

# Surgical Treatment for Cervical Carotid Artery Stenosis in the Elderly: Importance of Perioperative Management of Ischemic Cardiac Complications

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## Abstract

Ischemic cardiac complication is one of the major perioperative complications of surgical treatment for cervical carotid stenosis, carotid endarterectomy (CEA), and carotid artery stenting (CAS), and may greatly affect surgical outcome, especially in elderly patients aged  $\geq 80$  years. We retrospectively analyzed the records of 259 patients (34 patients aged  $\geq 80$  years) treated by CEA and 61 patients (12 patients aged  $\geq 80$  years) treated by CAS at Aizu Chuo Hospital from January 2000 to September 2010. Preoperative ischemic heart disease screening was performed in all patients. If high risk of coronary atherosclerotic stenosis was detected, treatment for coronary lesion was performed prior to CEA or CAS. There was no preoperative ischemic cardiac complication in both the CEA and CAS groups. Perioperative complications (morbidity + mortality) occurred in 2.9% of patients aged  $\geq 80$  years and 1.7% of patients aged  $\leq 79$  years in the CEA group, and 8.3% and 8.1% of patients, respectively, in the CAS group. There was no statistically significant difference by age in either group. CEA could be safely performed with tolerable complication rates even in elderly patients. However, the complication rate in the CAS group was relatively high. New ischemic lesion on diffusion-weighted magnetic resonance imaging, both symptomatic and asymptomatic, tended to occur at a higher rate in the CAS group, especially in the elderly patients. Thorough perioperative management may minimize ischemic cardiac complications even in elderly patients. Efforts must be continued to minimize surgical complications, especially for CAS. Noninvasive medical treatment should also be considered for elderly patients.

Key words: cervical carotid artery stenosis, carotid endarterectomy, carotid artery stenting, elderly, perioperative ischemic cardiac complications

## Introduction

Global life expectancy has increased continuously and substantially in the past 40 years.<sup>1)</sup> Consequently, medical care for the elderly population is becoming more important worldwide. Stroke is one of the leading causes of death and a major cause of acquired disability in adults. Treatment for stroke, especially preventive treatment, in the elderly population has recently become a major medical issue. Cervical carotid artery stenosis is one of the common causes of ischemic stroke. Preventive treatment for cervical carotid artery stenosis includes medical (nonsurgical) and surgical interventions. Severe carotid artery stenosis is frequently treated by surgical intervention, carotid endarterectomy (CEA), based on the findings of randomized control

studies.<sup>2–5)</sup> Endovascular intervention, carotid artery stenting (CAS), is also another surgical option with similar perioperative complications to CEA, as confirmed by a recent randomized control trial, The Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST).<sup>6)</sup>

Noninvasive medical treatment may be superior to surgical treatment, especially for asymptomatic severe carotid artery stenosis, because of the significant advances in medical intervention for vascular disease since the large randomized trials for carotid stenosis were conducted.<sup>7)</sup> The fundamental goals of the treatment of carotid artery stenosis are extension of healthy life expectancy, and improvement of the quality of life. Therefore, the selection of noninvasive medical treatment or invasive surgery must be considered carefully, and is even more important for the elderly. On the other hand, some patients with severe carotid stenosis suffer deterioration of

the quality of life caused by repeated relapses of cerebral infarction. CEA and CAS would be very effective for such patients or patients with long life expectancy. Performance of CEA and CAS with few perioperative complications is important in these patients. The CREST showed that CEA has superior perioperative complication rates compared to CAS in the elderly population. However, both CEA and CAS for carotid stenosis still carry high risk for the elderly.<sup>8)</sup> The appropriate perioperative management for the elderly has not yet been established.

Ischemic heart disease is one of the major perioperative complications of CEA and CAS. Atherosclerosis of the cardiac coronary arteries often occurs together with cervical carotid arteriosclerosis, extracranial atherosclerotic lesion, and both diseases are believed to have histopathological similarities.<sup>9)</sup> Perioperative occurrence of ischemic heart disease or myocardial infarction greatly influences the surgical outcomes, as shown by the CREST.<sup>6)</sup> Efficient management of perioperative ischemic cardiac complications is essential for better surgical outcome, especially in the elderly.

