Risk Stratification for Combined Carotid and Peripheral Vascular Diseases

KOMBİNE KAROTIS VE PERİFERAL ARTER HASTALIKLARINDA RİSK PLANLAMASI

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Summary

Objective: The objective of this study was to determine the predictive values of multiple atherosclerotic risk factors for screening of carotid artery stenosis in patients with peripheral vascular disease.

Materials and Methods: 120 patients admitted for peripheral vascular reconstruction to our institution, from 1998 through 2000 were preoperatively screened for carotid artery stenosis. Patients were examined for neurologic status and cervical bruits. As atherosclerotic risk factors, hyperlipidemia, diabetes, smoking, sex and age, coronary artery disease (CAD), coronary artery bypass surgery (CABG), and previous vascular operation were recorded. Preoperative ankle-brachial pressure indexes (ABI) were calculated. A11 patients underwent routine carotid color duplex examinations preoperatively.

Results: 94 patients (78.3%) had mild (<50%) or no carotid artery stenosis, and 26 patients (21.7%) had significant (>50%) carotid artery stenosis. Age (>60 years), coronary artery disease, carotid bruit as individual factors, and the combination of age >55 and hyperlipidemia had a significant value in predicting presence of >50% stenosis of one or both carotid arteries by univariate analysis. By multivariate logistic regression analysis, however, only carotid bruit was associated with carotid artery stenosis of>50%($p<0.001$).

Conclusion: Carotid artery bruit and somewhat older age are only significant risk factors indicating to screen for carotid artery stenosis in patients with peripheral vascular disease. Routine screening for asymptomatic carotid artery stenosis in all patients is not an effective strategy.

Key Words: Carotid artery stenosis, Peripheral vascular disease, Duplex

T Klin J Med Res 2001, 19:42-47

Received: Sep. 15, 2000

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Özet

Amaç: Bu çalışmanın amacı, periferal vasküler hastalığı olan hastalarda mevcut çeşitli aterosklerotik risk faktörlerinin yandaş karotis arter stenozunun araştırılmasının gerekliliğini göstermedeki rollerini değerlendirmekti.

Materyal ve Metodlar: Prospektif olarak planlanan çalışmamızda 1998 ile 2000 yılları arasında çeşitli periferal arteryel hastalıklar nedeni ile kliniğimizde tedavi edilen 120 hasta preopcratif olarak karotis arter stenozu yönünden taranmıştır. Hastaların nörolojik muayene ve karotis oskültasyon bulguları dikkatli bir şekilde değerlendirilmiştir. Aterosklerotik risk faktörleri olarak, hiperlipidemi, diyabet, sigara alışkanlığı, cinsiyet ve yaş, koroner arter hastalığı, geçirilmiş koroner arter bypass operasyonu ve önceki vasküler operasyonlar araştırılıp not edilmiştir. Preoperatif ayak bileği-kol arteriyel basınç indeksleri saptanmıştır. Bütün hastalara preoperatif olarak rutin karotis arteryel renkli doppler tetkikleri yapılmıştır.

Bulgular: 94 hastada (%78.3) hafif dereceli (<%50) karotis arter stenozu saptanmış veya hiç bulunmamış iken 26 hastada (%21.7) önemli derecede (>%50) karotis arter stenozu olduğu görülmüştür. Varyans analizlerinde, bağımsız faktörler olarak yaş (>60 yıl), koroner arter hastalığı, karotis üfürümü ve yaş (>55) ile hiperlipidemi kombinasyonu, %50 ve üzerindeki ciddi tek ya da bilateral karotis arter stenozu varlığım gösteren anlamlı risk faktörleri olarak bulunmuşlardır. Bununla birlikte multivaryans lojistik regresyon analizlerinde ise sadece karotis üfürümü varlığı ile %50 ve üzerindeki ciddi karotis arter stenozu arasında anlamlı bir ilişki olduğu saptanmıştır ($p< 0.001$).

Sonuç: Periferal arteriyel hastalığı olanlarda karotis üfürümü ve ileri yaş, yandaş karotis arter stenozunun araştırılması gerektiğini gösteren başlıca risk faktörleridir. Bütün hastaların asemptomatik karotis arter stenozu açısından rutin olarak taranması gereksiz ve etkili olmayan bir işlemdir.

