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Original Article

Preventive Strategies for Perioperative Ischemic Heart Disease during Carotid Artery Stenting

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Objectives: We have been performing preoperative coronary artery assessments and implementing coronary revascularization or intraoperative adjunctive therapies as needed in patients scheduled for carotid artery stenting (CAS) to prevent ischemic heart disease. In this study, we report the results of a retrospective observation of patients who underwent CAS under our treatment strategy to prevent perioperative coronary ischemic complications.

Methods: A total of 224 cases from January 2014 to December 2021 were included. Following preoperative coronary artery CTA, preoperative coronary artery treatment or intraoperative adjunctive therapy (temporary transcutaneous cardiac pacemaker [TTCP] or intra-aortic balloon pumping [IABP]) was performed based on the degree of stenosis. We analyzed the outcomes of patients treated with CAS under this strategy at our institution.

Results: Coronary artery disease was detected preoperatively in 143 cases (64%), with 91 cases (41%) indicated for coronary revascularization. Preoperative coronary artery treatment was performed in 76 cases (34%) prior to CAS, and adjunctive therapy with TTCP or IABP was provided in 28 cases (13%) during the procedure. No case developed perioperative coronary ischemic complication.

Conclusion: In patients who have undergone CAS, perioperative coronary ischemic complications might be reduced by evaluating the risk of ischemic heart disease preoperatively, performing pre-CAS coronary artery intervention based on the severity of the lesions, and administering intraoperative adjunctive therapy.

Keywords carotid artery stenting, coronary artery disease, hemodynamic depression, perioperative complication

Introduction

Carotid artery stenosis and coronary artery disease (CAD) are arteriosclerotic diseases that frequently coexist.[1)] Carotid artery stenting (CAS) has become an effective treatment for carotid artery stenosis and offers the advantage of being a less invasive treatment than carotid endarterectomy (CEA). However, ischemic heart disease is listed as one of the perioperative complications of CAS, with reported incidence rates of 2.4% in the SAPPHIRE study[2)] and 1.1% in the CREST study.[3)] The mechanism of its occurrence is considered to be related to triggering of the carotid sinus reflex during CAS, leading to hemodynamic depression (HD) characterized by bradycardia and hypotension,[4)] which can result in myocardial ischemia in patients with CAD. Preventing perioperative myocardial ischemia is crucial due to its potential severity. However, there is currently no established view regarding the prevention of coronary ischemic complication during CAS, including the efficacy of preoperative revascularization for concomitant CAD.

At our institution, patients scheduled for CAS undergo comprehensive coronary artery assessments preoperatively and coronary artery treatment is performed prior to CAS based on the severity of the lesions. In addition,

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in anticipation of HD during CAS, we actively provide adjunctive therapy such as a temporary transcutaneous cardiac pacemaker (TTCP) or intra-aortic balloon pumping (IABP) in patients at risk of coronary artery events. The aim of this study was to report on the strategy of scheduled CAS to prevent complications of ischemic heart disease, based on retrospective observation of the treatment outcomes at our institution.

Materials and Methods

This was a retrospective, observational study conducted at a single institution. Patients who underwent CAS as initial treatment for carotid artery stenosis between January 2014 and December 2021 were included.

Lifestyle diseases were defined as follows. Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg at home, patients already diagnosed with hypertension, or patients taking antihypertensive medication. Diabetes mellitus (DM) was defined as HbA1c (National Glycohemoglobin Standardization Program) >6.9%, patients already diagnosed with DM, or patients receiving treatment. Dyslipidemia was defined as low-density lipoprotein cholesterol >140 mg/dL, patients already diagnosed with dyslipidemia, or patients receiving treatment.

Symptomatic carotid stenosis was defined as ischemic stroke, transient ischemic attack (TIA), and amaurosis fugax attributed to ipsilateral carotid stenosis, and clinical signs due to CAD were defined as chest symptoms such as angina pectoris or elevated cardiac enzymes on blood tests.

