INTRODUCTION

Erectile dysfunction (ED) is increasingly recognized as a public health problem with both psychosocial correlates and associations with clinical comorbidities. The understanding and management of ED has evolved greatly, as evidenced by the increased recognition of its organic etiologies. This condition greatly affects patient quality of life, self-esteem, and ability to maintain intimate relationships ***(Traish and Guay, 2016).***

ED is now defined as the consistent inability to attain or maintain penile erections of sufficient quality to allow satisfactory sexual intercourse ***(Traish et al., 2017).***

ED was previously believed to be largely psychogenic in origin. While there are strong psychosocial correlates, there is increasing recognition of its relationship to clinical comorbidities that indicate an organic basis in the majority of presentations. It is also considered to be a significant public health problem, given its relationship to diabetes, vascular diseases, dyslipidemia, hypertension, and cigarette smoking. ***(Nehra, 2016).***

New insights suggest that ED may be viewed as a vascular disease and plausibly represents an early manifestation or indicator of covert cardiovascular disease existing beyond the genital organ. An additional element that contributes to the

significance of the problem is that ED is frequently an issue of the couple. Both the patient and his partner may be affected by the problem and should be involved in management decisions. ***(Grant, 2015).***

The National Health and Social Life Survey, which defined various types of sexual dysfunction in men and women, documented an ED incidence of 18% in men 50 to 59 years old and showed an incidence of erectile dysfunction in 52% of men 40 to 70 years old. Worldwide prevalence of erectile dysfunction around 177 million cases - has been predicted to double (and reach 322 million cases by the year 2025) ***(Angulo and Cuevas, 2012).***

As more epidemiological data accrue, information is emerging regarding the extent and impact of risk factors and comorbidities associated with ED. In addition to CV disease, pelvic trauma, neurological disease/injury, and aging have all been associated with the disorder. ED has recently been established for conditions such as diabetes, hypertension, and various cardiac and vascular diseases; diabetes alone quadruples the risk. Recent studies have supported the association between lower urinary tract symptoms, bladder outlet obstruction, and BPH with ED, although the exact pathophysiological relationship between prostate disease and ED remains unclear ***(Annamaria and Filippi, 2013).***

In addition to the increased risk related to chronic disease, ED may be associated with medication use in up to25% of all cases. Certain antihypertensive agents, particularly diuretics and _B-blockers, are highly associated with ED. ***(Arthur, 2013).***

Other medications associated with ED include hormonal agents (eg antiandrogens), protease inhibitors, cytotoxic agents, H2 antagonists, and selective serotonin reuptake inhibitors.

Selective serotonin reuptake inhibitors are known to be effective for treating depression, which in itself is associated with a higher incidence of ED.

several emotional conditions have been determined to be risk factors for ED, including depression, stress, general unhappiness, dissatisfaction with partner, greater than 20% decrease in income, pessimistic attitude, marital change, and employment change ***(La Fuente and Pomerol, 2014).***

A number of modifiable life-style factors contribute to ED. Sedentary life-style, obesity, heavy drinking, recreational drug use, and smoking all increase the risk of ED. This is an area of increasing interest, because it suggests several ways that patients can decrease their own symptoms ***(Barbara et al., 2015).***

Aim of the Work

The purpose of our study is to evaluate the feasibility, efficacy, and safety of LI-ESWT in men with mild to moderate ED as We investigated the clinical and physiological effect of LI-ESWT on men with organic erectile dysfunction who are phosphodiesterase type 5 inhibitor responders.

Chapter One

ANATOMY

The penis can be divided into three parts: the root, the body, and the glans. The root, or penile bulb, is located within the superficial perineal pouch, the body is formed by the three spongy erectile anatomic entities: two corpora cavernosa and one corpus spongiosum, and the glans is the distal end of the corpus spongiosum.

