

Pharmacodynamic Changes in Penile Color-Doppler Ultrasound of Diabetic Patients

SAMEH M. SARSIK, M.Sc.*; TAREK A. AMIN, M.D.*; NAEIM M. ABD EL-NABY, M.D.* and MOHAMED M. HEFEDA, M.D.**

The Departments of Dermatology, Venereology and Andrology and Diagnostic Radiology**, Faculty of Medicine, Tanta University*

Abstract

Background: Erectile dysfunction in diabetic patients leads to changes of intima, media, and Lumina of arteries resulting in atherosclerosis.

Aims of Study: To determine the association between diabetes mellitus and penile Doppler ultrasonography changes in patients with erectile dysfunction. Also, the influence of duration, control of diabetes and diabetes complications on Doppler parameters.

Settings and Design: Prospective cohort study, Andrology Unit of Dermatology, Venereology and Andrology Department, Tanta University Hospital.

Material and Methods: Thirty diabetic patients with ED and 10 age matched healthy controls were enrolled. Patients underwent assessment with international index of erectile function score, cavernosal artery ultrasonography during flaccid state for measurement of internal diameter, intima media thickness and arterial wall mass index. Followed by ICI to measure peak systolic velocity, end diastolic velocity and resistive index.

Statistical Analysis Used: Mean, standard deviation and Chi-square test by SPSS V.16.

Results: Diabetic patients with ED showed statistically significant decrease in IIEF score and PSV, increase in IMT and AWMI compared to controls. Positive correlation between duration of diabetes, blood glucose level and IMT and AWMI, Negative correlation between duration of diabetes and IIEF, PSV and erectile response. Negative correlation between blood glucose level and IIEF, PSV. Negative correlation between IMT, AWMI with IIEF.

Conclusions: Diabetic patients with ED have a higher prevalence of atherosclerosis represented as increased IMT and AWMI compared with controls. Diabetes was an independent risk factor associated with atherosclerosis. Cavernosal artery IMT and AWMI interpreted clinically as negative correlation with erectile function domain of IIEF. These new parameters give good prediction for atherosclerosis and could replace more invasive ICI.

Correspondence to: Dr. Sameh M. Sarsik, The Department of Dermatology, Venereology and Andrology, Faculty of Medicine, Tanta University

Key Words: Erectile dysfunction – Intima media thickness – Arterial wall mass index.

Key Messages: Ultrasound changes of diabetic patients include; increased IMT, AWMI, decreased PSV. IMT, AWMI are new parameters could be done in flaccid state and give the same level of accuracy considering predicting data for cavernosal arteries pathological changes which affect erectile function and could replace ICI and avoid its side effect.

Introduction

ERECTILE Dysfunction (ED) is consistent inability to obtain and maintain an erection for satisfactory sexual intercourse [1,2].

The penis is a highly vascularized organ, and erections are primarily vascular events [3]. Sexual stimulation causes the release of neurotransmitters from the corpus cavernosa and a relaxing factor, Nitric Oxide (NO), from the endothelial cells of the penis. The neurotransmitters, together with NO, cause the corpus cavernosa to relax and allow blood to flow into the penis, causing the penis to expand and sustain an erection until the process is reversed [4]. Any disorder inducing Endothelial Dysfunction (END) will also interfere with vasodilatation, preventing the erection [5].

Diabetes is commonly associated with ED. ED develops in 25 to 75% of diabetic men [6-8]. Proposed mechanisms includes; impaired Nitric Oxide (NO) synthesis, increased endothelin B receptor binding sites, NO-dependent nitrergic nerve degeneration and impaired cyclic guanosine monophosphate (cGMP) [9].

Duplex is used to determine the integrity of the vascular mechanism. After an intracavernosal injection of a vasodilatory agent [10].

Endothelial dysfunction is intimately linked to atherogenesis [5]. Endothelial dysfunction due to an abnormality in the release and/or action of NO is characterized by vasoconstriction, coagulation, increased leucocyte adhesion and stimulation of Smooth Muscle (SM) cell growth, and is, therefore, central to atherogenesis. Atherogenesis is likely to present earlier with clinical symptoms in arteries of a smaller diameter, such as in the penis, than in larger sized arteries, such as in the coronary circulation [11].

Diabetes is associated with intimal, medial, and luminal changes within the artery leading to atherosclerosis. Atherosclerosis can affect the penile and pudendal arteries limiting blood flow to the corpus cavernosum. Among the men with significant peripheral arterial disease, 40% to 50% complain of some degree of ED [12].

Subjects and Methods

Subjects:

The present study was carried out on 30 diabetic male patients with ED and 10 healthy controls of matched age were collected from the Outpatient Clinic of Andrology Unit of Dermatology, Venereology and Andrology Tanta University Hospital from a period of January 2017 to January 2018.

Methods:

All patients and controls were subjected to detailed history taking, thorough clinical examination. During examination all patients and controls were subjected to assessment of erectile function using (IIEF) [13]. It is principal components analysis to identify five domains of male sexual function (which are; erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction). For erectile function evaluation, questions from 1 to 5 and 15 were used which represents the erectile function domain of the IIEF (Table 1).

Table (1): Interpretation of erectile function domain of IIEF score.

Score	Interpretation
0-6	Severe dysfunction
7-12	Moderate dysfunction
13-18	Mild to moderate dysfunction
19-24	Mild dysfunction
25-30	No dysfunction

Both patients and controls were subjected to laboratory investigations including; blood glucose levels (fasting and 2 hours post prandial, lipid profile, hormonal profile (testosterone, prolactin,

FSH, LH, T3, T4 and TSH), complete blood picture, hepatic and renal function tests.

Pharmaco-dynamic study:

First gray scale imaging of flaccid penile shaft in transverse and sagittal planes was done to measure the diameter of the left cavernosal artery, IMT and rule out any calcifications or fibrosis. Later pharmaco penile Duplex ultrasonography was done following ICI of Trimix; starting dose was 5 units (0.05ml) of Trimix ((2.5ml) of papaverine 30mg/ml, (0.25ml) of phentolamine 10mg/ml, (0.05ml) PGE1 of 10 μ /ml and 1.2ml of normal saline) that may increase to 10 units (0.1ml) to reach best erection using 30G needle in either of corpora cavernosa [14]. The erectile response is graded visually from E0 to E5 as designed by Broderick et al. [15]. Post ICI spectral wave forms were recorded once in 10 minutes up to 30 minutes. PSV, EDV, IR were recorded in all patients and controls.

Primary diagnostic criteria for arterial insufficiency include PSV of less than 25cm/sec and wave form dampening while for venous ED, most investigators used to diagnose venous leakage when arterial EDV is greater than 5cm/sec or RI less than 0.816.

Measurement of cavernosal artery intima media thickness, internal diameter and arterial wall mass index.

Left cavernosal artery IMT was measured as a marker of subclinical atherosclerosis and to assess structural changes in the vascular wall using a high-resolution B-mode ultrasound with 11.4MHz linear vascular probe (VF 15-3 transducer, ACSON X300 SIEMENS Ultrasound).