The degree of stenosis of the lesion was evaluated by cerebral angiography using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method. The vulnerability of plaques was represented by the plaque-to-sternocleidomastoid muscle signal intensity ratio using an MRI T1 black blood (sampling perfection with application optimized contrasts using different flip angle evolutions [SPACE] sequence), and the presence of calcification in the lesion was evaluated using cervical contrast-enhanced CTA.

HD was defined as hypotension (systolic blood pressure <90 mmHg or its decrease of >20 mmHg) or bradycardia (heart rate <60 bpm or its decrease of >10 bpm) during CAS.

Clinical and examination information for each patient was obtained retrospectively from medical records, and the treatment information for CAS and perioperative complications of ischemic stroke and ischemic heart disease were investigated.

Since this study was an anonymized, retrospective, observational study, written, informed consent was not obtained from the patients, but the study was approved by the institutional ethics committee in compliance with the current ethical regulations. Opt-out materials were also displayed, and information of subjects who refused to participate in the study was removed from the analysis and promptly discarded.

Treatment management

The indications for CAS included asymptomatic lesions with NASCET stenosis ≥70% or symptomatic lesions with stenosis ≥50% (TIA, amaurosis fugax, or cerebral infarction) as assessed by cerebral angiography. Cases with inappropriate access routes, severely calcified lesions, or high-volume vulnerable plaques were considered at high risk for CAS, and CEA was performed instead of CAS.

Coronary artery CTA was evaluated for the presence of concomitant CAD prior to CAS. A coronary artery stenosis ≥75%, regardless of its site, was diagnosed as CAD, and coronary angiography (CAG) was performed by a cardiologist.

Percutaneous coronary intervention (PCI) for CAD preceding CAS was indicated in patients with CAG and confirmed coronary artery stenosis ≥90% in the proximal major coronary artery. In cases of coronary artery stenosis that did not meet the above categories and cases in which the perioperative risk of PCI was judged to be high, CAS had been performed with TTCP or IABP on standby by the cardiologist, after consultation with the cardiologist. Even if CAD revascularization was performed prior to CAS, there were no rules for the interval until CAS was performed. The treatment strategy of our institution for patients with concurrent carotid and coronary artery stenosis is shown in **Fig. 1**.

Cardiologic support during the CAS procedure

Dual antiplatelet therapy was initiated 2 weeks prior to the CAS procedure. When necessary, a TTCP was placed, and for patients deemed at higher risk, an IABP was inserted before the procedure. In cases of bradycardia during the procedure, a bolus injection of atropine sulfate 0.5 mg was administered intravenously, and ephedrine or norepinephrine was administered intravenously for hypotension. In cases of sustained bradycardia or persistent hypotension,

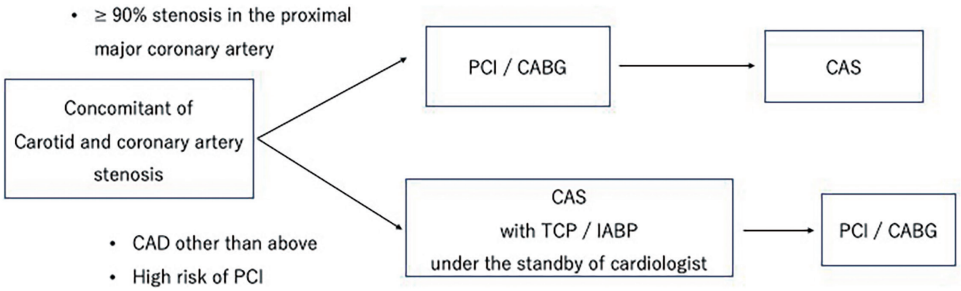

Fig. 1 Schema of treatment strategies for patients with concomitant coronary and carotid artery stenosis. CABG: coronary artery bypass grafting; CAD: coronary artery disease; CAS: carotid artery stenting; IABP: intra-aortic balloon pumping; PCI: percutaneous coronary intervention; TCP: transcutaneous cardiac pacemaker

