The Timing of Carotid Endarterectomy Post Stroke

Eli M. Baron, MD, Darric E. Baty, MD,
Christopher M. Loftus, MD, DHC (Hon.), FACS*

KEYWORDS

• Stroke • Endarterectomy • Acute intervention

The timing of carotid endarterectomy (CEA) post stroke remains a controversial area. Based on reports of hemorrhage and increased stroke rates with early surgery,[1–5] most authorities have advocated waiting at least 2 to 6 weeks after stroke before performing a CEA. More recently, prospective studies, meta-analyses of existing data, and review of the North American Symptomatic Carotid Endarterectomy Trial and European Carotid Surgery Trial have challenged these recommendations.[6–8] This article reviews the background leading to advocacy of delayed CEA after stroke, current literature recommendations regarding CEA after subacute stroke, current literature regarding neuroradiologic imaging findings and their implications in decision making regarding CEA after stroke, and the role of CEA for stroke in evolution.

BACKGROUND REGARDING DELAYED SURGERY

Most of the early literature regarding CEA after a stroke supports performing CEA in a delayed manner. In 1963, before the advent of CT scanning, Bruetman and colleagues[3] published a series of 900 patients undergoing CEA, six of whom had postoperative cerebral hemorrhage; this was confirmed at autopsy (5) or surgery for removal of a suspected clot (1). They noted that 5 of the 6 had a new neurologic deficit at the time of surgery; two of these patients had deteriorated after angiography and were taken to the operating suite emergently. Three of four patients (including one patient who did not have a preoperative neurologic deficit) had abnormal preoperative electroencephalograms (EEGs). The intracerebral hemorrhages (ICHs) occurred in a delayed fashion—3 to 6 days after surgery—and all patients were improving neurologically, even ambulatory, at the time of their acute deterioration. The investigators suggest that patients post recent ischemic event, ''be allowed to stabilize for at least one to two weeks and serial EEG be obtained as a monitor of the damaged area.'' They also state that their findings support the theory of Adams and Fischer,[9] that the reason for ICH was restoration of blood flow into a recently ischemic area.

One year later, Wylie and coworkers[1] described their experience with nine patients who had acute stroke undergoing CEA. They noted a 56% (5/9) fatal ICH rate in this group of patients, although their overall mortality rate after surgery for transient ischemic attacks (TIAs) or chronic cerebral insufficiency was 5%. Four of the patients were operated 3 to 10 days after a probable cerebral infarction, and the fifth was 22 days out from the initial stroke. No single patient was symptomatic from the ICH immediately after the operation; the time to symptom onset ranged from 2 hours to 3 days. Wylie and coworkers noted that, ''There appears to be a critical period following cerebral infarction during which restoration of flow of blood may cause serious or fatal intracranial hemorrhage adjacent to the infarcted zone and that reconstructive vascular operations may be performed safely during this period only when infarction has not

This article originally appeared in the November 2006 issue of Neurologic Clinics.
Temple University School of Medicine, Department of Neurosurgery, #580, Parkinson Pavilion, 3401 N. Broad Street, Philadelphia, PA 19140, USA
* Corresponding author.
E-mail address: cloftus@temple.edu (C.M. Loftus).

Neurosurg Clin N Am 19 (2008) 425–432
doi:10.1016/j.nec.2008.07.010
1042-3680/08/$ – see front matter

occurred. Additional clinical and experimental observations are now needed to define more accurately the limits of this critical period.'' They cited the experimental work of Meyer[10] on monkeys, in which minimal perivascular hemorrhage was seen in pial vessels adjacent to experimental infarction as early as 24 hours after infarct. Although microscopic hemorrhage was seen, gross, extensive hemorrhage was seen only when animals were given anticoagulants or with wide blood pressure fluctuations.

Data from the Joint Study of Extracranial Arterial Occlusion also seemed to support the practice of delayed surgery after stroke.[4] In one subgroup of patients who had acute stroke and altered mental status, the postoperative mortality was twice that of the medically treated group (42% versus 20%, respectively) when surgery was performed within 2 weeks of the onset of neurologic symptoms. The investigators noted that CEA performed 14 days after stroke was associated with better outcomes (17% mortality) than the medically treated group but also noted that the groups were not really comparable because many of the patients in the medically treated group had expired before 14 days had passed.