Anahtar Kelimeler: Karotis arter stenozu, Periferal arteriyel hastalık, Doppler

T Klin Araştırma 2001, 19:42-47

Stroke as a complication of carotid artery stenosis is one of the major leading cause of death (1). Recent improvements in preventive medicine has focused vascular surgeons attention on value of carotid duplex scanning for asymptomatic carotid artery disease in peripheral vascular disease, especially in the presence of significant atherosclerotic risk factors. Several reports have indicated that the prevalence of hemodynamically significant (>50%) carotid stenosis or occlusion in patients with peripheral arterial disease ranges from 10% to 15% (2,3) and therefore it becomes clinically important to identify subgroups of patients who have asymptomatic carotid artery stenosis.

Some multicenter prospective randomized trials demonstrated the benefit of performing carotid endarterectomy in asymptomatic patients.(4,5) Asymptomatic Carotid Atherosclerosis Study (ACAS) showed that patients with asymtomatic carotid stenosis of 60% or greater treated with aspirin and carotid endarterectomy had a reduced 5-year risk of fatal and non-fatal ipsilateral carotid stroke compared with patients treated with aspirin alone (4). Coinciding with this report, the Department of Veterans Affairs hospital carotid trial demostrated a decrease in the ipsilateral stroke rate in surgically treated group in patients who have a > 50% carotid artery stenosis (5).

Most important question is which patients with a peripheral vascular disease should undergo screening for carotid artery stenosis. Some clinicians have recommended that all patients with peripheral vascular disease undergo routine screening for asmyptomatic carotid artery disease and others do not (6).

The purpose of this study was to determine the predictive values of multiple atherosclerotic risk factors for screening of carotid artery stenosis in Patients with peripheral vascular disease.

Patients and Methods

Between 1998 and 2000, 120 patients admitted for peripheral vascular reconstruction were preoperatively screened for carotid artery stenosis. All Patients were carefully examined for symptoms of cerebrovascular insufficiency and for cervical T^its. Atherosclerotic risk factors, such as hyper-^Pidemia, diabetes, smoking, sex and age, coronary artery disease (CAD), coronary artery bypass surgery (CABG), and previous peripheral vascular operation were also carefully recorded. CAD of patients other than undergoing CABG and having coronary angiograms was diagnosed via thallium-201 perfusion scintigraphy. Preoperative peripheral arterial angiographic findings and diagnoses for arterial lesions of patients were classified as aorta-iliac, femora-popliteal, infragenicular, and multipl vascular lesions. Preoperative ankle-brachial pressure indexes (ABI) were calculated. Preoperative neurologic symptoms were classified as either a stroke or a transient ischemic attack (TIA). Transient neurologic symptoms that had been evaluated by a physcian were considered as TIAs; permanent neurologic deficits were defined as stroke.

All patients were examined before operation according to a standard protocol for carotid duplex scanning performed with a color duplex scanner (Toshiba -Sonolayer SSA-270A, Tochigi-Ken 329-26 Japan) which evaluates peak systolic velocity. An angle adjusted peak-systolic velocity greater than 1.25 m/sec indicated carotid artery stenosis greater than 50%. The end-diastolic velocity greater than 1.4 m/sec was considered as the carotid artery having 80% to 99% stenosis (7). According to this evaluation protocol carotid artery lesions were grouped as following; grade 1: < 15% stenosis, grade 2: 16% to 49% stenosis, grade 3: 50% to 79%> stenosis, grade 4: 80% to 99% stenosis, grade 5: total occlusion or no detected flow, grade 6: bilaterally detected mild to moderate (< 80%o) carotid artery stenosis, grade 7: bilaterally detected unilateral severe (>80%) stenosis, grade 8: bilaterally detected severe (>80%) carotid artery stenosis.

We then carefully investigated for the relation between carotid artery stenosis and all these various risk factors, and examination findings. We attempted to determine which of these risk factors and examination findings would indicate and predict a significant carotid artery stenosis.

Statistical analyses were performed by SPSS / PC+ (ver 8.0) computer program. The probabilty (p) less than 0.05 was considered significant. The data were analysed by using chi-square test, Mann Whitney-U Test, and all factors were assessed for their ability to predict the carotid artery stenosis and routine duplex scan requirement by using a lo-

gistic regression model that was suited for each variable and multivariate logistic regression analysis. The p value, standard deviations, risk ratio, and 95% confidence interval for each variable were determined. A11 proportions were compared with Fisher's Exact Test and all p values were two tailed.

