Long-term Morbidity and Mortality of Carotid Endarterectomy in Patients with End-stage Renal Disease Receiving Hemodialysis

Masakazu Okawa, MD, Tetsuya Ueba, MD, PhD, Toshiyasu Ogata, MD, PhD, Hiroshi Abe, MD, PhD, Toshio Higashi, MD, PhD, and Tooru Inoue, MD, PhD

Background and Purpose: Renal insufficiency is a known risk factor for stroke. However, the impact of carotid endarterectomy (CEA) on stroke incidence in patients requiring dialysis remains controversial. We hypothesized that patients undergoing dialysis have no greater risk for periprocedural adverse events. *Methods:* We performed a retrospective chart review of 12 CEA patients who were on dialysis at the time of CEA. The charts were reviewed for patient demographics, systemic vascular disease, perioperative morbidity and mortality rates, and long-term outcome. Outcomes were recorded in terms of modified Rankin Scale (mRS). *Results:* The mean patient age at the time of CEA was 66.9 ± 7.3 years, with 1 patient having received carotid artery stenting for restenosis. Of the 12 patients undergoing 15 CEAs while being dialysis dependent, none exhibited periprocedural complications including stroke and myocardial infarction. During the follow-up period (mean, 56.1 ± 38.8 months), 3 patients had strokes unrelated to the target vessels for CEA, and 3 patients died from acute myocardial infarction, congestive heart failure, and sepsis. The calculated 5-year survival rate in our series was 58.3% in all cases, 40.0% in symptomatic patients, and 71.4% in asymptomatic patients. Eight patients (66.6%) had a good outcome. *Conclusions:* These data suggest that patients undergoing dialysis were at no greater risk for periprocedural complications when undergoing CEA. Thus, CEA may be effective for stroke prevention in hemodialysis patients. **Key Words:** Hemodialysis—carotid endarterectomy—symptomatic—long-term follow-up.

Introduction

End-stage renal disease (ESRD) requiring hemodialysis (HD) represents a major public health problem in Japan and is related to an aging population and an increasing incidence of risk factors such as diabetes mellitus.[1] In HD patients, cerebrovascular disease is one of the main causes of death.[1-4] For example, in an American prospective cohort study of patients initiating dialysis therapy for ESRD, cerebrovascular events, including fatal and nonfatal clinical stroke and carotid endarterectomy (CEA), occurred 10 times more frequently than in the general population, with an incidence rate of 4.9 events/100 person-years.[3] Most of those events were related to ischemic stroke in dialysis patients. Nevertheless, there is no long-term outcome study of HD patients, in particular those including outcomes after CEA. Although carotid artery stenting is an alternative modality, its outcome for the patients with chronic kidney disease is generally worse.[5] Moreover, marked calcification is frequently found in systemic arteries of HD patients,[6] which would make us difficult to place the carotid artery

From the Department of Neurosurgery, Faculty of Medicine, Fukuoka University, Fukuoka, Japan.

Received April 11, 2013; revision received May 7, 2013; accepted May 10, 2013.

Address correspondence to Masakazu Okawa, MD. Department of Neurosurgery, Fukuoka University, 7-45-1 Nanakuma, Jonan-ku, Fukuoka 814-0180, Japan. E-mail: okawam@fukuoka-u.ac.jp.

1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2013.05.012

stent and to perform needle puncture. Aortic calcification is also one of the risk factor of cholesterol emboli. Therefore, we conducted CEA as a first-line modality. The aim of the present study was to evaluate the perioperative morbidity and mortality and long-term outcomes of CEA in Japanese HD patients.

Methods

All patients diagnosed as ESRD were cross-referenced with those who underwent CEA at the Kyushu Medical Center and Fukuoka University between April 2002 and July 2012. Patients with maintenance HD at the time of their CEA were enrolled in this evaluation. The degree of stenosis was calculated on the basis of angiography according to the criteria of the North American Symptomatic Carotid Endarterectomy Trial (NASCET) study.[7] The surgical indications were 70% or greater stenosis for symptomatic cases and 60% or greater stenosis for asymptomatic cases and non-HD patients.