Harrison and Marshall[11] note that in their series of patients undergoing CEA less than 4 weeks after their most recent TIA, 66% (16/24) had thrombus or friable material present at surgery or in the pathologic specimen, whereas only 21% (6/28) of persons more than 4 weeks from their most recent TIA had such findings. This may suggest an increased risk of intraoperative carotid-origin embolus in patients undergoing CEA early after stroke.

Looking further at the risk for ICH after CEA, Caplan and coworkers[12] published a report of two cases in which preoperative near-carotid occlusion and postoperative hypertension preceded fatal ICH. The investigators believed that uncontrolled postoperative hypertension and prior stroke were causative factors of the ICH and emphasized (again) that postoperative hemorrhages seem to occur in a delayed fashion. They conclude that this delay, and the almost universal neurologic improvement of patients before ICH, made the prior explanation of abnormal capillary permeability in an area of infarcted or ischemic brain receiving a sudden increase in blood flow untenable. Rather, they believed the hemorrhage to be related to the development of new-onset hypertension in the face of susceptible (dysautoregulated) vascular beds near the ischemic zone that were previously ''protected'' by the stenotic vessel. They argued that CEA is not safe in hypertensive patients who had a cerebrovascular accident, even up to 5 weeks after the event, as their patients were 4 and 5 weeks out from their strokes.

More recently (but still 20 years ago), Giordano and colleagues[2] published their series of patients undergoing early (within 5 weeks) and delayed (greater than 5 weeks) surgery. The patients in the early surgery group had a statistically significant, increased postoperative stroke rate, at 18.5% (5/27), whereas those in the delayed surgery group experienced no strokes. Only one of the postoperative strokes was noted to be a hemorrhagic infarction. The investigators conclude that surgery after a stroke is contraindicated within 5 weeks of the neurologic event. Nevertheless, in a critical look at their data, Paty and coworkers[13] note that one of the reported subsequent strokes occurred in the cerebral hemisphere contralateral to the initial infarction and that there were no strokes in the 9 patients treated within 2 weeks of prior infarction, questioning the significance of Giordano and colleagues' conclusions.

TIMING OF SURGERY IN PATIENTS WHO HAVE STABLE, NONDISABLING, OR MILDLY DISABLING STROKES

Despite the aforementioned concerns in years past that, to reduce complications, a waiting period post stroke of at least 4 to 6 weeks is optimal before performing CEA, the vast majority of studies in the past 20 years have demonstrated no increased risk of infarction for early CEA after stroke. Rather, they suggest a distinct benefit (in terms of preventing recurrent stroke during medical observation) to quick surgical intervention. The early reports detailing high mortality rates from ICH described heterogenous groups of patients, many of whom had severe neurologic deficits and probable hemorrhagic complications preoperatively. The lack of brain imaging techniques at the time of many of the reports makes it impossible to determine with any accuracy the extent of preexisting infarction or hemorrhage.[14] Compelling evidence now exists to suggest that patients may benefit from endarterectomy performed shortly after symptoms have stabilized (in the subacute phase), in patients who have nondisabling or mildly disabling strokes.

Current evidence suggests that surgical delay, and any arbitrarily assigned waiting before consideration of CEA after stroke, seems to leave patients at great risk for recurrent cerebral ischemia. Dosick and colleagues[15] report a 9.5% stroke rate (new dense neurologic deficit) in surgical candidate patients undergoing a 6-week waiting period post stroke. Similarly, in the North American Symptomatic Carotid Endarterectomy Trial, 4.9%

of the 103 medically treated patients diagnosed with stroke and severe internal carotid artery stenosis experienced a recurrent ipsilateral stroke within 30 days of trial entry.[16]

