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Thirty-day outcome of delayed versus early management of symptomatic carotid stenosis.

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Abstract

***Objective**:* Compare outcomes of early (<15 days) versus delayed carotid endarterectomy in symptomatic patients.

Methods: All CEA procedures performed for symptomatic carotid stenosis between January 2006 and May 2010 were retrospectively reviewed. Postoperative mortality (within 30 days), stroke, and Myocardial Infarction (MI) rates were analysed in the early and delayed CEA groups.

Results: During the study period, 149 patients were included. Carotid revascularization was performed within 15 days after symptom onset in 62 (41.6%) patients and longer than 15 days after symptom onset in 87 (58.4%). The mean time lapse between onset of neurological symptoms and surgery was 9.3 days (range, 1-15) in the early surgery group and 47.9 days (range, 16-157) in the delayed surgery group. 30-day combined stroke & death rates were respectively 1.7% and 3.5% in the early and the delayed surgery groups. 30-day combined stroke, death, & MI rates were respectively 1.7% and 5.9% in the early and the delayed surgery groups.

Conclusions: During the study period, the reduction of the symptom to knife time in application to the carotid revascularization guidelines did not impact our outcomes suggesting that early CEA achieves 30-day mortality and morbidity rates at least equivalent to those of delayed CEA.

Introduction

Randomised controlled trials have clearly shown the benefit of carotid endarterectomy (CEA) in symptomatic patients[1] with a perioperative complication rate less than 6%[2]. More recent reports present convincing evidence in favour of early revascularization after symptom onset[3,4]. An important finding in this regard is that cerebrovascular ischemic events exhibit an exponential recurrence rate reaching 8% and 11,5% at 7 days after a transient ischemic attack (TIA) or minor stroke respectively[5-7]. However, since the actual benefit of this prevention strategy in relation to perioperative complications has not been demonstrated[8] and considering the lacks of early surgery protocols, some vascular surgery centres worldwide continue to perform delayed surgery. The adoption of the carotid guidelines[2] in 2008 by reducing symptom to knife time required a new organization of our unit, therefore we decided to retrospectively review and compare outcomes of early (<15 days) versus delayed carotid revascularization performed before and after this shift, on symptomatic patients in order to discuss this attitude.

Material and Methods

Patient selection and preoperative management

All CEA procedures performed for symptomatic carotid stenosis at our center between January 2006 and May 2010 were retrospectively reviewed in accordance

with approved institutional review board protocols. Patients were classified as symptomatic if, within 3 months of their procedure, they presented hemispheric stroke or transient ischaemic attack (TIA) resulting in facial or upper/lower extremity weakness, aphasia, or amaurosis fugax documented by formal neurology evaluation. Crescendo transient ischemic attack (cTIA) was defined as repeated TIA over a relatively short time period. Stroke in evolution (SIE) was defined as worsening or fluctuating neurological deficit with no improvement between episodes. Referral to our stroke care unit was by primary care practitioners and neurologists. None of the patients of this study underwent preoperative thrombolytic therapy.

In all patients, preoperative bilateral carotid artery duplex ultrasonography demonstrated ≥ 50% stenosis on the symptomatic side according to the NASCET measurement[9]. According to French recommendations, all patients underwent CT angiography and/or MR angiography of the neck and brain to assess carotid and cerebral circulation and identify the location and size of any infarct. . If not already on-going, antiplatelet therapy (aspirin 75 or 160 mg/day) was implemented preoperatively. In some cases, Clopidogrel therapy (75 mg) prescribed by the referring physician was continued.

Before 2008, only patients presenting unstable symptomatic carotid stenosis associated or not with cerebral infarct less than 3 cm in diameter underwent early revascularization (<15 days) at our institution. Since January 2008, this policy has changed with revascularization being performed within 15 days of symptom onset in all patients, whenever possible[10]. Patients with extensive ischemic lesions were always re-evaluated 6 weeks later and proposed delayed surgery. In the present study, patients who underwent CEA within 15 days of symptom onset were included in the early CEA group while patients treated later were included in the delayed CEA

group. Symptomatic patients treated by carotid angioplasty due to hostile neck, surgically inaccessible lesions, or fibrotic restenosis were excluded from study. Surgical treatment was not proposed to patients with acute carotid occlusion, haemorrhagic stroke, or extensive permanent neurologic deficits.