Conventional CEA was performed while the patient was under general anesthesia, using an operating microscope and electroencephalographic monitoring. Shunts were used in all patients. No patients underwent patch closure. Hemodialysis was performed continuously 2 days before the operation and restarted 2 days after the operation to prevent hemodynamic change and hemorrhage; HD requires anticoagulation drugs, such as heparin. After CEA, propofol sedation was continued until the next morning. Transcranial color-coded real-time sonography was then performed serially to evaluate flow velocity of the middle cerebral artery for diagnosis of hyperperfusion.[8] Blood pressure was controlled to levels less than 150 mm Hg in systole and more than 90 mm Hg in diastole in all patients using nitroglycerin and/or diltiazem until 7 days after CEA.

The charts were reviewed for patient demographics, systemic vascular disease, perioperative morbidity and mortality rates, and long-term follow-up. Outcomes were evaluated in terms of modified Rankin Scale (mRS) at the latest follow-up and the change in mRS from before the operation to the final follow-up. Good outcome was defined as a final mRS score of 0-2, and poor outcome was defined as a final mRS score greater than 2. Five-year survival rate was calculated using Kaplan–Meier methodology. Data were analyzed using SPSS 14.0.J program (SPSS Inc., Chicago, IL).

Results

Demographics

The demographics of cases are reported in Table 1. Between April 2002 and July 2012, 592 CEAs were performed at our institution, of which 15 (2.5%) CEAs were performed in 12 patients undergoing HD. There were 9 male and 3 female patients, with ages ranging from 56 to 81 years (mean age, 66.9 years). Five lesions (33.3%) were symptomatic carotid stenosis, and the other 10 were asymptomatic. Two of 10 asymptomatic lesions were indicated because of stenosis progression under medical treatment. The mean stenotic rate measured by the NASCET method was 79.3% ± 9.1%. Eight patients had diabetic nephropathy as the original kidney disease that resulted in HD, whereas the other 4 had chronic

Table 1. *Characteristics of the 12 patients and the 15 lesions*

Case	Age/sex	Side	Symptom	NASCET	Plaque calcificatio	Original	Duration	HT	HL	DM	IHD	PVD
1	74/M	R	TIA	80	(+)	DM	0.5	(+)	(+)	(+)	(+)	(+)
2	64/M	R	TIA	79	(+)	DM	6	(+)	(−)	(+)	(−)	(−)
3	63/M	R	TIA	75	(+)	CGN	7	(+)	(−)	(−)	(−)	(−)
	66/M	L	Asymptomatic	82	(+)	CGN	9	(+)	(−)	(−)	(−)	(−)
4	76/F	R	TIA	80	(+)	CGN	9	(+)	(−)	(−)	(−)	(−)
5	56/M	R	TIA	91	(+)	CGN	10	(+)	(−)	(−)	(+)	(−)
6	81/M	R	Asymptomatic*	80	(+)	DM	1	(+)	(+)	(+)	(+)	(+)
7	70/M	L	Asymptomatic	88	(+)	DM	2	(−)	(−)	(+)	(+)	(+)
8	58/F	R	Asymptomatic	90	(+)	DM	2	(+)	(−)	(+)	(−)	(−)
	64/F	L	Asymptomatic*	75	(+)	DM	8	(+)	(−)	(+)	(−)	(−)
9	61/M	L	Asymptomatic	78	(+)	DM	4	(+)	(+)	(+)	(+)	(+)
	61/M	R	Asymptomatic	73	(+)	DM	4	(+)	(+)	(+)	(+)	(+)
10	75/M	L	Asymptomatic	63	(+)	DM	4	(+)	(−)	(+)	(−)	(+)
11	72/F	L	Asymptomatic	93	(−)	CGN	5	(+)	(−)	(−)	(−)	(−)
12	63/M	R	Asymptomatic	62	(+)	DM	7	(+)	(+)	(+)	(−)	(−)

