Rethinking The Six Weeks Waiting Approach To Carotid Intervention After Ischemic Stroke

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Citation

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Abstract

Atherosclerotic disease of extracranial carotid arteries is responsible for approximately 20% to 30% of strokes in North America each year. Currently, there are two treatment modalities for treatment of symptomatic carotid artery disease: Carotid endarterectomy (CEA) and Carotid artery stenting (CAS). Timing of carotid intervention after acute stroke is controversial. This text is meant to review literature on this controversial issue. Initially it was thought that any carotid intervention should not be done within six weeks after the onset of acute stroke, however newer data shows the risk of postoperative intracranial hemorrhage depends on the type of initial neurological defect, vascular territory of the stroke, infarct size, degree of midline shift on CT and the level of consciousness. We conclude that in appropriately selected patients, carotid intervention should be done as soon as possible after acute stroke.

INTRODUCTION

Atherosclerotic disease of extracranial carotid arteries is responsible for approximately 20% to 30% of strokes in North America each year. Currently, there are two treatment modalities for treatment of symptomatic carotid artery disease: Carotid endarterectomy (CEA) and Carotid artery stenting (CAS). Timing of carotid intervention after acute stroke is controversial. We will review literature on both of these treatment modalities and timing of treatment after acute stroke. The first successful CEA was performed by DeBakey in 1953. Currently, approximately 200.000 carotid endarterectomies are done in the US per year. CAS was first performed in 1994. Both single-center reports[1] and worldwide surveys[2] of CAS have demonstrated results approaching those of endarterectomy, typically in high-risk patients with significant comorbidities excluded from previous surgical trials[3].

PATHOPHYSIOLOGY

After carotid intervention has restored a normal carotid bifurcation lumen and normal blood flow, hyperperfusion will occur in the ipsilateral hemisphere until resistance vessels regain their ability to constrict and autoregulation is reestablished[4]. Post operative ipsilateral hyperperfusion can last as long as 11 days after endarterecomy. Because of the poor results of CEA in 1960, and reports of deaths from post operative intracranial hemorrhage[5], there has been a fear that early CEA after stroke might convert a non hemorrhagic stroke into a hemorrhagic stroke or increase the size of infarcted area. So an arbitrary time period of six weeks after stroke was chosen to be the optimal time for surgery, although there has been no scientific evidence to prove this myth.

Retrospectively, patients who developed postoperative intracranial hemorrhage had several features in common. They had high-grade carotid stenosis, and hypoperfusion based on physiologic measurements. Postoperatively, they had ipsilateral increased cerebral flow[7].

Incidence of post operative intracerbral hemorrhage ranges from 0.3% to 1.2%[8]. The risk factors include postoperative hypertension, history of previous cerebral infarction and postoperative anticoagulation[9].

LITERATURE AGAINST EARLY CEA AFTER STROKE

The first study which reported cerebral hemorrhage after CEA was a retrospective study of 900 patients who underwent CEA. Six patients had post operative cerebral hemorrhage, five out of these six had surgery between 2 and hours after angiography. All had this complication at 3 to 6 days after surgery. All vessels were patent postoperatively. The study concluded that the patients with recent cerebral infarction should wait for at least 1-2 weeks before they can

safely undergo CEA.[5]

Figure 1

Table 1: Reports against early CEA after stroke

Study	Year	Type of Study	No. of patients with cerebral hemorrhage after CEA	Total number of patients	Suggested wait time
DeBakey et al [5]	1963	Retrospective analysis	6	900	1-2 weeks.
Wylie et al [10]	1964	Retrospective analysis	5	179	
Blaisdell et al [11]	1969				At least 2 weeks
Caplan et al [12]	1978	Case report	2	2	6 weeks
Giordanoa et al [13]	1985	Retrospective analysis	5	330	5 weeks

Wylie et al. reported a series of 179 patients who underwent CEA. Five out of these patients developed cerebral hemorrhage after CEA. Two of these five patients had carotid stenosis, 3 had cerebral occlusion. In patients with carotid stenosis, the symptoms began after several hours in first case and after 3 days in second case. Autopsy of both patients showed patent carotid arteries and intracranial hemorrhage.[10] A joint study of extracanial arterial occlusion[11] compared the patients who had surgery within two weeks after the onset of stroke to those who had surgery after two weeks of the onset of acute stroke. Mortality was 42% for patients who had surgery within 2 weeks after stroke (vs. 5% mortality in patients who had surgery after 2 weeks of stroke). The study did not mention the number of patients undergoing CEA for a stenotic versus an occluded internal carotid artery lesion.