Operative technique

Standard endarterectomy with patch closure or eversion endarterectomy was performed under general anaesthesia by experienced board-certified vascular surgeons. Common-to-internal-carotid-artery bypass was used in cases involving long-segment stenosis or associated pathologies such as post-stenotic dilatation. All patients received an intravenous bolus of heparin (50 UI/kg). The common carotid artery was clamped if mean arterial pressure (MAP) exceeded 100 mmHg. Carotid stump pressure was the only method used to assess cerebral haemodynamic status. Selective shunting was utilized at the discretion of the operating surgeon in patients with MAP <100mmHg or stump pressure <40mmHg. Postoperatively, patients were kept in the anaesthesia recovery area to allow close monitoring of arterial pressure for 24 hours and then transferred to the standard surgical ward. Following the procedure, all patients continued single-antiplatelet therapy and, if not already prescribed, began single-statin therapy.

Definitions

Postoperative stroke was defined as occurrence of any new central neurologic deficit persisting more than 24 hours with or without CT or MRI evidence of cerebral infarct. Postoperative TIA was defined as any new central neurologic deficit resolving within 24 hours. Unstable patients were defined as patients presenting crescendo TIA

(CTIA) or stroke in evolution (SIE). Myocardial infarction (MI) was defined as any combination of two or more of the following criteria: typical chest pain lasting 20 minutes or longer; serum levels of creatine kinase (CK), CK-MB, or troponin two or more times higher than the upper normal limit; and presence of new Q waves on at least two adjacent derivations or predominant R waves in V1 (R wave ≥1 mm > S wave in V1).

Follow-up

All patients underwent neurological examination by the operating surgeon using the standard scoring form at discharge and 30 days after surgery. In case of doubt or sign of deterioration, advice from the neurologist was sought. Doppler ultrasound surveillance was performed at 1, 6 and 12 month and yearly thereafter.

Outcomes

Postoperative mortality (within 30 days), stroke, and MI rates were analysed in the early and delayed CEA groups.

Statistical analysis

Baseline patient characteristics and postoperative outcomes in the early and delayed CEA groups were compared using the Fischer and Student t tests. Data were summarized using descriptive statistics, i.e., count and frequency for categorical variables and mean and range for continuous variables. Statistical significance was determined at a two-sided P value of < 0,05. All statistical analyses were conducted using SAS v. 9.2 (SAS Inc, Cary, NC).

RESULTS

Patient characteristics

During the study period, a total of 621 CEA were performed in our unit including 149 symptomatic carotid stenosis. Procedures for symptomatic carotid stenosis were performed within 15 days after symptoms onset (early surgery) in 62 (41.6%) patients and later (delayed surgery) in 87 (58.4%). Mean age was 71,5 years (range, 47-93), 79,9% of patients were males and 73,8% presented hypertension. History of ischemic cardiac disease was more frequent in the delayed surgery group (p=0.03). Patient characteristics are summerized in **Table I**.

Neurological events and carotid lesions

Neurologic event was stroke in 75% of cases, TIA in 60% and amaurosis fugax in 9,4%. There were no statistical differences between the two groups. The carotid lesion was considered as neurologically “unstable” in 25 patients including 13 in the early surgery group and 12 in the delayed surgery group. Among the 62 patients in the early surgery group, 11 (17,7%) presented cTIA and 2 (3,2%) SIE. In the delayed surgery group, 21,8% presented cTIA and 4,6% presented SIE. These preoperative neurologic status and carotid lesions are described in **Table II**.

All 149 patients underwent preoperative duplex ultrasonography followed by CT angiography in 103 patients and/or MR-angiography in 61.

Intervention

The mean time lapse between onset of neurological symptoms and surgery was 9.3 days (range, 1-15) in the early surgery group and 47.9 days (range, 16-157) in the delayed surgery group. The procedure consisted in CEA in 147 patients and common-to-internal-carotid-artery bypass in 2. Patch-closure was performed in 34,2% of procedures, and a shunt was used in 19,5% of the procedures. There was no statistical difference between the two groups. Technical details of carotid revascularization are reported in **Table III**.

Outcomes

Both clinical examination and duplex ultrasonography at one-month were available in 144 patients. The remaining 5 patients were lost to follow-up after discharge. Complications occurring during hospitalization and the 30-day postoperative period are summarised in **Table IV**. No significant difference in postoperative complications was noted between the two groups. Injury of the facial or hypoglossal nerves occurred in 3 patients in each group. In the recovery room, TIA characterized by worsening of preoperative symptoms that resolved within 6 hours with a normal cerebral MR scan was observed in 5 cases.

