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## Preoperative Carotid Artery valuation in 1045 Patients Undergoing Coronary Artery Bypass Graft Surgery

**Backgrounds/Objectives:** To evaluate the prevalence of significant carotid artery stenosis and its determining factors in candidates of coronary artery bypass graft (CABG) surgery.

**Patients and Methods:** 1045 consecutive CABG candidates underwent carotid artery Doppler examination in a cross sectional study. The relation of age, gender, history of smoking and diabetes, as well as lipid profile to significant carotid stenosis was evaluated.

**Results:** In study subjects, mean age of  $60.57 \pm 9.3$  years, the prevalence of significant carotid stenosis ( $>60\%$ ) was 6.9%. In subjects older than 65 years the significant stenosis tolled to 12.5%. Over 50 years of age, female gender, hypercholesterolemia and diabetes were independent determining factors for significant carotid stenosis.

**Conclusion:** Significant carotid stenosis has significantly higher prevalence among patients over 50 years of age. Cost benefit studies are recommended to revise the current evaluation protocols.

**Keywords:** Doppler sonography, CABG, carotid artery

### Introduction

Excluding intraoperative death, stroke is the most dreaded perioperative complication in patients that undergo coronary bypass surgery. The prevalence of stroke is 2.1-5.2% in bypass surgery patients with a mortality rate up to 38%.<sup>1</sup>

Detachment of debris from carotid or aortic atherosclerotic plaques, embolization of the intracardiac clot and a decrease in perfusion pressure to  $<60$  mmHg are the etiologic causes of stroke in bypass surgery.<sup>2</sup> Carotid stenosis can be diagnosed and managed preoperatively. Therefore, several studies recommend preoperative carotid evaluation in all bypass candidates.<sup>3,4</sup> However, some others recommend it only in high risk patients. The stated determining factors are over 65 years of age, carotid bruit on physical examination, female gender, previous cerebrovascular accident or transient ischemic attack, peripheral vascular stenosis, hypertension, left main coronary stenosis, history of smoking, and diabetes.<sup>1,5-8</sup>

In this study, we aimed to assess the prevalence of significant carotid artery stenosis and its pertaining determining factors among the patients of a referral heart center who should undergo coronary bypass surgery.

### Patients and Methods

Over June 2004-May 2005, carotid Doppler study was performed on all the patients (n=1045) who referred to Tehran Heart Center (a university referral center) for coronary bypass surgery. Carotid Doppler was done by an expert radiologist who had been practicing Doppler studies on a daily basis for

more than 5 years. The device was a Toshiba Eccocee with linear 7.5 MHz and convex 3.75 MHz transducers. A standard protocol based on Nicolaidis criteria (Table 1) was applied to all patients.<sup>9</sup> Common carotid arteries, carotid bulbs, and internal carotid arteries were assessed for stenosis using the gray scale, color Doppler and pulse Doppler techniques. If the 7.5 MHz transducer could not be used due to the patient's obesity, a 3.75 MHz transducer would be chosen.

All patients had a lipid profile (triglyceride, cholesterol, LDL, HDL, Lipoprotein a [LPa]). Cholesterol and triglyceride levels were measured by enzymatic methods, HDL by direct method, LDL by Friedewald's formula, and LPa by immunoturbidometry. All of them were measured using Pars Azmon reagents licensed by German diagnostics. Diabetes was defined as fasting blood sugar >120 mg/dL on two separate examinations or a history of antihyperglycemic drug therapy. All the laboratory measurements were done within 24 hours of Doppler studies. This study was approved by the ethics committee of the hospital.

We considered carotid stenosis more than 60% as significant.<sup>6-8</sup> Triglyceride levels equal to or lower than 200mg/dl was considered as desirable, 201-400mg/dl as borderline and more than 400 mg/dl as high triglyceride level. Also cholesterol levels equal or lower than 200mg/dl was considered as desirable, 201-240mg/dl as borderline and more than 240mg/dl as high cholesterol level. Besides computing descriptive indices. We used the chi square test and t-test and logistic regression methods for statistical analysis. The SPSS ver.11.5 was used for statistical analysis. P values lower than 0.05 were considered as significant.

