International Journal of Impotence Research (2007) 19, 577–583
© 2007 Nature Publishing Group All rights reserved
0955-9930/07 $30.00
www.nature.com/ijir

ORIGINAL ARTICLE

The combined use of brachial artery flow-mediated dilatation and carotid artery intima-media thickness measurements may be a method to determine vasculogenic erectile dysfunction

G Ucar[1], M Secil[1], O Demir[2], T Demir[3], A Comlekci[3], S Uysal[4] and AA Esen[2]

[1]*Faculty of Medicine, Department of Radiology, Dokuz Eylul University, Inciralti, Izmir, Turkey;* [2]*Faculty of Medicine, Department of Urology, Dokuz Eylul University, Inciralti, Izmir, Turkey;* [3]*Faculty of Medicine, Department of Endocrinology, Dokuz Eylul University, Inciralti, Izmir, Turkey and* [4]*Faculty of Medicine, Department of Biochemistry, Dokuz Eylul University, Inciralti, Izmir, Turkey*

The aim of this study was to investigate the relationship between penile color Doppler sonography (CDS) findings and sonographic endothelial parameters in patients with erectile dysfunction (ED), including intima-media thickness (IMT) of common carotid arteries (CCA) and flow-mediated dilatation (FMD) of brachial artery. Fifty-six ED patients were included in the study. Penile CDS, IMT of CCA and FMD of brachial artery were performed in all patients. According to penile CDS findings, 27 (48%) patients had non-vasculogenic and 29 (52%) patients had vasculogenic ED. Among 29 patients, 17 (30%) patients had cavernous veno-occlusive disease (CVOD) and 12 (22%) patients had arterial/combined insufficiency (AI). Median (interquartile range) FMD values of non-vasculogenic ED, CVOD and AI were 12.50 (6.54)%, 12.82 (7.41)% and 6.25 (7.17)%, respectively. FMD was found to be impaired significantly in AI group when compared to the other groups. FMD values of CVOD group were lower when compared to non-vasculogenic group, but the difference was not statistically significant. IMT values of vasculogenic ED patients were higher than non-vasculogenic ED patients ($P<0.05$). Although IMT values were higher in AI group when compared to CVOD, the difference was not statistically significant. The combined use of IMT and FMD established the diagnosis of vasculogenic ED with 100% sensitivity and 59.2% specificity. The positive predictive value was 72%, negative predictive value 100% and accuracy 80%. The combined use of brachial artery FMD and carotid arteries IMT measurements may be suggested as an alternative method to evaluate vasculogenic ED.
International Journal of Impotence Research (2007) **19,** 577–583; doi:10.1038/sj.ijir.3901572; published online 14 June 2007

Keywords: erectile dysfunction; endothelial dysfunction; imaging; flow-mediated dilatation; intima–media thickness; penile Doppler sonography

Introduction

Atherosclerotic disease of penile arteries has been known to be the major cause of erectile dysfunction (ED). The risk of ED increases with diabetes mellitus (DM), hypercholesterolemia, coronary heart disease and hypertension, which are also known to be associated with atherosclerosis and endothelial dysfunction.[1] It is presumed that ED and vascular diseases are linked at the level of endothelium.[2] Endothelial dysfunction results in decreased release of endothelial nitric oxide (NO), and impaired NO activity seems to play an important role in the pathogenesis of ED.[3]

Intima-media thickness (IMT) of common carotid arteries (CCA), as measured by B-mode ultrasound, is a noninvasive and reproducible morphological marker of generalized early atherosclerosis, which has been shown to be a predictor of severe ED in men.[4,5] Flow-mediated dilatation (FMD) of brachial artery is frequently used as a noninvasive ultrasonographic technique for assessment of endothelial function. Endothelial dysfunction is the inability of the endothelial cells to stimulate vasodilatation properly.[3] FMD induced by reactive hyperemia has been known to be an endothelium-dependent

Correspondence: Dr M Secil, Faculty of Medicine, Department of Radiology, Dokuz Eylul University, Inciralti, Izmir, 35340, Turkey.
E-mail: mustafa.secil@deu.edu.tr
Received 5 December 2006; revised 11 April 2007; accepted 1 May 2007; published online 14 June 2007

phenomenon that can be detected during reactive hyperemia by sonography in superficial arteries.[6] By using FMD, it has been shown that endothelial function was impaired in ED patients with no apparent cardiovascular disease and DM.[7,8] Since its introduction in 1985, penile Doppler sonography has been used as a radiological test to assess the vascular status of patients with ED.[9]

The aim of this study was to investigate the relation between penile Doppler sonography findings and sonographic endothelial function parameters, including IMT of CCA and FMD of brachial artery.

