Carotid artery stenosis in asymptomatic patients undergoing coronary artery bypass grafting: who and when should be screened?

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KEY WORDS
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ABSTRACT

BACKGROUND Carotid artery stenosis (CAS) is one of the major causes of stroke in coronary artery bypass grafting (CABG).

AIMS The aim of this study was to determine which age groups require screening for CAS using carotid duplex ultrasound in asymptomatic patients undergoing CABG.

METHODS We included 644 neurologically asymptomatic consecutive patients (mean [SD] age, 63.9 [8.8] years; men, 453 [70.3%]) who underwent elective isolated CABG between June 2015 and June 2020. Clinical, demographic, and radiological data as well as coronary angiography results were retrospectively reviewed. Patients were classified into 4 age groups: 40 to 50, 51 to 60, 61 to 70, and >70 years, as well as 3 groups depending on the CAS degree: 50% or less, 50% to 70%, and 70% or greater. Regression analysis was applied across the selected parameters to identify risk factors for significant CAS, and receiver operating characteristic analysis, to determine cutoff age and SYNTAX score of patients who had to be screened before CABG.

RESULTS Overall, 8 (1.1%) patients included in the present study had stroke following CABG. Cutoff values of the SYNTAX score and CAS of 70% or greater were found to be 27 and 64 years, respectively. The sensitivity and specificity of the cutoff value were 98.4% to 98.3% and 74.3% to 55.1%, respectively. The area under the curve was 0.98 and 0.73, respectively.

CONCLUSIONS Based on the receiver operating characteristic analysis, we recommended to perform screening for CAS in patients older than 64 years and with a SYNTAX score of 27 or higher, even if they are asymptomatic.

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INTRODUCTION Neurological complications after coronary artery bypass graft ing (CABG) can occur due to various reasons, such as emboli sms caused by atrial fibrillation and manipulation of the atherosclerotic aorta.[1] Additionally, carotid artery stenosis (CAS) accompanying coronary artery disease caused by atherosclerosis plays a role in the neurological complications that occur after CABG in adults.[2] Although atheroembolisms from the aortic arch play a more significant role than CAS in postoperative stroke, carotid artery stenosis of 70% or greater detected by Doppler ultrasonography is an independent predictor of serious aortic arch disease.[3] In addition to these etiological causes, independent from atheroembolism, the presence of extracranial CAS during coronary surgery results in cerebral hypoperfusion, thereby increasing the frequency of postoperative neurological phenomena.[4] The risk of postoperative stroke is increased in cases where extracranial CAS and coronary artery disease coexist; therefore, patients should be examined for CAS prior to CABG.[5] Based on the recent guidelines, patients (aged >70 years) with left main coronary artery disease (LMCA) and with a history

WHAT'S NEW?

Coronary artery bypass grafting (CABG) is used in the treatment of ischemic heart disease. This surgery is associated with life-threatening complications, and neurological complications play an essential role, affecting mortality and morbidity. Carotid artery stenosis (CAS) is an important factor in neurological complications after CABG. CAS is curable can be detected with simple tests such as ultrasound before surgery. Current guidelines recommend that patients over 70 years of age who have symptoms of neurological disease should be routinely screened for CAS before CABG. In this study, all patients who underwent CABG were screened for CAS before the operation. Severe CAS was seen in young and nonsymptomatic patients. Our data may serve as a benchmark for future studies to reduce the neurological complications of CABG.

of a cerebrovascular event (CVE) or transient ischemic attack (TIA) are recommended to undergo routine screening.[4] However, contradictory data show that the prevalence of CAS is high in young people.[6] Therefore, whether routine screening is necessary for young and asymptomatic patients is disputed. Patients in all age groups are routinely screened using carotid artery Doppler at most healthcare centers due to medicolegal reasons and to prevent catastrophic outcomes of stroke. In this study, we aimed to determine the age groups that required screening for CAS in the population of patients who were referred for CABG.

METHODS

The study protocol was approved by the Hitit University Clinical Research Ethics Committee (no. 101, November 13, 2019). This study is retrospective and there was no need to obtain written informed consent from patients. Patients (n = 692) who underwent elective isolated CABG between June 2015 and June 2020 at the Cardiovascular Surgery Clinic were retrospectively analyzed. Those with a history of CVE/TIA and those who had neurological symptoms during the preoperative period (n = 48 [6.9%]), were excluded. Out of the neurologically asymptomatic patients, we included 644 patients (male sex, 453; mean [SD] age, 64.4 [8.6] years; female sex, 191; mean [SD] age, 63.2 [7.8] years) who were screened using carotid artery Doppler during the preoperative period. The patients were classified into 4 groups based on age (40–50, 51–60, 61–70, and >70 years).