Caplan et al. [12] presented a case report of 2 patients who had CEA within 6 weeks of onset of acute stroke, both of them had post operative intracranial hemorrhage. They suggested to wait for at least 6 weeks after acute stroke.

Giordano et al. [13] reported a retrospective study including 303 endarterectomies. Forty-nine of them were performed on patients with a deficit lasting more than 24 hours. Of these, 27 carotid endarterectomies were performed in an interval less than 5 weeks after stroke (early interval) and 22 operations were performed in an interval of more than 5 weeks after stroke (late interval). Five strokes occurred in the 27 patients operated on within 5 weeks, an incidence of 18.5%; none of the patients operated on after 5 weeks exhibited worsening of their preoperative neurologic status.

LITERATURE IN FAVOR OF EARLY CEA AFTER STROKE

Figure 2

Table 2: Reports in favor of early CEA after stroke

Study	Year	Type of Study	No. of patients with cerebral hemorrhage after CEA	Total number of patients	Suggested wait time
Whittemore et al [13]	1985	Retrospective analysis	0	28	Within 7 days(average day 11)
Dosick et al [15]	1985	Retrospective analysis	0	245	Within 2 weeks (average day 10)
Pritz et al [16]	1986	Case report	0	3	Within 24 hours.
Khana et al [17]	1988	Retrospective analysis	0	774	Within one week.
Rosethal et al [18]	1988	Retrospective analysis	2	29	Within 3 –21 days
Little et al [19]	1989	Prospective clinical trial	2	27	Within 30 days(average day 14)
Pitrowski et al [20]	1990	Prospective clinical trial		129	No difference between < / > 6 weeks.
Gasecki et al [21]	1990	Retrospective		100	No difference between < / > 30 days.
Khan et al [22]	1999	Retrospective study		1065	Within 30 days.

Whittemore et al. [13] described a retrospective study of total 337 patients who underwent CEA. A subgroup of 28 patients who underwent surgery within 2 to 30 days after stroke was identified. Each of the patients in this subgroup had a small neurologic defect with >75% stenosis of the ipsilateral carotid artery. Fifteen (53%) of these patients had CEA within 7 days after stroke (average day 11). None of the patients deteriorated neurologically in the post operative period. One patient died of pulmonary embolus on postoperative day 2.

Dosick et al. [13] performed a retrospective analysis of 245 patients who underwent CEA between 1980 and 1983. Out of these patients, 110 patients underwent CEA within 14 days (mean 10 days) of the initial onset of their neurologic deficit. None of these patients had another neurological deficit within 30 days of surgery. The study concluded that CEA can be safely performed within 2 weeks of onset of acute stroke.

Pritz et al. [16] described a case report of 3 patients, who underwent CEA 1, 4 and 8 days after the onset of maximal symptoms. All patients had CT scans with evidence of recent infarction and angiography showing high grade carotid

stenosis. None of the patients had any neurologic deficit postoperatively. They suggested that CEA can be performed safely after acute stroke under certain conditions: normal level of consciousness, small cerebral infarction, no mass effect on CT, and meticulous control of perioperative blood pressure.