The present study assesses our perioperative management during surgical treatment for carotid artery stenosis, both CEA and CAS, in the elderly to minimize perioperative complications, especially ischemic cardiac complication, and describes our surgical results in the elderly including the perioperative complications.

## Materials and Methods

We retrospectively analyzed the hospital records of patients who underwent surgical treatment (both CEA and CAS) for cervical carotid stenosis at Aizu Chuo Hospital from January 2000 to September 2010. We assessed the effectiveness of preoperative screening and the incidence of perioperative complications by comparing these findings in elderly patients aged  $\geq 80$  years with patients aged  $\leq 79$  years at surgery. We also compared the outcomes of CEA and CAS in the elderly patients.

On the basis of various randomized control studies, surgery was indicated for symptomatic patients with cervical carotid stenosis of  $\geq 50\%$  and asymptomatic patients with stenosis of  $\geq 80\%$ .<sup>10)</sup> CEA was the first choice for the surgical treatment. CAS was selected for high position carotid plaque extending distally to the height of the vertebral body of C2, because of the difficulty of the surgical approach to high position carotid plaque. CAS was also selected for restenosis after CEA. Characteristics of carotid plaque findings on carotid artery ultrasound or magnetic resonance (MR) imaging were

not considered in the inclusion criteria for surgery or in the selection of CEA or CAS.

Here, we will describe our perioperative management strategy. Preoperatively, digital subtraction angiography (DSA) of the cerebral vessels was performed for the evaluation of the degree of stenosis, identification of anatomical height, and evaluation of intracranial vessels and collateral flow. Carotid artery ultrasound was performed for the evaluation of plaque characteristics and measurement of flow rate. Single-photon emission computed tomography (SPECT) was performed to evaluate cerebral blood flow and to predict postoperative hyperperfusion. Physicians from the department of internal medicine were consulted as required with regard to medical complications such as diabetes, chronic obstructive respiratory disease, etc., and they exercised medical control in preparation for surgery. Medication for anti-platelet therapy included monotherapy for CEA patients and combination therapy for CAS patients. Anti-platelet therapy was continued until surgery.

All patients underwent preoperative screening for ischemic heart disease including echocardiography and Holter electrocardiography to prevent perioperative ischemic cardiac complications. We then consulted the cardiology department and, if required, performed a treadmill stress electrocardiography and coronary DSA. If severe stenosis of coronary artery was detected by coronary DSA and the cardiology department judged the patient had high risk for coronary lesions, we performed percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) prior to the surgery (both CEA and CAS). If severe stenosis of the coronary artery was detected by the preoperative screening, PCI or CABG was performed prior to surgery regardless of the presence or absence of symptoms of angina pectoris. Continuous intravenous administration of coronary vasodilator (nicorandil) was performed prior to surgery in patients with high risk of developing perioperative ischemic cardiac complications.

CEA was performed under general anesthesia and CAS was performed under local anesthesia. CEA was a macroscopic surgery performed without the use of a surgical microscope. After exposing the blood vessels, systemic heparinization was continued while the blood vessels were blocked. An internal shunt was used as required according to the comprehensive preoperative evaluation of the degree of collateral circulation. During CAS, systemic heparinization was performed after inserting a sheath for catheter insertion, and distal protection was employed for the prevention of intraoperative embolic events. A stent was placed in the stenotic segment after dilation

with a balloon catheter. As a rule, dilation was not performed after placing the stent.

The patient was comprehensively managed in the intensive care unit during the night after surgery, with the prime focus on blood pressure control. MR imaging was performed on the first postoperative day and new ischemic lesions were evaluated on diffusion-weighted MR imaging. Cerebral blood flow was evaluated with SPECT on the first or second postoperative day, and immediate strict blood pressure control was enforced in the event of hyperperfusion. Blood vessels were evaluated at 1 week after surgery by DSA or three-dimensional computed tomography angiography.

In this study, perioperative complications included any episodes of cerebral stroke, myocardial infarction, or death within 30 days after the operation. Arteriosclerosis obliterans which worsened after CAS and required additional treatment was considered to be a perioperative complication. Stroke was defined as an acute neurological event with focal symptoms and signs that were consistent with focal cerebral ischemic lesion detected on MR imaging. Myocardial infarction was defined as chest pain or symptoms consistent with ischemia on electrocardiogram, in addition to elevation of cardiac enzyme levels including creatine kinase-MB or troponin test. New ischemic lesion was defined as any new ischemic lesion detected on diffusion-weighted MR imaging performed on the first postoperative day regardless of the presence or absence of focal neurological symptoms.