Results

Thirty patients (25%) demonstrated some evidence of atherosclerotic carotid artery disease, in duplex scanning. Four patients (3.3%) had a carotid artery stenosis of 16% to 49%, 9 patients (7.5%) had a carotid artery stenosis of 50% to 79%, 4 patients (3.3%) had a carotid stenosis of 80% to 99%, 5 patients (4.1%) had unilateral totally occluded carotid artery, 1 patient (0.7%) had bilateral mild to moderate (< 80%) stenosis, 1 patient (0.7%) had bilaterally detected unilateral severe (>80%) stenosis, and 6 patients (5%) had bilateral severe (>80%) carotid artery stenosis. When divided into broad clinical subgroups, 94 patients (78.3%) had mild (< 50%) or no carotid artery stenosis, and 26 patients (21.7%) had 50% or greater, significant carotid artery stenosis.

Table 1 tabulates the prevalence of the various atherosclerotic risk factors in the patients with a carotid stenosis greater than or equal to 50% versus the prevalence in patients having carotid artery stenosis less than 50%» (Table 1).

The indications for hospitalization were claudication in 70 (58.3%) patients, rest pain in 28 (23.3%) patients, and ulcer or gangrene in 21 (17.5%o) patients. There was not any symptom in one (0.9%) patient whose vascular disease was diagnosed following a routine examination. Of the 70 patients with claudication, 53 (56.3% of 94) had carotid stenosis of less than 50% and 17 (65.3% of 26) had carotid stenosis of 50 % or greater. Of the 28 patients with rest pain, 20 (21.2%) had mild (<50%) or no carotid stenosis and 8 (30.4%) had significant (>50%) carotid artery stenosis. Of the 21 patients with ulcer, 20 (21.2%) had mild or no carotid stenosis and 1 (3.8%) had severe carotid artery stenosis. One (1.1%) asymptomatic patient had no carotid artery stenosis. There was not any significant relation between the degree of stenosis and indication for hospitalization of peripheral vascular disease (p= 0.258, by chi-square test).

Table 1. Predictive value and prevalence of various risk factors for significant carotid artery stenosis

	Carotid Stenosis >50% n=26	Carotid Stenosis <50% n=94	p Value
Age<50	1 (3.8%)	10(10.6%)	0.655
Age >50	25 (96.1%)	84 (89.3%)	0.454
Age >55	23 (88.4%)	73 (77.6%)	0.095
Age >60	22 (84.6%)	50 (53.1%)	0.012
Age >65	11 (42.3%)	30(31.9%)	0.095
Hypertension	13 (50%)	39(41.4%)	0.358
Diabetes	7 (26.9 %)	30(31.9%)	0.402
Hyperlipidemia	15 (57.7%)	34 (36.1%)	0.095
CAD	22 (84.6%)	52 (55.3%)	0.007
Previous MI	9 (34.6%)	26 (27.6%)	0.611
P.vascular operation	10(38.5%)	28(38.5%)	0.632
CABG	10(38.5%)	19 (20.2%)	0.096
Carotid bruit	20 (76.9%)	9 (9.6%)	< 0.001
Stroke	2 (7.7%)	2(2.1%)	0.196
TIA	2 (7.7%)	2(2.1%)	0.196
Right ABI	0.54 ± 0.35	0.48 ± 0.24	0.363
Left ABI	0.53 ± 0.36	0.48 ± 0.34	0.612
Male/ Female	26/0 (100%/0)	91/3 (96.8%/3.2%)	1

(CAD: Coronary artery disease, MI: Myocardial infarction, P: Previous, CABG: Coronary artery bypass surgery, TIA: Transient ischemic attack, ABI: Ankle-brachialpressure index)

Table 2. Predictive value of preoperative angiographic diagnoses

	Carotid Stenosis >50% n=26	Carotid Stenosis <50% n=94	p Value (X^2 test)
Aorta-iliac disease	12 (46.2%)	33 (35.1%)	
Femora-popliteal	3(11.5%)	26 (27.7%)	0.282
Infragenicular	2 (7.7%)	10(10.6%)	
Multipl	9 (34.6%)	25 (26.6%)	

Preoperative angiographic findings of patients did not yielded a significant correlation with the severity of carotid artery stenosis (Table 2).

