The value of international index of erectile function - 5 in assessment of the severity of vasculogenic erectile dysfunction.

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By

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ABSTRACT

It is unclear whether the IIEF-5 is capable of diagnosing the severity and cause of ED. **The aim** of this study is to evaluate the possible value of IIEF-5 in the assessment of the severity of vasculogenic erectile dysfunction in comparison to the results of penile duplex**. Patients and methods** This study was carried out on one hundred and fifty subjects complaining of ED for more than 6 months. Divided into two groups according to their response to ICI test: **Good responders group**: fifty patients who showed good response (E4) or more to any dose of ICI And **Poor responders group:** One hundred patients who showed poor response to ICI less than (E4) up to maximum dose of 1 cc Quadmix with abnormal penile duplex. All patients were subjected to full history taking including the demographic data, filling the questions of (IIEF-5), and penile duplex with 1 cc Bimix. The poor responders then divided in to arteriogenic ED with PSV within 5 minutes of injection was less than 30 cm/sec n=81, and into venogenic ED group if EDV on both sides was more than 5 cm/sec n=12, and into combined ED group n=7. The results of the duplex are correlated to the IIEF-5 score of the patients. **Results**: there is statistically significant difference between mean value of I.I.E.F-5 in both good and poor responders (P value =0.0000), significant difference between mean value of (age, duration, PSV Rt & Lt, EDV Rt & Lt, diameter of artery after in both Rt & Lt, percent of increase in arterial diameter Rt & Lt and RI Rt & RI Lt) between the good & poor responders. Statistically insignificant difference between mean value of I.I.E.F-5 in both arteriogenic and venogenic subgroups of poor responders group. Statistically insignificant correlations between I.I.E.F-5 & penile duplex results in both good & poor responders groups, Also there is Statistically insignificant correlations between I.I.E.F-5 & penile duplex results in arteriogenic & venogenic & combined subgroups. **Conclusion:** I.I.E.F-5 can't be used to diagnose the severity of vasculogenic ED or detect the cause.

Key Words: Erectile dysfunction, I.I.E.F-5, Penile duplex, SHIM.

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Table of Contents

List of abbreviations

AI	: Arterial insufficiency.
CAD	: Coronary artery disease.
CVOD	: Cavernous venous occlusive disease.
CDDU	: Colour Duplex Doppler ultrasonography.
cGMP	: Guanosine cyclic monophosphate.
CRF	: Chronic renal failure.
DUS	: Duplex ultrasonography.
ED	: Erectile dysfunction**.**
EDV	: End diastolic velocity**.**
EF	: Erectile function.
HDL	: High density lipoproteins.
ICI	: Intracavernous injections.
IIEF -5	: The International Index of Erectile Function-type 5.
IIEF-15	: International index of erectile function-type 15.
NS	: Nerve-sparing.
n	: Number.
PBFS	: Penile blood flow study.
PDE	: Phosphodiesterase enzyme.
PPDU	: Pharmaco penile duplex ultrasonography.
PSV	: Peak systolic velocity.
RA	: Rheumatoid arthritis**.**
RI	: Resistance index**.**
ROC	: Receiver operating characteristic.
RP	: Radical prostatectomy.
SHIM	: Sexual Health Inventory for Men.
SSc	: Systemic sclerosis.
VSMC	: Vascular smooth muscle cells.

List of Figures

List of Tables

INTRODUCTION

The National Institutes of Health (NIH) Consensus Panel has defined erectile dysfunction (ED) as the inability to achieve and/or maintain penile erection that is sufficient for satisfactory sexual performance **(NIH Consensus Development Panel 1993)**. Evidence-based approaches in the diagnosis of ED have included cavernosometry, nocturnal penile tumescence testing, and penile blood-flow studies (PBFS).

In the clinical office an excellent and fast response to intracavernosal vasoactive agents (in neurologically normal men) may support the diagnosis of psychogenic impotence **(Virag et al., 1984)**. PBFS provide an objective, minimally invasive evaluation of a suboptimal/equivocal erectile response **(Broderick et al., 1998)**. Although laboratory based diagnostic procedures are available, recently sexual questionnaires have gradually replaced them for evaluating ED because they are easy to use.