Abbreviations: CGN, chronic glomerulonephritis; DM, diabetes mellitus; F, female; HD, hemodialysis; HL, hyperlipidemia; HT, hypertension; IHD, ischemic heart disease; L, left; M, male; NASCET, North American Symptomatic Carotid Endarterectomy Trial; PVD, peripheral vascular disasel; R, right; TIA, transient ischemic attack.

*Stenosis progression during follow-up.

glomerulonephritis. Plaque calcification was found in 14 of 15 plaques (93.3%). Eight patients (66.6%) had hypertension. Coronary artery disease was found in 8 patients (66.6%), and percutaneous transluminal coronary angioplasty (PTCA) had been performed in 4 patients before CEA. The mean dialysis duration of the patients with HD was 5.2 ± 3.1 years before the operation. Five patients (41.7%) had peripheral artery disease. The mean follow-up period was 56.1 ± 38.8 months.

Perioperative Results

The perioperative stroke and death rate was 0% (0 strokes, 0 myocardial infarctions, and 0 deaths). Hyperperfusion was found in only 1 patient by transcranial color Doppler on the day following CEA. We sedated this patient with propofol for a few days, and he was discharged from the hospital 3 weeks after his CEA without any complications, including intracerebral hemorrhage. Bradycardia and an electrocardiographic change resulting from hyperkalemia occurred in 1 patient several hours after CEA, but he improved after emergency dialysis.

Long-term Morbidity and Mortality

Late neurologic events and long-term outcomes are shown in Table 2. In the follow-up period, late strokes occurred in 2 (16.6%) patients. Strokes occurred on the ipsilateral side of previous CEA in 1 patient (8.3%) at 23 months after surgery, which was caused by a newly generated middle cerebral artery stenosis; the ipsilateral carotid artery of the neck revealed no sign of restenosis in this case. Strokes on the contralateral side occurred in 1 patient, which resulted from anterior choroidal artery occlusion at 46 months after surgery. A cerebellar hemorrhage occurred in 1 patient at 2 years after CEA. Only 1 patient underwent carotid artery stenting because of progression of asymptomatic restenosis. Other lesions had been patent during follow-up period. The survival rate in our series was 75.0% at a mean follow-up of 56.1 ± 38.8 months, and the calculated 5-year survival rates were 58.3% in all cases (Fig 1), 40.0% in symptomatic patients, and 71.4% in asymptomatic patients. There were 3 deaths in our series: 1 died of congestive heart failure at 42 months after surgery, 1 died of myocardial infarction, and 1 died of sepsis after amputation of his foot at 58 months after surgery. No patient died of cerebral vascular disease. Eight patients (66.6%) had a good outcome, whereas 1 patient required a wheelchair.

Discussion

Early Benefit for Symptomatic Lesions

Symptomatic carotid stenoses have an early risk for stroke, suggesting that CEA could be useful for prevention of stroke and TIA.[9] In the present study, the risk of ipsilateral stroke among patients with symptomatic

