

Predictive value of cavernosal peak systolic velocity in the flaccid penis

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ABSTRACT

Purpose: The routine use of intracavernosal injection before Doppler investigation may cause time loss, side effects due to vasoactive agents used and incorrect evaluation in the diagnosis of arterial insufficiency because of psychological inhibition and anxiety. Doppler investigation without intracavernosal injection avoids these pronounced disadvantages. In our study we tried to evaluate whether PSV values prior to intracavernosal injection are predictive in the diagnosis of arterial insufficiency in diabetic and non-diabetic cases.

Material and Methods: 120 male diabetic (type-2) and non-diabetic patients affected by erectile dysfunction (ED) were enrolled in this study. The Doppler parameters - PSV, end diastolic velocity (EDV) of both cavernosal arteries - were recorded before intracavernosal injection (ICI) (60mg-2ml- papaverine hydrochloride (HCl)) and 5, 10 and 30 minutes after ICI into corpus cavernosum. Based on our results we chose 2 cut-off values for the pre-ICI PSV- 10cm/sec and 15cm/sec. A PSV value less than 25 cm/sec after ICI was used as the diagnostic criteria for arterial insufficiency. We calculated the sensitivity, specificity, positive and negative predictive value of pre-ICI PSV in predicting arteriogenic impotence as diagnosed by post-ICI Doppler sonography. Only type 2 DM patients were included in our study.

Results: Statistically significant differences were found in the PSV values before and after ICI, ICI response and EDV values after ICI in both cavernous arteries when diabetic and nondiabetic groups compared

Conclusions: Flow in the cavernosal arteries in the flaccid state could determine nondiabetic patients with vasculogenic impotence with a high accuracy rate.

Key words: penile, Doppler, flaccid, intracavernosal injection

INTRODUCTION

Erectile dysfunction (ED) is a common world-wide problem in men with diabetes mellitus (DM). The overall incidence of ED in the general population (40-70 years) is nearly 50%. But the prevalence is significantly higher in men with diabetes, up to 80%. Especially the non-insulin-dependent DM (type-2) accounts for 90% of diagnosed diabetic patients. Although the aetiologies of diabetic impotence are variable- psychogenic, hormonal, neurologic and vascular, the vascular aetiology accounts for nearly 90% of the whole reasons [1-3].

Color Doppler Ultrasound is the preferred method for the functional evaluation of the penile arterial system [1,4,5]. Tumescence is commonly simulated by intracorporeal

(intracavernosal) vasoactive agent injection. When administered into the cavernosal tissue, substances like papaverine HCl or prostaglandin E1 (PGE1) increase the arterial inflow in penile arteries, induce smooth muscle relaxation and subsequently cause passive venous outflow obstruction by compression of penile emissary veins [6]. But the Doppler investigation before and after intracavernosal vasoactive agent injection is a-time-requiring technique and also have some possible side effects due to vasoactive agents used. Doppler investigation without intracavernosal injection (ICI) avoids these pronounced disadvantages. In the literature, some issues have reported that peak systolic velocity (PSV) values measured from flaccid penis might be predictive in the determination of arterial insufficiency [7,8].

In this prospective study we tried to evaluate whether PSV values prior to ICI are predictive in the diagnosis of arterial insufficiency in diabetic (type 2) and non-diabetic cases.

MATERIALS AND METHODS

132 male diabetic (type-2) and non-diabetic patients affected by erectile dysfunction (ED) were enrolled in this study. 12 patients (2 with Peyronie's disease, 5 with type-1 DM, 1 chronic renal failure patient on dialysis, 1 renal transplant patient, 2 by-pass patients, 1 patient with toxic hepatitis) were excluded from the study. Of the 120 patients 40 had diabetes and 80 did not. Patients were assessed for ED using the International Index of Erectile Function (IIEF-5). All the patients were interviewed for their detailed medical history including about diabetes and smoking. All patients underwent routine laboratory investigations.

After providing written informed consent, all patients were examined using a linear probe (Esaote Technos MPX and Hitachi EUB 8500) with 7,5 MHz frequency. The patients were placed on the examination table in supine position. The penis was evaluated as the dorsum being parallel to the anterior abdominal wall and its long axis parallel to the body axis. In this position the Doppler parameters -PSV, end diastolic velocity (EDV) of both cavernosal arteries- were recorded before ICI and 5, 10 and 30 minutes after ICI (60mg-2ml-papaverine hydrochloride) into corpus cavernosum near the penile root via 25 gauge short needle injector. Color Doppler recording of the cavernous arteries were performed along an arterial segment corresponding to a Doppler angle of 60° and a sample volume of 1mm in all patients.