Postoperative stroke occurred in 4 patients. In the first case, duplex ultrasonography revealed ICA occlusion that was successfully treated by surgical revision with restoration of blood flow allowing reversal of postoperative aphasia but not of hemiplegia. In the second, the ICA was patent but MR-angiography showed minor ischemic lesions in the territory of the middle cerebral artery (MCA) probably due to micro-embolism. In the remaining 2 patients including one with crescendo TIA, the

ICA was patent but MR angiography showed massive ischaemic lesions in territories supplied by the MCA and anterior cerebral artery (ACA). Both of these patients died, one on postoperative day 3 and the other of postoperative day 6. Mean duration of hospitalisation was 6,1 days in the early CEA group versus 6,7 days in the delayed one (p NS).

In the subgroup of 25 patients whose preoperative neurologic status was considered as unstable, 6 presented SIE and 19 presented cTIA. The percentage of these patients undergoing early revascularization rose from 33% (5/15) before 2008 to 80% (8/10) thereafter. Thirty-day postoperative complications in this subgroup are summarised in **Table V.**

Discussion

Perusal of the literature clearly demonstrates that early revascularization of symptomatic carotid stenosis is associated with a reduction in symptoms recurrence rate[3,10]. However, despite Naylor's suggestion that "a 30-day death/stroke risk of 8% is acceptable if CEA is performed within 2 weeks of the index event"[8], the exact risk-to-benefit ratio of early revascularization remains unclear[11]. Our centre has adopted a policy of revascularizing every symptomatic carotid lesion ≥50% within 15 days after onset of neurological symptoms. As described herein, our outcomes suggest that early CEA achieves 30-day stroke and death rate at least equivalent to those of delayed CEA. Few authors describing early CEA[12-42] have provided information allowing comparative analysis with their own previous delayed CEA experience (**table VI**). However, some authors[35-37,40,42] have recently reported that early CEA within 2 weeks in comparison with a delayed surgery was not associated with higher perioperative stroke and death risk, thus supporting our findings. In her study describing very early CEA, i.e., within 2 days, Stromberg et al[34] showed an impressive 30-day stroke and death rate of 11.5% but this observation was not confirmed by the most recent publications[35-38] in which 30-day stroke and death rate range from 2.4% to 4.5%.

In 2008, our vascular surgery team began introducing measures designed to give scheduling priority to revascularization of newly symptomatic carotid artery stenosis. The goal was to shorten our "symptom-to-knife time" as much as possible, in accordance with recently published experiences[43,44]. Despite implementation of this policy, mean waiting time for surgery stayed at 9.3 days and treatment was delayed

beyond the set 2-week limit in some cases. As previously reported, the main sources of delay were: failure to recognize symptoms immediately and/or late referrals by general practitioners. Another obstacle for early revascularization involved obtaining test results on short notice, underlining the need for re-organization at the institutional level[5].

The need for more extensive assessment in high-risk patients is also a major issue in scheduling early revascularization. The number of patients with a history of cardiac ischemic disease was significantly higher in the delayed surgery group (25%) than in the early surgery group (11%). In our experience, the percentage of patients with unstable neurologic status operated within 15 days after symptom onset rose from 33% at the beginning of our study to 80% after 2008. At the end of the study, the main reason for delayed surgery was the need for additional cardiac testing and interventions. Cardiac-related factors also explain higher morbidity rates as pointed out by Karkos et al[45] in a review of 28 series describing emergency carotid surgery in patients with SIE and cTIA. The combined stroke/death/major cardiac event rate was 10.9% for cTIA and 20.8% for SIE. In our experience, the overall combined stroke/death rate was higher in this subgroup of patients (12%) than in stable patients but the rate in the early CEA subgroup was lower than in delayed CEA group (7.7% vs. 16.7%, p=0.49).

At the beginning of the present study, patients presenting cerebral lesions greater than 3 cm were systematically considered ineligible for early revascularization as suggested by Sbarigia et al[24]. This policy was changed since, as subsequently reported by the same author[46], we now know that the real limit is infarction > 2/3 of the middle cerebral artery territory. Following this principle, haemorrhagic conversion of cerebral ischaemic lesions was never required.

