INTRODUCTION

Prostate cancer (PCa) represents a significant societal burden, accounting for substantial morbidity and mortality in men with an annual worldwide incidence of about 1 million newly diagnosed cases and about 250 000 deaths ***(Jemal et al., 2012).***

Inspite of a significant worldwide prevelance of PCa especially in Western countries, the ratio of PCa incidence to mortality appears to be relatively high, with nearly 8 times as many men diagnosed with PCa each year than will die of the disease ***(Dall'Era et al., 2012).***

PCa is typically characterized by a heterogenous natural history with remarkable variability in prognosis sequelae and potentiality for aggressive behavior. The majority of detected tumors have a protracted course ***(Klotz, 2007).***

Screening programs for PCa have been widely used worldwide. Compared with clinical diagnosis, PCa screening has resulted in the identification of potentially lethal tumors at a much more curable stage. The widespread use of PCa screening has been associated with significant falls in PCa mortality estimated in some series to range from 30 to 50% ***(Hugosson et al., 2010).***

As a result of PCa screening, the incidence of small, localized, well-differentiated PCa has been increasing.

Currently, most men are diagnosed with localized (organ-confined) PCa at a relatively younger age ***(Klotz, 2013).***

Diagnosis of localized PCa is mainly by measuring of serum prostatic specific antigen (PSA), digital rectal examination (DRE) and trans-rectal ultrasound (TRUS)-guided prostate biopsy. Different imaging modalities seem to have a role in staging rather than diagnosis of localized PCa ***(Madu and Lu, 2010).***

Patients diagnosed with localized PCa have a variety of primary treatment options including radical prostatectomy (RP), definitive radiatiaon therapy (RT), conservative treatment and others. Inspite of such variability, there is a great lack of prospective randomized controlled trials which assess the comparative effectiveness and harms of such treatment options especially for men with screening detected disease. So, it is usually impossible to state that one therapy is clearly superior over another ***(Dall'Era et al., 2012).***

Watchful waiting (WW) have been known as an option for conservative treatment of localized PCa in older men. It was coined in the pre-PSA screening era based on the observation that PCa often progresses slowly, and is diagnosed in older men, in whom there is a high incidence of co-morbidity and related high competitive mortality. At the same time, radical therapy may lead to substantial effects on the patients' quality

of life. Treat was delayed until disease progression and used to be on palliative basis ***(Johansson et al., 2011).***

Active surveillance is the new term for conservative treatment coined in the PSA-screenig era which involves an active decision to delay treatment in well selected groups of patients with low risk PCa and closely follow up patients for any sign of risk upgrading. If happened, treatment will be with curative intent ***(Dall'Era et al., 2012).***

Radical prostatectomy (RP) remains one of the gold treatment standards for localized PCa achieving almost the best cancer control results. RP has been longely performe via an open retropubic or perineal approaches. Recent advances in laparoscopic surgery yielded the laparoscopic approach for RP and the robotic-assisted laparpscopic RP with promising short term results ***(Røder et al., 2012).***

Definitive radiation therapy (RT) have been considered aother main item for localized PCa treatment with long term cancer control results comparable to those of RP. With improved technology of imaging and dosimetry and evolution of computer-based treatment planning systems, conventional RT techniques have largely been supplanted by modern techniques as 3D-conformal RT, intensity-modulated RT and brachytherapy. This provoked further improvement of treatment outcomes ***(Zietman et al., 2010).***

Whole prostate gland ablation using enrgy sources as cryotherapy and high intensity focused ultrasound (HIFU), although have inferior reported tumor control outcomes compared to surgery or radiation, may be potential alternatives in selected group of patients with localized PCa ***(Nomura et al., 2012).***

Minimally invasive modalities of focal therapy represent a hybrid approach which utilize variable energy sources to eradicate known cancer foci within the prostate with the highest likelihood of progressing or metastasizing while attempting to diminish collateral damage to vital structures essential for maintaining normal urinary and sexual function. The results of such techniques in treatment of localized PCa are promising ***(Challacombe et al., 2013).***

Aim of the Work

The aim of this work is to review recent tools and modalities in the treatment of localized prostate cancer, discussing the efficacy of each, treatment outcomes and associated morbidity & complications.

