Prevalence of Carotid Artery Stenosis in Patients With Coronary Artery Disease in Japanese Population

Shuzou Tanimoto, MD; Yuji Ikari, MD, PhD; Kengo Tanabe, MD, PhD; Sen Yachi, MD; Hiroyoshi Nakajima, MD, PhD; Tomohiro Nakayama, MD; Mitsuharu Hatori, MD; Gaku Nakazawa, MD; Yoshinobu Onuma, MD; Yasutomi Higashikuni, MD; Hirosada Yamamoto, MD; Eiichi Tooda, RMS; Kazuhiro Hara, MD, PhD

Background and Purpose—Prevalence of carotid artery stenosis in patients with coronary artery disease (CAD) is unknown in Japanese population.

Methods—The study populations consisted of 632 consecutive patients who underwent coronary angiography because of suspicion of CAD. All patients underwent carotid ultrasonography to screen carotid artery stenosis before coronary angiography. We defined echographic carotid stenosis as area stenosis of $>50\%$ or peak systolic velocity of $>200\, \text{cm/s}$. 

Results—Echographic carotid stenosis was observed in 124 patients (19.6%). Coronary angiography revealed 433 patients had CAD. Prevalence of echographic carotid artery stenosis was 14 of 199 (7.0%), 18 of 124 (14.5%), 28 of 131 (21.4%), and 64 of 178 (36.0%) in patients with 0-, 1-, 2-, and 3-vessel CAD, respectively ($P<0.0001$). The prevalence rate with carotid stenosis and CAD was 25.4%. Multivariate stepwise logistic regression analysis showed that age and the extent of CAD were independently related to the presence of carotid stenosis ($P<0.0002$ and $<0.0001$, respectively).

Conclusions—Prevalence of carotid stenosis in patients with CAD is high in Japan as well as in Western countries. Screening of carotid artery stenosis is recommended especially in older patients with multivessel CAD. (Stroke. 2005; 36:2094-2098.)

Key Words: carotid stenosis ▪ coronary artery disease ▪ epidemiology ▪ Japan

Atherosclerosis frequently occurs at the carotid bifurcation and the proximal internal carotid artery. Carotid atherosclerosis is an important cause of ischemic brain attack and stroke. In Western countries, extracranial carotid atherosclerosis accounts for $\approx 30\%$ to $40\%$ of cases of ischemic cerebrovascular disease, depending on the population studied. $^1$ It was reported that there were racial differences in the severity and distribution of carotid atherosclerosis. $^2$ Compared with patients in Western countries, Japanese patients had predominantly intracranial artery lesions, and extracranial carotid stenoses were less frequent. $^3$-$^5$ But recently, the incidence of ischemic cerebrovascular disease attributable to extracranial carotid lesions has steadily increased in the Japanese population because of the change in lifestyle toward Western habit. $^6$

An association between carotid atherosclerosis and coronary artery disease (CAD) has been well established $^7$-$^9$ because atherosclerosis is considered to be a generalized disease. It has been reported that Japanese patients who underwent coronary artery bypass grafting (CABG) because of severe CAD had a high incidence of carotid stenosis. $^10$-$^11$ But there are few reports about the complication rate of carotid artery disease in Japanese patients with CAD other than the candidates for bypass surgery.

The aim of this study was to investigate the prevalence of carotid stenosis in patients with CAD and to determine any factors related to carotid stenosis in Japanese population.

Methods

Study Population
The study populations consisted of 632 consecutive patients who were scheduled to undergo coronary angiography because of suspicion of CAD during the period June 2002 to April 2004. Subjects were administered a questionnaire to assess symptoms, risk factor profile, and previous diagnostic evaluations. All patients gave written informed consent to participate in this study.

Evaluation of Risk Factor Variables
We evaluated the risk factor variables including sex, age, body mass index, hypertension, diabetes mellitus, hyperlipidemia, smoking, familial history of CAD, hemodialysis, past history of myocardial infarction, previous percutaneous coronary intervention and CABG, and previous transient ischemic attack or stroke.

