ORİGİNAL ARTİCLE

Carotid artery screening in high risk asymptomatic individuals: outcomes of 3000 carotid screening

Cribado de arterias carótidas en individuos asintomáticos de alto riesgo: resultados del cribado de 3000 carotidos

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Abstract

Objectives: *The primary aims of the study to evaluate the efficacy of carotid screening tests to identify asymptomatic carotid artery stenosis among high-risk patients and early prevention of stroke.* **Background:** *The estimated prevalence of asymptomatic severe carotid stenosis (≥ 70%) in the general adult population ranges up to 3.1%. However, the prevalence is higher in comorbid individuals. This makes it important to perform screening testing for early diagnosis and treatment in predetermined high-risk patients.* **Material and methods:** *In this prospective study, 3000 selected patients screened during March 2017 and September 2018 at the most populated family health center. Participants selected among registered individuals who have at least one of the risk factors such as hypertension, hyperlipidemia, diabetes mellitus, obesity, and smoking. All the participants were asymptomatic and above the age of 55. Bilateral carotid artery screening performed by Duplex Ultrasonography (DUSG) at the first call and one year later. Patients with severe carotid and/or coronary artery stenosis treated by surgical revascularization or stent implantation in the light of the latest guidelines.* **Conclusion:** *Carotid screening among high-risk asymptomatic individuals is of great importance to identify severe carotid artery as well as coronary artery stenosis. Patient education during screening may play a crucial role in preventing the disease.*

Keywords: *Carotid artery stenosis. Duplex ultrasonography. Endarterectomy. Modifiable risk. Stroke.*

Resumen

Objetivos: *Los objetivos principales del estudio fueron evaluar la eficacia de las pruebas de detección de carótidas para identificar la estenosis asintomática de la arteria carótida en pacientes de alto riesgo y la prevención temprana del accidente cerebrovascular.* **Antecedentes:** *La prevalencia estimada de estenosis carotídea grave asintomática (≥ 70%) en la población adulta general varía hasta el 3,1%. Sin embargo, la prevalencia es mayor en individuos comórbidos. Esto hace que sea importante realizar pruebas de detección para el diagnóstico y el tratamiento tempranos en pacientes predeterminados de alto riesgo.* **Material y métodos:** *En este estudio prospectivo, 3000 pacientes seleccionados fueron evaluados durante marzo de 2017 y septiembre de 2018 en el centro de salud familiar más poblado. Participantes seleccionados entre individuos registrados que tienen al menos uno de los factores de riesgo como hipertensión, hiperlipidemia, diabetes mellitus, obesidad y tabaquismo. Todos los participantes estaban asintomáticos y tenían más de 55 años. Cribado bilateral de la arteria carótida rea-*

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lizado por ecografía dúplex (DUSG) en la primera llamada y un año después. Pacientes con estenosis severa de carótidas y/o arterias coronarias tratados mediante revascularización quirúrgica o implantación de stents a la luz de las últimas guías. **Conclusión:** *El cribado carotídeo en individuos asintomáticos de alto riesgo es de gran importancia para identificar la estenosis grave de la arteria carótida y la arteria coronaria. La educación del paciente durante el cribado puede desempeñar un papel fundamental en la prevención de la enfermedad.*

Palabras clave: *Estenosis de la arteria carótida. Ecografía doppler. Endarterectomía. Riesgo modificable. Ictus.*

Introduction

Stroke is defined as a neurological deficit of vascular origin, which can result in death within 24 hours. The severity of the syndrome varies widely, including the possibilities of complete recovery, partial recovery, disability and death. Transient ischemic attacks (TIA) refers to episodes of loss of focal cerebral function, which are thought to be of ischemic origin usually localized to a vascular area that lasting maximum 24 hours. The prevalence of stroke is around 6/1000[1]. Stroke is the second leading cause of death in the population after coronary heart disease for the age of 60's[2]. Strokes are in the form of the first ischemic attack at the rate of 80%. Studies have shown that stroke incidence can be reduced by up to 40% when primary protection is provided[3].

There are risk factors such as age, gender, low birth weight, race, and genetic history that directly affect the prevalence of stroke. The risk of stroke in male is higher than in female gender[4]. There are also modifiable risk factors that can reduce the incidence of stroke with primary protection[5]. The most important modifiable risk factor is hypertension. Besides, smoking is one of the definite modifiable risk factors as diabetes and obesity.

