Angiographic study of internal pudendal artery in patients with erectile dysfunction and ischemic heart disease

Thesis

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By

Khaled Ahmed Mahmoud El-Nahas
M.B.B.Ch, M.Sc., Dermatology, Venereology and Andrology
Faculty of Medicine, Ain Shams University

Supervised by

Prof. Dr. Hanan Mohamed Saleh
Professor of Dermatology, Venereology and Andrology
Faculty of Medicine - Ain Shams University

Prof. Dr. Nehal Mohammed Zu Elfakkar
Professor of Dermatology, Venerelogy and Andrology
Faculty of Medicine - Ain shams University

Prof. Dr. Khaled Mohamed Said
Assistant Professor of Cardiovascular Diseases
Faculty of Medicine - Ain shams University

Faculty of Medicine
Ain Shams University
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INTRODUCTION

Erectile dysfunction (ED) is an important health problem which is defined as the recurrent inability to achieve and/or maintain an erection satisfactory for sexual intercourse ***(Teles et al., 2008).***

ED is increasingly being recognized as a vascular disorder, with predictive value for ensuing cardiac events. Men presenting with ED often have risk factors for atherosclerosis and, conversely, ED is frequently reported in men with vascular syndromes, such as coronary artery disease (CAD), hypertension, cerebrovascular disease, peripheral arterial disease and diabetes mellitus ***(Montorsi et al., 2005)***.

Atherosclerosis is a chronic systemic disease that involves cardiac and peripheral arteries and is the leading cause of death. Exposure to the known atherosclerosis risk factors leads to intima-media thickening and development of atheromatous plaques, causing vascular lumen stenosis and obstruction ***(Montorsi et al., 2006; Malik and Tivakaran, 2018).***

ED and coronary artery disease (CAD) have been shown to share common risk factors such as advanced age, diabetes, hypertension, dyslipidemia, and tobacco use ***(El-Sakka et al., 2004; Gazzaruso et al., 2004).***

ED is emerging as an identifiable risk factor for the subsequent development of cardiovascular events, and it has been shown that up to 70% of men with new onset angina and angiographically documented CAD have a history of antecedent ED ***(Ahmadi et al., 2014; Lane-Cordova et al., 2017).***

Essentially, ED and CAD are different clinical manifestations of the same spectrum of disease; however, because the penile arteries are smaller and require great flexibility, symptoms are likely to appear earlier than in the coronary or carotid arteries. The artery size hypothesis has been proposed to address this association ***(Montorsi et al., 2005)***.

Owing to the systemic nature of atherosclerosis, one would expect that all major vascular beds would be affected to the same extent. However, symptoms usually appear at different points in the system at different times. This is likely because larger vessels are able to better tolerate the same amount of plaque than smaller ones. Coronary circulation is, therefore, not critically affected because of its larger size, which might explain why CAD is not evident in early-stage ED, because of its smaller diameter, the plaque burden that produces significantly impaired circulation in the small arteries of the penis may cause only 30% to 40% occlusion of the larger coronary, internal

carotid, and femoral arteries. Therefore, while atherosclerosis sufficient to trigger ED may not cause clinically apparent cardiovascular disease, progression of the atherosclerotic process in the larger arteries may subsequently result in CAD, stroke, or claudication (***Brock, 2014).*** Sexual dysfunction may be the only reason men present to the doctor. This presents an opportunity, not only to treat the sexual dysfunction, but to also screen for cardiac risk. Even men with mild arteriogenic ED may be at risk for cardiovascular disease. It is important for these patients to have their risk assessed early, before sequelae develop, and to manage any risks aggressively ***(Lane-Cordova et al., 2017).***

Aim of the Work

The aim of this study was to describe the angiographic characteristics of pelvic arterial disease in patients with ED who have coronary artery disease (CAD), and to angiographically correlate the presence and severity of internal pudendal artery disease with CAD. In addition, to investigate the association between the severity of ED and the number of occluded coronary vessels. Thereby, evaluating the value of percutaneous revascularization techniques as a treatment for ED.