The root of the penis is located in the superficial perineal pouch, and consists of the crura, bulb, ischiocavernosus and bulbospongiosus muscles (Fig. 1) ***(Keith et al., 2007).***

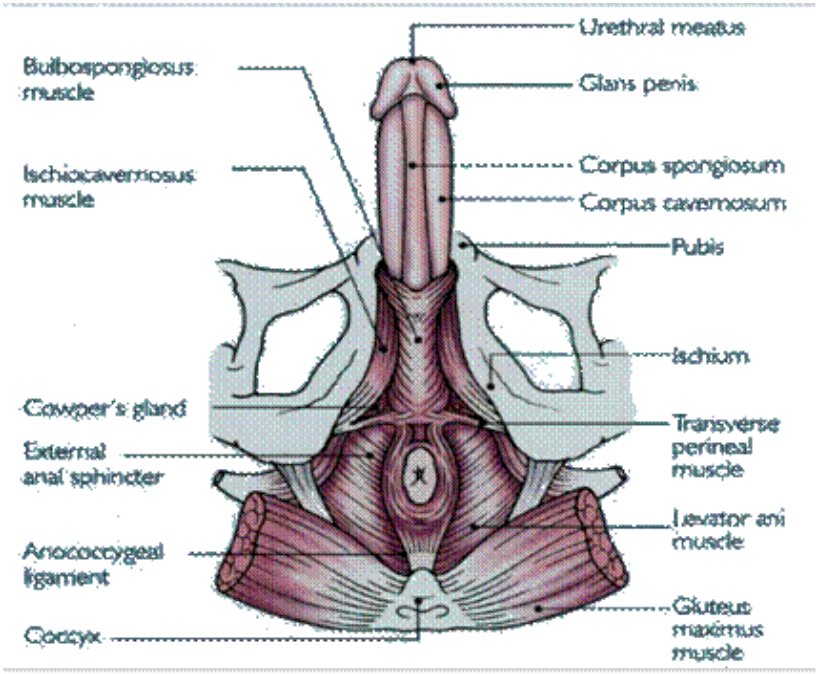

Figure (1): Muscles of the pelvic floor surround and support the erectile bodies and corpus spongiosum ***(Keith et al., 2007).***

The body of penis is composed of **2** dorsal cylindrical bodies, the corpora cavernosa, and the ventral corpus spongiosum which encloses the urethra and expands distal to form the glans penis. The corpora cavernosa are enclosed in a thick bilayer fibrous sheath, the tunica albuginea, whose fibers unite medial to form a perforated septum that allows the 2 bodies to function as a unit. The corpus spongiosum has a thinner tunica albuginea. The 3 corporal bodies are surrounded by deep fibrous tissue, Buck's fascia. Cavernosal tissue is sponge-like with a mesh of interconnected cavernosal spaces also known as sinusoidal or lacunar spaces. These cavernosal spaces are lined with vascular endothelium and separated by trabeculae composed of bundles of smooth muscle fibers with an extracellular matrix of collagen, elastin and fibroblasts. Gap junctions, hexamer protein lined aqueous intercellular channels, connect the smooth muscle cells of the corpora cavernosa. ***(Bagcivan et al., 2013).***