Mean age was compared using the *t*-test. The number of male patients was compared with Fisher's

exact test. The number of patients with each underlying disease, number of patients who underwent preoperative coronary treatment, and the rate of perioperative complications were also compared with Fisher's exact test. All statistical analysis was carried out using JMP 9.0.0 (SAS Institute Inc., Cary, North Carolina, USA), and statistical significance was set at  $p < 0.05$ .

## Results

CEA was performed in 259 patients and CAS in 61 patients between January 2000 and September 2010. There were 34 elderly patients aged  $\geq 80$  years in the CEA group (symptomatic 22, asymptomatic 12) and 12 in the CAS group (symptomatic 4, asymptomatic 8). The patients' characteristics are shown in Table 1. The proportion of symptomatic patients was significantly higher among elderly patients aged  $\geq 80$  years ( $p = 0.008$ ), and the proportion of male subjects was significantly higher among patients aged  $\leq 79$  years in the CEA group ( $p = 0.006$ ). In contrast, there was no significant difference between elderly patients aged  $\geq 80$  years and patients aged  $\leq 79$  years in the CAS group.

Underlying diseases in the CEA and CAS groups are shown in Table 1. The proportion of patients with diabetes was significantly higher in patients aged  $\leq 79$  years than in elderly patients aged  $\geq 80$  years in the CEA group ( $p = 0.001$ ). No other significant differences were found in underlying diseases between patients aged  $\geq 80$  years and  $\leq 79$  years in the CEA and CAS groups, including ischemic heart disease.

**Table 1** Clinical characteristics

	Carotid endarterectomy			Carotid artery stenting		
	Age $\geq 80$ yrs	Age $\leq 79$ yrs	<i>p</i> -value	Age $\geq 80$ yrs	Age $\leq 79$ yrs	<i>p</i> -value
Number of subjects	34	225		12	49	
Age (yrs)						
Mean $\pm$ SD	82.9 $\pm$ 2.8	70.1 $\pm$ 7.5	<0.001*	81.9 $\pm$ 1.7	71.5 $\pm$ 7.0	<0.001*
Range	80–91	38–79		80–85	54–79	
Symptomatic subjects	22 (64.7%)	89 (39.5%)	0.008**	4 (33.3%)	19 (38.7%)	1.00
Male	22 (64.7%)	192 (85.3%)	0.006**	9 (75.0%)	42 (85.7%)	0.39
Underlying diseases						
Hypertension	23 (67.6%)	141 (62.6%)	0.70	6 (50.0%)	29 (68.4%)	0.74
Diabetes	2 (5.8%)	71 (31.5%)	0.001**	1 (8.3%)	18 (5.2%)	0.08
Hyperlipidemia	5 (14.7%)	27 (12.0%)	0.58	2 (16.6%)	6 (13.1%)	0.65
Angina, myocardial infarction	8 (23.5%)	35 (15.5%)	0.32	4 (33.3%)	15 (30.6%)	1.00
Arteriosclerosis obliterans	1 (2.9%)	9 (4.0%)	1.00	2 (16.6%)	5 (10.2%)	0.61
Chronic respiratory disease	0 (0%)	7 (3.1%)	0.59	0 (0%)	2 (4.0%)	1.00

\*Statistically significant by *t*-test, \*\*Statistically significant by Fisher's exact test. SD: standard deviation.

The outcomes for patients treated for coronary lesions prior to the surgery are shown in Table 2. The rate of patients requiring treatment for coronary lesions was 8.8% in patients aged  $\geq 80$  years and 12.8% in patients aged  $\leq 79$  years in the CEA group, and 8.3% and 4.0%, respectively, in the CAS group, both with no significant difference.