Patients and controls were examined in supine position. IMT of left cavernosal artery was measured in the proximal artery, choosing the straight portion that offered the best visualization during flaccid state of the penis.

The IMT was defined as a distance between the leading edge of the first echogenic line and the leading edge of the second echogenic line. The first line represent the luminal intimal interface and the second line is produced by the collagen containing upper layer of adventitia close to the medial adventitial interface [17]. Normally cavernosal artery IMT is less than 0.3mm, therefore; an increased cavernous IMT (≥ 0.3 mm) is an indicative of atherosclerotic plaque [18].

The following data were measured:

- 1- Internal Diameter (ID) at the end of diastole.
- 2- Intima Media Thickness (IMT) at the end of diastole.
- 3- Arterial Wall Mass Index (AWMI) was calculated by this equation:

$$\text{AWMI (g/cm)} = \pi (\text{ID}/2 + \text{IMT})^2 - \pi (\text{ID}/2)^2 \quad [17]$$

$$\text{Where } \pi = 22/7.$$

Results

Age in patient group ranged from 45-64 years (mean 57.43 ± 4.73 years). In the control group it ranged from 39-63 (mean 55.0 ± 6.07 years). Duration of diabetes ranged between 2-18 years (mean 6.93 ± 3.54 years). In addition, the duration of ED ranged from 1-11 years (mean 4.20 ± 2.80 years).

Regarding IIEF; in patient group it ranged from 3-22 (mean 12.50 ± 4.97), in the control group it ranged from 25-29 (mean 27.10 ± 1.52) with high significant difference ($p < 0.001$). Regarding the patients group 6.7% showed mild ED (n=2), 46.7% showed mild to moderate ED (n=14), 30% showed moderate ED (n=9), 16.7% showed severe ED (n=5), while none of the control group showed ED (n=10) ($p < 0.001$) (Table 2).

Table (2): Comparison between the two studied groups regarding IIEF-5.

	Patients (n=30)		Control (n=10)		Test of sig.	p
	No.	%	No.	%		
Interpretation of IIEF:						
No dysfunction	0	0.0	10	100.0	$\chi^2 = 34.708^*$	MC $p < 0.001^*$
Mild	2	6.7	0	0.0		
Mild to moderate	14	46.7	0	0.0		
Moderate	9	30.0	0	0.0		
Severe	5	16.7	0	0.0		
Min.-max.	3.0-22.0		25.0-29.0		$t =$	$< 0.001^*$
Mean \pm SD.	12.50 \pm 4.97		27.10 \pm 1.52		14.217*	
Median	13.0		27.50			

t : Student t-test.

p: p-value for comparing between the two groups.

*: Statistically significant at $p \leq 0.05$.

Fasting blood glucose in patients group ranged from (109-244) mg/dl (mean 160.1 ± 32.75 mg/dl), two hours post prandial blood glucose ranged from (203-399) mm/Hg (mean of 280.5 ± 6.8 mg/dl). In the control group fasting blood glucose ranged from (70-100) mg/dl with a mean of (86.70 ± 9.97) mg/dl, two hours post prandial blood glucose ranged from (143-176) mm/Hg with a mean of (162.1 ± 12.16) mg/dl with highly significant difference $p < 0.001$.

Regarding the erectile response after trimix injection; in patients group 10% (n=3) showed E1, 10% (n=3) showed E2, 66.7% (n=20) showed E3, 10% (n=3) showed E4, 3.3% (n=1) showed E5. In the control group 100% (n=10) showed E5, with high significant difference $p < 0.001$ (Table 3).

Table (3): Comparison between the two studied groups regarding erectile response.

Erectile response	Patients (n=30)		Control (n=10)		χ^2	MC p
	No.	%	No.	%		
E1	3	10.0	0	0.0	30.664*	$< 0.001^*$
E2	3	10.0	0	0.0		
E3	20	66.7	0	0.0		
E4	3	10.0	0	0.0		
E5	1	3.3	10	100.0		

χ^2 : Chi square test.

MC: Monte Carlo.

p : p-value for comparing between the two groups.

*: Statistically significant at $p \leq 0.05$.

Cavernosal artery ultrasonography results:

Regarding left cavernosal artery ID in flaccid state; in patients group it ranged from 0.2-0.5mm (mean 0.34 ± 0.08 mm) Fig. (1A-C) respectively, in the control group it ranged from 0.3- 0.5mm (mean 0.37 ± 0.08 mm) (Table 4).

Concerning cavernosal artery IMT; in patients group it ranged from 0.3-0.5mm (mean 0.35 ± 0.07 mm) Fig. (1A-C), in control group it ranged from 0.10-0.30mm (mean of 0.18 ± 0.06 mm) (Table 4).

Regarding the AWMI; in patients group it ranged from 0.006-0.085gm/cm with a mean of (0.013 ± 0.020) gm/cm, in the control group it ranged from 0.002-0.006gm/cm (mean of 0.003 ± 0.001 gm/cm) (Table 4).

Table (4): Comparison between the two studied groups regarding ID, IMT and AWMI.

Flaccid state	Patients (n=30)	Control (n=10)	Test of sig.
Left cavernosal artery internal diameter ID (mm):			
Min.-max.	0.20-0.50	0.30-0.50	$t = 0.359$
Mean \pm SD.	0.34 \pm 0.08	0.37 \pm 0.08	0.929
Median	0.30	0.35	
Intima media thickness IMT (mm):			
Min.-max.	0.30-0.50	0.10-0.30	U= $< 0.001^*$
Mean \pm SD.	0.35 \pm 0.07	0.18 \pm 0.06	8.50*
Median	0.30	0.20	
Arterial wall mass index AWMI (gm/cm):			
Min.-max.	0.006-0.085	0.002-0.006	U= $< 0.001^*$
Mean \pm SD.	0.013 \pm 0.020	0.003 \pm 0.001	4.50*
Median	0.007	0.003	

t : Student t-test.

U: Mann Whitney test.

p: p-value for comparing between the two groups.

*: Statistically significant at $p \leq 0.05$.



Fig. (1A): Cavernosal artery ID 0.4mm, IMT 0.3mm.

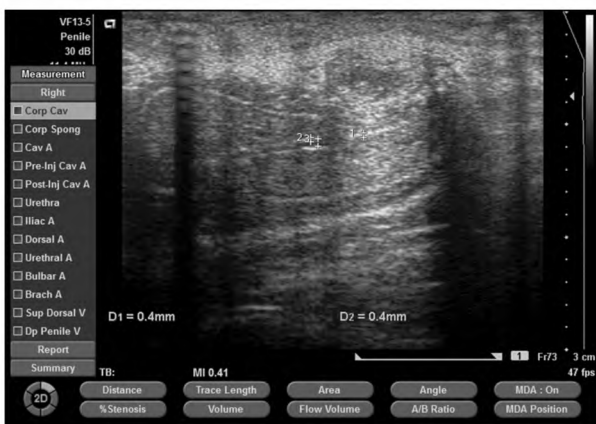


Fig. (1B): Cavernosal artery ID 0.4mm, IMT 0.4mm.