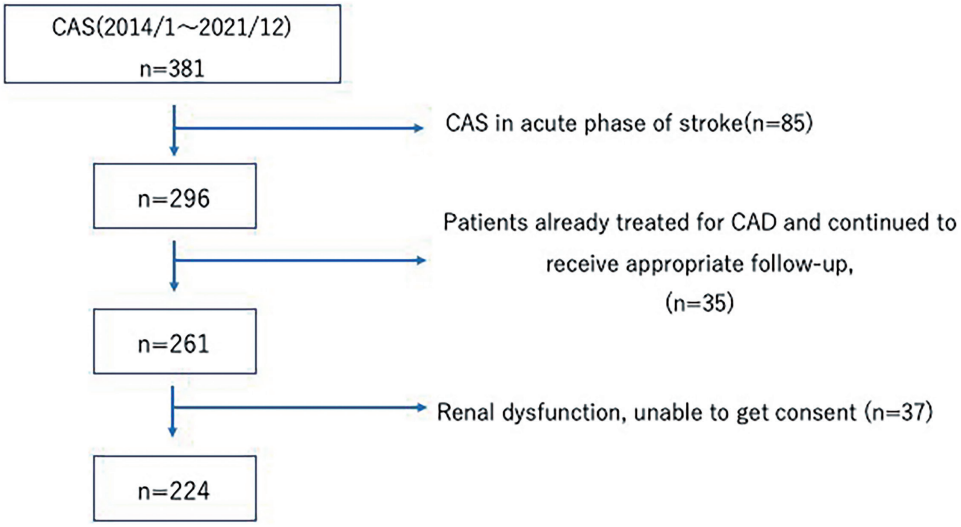

Fig. 2 Inclusion criteria. CAD: coronary artery disease; CAS: carotid artery stenting

continuous intravenous infusion of norepinephrine was administered.

Results

Of a total of 381 cases who underwent CAS as initial treatment for carotid stenosis between January 2014 and December 2021, 85 underwent CAS during the acute phase within 14 days after the onset of stroke, 35 cases who had already been treated for CAD continued to receive appropriate follow-up, and 37 cases were excluded for reasons such as renal dysfunction contraindicating the use of contrast media, inability to remain at rest during the examination, or lack of consent for coronary CTA. A final total of 224 cases were included in this study (**Fig. 2**).

Patients' background characteristics are shown in **Table 1**. The median age was 76 years, with 198 cases (88%) being male. Preexisting conditions included hypertension in 153 cases (67%), DM in 60 cases (27%), dyslipidemia in 145 cases (65%), and 112 cases (50%) were symptomatic. The median stenosis rate of the lesions was 60% according to the NASCET criteria. No cases presented with clinical signs caused by CAD prior to CAS. Preoperative coronary artery CTA showed concomitant CAD in 143 cases (64%), and subsequent CAG in these cases identified CAD that was indicated for revascularization in 91 cases (41%). The treatment information is presented in **Table 2**.

Of the 91 patients eligible for treatment for CAD, 76 underwent coronary artery treatment preceding CAS, excluding 15 patients who were judged to be at high risk for PCI prior to CAS according to consultation with a cardiologist. PCI was performed in 73 cases (33%), plain old balloon angioplasty in 2 cases (0.9%), and coronary artery bypass grafting (CABG) in 1 case (0.4%). In cases where CAD was present during CAS (28 cases, 13%), a TTCP

Table 1 Patients' background characteristics

	n = 224
Age (years)	76 (70–81)
Male	198 (88%)
Atherosclerotic-related disease	
Hypertension	153 (67%)
DM	60 (27%)
Hyperlipidemia	145 (65%)
Symptom due to cervical stenosis	
Stroke/TIA/Amaurosis	104/5/3
Asymptomatic	112 (50%)
Cervical stenosis lesion	
Right side	116 (52%)
NASCET	60 (49–76)
SIR	1.5 (1.2–2)
Calcification (>180° of circumference)	46 (21%)
Concomitant of CAD	143 (64%)
CAD indicated for revascularization	91 (41%)
Clinical sign due to CAD	0