Table 3 shows the results of perioperative complications and Table 4 shows the details of perioperative complications in each group. Morbidity occurred in 2.9% of patients aged  $\geq 80$  years and in 1.3% of patients aged  $\leq 79$  years in the CEA group, showing a tendency to more complications in patients aged  $\geq 80$  years. All complications included in morbidity were cerebral stroke. No myocardial infarction or ischemic cardiac complication occurred perioperatively. Only one patient aged  $\leq 79$  years died of postoperative pneumonia in the CEA group. In addition, the total of morbidity and mortality did not show any significant difference between patients aged  $\geq 80$  years (2.9%) and patients aged  $\leq 79$  years (1.7%). Morbidity occurred in 8.3% of patients aged  $\geq 80$  years and in 8.1% of patients aged  $\leq 79$  years in the CAS group, with no significant difference. No perioperative ischemic cardiac complication occurred. Two patients aged  $\leq 79$  years suffered worsening of arteriosclerosis obliterans and required surgical treatment.

Postoperative diffusion-weighted MR imaging demonstrated new ischemic lesion in 8.8% of patients aged  $\geq 80$  years and 3.1% of patients aged  $\leq 79$  years in the CEA group, indicating a tendency to form new lesions in patients aged  $\geq 80$  years. However, there was no significant difference. Postoperative diffusion-weighted MR imaging demonstrated new lesions in 50.0% of patients aged  $\geq 80$  years and 24.4% of patients aged  $\leq 79$  years in the CAS group, showing a tendency to form new ischemic lesions in patients aged  $\geq 80$  years. However, there was no significant difference.

Comparison of the CEA and CAS treatment outcomes showed a trend for higher complication rate (including new ischemic lesions) in the CAS group in both patients aged  $\geq 80$  years and patients aged  $\leq 79$  years.

## Discussion

The main result of this study is that the occurrence of perioperative ischemic cardiac complications could be minimized by thorough preoperative screening and perioperative management before surgery for carotid stenosis (both CEA and CAS) even in elderly patients aged  $\geq 80$  years. In particular, CEA could be safely performed with tolerable perioperative complication rate.

**Table 2 Preoperative cardiovascular treatment**

	Carotid endarterectomy			Carotid artery stenting		
	Age $\geq 80$ yrs (n = 34)	Age $\leq 79$ yrs (n = 225)	p-value	Age $\geq 80$ yrs (n = 12)	Age $\leq 79$ yrs (n = 49)	p-value
PCI	1 (2.9%)	29 (12.8%)		1 (8.3%)	2 (4.0%)	
CABG	2 (5.8%)	0 (0%)		0 (0%)	0 (0%)	
Total	3 (8.8 %)	29 (12.8%)	0.77	1 (8.3%)	2 (4.0%)	0.48

CABG: coronary artery bypass grafting, PCI: percutaneous coronary intervention.

**Table 3 Perioperative complications**

	Carotid endarterectomy			Carotid artery stenting		
	Age $\geq 80$ yrs (n = 34)	Age $\leq 79$ yrs (n = 225)	p-value	Age $\geq 80$ yrs (n = 12)	Age $\leq 79$ yrs (n = 49)	p-value
Morbidity	1 (2.9%)	3 (1.3%)	0.43	1 (8.3%)	4 (8.1%)	1
Cerebral stroke	1	3		1	2	
Myocardial infarction	0	0		0	0	
Atherosclerosis obliterans deterioration	0	0		0	2	
Mortality	0 (0%)	1 (0.4%)	1	0 (0%)	0 (0%)	1
Morbidity + mortality	1 (2.9%)	4 (1.7%)	0.50	1 (8.3%)	4 (8.1%)	1
New ischemic lesion on DWI	3 (8.8%)	7 (3.1%)	0.13	6 (50.0%)	12 (24.4%)	0.15

DWI: diffusion-weighted magnetic resonance imaging.

**Table 4** Details of perioperative complications

CEA complications	
Age $\geq$ 80 years	One case of postoperative cardiogenic embolism on the contralateral side
Age $\leq$ 79 years	Two cases of intraoperative embolism, one case of intraoperative ophthalmic artery occlusion (loss of vision), and one case of death from postoperative pneumonia
CAS complications	
Age $\geq$ 80 years	One case of intraoperative embolism
Age $\leq$ 79 years	One case of intraoperative embolism, one case of brain-stem infarction, and two cases of worsening atherosclerosis obliterans

CAS: carotid artery stenting, CEA: carotid endarterectomy.