Demographic and echocardiographic data, carotid Doppler examination results, the Synergy Between PCI With Taxus and Cardiac Surgery (SYNTAX) score and Euroscore II results, and postoperative follow-up parameters of patients were obtained from the medical records of the clinic and the hospital automation system.

All coronary angiography data were blindly evaluated by an experienced cardiologist and a cardiovascular surgeon. If the results were not the same, lesions were additionally evaluated by a different cardiologist and a cardiovascular surgeon. A joint decision was made by these 4 people. The SYNTAX score was calculated using SYNTAX algorithms.[7]

The degree of CAS was determined using B-Mode and duplex ultrasound on the LOGIQ (Ultrasound; GE Healthcare Technologies, Milwaukee, Wisconsin, United States) ultrasound device. The attending radiologists were not informed about the results of the coronary angiography. Patients were also divided into 3 groups depending on CAS degree: 50% or less, 50% to 70%, and 70% or greater. In addition to internal carotid artery (ICA) peak systolic velocity (PSV) and ICA end-diastolic velocity measurements, the presence and degree of CAS were determined by checking whether there is plaque using B-Mode and Doppler.[8] According to this method, group 1 (stenosis of ≤50%) included patients who had ICA PSV of less than 125 cm/s and did or did not have plaque. Group 2 (stenosis of 50%–70%) included patients who had ICA PSV of 125 to 230 cm/s and had visible plaque. Group 3 (stenosis of ≥70%) included patients with ICA PSV greater than 230 cm/s and an end-diastolic velocity of 100 cm/s. Moreover, patients with no lumen or flow visible on B-Mode were determined to be completely occluded and included in group 3. The type of surgical procedure (reverse staged, staged, and combined) was decided based on the patient's cardiac symptoms and the severity of coronary disease or CAS. All carotid endarterectomy (CEA) operations were performed as patch plasty procedures with the saphenous vein or a knitted Dacron patch (HEMAGARD, Maquet Gentinge Group, Rastatt, Germany).

Statistical analysis

Data were stored and analyzed using SPSS 22.0 (IBM Corp., Armonk, New York, United States). Descriptive statistics were presented as mean (SD) and frequency. The Pearson χ^2 test was used to compare categorical data. Normality of data distribution was analyzed using the Kolmogorov–Smirnov test. A multinomial logistic regression analysis was conducted to determine the factors affecting CAS (dependent variable) using age and the SYNTAX score as predictors. Odds ratio (OR) and 95% CI values were calculated for the parameters found to be statistically significant in the logistic regression models. The dependent variable, CAS, consisted of 3 categories (≤50%, 50%–70%, ≥70%), and the independent variable, age, consisted of 4 categories (40–50, 51–60, 61–70, and >70 years). The SYNTAX score was a continuous variable. The reference category is less than 50% for CAS. In our study, whether age and SYNTAX score values could be diagnostic and prognostic markers in the diagnosis of CAS was assessed using the receiver operating characteristic (ROC) analysis. The ROC curve, area under the curve (AUC), and 95% CI of this area were

TABLE 1 Demographic and clinical data

Characteristic		Value
Age, y	Mean (SD)	63.9 (8.8)
	40–50	49 (7.6)
	51–60	174 (27.0)
	61–70	240 (37.3)
	>70	181 (28.1)
Sex	Male	453 (70.3)
	Female	191 (29.7)
DM		228 (35.5)
HT		490 (76)
Hyperlipidemia		244 (37.8)
Chronic renal failure		10 (1.5)
Peripheral arterial disease		35 (5.4)
SYNTAX score, mean (SD)		23.2 (8.3)
Three-vessel disease		313 (48.6)
LM-CAD		34 (5.2)
CAS	<50%	454 (70.5)
	50%–70%	62 (9.6)
	>70%	128 (19.9)

Data are presented as number (percentage) of patients unless otherwise indicated.

Abbreviations: CAS, carotid artery stenosis; DM, diabetes mellitus; HT, hypertension; LM-CAD, left main coronary artery disease

TABLE 2 Multinomial logistic regression analysis of age and carotid artery stenosis

CAS	Age, y	Odds ratio (95% CI)	*P* value
50%–70%	40–50	0.214 (0.069–0.723)	<0.001
	51–60	0.334 (0.138–0.81)	<0.001
	61–70	1.112 (1.008–1.238)	<0.001
	>70	1.486 (1.126–2.082)	<0.001
>70%	40–50	0.129 (0.066–0.252)	<0.001
	51–60	0.243 (0.098–0.606)	<0.001
	61–70	1.624 (1.116–2.358)	<0.001
	> 70	2.256 (1.467–3.690)	<0.001

Dependent variable: carotid artery stenosis; independent variable: age. The reference category is <50% for carotid artery stenosis.