## Results

Patients aged 27-88 years; mean age of  $60.57 \pm 9.3$  years. Patients of 61-70 years of age constituted the largest age group (38.9%, n=406) followed by the 51 to 60-year-old age group (31.7%, n=331) (Figure 1).

All patients were coronary bypass candidates; however, some of them were concomitantly undertaking another operation too (Table 2).

Of 1045 patients studied, 728 (69.7%) were male. Two hundred forty-four (23.3%) had diabetes (fasting

blood sugar >120 mg/dL on two separate occasions or history of antihyperglycemic drug therapy). Seven hundred fourteen (68.3%) were nonsmoker, two hundred thirty (22%) were active smokers, and 101 (9.7%) were ex-smokers that had quit smoking for more than 1 year.

The biochemical results are shown in Table 3. Doppler study revealed bilateral carotid atherosclerotic plaques in 329 (31.5%), unilateral carotid plaque in 313 (30%), and normal in 403 of patients. Of 313 patients with unilateral carotid plaques, in 53% of patients it occurred on the right side.

Carotid stenosis was estimated according to Nicolaidis criteria that has high sensitivity (98%) and negative predictive value (98%).<sup>10</sup> The results are displayed in Table 4.

In patients with atheromatous plaques, 1 had occlusion of the left internal carotid, and 5 had occlusion of the right internal carotid artery. Totally, 72 patients had significant carotid stenosis (more than 60% stenosis) that constituted 6.9% of all the subjects. Of these patients, 59 had unilateral and 13 had bilateral significant stenosis. Ten patients had carotid stenosis more than 80%; 6 on the right side and 4 on the left. Six patients had obstruction in their internal carotid artery.

As shown in Table 5, the mean age, HDL and cholesterol are significantly higher in significant carotid stenosis.

Three hundred ninety-two patients aged 65 years and more, 12.5% (n=49) of them had more than 60%

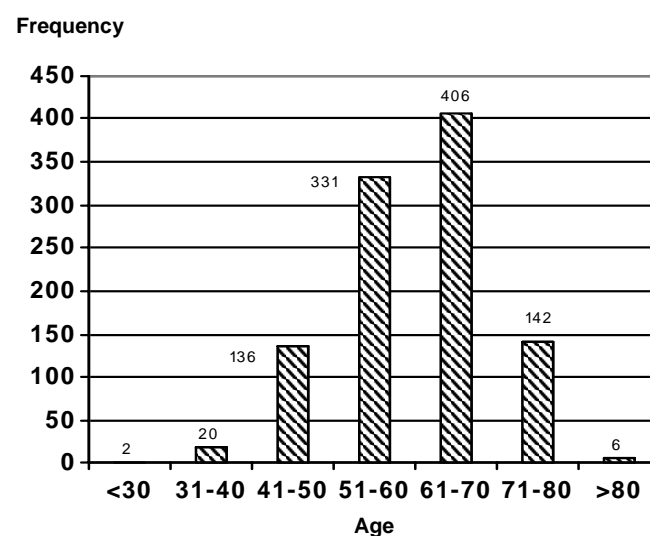


Figure 1. Distribution of patients over different decades of life.

**Table 1.** Duplex ultrasound criteria used to quantify ICA stenosis according to Nicolaides .The velocities are measured as cm/s. PSV; peak systolic velocity, EDV;end diastolic velocity, ICA; internal carotid artery, CCA; common carotid artery.

NASCET stenosis grade	PSV	EDV	PSV ICA/ PSV CCA	PSVICA/EDVCCA	EDVICA/EDVCCA
1-49%	<150	<80	<2	<10	<2.6
50-59%	<250	<130	<3.2	<10	<2.6
60-79%	>250	>130	>4	<25	<5.5
80-89%	>250	>130	>4	>25	>5.5
90-99%	Trickle flow				
100%	No flow				

stenosis and 3% (n=12) had more than 80% stenosis.

The most common site for atheromatous plaques was the carotid bulb (84% of right-sided, and 78% of left-sided plaques) followed by the cervical portion of the internal carotid artery and the common carotid artery, respectively.

Thirteen percent of women and 4.3% of men had significant stenosis (P=0.002). Also, 11% of the patients with diabetes and 5.6% of nondiabetic patients had significant stenosis (P=0.003).The prevalence of significant stenosis was 1.3% in patients younger than 50 years of age, and 7.9% at 50 or older age (P<0.0001).