An interesting observation in this study involves symptoms during the postoperative wake-up period. Five patients in this series displayed initial worsening of neurological clinical status at wake-up that regressed spontaneously in the recovery room. A possible explanation is injury to the penumbra zone due to carotid clamping shortly after stroke. To our knowledge, this observation frequently debated during carotid meetings has never been specifically studied in relation to the timing of CEA.

The main limitations of present study are retrospective design with data collection from medical charts and lack of independent neurologic assessment and neuroimaging details.

Conclusions

During the study period, the reduction of the symptom to knife time obtained by applying the carotid revascularization guidelines had no effect on outcomes suggesting that early CEA achieves 30-day mortality and morbidity rates at least equivalent to those of delayed CEA.

References

[1] Rothwell PM, Eliasziw M, Gutnikov SA, Fox AJ, Taylor DW, Mayberg MR, et al. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. Lancet 2003;361(9352):107□116.
[2] Liapis CD, Bell PRF, Mikhailidis D, Sivenius J, Nicolaides A, Fernandes e Fernandes J, et al. ESVS guidelines. Invasive treatment for carotid stenosis: indications, techniques. Eur J Vasc Endovasc Surg 2009;37(4 Suppl):1□19.
[3] Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJM. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. Lancet 2004;363(9413):915□924.
[4] Ferrero E, Ferri M, Viazzo A, Labate C, Berardi G, Pecchio A, Piazza S, Ripepi M, Nessi F. A retrospective study on early carotid endarterectomy within 48 hours after transcient ischemic attack and stroke in evolution. Ann Vasc Surg 2014;28(1):227-38
[5] Coull AJ, Lovett JK, Rothwell PM. Population based study of early risk of stroke after transient ischaemic attack or minor stroke: implications for public education and organisation of services. BMJ 2004;328(7435):326.
[6] Lisabeth LD, Ireland JK, Risser JM, Brown DL, Smith MA, Garcia NM, Morgenstern LB. Stroke risk after transcient ischemic attack in a population-based setting. Stroke 2004;35:1842-1846
[7] Eliasziw M, Kennedy J, Hill MD, Buchan AM, Barnett HJM. Early risk of stroke after a transcient ischemic attack in patients with internal carotid artery disease. CMAJ 2004; 170(7)
[8] Naylor AR. Delay may reduce procedural risk, but at what price to the patient? Eur J Vasc Endovasc Surg 2008;35(4):383□391.
[9] Barnett HJ, Taylor DW, Eliasziw M, Fox AJ, Ferguson GG, Haynes RB, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med 1998;339(20):1415□1425
[10] Naylor AR. Time is brain! Surgeon 2007;5(1):23□30.
[11] De Rango P. Carotid stenosis: an unknown disease.. Eur J Vasc Endovasc Surg 2012;44(1):18□19.
[12] Mentzer RM Jr, Finkelmeier BA, Crosby IK, Wellons HA Jr. Emergency carotid endarterectomy for fluctuating neurologic deficits. Surgery 1981;89(1):60□66.
[13] Whittemore AD, Ruby ST, Couch NP, Mannick JA. Early carotid endarterectomy in patients with small, fixed neurologic deficits. J Vasc Surg 1984;1(6):795□799.
[14] Dosick SM, Whalen RC, Gale SS, Brown OW. Carotid endarterectomy in the stroke patient: computerized axial tomography to determine timing. J Vasc Surg 1985;2(1):214□219.
[15] Gasecki AP, Ferguson GG, Eliasziw M, Clagett GP, Fox AJ, Hachinski V, 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(2):288□295.
[16] Ricco JB, Illuminati G, Bouin-Pineau MH, Demarque C, Camiade C, Blecha L, et al. Early carotid endarterectomy after a nondisabling stroke: a prospective study. Ann Vasc Surg 2000;14(1):89□94.
[17] Ballotta E, Da Giau G, Baracchini C, Abbruzzese E, Saladini M, Meneghetti G. Early versus delayed carotid endarterectomy after a nondisabling ischemic stroke: a prospective randomized study. Surgery 2002;131(3):287□293.