Whittemore and coworkers[17] confirm the feasibility of performing CEA within 4 weeks of stroke in 28 patients sustaining small fixed, neurologic deficits. They reported a mean time from onset of stroke to surgery of 11 days and also that 53% of patients were operated on within 7 days of onset of symptoms. Postoperatively, there was one death resulting from pulmonary embolism and no patient sustained a new stroke. Rosenthal and coworkers[18] noted a seemingly protective effect of CEA against stroke when performed on patients sustaining a reversible ischemic neurologic deficit or stroke. Twenty-nine of their patients who had limited stable strokes and abnormal CT scans underwent CEA within 3 weeks of their event, whereas 75 patients who had strokes and significant infarction on CT scan underwent surgery greater than 3 weeks after their events. Of these, those undergoing surgery less than 3 weeks from onset of stroke had a 3% recurrent stroke rate whereas those undergoing surgery greater than 3 weeks from stroke had a recurrent stroke rate of 5.3%. In the 10-year follow-up, the cumulative incidence of recurrent stroke was 7% in the endarterectomy group versus 18% in a nonoperative control group.

In a retrospective study of 129 patients experiencing stroke, Piotrowski and colleagues[19] note no significant difference in cerebrovascular events or death between patients operated on within 6 weeks and more than 6 weeks after stroke. For the group operated with early surgery, the investigators waited until neurologic recovery reached a plateau, as determined clinically by a neurologist (76% of these patients had surgery within 4 weeks of their event). They conclude that early CEA could be performed without an increase in morbidity or mortality after stroke as long as neurologic recovery has reached such an equilibrium.

In a retrospective analysis of 100 patients entered in to the North American Symptomatic Carotid Endarterectomy Trial who had severe (70%–99%) angiographically defined carotid artery stenosis, Gasecki and coworkers[16] studied patients who were operated on within 30 days of stroke versus those operated beyond 30 days. They note the baseline clinical characteristics of the groups to be comparable and they note similar postoperative complication rates, with the group undergoing early CEA having a slightly lower complication rate (4.8% in the early group and 5.2% in the delayed group). They conclude, ''Delaying the procedure by 30 days for patients with symptomatic high-grade stenosis exposes them to risk of a recurrent stroke, which may be avoidable by earlier surgery.''

Hoffman and Robbs[20] performed a retrospective study in which they compared 86 patients who underwent early CEA (less than 6 weeks) for stable strokes with minor deficits or crescendo TIAs with stroke to 121 patients who had strokes and underwent delayed CEA. There were no statistical differences regarding baseline medical comorbidities, neurologic deficits, or degree of carotid stenosis. No significant differences were seen between groups in postoperative morbidity (defined as myocardial infarction and stroke) or mortality, although the odds ratio of morbidity and mortality of the delayed group over the early group was 1.6. The investigators thus advocated reconsideration and abandonment of the dogmatic 6-week waiting period for CEA post stroke.

Many of the series discussed in this article were studied in an important Mantel-Haenszel meta-analysis performed by Bond and coworkers.[7] Using pooled studies performed between 1980 and 2000, they noted 11 studies comparing early (<3 to 6 weeks) versus late (>3 to 6 weeks) CEA in patients who had stable symptoms post stroke. Using their methodology, 794 patients were studied in the early group and 3424 patients were studied in the late group. An odds ratio of 1.13 regarding stroke or death was calculated in the early group (stroke or death rate of 5.04%) versus the group undergoing later surgery (stroke or death rate of 4.26%) ($P = 0.62$). They conclude, ''There was no excess risk associated with early vs. late CEA in patients with stable symptoms.''

Ballotta and colleagues[6] performed a prospective randomized trial, in which patients underwent CEA within 30 days (n = 45) or more than 30 days (n = 41) after nondisabling ischemic stroke. The mean ipsilateral stenosis rate was 85% in those undergoing early operation, whereas the mean ipsilateral rate of stenosis was 83% in those undergoing later operation. The presence of an ulcerated plaque was noted in 33% of those patients undergoing early operation and in 27% of patients undergoing delayed operation. Both groups were noted to have 2% perioperative stroke rates and similar 3-year survival rates. The investigators conclude that, ''Early CEA after a nondisabling ischemic stroke can be performed safely with perioperative mortality and stroke rates comparable with those of delayed CEA. The timing of surgery does not seem to influence the benefit of the CEA.''