In this study, we aimed to investigate the efficacy of the carotid screening tests among high-risk asymptomatic individuals to find out severe carotid stenosis and predict the possibility of early treatment to prevent stroke.

Patients and methods

Ethical consideration

This prospective study carried out after approval of the Ethics Committee (Number:1024). Patient consent forms were signed by participants before inclusion. The study results were accepted by hospital authority, and all of the authors were admitted to the publication of the article.

Inclusion and exclusion

The study included 3000 registered patients of a Family Health Center at our region, a facility which has 55-60 thousand of the registered patients. The survey carried out during March 2017 and September 2018. All the participants were over the age of 55, and have at least one of the risk factors of hypertension, hyperlipidemia, diabetes mellitus (DM), obesity and smoking.

Patients with the previous diagnosis of carotid arterial or coronary artery disease; under the age of 55; without any registered risk factors of hypertension, DM, obesity, smoking were not included in the study. Chronic renal failure requiring hemodialysis patients also excluded.

Study design and patient management

According to the predefined condition, high-risk patients among the registered population were contacted by phone call. Who agreed to have duplex ultrasonography (DUSG) were appointed to the facility. Bilateral carotid artery were examined with DUSG by two radiologists and two cardiovascular surgeons in turn.

The patients were divided into four groups after DUSG evaluation by NASCET system; The first group was no detectable stenosis. The second group included carotid stenosis of <50%, medical therapy, and annual DUSG was recommended for this group. The last two groups were those with 50-70% and >70% stenosis. Patients with bilateral stenosis and multiple risk factors were undergone cardiology consultation for coronary and carotid angiography in these groups. The carotid revascularization plan was decided by the council formed of neurology, cardiology, and cardiovascular surgeons based on the latest guideline and meta-analysis after the angiogram images were evaluated[6,7].

In addition to focusing on reducing the impact of modifiable risk factors in patients with 0-50% stenosis, aspirin, and lipid-lowering treatment were started, and DUSG was performed one year after initial screening.

Table 1. Patients demographics and risk factors

	Number of patient (N=3000) (%)	Degree of stenosis of each carotid artery			
		0 n (%)	<50% n (%)	50-70% n (%)	>70% n (%)
Female	1390 (46.3)	2487 (89.5)	178 (6.4)	89 (3.2)	26 (0.94)
Male	1610 (56.7)	2791 (86.7)	260 (8.1)	126 (3.9)	43 (1.34)
Smoking	1406 (46.9)	2588 (92.0)	155 (5.5)	47 (1.72)	22 (0.78)
Hypertention	2090 (69.7)	3463 (82.8)	514 (12.3)	183 (4.0)	20 (0.9)
Hyperlipidemia	1427 (47.6)	2481 (87.0)	303 (10.6)	51 (1.73)	19 (0.67)
DM	1263 (42.1)	2018 (79.9)	432 (17.1)	58 (2.3)	18 (0.7)
BMI<25	321 (10.7)	592 (92.2)	39 (6.1)	9 (1.4)	2 (0.3)
BMI: 25-30	978 (32.6)	1780 (91.0)	141 (7.2)	35 (1.8)	0
BMI>30	1701 (56.7)	3028 (89.0)	213 (6.3)	139 (4.05)	22 (0.65)
Patients of					
Unilateral stenosis	274 (9.13)	196 (6.5)	132 (4.4)	105 (3.6)	37 (1.23)
Bilateral stenosis	241 (8.03)	2289 (76.3)	153 (5.1)	72 (2.4)	16 (0.53)
Subtotal	515 (17.2)	2485 (82.8)	285 (9.5)	177 (6.0)	53 (1.76)

DM: Diabetes mellitus
BMI: Body mass index.

Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics software (SPSS Inc. Chicago Illinois, United States of America), version 24.0. The normal distribution of variables was analyzed with the Kolmogorov–Smirnov test. Normally distributed continuous variables are stated as Mean±SD (Standard deviation). Categorical variables are stated as absolute numbers and proportions. Univariate analysis was performed to establish the relationship with the risk factor and the disease, and multivariate analysis was conducted to find out the independent risk factor for the disease. P value <0.05 accepted as statistically significant.

