication rates in these studies compared with randomized controlled trials are not unexpected. In randomized controlled trials artificial constraints such as stringent inclusion and exclusion criteria, generally excellent patient care and close patient follow-up may result in better outcomes than in routine clinical practise.

Several groups have described potential risk factors for surgical complications after CEA (2, 4, 6, 9). In 1975, Sundt et al. (4) provided evidence that patients with certain cardiovascular and neurological risk factors were at a highest risk for postoperative myocardial infarction and stroke. Some of these same risk factors have been confirmed statistically in a retrospective analysis of 463 CEA patients (5). The authors of the latter study found predictors that can stratify candidates for CEA at higher risk of stroke and cardiac complications: female gender, age over 75 years, history of congestive heart failure, CEA in combination with coronary surgery. In ACAS, several baseline variables emerged as significant predictors of perioperative complications. Diabetes mellitus, contralateral siphon stenosis and never drinking were associated with higher risk of perioperative stroke; prior history of stroke, contralateral stenosis greater than 60% and never drinking were associated with a higher risk of all perioperative complications combined. Of the operative variables, the length of external carotid artery plaque was associated with subsequent stroke and all-event rates; the use of local or regional anesthesia was associated with a higher risk of TIA and MI (6). Our analysis of a smaller group of patients identifed only diabetes mellitus as a preoperative independent variable associated with stroke or death.

In patients who are the candidates for vascular surgery, the prevalence of coexisting coronary lessions is high (7, 8). The risk of myocardial infarction after CEA in symptomatic patients has been reported but varies in different settings (5, 9). Fatal perioperative myocardial infarction varies in incidence from 1% to 1.7% (10, 11). A routine of preoperative noninvasive cardiac investigation is generally adequate to identify patients at the risk of future coronary events (12). The preoperative investigation must include careful history taking with particular emphasis on previous myocardial infarction, past or persisting angina, decreased exercise tolerance, other evidences of past or persisting congestive failure and history of or persistence of rhythm disorder. ECG and chest radiography to ascertain heart size should be routine (13, 14). A transthoracic and, when indicated, a transesophageal echocardiogram, a stress test and rhythm monitoring should be obtained in doubtful cases. The risk in the postoperative period of cardiac complications was higher in patients who had CEA in comparison to medically treated patients within the same period (15). These comparisons suggest that most of the cardiovascular complications were triggered by the procedure. Previous studies have also identified an increased incidence of cardiac complications. Wong et al. (16) reported at least complications of angina, myocardial infarction, congestive heart failure or dysrhythmia in 8.9% of 291 patient. **We had no fatal cardiac complications and the occurrence of perioperative myocardial infarction was uncommon (0.9%).** Nevertheless, since CEA is a relatively common vascular procedure, neurologist and surgeons must strive to reduce the incidence of postoperative complications to an absolute minimum. Special attention to risk factors, detailed preoperative cardiac investigations can reduce complications in high-risk patients. Although risk factors for cardiac complications alone after CEA have been less commonly studied in the literature, patients undergoing CEA frequently harbor occult or symptomatic cardiac disease (17). Our present study identified history of myocardial infarction as an independent preoperative variable predictive of cardiac complications after CEA. The detection of these risk factors may allow the preoperative identification of high-risk patients who may then be given more intensive perioperative monitoring or treatment.

Assessments of the appropriateness of CEA in surgical series are rare. C. M. Winslow and colleagues (18) examined the surgical indications of 1302 Medicare patients who underwent CEA and determined that 75 underwent CEA inappropriately: 48 of this group underwent surgery for minimal carotid stenosis, 11 were at excessively high preoperative risk, 9 had cerebrovascular symptoms contralateral to the oprated side and 6 received surgery for carotid occlusion.

On a smaller scale, J. W. Asaph and colleagues (19) found that in a retrospective community surgical audit of 243 patients, 37 of them underwent surgery for <80% asymptomatic stenosis. After these results were published, the indications for CEA were restricted. As a result, there was a drop in the number of operations performed, the surgical complication rate and the number of "inappropriate" operations for asymptomatic carotid stenosis.