[18] Eckstein HH, Ringleb P, Dörfler A, Klemm K, Müller BT, Zegelman M, et al. The Carotid Surgery for Ischemic Stroke trial: a prospective observational study on carotid endarterectomy in the early period after ischemic stroke. J Vasc Surg 2002;36(5):997□1004.
[19] Huber R, Müller BT, Seitz RJ, Siebler M, Mödder U, Sandmann W. Carotid surgery in acute symptomatic patients. Eur J Vasc Endovasc Surg 2003;25(1):60□67.
[20] Paty PSK, Darling RC 3rd, Feustel PJ, Bernardini GL, Mehta M, Ozsvath KJ, et al. Early carotid endarterectomy after acute stroke. J Vasc Surg 2004;39(1):148□154.
[21] Wölfle KD, Pfadenhauer K, Bruijnen H, Becker T, Engelhardt M, Wachenfeld-Wahl C, et al. Early carotid endarterectomy in patients with a nondisabling ischemic stroke: results of a retrospective analysis. VASA 2004;33(1):30□35.
[22] Rantner B, Pavelka M, Posch L, Schmidauer C, Fraedrich G. Carotid endarterectomy after ischemic stroke--is there a justification for delayed surgery? Eur J Vasc Endovasc Surg 2005;30(1):36□40.
[23] Aleksic M, Rueger MA, Lehnhardt FG, Sobesky J, Matoussevitch V, Neveling M, et al. Primary stroke unit treatment followed by very early carotid endarterectomy for carotid artery stenosis after acute stroke. Cerebrovasc Dis 2006;22(4):276□281.
[24] Sbarigia E, Toni D, Speziale F, Falcou A, Sacchetti ML, Panico MA, et al. Emergency and early carotid endarterectomy in patients with acute ischemic stroke selected with a predefined protocol. A prospective pilot study. Int Angiol 2003;22(4):426□430.
[25] Rantner B, Eckstein H-H, Ringleb P, Woelfle KD, Bruijnen H, Schmidauer C, et al. American Society of Anesthesiology and Rankin as predictive parameters for the outcome of carotid endarterectomy within 28 days after an ischemic stroke. J Stroke Cerebrovasc Dis 2006;15(3):114□120.
[26] Dorigo W, Pulli R, Barbanti E, Azas L, Troisi N, Pratesi G, et al. Carotid endarterectomy in patients with acute neurological symptoms: a case-control study. Interact Cardiovasc Thorac Surg 2007;6(3):369□373.
[27] Ballotta E, Meneghetti G, Da Giau G, Manara R, Saladini M, Baracchini C. Carotid endarterectomy within 2 weeks of minor ischemic stroke: a prospective study. J Vasc Surg 2008;48(3):595□600.
[28] Gorlitzer M, Froeschl A, Puschnig D, Locker E, Skyllouriotis P, Meinhart J, et al. Is the urgent carotid endarterectomy in patients with acute neurological symptoms a safe procedure? Interact Cardiovasc Thorac Surg 2009;8(5):534□537.
[29] Ferrero E, Ferri M, Viazzo A, Gaggiano A, Ferrero M, Maggio D, et al. Early carotid surgery in patients after acute ischemic stroke: is it safe? A retrospective analysis in a single center between early and delayed/deferred carotid surgery on 285 patients. Ann Vasc Surg 2010;24(7):890□899.
[30] Rantner B, Kollerits B, Schmidauer C, Willeit J, Thauerer M, Rieger M, et al. Carotid endarterectomy within seven days after the neurological index event is safe and effective in stroke prevention. Eur J Vasc Endovasc Surg. déc 2011;42(6):732□739.
[31] Capoccia L, Sbarigia E, Speziale F, Toni D, Fiorani P. Urgent carotid endarterectomy to prevent recurrence and improve neurologic outcome in mild-to-moderate acute neurologic events. J Vasc Surg 2011;53(3):622□627; discussion 627□628.
[32] Leseche G, Alsac J-M, Castier Y, Fady F, Lavallee PC, Mazighi M, et al. Carotid endarterectomy in the acute phase of crescendo cerebral transient ischemic attacks is safe and effective. J Vasc Surg 2011;53(3):637□642.
[33] Annambhotla S, Park MS, Keldahl ML, Morasch MD, Rodriguez HE, Pearce WH, et al. Early versus delayed carotid endarterectomy in symptomatic patients. J Vasc Surg