Results

All of the patients in the study were asymptomatic. A total of 6000 carotid arteries of the 3000 selected individuals were screened by DUSG. The mean age was 61±7.6 years. 46.3% of patients were female. Hypertension, obesity and hyperlipidemia were the most common risk factors of the included patients. Nearly half of the patients were smokers. DM was the 5th most common risk factor for inclusion (Table 1).

In 2485 (82.8%) patients, there was no detectable carotid stenosis. There were 37 (1.23%) patients had unilateral and 16 (0.53%) patients had 70-100% carotid stenosis (Table 1). All of these patients were performed carotid and coronary angiography. 14 (0.47%) of them underwent carotid endarterectomy, and 15 (0.5%) patients underwent stent implantation successfully subsequently. Another 8 (0.27%) patients underwent carotid endarterectomy and coronary artery bypass grafting (CABG) simultaneously. Among the patients with 50-70% stenosis, 26 (0.87%) out of 177 (6%) patients underwent carotid and coronary angiography after cardiology consultation due to bilateral stenosis and multiple risk factors. As a result, carotid endarterectomy and CABG were performed simultaneously 5 (0.17%) of them, and carotid stent implanted 3 (0.1%) of them. 12 (0.4%) patients underwent percutaneous coronary intervention (Table 2).

TIA and complete paralysis developed in 7 (0.23%) patients during the follow-up period. In 3 (0.1%) of them, the surface of the plaque was evaluated irregularly. Carotid stent implantation was performed to these patients. The other 4 (0.13%) patients underwent carotid endarterectomy after CT angiography. 3 (0.1%) patients with 50-70% carotid stenosis died due to cardiac causes during the year. Stenosis advanced by >10% at second DUSG after one year in 27 (0.9%) participants who have 0-50% stenosis

Table 2. Treatment choices for patients had severe carotid stenosis, and events that occurred after or before treatment

Events	Incidence (%) (N=3000)
One year mortality	3 (0.1%)
Carotid endarterectomy	18 (0.77%)
Carotid stent implantation	21 (0.7%)
Coronary+carotid angiography	63 (1.8%)
Percutaneous coronary intervention	12 (0.8%)
Carotid endarterectomy + CABG	13 (0.43%)
Stroke	7 (0.23%)
TIA	3 (0.1%)
Complete paralysis	4 (0.13%)
Stenosis advanced by >10%	27 (0.9%)

CABG: Coronary artery bypass graft
TIA: Transient ischemic attack.

Table 3. Risk factors' comparision between patients had severe and mild carotid stenosis

	Stenosis <50		Stenosis >50		P
	n	%	n	%	
Gender					
Female	989	(71.15)	401	(28.85)	0.012
Male	1211	(75.22)	399	(24.78)	
Smoking	1024	(72.83)	382	(27.17)	0.559
Hypertension	1401	(67.03)	689	(32.97)	<0.001
Hyperlipidemia	894	(62.65)	533	(37.35)	<0.001
DM	752	(59.54)	511	(40.46)	<0.001
BMI					
BMI<25	264	(82.24)	57	(17.76)	<0.001
BMI: 25-30	846	(86.50)	132	(13.50)	
BMI>30	1090	(64.08)	611	(35.92)	

(Table 2). No complications occurred in patients undergoing carotid endarterectomy or stenting.

We also performed univariate and multivariate analyses. Univariate analysis showed that hypertension, hyperlipidemia, DM, and BMI have a significant relationship with the severity of carotid artery stenosis (Table 3).

Similarly, multivariate analysis revealed that the increased age, hypertension, hyperlipidemia, DM, and obesity as independent risk factors for >50% of carotid stenosis (Table 4).