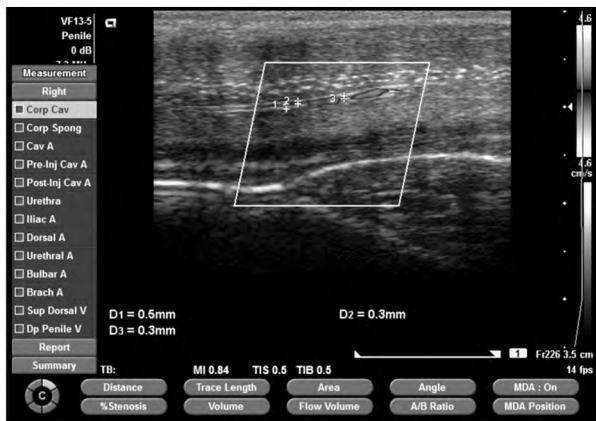


Fig. (1C): Cavernosal artery ID 0.5mm, IMT 0.3mm.

Regarding PSV; in the patients group, after 5 minutes of ICI it ranged from 8.20-32.80cm/sec (mean 20.97±7.08cm/sec), after 10 minutes ranged from 9.60-31.50cm/sec (mean of 22.29 ±6.62 cm/sec), after 30 minutes ranged from 9.30-31.63 cm/sec (mean of 23.83 ±5.69cm/sec). In control group, after 5 minutes of ICI PSV ranged from 28.80-42.90cm/sec (mean 37.77±4.33cm/sec), after 10 minutes it ranged from 27.10-47.0cm/sec (mean 39.68±6.46cm/sec), after 30 minutes it ranged from

31.20-45.40cm/sec (mean 40.25 ±4.24cm/sec). Comparison of the two studied groups showed high significant difference ($p<0.001$) (Table 5), Figs. (2-4A-C) respectively.

Table (5): Comparison between the two studied groups regarding PSV.

PSV (cm/sec)	Patients (n=30)	Control (n=10)	t	p
5 minutes:				
Min.-max.	8.20-32.80	28.80-42.90	8.922*	<0.001*
Mean ± SD.	20.97±7.08	37.77±4.33		
Median	20.90	39.45		
10 minutes:				
Min.-max.	9.60-32.60	27.10-47.0	7.230*	<0.001*
Mean ± SD.	22.29±6.62	39.68±6.46		
Median	23.65	41.20		
30 minutes:				
Min.-max.	9.30-31.50	31.20-45.40	8.355*	<0.001*
Mean ± SD.	23.83±5.69	40.25±4.24		
Median	24.90	41.15		
Average:				
Min.-max.	9.97-31.63	30.90-43.43	8.154*	<0.001*
Mean ± SD.	22.36±6.0	39.23±4.44		
Median	22.58	40.82		

t : Student t-test.

p : p-value for comparing between the two groups.

*: Statistically significant at $p\leq 0.05$.

Regarding EDV; in the patients group, after 5 minutes of ICI it ranged from 2.60-15.80cm/sec (mean 7.28±4.37cm/sec). After 10 minutes it ranged from 2.40-16.80cm/sec (mean 7.41 ±4.34cm/sec), after 30 minutes it ranged from 2.20-23.80cm/sec (mean 7.85±5.45) cm/sec). In control group, after 5 minutes of ICI EDV ranged from 2.40-4.90cm/sec (mean 3.67±0.87cm/sec), after 10 minutes it ranged from 0.0-4.90cm/sec (mean 3.05 ± 1.88cm/sec), after 30 minutes it ranged from 0.0-4.20cm/sec (mean 2.99± 1.60cm/sec). With high significant difference ($p<0.001$) (Table 6), Figs. (2-4A-C) respectively.

Concerning RI; in the patients group, after 5 minutes of ICI it ranged from 0.41-0.86 (mean 0.67±0.14), after 10 minutes it ranged from 0.39-0.88 mean 0.68±0.13), after 30 minutes of ICI it ranged from 0.15-0.89 (mean 0.68±0.18). In control group, after 5 minutes of ICI RI ranged from 0.83-0.92 (mean 0.88±0.03), after 10 minutes it ranged from 0.82-1.0 (mean 0.91 ±0.06), after 30 minutes it ranged from 0.87-1.0 (mean 0.92±0.05). With high significant difference between compared groups ($p<0.001$) (Table 7), Figs. (2-4A-C) respectively.

Table (6): Comparison between the two studied groups regarding EDV.

EDV (cm/sec)	Patients (n=30)	Control (n=10)	U	p
5 minutes:				
Min.-max.	2.60-15.80	2.40-4.90	81.50*	0.032*
Mean ± SD.	7.28±4.37	3.67±0.87		
Median	6.55	3.70		
10 minutes:				
Min.-max.	2.40-16.80	0.0-4.90	54.50*	0.003*
Mean ± SD.	7.41±4.34	3.05±1.88		
Median	6.90	3.90		
30 minutes:				
Min.-max.	2.20-23.80	0.0-4.20	58.50*	0.004*
Mean ± SD.	7.85±5.45	2.99±1.60		
Median	6.80	3.60		
Average:				
Min.-max.	2.60-17.43	1.63-4.32	43.0*	0.001*
Mean ± SD.	7.51±4.39	3.24±1.01		
Median	6.72	3.65		

U : Mann Whitney test.

p : p-value for comparing between the two groups.

* : Statistically significant at p≤0.05.

Table (7): Comparison between the two studied groups regarding RI.

RI	Patients (n=30)	Control (n=10)	t	p
5 minutes:				
Min.-max.	0.41-0.86	0.83-0.92	7.966*	<0.001*
Mean ± SD.	0.67±0.14	0.88±0.03		
Median	0.68	0.88		
10 minutes:				
Min.-max.	0.39-0.88	0.82-1.0	5.078*	<0.001*
Mean ± SD.	0.68±0.13	0.91±0.06		
Median	0.70	0.89		
30 minutes:				
Min.-max.	0.15-0.89	0.87-1.0	3.952*	<0.001*
Mean ± SD.	0.68±0.18	0.92±0.05		
Median	0.72	0.90		
Average:				
Min.-max.	0.36-0.85	0.86-0.94	8.505*	<0.001*
Mean ± SD.	0.68±0.14	0.90±0.03		
Median	0.70	0.89		

t : Student t-test.

p : p-value for comparing between the two groups.

* : Statistically significant at p≤0.05.

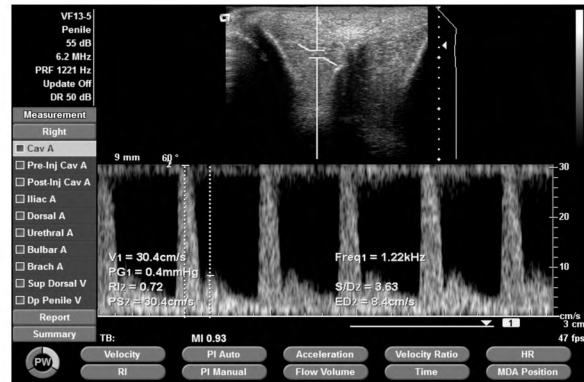


Fig. (2B): Real time US of venogenic ED PSV 30.4cm/sec, EDV 8.4cm/sec and RI 0.72.