Materials and methods

Patients

Between April 2005 and June 2005, 60 consecutive patients who presented with the complaints of ED were included in this prospective study. Written informed consent form was obtained from all participants. The study protocol was approved by the Local Ethical Committee of our Institute.

The diagnosis of ED was determined using the full version International Index of Erectile Function (IIEF) scoring.[10] According to the IIEF questionnaires, patients with scores $\leqslant 25$ were accepted to have ED. Each patient also completed a detailed questionnaire as a part of the initial visit to assess medical and sexual history. A detailed survey of basic demographic data of the patients was obtained. The measurements of systemic arterial pressure, body mass index (BMI) and waist circumference were performed. DM was particularly explored and diabetic participants were noted. For nondiabetic patients, based on the diagnostic criterion of the American Diabetes Association, 75 g oral glucose tolerance test (OGTT) was used to determine impaired glucose tolerance. Diabetic patients and patients who had impaired OGTT underwent an autonomic neuropathy test by an endocrinologist to exclude diabetic neuropathy.

Exclusion criteria of the study included pelvic surgery or trauma, liver and renal insufficiency, urogenital abnormalities, ongoing medication for ED at the time of presentation and positive autonomic neuropathy test.

Laboratory tests

In the morning, after a 12 h overnight fasting, 10 ml venous blood was sampled for serum concentrations of lipid panel, liver and kidney function tests, and glucose. Additional 2 ml of fasting blood sample was drawn into serum ethylenediaminetetraacetic acid (EDTA)-containing tube and stored at $+4^{\circ}$C for ADMA (asymmetric dimethylarginine) analysis by enzyme-linked immunosorbent assay (ELISA) method. For OGTT, 75 g oral glucose load was administered to all subjects who had no history of DM, and repeat venous sampling was performed 2 h later for measurement of serum glucose.

Sonographic examinations

Sonographic examinations were performed in a semi-darkened, isolated and temperature-controlled room (20–25°C). Images were obtained by high-resolution Doppler sonography machine (HDI-5000; ATL, Bothell, WA, USA) with a 5–2 MHz broadband linear-array transducer. All of the sonographic examinations were performed by the same examiner (GU).

IMT of carotid arteries. Longitudinal plane sonographic images of the right and the left CCA of each patient, at approximately 1 cm proximal to the carotid bulb, were obtained and archived in the picture archiving and communication system (PACS) system. Care was taken to keep the frequency level and other imaging parameters (general 2D optimization, persistence, and so on) the same in each patient. Archived images were retrospectively analyzed in a blinded fashion using computer software program (Q-LAB, ATL-Philips, Bothell, WA, USA) in which IMT measurements were semi-automatically made.[11] The value of <0.70 mm was accepted as normal and that of $\geqslant 0.70$, as abnormal, based on the results of a previous cohort study.[12]

A normal age-matched group was also constituted with 12 subjects having IMT values obtained in the same laboratory.

FMD of brachial artery. Each subject was studied for FMD in the morning hours (0800–0900 hours) after being abstaining from alcohol, caffeine, tobacco, vasoactive agents and food for 12 h before the examination. Subjects were in the supine position with the arm outstretched. The brachial artery was imaged over a longitudinal section approximately 5 cm proximal to the brachial artery curve in the antecubital fossa. After baseline measurements, a blood pressure cuff was placed around the arm above the scanned part of the artery and was inflated to 250 mm Hg for 5 min. The blood pressure cuff was then deflated, resulting in a reactive hyperemia, to cause an increase in shear stress and dilatation of the brachial artery. After cuff deflation, brachial artery diameters at 30, 60 and 90 s were measured and sonographic images were recorded. After 10 min of rest, a single dose of sublingual isordile dinitrate of 5 mg was administered, and brachial artery diameter was measured after 3 min in order to evaluate endothelium-independent dilatation. Among 30, 60 and 90 s measurements, the largest value of the brachial artery diameter was accepted as the reference value for dilatation and FMD was

expressed as the percentage of change in brachial artery diameter from baseline value. Likewise, nitrate-mediated endothelium-independent dilatation (NMD) was expressed as the percentage change in brachial artery diameter 3 min after sublingual nitrate administration, relative to baseline values. It is accepted that the value of $\geqslant 10\%$ dilatation was normal and that of $<10\%$ dilatation was abnormal, based on the results of a previous studies.[12,13]

A normal age-matched group was also constituted with 12 subjects having FMD values obtained in the same laboratory.