Khanna et al. [17] described a retrospective study of 774 patients who underwent CEA. 363 of these were done for completed strokes and 411 for transient ischemic attacks. The lowest mortality (1.6%) was in those patients who had CEA done in the first week, while 3.4% mortality occurred in the second week and 23.3% in the third week or later. In addition, 2.2% of this entire group deteriorated. The low mortality and morbidity in patients who underwent surgery within the first week were attributed to strict control of blood pressure. The high mortality in patients in whom surgery was performed in the third week or later was associated with recurrent strokes preoperatively. Death in these 14 patients was not due to neurological complications of endarterectomy but to myocardial infarction (7 patients), pulmonary embolus (4 patients), gastrointestinal bleeding (1 patient), associated head injury (1 patient), and brain stem stroke (1 patient).

Rosenthal et al. [18] described a retrospective analysis of 253 patients who suffered either a complete stroke or RIND. A subset of 29 patients with a limited and stable stroke had CEA from 9 to 21 days after the onset of symptoms. One patient sustained a postoperative stroke (3%), and 3 patients (10%) suffered postoperative minor TIAs that resolved. Thirty-one patients with a reversible ischemic neurological deficit (defined as a deficit lasting longer than 24 hours, resolving completely within 3 weeks, and having no CT evidence of infarction) underwent CEA from 3 to 21 days. In this group, one postoperative stroke (3%) and one TIA (3%) occurred.

Little et al. [19] performed a prospective trial of a total of 302 patients. A subset of 27 patients out of this group underwent CEA within 30 days after recent stroke. Twenty-two neurologically stable patients with mild deficits and normal CT and 2 patients with moderate neurological deficits and CT findings of recent infarction experienced no morbidity and no mortality. Two of 3 patients with progressive neurological deficits and CT findings of recent infarction experienced infarct extension. One of these 2 patients died. The study concluded that patients who have minimal residual neurological deficits and whose CT scans show normal findings are at low surgical risk, perhaps approaching that of patients with transient ischemic attacks.

Piotrowski JJ [20] described a prospective trial on 129 patients with recent stroke. The patients were preoperatively divided into two groups: early (<6 weeks, 82 patients) and late (>6 weeks, 47 patients) surgery. No significant difference in outcome was found between patients operated early versus late. No significant difference was observed between patients operated on at 2, 4, 6, or more than 6 weeks after stroke.

Gasecki et al. [21] did a retrospective study on 100 patients with severe carotid stenosis (70-99%) and nondisabling hemispheric stroke at entry into the North American Symptomatic CEA Trial. The patients were divided into two groups: early and late. Early patients had CEA within 30 days (2 to 30 days) of stroke, while the late group had surgery after 30 days. The postoperative stroke rate was comparable between the two groups. Both strokes in the early group were in patients who had a normal noncontrast CT and an acute carotid thrombus.

Klein et al. [22] reported a retrospective study of 34 patients who underwent CEA within 30 days of a hemisphere stroke. Neurological deficits were noted in 1 patient contralateral to the endarterectomized carotid. No deaths occurred.

LITRATURE AGIANST EARLY CAROTID ARTERY STENTING

CAS is a newer modality as compared to CEA. There has been one retrospective study, including 39 patients who had CAS after a mean time of 55 +/- 34 hours. Degree of carotid artery stenosis was 86 +/- 11%. In 37 procedures, complete recanalization was achieved, and in 2 procedures the residual stenosis was mild. Minor disabling stroke was reported in 2 patients and death subsequent to intracranial hemorrhage in 1 patient. The study concluded that CAS is safe after acute ischemic stroke if infarction volume is small and neurological deficit is mild[23].

Figure 3

Table 3: Reports in favor of early CAS after stroke

Study	Year	Type of Study	No. of patients with cerebral hemorrhage after CEA	Total number of patients	Suggested wait time
Zaidat *et al*[23]	2004	Prospective study	2	39	Within 60 hours.

LITERATURE IN FAVOR OF CAROTID ARTERY STENTING

Chamorro et al. [30] published a case report of a 43-year-old male, who had CAS 48 hours after an acute stroke complicated by intracranial hemorrhage within 24 hours after stenting and later on death in 7 days.

Thijs et al. [31] reported a retrospective review of 52 patients who underwent urgent CAS after failure of medical therapy for acute stroke. Four of the patients had intracerebral hemorrhage. It was thought that use of anticoagulants prior to stenting was responsible for this hemorrhage.

