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【 ORIGINAL ARTICLE 】

Long-term Clinical Outcomes of Elective Carotid Artery Stenting in Patients Undergoing Maintenance Hemodialysis

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Abstract:

Objective Carotid artery stenting (CAS) in patients undergoing maintenance hemodialysis is characterized by high complication rates. These patients are excluded from clinical trials of CAS. The purpose of our retrospective study was to investigate the long-term clinical outcomes of CAS in patients undergoing maintenance hemodialysis.

Methods CAS was performed under local anesthesia. The technical success rate, periprocedural complications, 30-day major vascular event rate (stroke, myocardial infarction, and/or death), 3-month morbidity and mortality rates, and 5-year survival probability were investigated.

Patients Nineteen patients undergoing maintenance hemodialysis were identified.

Results The mean age of the patients was 69 years. Periprocedural complications occurred in two patients (confusion following CAS in one and transient hemiparesis in the other). Complete neurological recovery was achieved in both patients. No major cardiovascular events occurred within 30 days after CAS. Asymptomatic intracranial hemorrhage only occurred in one patient, and seven patients died during the follow-up period at a mean of 3.5 years after the procedure (range, 6 months to 8 years). No permanent neurologic deficit remained in the patient with intracranial hemorrhage. The causes of death were cardiovascular disease (n = 4), cancer (n = 2), and pneumonia (n = 1). No patients died of stroke. The 5-year survival probability in patients undergoing maintenance hemodialysis was 57%.

Conclusion CAS in maintenance hemodialysis patients may be feasible and effective for the prevention of stroke with proper case selection, appropriate technique and strict perioperative management. The most common causes of death during the follow-up of maintenance hemodialysis patients were diseases other than stroke.

Key words: carotid artery stenting, hemodialysis, long-term outcome, 3-month morbidity and mortality rates, 5-year survival probability

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Introduction

Stroke is the leading cause of disability and death (1). The number of patients undergoing maintenance hemodialysis is increasing worldwide (2). In a previous study, patients undergoing maintenance hemodialysis had an increased risk of stroke (3). Despite the high frequency of cerebrovascular disease among patients on dialysis (4, 5), few studies have assessed the long-term outcomes after carotid revascularization in these patients (6).

The risk of ischemic stroke is very high in patients with carotid stenosis (7). Patients undergoing maintenance hemodialysis have a high prevalence of carotid artery stenosis. Some previous studies have shown that carotid endarterectomy (CEA) might be effective for stroke prevention in patients undergoing maintenance hemodialysis (8-10). However, these patients are excluded from landmark trials evaluating CEA. Carotid artery stenting (CAS) is an alternative to CEA for the treatment of carotid artery stenosis, and the

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Table 1. Patients Characteristics.

Age, y, average (SD)	69 (10)
Sex, Male, no., (%)	17 (85%)
Symptomatic, no., (%)	13 (65%)
Carotid stenosis, Left, no., (%)	14 (70%)
Minor complication, no., (%)	2 (10%)
Major complication, no., (%)	0 (0%)
3-month morbidity/mortality, no., (%)	0 (0%)
Estimated survival probability at 5 years, %	57%

long-term functional outcomes and risks of fatal or disabling stroke are similar (11). Landmark trials, such as the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Trial and the Carotid Revascularization Endarterectomy vs. Stenting Trial have often excluded patients undergoing hemodialysis (12, 13). CAS is associated with higher complication rates in these patients (14). Additionally, the long-term efficacy of CAS in patients on maintenance hemodialysis is uncertain. Few studies have evaluated the long-term outcome of CAS in patients undergoing maintenance hemodialysis.

The purpose of our retrospective study was to investigate the long-term outcomes of CAS in patients undergoing maintenance hemodialysis.

Materials and Methods

Maintenance hemodialysis patients who underwent elective CAS in the Shonan Kamakura General Hospital Stroke Center from September 2003 to July 2014, and who were over 18 years of age were included in this retrospective study. The inclusion criteria were 1) either symptomatic carotid stenosis of >50% or asymptomatic high-grade carotid stenosis (>70%), 2) a modified Rankin scale score of <2 before CAS, and 3) small or no brain infarction on magnetic resonance imaging. We excluded patients with malignant tumors.