Penile Doppler sonography. Penile Doppler sonography was performed in all participants after 50 mg papaverine hydrochloride (the only commercially available intracavernous vasoactive agent in our country) injection into the corpus cavernosum, and cavernous artery waveforms were recorded at 5, 10 and 20 min. The spectral waveforms performed included peak-systolic velocity (PSV), end-diastolic velocity (EDV) and resistance index (RI = PSV−EDV/PSV). Values of PSV higher than 35 cm/s and EDV lower than 5 cm/s were considered as normal responses. The diagnosis criteria for abnormal response included arterial insufficiency for PSV < 35 cm/s; cavernous venous occlusive disease (CVOD) for PSV $\geqslant$ 35 cm/s, EDV $\geqslant$ 5 cm/s and RI < 0.9; and combined insufficiency for PSV < 35 cm/s, EDV $\geqslant$ 5 cm/s and RI < 0.9.

The patients were grouped according to penile Doppler findings as non-vasculogenic and vasculogenic ED. Vasculogenic ED group was further subclassified into two groups as (1) CVOD and (2) arterial or combined insufficiency (AI).

Data analysis and statistics

The IMT and FMD measurements of the archived images were made by two investigators (MS, GU), and the mean of the obtained values were taken into consideration. Interobserver correlation (r) of the IMT and FMD measurements was 0.97 and 0.94, respectively. As the data were not normally distributed, the cumulative results of the study groups were shown as median ± interquartile range; also, nonparametric tests were used for statistical analysis. Statistical analysis was performed by SPSS 11.0 (SPSS, Chicago, IL, USA) using chi-square test, Pearson correlation analysis, Mann–Whitney U-test and multivariate analysis as appropriate.

Results

Four of 60 patients lost follow-up, and the study was completed with 56 patients. Out of 56 patients, 10 had a history of DM and were on medication. The remaining 46 patients underwent OGTT and 2 patients were detected to have impaired glucose tolerance. Autonomic neuropathy test was performed in this group of 12 patients, and none of the patients had a positive result suggestive of diabetic neuropathy.

According to penile Doppler sonography findings, 27/56 (48%) patients had non-vasculogenic and 29/56 (52%) patients had vasculogenic ED. In the vasculogenic group, 17/56 (30%) patients had CVOD and 12/56 (22%) patients had AI.

Multivariate analysis of combined data of the demographic, clinical characteristics and sonographic parameters of the study population are summarized in Table 1. The statistically significant rates of sonographic parameters of IMT and FMD between two groups was found to be lower than 0.01. The other statistically significant parameters between groups included the age, waist circumference and IIEF scores.

In the vasculogenic ED group (CVOD + AI patients), IMT values of both right and left CCA were significantly higher than the non-vasculogenic and the control groups (Table 2). Although IMT values were higher in the AI group than the CVOD group, the difference was not statistically significant (Figure 1).

The FMD values of non-vasculogenic, CVOD and AI groups were found to be lower than the control group ($P<0.05$). AI group showed the lowest FMD values, and there was statistically significant difference between CVOD and AI patients ($P<0.05$) (Figure 2). Nitrate-mediated dilatation did not show statistically significant difference between the groups.

On Pearson correlation test, IMT and FMD showed weak negative correlation ($r=-0.315$, $P<0.05$). Table 3 shows the statistical values of IMT and FMD and the combined use of IMT and FMD for determination of vasculogenic ED when penile Doppler sonography findings are accepted as standard.

Discussion

ED is a common medical disorder that has a negative impact on the quality of life and psychological well-being of millions of men worldwide. The Massachusetts Male Aging study on 1290 men, aged 40–70 years, showed that 52% of men reported some degree of ED.[1] The major cause of vasculogenic ED is atherosclerosis, which may be caused by several factors as DM, hypertension, hyperlipidemia and smoking. There is growing evidence demonstrating that these conditions are associated with endothelial dysfunction. Impaired endothelial function and the consequent decreased capacity of the vascular smooth muscle to relaxation are regarded as the precursor of atherosclerosis and also subsequent impaired cavernosal relaxation.