ERECTILE DYSFUNCTION

Male erectile dysfunction (ED) is the persistent inability to obtain and/or maintain an erection sufficient for sexual intercourse ***(Hackett et al., 2010).***

A. Anatomy of penis:

The penis is formed of three parts, with two corpora cavernosa on each side which function as the main erectile tissue, and ventral corpus spongiosum which contains the urethra. The three corpora are covered by loose subcutaneous tissue and skin ***(Romans, 2006).***

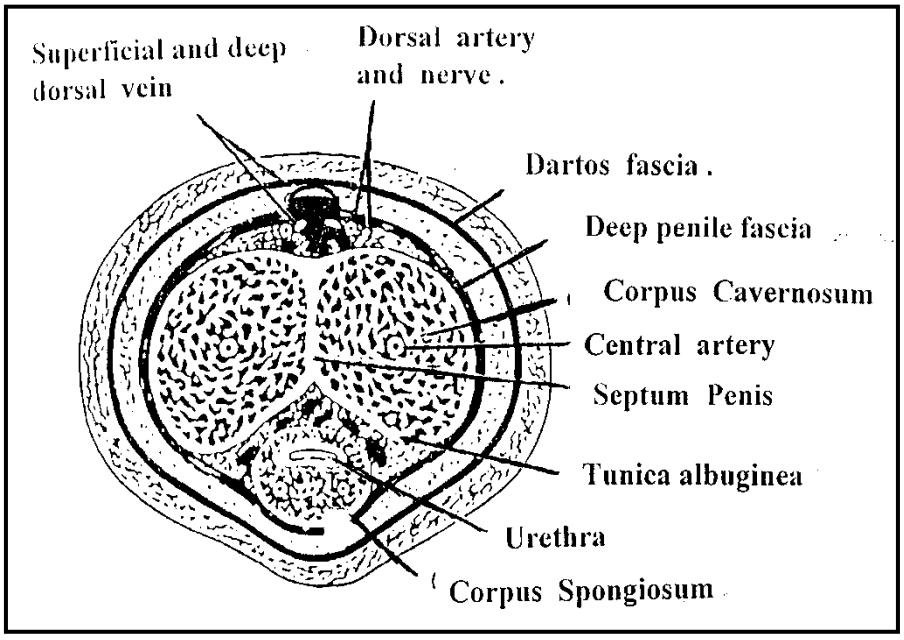

Fig. (1): Cross section of the penis ***(Lue et al., 1992)***

Each corpora cavernosa originate separately under the ischiopubic rami, and then merge as they pass under the pubic arch. Although the septum in between is incomplete, it is complete in some other species. Corpora cavernosa are supported by many fibrous structures that include the surrounding tunica albuginea ***(Lewis, 2004).*** The spongy inner tissue of the corpora is formed of interconnected sinusoids separated by smooth muscle trabeculae, and surrounded by collagen and elastic fibers. Tunica albuginea is a strong structure formed of heterogenous thickness and anatomy, whose function is to provide rigidity of the erectile bodies and allows proper veno occlusive mechanism ***(Rosen et al., 2008).***

Internal pudendal artery (IPA) is the main source of blood supply to the penis; it is a branch of the internal iliac artery ***(Breza et al., 1999).***

After giving off a branch to the perineum, the internal pudendal artery becomes the common penile artery. The common penile artery divides into three branches, the dorsal, bulbourethral, and cavernous arteries. Cavernous artery supplies the corpus cavernosum leading to tumescence during erection. The dorsal artery supplies the glans penis leading to its engorgement during erection (Fig. 2) ***(Kim et al., 1994; Aboseif et al., 2000).***