Based on our results we chose 2 cut-off values for the pre-ICI PSV- 10cm/sec and 15cm/sec. A PSV value less than 25 cm/sec after ICI was used as the diagnostic criteria for arterial insufficiency [1,2,7,8]. We calculated the sensitivity, specificity, positive and negative predictive value of pre-ICI PSV in predicting arteriogenic impotence as diagnosed by post-ICI Doppler sonography. Patients with a suspicion of venous incompetence on Doppler sonography were excluded from this series (15 of 40 patients with diabetes and 45 of 80 patients without diabetes were excluded) [7]. The PSV after ICI was also classified as less than 25cm/sec (arterial insufficiency), 25-35cm/sec (indeterminate), greater than 35cm/sec (normal) (1). The EDV was classified as less than 5cm/sec and greater than 5cm/sec. EDV value > 5 cm/sec measured from any cavernosal artery was accepted venous insufficiency [1]. The response to ICI was classified as grade 0 (no response), grade 1 (tumescence), grade 2 (incomplete erection), grade 3 (rigid erection) [1,9]. Only type 2 DM patients were included in our study. Five patients with type-1 diabetes were excluded from the study because of their low number. Diabetic patients were divided into two groups according to the disease duration (less than 5 years, and 5 years or more). Smoking consumption

was recorded in terms of lifetime pack-years smoked. The institutional review board of our hospital approved the study and the written consent was taken from every patient. The data were analyzed using the Statistical Package for Social Sciences (SPSS), version 11.5, software program. Chi square test and t test were used for the statistical analysis. A *p* value of 0.05 or less was considered statistically significant.

RESULTS

A total of 120 male patients aged between 25 and 78 years (mean 48.9 years) were included into the study. The duration of erectile dysfunction of patients ranged between 6 months and 25 years (mean 2.53 years). Among these patients 40 (33.3%) were diabetic (mean age 51.1) and 80 (66.6%) were non-diabetic (mean age 47.8). Mean ages of the diabetic and non-diabetic patients were not statistically different (*p*=0.098).

In 22 patients (55%) diabetes duration were less than 5 years, in 18 patients (45%) it was equal or more than 5 years. 20 of the patients (50%) were smokers in diabetic group, and 30 of the patients were smokers (37,5%) in the non diabetic group. The duration of smoking among smokers ranged between 1 to 30 years. Patients had varying degrees of ED (mild in 55%, moderate in 30%, severe in 15%) in diabetic group and (mild in 62.5%, moderate in 30% and severe in 7.5%) in non-diabetic group.

Statistically significant differences were found in the PSV values before and after ICI, ICI response and EDV values after ICI in both cavernous arteries when diabetic and nondiabetic groups compared (*Tab. 1*).

No statistical significance were found in the PSV values before and after ICI and EDV after ICI in both cavernous arteries according to the diabetes duration. A statistically significant difference was found in the ICI response according to the diabetes duration (*Tab. 2*).

With the threshold of 10cm/sec (before ICI) and 25cm/sec (after ICI) the accuracy values of PSV in the diagnosis of arteriogenic impotence in diabetic patients from the right (r) and the left (l) cavernosal arteries were respectively: sensitivity 69(r)-77(l)%, specificity 33(r)-50(l)%, positive predictive value 65(r)-63(l)%, negative predictive value 37.5(r)-67(l)%. With the threshold of 15cm/sec (before ICI) and 25cm/sec (after ICI) the accuracy values of PSV were: sensitivity 83(r)-86(l)%, specificity 37(r)-45(l)%, positive predictive value 29(r)-37.5(l)%, negative predictive value 88(r)-89(l)% (*Tab. 3*).

With the threshold of 10cm/sec (before ICI) and 25cm/sec (after ICI) the accuracy values of PSV in the diagnosis of arteriogenic impotence in nondiabetic patients from the 'right' and the 'left' cavernosal arteries were respectively: sensitivity 96(r)-86(l)%, specificity 63(r)-83(l)%, positive predictive value 90(r)-96(l)%, negative predictive value 83(r)-56(l)%. With the threshold of 15cm/sec (before ICI) and 25cm/sec

Table 1. Relationship between diabetes and Doppler parameters.