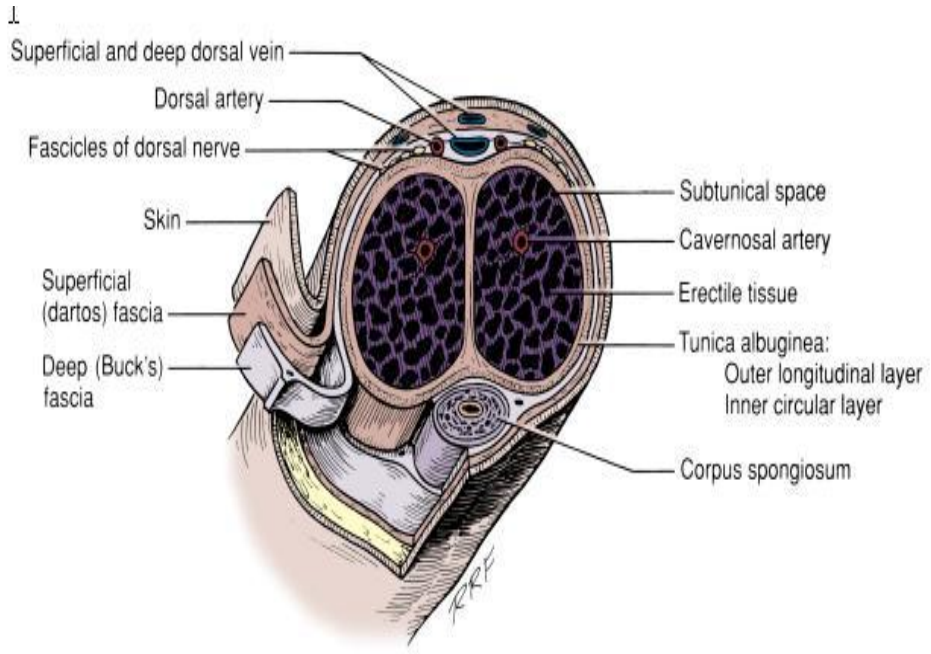

Figure (2): Cross section of the penis, demonstrating the relationship between the corporal bodies, penile fascia, vessels, and nerves ***(James, 2007).***

The blood supply to the penis originates predominantly from the internal pudendal artery, which after giving off the perineal artery becomes the penile artery.

The penile artery branches into the bulbar, urethral (spongiosal), dorsal and cavernous arteries. The cavernous artery enters the corpora cavernosa and subsequently divides into many branches called the helicine arteries, which open into the cavernosal spaces. The **3** sets of veins that drain blood from the penis are the superficial, intermediate and deep veins. The deep veins drain the corpora cavernosa and corpus spongiosum. The penis is innervated mainly by the sympathetic nervous system which originates in the thoracolumbar spinal cord and

the parasympathetic nervous system which originates in the sacral spinal cord ***(Robert and Tom, 2015).***

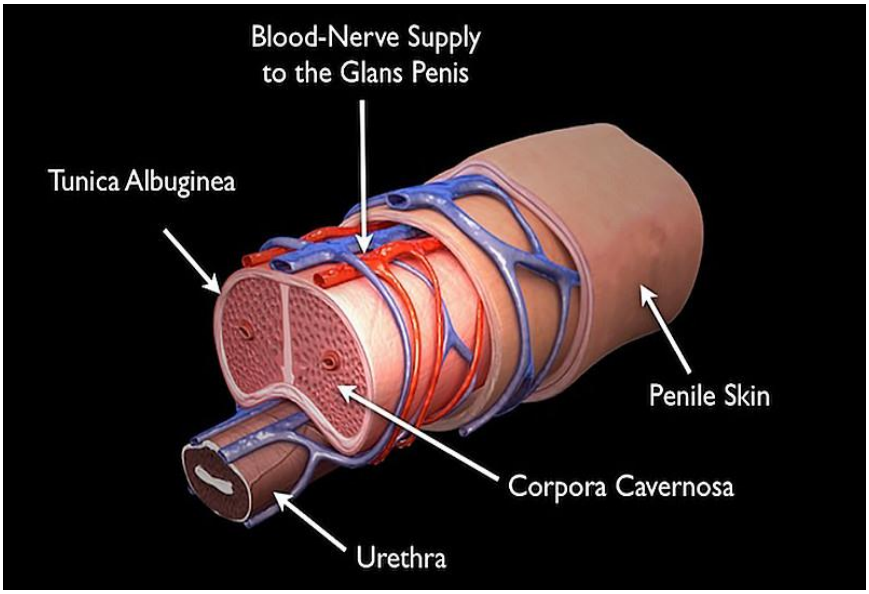

Figure (3): Vascular supply of the penis. ***(John et al., 2004).***

Corpora cavernosa penis:

Each corpora cavernosa begins at the inferior ramus of the pubic bone (*crura penis*) and extends through the penis to the glans ***(Andersson, 2015).***

Corpus spongiosum penis:

The unpaired corpus spongiosum surrounds the urethra and begins between the two crura penis as a thickening (*Bulbus penis*). At the tip of the penis, the corpus spongiosum forms the glans penis. Connective tissue fibers provide a strong connection to the corpora cavernosa ***(Robert and Tom, 2015).***

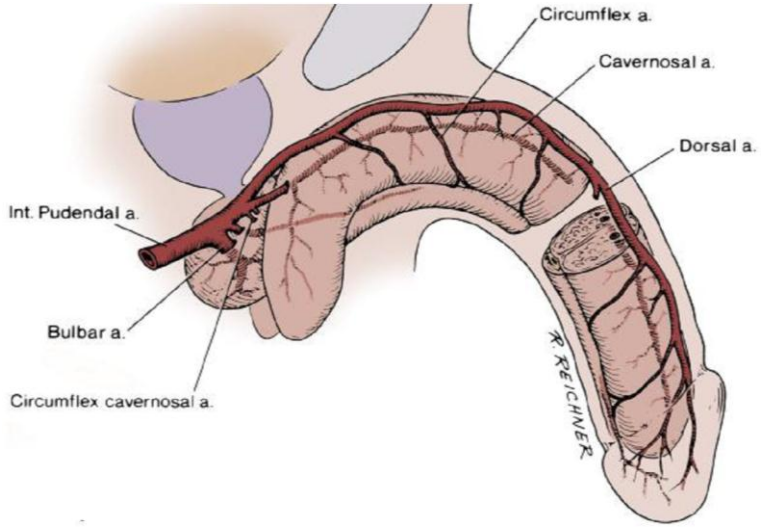

Figure (4): Arterial supply of the penis. ***(John et al., 2015).***

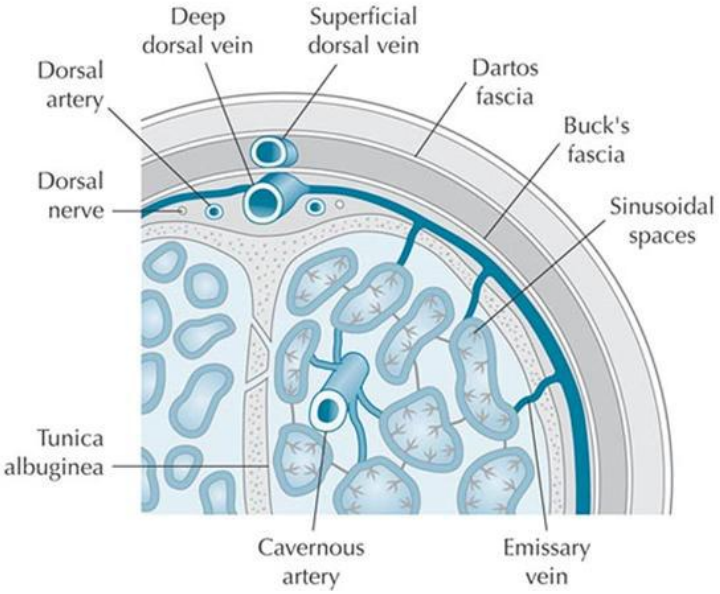

Figure (5): Venous drainage of the penis. ***(John et al., 2015).***

Lymphatics of the penis

The lymphatics of the penile skin drain into the superficial inguinal and subinguinal lymph nodes, the lymphatics of the glans penis empty into the subinguinal and external iliac lymph nodes. The deep lymphatics drain into hypogastric and common iliac lymph nodes ***(Porst and Ira, 2016).***

Innervation of the Penis

CNS:

The processing of sensory stimuli in the limbic system and hypothalamus stimulates the spinal autonomic centers of the erection. The main centers in the hypothalamus are the paraventricular nucleus and the medial area praeoptica.