Table 1 Demographic, clinical and sonographic parameters of the groups

	Non-vasculogenic ED (n = 27) median (interquartile range)	*Vasculogenic ED (n = 29)median (interquartile range)*	P
Age (years)	50.0 (11.0)	60.0 (13.5)	0.004*
Mean IIEF score	13.0 (9.0)	10.0 (13.0)	0.018*
Waist circumference (cm)	92.0 (12.0)	96.0 (13.5)	0.034*
BMI	25.60 (3.03)	26.25 (5.97)	0.190
Systolic BP (mm Hg)	130 (10)	130 (35)	0.985
Diastolic BP (mm Hg)	80 (10)	80 (10)	0.750
Total cholesterol (mg/dl)	163.0 (52.0)	163.0 (39.0)	0.592
HDL (mg/dl)	50.0 (12.0)	48.0 (19.0)	0.236
LDL (mg/dl)	88.0 (49.0)	85.0 (41.5)	0.747
ADMA (μM/l)	0.74 ($\pm$0.48)	0.53 ($\pm$0.53)	0.310
Triglycerides (mg/dl)	99.0 (53.0)	106.0 (87.5)	0.173
ALT (μ/l)	16.0 (7.0)	20.0 (14.5)	0.123
AST (μ/l)	18.0 (7.0)	21.0 (8.5)	0.065
BUN (mg/dl)	17.0 (5.0)	16.1 (5.2)	0.470
Cr (mg/dl)	1.05 (0.15)	1.08 (0.14)	0.992
R IMT (mm)	0.63 (0.26)	0.83 (0.19)	0.000*
L IMT (mm)	0.63 (0.23)	0.86 (0.20)	0.000*
FMD (%)	12.5 (6.54)	9.75 (7.67)	0.004*

Abbreviations: BMI, body mass index; FMD, flow-mediated dilatation; HDL, high-density lipoprotein; IMT, intima-media thickness; LDL, low-density lipoprotein.
P-values represent significance rates between two groups according to multivariate analysis.
*Significant at the level of 0.05.

Table 2 Sonographic parameters of subgroups

	Normal control	*Non-vasculogenic ed*	*CVOD*	*AI*
R CCA IMT (mm)	0.5800 (0.1875)	0.6300 (0.2600)	0.8100 (0.2300)[a]	0.8450 (0.1675)[a]
L CCA IMT (mm)	0.6300 (0.2100)	0.6300 (0.2300)	0.8400 (0.2150)[a]	0.8650 (0.1400)[a]
FMD (%)	15.9 (7.69)	12.50 (6.54)[b]	12.82 (7.41)[b]	6.25 (7.17)[c]
Nitroglycerine-induced dilatation (%)	16.47 (10.41)	14.63 (7.80)	12.82 (6.83)	10.92 (16.32)

Abbreviations: CVOD, cavernous veno-occlusive disease; ED, erectile dysfunction; FMD, flow-mediated dilatation; IMT, intima-media thickness.
The values presented are median (interquartile range).
[a]Statistically significant when compared to normal control and non-vasculogenic ED group.
[b]Statistically significant when compared to normal control group.
[c]Statistically significant when compared to other groups.

Carotid IMT is associated with atherosclerotic disease.[14,15] It has also been shown that IMT of CCA is a predictor of severe ED in men without clinical atherosclerosis.[4] Measuring IMT in patients has several advantages, the most important being its noninvasive and non-embarrassing nature and the fact that it has been validated.[16] Another advantage of measuring IMT is the ability to detect early changes that occur in the subclinical phase of atherosclerosis.[5] However, there are no published scales of IMT values for a normal population. In a cohort study, Yan *et al.*[12] found that the average mean values of IMT in 1578 middle-aged healthy men (mean age 49.37 $\pm$ 9.92) was 0.72 $\pm$ 0.18, which was similar to previous published data in similar populations. On the basis of these cohort data, we accepted the cutoff pathological value of IMT as 0.70 mm. The measurement of IMT can be performed in all high-resolution sonography machines. In this study, we preferred to use a semi-automated computer program for IMT measurements. This might seem to result in an increase of the cost and time for the examinations; however, these computer programs are validated software and have been shown to provide objective and reliable data when compared to manual measurements.[11]