Chapter One

ANATOMY OF THE PROSTATE

Anatomic relations

The prostate is a pyramidal compound tubuloalveolar gland which surrounds the prostatic urethra from the bladder base to the membranous urethra. It lies at a low level in the lesser pelvis, behind the inferior border of the symphysis pubis and pubic arch and anterior to the rectal ampulla, through which it may be palpated ***(Hammerich et al., 2009).***

The gland is 2 cm in anteroposterior and 3 cm in its vertical diameters, and its normal weight ranges from 18-22gm. Superiorly the base is largely contiguous with the bladder neck. The urethra enters the prostate near its anterior border. The apex is inferior, surrounding the junction of the prostatic and membranous parts of the posterior urethra ***(Hammerich et al., 2009).***

Being somewhat pyramidal, the prostate presents a base or vesical aspect superiorly, an apex inferiorly and posterior, anterior and two inferolateral surfaces. The prostatic base measures about 4 cm transversely ***(Hammerich et al., 2009).***

The anterior surface lies in the arch of the pubis, separated from it by a venous plexus (Santorini's plexus) and loose adipose tissue. It is transversely narrow and convex,

extending from the apex to the base. Near its superior limit it is connected to the pubic bones by the puboprostatic ligaments. The urethra emerges from this surface anterosuperior to the apex of the gland. The anterior part of the prostate is relatively deficient in glandular tissue and is largely composed of fibromuscular tissue ***(Villers et al., 2008).***

The two inferolateral surfaces are related to the muscles of the pelvic sidewall: the anterior fibres of levator ani muscle embrace the prostate in the pubourethral sling or pubourethralis. These muscles are separated from the prostate by a thin layer of connective tissue ***(Villers et al., 2008).***

The posterior surface is transversely flat and vertically convex. Near its superior (juxtavesical) border is a depression where it is penetrated by the two ejaculatory ducts. Below this is a shallow, median sulcus, usually considered to mark a partial separation into right and left lateral lobes ***(Villers et al., 2008).***

Prostate capsule

The capsule of the prostate gland is an inseparable condensation of stromal elements composed of collagen, elastin, and abundant smooth muscle that is incomplete at the apex; it does not represent a true capsule ***(Ishidoya et al., 2007).***

At the apex of the prostate, normal prostatic glands can be found to extend into the striated muscle with no capsule. At the base of the prostate, outer longitudinal fibers of the detrusor fuse and blend with the fibromuscular tissue of the capsule. Fibrous septa emanate from the capsule, pierce the underlying parenchyma, and divide it into multiple lobules ***(Ishidoya et al., 2007).***

Prostate fascia

The prostate is covered with three distinct and separate fascial layers: Denonvilliers' fascia, the prostatic fascia, and the levator fascia

Denonvilliers' fascia is a filmy, delicate layer of connective tissue that is a dense condensation of pelvic fascia, developed by obliteration of the rectovesical peritoneal pouch located between the anterior walls of the rectum and prostate. This fascial layer covers the posterior surface of the prostate and extends cranially to cover the posterior surface of the seminal vesicles and the ampullae of the vasa deferentia separating them from the rectum. It terminates below at the striated urethral sphincter ***(Cornu et al., 2010).***

The prostatic fascia is a layer of fascia derived from the endopelvic fascia, continuous anteriorly and anterolaterally with the true capsule of the prostate. The major tributaries of the dorsal vein of the penis and Santorini's plexus travel within the anterior prostatic fascia. Anteroinferiorly the fascia and the capsule of the prostate merge and blend with the puboprostatic ligaments ***(Cornu et al., 2010).***

The levator fascia, which covers the pelvic musculature, fuses anterolaterally with the prostatic fascia to form the lateral pelvic fascia. Posterolaterally, the levator fascia separates from the prostate to travel immediately adjacent to the pelvic musculature surrounding the rectum. The neurovascular bundles (NVBs) are located in the lateral pelvic fascia between the prostatic and levator fascia ***(Raychaudhuri and Cahill, 2008).***