Hypertension was defined as present if a subject took medication for hypertension or if the subject’s blood pressure was $>140\, \text{mm Hg}$ in systole or $>90\, \text{mm Hg}$ in diastole for $\geq 2$ repeated measurements. Diabetes mellitus was defined as a serum glycosylated hemoglobin...
concentration of $>5.8\%$, if the repeated fasting plasma glucose exceeded 126 mg/dL, or if the patients took medication for diabetes. Hyperlipidemia was defined as taking lipid-lowering medications, a fasting serum total cholesterol concentration of $>220$ mg/dL, low-density lipoprotein cholesterol concentration of $>140$ mg/dL, high-density lipoprotein cholesterol concentration of $<40$ mg/dL, or triglyceride concentration of $>150$ mg/dL. A familial history of CAD was defined as a history of CAD in any first-degree relative $<60$ years of age. Hemodialysis was defined as undergoing maintenance hemodialysis regardless of etiology.

**Assessment of Coronary Angiography**

Coronary angiography was performed to investigate CAD. The diameter stenosis was calculated by quantitative coronary angiography with an automated coronary analysis system (CMS Medis Medical Imaging Systems). CAD was defined as a lumen diameter stenosis of $>50\%$ in $\geq 1$ major coronary artery. Each patient was classified into 1 of the following groups according to the number of diseased vessels: 0-vessel disease (ie, patients without diseased vessels [group 0]), 1-vessel disease (ie, patients with disease in 1 vessel [group 1]), 2-vessel disease (ie, patients with disease in 2 vessels or left main trunk disease without right coronary artery stenosis [group 2]), 3-vessel disease (ie, patients with disease in 3 vessels or left main trunk disease with right coronary artery stenosis [group 3]).

**Assessment of Carotid Atherosclerosis**

Atherosclerosis of carotid artery was analyzed by duplex ultrasound scanning within a month before coronary angiography in the all enrolled patients. A commercially available machine (Vingmed; General Electric) with a 10-MHz linear array transducer was used. Imaging was performed while subjects were lying in a supine position with the head turned away from the side being scanned and the neck extended. Transverse and longitudinal scans were obtained on the common carotid artery, the carotid bifurcation, and the internal and external carotid artery by B-mode and color Doppler ultrasound. Area stenosis (percent) was measured as: $1 - (\text{the area of residual lumen/the area of the normal vessels}) \times 100$ by B-mode ultrasound. Doppler spectral analysis can determine the peak systolic velocity (PSV) by sampling at the area of turbulence. The PSV was measured only when the turbulence was found. To measure blood flow velocity on longitudinal scans, a 5- to 7-mm sample was set in the carotid artery and displayed as linearly as possible. Special care was taken to maintain the incident angle between the carotid artery and the beam at $30^\circ$ to $60^\circ$. We defined echographic carotid artery stenosis as the carotid atherosclerosis with area stenosis of $>50\%$ or PSV of $>200$ cm/s on the common carotid artery, the carotid bifurcation, and the internal carotid artery.

Coronary angiography and carotid angiography were performed when echographic carotid artery stenosis was identified. Selective carotid angiography was performed in lateral and frontal views. The view showing the maximum stenosis was selected for quantitative angiographic analysis. The lumen diameter at the point of maximum stenosis and the diameter of the normal distal internal carotid artery were measured; percent stenosis was then calculated using the method described in the North American Symptomatic Carotid Endarterectomy Trial (NASCET) study. We defined angiographic carotid stenosis, according to the NASCET criteria, as a diameter stenosis of $>70\%$ on the common carotid artery, the carotid bifurcation, and the internal carotid artery.