Table 4. Multivariate analysis of independent risk factors for patients had >50% of carotid stenosis

	P	Odds ratio	95% Confidence Interval
Age	0.000	1.036	1.025-1.047
Gender	0.150	0.462	0.695-1.057
Smoking	0.236	0.658	0.919-1.408
Hypertension	0.000	2.025	1.558-2.632
Hyperlipidemia	0.000	3.209	2.464-4.181
DM	0.008	1.396	1.090-1.789
BMI>30	0.000	3.381	2.385-4.791

Discussion

Stroke is a significant healthcare problem throughout the world. Identification of patients who are at risk of stroke as well as cardiovascular disease allows early medical treatment or surgical intervention[8]. Screening for carotid artery stenosis offers one pathway for this, as there is some correlation between carotid stenosis and coronary artery disease[9,10]. There are no randomized control trials to compare the benefits of screening vs. no screening in the general population and the effect on rates of stroke and cardiovascular disease. Study suggests both medical and surgical interventions to reduce the risk of stroke in asymptomatic patients be effective[11] Nevertheless, the biggest problem is who will be screened[12]. In our study, we defined five more common modifiable risk factors among our population as inclusion criteria.

Hypertension is one of the leading modifiable risk factors in stroke, which accelerates atherosclerosis. In a study lasting nearly 50 years, it was revealed that stroke and vital organ damage were prevented by the treatment of hypertension. Hypertension is the most crucial parameter in establishing health policies to prevent stroke. In patients over the 7th decade, a decrease of 30% in stroke incidence has been shown with 10 mmHg blood pressure drop[13]. In this series, there were 2090 (69.7%) hypertension patients using antihypertensive drugs. Among the hypertensive patients, we found 0.9% of patients with >70% stenosis and 32.1% patients with 50-70% stenosis in the internal carotid artery. Another important risk factor in stroke is smoking. Regardless of all other risk factors, the risk of stroke is doubled in smokers[14]. Smoking increases the

formation of atherosclerosis and thrombus development in atherosclerotic vessels, as hypertension[15,16].

Diabetes is one of the preventable causes of death in stroke and ischemic heart disease. It has been shown in studies that vascular diabetic complications and stroke rates are higher in individuals with HbA1c level above 6%. The increased risk of stroke in patients with diabetes is independent of age and blood pressure. Decreased insulin release in diabetic patients increases the risk of atherosclerosis, as well as substances such as glutamate, accumulate after a series of immunological reactions and vascular damage occurs[17].

Treatment of hyperlipidemia is also essential in preventing the development of atherosclerosis in diabetic patients. It has been found that a high cholesterol level is associated with ischemic stroke. Serum high total cholesterol and carotid intima-media thickness were found to be correlated[18,19]. High HDL cholesterol has been shown to reduce the risk of ischemic stroke. With every 10 mg/dl HDL increase, the risk of stroke decreases by 11-15%[20]. It has been observed that in individuals with better control of blood glucose, lipid parameters, and blood pressure, a 50% significant decrease in risk is achieved in cardiovascular and microvascular events[17]. In our study, 1427 patients were diagnosed with dyslipidemia and LDL blood biochemical value was followed with >160 mg/dl. All patients were started to be given a higher dose of statin group medication.

Obesity is associated with high blood pressure, blood glucose, and serum lipids in individuals. The susceptibility of individuals with central obesity to atherosclerosis has been demonstrated in studies. Although the frequency and duration of physical activity have not been determined for these patients, 30 minutes of exercise is recommended every day by the American National Institute of Health[21].

From this study, we acknowledged that the screening test not only reveals the disease but, more importantly, it contributes positively to the modifiable risk factors. This observation may explain the low mortality and stroke rates during a one-year follow-up.

In conclusion, carotid screening among high-risk asymptomatic individuals is of great importance to detect severe carotid as well as coronary artery stenosis; thus, early diagnosis and treatment can be possible. Moreover, patient awareness will be more effective in preventing the disease as a result of educating and informing the high-risk patients during the screening test.

Limitation of the study

This is a unilateral prospective study and has not been randomized. Also, since DUSG is practitioner dependent, there is a margin of error. Because patients under the age of 55 are excluded from the study, the incidance of the disease of this age group is still not known.

The risk factor for carotid stenosis is not limited to we mentioned above. Valvular or non-valvular atrial fibrillation, left ventricular hypertrophy, and hyperhomocysteinemia are also risk factors for both stroke and atherosclerosis. This high-risk group was also not included in the study. Finally, lack of cost-effective analysis is another most important limitation of the study. Each country has its unique health insurance system and resources devoted to health protection, the cost-effective analysis should be made first before screening a large population.

Conflict of interest

The authors declare no conflicts of interest in this study.

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Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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