Spinal autonomic centers:

Cortical and peripheral stimuli activate spinal centers and cause the erection. The Nucleus intermediolateralis (S2–S4) is the parasympathetic spinal center, the sympathetic spinal center is located T12–L2.

Inferior hypogastric plexus:

Gets nerve fibers from the above mentioned centers. The inferior hypogastric plexus sends nerve fibers to the pelvic organs.

Cavernous nerves of the penis:

Autonomic nerve fibers for the penis from the inferior hypogastric plexus, located posterolateral to the seminal vesicles and pass lateral to the prostate (mainly located between 5 to 7 o'clock). In the membranous portion of the urethra, the nerve fibers are located at 3 and 9 o'clock, at the distal bulb of penis they are located at 1 and 11 o'clock, where they enter into the penis. In addition, nerve fibers accompany the arteries or sensory nerves. The autonomic nerve fibers innervate the helicine arteries. The cholinergic nerve endings stimulate the NO-synthase and therefore the release of NO (nitric oxide). The exact mechanism is explained in the section physiology of erection ***(Robert and Tom, 2015).***

Motor neuron innervation:

The pudendal nerve (S2-4) innervates the M. bulbocavernosus and M. ischiocavernosus.

Sensory innervation:

Afferent nerve fibers to move from the receptors via the dorsal penile nerve and pudendal nerve into the spinal cord. Next steps are either the medial lemniscus or spinothalamic tract.

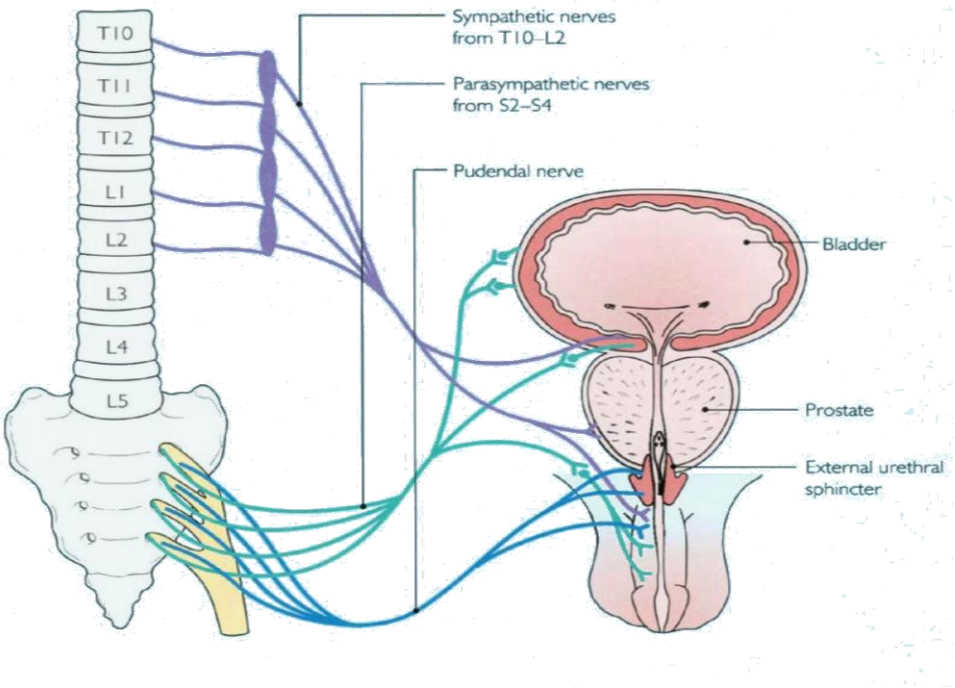

Figure (6): Nerve supply of the penis. ***(Roger et al., 2014)***

Chapter Two

PHYSIOLOGY OF ERECTION

Penile erection is a neurovascular event modulated by psychological factors and hormonal status ***(Lue, 2016).*** Erection is the ultimate response to multiple psychogenic and sensory stimuli from imaginative, visual, auditory, olfactory, gustatory, tactile, and genital reflexogenic sources, which affect several neurological and vascular cascades that lead to penile tumescence and rigidity sufficient for vaginal penetration ***(Kandeel et al., 2016).***