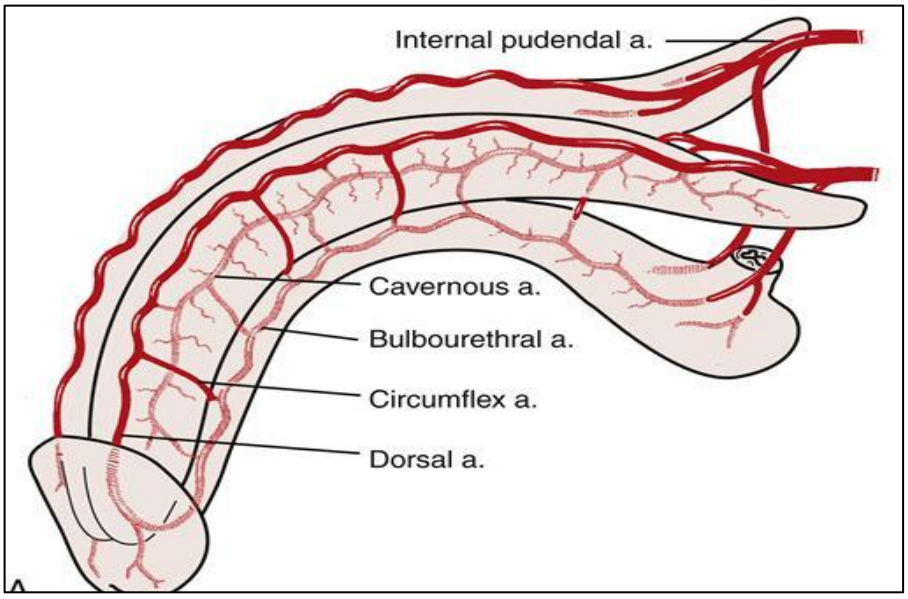

Fig. (2): Arterial anatomy of the penis ***(Montorsi et al., 2001).***

Venous drainage starts as tiny venules leading from the peripheral sinusoids under the tunica albuginea forming the subtunical plexus of veins which penetrate the tunica albuginea as emissary veins ***(Breza et al., 1999).*** Emissary veins located dorsally drain into the deep dorsal, laterally to the circumflex, and ventrally to the periurethral veins. Glans penis, corpus spongiosum, and distal corpora cavernosa drain into the deep dorsal vein (Fig. 3) ***(Walsh and Donker, 1997).***

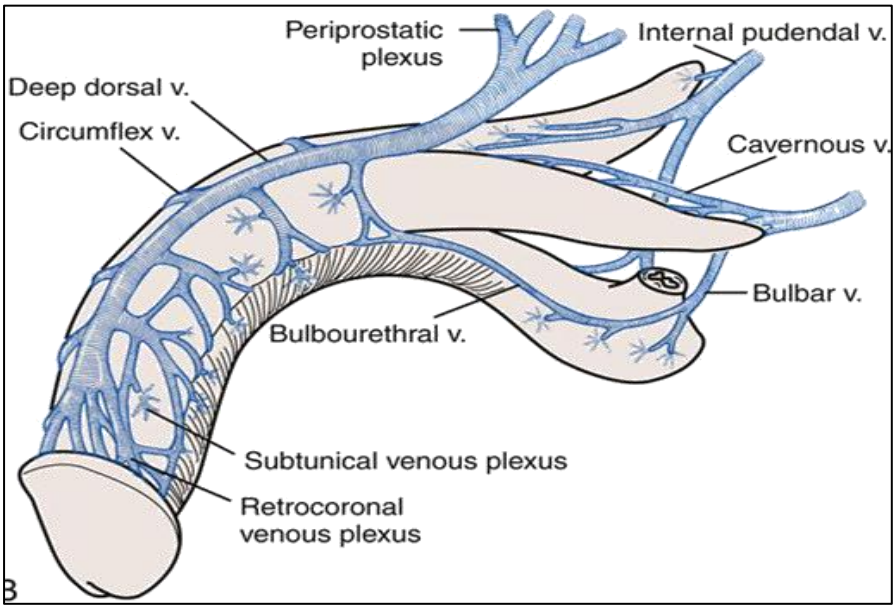

Fig. (3): Venous anatomy of the penis ***(Montorsi et al., 2001).***

Somatic nerve supply is derived from S2, S3, S4 nerve roots, passing through pudendal nerve, which pass through the pudendal canal during its pathway, then continues as the dorsal nerve of penis ***(Romans, 2006).***

