



Natural History of Asymptomatic Moderate Carotid Artery Stenosis in the Era of Medical Therapy

Yang-Jin Park^{1,4}, Dong-Ik Kim^{1,4}, Gyeong-Moon Kim^{2,4}, Duk-Kyung Kim^{3,4}, Young-wook Kim^{1,4}

■ **OBJECTIVE:** To determine the incidence and risk factors of carotid stenosis progression in patients with asymptomatic moderate carotid artery stenosis (CAS).

■ **METHODS:** Patients with asymptomatic moderate CAS in duplex ultrasound (DUS) were identified from 2003 to 2008, and only those with more than 1 DUS were included during a 5-year follow-up after index DUS. Study end-points were carotid stenosis progression to severe stenosis $\geq 70\%$, development of ipsilateral neurologic symptoms (INS), and death.

■ **RESULTS:** One hundred twenty-nine carotid arteries in 124 patients were included in the study. Carotid stenosis progression occurred in 41 (31.8%) arteries, and 4 (3.2%) patients developed INS during a mean follow-up of 49 months (range, 2–128 months). The 5-year freedom from carotid stenosis progression and development of INS were $63.5\% \pm 5.3\%$ and $98.1\% \pm 1.4\%$, respectively, with no difference from those of statin. There was no significant predictor of carotid stenosis progression, and it was not significantly associated with development of INS. The 5-year actuarial patient survival and symptom-free survival were $95.3\% \pm 2.7$ and $93.4\% \pm 3.0\%$, respectively, with no difference from those of statin. The only independent predictor of death and INS/death was a remote history of INS (hazard ratio 18.166, $P = 0.021$, hazard ratio 4.840, $P = 0.046$).

■ **CONCLUSIONS:** The incidence of carotid stenosis progression in asymptomatic moderate CAS was high even in

popular use of aspirin and statin. Although development of INS was not associated with carotid stenosis progression, it was a risk factor of long-term morbidity and survival.

INTRODUCTION

Cerebrovascular disease is the fourth-leading cause of death in the United States.¹ Carotid artery stenosis (CAS) accounts for 10%–20% of all strokes and is an important cause of ischemic stroke, and the treatment of CAS has been a topic of intense debate during the last 30 years.² It has an estimated prevalence of 9.3% for patients aged ≥ 70 years.³ Although the prevalence of CAS in the Asian population has not been reported widely, our previous reports showed that the prevalence of asymptomatic, moderate-to-severe CAS (50%–99%) was 3.1% for patients aged ≥ 65 years participating in a health-screening program and 14.7% for patients with peripheral vascular disease.^{4,5}

In contemporary practice, the practice guidelines currently support carotid endarterectomy (CEA) as the treatment in asymptomatic CAS patients with a severity greater than 70%, who demonstrate an estimated perioperative morbidity and mortality risk of 3%.^{6,7} Recently, there is emerging evidence in favor of aggressive medical management that reduces the compelling indications for CEA/stenting in asymptomatic populations.⁸ The best medical therapy includes smoking cessation, antiplatelet therapy, control of hypertension and diabetes, and lipid reduction with statin.⁶ Although there is no current guideline

Key words

- Carotid stenosis
- Natural history
- Plaque
- Stroke
- Transient ischemic attack

Abbreviations and Acronyms

- CAS:** Carotid artery stenosis
- CEA:** Carotid endarterectomy
- CMT:** Compliant medical therapy
- DUS:** Duplex ultrasound
- ICA:** Internal carotid artery
- INS:** Ipsilateral neurologic symptom
- LDL:** Low-density lipoprotein

MI: Myocardial infarction

TIA: Transient ischemic attack

From the ¹Division of Vascular Surgery, Department of Surgery, ²Department of Neurology, and ³Division of Cardiology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine; and ⁴Heart Stroke Vascular Institute, Samsung Medical Center, Seoul, Korea

To whom correspondence should be addressed: Yang-Jin Park, M.D., Ph.D.
[E-mail: yjpark1974@gmail.com]

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regarding the management of asymptomatic moderate CAS measuring 50%–69%, there is a general consensus that asymptomatic moderate CAS be managed medically first.

Currently, convincing data from pooled randomized trials have demonstrated that statin use reduces the risk of stroke in the general population and to some extent in patients with asymptomatic CAS, but there are few studies showing the effect of statins on carotid stenosis progression, which is considered a significant predictor of stroke risk.^{9–11} In addition, there have been few studies about the natural history of asymptomatic moderate CAS in Asian population. Hence, the aim of this study was to determine the natural history of asymptomatic moderate CAS in the setting of popular use of medical treatment.