Every CAS procedure was started under local anesthesia. Elective CAS was defined as CAS in asymptomatic patients or CAS in patients who experienced their last ischemic attack ≥30 days previously. The technical success rate, periprocedural complications, 30-day major vascular event rate (stroke, myocardial infarction and/or death), 3-month morbidity and mortality rates, and 5-year survival probability were investigated.

Procedural technique

Patients provided written informed consent to undergo CAS. CAS was performed by transfemoral or transbrachial catheterization under local anesthesia by the same neuroendovascular team. For the transfemoral approach, an ultralong sheath (6-Fr Shuttle; Cook Medical, Bloomington, IN or 6-Fr Axcelguide; Medikit, Tokyo, Japan) or guiding catheter (8-Fr Brite Tip; Cordis, Johnson & Johnson, Miami, USA) was used. For the transbrachial approach, a 6-Fr (2.24-mm or 0.088-inch internal diameter) guiding sheath with a 90-cm length (MSK-guide 7.5×90; Medikit, Tokyo, Japan) was positioned in the affected common carotid artery proximal to the carotid stenosis (15, 16). The MSK-guide 7.5 became commercially available in October 2010, and transbrachial CAS was performed from 2010 onward. A filter embolic protection device was used during CAS. We did not perform balloon-dilatation immediately after carotid stent deployment because post-CAS balloon-dilatation may cause distal embolization or sufficient dilatation of carotid stenosis may induce hyperperfusion syndrome (17).

Management before and after CAS

For at least 3 days before CAS, patients received dual antiplatelet therapy, which involved aspirin (100 mg/day) and ticlopidine (100 mg/day) until March 2006 and aspirin (100 mg/day) and clopidogrel (75 mg/day) after April 2006. Dual antiplatelet therapy was continued immediately after stenting, but clopidogrel 75 mg was discontinued 30 days after stenting. Antihypertensive drugs were used until 5 days after CAS to reduce the systolic blood pressure to <150 mmHg and diastolic blood pressure to <90 mmHg when the blood pressure was elevated after CAS. Close neurologic monitoring and strict blood pressure control were performed as postoperative management for the patients, and were initiated immediately after CAS.

Follow-up evaluation

Brain magnetic resonance angiography, carotid ultrasound, or digital subtraction angiography were performed at 3 and 12 months after CAS in addition to the evaluation of the clinical outcome. In-stent restenosis was defined as stenosis of ≥50% on digital subtraction angiography.

Statistical analysis

We investigated the clinical and angiographic data of maintenance hemodialysis patients who underwent CAS. We reported continuous variables as the mean and standard deviation, and categorical variables as frequencies and percentages. Cumulative life table analyses (Kaplan-Meier) were used to assess the long-term survival and stroke-free survival rates. We compared the long-term survival outcomes of asymptomatic and symptomatic patients after CAS. P values of <0.05 were considered to indicate statistical significance. All analyses were performed using JMP Pro version 11.0 (SAS Institute, Cary, USA).

Results

During the study period, 560 patients with carotid stenosis underwent CAS. Among these, 19 patients (20 carotid stenoses) undergoing maintenance hemodialysis were identified (Table 1, 2). CAS was performed for 7 asymptomatic (35%) and 13 symptomatic (65%) carotid stenoses. The mean age of the 19 patients was 69 years (range, 46-82 years). Periprocedural complications occurred in two pa-

Table 2. Clinical and Angiographic Variables of the 19 Patients with 20 Carotid Stenoses.