Wolfle and coworkers[21] note similar results in a retrospective series of 66 patients who were neurologically stable and undergoing CEA for greater than 50% symptomatic stenosis after a mean interval of 10 days post stroke. They

reported an operative mortality of 0% and (mostly) transient neurologic worsening in 5 (12.1%) patients, with resolution of symptoms within 4 days in 80%. Thus, only one patient (1.5%) sustained a permanent deficit. They noted stroke severity on admission, as graded by the modified Rankin scale, to be a significant determinant of postoperative outcome. "While 6/23 patients (26%) with an initial deficit > or = 3 on the modified Rankin scale developed neurologic worsening, this was the case in only 2/43 patients (4.6%) with a deficit < or = 2 (Odds Ratio 7.2; 95% CI, 1.32–39.49; two-sided $P = 0.01$)." They conclude that patients who have minor strokes could undergo early CEA safely.

Patients who have stroke of carotid origin are at highest risk for recurrent ischemia within the first 2 weeks. Perhaps the largest data pool regarding the timing of CEA after stable stroke was analyzed by Rothwell and coworkers[8] in their analysis of data from the European Carotid Surgery Trial and North American Symptomatic Carotid Endarterectomy Trial. A total of 5893 patients with 33,000 patient-years of follow-up were studied, with patients randomized to medical treatment or surgery at intervals of less than 2 weeks (20.1%), 2 to 4 weeks (17.9%), 4 to 12 weeks (39.2%), and greater than 12 weeks (22.8%) from patients' last symptoms. Entry neurologic events included ocular symptoms only (19.8%), TIAs (35.8%), and nondisabling ischemic strokes (44%). A total of 3157 patients underwent surgery. In patients who had greater than or equal to 70% carotid stenosis, risk reduction of ipsilateral ischemic stroke was greatest over 5 years in those who had experienced prior stroke (absolute risk reduction of 17.7%) and least in those experiencing ocular symptoms alone (absolute risk reduction of 5.5%).

The 5-year risk reduction for ipsilateral ischemic carotid stroke seen in the surgical arm was greatest in patients randomized within 2 weeks of symptoms (23.0%) and tapered off with increasing time for the other groups (reductions of 15.9%, 7.9%, and 7.4%, respectively). The cumulative 5-year absolute risk reduction for ipsilateral stroke, any stroke or death within 30 days of surgery, for those patients who had greater than or equal to 70% stenosis (but not nearly occluded) was 30.2% for the group randomized within 2 weeks of symptoms, 17.6% for the group randomized within 2 to 4 weeks of symptoms, 11.4% for those randomized within 4 weeks after symptoms, and 8.9% for those randomized 12 weeks after symptoms. The fall-off in benefit of CEA seen with time was highly significant ($P = 0.009$). The investigators conclude, "The procedure should be ideally done within 2 weeks of the patient's last symptoms."

IMAGING FINDINGS AND THEIR RELATIONSHIP TO THE TIMING OF SURGERY

Can imaging data predict patients at risk for postoperative complications and allow choosing the best surgical candidates? After the introduction of readily available CT scanning, a great deal of effort has gone into using this technology to risk stratify patients and, ultimately, predict which patients benefit from early versus delayed surgery. Negative CT scans are one encouraging sign. Dosick and colleagues[15] find that in patients who have neurologic deficits lasting longer than 24 hours and appropriate carotid lesions at angiography, negative serial preoperative CT scans were predictive of a 0% mortality and a 0.9% (1/110) morbidity (one postoperative stroke in a vascular territory separate from the operated artery) in their series of patients operated on within the first 14 days. Unlike the authors' preference,[22] they used an indwelling carotid shunt in every case, regardless of other factors usually used for selective shunting, such as stump pressures, EEG findings, back-bleeding, or neurologic examination. In the group of patients who had positive CT scans, 9.5% (7/74) had at least one event while waiting for delayed surgery at 4 to 6 weeks; angiography revealed significant lesions in 69% (51/74) of this subgroup, and all patients who had additional neurologic events had positive angiograms. The postoperative stroke rate was 2.0% (1/51).