Table 2. *Perioperative complications and long-term outcomes*

Patient no.	Follow-up period (mo)	HP	Perioperative stroke	Perioperative IHD	Other adverse events	Restenosis	Ipsilateral stroke	Any stroke and death	mRS		
									On admission	At discharge	Final
1	27	(−)	(−)	(−)	(−)	(−)	(−)	(−)	0	0	0
2	34	(−)	(−)	(−)	(−)	(−)	(−)	(−)	0	0	0
3	102	(+)	(−)	(−)	(−)	(+)	(−)	(+)	0	0	6
	100	(−)	(−)	(−)	(−)	(−)	(−)	(+)	0	0	6
4	27	(−)	(−)	(−)	(−)	(−)	(−)	(−)	0	0	0
5	97	(−)	(−)	(−)	Hyperkalemia	(−)	(−)	(−)	0	0	0
6	26	(−)	(−)	(−)	(−)	(−)	(−)	(−)	0	0	0
7	49	(−)	(−)	(−)	(−)	(−)	(−)	(+)	0	0	6
8	96	(−)	(−)	(−)	(−)	(−)	(−)	(−)	0	0	0
	24	(−)	(−)	(−)	(−)	(−)	(−)	(−)	0	0	0
9	6	(−)	(−)	(−)	(−)	(−)	(−)	(−)	0	0	0
	4	(−)	(−)	(−)	(−)	(−)	(−)	(−)	0	0	0
10	58	(−)	(−)	(−)	(−)	(−)	(−)	(+)	0	0	6
11	118	(−)	(−)	(−)	(−)	(−)	(−)	(+)	0	0	4
12	75	(−)	(−)	(−)	(−)	(−)	(+)	(+)	0	0	1

Abbreviations: HP, hyperperfusion; IHD, ischemic heart disease; mRS, modified Rankin scale.

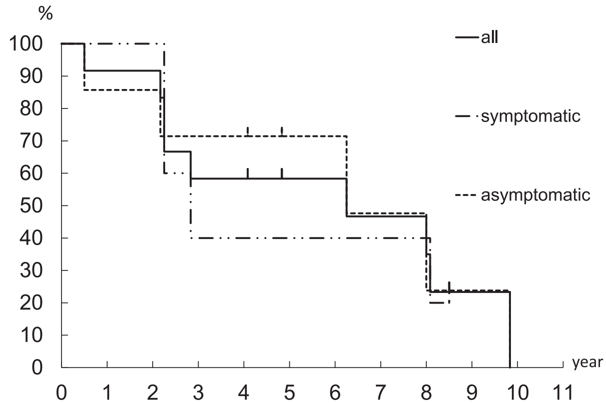

Figure 1. *Survival rate Kaplan–Meier curve. The 5-year survival rates are 58.3% in all cases, 40.0% in symptomatic patients, and 71.4% in asymptomatic patients.*

internal carotid artery disease was 5.5% within the first 2 days after a first recorded hemispheric TIA and 20.1% within the first 90 days. Furthermore, using the NASCET criteria, the Kaplan–Meier curves for stroke diverged between the medically and surgically treated groups at approximately 3 months of follow-up,[9] with a clear benefit in the surgical group by 6-12 months. Thus, if the degree of perioperative risk can be controlled, CEA would be justified for HD patients who have symptomatic carotid stenosis, without any effects on their long-term survival.

Long-term Benefit for Asymptomatic Lesions

To our knowledge, there are no reports on the natural history or long-term outcome of use of CEA in HD patients with carotid artery stenosis. Because asymptomatic patients do not have early benefit like symptomatic patients, long-term outcome is more important. The indication for use of CEA for asymptomatic stenosis (American Academy of Neurology recommendation) requires an expected life expectancy of at least 5 year.[10] According to a Japanese review of HD patients,[1] the 5-year survival rate after HD initiation was only 59.7% (mean age, 64.9 years). As for asymptomatic patients who exhibit a lower incidence of stroke, CEA produces no significant benefits in patients with low long-term survival rates. However, stroke, which is mainly ischemic, occurs 10 times more frequently in dialysis patients than the general population.[11] In our series, the 5-year survival rate was higher than the natural history of asymptomatic HD patients (71.4% versus 59.7%, mean age, 66.9 years versus 64.9 years), and all surgical sites were patent, with no infarction. Thus, our data suggest that CEA might be effective for stroke prevention for HD patients, even in those who are asymptomatic.