2012;56(5):1296□1302; discussion 1302.
[34] Strömberg S, Gelin J, Osterberg T, Bergström G, Karlström L, Osterberg K. Very urgent carotid endarterectomy confers increased procedural risk. Stroke 2012;43:1331-5
[35] Mono ML, Steiger I, Findling O, Jung S, Reinert M . Risk of very early recurrent cerebrovascular events in symptomatic carotid artery stenosis. J Neurosurg 2013;119(6):1620-6.
[36] Sharpe R, Sayers RD, London NJM, Bown MJ, McCarthy MJ, Nasim A, Davies RSM, Naylor AR. Procedural risk following carotid endarterectomy in the hyperacute period after onset of symptoms. Eur J Vasc Endovasc Surg 2013;46(5):519-24
[37] Rantner B, Schmidauer C, Knoflach M, Fraedrich G. Very Urgent Carotid Endarterectomy Does Not Increase the Procedural Risk. Eur J Vasc Endovasc Surg 2014;1078-5884(14)00524-3
[38] Ferrero E, Ferri M, Viazzo A, Labate C, Berardi G, Pecchio A, Piazza S, Ripepi M, Nessi F. A retrospective study on early carotid endarterectomy within 48 hours after transient ischemic attack and stroke in evolution. Ann Vasc Surg 2014;28(1):227-38
[39] Tsivgoulis G, Krogias C, Georgiadis GS, Mikulik R, Safouris A, Meves SH, Voumvourakis K, Haršány M, Staffa R, Papageorgiou SG, Katsanos AH, Lazaris A, Mumme A, Lazarides M, Vasdekis SN. Safety of early endarterectomy in patients with symptomatic carotid artery stenosis: an international multicenter study. Eur J Neurol 2014;21(10):1251-7
[40] Chisci E, Pigozzi C, Troisi N, Tramacere L, Zaccara G, Cincotta M, Ercolini L, Michelagnoli S. Thirty-day neurological improvement associated with early versus delayed carotid endarterectomy in symptomatic patients. Ann Vasc Surg 2014;0890-5096(14)00657-8
[41] Merlini T, Péret M, Lhommet P, Debiais S, Marc G, Godard S, Martinez R, Enon B, Picquet J. Is early surgical revascularization of symptomatic carotid stenoses safe? Ann Vasc Surg 2014;28(6):1539-47
[42] Kretz B, Kazandjian C, Bejot Y, Abello N, Brenot R, Giroud M, Steinmetz E. Delay between symptoms and surgery for carotid artery stenosis : modification of our practice. Ann Vasc Surg. 2014 ;0890-5096(14)00531-7
[43] Den Hartog AG, Moll FL, van der Worp HB, Hoff RG, Kappelle LJ, de Borst GJ. Delay to carotid endarterectomy in patients with symptomatic carotid artery stenosis. Eur J Vasc Endovasc Surg 2014;47(3):233□239.
[44] Vikatmaa P, Sairanen T, Lindholm J-M, Capraro L, Lepäntalo M, Venermo M. Structure of delay in carotid surgery--an observational study. Eur J Vasc Endovasc Surg 2011;42(3):273□279.
[45] Karkos CD, Hernandez-Lahoz I, Naylor AR. Urgent carotid surgery in patients with crescendo transient ischaemic attacks and stroke-in-evolution: a systematic review. Eur J Vasc Endovasc Surg 2009;37(3):279□288.
[46] Sbarigia E, Toni D, Speziale F, Acconcia MC, Fiorani P. Early carotid endarterectomy after ischemic stroke: the results of a prospective multicenter Italian study. Eur J Vasc Endovasc Surg 2006;32(3):229□235.

Titles of tables

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Table II. Neurological symptoms and preoperative carotid artery status in early and delayed surgery groups.

Table III. Technical aspects of revascularization in early and delayed surgery groups.

Table IV. Perioperative and thirty-day complications in early and delayed surgery groups.

Table V. Thirty-day postoperative complications in unstable carotid artery stenosis group. cTIA : crescendo transient ischemic attack. SIE : stroke in evolution. MI : myocardial infarction.

Table VI. Studies reporting early carotid revascularization following neurological events. SIE: stroke in evolution. cTIA: crescendo transient ischemic attack.