Autonomic nerve supply of genitalia is through the pelvic plexus, which is formed of both parasympathetic, and sympathetic fibers. Parasympathetic nerve supply is formed of visceral efferent preganglionic fibers arising from S2-S4 roots. Sympathetic fibers are the contribution of thoracolumbar sympathetic fibers and are derived from L1 and L2 roots. These fibers pass through the hypogastric nerve, sacral sympathetic chain, and fibers originate from the autonomic inferior mesenteric plexus accompanying the superior hemorrhoidal artery ***(Kim et al., 2004).***

Cavernous nerves supplying each corpus cavernosum start as fine fibers from the pelvic plexus, they are mixed nerves with the parasympathetic component producing vasodilatation and the sympathetic one producing vasoconstriction, regulating blood flow during erection and detumescence ***(Romans, 2006; Meulman and Diemont, 2006).***

B. Physiology of erection:

Penile erection is primarily a neurovascular event modulated by psychological and hormonal status ***(Nicolosi et al., 2003).***

Increase in the blood flow by several times is due to relaxation of cavernous smooth muscle. Expansion of the cavernous tissue leads to compression of subtunical venular plexuses against the tunica albuginea resulting in almost complete occlusion of venous outflow ***(Fournier et al., 2007; Banya et al., 2009),*** that may get the blood trapped within the corpora cavernosa increasing the intracavernous pressure to approximately 100 mmHg, leading to an erect state (the full erection phase). Bulbocavernosus reflex, stimulating the ischiocavernosus muscles to compress the base of the corpora cavernosa leads to increased rigidity with intracavernous pressure reaching several hundred mmHg with stoppage of both the inflow and outflow of blood ,(the rigid erection phase) ***(Aboseif and Lue, 1999).***

Nitric oxide released from nonadrenergic-noncholinergic fibers and the endothelium, is the main neurotransmitter for penile erection ***(Lue, 2000).*** The parasympathetic fibers release acetylcholine (ACh), vasoactive intestinal polypeptide (VIP) and nitric oxide (NO). Although ACh causes penile smooth muscles to contract invitro, it activates endothelial cells to release NO assisting penile erection ***(Andersson, 2001).***

Nitric oxide activates the enzyme guanylyl cyclase to covert Guanosine triphosphate (GTP) to cyclic Guanosine monophosphate (cGMP). cGMP activates the enzyme cGMP dependent protein kinase to phosphorylate multiple intracellular proteins and ion channels, leading to opening of certain potassium channels and hyperpolarization ***(Corona et al., 2004).***

Hyperpolarization decreases intracellular calcium by closure of calcium channels and sequestration of calcium by the endoplasmic reticulum, leading to smooth muscle relaxation. In order to return to the flaccid state, cGMP is hydrolyzed by phosphodiesterase enzyme type 5 (Fig.4) ***(Corona et al., 2004).***

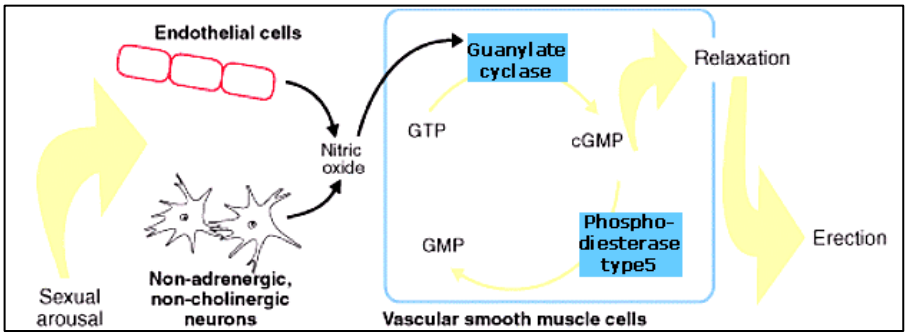

Fig. (4): Neurophysiology of erection ***(Lobo and Nehra, 2005).***

C. Erectile dysfunction:

Erectile dysfunction (ED) is classified as two main categories: Psychogenic ED and Organic ED. Up to 80 to 90% of patients fall into the organic group. Approximately 85% of these patients have some degree of vascular origin (arteriogenic and venogenic erectile dysfunction) ***(Benson and Vicker, 2000).***