The mean right A B I were 0.48 ± 0.24 and 0.54 ± 0.35 for patients having less than 50%) and greater than or equal to 50% carotid artery stenosis, respectively. The difference was not significant (p=0.363). Likewise, the comparison of left mean

Table 3. Predictors of 50% or greate stenosis of one or both carotid arteries by univariate and multivarate analysis

Variable	Univariate p value	Risk ratio	95% Confidence limits	Multivariate p value
C A D	0.007	0.636	0.496-0.815	0.1142
Carotid bruit	< 0.001	0.127	0.063 -0.257	< 0.001
Age (>60)	0.012	0643	0.489 - 0.858	0.1083

(CAD: Coronary artery disease)

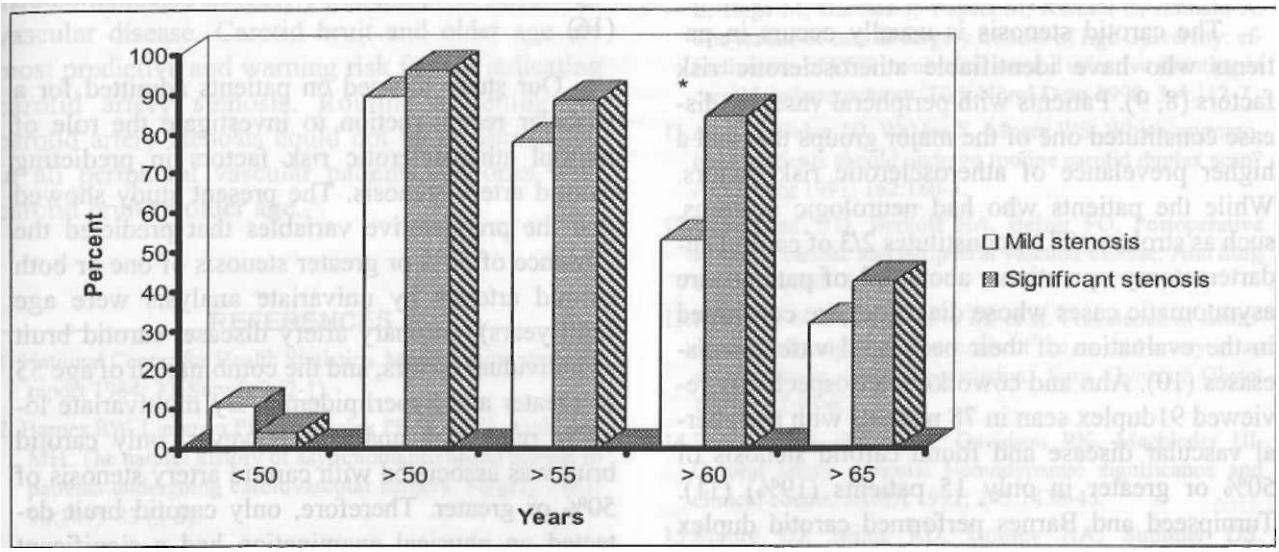

Figure 1. Prevalence of mild (<50%) and significant (>50%) carotid artery stenoses according to age (year) limits (asterisk indicates significant age limit: 60 years).

ABI measurements was not significantly different between two broad carotid artery stenosis groups (0.48 ± 0.34 versus 0.53 ± 0.36 for mild and 50% or greater carotid artery stenosis groups, respectively, p=0.612).

Furthermore, the various combinations of each variable were also evaluated to look for some possible significant correlations between these combined factors and the carotid stenosis greater than or equal to 50%. The most notable combination was age 55 or greater and the hyperlipidemia. Of the 33 patients aged 55 or greater with hyperlipidemia, 15 (57.7% of 26) had carotid stenosis of 50% or greater, whereas 18 (19.1% of 94) had mild carotid artery stenosis. Age 55 or greater and hyperlipidemia combination was a significant predictor of carotid artery stenosis greater than or equal to 50% (p=0.032).

Consequently the preoperative variables that predicted the presence of 50% or greater stenosis of one or both carotid arteries by univariate analysis were age (>60 years), coronary artery disease, carotid bruit as individual factors, and the combination of age 55 or greater and hyperlipidemia. By multivariate logistic regression analysis, however, only carotid bruit was associated with carotid artery stenosis of 50% or greater (p< 0.001) (Table 1, 2,3) (Figure 1).

Discussion

The Asymptomatic Carotid Atherosclerosis Study (ACAS) demostrated the benefit of performing carotid endarterectomy in selected asymptomatic patients who have > 60% carotid stenosis.(4). However, the screening of all asymptomatic population for carotid stenosis is an inefficient and ex-

pensive strategy. Ramsey and coworkers evaluated 102 asymptomatic volunteers older than 50 years of age with duplex scan and found that only 2% of population needed surgical intervention (8). Likewise, Colgan and coworkers performed duplex scanning in 348 asymptomatic volunteer and they identified only 4% of patients having a stenosis of internal carotid artery greater than 50% (9). These previous studies have shown that prevalence of severe carotid stenosis in asymptomatic patients selected by chance is quite low.