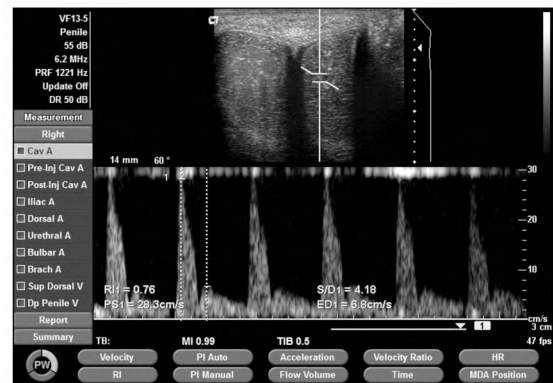


Fig. (2C): Real time US of venogenic ED PSV 28.3cm/sec, EDV 6.8cm/sec and RI 0.76.

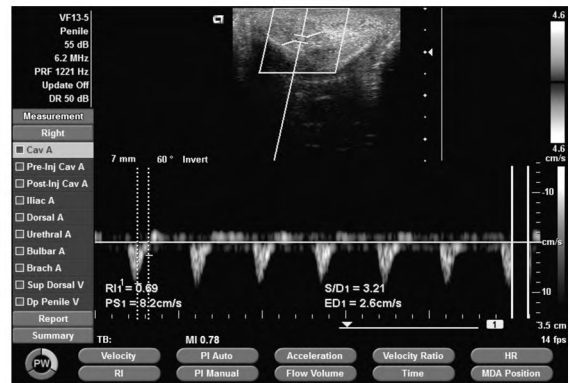


Fig. (3A): Real time US of arterial ED PSV 8.2cm/sec, EDV 2.6cm/sec and RI 0.69.

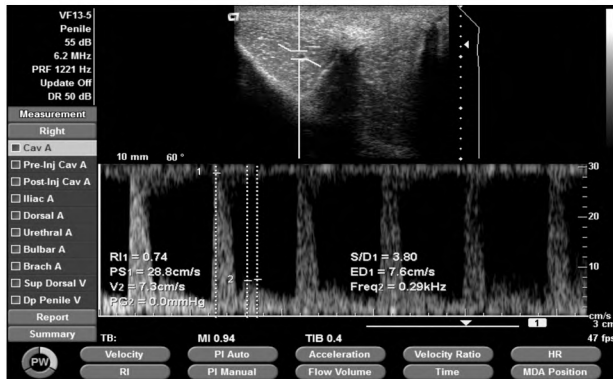


Fig. (2A): Real time US of venogenic ED PSV 28.8 cm/sec, EDV 7.3cm/sec and RI 0.74.

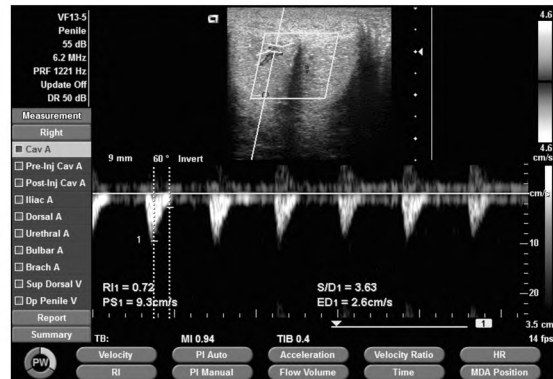


Fig. (3B): Real time US of arterial ED PSV 9.3cm/sec, EDV 2.6cm/sec and RI 0.72.

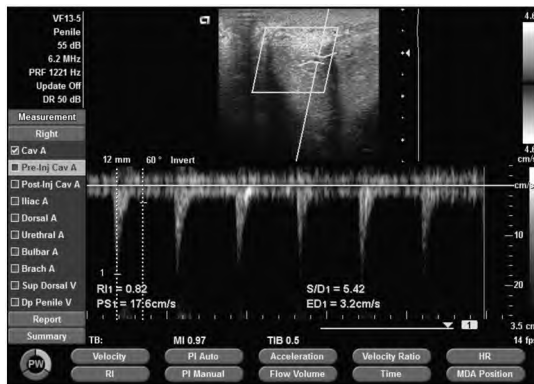


Fig. (3C): Real time US of arterial ED PSV 17.6cm/sec, EDV 3.2cm/sec and RI 0.82.

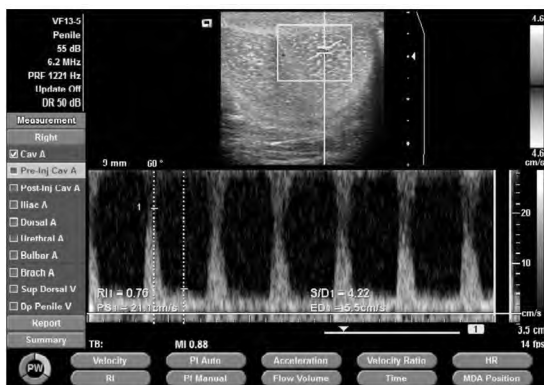


Fig. (4A): Real time US of mixed ED PSV 21.1cm/sec, EDV 15.5cm/sec and RI 0.76.

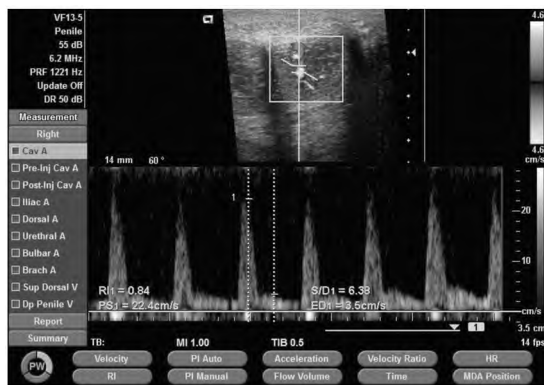


Fig. (4B): Real time US of mixed ED PSV 22.8cm/sec, EDV 8.5cm/sec and RI 0.78.

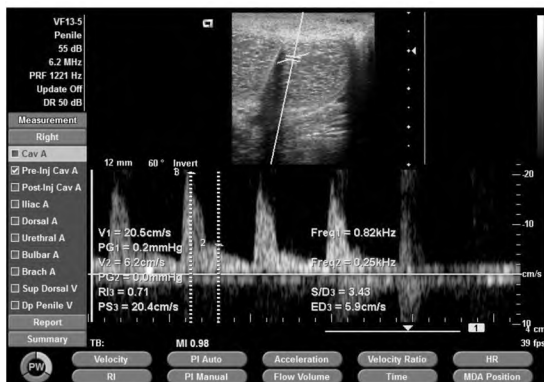


Fig. (4C): Real time US of mixed ED PSV 20.4cm/sec, EDV 5.9cm/sec and RI 0.7.