Little and coworkers[23] analyzed a subgroup of CEA patients who had surgery within 30 days of onset of their neurologic symptoms. They conclude that patients who have negative CT scans and minimal residual neurologic symptoms are at low risk for early surgery, perhaps even approaching the risk of patients presenting with TIAs alone; of the 22 patients in this subgroup, none experienced new postoperative permanent neurologic deficits. Patients who had positive scans and moderate, stable neurologic deficits were at intermediate risk. In addition, two patients who had repeat TIAs and normal CT scans had an uncomplicated postoperative course. The high-risk category comprised patients who had deteriorating neurologic examinations and positive CT scans. Two of three patients in this subgroup had postoperative extension of their infarctions and one patient died, representing 66% morbidity and 33% mortality rates.

Despite Little and colleagues[23] having advocated early surgery only in the presence of normal cranial imaging findings, most series looking at brain CT stroke-related imaging findings fail to

note a substantial correlation in relation to outcomes of patients undergoing CEA post stroke. In their series of 66 patients undergoing CEA after stroke, Wolfle and coworkers[21] note, ''no correlation between timing of surgery or the presence of acute ipsilateral cranial CT defects with the occurrence of postoperative stroke.'' Similarly, in their study of 200 patients undergoing CEA within 6 months of a stroke, Paty and colleagues[13] note, ''no correlation between timing of surgery, extent of infarct on computed tomography/magnetic resonance imaging, and postoperative neurologic complications with the occurrence of postoperative stroke.'' Gasecki and colleagues[16] also note that, ''No association was found between an abnormal preoperative computed tomography scan result and the subsequent risk of stroke when early operation was used.'' Nevertheless, this indifference to positive CT findings may be only in the presence of stable symptoms; in their retrospective study, Ricotta and coworkers[24] note CT findings of prior infarction not correlated with neurologic deficits postoperatively but noted a significant increase in neurologic morbidity and mortality in those patients who had positive CT scans undergoing urgent CEA in the presence of acute neurologic deterioration.

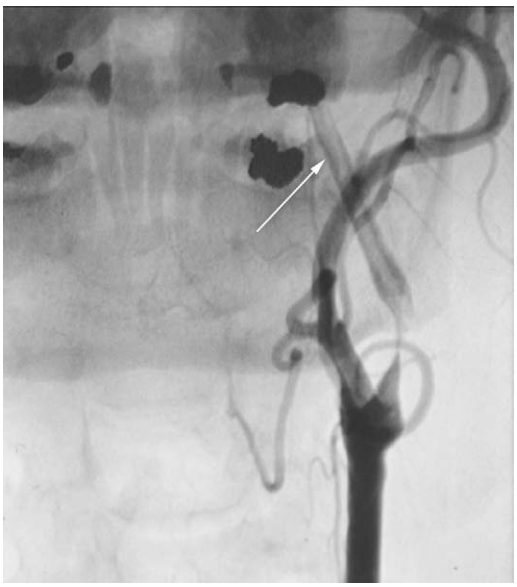

Fig. 1. Anteroposterior view of left common carotid injected angiogram demonstrating a high-grade stenosis of the left internal carotid artery. Also seen is evidence of a thrombus (*arrow*) extending from the distal plaque into the skull base. Subsequently this patient was anticoagulated and brought back 6 weeks later for routine CEA.

SURGERY IN PATIENTS WHO HAVE CRESCENDO TRANSIENT ISCHEMIC ATTACKS OR STROKE IN EVOLUTION

The indications for urgent or emergency CEA are controversial. Given that the risk of CEA is significantly higher in patients who are neurologically unstable versus patients who are neurologically stable,[25] emergency surgery should be indicated only if it offers improved outcomes over medical treatment.[26] Regarding crescendo TIAs, there are reports of patients doing well with emergency surgery.[27–29] Equally compelling reports exist with good results in patients undergoing anticoagulation followed by delayed CEA.[30,31] Given the lack of a direct comparison of emergency surgery versus anticoagulation initially and the lack of compelling evidence of the superiority of emergency CEA over initial anticoagulation followed by CEA, some experienced investigators recommend treatment of crescendo TIAs with anticoagulation and delayed CEA, with emergent CEA indicated only for those who have progressive symptoms despite anticoagulation.[26] The authors' policy differs from this: crescendo TIAs are treated urgently, once they have been heparinized, and operations are within 24 hours on patients who are fully heparinized. The only exception is when a propagating intraluminal thrombus beyond the reach of the surgical field is identified (**Fig. 1**). These patients have a very high surgical risk (from operative carotid manipulation and dislodgment) and the preference is to anticoagulate them for 6 weeks and return for delayed routine CEA at that time.[22,32]