Totally, 8.7% of patients with no history of smoking had significant stenosis versus 3% of patients with positive history of smoking (P=0.001).

Regarding the low number of female smokers in our study (16 active smokers and 6 ex-smokers), the association of smoking and carotid stenosis was evaluated only in men. Thus, 5.8% of the nonsmoker men had more than 60% stenosis; respectively 2.3% and 2.1% in active smokers and those with history of smoking (P=0.063).

The effect of atherogenic factors (triglyceride, cholesterol, LDL and LPa) were assessed in regard with carotid stenosis. Patients were grouped for LPa level as normal (<30 mg/dL) and high ( $\geq$ 30 mg/dL); for cholesterol level as desirable (<200 mg/ dL), moderate risk (200-240 mg/dL), and high risk ( $\geq$ 240 mg/dL); for triglyceride level as normal (<200 mg/dL), moderately high (200-400 mg/dL), and high ( $\geq$ 400 mg/dL); and for LDL level as normal (<160 mg/dL), and high ( $\geq$ 160 mg/dL).

Accordingly, significant stenosis was 7.1% in patients with normal LPa and 6.7% in the high LPa group (P=0.78). Normal LDL and high LDL groups had respectively 5.4% and 12.6% significant carotid stenosis (P=0.0006). Significant carotid stenosis oc-

curred in 5.6% of patients with desirable cholesterol levels, in 4.6% of the moderate risk group, and in 13.4% of the high risk group (P=0.0001). Carotid artery stenosis of more than 60% was observed in 6.5% of patients with normal TG, 7% with moderately high TG, and 17.4% with high TG (P=0.12). Only 23 patients had high TG (>400mg/dL).

**Table 2.** Reasons for additional operations concomitantly with the bypass surgery.

Frequency	Reasons
9	AVR+MVR
2	AVR
1	MVR+AVR+TVR
3	MVR+TVR
11	MVR
1	TVR

AVR; aortic valve replacement, MVR; mitral valve replacement, TVR; Tricuspid valve replacement.

**Table 3.** Biochemical results for all patients. LPa, Lipoprotein a; LDL, low-density lipoprotein; TG, triglyceride.

	level	number
LPa	= < 30	621(%59.4)
	>30	421(%40.3)
LDL	= < 160	819(%78.4)
	>160	223(%21.3)
Cholesterol	= < 200	663(%63.4)
	201-240	358(%34.3)
	>240	23(%2.2)
TG	= < 200	663(%63.4)
	201-400	358(%34.3)
	>400	23(%2.2)

**Table 4.** Distribution of right and left arterial stenosis

	Right	Left
<15%	373(%74.0)	365(%77.8)
15-60%	84(%16.7)	66(%14.1)
60-79%	36(%7.1)	33(%7.0)
80-99%	6(%1.2)	4(%0.9)
100%	5(%1.0)	1(%0.2)

**Table 5.** Comparison of age and biochemical measures in the two groups of significant and nonsignificant carotid stenosis.

	Mean in all patients		Mean	P-Value
Triglyceride	192.1±105.1	No significant stenosis	191.3±99.3	0.54
		Significant stenosis	203.4±165.2	
Cholesterol	205.5±58.0	No significant stenosis	204.4±58.1	0.021
		Significant stenosis	220.5±56.0	
HDL	36.9±8.9	No significant stenosis	36.7±8.7	0.006
		Significant stenosis	40.3±10.5	
LDL	131.6±52.1	No significant stenosis	131.1±52.5	0.19
		Significant stenosis	139.4±45.7	
Lipoprotein A2(CRP)	10.5±9.9	No significant stenosis	10.5±10.1	0.94
		Significant stenosis	10.4±7.3	
Lipoprotein A1	36.3±32.4	No significant stenosis	36.3±32.3	0.99
		Significant stenosis	36.3±33.7	
LDL to HDL Ratio	3.9±3.9	No significant stenosis	3.9±4.1	0.12
		Significant stenosis	3.6±1.2	
Age	60.5±9.5	No significant stenosis	60.1±9.4	<0.0001
		Significant stenosis	66.5±8.1	