Inability of the endothelial cells to stimulate vasodilatation properly is referred to as endothelial dysfunction. It is correlated with subclinical measures of cardiovascular disease and prospectively associated with an increased risk for ED events. Impaired NO formation is considered a key pathophysiological mechanism in both endothelial dysfunction and ED.[13] FMD induced by reactive hyperemia has been known to be an endothelium-dependent phenomenon that can be detected during

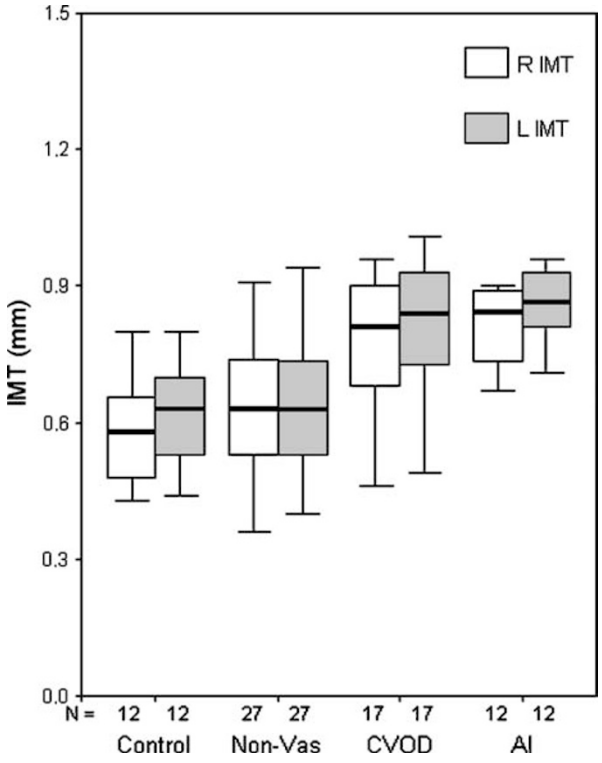


Figure 1 Right and left common carotid artery IMT (R IMT, L IMT, respectively) values of groups. AI, arterial or combined insufficiency group; control, the control group; CVOD, cavernous veno-occlusive disease group; non-vas, non-vasculogenic ED group.

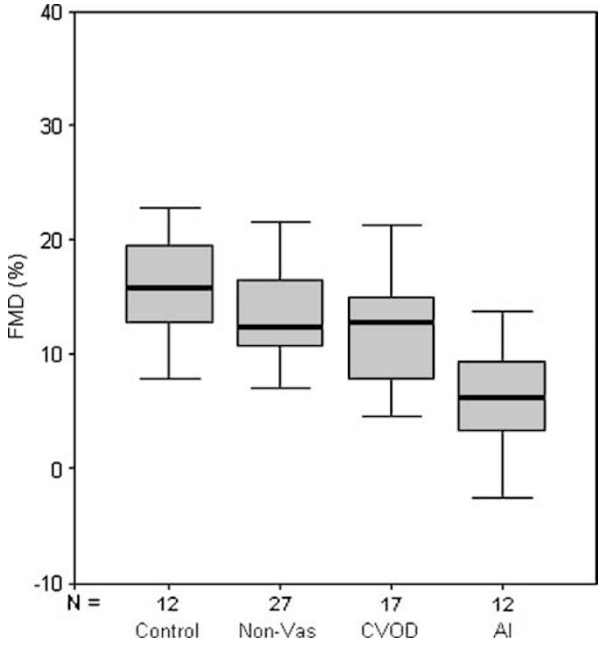


Figure 2 FMD values of brachial artery. AI, arterial or combined insufficiency group; control, the control group; CVOD, cavernous veno-occlusive disease group; non-vas, non-vasculogenic ED group.

Table 3 Statistical analyses of the tests when penile Doppler sonography is accepted as standard

	Sensitivity (%)	*Specificity (%)*	*Positive predictive value (%)*	*Negative predictive value (%)*	*Accuracy (%)*
IMT	89.6	62.9	72.2	85	76
FMD	58.6	92.5	89.4	67.5	75
IMT + FMD	100	59.2	72	100	80

Abbreviations: FMD, flow-mediated dilatation; IMT, intima-media thickness.

reactive hyperemia by sonography in superficial arteries.[6] This method is widely accepted as a well tolerated, reproducible and noninvasive technique for evaluation of endothelial function. FMD is approximately 10% which is the generally accepted normal lower range for this test.[13] In a cohort study, Yan *et al.*[12] found that average mean values of FMD in 1578 middle-aged healthy men (mean age 49.37 ± 9.92) was $8.59 \pm 4.05\%$. In our study, we accepted the values of $<10\%$ dilatation as abnormal.