CEA for acute stroke and stroke in evolution also is controversial. In general, the severity of acute neurologic deficit at the time of surgery is the greatest risk factor for poor outcomes.[26] Acute stroke with associated debilitating fixed deficits or changes in level of consciousness generally are considered contraindications to CEA; patients undergoing emergent CEA for stroke with profound deficits are reported to have mortalities ranging between 20% and 37%.[33,34] Nevertheless, Meyer and colleagues,[33] in their series of patients undergoing emergent CEA for carotid occlusion presenting with severe neurologic deficits, note 38% of their patients made a dramatic recovery. They conclude, ''An emergency carotid endarterectomy may be indicated in selected patients with acute internal carotid artery occlusion with profound neurological deficits.''

The overall data, however, may not support a general policy of emergency CEA for unselected patients who have stroke in evolution or crescendo TIAs. In their meta-analysis looking at 13 studies reporting results for patients undergoing emergency CEA for crescendo TIAs, stroke in evolution,

or "urgent" CEA, Bond and colleagues[7] calculate an overall odds ratio of 4.9 (3.4–7.1; 95% CI) of stroke or death over stable stroke patients undergoing CEA. Given that the overall risk of stroke and death, based on their calculations, was approximately 20%, they note that the data do not seem to support a policy of urgent CEA for any of the indications discussed previously.

More recently, some investigators advocate urgent surgery in highly selected patients for acute stroke and stroke in evolution,[35–39] as clearly it does reduce the risk of further progression of symptoms by removing a source of further emboli and increasing flow to the ischemic penumbra.[40] These investigators also report a 1-month mortality, ranging from 0 to 9.5%. Schneider and coworkers report excellent results in a retrospective study of 43 patients undergoing emergent CEA in the setting of stroke with profound deficits, stroke in evolution, crescendo TIAs, and prolonged reversible ischemic neurologic deficit compared with a control group of 237 patients who had greater than or equal to 70% carotid stenosis undergoing elective CEA. The investigators excluded patients from the emergent group who were comatose or who had signs of acute hemorrhagic or ischemic infarction on preoperative CT scan. Outcomes of both groups at 90 days statistically were not different, with none of the patients who were operated on emergently experiencing a new-onset stroke or death. Additionally, any major preoperative deficits seen in the emergent group had resolved by 90 days.

Gay and coworkers[39] report good results in 21 patients who underwent carotid artery repair less than 24 hours after diagnostic work-up for crescendo TIAs (5 cases), fluctuating neurologic deficits (11 cases), and stroke in evolution (5 cases). Two deaths were noted within 30 days, but survival rates at 1 and 5 years were 90% and 62%, respectively, with neurologic deficit-free rates at 1 and 5 years being 95% and 76%, respectively. Their work-up included CT in 15 cases, with infarction noted in 13 cases. They note in their discussion that patients suffering ongoing attacks with moderate deficit may be candidates for urgent repair even if the CT scan depicts infarction. They also note that the decision to perform urgent CEA should be made on a case-by-case basis and that patients experiencing a frank stroke with severe symptoms or disturbances in consciousness most likely would not benefit from CEA. Likewise, Van der Mieren and colleagues[35] advocate urgent CEA in selected patients but note absolute contraindications to be coma, ICH, and CT scan depicting infarction in more than one third of the middle cerebral artery territory. Others suggest that evidence of blood-brain barrier damage on CT scan or MRI resulting from acute stroke also may contraindicate emergent CEA.[41]

SUMMARY

Despite the earlier accepted notion that CEA should be delayed 4 to 6 weeks after a stroke, current evidence suggests that CEA may be performed safely earlier than this in most patients who have mild to moderate deficits once symptoms stabilize. The gray areas, however, remain gray, as outlined. Crescendo TIAs are urgent cases in the authors' practice; others advocate a more moderate delayed approach in such cases. Almost everyone agrees that propagating intraluminal thrombus is treated best with a moderate delayed approach that allows the thrombus to resolve first with anticoagulants. Acute carotid occlusion must be assessed on an individual basis: cases that occlude under observation should be explored immediately; cases that come from the field with profound deficits have dismal outcomes, but even here surgery may be effective in salvaging a small group of good functional survivors, and the natural history without surgery is atrocious. Surgery for stroke in evolution is associated with higher morbidity and mortality rates; selected patients may benefit from emergency surgery.