There are several questionnaires available; as International Index of Erectile Function (IIEF-15) **(Rosen et al., 1997)** which has been used for many clinical studies; is a brief and reliable measure of ED that is culturally, linguistically and psychometrically valid it can be used for routine office practice as well. And there are simpler questionnaires in use; one of them is the Sexual Health Inventory for Men (SHIM) which deals specifically with erectile activity using a five-point Likert type Scale **(Rosen et al., 1997)**.

Aim of the work

It is unclear whether the IIEF-5 is capable of diagnosing the severity and cause of ED. The present study aimed to evaluate the ability of the IIEF-5 to detect the severity of vasculogenic erectile dysfunction, and to compare it with pharmacological testing and duplex Doppler ultrasonography (DUS).

Risk factors of vasculogenic ED

Erection is a vascular event under neural control and is determined by the balance between arterial inflow and venous outflow. Vascular arterial abnormalities will therefore affect erectile function and it is vasculogenic ED that has been the subject of detailed evaluation. **(Jackson 2006 and Montorsi et al., 2006).**

Endothelial dysfunction is now recognized to be the fundamental fault leading to ED. As the endothelium is the same in the penile arteries as the coronary arteries, ED and coronary artery disease (CAD) share the same vascular risk factors. The greater weight of endothelium relative to the smaller penile arteries might explain why ED can precede a cardiac event or predict subclinical CAD and in turn why ED is common in the presence of known CAD **(Jackson 2006)**.

Risk factors are associated with but not necessarily causative of vascular disease. They can be considered unavoidable (age, sex, family history) or modifiable (lifestyle, obesity, physical inactivity, cigarette smoking, diabetes, hypertension, and hyperlipidemia) **(Lloyd-Jones et al., 1999)**. In addition, the metabolic syndrome, which is a group of vascular risk factors, including central obesity, hyperlipidemia, hypertension, and insulin resistance, is associated with ED **(Corona et al., 2006)**.

- ## Lifestyle

One of the most important factors is the role of intensive lifestyle modification in improving erectile function and decreasing cardiovascular inflammatory markers of risk **(Bacon et al., 2006).** Atheromatous plaques are complex and dynamic and it is plaque composition rather than volume that influences the risk of a clinical cardiac event **(Davies et al., 1993).**

A reduction in lipid content of the plaque and the accumulation of macrophages and lymphocytes, whilst increasing vascular smooth muscle cells (VSMC) and the thickness of the fibrous cap, will improve endothelial function, whereas VSMC apoptosis will reduce cap thickness, increase the necrotic content and plaque inflammation, leading to plaque instability and vulnerability **(Bennett, 2007)**. Most atheroma is sub-clinical and in its early phases more easily influenced in a beneficial way, emphasizing the important link between ED and early phase silent coronary artery disease (CAD) with regard to using ED as a marker for aggressive risk reduction **(Jackson, 2006).**

- ## Smoking

Smoking increased the risk of developing ED by 50% **(Bacon et al., 2006)**. Men who smok increased their risk of developing moderate or total ED to 24% compared to non-smokers, at 14 % ($p = 0.01$) **(Johannes et al., 2000).** In hypertensive men the probability of complete ED was doubled. Smoking has been shown to interfere significantly and adversely with the cavernous veno-occlusive mechanism and to reduce erectile response to intracavernous injections **(Juenemann et al., 1987 and Glina**

et al., 1988). The benefit of smoking cessation on ED is not proven, perhaps due to an irreversible effect from prolonged tobacco use **(Derby et al., 2000).**

- ## Diabetes Mellitus

Several studies confirmed the role of diabetes as an etiology of erectile dysfunction (ED). ED developed in 35-75% of diabetics **(Hatzichritou et al., 1994)**. ED in diabetics has been reported to be more common than retinopathy or nephropathy **(Lehman and Jacobs 1983)**. Peak systolic velocity (PSV) in the cavernous artery was found to be lower in diabetics in a study of 105 patients **(Jonler et al., 1995).**

- ## Hypertension

Hypertension is a major risk factor for both ED and CAD. Cavernous artery insufficiency was reported in 85% of 117 hypertensive patients **(Muller et al., 1991)**. ED is present in up to 17% of men at the initial hypertensive diagnosis. The incidence rate of ED in treated hypertensives is 68% (7.6% mild, 15.4% moderate and 45.2% severe according to the IIEF), Although correlations of antihypertensive medications with incidence of erectile dysfunction did not reach statistical significance, there was a clear trend with patients treated with diuretics and beta-blockers having the highest incidence and those treated with alpha-blockers having the lowest incidence of erectile dysfunction. **(Burchardt et al., 2000)**.