Variable	Number of patients with Diabetes (+) (total n: 40)	Number of patients with Diabetes (-) (total n: 80)	P Value
PSV(cm/sn) before ICI			
Right cavernosal artery			
< 10	29 (%72.5)	18 (%22.5)	<0.05
≥ 10	11 (%27.5)	62 (%77.5)	
Left cavernosal artery			
< 10	27 (%67.5)	17 (%21.3)	<0.05
≥ 10	13 (%32.5)	63 (%78.8)	
ICI response			
No response	2 (%5)	0 (%0)	<0.05
Tumescence	8 (%20)	6 (%7.5)	
Incomplete erection	13 (%32.5)	26 (%32.5)	
Rigid erection	17 (%42.5)	48 (%60)	
PSV (cm/sn) after ICI			
Right cavernosal artery			
<25	13 (%32.5)	12 (%15)	<0.05
25-35	9 (%22.5)	13 (%16)	
>35	16 (% 40)	55 (%69)	
Left cavernosal artery			
<25	12 (%30)	11 (%14)	<0.05
25-35	10 (%25)	11 (%14)	
>35	18 (% 45)	58 (%72.5)	
EDV (cm/sn) after ICI			
Right cavernosal artery			
≤ 5	30 (%75)	45 (%56.3)	<0.05
> 5	10 (%25)	35 (%43.8)	
Left cavernosal artery			
≤ 5	27 (%67.5)	38 (%47.5)	<0.05
> 5	13 (%32.5)	42 (%52.5)	

*ICI: intracavernosal injection, PSV: peak systolic velocity, EDV: end-diastolic velocity

sec (after ICI) the accuracy values of PSV were: sensitivity 100(r)-100(l)%, specificity 35(r)-53(l)%, positive predictive value 62(r)-69(l)%, negative predictive value 38(r)-100(l)% (Tab.4).

In the flaccid state there was not a statistically significant difference between the mean PSV values in diabetic and nondiabetic patients ($p=0.134$).

No differences were found between smokers and non-smokers regarding the post-ICI PSV and EDV values in diabetic and nondiabetic patients ($p>0.05$).

Venous insufficiency was observed with the frequency of 37.5% in diabetic patients and 56.3% in nondiabetic patients. But no statistically significant difference was calculated between diabetic and nondiabetic patients ($p=0.053$).

DISCUSSION

The diagnosis of arterial insufficiency of the penis can be established most reliably by selective penile angiography [10-12]. However, this technique is an invasive procedure, time consuming, expensive and painful [7]. The introduction of duplex sonography and color Doppler imaging allowed non-invasive evaluation of the patients with suspected vasculogenic impotence. It is generally accepted that below 35cm/ sec the likelihood and severity of arterial disease increase, with a PSV less than 25cm/sec indicating a high probability of severe arterial disease [7, 13]. However penile Doppler examination is also time consuming technique lasting up to 30 minutes for better results [14]. There is also several conflicting studies about the sensitivity and the specificity of the penile Doppler examination and the validity of the

Table 2. Relationship between diabetes duration and Doppler parameters.

Variable	Patients with diabetes duration < 5 years(total n: 22)	Patients with diabetes duration ≥ 5 years(total n: 18)	P Value*
PSV(cm/sn) before ICI			>0.05
Right cavernosal artery			
< 10	7 (%32)	4 (%22)	
≥ 10	15 (%68)	14 (%78)	
Left cavernosal artery			
< 10	16 (%73)	11(%61)	
≥ 10	6 (%27)	7 (%39)	
ICI response			<0.05
No response	1 (%4.5)	1 (%5.6)	
Tumescence	2 (%9)	6 (%33.3)	
Incomplete erection	11 (%50)	2 (%11.1)	
Rigid erection	8 (%36)	9 (%50)	
PSV (cm/sn) after ICI			>0.05
Right cavernosal artery			
<25	7 (%32)	6 (%33.3)	
25-35	4 (%18.2)	5 (%27.8)	
> 35	11 (%50)	7 (%39)	
Left cavernosal artery			
<25	6 (%27)	6 (%33.3)	
25-35	4 (%18.2)	6 (%33.3)	
> 35	12 (%54.5)	6 (%33.3)	
EDV (cm/sn) after ICI			>0.05
Right cavernosal artery			
≤ 5	15 (%68)	15 (%83.3)	
> 5	7 (%32)	3 (%16.7)	
Left cavernosal artery			
≤ 5	13 (%59)	14 (%78)	
> 5	9 (%41)	4 (%22)	

ICI: intracavernosal injection, PSV: peak systolic velocity, EDV: end-diastolic velocity

*Chi-square test; significance level at P < 0.05

Table 3. Comparison between Pre-ICI and Post-ICI Values using various thresholds in diabetic patients.