The carotid stenosis is usually occurs in patients who have identifiable atherosclerotic risk factors (8, 9). Patients with peripheral vascular disease constituted one of the major groups that had a higher prevelance of atherosclerotic risk factors. While the patients who had neurologic syptoms, such as stroke or TIAs constitutes 2/3 of carotid endarterectomy operations, about 1/3 of patients are asymtomatic cases whose diagnoses are confirmed in the evaluation of their peripheral vascular diseases (10). Ahn and coworkers retrospectively reviewed 91 duplex scan in 78 patients with peripheral vascular disease and found carotid stenosis of 50% or greater in only 15 patients (19%) (11). Turnipseed and Barnes performed carotid duplex scan before surgery in 330 and 449 patients who underwent coronary artery surgery or peripheral vascular surgery, respectively (2,12). They found that, prevalence of carotid artery disease was significantly higher in patients who had peripheral vascular disease (52% and 28.8% in Turnipseed and Barnes studies, respectively) than in patients who had coronary artery disease (11.7% and %15.1 in Turnipseed and Barnes studies, respectively) (2,12) .Our present study also showed that, significant carotid artery stenosis was found in 26 (21.7%) of 120 patients with peripheral vascular disease.

Fowl and coworkers screened two patient groups to look for the incidence of asymptomatic carotid artery stenosis. The incidence of >50% carotid stenosis was found as 6.5% in the first group of patients having no evidence of peripheral vascular disease, and 12% in the second group of patients with significant peripheral vascular disease in this study (13). Our study and the former ones showed that there was a clear relationship between peripheral vascular disease and carotid artery disease. Likewise, an association has been recognized also between asymptomatic carotid stenosis and increased stroke risk, transient cerebral ischemic attack, and death, with the risk ranging from less than 5% to 18%> per year, depending on the degree of asymptomatic stenosis and the spesific outcome variables (14-16). However, both Turnipseed et al. (12) and Hertzer et al. found no clear benefit of a prophylactic carotid endarterectomy in patients with asymptomatic carotid artery stenosis undergoing cardiac or peripheral vascular reconstruction (16).

Our study focused on patients admitted for a vascular reconstruction to investigate the role of multipl atherosclerotic risk factors in predicting carotid artery stenosis. The present study showed that the preoperative variables that predicted the presence of 50% or greater stenosis of one or both carotid arteries by univariate analysis were age (>60 years), coronary artery disease, carotid bruit as individual factors, and the combination of age 55 or greater and hyperlipidemia. By multivariate logistic regression analysis, however, only carotid bruit was associated with carotid artery stenosis of 50%) or greater. Therefore, only carotid bruit detected on physical examination had a significant value to predict a severe carotid artery stenosis requiring a preoperative carotid screening. Similarly, Gentile et al. showed that the presence of carotid bruit was associated with carotid stenosis of 50% or greater in patients undergoing infrain^uinal bypass surgery (6). As contrary to this report, however, Turnipseed and coworkers found no direct relationship between cervical bruit and severity of carotid disease (12).

Marek and associates found that patients older than 65 years of age who had claudication, an ankle-brachial blood pressure index (ABI) less than 0.7, and a carotid bruit, had a 45% incidence of carotid disease (18). It was also indicated in this report that there was a significant correlation between decreasing ABI and severity of carotid stenosis (18). Likewise, Gentile et al. found a similar inverse relationship between the value of ABI and degree of carotid stenosis, but the association was weak (6). In our present study, however, there was not a clear association between ABI measurements and carotid artery stenosis.

Results of our prospective study showed that 25% of patients with peripheral vascular disease had some degree of carotid artery disease, that 21.7%) had 50% or greater, significant carotid artery stenosis, and that only 14.2% of patients, however, had critical stenosis of 75% or geater. It could be considered that screening for asymptomatic carotid artery stenosis is indicated in patients with only carotid artery bruit. In the light of the conclusions of other, former studies, however, screening could also be indicated in elderly patients with peripheral vascular disease. Carotid bruit and older age are most predictive and warning risk factors indicating carotid artery stenosis. Routine screening for carotid artery stenosis could not be recommended in all peripheral vascular patients but ones with carotid bruit or older age.

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