- ## Dyslipidemia

A high level of total cholesterol or a low level of high density lipoproteins (HDL) were reported as important risk factors for ED **(Feldman et al., 1994 and Wei et al., 1994)**. In clinical studies HDL and LDL (low density lipoprotein) values were associated with Vascular ED and veno-occlusive dysfunction **(Manning et al., 1996)**.

- ## Cardiovascular risk factors

Atherosclerosis appears to be the most common cause of vasculogenic ED. Smoking, hypertension, diabetes mellitus and dyslipidemias have been shown to initiate the cascade of events resulting in atherosclerosis. These include endothelial injury, cellular migration and smooth muscle proliferation **(Sullivan et al., 2001)**. These risk factors are common between ED and coronary artery disease. Studies suggest ED as a strong predictive factor for coronary artery disease **(Shamloul et al., 2004 and Billups et al., 2005)**.

- ## Post-trumatic vasculogenic ED

Patients with a history of pelvic fracture with associated urethral trauma could suffer from ED due to disruption of the neurovascular pathway **(Van Arsdalen et al., 1984)**. Perineal trauma either acute or chronic may result in vasculogenic ED, as in acute perineal (straddle) trauma may result in ED due to disruption of neurovascular bundle **(Munarriz et al., 1995)**.

In chronic perineal trauma as in chronic compression syndrome, which occationally observed in cyclist who spend long time in the saddle, may lead to impairment of the penile blood supply with effects on pudendal nerve (numbness of penis), and subsequent manifestation of ED **(Mulhall et al., 1996 and Sommer et al., 2001).**

- ## Radiogenic risk factor

Studies have shown that 20 to 70% of patients who received radiation for malignant diseases suffered from ED, with an onset as early as one month up to four years. Vasculogenic impotence is the most consistent organic erectile abnormality in post irradiation ED **(Goldstein et al., 1984)**.

- ## Iatrogenic vasculogenic ED

Injury to neurovascular bundle supplying penis during pelvic surgery may result of ED. Hypoxia of penile tissue result in fibrosis of penile structures and development of venous leak following operations treating colorectal carcinoma **(Sutorý 2009)**.Also, aorto-femoral surgery either endarterectomy or reconstruction may carry risk of worsen the pre existing ED in these patients **(Cormio et al., 1996).**

Pharmacopenile duplex in diagnosis of erectile dysfunction

Penile sonography should be performed using high frequency linear probes with the patient in the supine position and the penis scanned from its ventral surface using longitudinal and transverse views. Evaluation should be carried out while the penis is flaccid and after intracavernosal injection of vasoactive drugs **(Doubilet et al., 1991)**.

Drugs used in pharmacopenile duplex study

Prostaglandin E1 injection at the dosage of 10 μg is usually adequate to obtain a suitable erectile response in potent patients **(Bertolotto and Neumaier, 1999)**. Some authors, however, routinely use 20 μg. A lower initial dosage of 5 μg is recommended in young patients in order to limit the risk of prolonged and painful erection **(Lin and Bradley, 1985).** Other drugs can be used in pharmacopenile duplex study as papaverine, the dose of papaverine ranged from 7.5 mg to grater than 60 mg but lower doses can be used in conjunction with phentolamine and PGE1 and the doses of PGE1 ranged from 10 to 40 ug when used alone, 10 ug or less when used in conjunction with the other two agents, Phentolamine has always been in compination with other two drugs in a dose around 0.5 mg. **(Meuleman and Diemont, 1995)**

Grey-Scale Ultrasound Anatomy

The different anatomical features of the penis are better evaluated during tumescence and erection. In the flaccid state, the corporal bodies present at ultrasonography as cylindrical structures with intermediate