**Statistical Analysis**

Data analysis was performed using the SAS version 8.02 (SAS Institute Inc). Continuous variables were expressed as mean $\pm$ SD. Two-sided unpaired $t$ test was performed for continuous variables and $\chi^2$ test (or Fisher’s exact test when appropriate) for discrete variables. Multivariate stepwise logistic regression analysis was performed to detect independent predictors of carotid artery stenosis using factors that had significant relation in univariate analysis. A value of $P<0.05$ was considered statistically significant.

**Results**

We studied 632 consecutive patients (476 men; mean age 65.3 $\pm$ 7.7; range 35 to 89 years). The demographic and clinical characteristics of the entire study population are presented in Table 1.

Among all the enrolled patients, echographic carotid stenosis was found in 124 patients (19.6%). In coronary angiography, CAD was present in 433 patients (68.5%). A total of 124 patients (19.6%) had 1-vessel disease, 131 patients (20.7%) had 2-vessel disease, and 178 patients (28.2%) had 3-vessel disease.

Univariate analysis revealed that the following factors were associated with echographic carotid stenosis: age, hypertension, diabetes mellitus, past history of myocardial infarction, previous CABG, and the extent of CAD (Table 2). From these factors, multivariate stepwise logistic regression analysis selected age ($P=0.0002$) and the extent of CAD ($P<0.0001$) as the independent predictors of the presence of echographic carotid stenosis (Table 3).

We also analyzed angiographic carotid stenosis based on the NASCET criteria. Of the 124 patients with echographic carotid stenosis, 46 had no available carotid angiography because of severe renal dysfunction ($n=6$), the difficulty of selective cannulation to carotid artery ($n=7$), onset of acute coronary syndrome before coronary angiography ($n=20$), and no patient’s consent ($n=13$). These 46 patients were excluded from the postanalysis because of unavailable carotid angiography. Carotid angiography was performed in the residual 78 patients. We found angiographic carotid stenosis in 47 patients.

Univariate analysis revealed that the following factors were associated with angiographic carotid stenosis: age, hypertension, diabetes mellitus, past history of myocardial infarction, previous CABG, and the extent of CAD (Table 4).
From these factors, multivariate stepwise logistic regression analysis selected age (P=0.0392) and the extent of CAD (P<0.0001) as the independent predictors of the presence of severe carotid stenosis (Table 3).

The extent of CAD had a strong association with echographic and angiographic carotid stenosis in univariate as well as multivariate analysis. We performed further analysis on the distribution of carotid stenoses according to the extent of CAD (Figure). The distribution of echographic carotid stenosis in the groups with degrees of CAD was 7.0%, 14.5%, 21.4%, and 36.0% of patients with 0-, 1-, 2-, and 3-vessel disease, respectively (P<0.0001). There was a stepwise increase in the number of patients with echographic or angiographic carotid stenosis among the patients with increasing severity of CAD. In patients with CAD, 25.4% had echographic stenosis, and 11.0% had angiographic carotid stenosis. The prevalence of echographic or angiographic carotid stenoses were 14.5% or 3.4%, respectively, in 1-vessel disease, whereas it was 29.8% or 14.2%, respectively, in multivessel disease (P<0.0001).

### Discussion

In this study, our main findings were: (1) the prevalence of carotid stenosis in patients with CAD was unexpectedly high in the sample Japanese population, and (2) age and the extent of CAD were independently related to the presence of carotid stenosis.

In the 1960s, there were few people in Japan with atherosclerosis in the extracranial carotid artery.3-5 But the incidence of extracranial carotid atherosclerosis has increased in the past few decades with the change in lifestyle toward Western habits.6 In 1997, Mannami T et al13 reported that the prevalence of carotid stenosis defined as area stenosis of >50% on ultrasound was 4.4% among Japanese people 50 years of age. In the present study, carotid stenosis was seen in 7% of patients without CAD. Colgan et al14 reported that in Western countries, 4% of 348 participants scanned at a health fair, whose average age was 61 years, had carotid stenoses of >50%. Puja et al15 reported that the prevalence of carotid stenosis of >50% was 5% in subjects ≥75 years of age. In the Framingham Study,16 8% of the 1189 members of the cohort 66 to 93 years of age had carotid stenosis of >50%. Taking these results into consideration, at present, the prevalence of carotid stenosis in Japan may be similar to that of Western countries.