Distribution of ED of the studied cases; Venogenic ED represented 46.7% (n=14), arterial ED represented 30% (n=9), mixed ED represented 20% (n= 6) and psychogenic ED represented 3.3% (n=1). Regarding the results of IIEF score; severity of ED was as the following, mild cases represented 10% (n=3), moderate cases represented 73.3% (n=22), severe cases represented 16.7% (n=5).

In the current study, one patient had developed priapism, which was of low flow in nature and treated by Emergency Decompression at Urology Department.

Correlations:

1- Correlations between diabetes duration and different parameters in patients group was illustrated in (Table 8).

There was no significant correlation between duration of diabetes and average RI ($r_s = 0.186$).

There were significant positive correlations between duration of diabetes and IMT, AWMI ($r_s = 0.751$, $r_s = 0.538$) Figs. (5,6) respectively.

There were significant negative correlations between duration of diabetes and erectile response, cavernosal artery IO Fig. (7), average PSV, average EDV ($r_s = -0.699$, $r_s = -0.476$, $r_s = -0.830$, $r_s = -0.542$).

Table (8): Correlations between diabetes duration and different parameters in patients group.

	Diabetes duration (years)	
	r_s	p
Erectile response	-0.699*	<0.001*
Cavernosal artery diameter (mm)	-0.476*	0.008*
IMT (mm)	0.751*	<0.001*
Arterial wall mass index (gm/cm)	0.538*	0.002*
Average PSV (cm/sec)	-0.830*	<0.001*
Average EDV (cm/sec)	-0.542*	0.002*
Average RI	0.186	0.325

r : Pearson coefficient.

*: Statistically significant at $p \leq 0.05$.

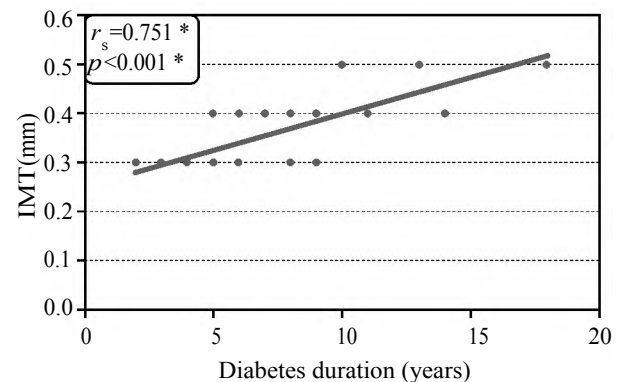


Fig. (5): Correlation between diabetes duration and IMT (mm) in patients group.

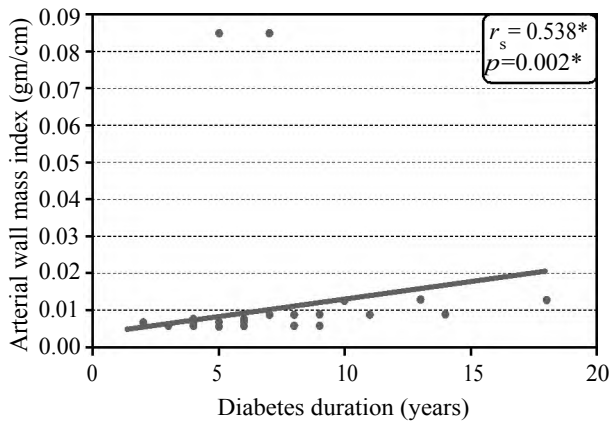


Fig. (6): Correlation between diabetes duration and arterial wall mass index (gm/cm) in patients group.

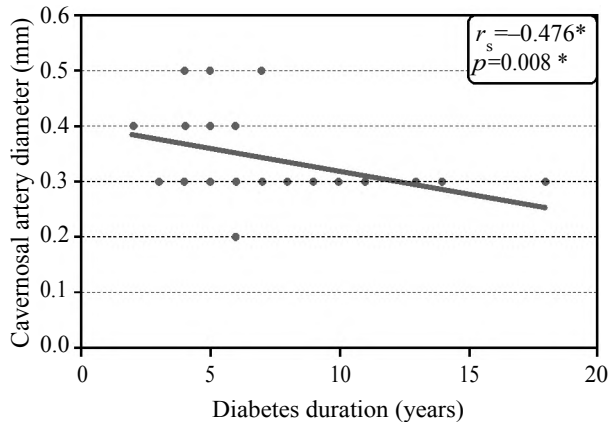


Fig. (7): Correlation between diabetes duration and Cavernosal artery diameter (mm) in patients group.

2- Correlations between age of diabetic patients and different parameters in patients group was illustrated in (Table 9).

There were no significant correlations between age of the diabetic patients and any of the following parameters; erectile response, cavernosal artery ID, IMT, AWTI, average PSV, average EDV and average RI ($r=-0.129$, $r=-0.166$, $r=0.236$, $r=0.163$, $r=-0.205$, $r=0.068$, $r=-0.205$) respectively.

3- Correlations between control of diabetes and different parameters in patients group was illustrated in (Table 9).

There were no significant correlations between FBG and cavernosal artery ID, AWTI and average RI ($r=-0.256$, $r=-0.045$, $r=0.177$).

There was significant positive correlation between FBG and IMT ($r=0.695$) Fig. (8).

There were significant negative correlations between FBG and erectile response, average PSV, average EDV ($r=-0.777$, $r=-0.661$, $r=-0.390$).

In addition, there were no significant correlations between 2 HPP and AWTI and average RI ($r=0.075$, $r=0.235$) respectively.

There was significant positive correlation between 2 HPP and IMT ($r=0.575$) Fig. (9).

There were significant negative correlations between 2 HPP and erectile response, cavernosal artery ID Fig. (10), average PSV, average EDV which showed statistical significance ($r=-0.782$, $r=-0.375$, $r=-0.677$, $r=-0.435$).

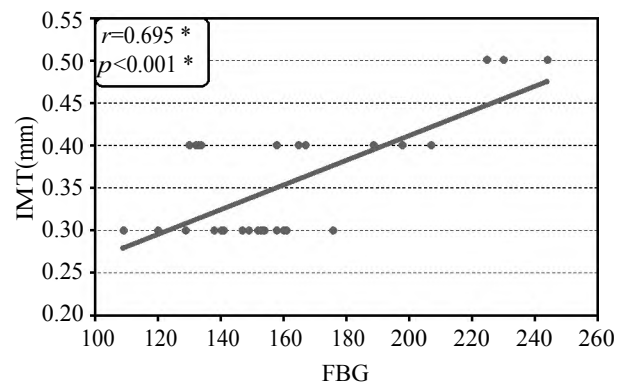


Fig. (8): Correlation between FBG with IMT (mm) in patients group.