Perioperative Morbidity and Mortality

Chronic renal insufficiency (CRI) is a perioperative risk factors for CEA.[12-16] Debing and van den Brande[14] compared 102 patients with CRI (creatinine > 1.5 mg/dL, creatinine clearance < 30 mL/min) with 909 healthy patients and found a significantly higher mortality in the CRI group (3.9% versus 1.0%), which was mainly caused by coronary artery disease. Furthermore, although Ascher et al[15] reported no differences in the stroke rate between 166 patients with renal disease and 443 healthy subjects, there was a higher mortality rate in renal disease patients with a creatinine more than 3.0 mg/dL than in the control group subjects (3.0% versus 0%). Interestingly, Reil et al[11] reported that the safety of CEAs performed in 370 renal insufficiency patients was similar to that in subjects without renal insufficiency as these subjects required preoperative cardiac evaluation and close cardiac monitoring because of increased risk of myocardial infarction. Similarly, in our series, preoperative evaluation of the systemic vascular lesions including coronary artery disease and peripheral artery disease using ultrasound allowed us to use CEA safely. Thus, it is important to co-operate with cardiologists, nephrologists, and cardiac surgeons, for example, before performing CEA.

Hyperperfusion syndrome after CEA in dialysis patients is likely to be a more significant problem than in nondialysis patients because of the increased frequency of cerebral hemorrhage.[2,3,17] In addition, it is difficult to perform dialysis if the blood pressure is too low. Our patients were sedated under general anesthesia until the following day to minimize blood pressure fluctuations immediately after surgery, while screening for hyperperfusion syndrome by ultrasound was also performed.[8] Similarly, the delay in reinstatement of dialysis until the second day after surgery was to reduce the impact of dialysis on blood pressure.

Significance of CEA for Hemodialysis Patients

There are a few reports on the efficacy of CEA in patients receiving HD. Nevertheless, there are some circumstances where CEA for HD patients may be critical to prevent stoke. For example, HD patients were reported to have a higher incidence of carotid artery atherosclerosis.[18,19] Pascazio et al[19] also found more carotid plaques in HD patients (73.8%) than in non-HD controls (44%). Furthermore, Maeda et al[18] reported that carotid plaques were found by ultrasonography in 87.0% of Japanese HD patients, whereas the incidence of carotid artery calcifications was 79.2%.

There is also evidence that the rates of mortality and worse outcomes are higher in HD patients. For example, based on the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study,[4] for every 100 dialysis patients with a stroke, 35 will die within 30 days and only 56 of the 100 patients will be able to go home or to an acute rehabilitation facility. Iseki et al[3] also reported an increased incidence of acute death (within 30 days after stroke) and cerebral infarction in HD patients (46.6%

and 27.9%, respectively) compared with the general population (12.3% and 6.5%, respectively).

Finally, there is evidence that severe stenosis of the carotid artery may result in hemodynamic infarction by HD. For example, Toyoda et al[17] reported that 34% of ischemic brain infarcts occurred within 30 minutes of the dialysis procedure because of a drastic decrease in intravascular blood volume secondary to HD and decreasing cerebrovascular response. Patients with severe stenosis are likely to be exposed to similar conditions while undergoing dialysis.

Recently, an increasing number of older patients and patients with multiple risk factors for arteriosclerosis, especially diabetic patients,[1] have started to receive HD therapy, suggesting that the risk for ischemic stroke, coronary disease, and peripheral artery disease may increase in HD patients overall. Interestingly, a long-term study showed that to prevent vascular events, diastolic blood pressure changes related to large-artery atherosclerosis were more important in HD patients than the patients without stenosis.[17] Thus, evaluation of the systemic arteries, including the carotid artery, the coronary artery, and the peripheral artery, during the follow-up period is of clinical importance.

Conclusions

We found that CEA was effective for patients with HD and may increase long-term survival. Further studies of CEA for HD patients are needed to further define criteria that will allow better prediction of patients likely to achieve long-term benefits. We suggest that CEA for HD patients could be performed as safe as non-HD patients and that CEA might contribute to stroke prevention and better outcome for them.