Pre-ICI threshold	Number of Patients by Post-ICI PSV(Total n: 25**)			
	Right Cavernosal Artery		Left Cavernosal Artery	
10cm/sn threshold	<25cm/sn	≥25cm/sn	<25cm/sn	≥25cm/sn
<10	3	6	6	6
≥10	5	11	3	10
15cm/sn threshold				
<15	7	12	8	10
≥15	1	5	1	6

ICI: Intracavernosal injection, PSV: Peak systolic velocity

*A post-ICI PSV ≥ 25cm/sn was accepted normal

** 15 of 40 diabetic patients were excluded due to venous incompetence

Table 4. Comparison between Pre-ICI and Post-ICI values using various thresholds in non-diabetic patients.

Pre-ICI threshold	Number of Patients by Post-ICI PSV(total n:35**)			
	Right Cavernosal Artery		Left Cavernosal Artery	
10cm/sn threshold	<25cm/sn	≥25cm/sn	<25cm/sn	≥25cm/sn
<10	5	3	5	1
≥10	1	26	4	25
15cm/sn threshold				
<15	6	11	9	8
≥15	0	18	0	18

ICI: Intracavernosal injection, PSV: Peak systolic velocity

*A post-ICI PSV ≥ 25cm/sn was accepted normal

** 45 of 80 nondiabetic patients were excluded due to venous incompetence

post-ICI Doppler. In large series studies in which patients underwent two Doppler examinations with ICI 2 weeks apart showed a poor correlation between the findings during the two examinations [5, 9, 15, 16].

Roy *et al.* [7] and Mancini *et al.* [8] proposed Doppler examination in flaccid penis in different studies. Roy supposed 10cm/sec, Mancini supposed 12.5 cm/sec for the pre-ICI PSV cut-off value of the cavernosal arteries in the flaccid penis in arterial insufficiency. But Pickard *et al.* [17] supposed that the PSV values taken in the flaccid state couldn't distinguish between patients with vasculogenic impotence and controls. In our study, the accuracy rates were the highest when the cut-off value assessed 10cm/sec for the lowest normal pre-ICI PSV in both diabetic and non-diabetic cases. But the total overall accuracy rates were very low in the diabetic group (51% in diabetic group, 85% in nondiabetic group). Our total accuracy rate in nondiabetic patient group is very similar to the previous studies of the Roy *et al.* [7] and Mancini *et al.* [8]. But in diabetic patients assessed cut-off values were failed in the prediction of the arterial insufficiency. This result is also meaningful when the statistically significant difference between two patient groups according to the PSV values pre-ICI, post-ICI and EDV values after ICI in both cavernosal arteries considered (*Tab.1*). How can we explain this difference between diabetic and nondiabetic patients? In our diabetic patient group mean diabetes duration was 5.86 years. The presence of diabetes even for the short term can affect the arterial system more than the venous system. However, higher incidence of cavernous arterial insufficiency was noted in patients with a longer duration of diabetes [3]. Chronic progressive impotence related directly to diabetes is the most frequent form. This form of impotence occur years after the diagnosis of the patient. This form is progressive, irreversible and is accepted as a natural result (neuropathic, vascular or both) of the diabetes [18]. Long term diabetes, poor metabolic control and atherosclerosis can result in atrophy of penile smooth muscle, loss of myofilaments, decreases in cell size, increases in collagen fibres and loss of gap junctions which ultimately lead to incomplete relaxation of the muscle and venous leakage [1]. Corporal dysfunction in diabetes has been

associated with structural alterations in sinusoidal architecture which could produce a loss of compliance and make it both difficult to fill and store blood in the penis for the adequate erection [2].

Impairments in the hemodynamics of erection have been demonstrated not only in diabetes but also with myocardial infarction, coronary artery disease necessitating bypass surgery, peripheral vascular disease and vascular risk factors such as hypertension and cigarette smoking [19]. Cigarette smoking incidence is relatively higher in our population. Several effects of cigarette smoking on male potency have been demonstrated in the literature. Inhibition of smooth muscle function, atherosclerotic changes, hypercoagulability, increased platelet aggregation, release of free fatty acids and catecholamines, direct toxic effect on the vascular endothelium have been also considered as possible mechanisms. But in our study no statistically significant difference was observed between diabetic and nondiabetic patients when cigarette smoking incidence considered [19, 20]. ED in men with diabetes has also been associated with increased age, poor glycemic control, smoking, increased alcohol intake, depression, use of specific type of medications and microvascular diabetic complications [6].

We also observed high frequency of venous insufficiency in our diabetic and nondiabetic patients which is consistent with the knowledge that ED aetiology is usually mixed (arterial and venous) rather than the arterial pathology alone [6, 20].

CONCLUSIONS

Our results show that nondiabetic patients with vasculogenic impotence could be determined with the flow in the cavernosal arteries in the flaccid state with 85% total accuracy. This technique may avoid excess invasive procedure and may reduce the duration of the investigation.

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