METHODS

Patient Identification

The protocol of this study was approved by the Institutional Review Board of Samsung Medical Center, Seoul, Korea, and informed consent was not required. All patients who underwent duplex ultrasound (DUS) at the vascular laboratory of our institute by Registered Vascular Technologists from January 1, 2003, to December 31, 2008 were searched to ensure at least 5 years of follow-up after the index study. DUS was used mainly for the preoperative evaluation of coronary arterial bypass grafting, peripheral arterial disease, and known CAS or for follow-up of the patients who underwent contralateral carotid revascularization. These DUS examinations were identified by in-hospital codes, which are designated for unilateral or bilateral duplex scans of extracranial carotid arteries. The initial query revealed 29,464 DUS in 23,973 patients, and 9335 DUS in 3844 patients were included after we excluded the patients who did not undergo at least 1 interval DUS study.

The results of the 9335 DUS studies were reviewed, and the patients were categorized based on severity of CAS. One-hundred forty-six carotid arteries of 141 patients with moderate (50%–69%) stenosis of at least 1 extracranial internal carotid artery (ICA) were identified, and their medical records were reviewed. An additional 17 carotid arteries were excluded because of the presence of ipsilateral neurologic symptom (INS) within the 6 months before the index DUS ($n = 14$), history of carotid revascularization ($n = 2$), or radiation-induced stenosis ($n = 1$). Thus, the final study cohort consisted of 124 patients (129 carotid arteries) with asymptomatic moderate CAS (Figure 1).

Asymptomatic Status

Asymptomatic patients had no history of INS, including transient ischemic attack (TIA), stroke, or amaurosis fugax, within the 6 months before the index DUS.^{12,13}

Moderate Carotid Stenosis

Moderate stenosis was defined as a 50%–69% diameter reduction in the ICA. Our laboratory uses ICA peak systolic velocity values between 125 and 230 cm/s, end-diastolic velocity of 40–100 cm/s, and an ICA/common carotid artery ratio of 2.0–4.0 to define moderate stenosis.¹⁴

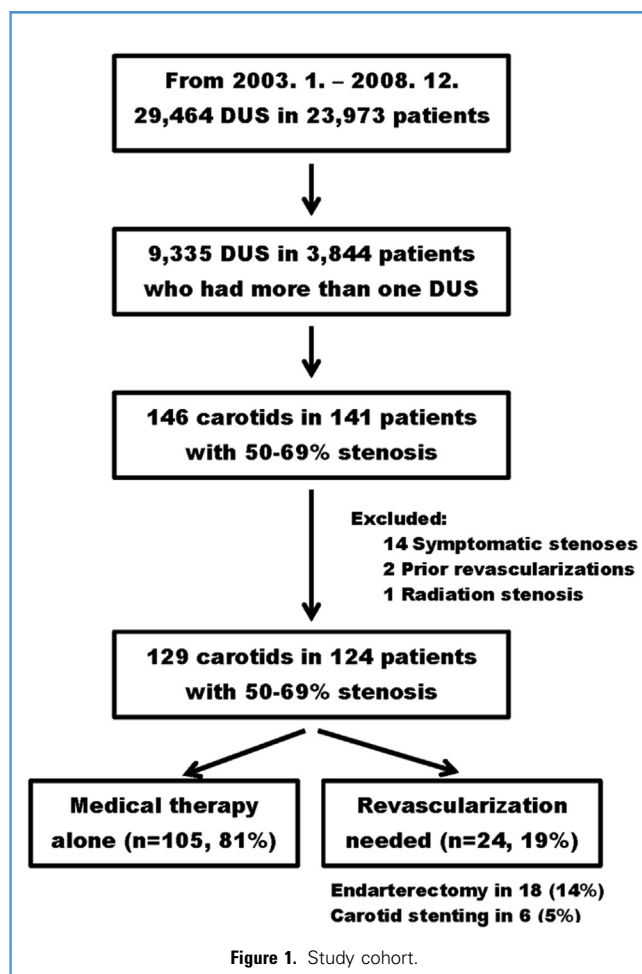


Figure 1. Study cohort.

Carotid Stenosis Progression

The protocol in cases of moderate carotid stenosis in our vascular laboratory is to perform DUS follow-up in 6 month-intervals after the index examination. Serial DUS images were evaluated, and patients who demonstrated change in peak velocities (peak systolic velocity >230 cm/s, end diastolic velocity >100 cm/s) or ICA/common carotid artery ratio (>4.0) that placed them in the severe (70%–99%) or occluded (100%) category were considered to have experienced carotid stenosis progression.

Ipsilateral Neurologic Symptoms

Patients who experienced an episode of stroke, TIA, or amaurosis fugax attributed to the ICA after the date of the index DUS were considered to have become symptomatic. All strokes were evaluated by a neurologist and were confirmed with brain imaging.

Carotid Revascularization

All ipsilateral procedures performed on the ICA were documented, including CEA and carotid stenting. The indications for and type of carotid revascularization were at the discretion of the physician and were often determined after discussion among the physicians.

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