References

1. Nakai S, Masakane I, Shigematsu T, et al. An overview of regular dialysis treatment in Japan (as of 31 December 2007). Ther Apher Dial 2009;13:457-504.
2. Kawamura M, Fijimoto S, Hisanaga S, et al. Incidence, outcome, and risk factors of cerebrovascular events in patients undergoing maintenance hemodialysis. Am J Kidney Dis 1998;31:991-996.
3. Iseki K, Fukiyama K, Okawa Dialysis Study Group. Clinical demographics and long-term prognosis after stroke in patients on chronic haemodialysis. The Okinawa Dialysis Study (OKIDS) Group. Nephrol Dial Transplant 2000;15:1808-1813.
4. Sozio SM, Armstrong PA, Coresh J, et al. Cerebrovascular disease incidence, characteristics, and outcomes in patients initiating dialysis: the choices for healthy outcomes in caring for ESRD (CHOICE) study. Am J Kidney Dis 2009;54:468-477.
5. Saw J, Gurm HS, Fathi RB, et al. Effect of chronic kidney disease on outcomes after carotid artery stenting. Am J Cardiol 2004;94:1093-1096.
6. Coll B, Betriu A, Martinez-Alonso M, et al. Large artery calcification on dialysis patients is located in the intima and related to atherosclerosis. Clin J Am Soc Nephro 2011;6:303-310.
7. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med 1991;325:445-453.
8. Fujimoto S, Toyoda K, Inoue T, et al. Diagnostic impact of transcranial color-coded real-time sonography with echo contrast agents for hyperperfusion syndrome after carotid endarterectomy. Stroke 2004;35:1852-1856.
9. Eliasziw M, Kennedy J, Hill MD, et al; North American Symptomatic Carotid Endarterectomy Trial Group. Early risk of stroke after a transient ischemic attack in patients with internal carotid artery disease. CMAJ 2004;170: 1105-1109.
10. Chaturvedi S, Bruno A, Feasby T, et al; Therapeutics, Technology Assessment Subcommittee of the American Academy of Neurology. Carotid endarterectomy—an evidence-based review: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2005;65:794-801.
11. Reil T, Shekherdimian S, Golchet P, et al. The safety of carotid endarterectomy in patients with preoperative renal dysfunction. Ann Vasc Surg 2002;16:176-180.
12. Sidawy AN, Aidinian G, Johnson ON III, et al. Effect of chronic renal insufficiency on outcomes of carotid endarterectomy. J Vasc Surg 2008;48:1423-1430.
13. Tarakji A, McConaughy A, Nicholas GG. The risk of carotid endarterectomy in patients with chronic renal insufficiency. Curr Surg 2006;63:326-329.
14. Debing E, van den Brande P. Chronic renal insufficiency and risk of early mortality in patients undergoing carotid endarterectomy. Ann Vasc Surg 2006;Vol 20: 609-613.
15. Ascher E, Marks NA, Schutzer RW, et al. Carotid endarterectomy in patients with chronic renal insufficiency: a recent series of 184 cases. J Vasc Surg 2005;41:24-29.
16. Sundt TM, Sandok BA, Whisnant JP. Carotid endarterectomy. Complications and preoperative assessment of risk. Mayo Clin Proc 1975;50:301-306.
17. Toyoda K, Fujii K, Fujimi S, et al. Stroke in patients on maintenance hemodialysis: a 22-year single-center study. Am J Kidney Dis 2005;45:1058-1066.
18. Maeda N, Sawayama Y, Tatsukawa M, et al. Carotid artery lesions and atherosclerotic risk factors in Japanese hemodialysis patients. Atherosclerosis 2003;169: 183-192.
19. Pascazio L, Bianco F, Giorgini A, et al. Echo color Doppler imaging of carotid vessels in hemodialysis patients: evidence of high levels of atherosclerotic lesions. Am J Kidney Dis 1996;28:713-720.