Figure 4

Table 4: Reports in favor of early CAS after stroke

Study	Year	Type of Study	No. of patients with cerebral hemorrhage after CEA	Total number of patients	Suggested wait time
Chamorro *et al*[30]	2000	Case report	1	1	
Thijs *et al*[31]	2000	Retrospective	4	52	

TRIALS COMPARING CEA & CAS

As discussed above, the recent literature supports the role of carotid intervention in the early phase after an acute stroke. Given that currently we have both CEA and CAS available as intervention in acute stroke, the question remains as to what is the best option after early stroke. CEA has been in practice for over 50 years now, and CAS is a relatively newer technique. Level I evidence supports CEA as the standard treatment of severe asymptomatic and symptomatic carotid stenosis.

The CAVATAS Trial[28] (Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid And Vertebral Artery Transluminal Angioplasty Study) was a randomized prospective trial which showed that rates of major outcome events within 30 days of first treatment did not differ significantly between endovascular treatment and surgery (6.4% vs 5.9%). The median delay from randomization to treatment was 20 days in patients assigned to endovascular treatment and 27 days (14-41) in patients allocated to the surgical group. However, the time period between the diagnosis and the treatment was not mentioned.

CA-RESS[84] (Carotid Artery Revascularization using Endarterecomy or Stenting Systems) is a multicenter prospective nonrandomized trial, which showed no significant differences in combined death/stroke rates at 30 days (3.6% CEA vs. 2.1% CAS) or at 1 year (13.6% CEA vs. 10% CAS). However the time period between the onset of stroke and the treatment was not mentioned.

Currently, SAPPHIRE trial (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy) showed results that only 5.8% of the stent patients had strokes compared to 7.7% of those who had surgery. The risk of myocardial infarction was 2.5% in the stent patients versus 8.1% of those who had surgery. The mortality rate was 7% for the stent patients at one year compared to 12.9% for the surgery patients.

DISCUSSION

Patients with a stroke who are candidates for carotid intervention represent a heterogenous group, and the risk of postoperative intracranial hemorrhage depends on the type of initial neurological defect, vascular territory of the stroke, infarct size, degree of midline shift on CT and the level of consciousness[24]. Toni et al. [25] showed that the risk of an ischemic stroke of being transformed into a hemorrhagic infarct can be predicted as early as 5 hours after the onset of stroke and only independent predictor of hemorrhagic stroke was early focal hypodensity. Flow to the hemisphere ipsilateral to the endarterectomized carotid is more direct to the middle cerebral artery under ordinary anatomic conditions than to other territories of the anterior circulation. Therefore patients with middle cerebral artery stroke may be at greater risk for complications than patients with cerebral infarctions in the distribution of other vascular territories. Patients with large cerebral infarcts are more prone to develop hemorrhagic transformation than those with small strokes.

Level of consciousness in stroke patients may be an independent predictor of the risk of hemorrhagic transfusion. Mortality is twice as great in patients with a depressed level of consciousness who had an operation within 13 days compared with those who underwent surgery after an interval of 2 weeks. [11]

Patients with a stable, acute stroke (neurological deficit lasting >24 hours), a normal CT scan, and a normal level of consciousness can probably undergo CEA shortly after the diagnosis is made and evaluation is complete. In this instance, the risk of stroke would seem to approximate that of patients who have suffered a TIA [26]

Patients with a low density on CT without significant shift, a stable neurological deficit, and a normal level of

consciousness have been reported to safely undergo early surgery with low risk[27]

CONCLUSION

Based on the data presented above, we conclude that every patient with acute stroke should be individulized on the basis of age, CT scan findings (absence or presence of midline shift, focal hypodensity), history of prior CEA or CAS. An expert opinion should be formed with the contribution from neurologist, vascular surgeon and interventional radiologist. High risk patients should be treated with urgent CAS after the correction of the coagulation cascade. Low risk patients should undergo carotid endarterctomy as soon as possible, because the patency rates after CEA are better than those of CAS.

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