Abbreviations: see TABLE 1

TABLE 3 Multinomial logistic regression analysis of SYNTAX score and carotid artery stenosis

Carotid artery stenosis	Odds ratio (95% CI)	*P* value
50%–70%	1.091 (1.032–1.153)	0.002
>70%	1.163 (1.101–1.228)	<0.001

Dependent variable: carotid artery stenosis; independent variable: SYNTAX score. The reference category is <50% for carotid artery stenosis.

calculated. In the interpretation, AUC was evaluated as follows: 0.9 to 1, excellent; 0.8 to 0.9, good; 0.7 to 0.8, medium; 0.6 to 0.7, weak; and 0.5 to 0.6, no discrimination. The Youden index (maximum sensitivity and specificity) was used to determine the best cutoff point in the ROC analysis. Sensitivity and specificity values were calculated using the cutoff points determined for age and the SYNTAX score after ROC analysis. Statistical significance was set at a *P* value of less than 0.05.

RESULTS The mean (SD) age of the patients was 63.9 (8.8) years, and the majority were men (453 [70.3%]; women, 191 [29.7%]). A total of 228 patients (35.5%) had type 2 diabetes and 490 (76%) had hypertension. The mean (SD) SYNTAX score of the patients was 23.2 (8.3). Patient demographic and clinical data are presented in TABLE 1. Multinomial logistic regression analysis results revealed that as the SYNTAX score and age increased, the incidence of CAS (50%–70% and >70%) increased (OR >1) compared to the reference category (<50%) (TABLES 2 and 3).

Overall, 8 (1.1%) patients had stroke following CABG. The mean age of patients who had a stroke was 61.8 years (range, 52–71). Of these, 6 had minor CVEs and were discharged without any sequela, 2 had major CVEs, and these 2 patients died following CVEs within the first postoperative week. A critical degree of carotid stenosis was detected in 6 (12%) of 49 patients in the young group aged 40 to 50 years. A total of 32 patients, with a mean age of 63.7 years (range, 56–72 years), underwent carotid artery surgery in addition to CABG. Of these, 4, 2, and 26 underwent reverse staged CABG + CEA (first CEA – after CABG), staged CABG + CEA (first CABG – after CEA), and combined CABG + CEA (simultaneous operation), respectively (TABLE 4).

The decision on the indication and type of carotid artery operation (staged, reversed staged, or simultaneous CABG + CEA) to be performed was made by the surgeon according to the clinical condition of the patient and the severity of the stenosis in the coronary arteries or carotid arteries. No postoperative mortality or stroke was observed in any of the patients who underwent coronary artery surgery in combination with any type of carotid artery surgery.

To determine the cutoff value of the SYNTAX score in CAS of 70% or greater, the ROC curve analysis was used, and the cutoff value was determined as 27. The sensitivity of the cutoff value was 98.4% and its specificity was 98.3%. The AUC was 0.98 (95% CI, 0.977–0.992) (FIGURE 1).

For the SYNTAX score, the ROC curve analysis was used to determine the cutoff value for age in patients who had carotid artery disease of 70% or greater. When patients with a SYNTAX score of 27 or greater were deemed positive,

TABLE 4 Procedure type

Procedure	Value
CABG + CEA	26 (81.25)
Staged CABG + CEA	2 (6.25)
Reverse Staged CABG + CEA	4 (12.5)

Data are presented as number (percentage).