This study is the first investigation that defines the relationship between penile Doppler sonography and combined use of IMT (as the morphologic parameter of endothelium) and FMD (as the physiological parameter of endothelium) in ED patients. The data of the present study showed that both IMT and FMD were abnormal in the vasculogenic ED group and that FMD was significantly decreased in AI patients when compared to the other groups. Mazo *et al.*[17] have reported similar findings that FMD of brachial artery were significantly impaired in patients with AI, where there were no differences between groups of patients with other forms of ED and control group. A few studies also determined impaired FMD in patients with ED. NMD has also been reported to be impaired in some of these studies.[7,18,19] The values of NMD in our study tended to be lower in ED patients, but the statistical difference was not significant.

Most of the previous studies did not include the comparison of all three sonographic methods of IMT, FMD and penile Doppler sonography. The only study including IMT, FMD and penile Doppler US together has not considered the CVOD group and used penile Doppler sonography only to determine arterial insufficiency.[18] Our results show that the differentiation of vascular and nonvascular ED may be achieved by IMT measurements. In the vasculogenic group, the FMD results may be used for differentiation of CVOD and AI patients. The combined use of IMT and FMD can determine vasculogenic ED with 100% sensitivity and 100% negative predictive value; however, the specificity of 59.2% is relatively low. This means that the tests may be used to detect vasculogenic ED patients, but

one should be aware that the tests have relatively low selectivity to disclose the disease in the non-vasculogenic ED patients.

Penile color Doppler sonography (CDS) with intracavernous vasoactive agent injection has been generally accepted procedure for a long time for the diagnostic evaluation of patients with ED. However, it has invasive nature and complication risks such as ecchymosis, penile hematoma and priapism, and the method is embarrassing for most of the patients. Also, invasiveness of intracavernous injection may elicit significant patient anxiety, and the resultant sympathetic stimulation may inhibit erectile response, leading to a false-positive diagnosis. Furthermore, the use of penile CDS routinely is questionable because, to date, there is no relationship with treatment options. Since the introduction of effective oral erectogenic treatments, oral therapy has become the standard first choice for most patients with ED without determining the underlying cause.[5]

According to our results, it may be proposed that the finding of abnormal carotid IMT could prompt a physician to specifically ask about ED in general practice settings, and more subclinical ED patients could be detected. On the other hand, in patients with the complaint of ED, the discrimination of types (vasculogenic/non-vasculogenic) and subtypes (non-vasculogenic/CVOD/AI) of ED may be possible by simple and non-invasive sonographic examinations, which may alter the treatment options. In an ED, a patient with normal IMT seems to have lower probability of vasculogenic origin, and medical treatment could be the choice of treatment. In patients with abnormal IMT, FMD examination should be performed. Impaired FMD seems to select patients with arterial insufficiency among the vasculogenic ED patients. Further investigation by angiographic examination, endovascular treatment of the arterial cause or surgical treatment with penile prosthesis may be considered in these patients.

This study has some limitations. First, prostaglandin E1, which is not available in our country, might have been preferred as an intracavernous vasoactive agent instead of papaverine. Second, a total of 20 (40%) patients were using drugs as statins and angiotensin-converting enzyme inhibitors, which may interfere with FMD results. Although medications were stopped 12 h before examining FMD, it would be unethical to stop medications for a long time to prevent the effect of drugs on FMD. Third, the measurement of brachial artery FMD has some technique and patient-related limitations, which were tried to be minimized during the evaluations. The cutoff value for abnormal FMD rate, which may seem to be artificial, may be accepted as a limitation of this study and also similar kinds of studies. In the literature, a clear cutoff value of FMD has not been described as yet. On the basis of a review article and on a large cohort study in this area,[12,13,20] we accepted $<10\%$ of FMD as abnormal and used this level to determine the sensitivity, specificity and accuracy rates of the tests which do not have gold standards. And last, the number of the study population was limited, particularly in subgroups, to make parametric statistical analyses and further conclusions. It should be stated that the results of this study are preliminary, and further investigations are needed in larger populations for validation of these results.

Conclusion

The combined use of brachial artery FMD and carotid arteries IMT measurements may be suggested as an alternative method to evaluate vasculogenic ED.