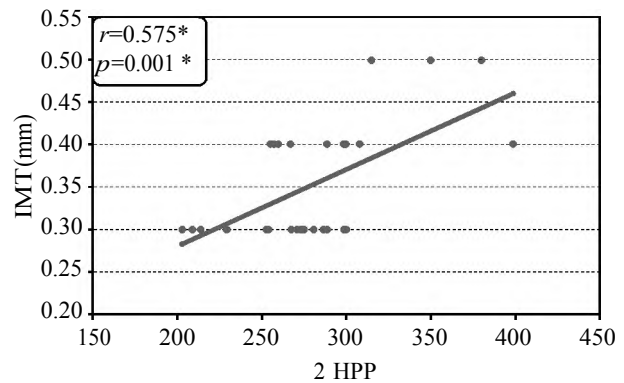


Fig. (9): Correlation between 2 HPP with IMT (mm) in patients group.

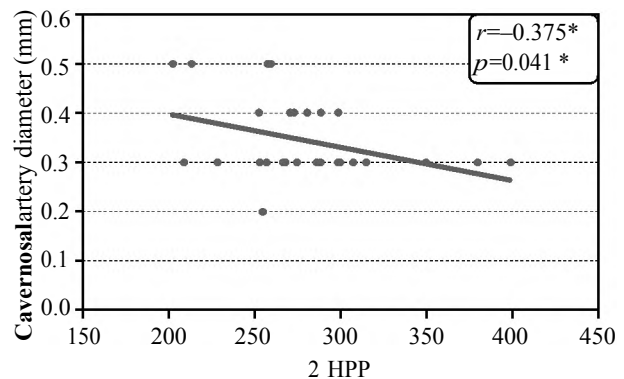


Fig. (10): Correlation between 2 HPP with Cavernosal artery diameter (mm) in patients group.

Table (9): Correlations between different parameters in patients group.

	Age (years)		FBG		2 HPP	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
Erectile response	-0.129	0.496	-0.777	<0.001*	-0.782	<0.001*
Cavernosal artery diameter (mm)	-0.166	0.381	-0.256	0.173	-0.375	0.041 *
IMT (mm)	0.236	0.209	0.695	<0.001*	0.575	0.001*
Arterial wall mass index (gm/cm)	0.163	0.389	-0.045	0.812	-0.075	0.695
Average PSV (cm/sec)	-0.205	0.278	-0.661	<0.001*	-0.677	<0.001*
Average EDV (cm/sec)	0.068	0.723	-0.390	0.033*	-0.435	0.016*
Average RI	-0.205	0.278	0.177	0.351	0.235	0.211

4- Correlations between IMT, AWMI and IIEF in patients group was illustrated in (Table 10).

There was significant negative correlation between IMT and IIEF ($r=-0.513$) Fig. (11), in addition, there was there was significant negative correlation between AWMI and IIEF ($r=-0.502$) Fig. (12).

Table (10): Correlation between IMT, AWMI and IIEF in patients group.

	r_s	<i>p</i>
IMT (mm) vs. IIEF	-0.513 *	0.004*
AWMI (gm/cm) vs. IIEF	-0.502*	0.022*

r_s : Spearman coefficient.

*: Statistically significant at $p \leq 0.05$.

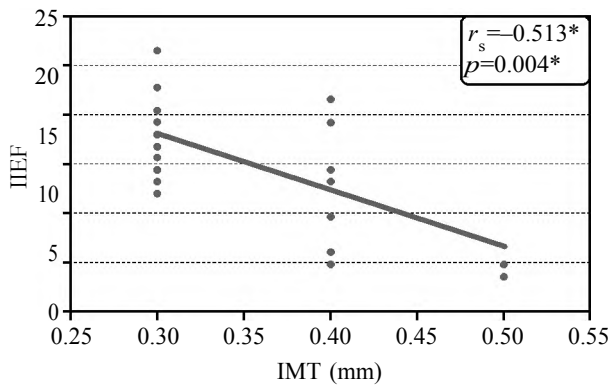


Fig. (11): Correlation between IMT (mm) with IIEF in patients group.

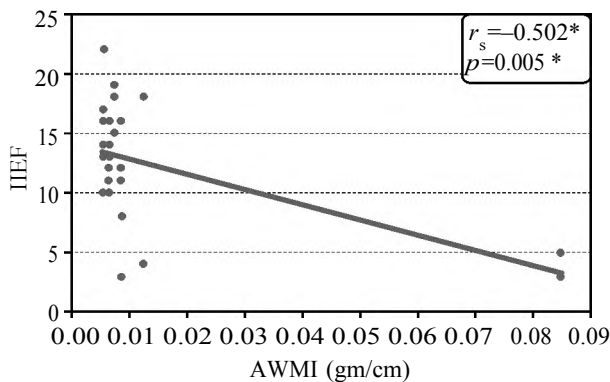


Fig. (12): Correlation between AWMI (gm/cm) with IIEF in patients group.

Discussion

The current study showed that prevalence of ED increased with increasing age that was agreed by many previous studies [19-21]. There was a significant association between severity of ED and age of the participant; 9.5% of patients below age of 60 had severe ED while 34% of patients over 60 had sever ED, this was agreed by Chaudhary et al., and Anwar et al., that reported, diabetes mellites patients with advanced age have a higher propensity of developing severe ED, which further deteriorates the already compromised health & quality of life [21,22].

Regarding the duration of diabetes and its effect on erection; the current study showed that longer the duration of diabetes the more severe ED and poorer erectile response in comparison with the non-diabetic controls, this is because as the age of the patient progresses and duration of diabetes increases various complications of diabetes and age related changes in body take place [23].

Our data showed that poor glycaemic control, as indicated by increased fasting blood glucose, two hours post prandial was more commonly seen in ED patients with means of 160.1 ± 32.75 mg/dl and 280.5 ± 43.44 mg/dl respectively, a study done by Weinberg et al., reported that a poor glycaemic control was associated with increased risk of ED [24] and Awad et al., considered poor glycaemic control as an independent risk factor for ED [25].

The current study showed that IIEF score declines with longer duration of diabetes and poorer glycaemic control using the questions directed to evaluate the erectile function, similar results reported by a study conducted by AlMogbel et.al 26 and agreed by the work published by Goyal et al., [27,28].

Regarding PSV; the current study showed that with longer diabetes duration and poorer glycaemic control PSV declines which indicates arterial insufficiency that adds to lower erectile response, such results was agreed by several previous studies

[29-32]. End diastolic velocity and RI showed insignificant correlation with diabetes duration and glycaemic control as regarding erectile response, but these parameters cannot rely on as they lack specificity for venous leakage in the presence of arterial insufficiency [33].

The initial scan of cavernosal ID in flaccid state was insignificant statistically in comparison with the control group. Such parameter should not be relayed on because normal values of cavernosal artery internal diameter could be any diameter between 0.2-1mm [34,35], Phani Chakravarty Mutnuru et al., showed that the cause may be attributed to that arterial flow is difficult to demonstrate in flaccid state, but sometimes can show damped and monophasic systolic wave form [36].

The current study patients group IMT mean was 0.36 ± 0.08 mm that indicates presence of atherosclerotic plaques in cavernosal arteries but not in control group, these results was agreed by Caretta et al., that included 109 subjects and defined cavernous atherosclerotic plaque as an intimal medial thickness ≥ 0.337 . Also similar results was reported by Prezioso et al., [16].