Patient characteristics	Early Surgery	Delayed Surgery	Overall	p
Patients. n (%)	62 (41 .6)	87 (58.4)	149	
Age. Mean (range)	70.3 (50-88)	72.3(47–93)	71.5	NS
Female. n (%)	11 (17.7)	19(21.8)	30 (20.1)	NS
Male. n (%)	51 (82.3)	68 (78.2)	119 (79.9)	NS
Risk Factors. n (%)				
Hypertension	45 (72.6)	65 (74.7)	110 (73.8)	NS
Diabetes	16 (25.8)	31(35.6)	47 (31.5)	NS
Dyslipidemia	31 (50)	43 (49.4)	74 (49.7)	NS
Tabacco use	29 (46.8)	40 (46)	69 (46.3)	NS
Obesity (Body Mass Index>30)	3 (4.8)	4 (4.6)	7 (4.7)	NS
Ischemic Cardiac Diseases. n (%)	7 (11.3)	22 (25.3)	29 (19.5)	0.0326
Cardiac Arythmia. n (%)	5 (7.9)	5 (5.7)	10 (6.7)	NS
Peripheral Vascular Disease. n.(%)	14 (22.6)	20 (23)	34 (22.8)	NS

Table I. Characteristics of patients in early and delayed surgery groups.

Neurological Event	**Early Surgery**	**Delayed Surgery**	**Total**	**p**
Patients. n (%)	62 (41.6)	87 (58.4)	149	
Stroke	27 (43.5)	48 (55.2)	75 (50.3)	NS
Stroke in Evolution	*2 (3.2)*	*4 (4.6)*	*6 (4)*	NS
TIA	29 (46.8)	31 (35.6)	60 (40.3)	NS
Crescendo TIA	*11 (17.7)*	*8 (21.8)*	*19 (12.7)*	NS
Amaurosis Fugax	6 (9.7)	8 (9.2)	14 (9.4)	NS
Ipsilateral Carotid stenosis. n (%)				
50-69%	7 (11.3)	19 (21.8)	26 (17.4)	NS
70-79%	17 (27.4)	18 (20.7)	35 (23.5)	NS
80-89%	13 (21)	19 (21.8)	32 (21.5)	NS
90-99%	25 (40.3)	31 (35.6)	56 (37.6)	NS
Contralateral Carotid status. n (%)				
No stenosis	48 (77.4)	55(63.2)	103 (69.1)	NS
50-69%	7 (11.3)	14 (16.1)	21 (14.1)	NS
70-99%	6 (9.7)	16 (18.4)	22 (14.8)	NS
Occlusion	1 (1.6)	2 (2.3)	3 (2)	NS

Table II. Neurological symptoms and preoperative carotid artery status in early and delayed surgery groups.

Procedure	Early Surgery	Delayed Surgery	Total	p
CEA. n (%)	61 (98)	86 (99)	147 (99)	NS
Patch Closure. n (%)	18 (29)	33 (38)	51 (34)	NS
Direct Suture. n (%)	15 (24)	13 (15)	28 (19)	NS
Eversion. N (%)	28 (45)	40 (46)	68 (46)	NS
Bypass. n (%)	1 (2)	1 (1)	2 (1)	NS
Shunt Use. n (%)	11 (17.7)	18 (20.7)	29 (19.5)	NS

Table III. Technical aspects of revascularization in early and delayed surgery groups.

Complication.	Early Surgery	Delayed Surgery	Total	P
Perioperative period				
Cervical hematoma. n (%)	3 (4.8)	9 (10.3)	12/149 (8)	0.36
Requiring surgical revision	1	5		
Cranial nerve injury. n (%)	2 (3.2)	4 (4.6)	6/149 (4)	0.99
Thirty-day period				
Lost to follow-up	3 (4.8)	2 (2.3)	5/149 (3.4)	
Myocardial infarction. n (%)	0	3 (3.5)	3/144 (2.1)	0.26
TIA. n (%)	3 (5.1)	2 (2.3)	5/144 (3.5)	0.65
Stroke. n (%)	1 (1.7)	3 (3.5)	4/144 (2.8)	0.64
Non-fatal stroke	0	2 (2.3)	2/144 (1.4)	0.51
Fatal stroke	1 (1.7)	1 (1.2)	2/144 (1.4)	0.99
Death. n (%)	1 (1.7)	1 (1.2)	2/144 (1.4)	0.99
Combined stroke & death. n (%)	1 (1.7)	3 (3.5)	4/144(2.8)	0.64
Combined stroke, death, & MI. n (%)	1 (1.7)	5 (5.9)	6/144 (4.2)	0.40

Table IV. Perioperative and thirty-day complications in early and delayed surgery groups.