Such concerns over the appropriateness of CEA, along with its unproven efficacy and possible excessive use, resulted in the initiation of a number of ramdomized controlled CEA trials, including

asymptomatic American Veterans Affairs Trials and ACAS (3, 20). The published results of ACAS study have supplied evidence to support indications for CEA for asymptomatic carotid disease, and they also provided benchmarks for acceptable complication rates associated with such indication. As this trial demonstrated, major strokes were not prevented, women did not appear to benefit from CEA, and the overall positive result for surgery was only realized with a very low (2.3%) perioprative stroke and death rate. Because the benefit of CEA for asymptomatic stenosis seems marginal and dependent on both the patients treated and a very low operative complication rate, we decided *a priori* in our analysis that stenosis < 75% would be considered uncertain or inappropriate. We determined that CEA was not overused in our hospital because of the inappropriate or uncertain indications (15%).

Although we found no correlation between the case loads of individual surgeons and surgical outcome, the perioperative complication rate of 3 surgeons who did 10 CEAs and more per year was lower than that of surgeons who performed the operation less frequently. Thus a greater number of surgeons performing CEAs with greater frequency may have played a role in decreasing the overall stroke rate.

Similar observations have been made in community surveys from Cincinnati and Cleveland. In 1986, Kempczinski et al. (21) reported that the combined stroke rate of surgeons who performed more than 50 CEAs annually was lower than that of surgeons who did not (3.5% *vs* 6.6%), but the difference between the two groups was not statistically significant. However, when W. S. Moore (22) reanalyzed the results of this study, separating the data into three subgroups based on increasing surgical activity, 5.5 CEA/year, 19.7 CEA/year and 76.6 CEA/year, a strong trend toward improved results with greater operative activity became apparent ($p = 0.07$). In a large community survey by Rubin et al. (23), involving more than 8000 CEAs performed by members of the Cleveland Vascular Society, statistically improved stroke rates were reported for members who performed a minimum of 15 CEAs per year compared with those who did fewer cases (1.7% *vs* 3.4%, $p < 0.0001$). These studies and ours support the thesis that an active surgical practice reduces the risk of perioperative stroke.

CONCLUSIONS

1. The combined rate of uncertain and inappropriate indications of CEA for asymptomatic patients was not high in our hospital.

2. The observed high number of complications suggets restricting the use of CEA for our asymptomic patients.

3. The preoperative identification of high-risk patients through risk factor analysis may offer an opportunity to reduce the complication rates.

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ASIMPTOMINĖS VIDINĖS MIEGO ARTERIJOS ENDARTEREKTOMIJOS INDIKACIJŲ TINKAMUMAS IR OPERACINIŲ KOMPLIKACIJŲ RIZIKOS VEIKSNIAI

S a n t r a u k a

Tikslas. Vadovaudamiesi vidinės miego arterijos endarterektomijos rezultatais, gautais tarptautinių randomizuotų klinikinių studijų, ištyrėme mūsų ligoninėje indikacijų parinkimą miego arterijos endarterektomijai asimptominiams asmenims ir nustatėme pooperacinių mirčių, insultų ir širdies komplikacijų dažnį bei jų išsivystymo rizikos veiksnius.

Metodika. Atlikome perspektyvinę miego arterijų endarterektomijų Vilniaus greitosios pagalbos universitetinėje ligoninėje studiją per 5 metus. Remiantis JAV Širdies asociacijos klinikinės praktikos rekomendacijomis, asimptominei miego arterijos endarterktomijos indikacijos buvo suskirstytos į šias kategorijas: priimtinos, kai vidinės miego arterijos stenozė ≥75%, abejotinos, kai stenozė <75%–50%, nepriimtinos – mažiau kaip 50%.

Rezultatai. Priimtinos chirurginės indikacijos nustatytos 85% ligonių (93/110). Insultas ir mirtis įvyko 5,4% (6/110), kardiologinės komplikacijos – 2 ligoniams (1,8%). Cukrinis diabetas buvo nepriklausomos pooperacinių komplikacijų rizikos veiksnys ligoniams, operuotiems dėl asimptominės vidinės miego arterijos.

Išvados. Abejotinos ir netinkamos asimptominės miego arterijos endarterektomijos indikacijos nėra dažnos mūsų ligoninėje. Galimas daiktas, kad didelis miego arterijos endarterektomijos komplikacijų skaičius paneigia operacijos naudą asimptominiams asmenims.

Raktažodžiai: asimptominė miego arterijos stenozė, miego arterijos endarterektomija, komplikacijos, rizikos veiksniai