The IMT in the current study showed positive correlation with the duration of diabetes, poor glycaemic control and PSV. Caretta et al., reported similar findings that a cavernous IMT ≥ 0.3 mm predicts the presence of cavernous plaque with a 100% sensitivity and 76.4% specificity and this parameter is better than PSV [37].

In addition, this study showed that higher IMT was associated with lower erectile response during ultrasonography and was reflected clinically as negative correlation with score of erectile function domain of IIEF, and this was agreed by Prezioso et al., [16].

The ultrasonographic results in the present study as regarding AWMi; in patients group the mean arterial wall mass index was 0.08 ± 0.028 gm/cm and in control group the mean was 0.032 ± 0.015 gm/cm. Comparison between patients and controls showed significant difference ($p < 0.001$). A significant positive correlation between duration of diabetes and AWMi was in patient group ($p < 0.001$). Furthermore, there was negative correlation between AWMi and erectile function domain score of IIEF. By reviewing the literature there were no data regarding AWMi and this is the first work studying AWMi of cavernosal arteries.

The use of AWMi and IMT is a good indicator to detect early atherosclerotic changes in the artery

and to avoid the use of plaque which is late indicator of atherosclerosis [17].

Several studies have demonstrated an increased risk of cardiovascular morbidity and mortality in diabetic patients. In the current study diabetic patients with ED showed evidence of subclinical atherosclerosis as indicated by increased cavernosal artery IMT and AWMi compared with controls. These changes were more pronounced in older patients having longer duration of diabetes. All these results suggest that diabetes itself is an independent risk actor associated with subclinical atherosclerosis. This leads us to speculate that diabetic patients with ED could be suggested as a group with an increased atherosclerotic risk especially in older ages with longer duration of diabetes and ED. So, such patients need frequent follow-up to reduce further cardiovascular morbidity and mortality.

Changes in the ultrasound of diabetic patients include; increased IMT, AWMi, decreased PSV, and it may add new parameters which are IMT, AWMi for evaluation of pathological vascular changes which have adverse effect on erectile function, interpreted by significant negative correlation IIEF.

In addition, this study proved these two parameters that could be done in flaccid state and give the same level of accuracy considering predicting data for cavernosal arteries vascular changes could replace the more invasive techniques with ICI and could avoid their side effects.

References

- 1- SELVIN E., BURNETT A.L. and PLATZ E.A.: Prevalence and Risk Factors for Erectile Dysfunction in the US. *Am. J. Med.*, 120 (2): 151-7. doi:10.1016/j.amjmed.2006.06.010, 2016.
- 2- CARETTA N., De KREUTZENBERG S.V., VALENTE U., et al.: Hypovitaminosis D is associated with erectile dysfunction in type 2 diabetes. *Endocrine*, 1-8. doi: 10.1007/s12020-015-0851-z, 2016.
- 3- BILLUPS K.L., BANK A.J., PADMA-NATHAN H., KATZ S.D. and WILLIAMS R.A.: Erectile dysfunction as a harbinger for increased cardiometabolic risk. *Int. J. Impot. Res.*, 20 (3): 236-42. doi:10.1038/sj.ijir.3901634, 2008.
- 4- BIRD I.M.: Endothelial nitric oxide synthase activation and nitric oxide function: New light through old windows. *J. Endocrinol.*, 210 (3): 239-41. doi:10.1530/JOE-11-0216, 2011.
- 5- SOLOMON H., MAN J.W. and JACKSON G.: Erectile dysfunction and the cardiovascular patient: Endothelial dysfunction is the common denominator. *Heart*, 89 (3): 251-3, 2003.