Lesion	Age	Sex	Side	Symptomatic	Stenosis	Complication	HT	DL	DM	IHD	PAD	Cause of death
1	75	M	L	Asymptomatic	70%		+	-	-	+	-	Cardiovascular disease
2	66	M	L	Symptomatic	99%		-	+	+	+	-	Cardiovascular disease
3	75	M	L	Symptomatic	90%	TIA	+	+	+	+	-	Cardiovascular disease
4	59	F	L	Symptomatic	99%		+	-	+	+	-	
5	65	M	L	Asymptomatic	92%		+	+	+	-	-	Pneumonia
6	58	F	L	Symptomatic	80%		+	-	+	+	-	Cancer
7	79	M	R	Asymptomatic	86%		+	-	-	+	-	Cardiovascular disease
8	73	M	L	Symptomatic	84%	Delirium	+	+	+	-	-	
9	73	M	R	Symptomatic	80%		+	+	+	-	-	
10	56	M	L	Symptomatic	60%		+	-	-	+	-	
11	79	M	L	Asymptomatic	90%		+	+	-	+	-	
12	80	M	L	Symptomatic	54%		+	-	-	+	-	
13	61	M	L	Symptomatic	50%		+	+	-	+	-	
14	82	M	R	Symptomatic	63%		+	-	+	+	-	
15	82	M	L	Symptomatic	56%		+	+	-	-	+	Cancer
16	66	M	L	Asymptomatic	70%		+	+	+	-	+	
17	46	F	R	Asymptomatic	70%		+	-	-	+	-	
18	64	M	L	Asymptomatic	70%		+	+	+	+	-	
19	76	M	R	Symptomatic	74%		+	-	+	+	-	
20	76	M	R	Symptomatic	79%		+	+	+	+	-	

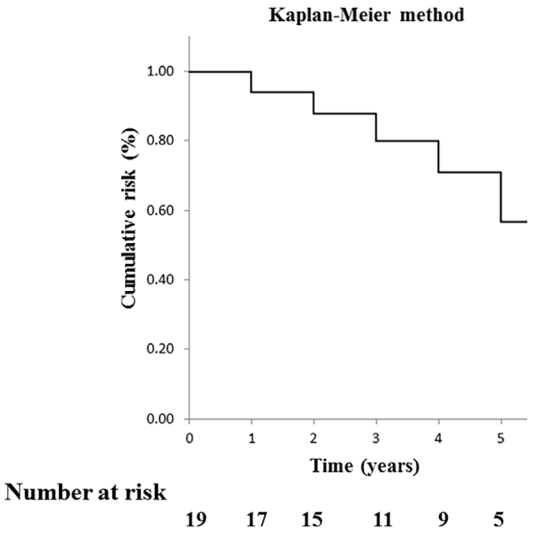

Figure 1. The Kaplan-Meier curve for long-term cumulative survival of all patients who underwent CAS.

tients: confusion following CAS in one and transient hemiparesis in the other. Complete neurological recovery was achieved within 7 days after CAS in both patients. No major cardiovascular events occurred within 30 days after CAS. Asymptomatic intracranial hemorrhage occurred in only one patient 33 days after CAS, and seven patients died during the follow-up period; the median time between CAS and death was 3.5 years. No permanent neurologic deficit remained in the patient with intracranial hemorrhage. During the follow-up period, no in-stent restenosis was detected in any of the 19 patients.

The causes of death were cardiovascular disease (n = 4), cancer (n = 2), and pneumonia (n = 1). The median survival time of the 19 patients was 5.7 years. The 5-year survival probability was 57% (Fig. 1). The calculated 5-year survival rate was 58% and 57% in patients with symptomatic and asymptomatic carotid stenosis, respectively (Fig. 2). There were no statistically significant differences in the long-term survival of the two groups (p = 0.861).

Discussion

In the present study, CAS was performed in 19 patients (20 carotid artery stenoses) undergoing hemodialysis. No 3-month morbidity or mortality occurred, and the median survival time of the 19 patients was 5.7 years. CAS may be effective for the prevention of stroke in maintenance hemodialysis patients with symptomatic carotid stenosis. However, considering the natural history, the present study did not demonstrate the effectiveness of CAS in patients with asymptomatic carotid stenosis.

A previous study showed that the risk of atherosclerotic cardiovascular disease in patients with end-stage renal disease was 5 to 30 times higher than that in the general population (18). Leskinen et al. (19) reported that the carotid plaque burden (as shown by carotid ultrasound) in patients with end-stage renal disease was higher than that in the general population. Additionally, Adil et al. (20) reported that both CAS and CEA were associated with a 4-fold higher odds of in-hospital mortality in patients with end-stage renal disease. Such observations raise concerns regarding the risk: benefit ratio of carotid revascularization in these patients.