Variable	Early Surgery (%)	Delayed Surgery (%)	Total (%)	P
Patients. n	13 (52)	12 (48)	25 (100)	
Preoperative cTIA	11 (85)	8 (67)	19 (76)	0.38
Preoperative SIE	2 (15)	4 (33)	6 (24)	0.38
TIA. n (%)	1 (7.7)	0	1 (4)	0.99
Stroke. n (%)	1 (7.7)	2 (16.7)	3 (12)	0.60
Fatal Stroke	1 (7.7)	0	1 (4)	0.99
Death. n (%)	1 (7.7)	0	1 (4)	0.99
MI. n (%)	0	1 (8.3)	1 (4)	0.48
Combined Stroke&Death. n (%)	1 (7.7)	2 (16.7)	3 (12)	0.60
Combined Stroke&Death&MI. n (%)	1 (7.7)	3 (25)	4 (16)	0.32

Table V. Thirty-day postoperative complications in unstable carotid artery stenosis group. cTIA : crescendo transient ischemic attack. SIE : stroke in evolution. MI : myocardial infarction.

Reference	Year	N°of Patients	Symptoms	Delay m (mean) M (Median)	Neurological Assessment	30-day stroke and death rate	Comparison with delayed surgery (n)
Mentzer[13]	1981	24	SIE/cTIA	emergent	/	4.1%	/
Whittemore[14]	1984	28	Stroke	11 days (m)	/	3.5%	/
Dosick[15]	1985	110	TIA	10 days (m)	/	0.9%	/
Gasecki[16]	1994	42	Stroke	<30 days	/	4.8%	5.2% (58)
Ricco[17]	2000	72	Stroke	<15 days	/	2.8%	/
Ballotta[18]	2002	45	Stroke	<18 days (M)	/	2%	2% (41)
Eckstein[19]	2002	164	Stroke	<17 days(M)	Rankin	6.7%	/
Huber[20]	2003	67	Stroke/TIA	2 days (M)	Rankin	16%	/
Paty[21]	2004	126	Stroke	< 15 days	NIHSS	3.1%	2.9% (102)
Wolfle[22]	2004	66	Stroke	10 days (M)	Rankin	10%	/
Rantner[23]	2005	36	Stroke	<28 days	/	3.4%	4.8% (62)
Aleksic[24]	2006	43	Stroke/TIA	4 days (M)	Rankin	6.9%	/
Sbarigia[25]	2006	33	Stroke	<7 days	/	3%	/
Rantner[26]	2006	226	Stroke	12 days (M)	Rankin	8.4%	/
Dorigo[27]	2007	70	TIA/cTIA	<1 day	/	1.4%	0.3% (352)
Ballotta[28]	2008	102	Stroke	8 days (M)	Rankin	0%	/
Gorlitzer[29]	2009	28	Stroke/cTIA	4 days (m)	Rankin	0 %	1% (302)
Ferrero[30]	2010	131	Stroke/TIA	<14 days	Rankin	3.8%	3.2% (154)
Rantner[31]	2011	241	Stroke/TIA	<7 days	Rankin	2.1%	4.7% (215)
Capoccia[32]	2011	62	Stroke	34 hours (m)	NIHSS	1.6%	/
Leseche[33]	2011	64	cTIA	5 days (M)	/	0%	/
Annambothla[34]	2012	44	Stroke/TIA	<14 days	/	2.2%	2.9% (267)
Stromberg[35]	2012	148	Stroke/TIA	<2 days	Rankin	11.5%	4.4% (2448)
Mono[36]	2013	21	Stroke/TIA	<2 days	NIHSS	4,5%	4,1% (73)
Sharpe[37]	2013	41	Stroke/TIA	<2 days	Rankin	2.4%	1.2% (434)
Rantner[38]	2014	219	Stroke/TIA	<2 days	/	4,4%	2,7%(542)
Ferrero[4]	2014	176	SIE/cTIA/TIA	<2 days	NIHSS	3,9%	/
Tsivgoulis[39]	2014	165	Stroke/TIA	<14 days	Rankin	5,5%	/
Chisci[40]	2014	100	Stroke/TIA	<14 days	NIHSS	3%	0,4% (222)
Merlini[41]	2014	91	Stroke/TIA	<14 days	Rankin	3,3%	/
Kretz[42]	2104	158	Stroke/TIA	<14 days	Rankin	3.2%	3,1% (259)
Present study	2014	62	Stroke/TIA	<15 days	/	1.7%	3.5% (87)

Table VI. Studies reporting early carotid revascularization following neurological events. SIE: stroke in evolution. cTIA: crescendo transient ischemic attack.