- 6- ALTHOF S.E.: Quality of life and erectile dysfunction. *Urology*, 59 (6): 803-10, 2002.
- 7- FEDELE D., BORTOLOTTI A., COSCELLI C., et al.: Erectile dysfunction in type 1 and type 2 diabetics in Italy. On behalf of Gruppo Italiano Studio Deficit Erettile nei Diabetici. *Int. J. Epidemiol.*, 29 (3): 524-31, 2000.
- 8- McCULLOCH D.K., CAMPBELL I.W., WU F.C., PRESCOTT R.J. and CLARKE B.F.: The prevalence of diabetic impotence. *Diabetologia*, 18 (4): 279-83, 1980.
- 9- MOORE C.R. and WANG R.: Pathophysiology and treatment of diabetic erectile dysfunction. *Asian J. Androl.*, 8 (6): 675-84. doi: 10.1111/j.1745-7262.2006.00223.x, 2006.
- 10- STEVEN W. FITZGERALD M., SCOTT J. ERICKSON M., W. DENNIS FOLEY M., ELLIOT O. LIPCHIK M. and THOMAS L. LAWSON M.: Color Doppler in the Sonography Evaluation of Erectile, 3-17, 1991.
- 11- MONTORSI P., RAVAGNANI P.M., GALLI S., et al.: The artery size hypothesis: A macrovascular link between erectile dysfunction and coronary artery disease. *Am. J. Cardiol.*, 96 (12B): 19M-23M. doi:10.1016/j.amjcard.2005.07.006, 2005.
- 12- LEWIS R.W.: Epidemiology of erectile dysfunction. *Urol. Clin. North Am.*, 28 (2): 209-16, vii. <http://www.ncbi.nlm.nih.gov/pubmed/11402575>, 2001.
- 13- ROSEN R.C., RILEY A., WAGNER G., OSTERLOH I.H., KIRKPATRICK J. and MISHRA A.: The international index of erectile function (IIEF): A multidimensional scale for assessment of erectile dysfunction. *Urology*, 49 (6): 822-30, 1997.
- 14- COOMBS P.G., HECK M., GUHRING P., NARUS J. and MULHALL J.P.: A review of outcomes of an intracavernosal injection therapy programme. *B.J.U. Int.*, 110 (11): 1787-91. doi:10.1111/j.1464-410X.2012.11080., 2012.
- 15- BRODERICK G.A. and ARGER P.: Duplex Doppler ultrasonography: Noninvasive assessment of penile anatomy and function. *Semin. Roentgenol.*, 28 (1): 43-56, 1993.
- 16- PREZIOSO D., IACONO F., RUSSO U., et al.: Evaluation of penile cavernosal artery intima-media thickness in patients with erectile dysfunction. A new parameter in the diagnosis of vascular erectile dysfunction. Our experience on 59 cases. *Arch. Ital. di Urol e Androl.*, 86 (1): 9-14, 2014.
- 17- AMIN T. and EL-SAIED A. S.H.A.: Atherosclerosis risk in psoriasis. *Pan. Arab J. Dermatol.*, 16: 39-45, 2005.
- 18- CARETTA N., PALEGO P., SCHIPILLITI M., FERLIN A., Di MAMBRO A. and FORESTA C.: Cavernous Artery Intima-Media Thickness: A New Parameter in the Diagnosis of Vascular Erectile Dysfunction. *J. Sex Med.*, 6 (4): 1117-26. doi:10.1111/j.1743-6109.2008.01112.x, 2009.
- 19- FEDELE D., COSCELLI C., SANTEUSANIO F., et al.: Erectile dysfunction in diabetic subjects in Italy. Gruppo Italiano Studio Deficit Erettile nei Diabetici. *Diabetes Care*, 21 (11): 1973-7. <http://www.ncbi.nlm.nih.gov/pubmed/9802753>, 1998.
- 20- MALAVIGE L.S. and LEVY J.C.: Erectile dysfunction in diabetes mellitus. *J. Sex Med.*, 6 (5): 1232-47. doi: 10.1111/j.1743-6109.2008.01168.x, 2009.
- 21- ANWAR Z., SINHA V., MITRA S., et al.: Erectile Dysfunction: An Underestimated Presentation in Patients with Diabetes Mellitus. *Indian J. Psychol. Med.*, 39 (5): 600-4. Doi:10.4103/0253-7176.217015, 2017.
- 22- CHAUDHARY R.K., SHAMSI B.H., TAN T., CHEN H. and XING J.: Study of the relationship between male erectile dysfunction and type 2 diabetes mellitus/metabolic syndrome and its components. *J. Int. Med. Res.*, 44 (3): 735-41. doi:10.1177/0300060515623122, 2016.
- 23- GARG S. and KUMAR K.: "Study of erectile dysfunction in type-2 diabetic patients." *Int. J. Healthc Biomed Res.*, 1 (3): 210-6, 2013.
- 24- WEINBERG A.E., EISENBERG M., PATEL C.J., CHERTOW G.M. and LEPPERT J.T.: Diabetes severity, metabolic syndrome, and the risk of erectile dysfunction. *J. Sex Med.*, 10 (12): 3102-9. doi:10.1111/jsm.12318, 2013.
- 25- AWAD H., SALEM A., GADALLA A., Wafa N.A. EL and MOHAMED O.A.: Erectile function in men with diabetes type 2: Correlation with glycemic control. *Int. J. Impot. Res.*, 22 (1): 36-9. doi:10.1038/ijir.2009.39, 2009.
- 26- ALMOGBEL T.A.: Erectile Dysfunction and Other Sexual Activity Dysfunctions among Saudi Type 2 Diabetic Patients. *Int. J. Heal Sci. Qassim. Univ.*, 8 (4): 348-59, 2014.
- 27- GOYAL A., SINGH P. and AHUJA A.: Prevalence and Severity of Erectile Dysfunction as Assessed by IIEF-5 in North Indian Type 2 Diabetic Males and Its Correlation with Variables. *J. Clin. Diagnostic Res.*, 7 (12): 2936-8. Doi: 10.7860/JCDR/2013/7718.3777, 2013.
- 28- ROMEO J.H., SEFTEL A.D., MADHUN Z.T. and ARON D.C.: Sexual Function in Men With Diabetes Type 2: Association with Glycemic Control. *J. Urol.*, 163: 788-91, 2000.
- 29- TO O., AFTER R., THE C., et al.: Usefulness of power Doppler ultrasonography in evaluating erectile dysfunction. *B.J.U. Int.*, (89): 779-82, 2002.
- 30- SIKKA S.C., HELLSTROM W.J.G., BROCK G. and MORALES A.M.: Standardization of vascular assessment of erectile dysfunction: Standard operating procedures for duplex ultrasound. *J. Sex Med.*, 10 (1): 120-9. Doi: 10.1111/j.1743-6109.2012.02825.x, 2013.
- 31- AVERSA A., BRUZZICHES R. and SPERA G.: Diagnosing Erectile Dysfunction: The penile dynamic colour duplex ultrasound revisited. *Int. J. Androl.*, 28: 61-3, 2005.
- 32- OLIVEIRA P., LEITAO T., OLIVEIRA T. and MARTINHO D.: Penile Dynamic Duplex Ultrasonography. *Austin J. Urol.*, 3 (3), 2016.
- 33- WILKINS C.J., SRIPRASAD S. and SIDHU P.S.: Colour Doppler Ultrasound of the Penis. *Clin. Radiol.*, 58 (7): 514-23. Doi: 10.1016/S0009-9260(03)00112-0, 2003.
- 34- MUTNURU P.C., RAMANJANEYULU H.K., SUSARLA R., YARLAGADDA J., DEVRAJ R. and PALANISAMY P.: Pharmacologic Penile Duplex Ultrasonography in the Evaluation of Erectile Dysfunction. *J. Clin. Diagn. Res.*, 11 (1): TC07-TC 10. Doi: 10.7860/JCDR/2017/25092.9270, 2017.
- 35- MIHMANLI I. and KANTARCI F.: Erectile dysfunction. *Semin Ultrasound CT MR*, 28 (4): 274-86, 2007.

36- MUTNURU P.C., RAMANJANEYULU H.K. and SUSARLA R.: Pharmaco Penile Duplex Ultrasonography in the Evaluation of Erectile Dysfunction. J. Clin. Diagnostic Res., 11 (1): 7-10. Doi: 10.7860/JCDR/2017/25092.9270, 2017.

37- CARETTA N., PALEGO P., SCHIPILLITI M., FERLIN A., MAMBRO A. Di and FORESTA C.: Cavernous Artery Intima-Media Thickness: A New Parameter in. J. Sex Med., 6: 1117-26. doi:10.1111/j.1743-6109.2008.01112.x, 2009.

التغيرات الدوائية الديناميكية للقضيب فى الدوبلر الملون لمرضى السكرى

مرض السكرى هو حالة إنتهايبية مزمنة تشبه الإضطرابات المناعية الإنتهايبية الأخرى. قد يعانى مرضى السكرى من خطر زائد للأصابة بأمراض القلب، وهو ما يمثل سبباً هاماً لم يتم التعرف عليه سابقاً للمرض والوفاة.

قياسات الشريان الكهفى مثل سمك الطبقة الداخلية ومؤشر كتلة جدار الشريان الكهفى هى أدوات واعدة للكشف عن تصلب الشرايين فى طورها تحت الإكلينيكي.

أوضحت الدراسة الحالية أن مرضى السكرى الذين يعانون من ضعف الإنتصاب بدون أعراض سريرية للأمراض القلبية الوعائية أو عوامل الخطر القلبية الوعائية لديهم أعلى من تصلب الشرايين تحت الإكلينيكي فى شكل زيادة سمك الطبقة الداخلية ومؤشر كتلة جدار الشريان الكهفى مقارنة مع المجموعة الضابطة. كما أن مرض السكرى يعتبر عامل خطر مستقل مرتبط بتصلب الشرايين.

يمكن تأويل الزيادة فى سمك الطبقة الداخلية ومؤشر كتلة جدار الشريان الكهفى سريرياً بوجود علاقة عكسية بينهما والمؤشر الدولى لوظيفة الإنتصاب.

يمكن أن تعطى هذه المؤشرات الجديدة تنبؤاً جيداً بتصلب الشرايين ويمكن أن تحل محل الحقن الكهفى الأكثر تعقيداً ويمكن أن تتجنب آثارها الجانبية.