1. Psychogenic Erectile Dysfunction:

Hypothalamus, the limbic system, and the cerebral cortex control the sexual behavior and penile erection through, stimulatory or inhibitory messages controlling the spinal erection centers ***(Steers, 1990).***

Psychological impotence is caused by, performance anxiety, traumatic previous experience as sexual abuse in childhood and fear of pregnancy or sexually transmitted diseases, premature ejaculation and excessive alcohol intake ***(Bacon et al., 2006).***

Two mechanisms may be involved in the inhibition of erection. First, reflexognic erection can be inhibited by psychogenic stimuli to the sacral cord preventing activation of the parasympathetic dilator impulses to the penis. Second, increase of penile smooth muscle tone, due to increased sympathetic outflow, elevated blood catecholamine levels or both opposing the smooth muscle relaxation of cavernous tissue during erection ***(De Tejada et al., 2005)***.

2. Neurogenic Erectile Dysfunction:

Penile sensitivity to genital stimulation is important to achieve and maintain erection reflexes. Decreased penile sensitivity especially in some diabetic patients with erectile dysfunction may be the main cause for their complaint ***(Rowland et al., 2003).***

Disorders affecting the parasympathetic sacral spinal cord or the efferent autonomic fibers cause partial or complete ED as a result of the inability to cause relaxation of the cavernous tissue smooth muscles. Affection of the afferent sensory fibers of the pudendal nerve or their representation in the sacral spinal cord also may lead to erectile dysfunction ***(Rowland et al., 2003).***

Multiple sclerosis, Parkinson's disease, Alzheimer's disease, temporal lobe epilepsy, and cerebral stroke are frequently associated with ED ***(Siddiqui et al., 2012).*** The

degree of ED in spinal cord injury patients is largely dependent on the degree and level of the spinal lesion. Incomplete lesions or injuries to the upper part of the spinal cord may preserve some erectile capabilities in comparison to complete, lower part injuries ***(Krane et al., 2004).*** Radical pelvic surgeries as radical prostatectomy may be complicated with high risk of cavernous nerve injury leading to neurogenic ED ***(Mulhall, 2008).***

3. Endocrinal Erectile Dysfunction:

Testosterone is mandatory for normal sexual desire and normal erection ***(Aversa et al., 2003; Bancroft, 2005; Zhang et al., 2005),*** it regulates the expression of NO synthase and phosphodiestrase enzyme 5 ***(Traish et al., 2003).***

Prolactin inhibits sexual desire and erection, some authors attribute the refractory period of the sexual cycle to post-orgasmic elevations in prolactin level. Hyper prolactinaemia inhibits secretion of gonadotropin-releasing hormones, which, in turn, decreases the secretion of luteinizing hormone, decreasing testosterone concentrations ***(Krüger et al., 2002).***

The most important causes of endocrinal impotence are hypogonadotropic hypogonadism which is associated with neoplastic, inflammatory, traumatic, vascular and degenerative disorders of the pituitary gland and the

hypothalamus. Hypergonadotrophic hypogonadism with low serum testosterone and elevated gonadotrophin levels which indicate testicular disease as seen in patients with Klinefelter syndrome. Hyperprolactinemia, which may be caused by drugs, chronic renal failure, primary hypothyroidism, pituitary tumors and may be idiopathic. Thyroid dysfunction as in both, hyper and hypothyroidism ***(Persu et al., 2009).***

4. Diabetic Erectile Dysfunction:

Diabetes mellitus (DM) is one of the leading causes of erectile dysfunction. 25% up 60% of all diabetic men are estimated to have ED of varying degrees at some stage of their sexual lives. It may be more common than retinopathy and nephropathy ***(Buvat et al., 1995).***

Insulin-resistance (IR) is a metabolic alteration that produces endothelial dysfunction. It affects most patients with obesity, metabolic syndrome, and DM2. Endothelial dysfunction is due to lower synthesis and release of NO, combined with higher NO consumption in tissues exposed to high concentrations of reactive oxygen species ***(Cersosimo and De Fronzo, 2006).*** The reduction in NO levels affects the different arteries of the body, impairing its vasodilator mechanism ***(McFarlane et al., 2001).*** Endothelial dysfunction caused by insulin resistance (IR) is