We used the logistic regression model to evaluate determining factors for significant carotid stenosis. Accordingly, we computed the odds ratios (OR) for significant stenosis in one model. According to the model, among all factors, age>50 (OR=5.7[1.3-24.4] Wald P=0.018), presence of diabetes (OR=1.8[1.1-3.2] Wald P=0.022), female gender (OR=2.2[1.3-3.9] Wald P=0.005), triglyceride>400 (OR=3.9[1.0-15.5] Wald P=0.046) and HDL>60 (OR=6.7[1.4-32.5] Wald P=0.017) were independent determining factors for significant carotid stenosis.

## Discussion

In coronary bypass surgery candidates, carotid stenosis is a risk factor for stroke, inhospital mortality and longer inhospital stay.<sup>1</sup> Evaluation of carotid arteries for stenosis combined with endarterectomy reduces preoperative as well as postoperative risk of stroke. It also helps with discovering and following cases of significant carotid artery stenosis that do not have any neurological symptoms. Presence of significant carotid artery stenosis can change the bypass schedule to a bypass with endarterectomy or endarterectomy followed by bypass surgery.<sup>8</sup>

Considering the costliness of carotid Doppler studies, it is important to determine those bypass candidates who would benefit from carotid evaluation. Age of more than 65 years, carotid bruit on examination, peripheral vascular stenosis, hypertension, left main

coronary stenosis, history of smoking, and diabetes have been stated as determining factors associated with carotid stenosis by different studies.<sup>1,5-8</sup> However, some other studies did not find any association between hypertension, hypercholesterolemia, smoking, and diabetes with carotid stenosis.<sup>1,11</sup>

In regard with the fact that atherosclerosis is a multifactorial phenomenon with both genetic and environmental factors playing a role, and considering the fact that previous studies have shown that coronary artery disease occur at an earlier age in Iran, this study sought to assess the prevalence of carotid stenosis and its pertinent determining factors in a large number of patients who were considered for CABG in a referral center.<sup>12,13</sup>

Of 1045 patients in this study with a mean age of 60.57 years, 72 patients (6.9%) had carotid stenosis of more than 60%. Significant stenosis was 12.5% in 65 year olds and above, which is in accordance with Berens' and Faggioli's results.<sup>8,11</sup> Faggioli reported that the prevalence of carotid stenosis significantly increased after 60 years of age; however, we observed the pattern at 50 (i.e. 1.3% at 50 years and less, and 7.9% at more than 50; P=0.002). Faggioli did not report hypercholesterolemia, hypertension, diabetes, and smoking as the determining factors for carotid stenosis, postoperative stroke or death. However, in our study, high risk hypercholesterolemia (>240 mg/dL) and diabetes were associated with significant

carotid stenosis (respectively  $P=0.0001$  and  $P=0.003$ ). The prevalence of carotid stenosis was 17.4% with TG more than 400 mg/dL, and 6.5% with TG less than 200 mg/dL. However, the small number of patient with TG more than 400 mg/dL in our study (33 out of 1045) rendered the statistical evaluation inconclusive. An LDL level higher than 160 mg/dL was also a determining factor for carotid stenosis ( $P=0.0006$ ).

In the current study, smoking was not a risk factor for carotid stenosis, and hypertension was not studied. Identifying diabetes as a risk factor in our study is against the findings in Dunard's study. Dunard observed that 32% of the patients with less than 70% carotid stenosis had a history of diabetes and the prevalence of diabetes was 34% in patients with stenosis of 70% and more. Female gender was reported a risk factor by Dunard and Figgioli ( $P\leq 0.005$  and  $P=0.02$  respectively). In our study, this association was seen too ( $P < 0.0001$ ).

High serum Lp(a) levels (more than 30 mg/dL) is a controversial atherogenic factor. We did not find any association between high Lp(a) and significant carotid stenosis.<sup>14</sup>

## Conclusion

Age of 50 years and more, female gender, diabetes, and hypercholesterolemia were identified determining factors for carotid artery stenosis among our patients. In regard with the early occurrence of carotid stenosis in our patients by one decade, it is recommended to assess the cost effectiveness of carotid evaluations after the age of 50 in a multicenteric Persian study.

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