Some previous studies have shown that CEA might be effective for stroke prevention in patients undergoing maintenance hemodialysis (21). Patients with renal dysfunction who have undergone CEA have been shown to have a

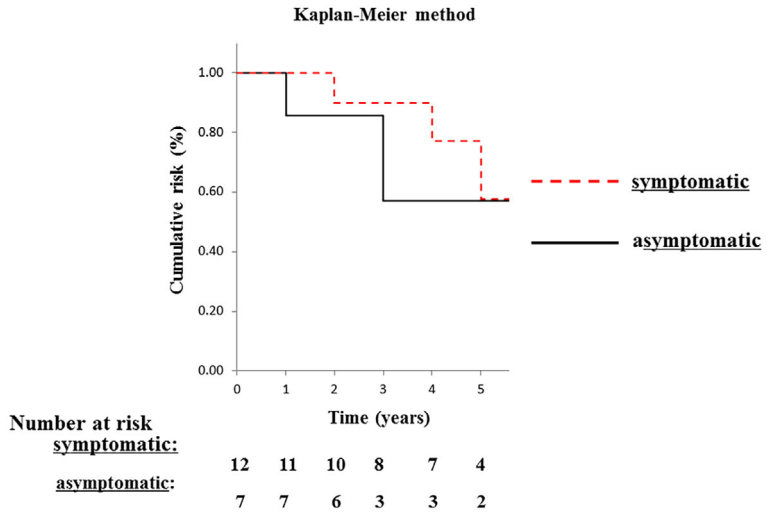

Figure 2. **Kaplan-Meier curves for long-term cumulative survival of asymptomatic and symptomatic patients who underwent CAS. Solid line: asymptomatic group (n=7), dotted line: symptomatic group (n=13). There was no statistically significant difference in the long-term survival of the two groups.**

higher risk of perioperative stroke and death in comparison to patients with a normal renal function (22). Protack et al. (23) reported that 750 and 250 patients with chronic renal insufficiency who underwent CEA and CAS had high 30-day mortality rates. However, a limitation of their study was that only 7 of the 921 patients underwent maintenance hemodialysis. Adil et al. (20) recently reported that 3,888 and 693 patients undergoing hemodialysis were treated by CEA and CAS, respectively, and that both CAS and CEA were associated with higher rates of in-hospital mortality and moderate to severe disability. Few studies of CEA and/or CAS have focused on patients undergoing maintenance hemodialysis. Carotid intervention for patients with chronic renal insufficiency might remain controversial because of the increased risk of perioperative complications and postoperative cardiovascular disease (24).

Few reports have described the long-term outcomes after carotid intervention versus medical therapy for hemodialysis patients with carotid artery stenosis. Aggressive medical treatment was recently shown to be the most effective therapy for asymptomatic carotid artery stenosis (25). Yuo et al. (26) reported that the median survival of 2,131 patients undergoing dialysis who were treated by CEA or CAS was 2.5 years (CAS, 2.0 years; CEA, 2.6 years). Medical therapy alone might be the best treatment for patients with asymptomatic carotid artery stenosis. The largest population-based study of outcomes after CAS in patients undergoing hemodialysis demonstrated relatively poor long-term survival and a prohibitive risk of operative stroke and death (27). In this background, it might be preferable avoid CAS in asymptomatic patients undergoing dialysis and to plan CAS for symptomatic patients with caution.

In the present study, the major causes of death in patients undergoing maintenance hemodialysis who were treated by CAS were cardiovascular disease and/or cancer. Screening tests for cardiovascular disease and/or cancer might be needed before carotid intervention for patients with chronic renal insufficiency.

Because of the small number of patients in the present study, larger studies are required to confirm our results.

Conclusion

With proper case selection, appropriate technique and strict perioperative management, CAS in maintenance hemodialysis patients may be feasible and effective for the prevention of stroke. Diseases other than stroke were the most common causes of death in patients undergoing maintenance hemodialysis.

Author's disclosure of potential Conflicts of Interest (COI).
Tomonori Iwata: Honoraria, Daiichi Sankyo and Eisai.

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