The haemodynamic mechanism of erection

Upon sexual stimulation, neurotransmitters are released from the cavernous nerve terminals and also vasoactive relaxing factors from the endothelial cells of the penis, which results in the following events:

1. Dilatation of the arterioles and arteries by increased blood flow in the diastolic and the systolic phases.

2. Trapping of the incoming blood by the expanding sinusoids.

3. Compression of the subtunical venular plexuses between the tunica albuginea and the peripheral sinusoids, reducing the venous outflow.

4. Stretching of the tunica to its capacity, which occludes the emissary veins between the inner circular and the outer longitudinal layers and further decreases the venous outflow to a minimum.

5. An increase in Po_2 (to about 90 mm Hg) and intracavernous pressure (around 100 mm Hg), which raises the penis from the dependent position to the erect state (the full-erection phase).

6. A further pressure increase (to several hundred millimeters of mercury) with contraction of the ischiocavernosus muscles (rigid-erection phase) ***(Robert et al., 2015).***

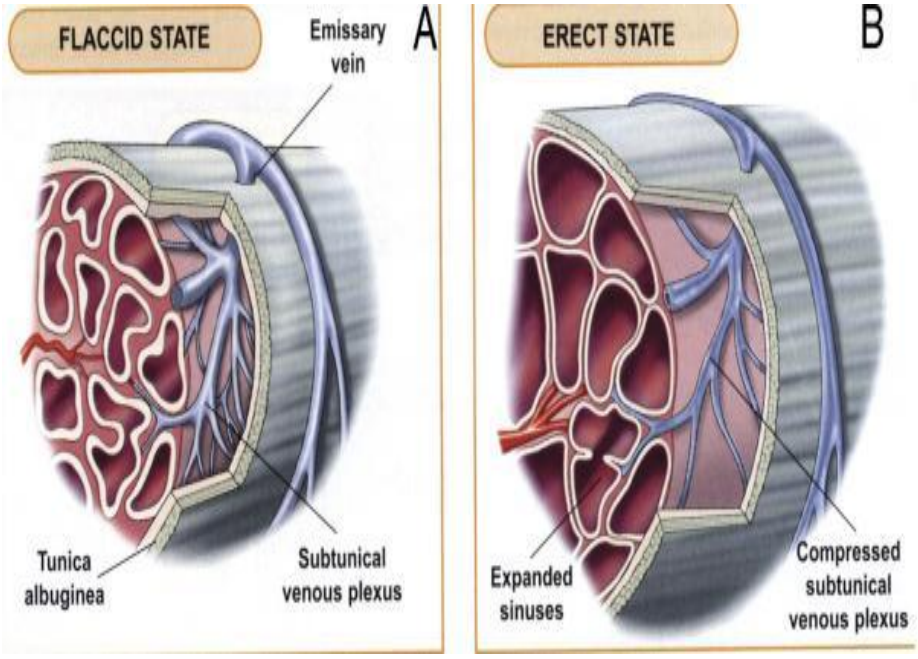

Figure (7): The mechanism of penile erection. (A) In the flaccid state, the arteries, arterioles, and sinusoids are contracted. (B) In the erect state, the muscles of the sinusoidal wall and the arterioles relax, allowing maximal flow to the compliant sinusoidal spaces ***(Lue, 2010).***