CAD: coronary artery disease; DM: diabetes mellitus; NASCET: North American Symptomatic Carotid Endarterectomy Trial; SIR: signal intensity ratio; TIA: transient ischemic attack

Table 2 Treatment information

	n = 224
Anesthesia during CAS	
General	34 (15%)
Local	190 (85%)
Protection device	
Distal balloon	118 (53%)
Distal filter	56 (25%)
Proximal protection	50 (22%)
Stent	
Open-cell stent	48 (21%)
Closed-cell stent	176 (79%)
Post-dilatation	175 (78%)
Prior treatment for CAD	
PCI	73 (33%)
POBA	2 (0.9%)
CABG	1 (0.4%)
Adjunctive therapy during CAS	
TTCP	28 (13%)
IABP	3 (1.4%)
HD	84 (38%)
Complication	
Symptomatic ischemic stroke	5 (2.2%)
Coronary ischemic event	0

CABG: coronary artery bypass grafting; CAD: coronary artery disease; CAS: carotid artery stenting; HD: hemodynamic depression; IABP: intra-aortic balloon pumping; PCI: percutaneous coronary intervention; POBA: plain old balloon angioplasty; TTCP: temporary transcutaneous cardiac pacemaker

was placed during CAS for treatment. Five of these 28 patients had undergone PCI prior to CAS but were treated with TTCP because of residual CAD, which is not eligible for treatment. In addition, in three cases (1.4%) with multivessel coronary artery stenosis or concurrent aortic valve stenosis, both a TTCP and an IABP were used during CAS. Hemodynamic decompression occurred in 84 patients (38%), and temporary pacing was activated in 5 (18%) of the 28 patients with a TTCP implanted. None of the 3 patients with IABP implanted had perioperative hypotension.

Ischemic stroke occurred as a perioperative complication of treatment in 5 cases (2.2%), but none developed ischemic heart disease. Furthermore, in 16 cases (7.1%), scheduled PCI was performed after CAS.

Discussion

The major finding of the present study is that no ischemic heart disease complication occurred during CAS under the treatment strategy of coronary artery intervention for CAD prior to CAS if indicated and adjunctive therapy for intraoperative HD.

The association between perioperative ischemic heart disease and carotid artery revascularization has been well-established, with previous studies demonstrating increased mortality risk in patients undergoing CEA with concomitant CAD compared to those without CAD.[5,6] Mackey et al.[7] reported 30-day mortality rates of 1.5% vs. 0% (p = 0.04) and acute myocardial infarction rates of 4.3% vs. 0.7% (p = 0.004). Considering the potential severity and the increased risk of fatality once ischemic heart disease occurs, to improve treatment outcomes it is essential to consider treatment strategies aimed at preventing complications of ischemic heart disease in CAS procedures. In the present study, preoperative evaluation of patients with carotid artery stenosis who were candidates for CAS revealed coexisting coronary artery stenosis in 64% of whom 41% exhibited severe stenotic lesions requiring revascularization. The coexistence of CAD in cases of carotid artery stenosis has been reported in previous studies[1,5–8] with a wide range of frequencies from 28% to 52%.[1,7–9] The slightly higher frequency in the present study than that in these previous reports is possibly due to the older age of the present patient (median age, 76 years). A randomized, controlled trial[10] compared patients undergoing CEA who were assigned to two groups: one group underwent preoperative CAG and subsequent revascularization if significant lesions were found (CAG/revascularization group, n = 216) and the other group did not undergo CAG (non-CAG group, n = 210). According to the report,

in the CAG/revascularization group, significant lesions were observed in 68 of 216 cases (31%), with 66 cases undergoing PCI. No perioperative ischemic events were reported in this group. In contrast, the non-CAG group had 9 cases with perioperative ischemic events (1 case with extensive myocardial infarction resulting in death and 8 cases with ischemic events amenable to medical treatment) (0% vs. 4.2%, p = 0.01). One death occurred in the non-CAG group (0.9%), whereas there were no deaths in the CAG group (p = 0.24). These findings suggest that preoperative coronary artery evaluation and, if necessary, intervention can reduce perioperative ischemic events in patients undergoing CEA. Unlike CEA, both CAS and PCI are performed under dual antiplatelet therapy. Considering this, in cases where preoperative evaluation for CAS demonstrates significant coronary artery stenosis, performing coronary artery intervention prior to CAS, if indicated, can be considered a safer preventive treatment for cardiac ischemic events than CEA.