Abbreviations: CABG, coronary artery bypass graft; CEA, carotid endarterectomy

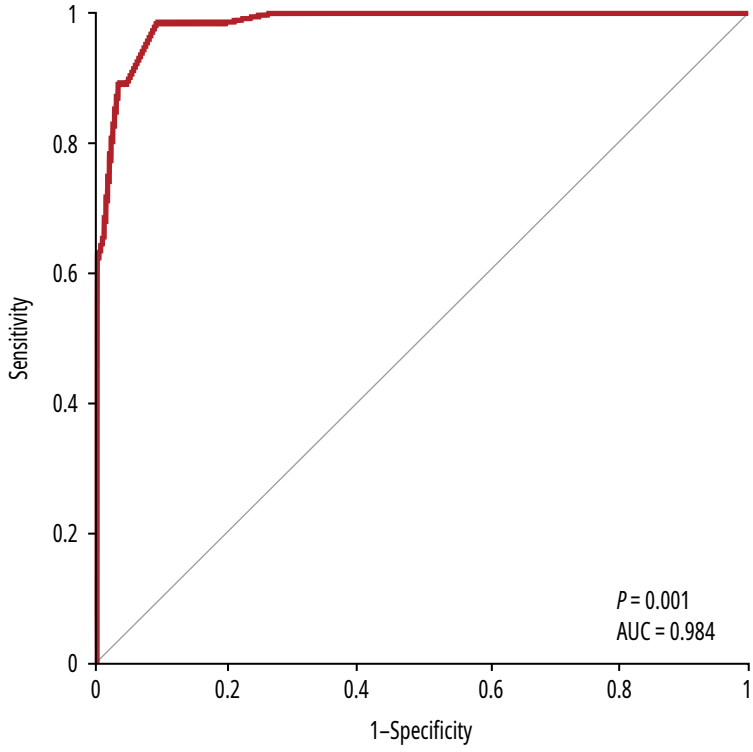

FIGURE 1 The receiver operating characteristic (ROC) curve for the SYNTAX score based on carotid artery stenosis of ≥70%
Abbreviations: AUC, area under the curve

the cutoff value for age was determined to be 64. The sensitivity of the cutoff value was 74.3% and its specificity was 55.1%. The AUC was 73.7% (95% CI, 0.696–0.779) (FIGURE 2).

DISCUSSION Stroke is a catastrophic complication, mainly due to noncardiac reasons, that is accompanied by atherosclerosis in postcardiac surgeries. Among these reasons, CAS is an important factor that can be detected and treated preoperatively. Performing a routine screening for CAS prior to CABG is controversial because of its cost. In the guidelines published by the European Society of Vascular Surgery in 2017, a routine screening for CAS is recommended only for patients aged 70 years or older, with a history of CVE / TIA or LMCA stenosis.[9] Although there are some reasons for such limited indications, it is a fact that the presence of 2 pathologies is a factor that dramatically increases the risk of postoperative stroke. Therefore, routine preoperative screening is performed in a larger group of patients using color Doppler based on clinical experiences at healthcare centers. The main finding from this study is that to detect a CAS of 70% or greater, the critical degree of stenosis in patients who undergo elective CABG, the cutoff value for the SYNTAX score is 27 and the cutoff value for age is 64 years. To minimize the risk of CVE following CABG in patients who will undergo elective CABG, we screen patients using carotid artery Doppler at our clinic. Carotid artery stenosis can also be observed in young people.[10-12] We detected a critical degree of carotid stenosis in 6 (12%) of 49 patients in the group of young patients aged 40 to 50 years, proving that this routine is reasonable.

Naylor et al[5] have reported a rate of postoperative stroke of 1% to 2% in all groups of patients who underwent CABG. In another study that included patients with critical asymptomatic carotid stenosis, the rate of postoperative stroke was 3%. The rate of postoperative stroke reaches 5% in patients with bilateral carotid stenosis and 11% in patients with total stenosis.[5] Therefore, detecting CAS prior to coronary bypass and then performing prophylactic carotid artery revascularization for treatment is necessary. There is a debate on whether stenting or surgical treatment is superior; moreover, if surgical treatment is preferred, it is also debated whether staged or simultaneous surgical treatment would be more efficient. According to a recent meta-analysis conducted on 21 000 patients, the rate of postoperative stroke was 3%, the rate of postoperative TIA was 1%, the rate of postoperative MI was 5%, and the rate of postoperative 30-day mortality was 4% in patients who underwent CABG + CEA simultaneously.[13] Thus, simultaneous CABG + CEA is safe. In this study, 81.25% patients with CAS of a critical degree underwent CABG + CEA simultaneously.