It is well known that carotid atherosclerosis strongly correlated with CAD. In the severe CAD patients who were scheduled to undergo CABG, the complication rate of carotid stenosis of >50% was 5% in subjects ≥75 years of age. In Western countries, 4% of 348 participants scanned at a health fair, whose average age was 61 years, had carotid stenoses of >50%. Puja et al15 reported that the prevalence of carotid stenosis of >50% was 5% in subjects ≥75 years of age. In the Framingham Study,16 8% of the 1189 members of the cohort 66 to 93 years of age had carotid stenosis of >50%. Taking these results into consideration, at present, the prevalence of carotid stenosis in Japan may be similar to that of Western countries.
stenosis was 2% to 18% in Western countries, whereas for the Japanese population, it was 13.7%. But the prevalence of carotid stenosis in patients with CAD other than the candidates for bypass surgery has not been well evaluated. In our study, the prevalence of echographic carotid stenosis with multivessel CAD was 29.8%. We also analyzed angiographic carotid stenosis in this study. Angiographic carotid stenosis is important for prognosis and to decide on surgical or interventional treatment. However, there have been few reports about the relationship between angiographic carotid stenosis and CAD. Our study showed that 19.4% of patients with 3-vessel disease had angiographic carotid stenosis and may require both coronary and carotid intervention. Histological relationship between carotid and coronary atherosclerosis has been seen in an autopsy study. The histological relationship may explain the high complication rate.

Open-heart surgery in patients without carotid atherosclerosis carries a risk of stroke of ≈1% to 2%, but in the presence of unoperated major carotid stenosis, it is associated with a 14% risk of perioperative stroke. Prognosis of CAD has improved in the past few years because of improvement in coronary revascularization. But neurologic complication represents the most frequent cause of mortality in patients undergoing myocardial revascularization. Therefore, it should be recommended that the patients with CAD, especially those with multivessel CAD, undergo carotid ultrasonography for screening of carotid atherosclerosis before treatment for CAD.

Screening of carotid stenosis in patients with CAD seems insufficient in Japan at present, probably because the high complication rate of carotid stenosis has been considered to be low in Japanese population. Previous studies reported high complication rates between carotid artery stenosis and severe CAD in patients undergoing coronary bypass surgery. Our study, including less severe CAD as well as severe CAD, supported these previous studies. The patients with CAD, especially those with multivessel CAD, should undergo carotid ultrasonography in Japan, as in Western countries.

There may be limitations in this study. First, we only studied a group of consecutive patients who were referred for coronary angiography because of suspected CAD. Second, a mean age of patients in this study was high. The prevalence of multivessel CAD was higher in advanced age, and the extent of CAD was affected with the incorporation of coronary risk factors including age. These selection biases could mean that our findings regarding the relationship between carotid stenosis and CAD are relevant only to this specific group and may not be applicable to the general population.

In conclusion, prevalence of carotid stenosis in patients with CAD is high in Japan as well as in Western countries, and screening of carotid artery stenosis should be recommended in patients with CAD, especially in older patients with multivessel CAD.

References

Prevalence of Carotid Artery Stenosis in Patients With Coronary Artery Disease in Japanese Population
Shuzou Tanimoto, Yuji Ikari, Kengo Tanabe, Sen Yachi, Hiroyoshi Nakajima, Tomohiro Nakayama, Mitsuharu Hatori, Gaku Nakazawa, Yoshinobu Onuma, Yasutomi Higashikuni, Hirosada Yamamoto, Eiichi Tooda and Kazuhiro Hara

Stroke. 2005;36:2094-2098; originally published online September 22, 2005;
doi: 10.1161/01.STR.0000185337.82019.9e

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/36/10/2094

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/