The CREST study, a randomized control trial comparing the surgical outcomes of CEA and CAS, indicated that the perioperative complication and mortality rates are similar for CEA and CAS, but the effectiveness of CEA compared to CAS increased with the age of the patient.<sup>6)</sup> In addition, the CREST study also highlighted the complications of perioperative cerebral infarction in CAS patients and perioperative ischemic heart disease in CEA patients.

Many reports have suggested the significance of ischemic cardiac complications occurring during surgical treatment for cervical carotid stenosis.<sup>11-13)</sup> In the present series, thorough preoperative cardiovascular screening of all patients and timely treatment of coronary lesions as required prevented the occurrence of perioperative ischemic cardiac complications. The proportion of patients requiring treatment for coronary lesions prior to CEA or CAS was not significantly different between the two age groups (aged  $\geq$  80 years and aged  $\leq$  79 years). In addition, continuous intravenous administration of nicorandil prior to performing surgery in the group at high risk of perioperative ischemic cardiac complications was presumably an additional factor suppressing the occurrence of perioperative ischemic cardiac complications.

Moreover, the rate of perioperative complications was not significantly different between subjects aged  $\geq$  80 years and those aged  $\leq$  79 years in both the CEA and CAS groups. Comparison of the surgical outcomes of CEA and CAS in age groups found better surgical outcomes for CEA in patients aged  $\geq$  80 years as seen in the CREST results.<sup>6)</sup>

However, our study also identified several disadvantages of the surgical treatment. There was a higher rate of perioperative complications in both patients

aged  $\geq$  80 and aged  $\leq$  79 years in the CAS group. The complication rate was as high as 8%. In contrast, the complication rate was less than 3% in the CEA group. According to retrospective investigations, there were some high risk cases in the CAS group, such as patients with vulnerable plaque according to carotid artery ultrasound or MR imaging.

Another disadvantage was the formation of new ischemic lesions on diffusion-weighted MR imaging. New ischemic lesions were observed at a higher rate in the elderly patients (in both CEA and CAS groups) and in the overall CAS group, to as high as 50% in the elderly patients in CAS group. A sub-analysis of the randomized International Carotid Stenting Study (ICSS) revealed that the rate of new ischemic lesions on postoperative diffusion-weighted MR imaging was three times higher in the CAS group than in the CEA group.<sup>14)</sup> The ICSS also analyzed results with the subjects split into a group aged  $\geq$  71 years and a group aged  $\leq$  70 years. Subjects of both age groups who underwent CAS demonstrated a significantly higher rate of new ischemic lesion, and the trend was stronger in the subjects aged  $\geq$  71 years. Our result is consistent with these findings. Ischemic lesion on diffusion-weighted MR imaging, thought to be asymptomatic, may be a possible cause of clinical symptoms such as deteriorated cognitive function, so efforts should be made to reduce the occurrence of such lesions.<sup>15)</sup>

Deterioration of arteriosclerosis obliterans is another specific complication related to CAS. In this study, two patients aged  $\leq$  79 years had worsening of arteriosclerosis obliterans as a result of CAS treatment, caused by the sheath inserted into the femoral artery during CAS. Surgical treatment was required in both patients, but neither suffered any physical impediments. Therefore, we suggest that adequate screening of the degree of atherosclerosis in the area of sheath insertion is necessary prior to CAS surgery.

Indeed there was a higher rate of operative complications found in the CAS group. However, the operative outcome could be improved, since the total number of the patients treated by CAS was relatively small in this study. Evaluation of high risk cases, such as the characteristic of plaques through ultrasound or MR imaging, might be important for the consideration of surgical indications and selection of the surgery.

In summary, our present study suggests that CEA and CAS can both be safely performed in elderly patients aged  $\geq$  80 years without ischemic cardiac complications after thorough preoperative screening and perioperative management. Our present study also indicates that CAS might not be safe enough for the elderly population. The fundamental goal of

the treatment of carotid artery stenosis is extension of healthy life expectancy, and improvement of the quality of life. We must be aware that noninvasive medical treatment may be the best treatment choice in some cases and surgery should not be easily indicated. However, surgical treatment is essential in other cases. Efforts must be continued to minimize the surgical complications.

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### Conflicts of Interest Disclosure

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices in the article. All authors who are members of The Japan Neurosurgical Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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