A final thought is that for patients who have routine TIA or small stroke, with minimal imaging evidence of infarction or mass effect, a stable deficit, and a normal level of consciousness, there is no reason to empirically delay carotid reconstruction, and patients are served best by a fast-track approach to surgical treatment.

REFERENCES

1. Wylie EJ, Hein MF, Adams JE. Intracranial hemorrhage following surgical revascularization for treatment of acute strokes. J Neurosurg 1964;21:212–5.
2. Giordano JM, Trout HH 3rd, Kozloff L, et al. Timing of carotid artery endarterectomy after stroke. J Vasc Surg 1985;2:250–5.
3. Bruetman ME, Fields WS, Crawford ES, et al. Cerebral hemorrhage in carotid artery surgery. Arch Neurol 1963;9:458–67.
4. Blaisdell WF, Clauss RH, Galbraith JG, et al. Joint study of extracranial arterial occlusion. IV. A review of surgical considerations. JAMA 1969;209:1889–95.
5. Thompson JE, Talkington CM. Carotid endarterectomy. Ann Surg 1976;184:1–15.
6. Ballotta E, Da Giau G, Baracchini C, et al. Early versus delayed carotid endarterectomy after

a nondisabling ischemic stroke: a prospective randomized study. Surgery 2002;131:287–93.
7. Bond R, Rerkasem K, Rothwell PM. Systematic review of the risks of carotid endarterectomy in relation to the clinical indication for and timing of surgery. Stroke 2003;34:2290–301.
8. Rothwell PM, Eliasziw M, Gutnikov SA, et al. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. Lancet 2004;363:915–24.
9. Adams RD, Fisher CM. Pathology of cerebral arterial occlusion. In: Fields WS, editor. Pathogenesis and treatment of cerbrovascular disease. Springfield (Illinois): Charles C Thomas; 1961.
10. Meyer JS. Importance of ischemic damage to small vessels in experimental cerebral infarction. J Neuropathol Exp Neurol 1958;17:571–85.
11. Harrison MJ, Marshall J. The finding of thrombus at carotid endarterectomy and its relationship to the timing of surgery. Br J Surg 1977;64:511–2.
12. Caplan LR, Skillman J, Ojemann R, et al. Intracerebral hemorrhage following carotid endarterectomy: a hypertensive complication? Stroke 1978;9:457–60.
13. Paty PS, Darling RC 3rd, Woratyla S, et al. Timing of carotid endarterectomy in patients with recent stroke. Surgery 1997;122:850–4 [discussion: 54–5].
14. Estes JM, Whittemore AD. Subacute carotid surgery in recent stroke patients. In: Loftus CM, Kresowik TF, editors. Carotid artery surgery. New York: Thieme; 2000. p. 209–13.
15. Dosick SM, Whalen RC, Gale SS, et al. Carotid endarterectomy in the stroke patient: computerized axial tomography to determine timing. J Vasc Surg 1985; 2:214–9.
16. Gasecki AP, Ferguson GG, Eliasziw M, et al. Early endarterectomy for severe carotid artery stenosis after a nondisabling stroke: results from the North American Symptomatic Carotid Endarterectomy Trial. J Vasc Surg 1994;20:288–95.
17. Whittemore AD, Ruby ST, Couch NP, et al. Early carotid endarterectomy in patients with small, fixed neurologic deficits. J Vasc Surg 1984;1:795–9.
18. Rosenthal D, Borrero E, Clark MD, et al. Carotid endarterectomy after reversible ischemic neurologic deficit or stroke: is it of value? J Vasc Surg 1988;8:527–34.
19. Piotrowski JJ, Bernhard VM, Rubin JR, et al. Timing of carotid endarterectomy after acute stroke. J Vasc Surg 1990;11:45–51 [discussion: 51–2].