Acknowledgments

This study was supported by Dokuz Eylul University Research Fund Study no. 04.KB.SAĞ.070.

References

1 Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. *J Urol* 1994; **151**: 54–61.
2 Dayan L, Greunwald I, Vardi Y, Jacob G. A new clinical method for the assessment of penile endothelial function using the flow mediated dilation with plethysmography technique. *J Urol* 2005; **173**: 1268–1272.
3 Sullivan ME, Thompson CS, Dashwood MR, Khan MA, Jeremy JY, Morgan RJ *et al.* Nitric oxide and penile erection: is erectile dysfunction another manifestation of vascular disease? *Cardiovasc Res* 1999; **43**: 658–665.
4 Bocchio M, Scarpelli P, Necozione S, Pelliccione F, Mhialca R, Spartera C *et al.* Intima-media thickening of common carotid arteries is a risk factor for severe erectile dysfunction in men with vascular risk factors but no clinical evidence of atherosclerosis. *J Urol* 2005; **173**: 526–529.
5 Speel TG, van Langen H, Wijkstra H, Meuleman EJ. Penile duplex pharmaco-ultrasonography revisited: revalidation of the parameters of the cavernous arterial response. *J Urol* 2003; **169**: 216–220.
6 Hashimoto M, Eto M, Akishita M, Kozaki K, Ako J, Iijima K *et al.* Correlation between flow-mediated vasodilatation of the brachial artery and intima-media thickness in the carotid artery in men. *Arterioscler Thromb Vasc Biol* 1999; **19**: 2795–2800.
7 Kaya C, Uslu Z, Karaman I. Is endothelial function impaired in erectile dysfunction patients? *Int J Impot Res* 2006; **18**: 55–60.
8 Yavuzgil O, Altay B, Zoghi M, Gurgun C, Kayikcioglu M, Kultursay H. Endothelial function in patients with vasculogenic erectile dysfunction. *Int J Cardiol* 2005; **103**: 19–26.
9 Lue TF, Hricak H, Marich KW, Tanagho EA. Vasculogenic impotence evaluated by high-resolution ultrasonography and pulsed Doppler spectrum analysis. *Radiology* 1985; **155**: 777–781.

10 Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The International Index of Erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology* 1997; **49**: 822–830.
11 Secil M, Altay C, Gulcu A, Cece H, Goktay AY, Dicle O. Automated measurement of intima-media thickness of carotid arteries in ultrasonography by computer software. *Diagn Interv Radiol* 2005; **11**: 105–108.
12 Yan RT, Anderson TJ, Charbonneau F, Title L, Verma S, Lonn E. Relationship between carotid artery intima-media thickness and brachial artery flow-mediated dilation in middle-aged healthy men. *J Am Coll Cardiol* 2005; **45**: 1980–1986.
13 Vogel RA. Measurement of endothelial function by brachial artery flow-mediated vasodilation. *Am J Cardiol* 2001; **88**: 31E–34E.
14 O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson Jr SK. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. *N Engl J Med* 1999; **340**: 14–22.
15 Chambless LE, Folsom AR, Davis V, Sharrett R, Heiss G, Sorlie P. Risk factors for progression of common carotid atherosclerosis: the Atherosclerosis Risk in Communities Study, 1987–1998. *Am J Epidemiol* 2002; **155**: 38–47.
16 Smilde TJ, Wollersheim H, Van Langen H, Stalenhoef AF. Reproducibility of ultrasonographic measurements of different carotid and femoral artery segments in healthy subjects and in patients with increased intima-media thickness. *Clin Sci (London)* 1997; **93**: 317–324.
17 Mazo E, Gamidov S, Anranovich S, Iremashvili V. Testing endothelial function of brachial and cavernous arteries in patients with erectile dysfunction. *J Sex Med* 2006; **3**: 323–330.
18 Kaiser DR, Billups K, Mason C, Wetterling R, Lundberg JL, Bank AJ. Impaired brachial artery endothelium-dependent and -independent vasodilation in men with erectile dysfunction and no other clinical cardiovascular disease. *J Am Coll Cardiol* 2004; **43**: 179–184.
19 Alkhayal S, Lehmann V, Thomas P. A simple noninvasive test to detect vascular disease in patients with erectile dysfunction: a novel method. *J Sex Med* 2006; **3**: 331–336.
20 Andersson KE. Erectile physiological and pathophysiological pathways involved in erectile dysfunction. *J Urol* 2003; **170**: S6–S13.