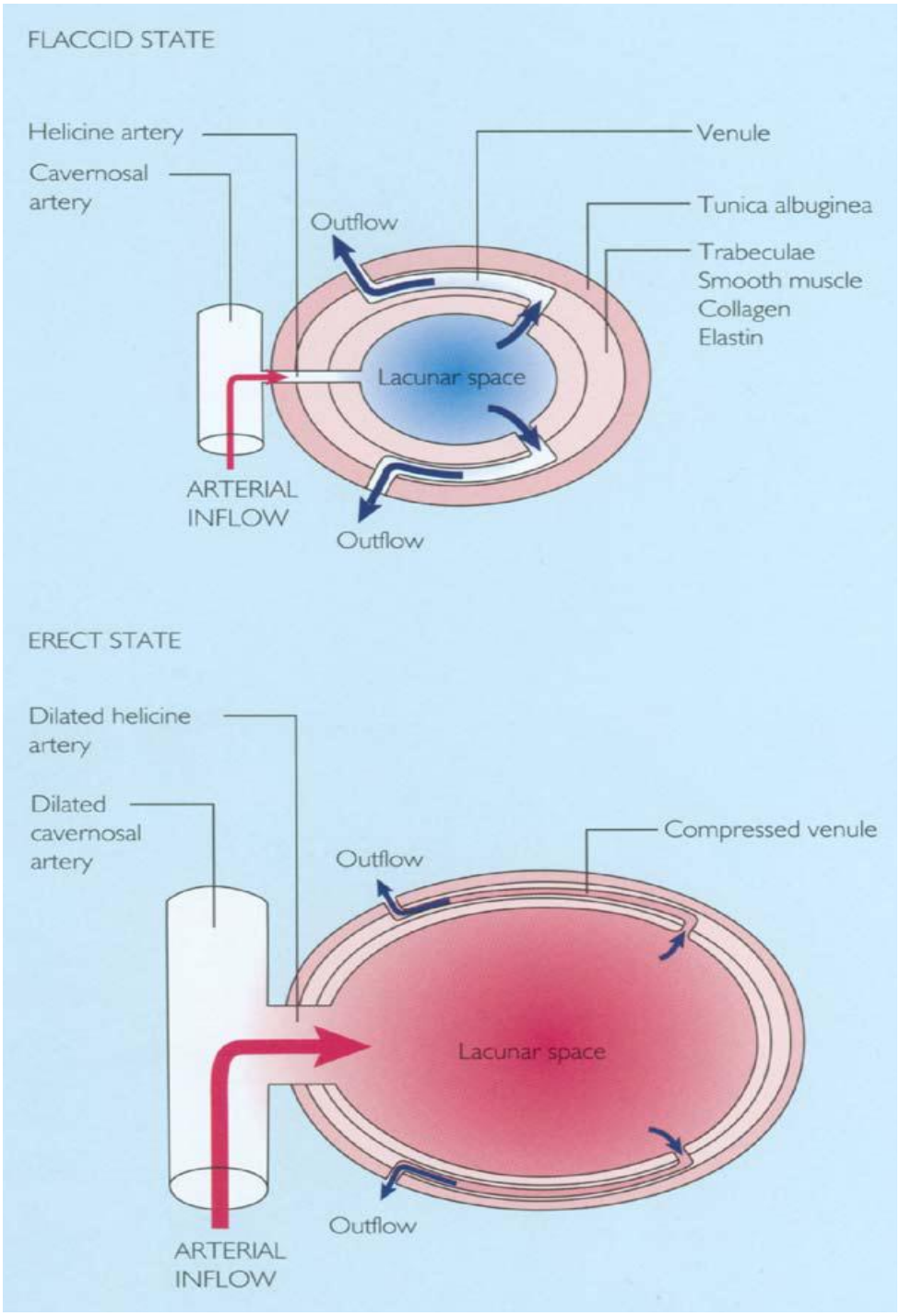

Figure (8): Schematic representation of the hemodynamics of flaccidity and erection ***(Roger et al., 2015).***