In patients with complex carotid plaques, complex coronary artery stenosis coexists and the degree of the stenosis detected during the carotid artery Doppler examination and the stage of coronary artery disease correlate significantly.[14-17] Additionally, the SYNTAX score and intima-media thickness of the carotid artery correlate significantly.[18] Akansel et al[19] reported a specificity of 90.4%, sensitivity of 85.9%, and SYNTAX score cutoff value of 27; moreover, they stated that a SYNTAX score of 70% or greater can be used as a predictor for CAS. Similar to the results of the ROC curve analysis conducted in this study, the SYNTAX score value that coincided with the cutoff value for CAS of 70% or greater was found to be 27. In addition, the specificity of this value was 98.4% and sensitivity was 98.3%. The value of 27 was taken as a reference, and we

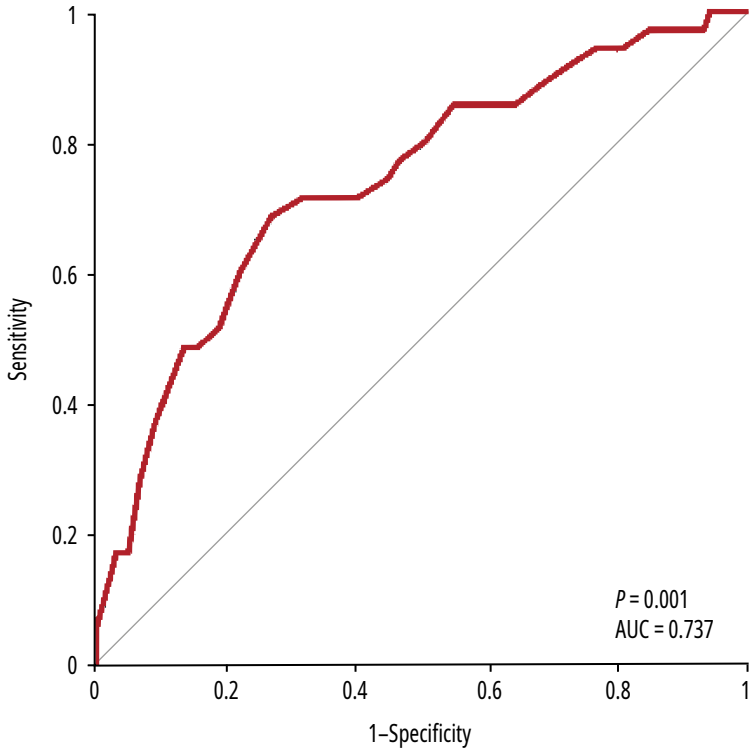

FIGURE 2 The receiver operating characteristic (ROC) curve for age based on a SYNTAX score >27
Abbreviations: see FIGURE 1

determined the cutoff age as 64 years for patients with CAS of 70% or greater as an accompanying disease. Although the specificity of this age cutoff is 74.3% and its sensitivity is 55.1%, which are low, the results are significant. Furthermore, as per the finding of the present study, the degree of CAS significantly increases with age.

In this study, the cutoff value for age was 64 years in patients with serious CAS (>70%) as an accompanying disease. Considering that only asymptomatic patients were included in the present study, it may be expected that atherosclerotic pathology is higher in symptomatic patients. Regarding the age of 70 years as the cutoff value for the routine screening performed in symptomatic patients and those with LMCA lesions, which is recommended by the latest guidelines, contradictory results have been obtained in the present study.[9,20,21] We maintain that CAS screening based on a high age cutoff may result in omitting patients with serious CAS during CABG.

Cost-effectiveness is one of the main reasons why the cutoff age of 70 is recommended in the 2017 guidelines of the European Society of Vascular Surgery. The cost of carotid artery Doppler procedure is 4 EUR at the state hospitals in Turkey. This procedure costs 16 EUR in Sweden.[22] In a study conducted by Hogberg et al[22] on males aged 65 years or older in Sweden, it was demonstrated that performing a screening using carotid artery Doppler is more cost-effective than the medical treatment itself for preventing stroke. For cost-effectiveness, performing CAS screening in patients in high-risk groups who will undergo CABG can be projected to be effective in the cost-effectiveness analysis for patients younger than 65 years in whom carotid artery Doppler cost is not high; further studies are thus warranted.

This study has some limitations. First, the study design is retrospective. In addition, data from a single healthcare center were analyzed and only elective patients were included. Therefore, the results from the study represent only a group of specific patients. Thus, it is not possible to make a generalization for all patients who undergo CABG. However, this study offers important deductions because neurologically--asymptomatic patients account for a majority of CABG patients. Because the present study is retrospective in nature, not all factors that affect postoperative stroke are dealt with in detail. Therefore, the correlation between stroke and CAS may not reflect accurate results. Moreover, the main objective of the study is not to detect stroke etiology, but to determine the age cutoff value for CAS screening; therefore, we suggest that these parameters should be considered as a finding of the study and evaluated based on their correlation with the SYNTAX score.

In conclusion, we recommend performing routine CAS screening for patients older than 64 years and with a SYNTAX score of 27 or greater, even if they are asymptomatic.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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