20. Hoffmann M, Robbs J. Carotid endarterectomy after recent cerebral infarction. Eur J Vasc Endovasc Surg 1999;18:6–10.
21. Wolfle KD, Pfadenhauer K, Bruijnen H, et al. Early carotid endarterectomy in patients with a nondisabling ischemic stroke: results of a retrospective analysis. Vasa 2004;33:30–5.
22. Loftus C. Carotid endarterectomy: principles and technique. 2nd edition. New York: Taylor and Francis; 2006.
23. Little JR, Moufarrij NA, Furlan AJ. Early carotid endarterectomy after cerebral infarction. Neurosurgery 1989;24:334–8.
24. Ricotta JJ, Ouriel K, Green RM, et al. Use of computerized cerebral tomography in selection of patients for elective and urgent carotid endarterectomy. Ann Surg 1985;202:783–7.
25. Sundt TM, Sandok BA, Whisnant JP. Carotid endarterectomy. Complications and preoperative assessment of risk. Mayo Clin Proc 1975;50:301–6.
26. Amin-Hanjani S, Ogilvy CS. Indications and techniques for emergent carotid exploration. In: Loftus CM, Kresowik TF, editors. Carotid artery surgery. New York: Thieme; 2000. p. 303–13.
27. Mentzer RM Jr, Finkelmeier BA, Crosby IK, et al. Emergency carotid endarterectomy for fluctuating neurologic deficits. Surgery 1981;89:60–6.
28. Najafi H, Javid H, Dye WS, et al. Emergency carotid thromboendarterectomy. Surgical indications and results. ArchSurg 1971;103:610–4.
29. Walters BB, Ojemann RG, Heros RC. Emergency carotid endarterectomy. J Neurosurg 1987;66: 817–23.
30. Nehler MR, Moneta GL, McConnell DB, et al. Anticoagulation followed by elective carotid surgery in patients with repetitive transient ischemic attacks and high-grade carotid stenosis. Surg 1993;128: 1117–21 [discussion: 21–3].
31. Putman SF, Adams HP Jr. Usefulness of heparin in initial management of patients with recent transient ischemic attacks. Arch Neurol 1985;42: 960–2.
32. Loftus CM. Propagating intraluminal carotid thrombus - surgery or anticoagulation? In: Loftus CM, Kresowik T, editors. Carotid artery surgery. New Tork: Thieme; 2000. p. 321–8.
33. Meyer FB, Sundt TM Jr, Piepgras DG, et al. Emergency carotid endarterectomy for patients with acute carotid occlusion and profound neurological deficits. Ann Surg 1986;203:82–9.
34. DeWeese JA. Management of acute strokes. Surg Clin North Am 1982;62:467–72.
35. Van der Mieren G, Duchateau J, De Vleeschauwer P, et al. The case for urgent carotid endarterectomy. Acta Chir Belg 2005;105:403–6.
36. Schneider C, Johansen K, Konigstein R, et al. Emergency carotid thromboendarterectomy: safe and effective. World J Surg 1999;23:1163–7.
37. Peiper C, Nowack J, Ktenidis K, et al. Prophylactic urgent revascularization of the internal carotid artery in the symptomatic patient. VASA. Zeitschrift Gefasskrankheiten 2001;30:247–51.

38. Huber R, Muller BT, Seitz RJ, et al. Carotid surgery in acute symptomatic patients. Eur J Vasc Endovasc Surg 2003;25:60–7.
39. Gay JL, Curtil A, Buffiere S, et al. Urgent carotid artery repair: retrospective study of 21 cases. Ann Vasc Surg 2002;16:401–6.
40. Mead GE, O'Neill PA, McCollum CN. Is there a role for carotid surgery in acute stroke? Eur J Vasc Endovasc Surg 1997;13:112–21.
41. Brandl R, Brauer RB, Maurer PC. Urgent carotid endarterectomy for stroke in evolution. Vasa 2001; 30:115–21.