Treatment strategies for concomitant carotid and coronary artery stenosis remain controversial. In general, it is reasonable to treat symptomatic lesions first, but treatment decision-making is particularly difficult when both lesions are asymptomatic or severe. The disadvantage of CAS preceding revascularization of CAD is that there is a certain risk of myocardial ischemia caused by perioperative HD during CAS. In such cases, adjunctive therapy with TTCP and IABP may be considered by a cardiologist as standby therapies. Conversely, if revascularization for CAD precedes CAS, cerebral infarction as a perioperative complication of CAS must be considered.

Although there is no settled view regarding the indications for treatment of coronary artery stenosis prior to CAS, in this study, we determined the indications for treatment of CAD prior to CAS according to the degree of stenosis. We consulted with a cardiologist to determine the indications, bearing in mind that even asymptomatic CAD carries a risk of inducing angina symptoms due to sudden hemodynamic changes during CAS. In all cases, it is important to have a thorough preoperative discussion with both the cardiologist and neurologist regarding the indication for revascularization for CAD, the order of treatments (whether CAS should precede coronary artery intervention), and the method of treatment (PCI or CABG).

The incidence of bradycardia associated with HD has been reported to range from 7.4% to 60%, and hypotension from 14% to 31%, although variations in definitions can lead to differences in reported rates.[11–14] Recent reports have also suggested an association between hemodynamic instability during CAS and perioperative myocardial infarction and death.[15] In the present study, TTCP was used in 28 cases (13%) and pacing was activated in 5.

The effectiveness of TTCP as an adjunctive therapy has been reported in previous studies.[16–18] One study reported that bradycardia requiring TTCP occurred in 73% of CAS-treated patients.[17] IABP, although more complex in technique, is effective for both bradycardia and hypotension. It is useful for preventing stroke due to excessive hypotension during the procedure, as well as preventing the development of heart failure and potentially fatal arrhythmias due to hemodynamic instability. In the present study, IABP was used in two cases with untreated multivessel lesions and one case with severe aortic valve stenosis. Treatment reports have described the use of IABP and TTCP for CAS in cases of carotid artery stenosis with three-vessel disease,[19,20] and although there are limited case reports, their effectiveness can be expected. The present findings suggest that our strategy of coronary artery intervention prior to CAS if indicated and intraoperative adjunctive therapy with TTCP or IABP with a cardiologist standby may help prevent perioperative complications of ischemic heart disease.

However, there are some limitations to this study. First, it was conducted at a single institution with a small sample size. In addition, being a retrospective study, there may be confounding factors. Second, those who underwent CEA for carotid artery stenosis were excluded and patients with renal dysfunction were also excluded because they did not undergo preoperative examination due to the risk of contrast media use. Moreover, selection bias might have been introduced because patients with a history of coronary artery treatment were excluded after checking their current condition to ensure that they did not have coronary risk. Finally, as this study was not a comparative study with a control group, we cannot assert that this treatment strategy was directly related to the prevention of ischemic heart disease. Further prospective studies with larger sample sizes are needed to accumulate more cases and validate the treatment outcomes and the effectiveness of the strategy proposed in this study.

Conclusion

Evaluating the coronary arteries prior to scheduled CAS, performing preoperative revascularization for CAD if indicated, and provision of adjuvant therapy with TTCP or

IABP for HD during CAS may help prevent coronary ischemic complications following CAS.

Disclosure Statement

The first author and all other authors have no conflict of interest.

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