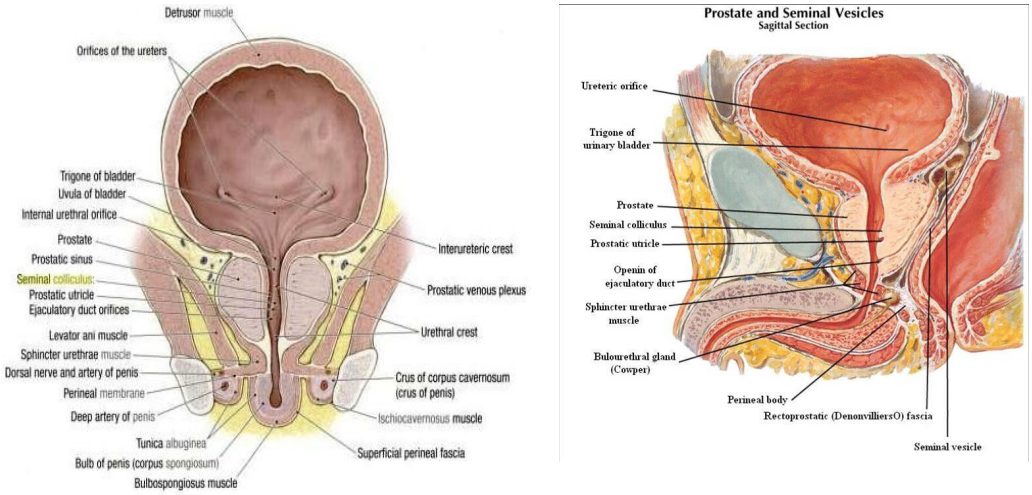

Fig. (1): Anatomy and relation of the prostate ***(Smith et al., 2012)***

Zonal anatomy

The prostate gland was initially thought to be divided into five anatomical lobes, but it is now recognized that five lobes can only be distinguished in the fetal gland prior to 20 weeks' gestation ***(Hammerich et al., 2009).***

Using transrectal ultrasound (TRUS), Mc Neal subdivided the prostate glandular tissue into five distinct zones:

- ***Central zone*:** (25% of volume) surrounds the ejaculatory ducts posterior to the pre-prostatic urethra and is more or less conical in shape with its apex at the verumontanum. Its ducts drain into the distal urethra immediately surrounding the ejaculatory duct orifices. It is rarely involved in any disease and shows certain histo-chemical characteristics which are different from the rest of the prostate and is thought to be derived from the Wolffian duct system.
- ***Transitional zone*:** (5-10% of volume) surrounds the distal part of the pre-prostatic urethra just proximal to the apex of the central zone and the ejaculatory ducts. Its ducts enter the proximal prostatic urethra just below the pre-prostatic sphincter.
- ***Peripheral zone:*** (70% of volume) cup-shaped and encloses the central and transition zones and the pre-prostatic urethra except anteriorly. It constitutes the bulk of the apical, posterior, and lateral aspects of the prostate. Its ducts open into the distal prostatic urethra from the base of the verumontanum to the prostate apex.
- ***Anterior fibro-muscular stroma zone:*** extends from the bladder neck to the stiated EUS, filling up the space between the peripheral zones anterior to the pre-prostatic urethra.

- ***Pre-prostatic sphincter zone:*** is composed of elastin, collagen, and smooth and striated muscle fibres ***(Hammerich et al., 2009).***

Clinically, the prostate have two lateral lobes, separated by a central sulcus that is palpable on rectal examination, and a middle lobe, which may project into the bladder in older men with BPH. These lobes do not correspond to histologically defined structures in the normal prostate but are usually related to pathologic enlargement of the transition zone laterally and the periurethral glands centrally ***(Hammerich et al., 2009).***

The zonal anatomy of the prostate is clinically important because most carcinomas arise in the peripheral zone, whereas BPH affects the transition zone, which may grow to form the bulk of the prostate ***(Hammerich et al., 2009).***

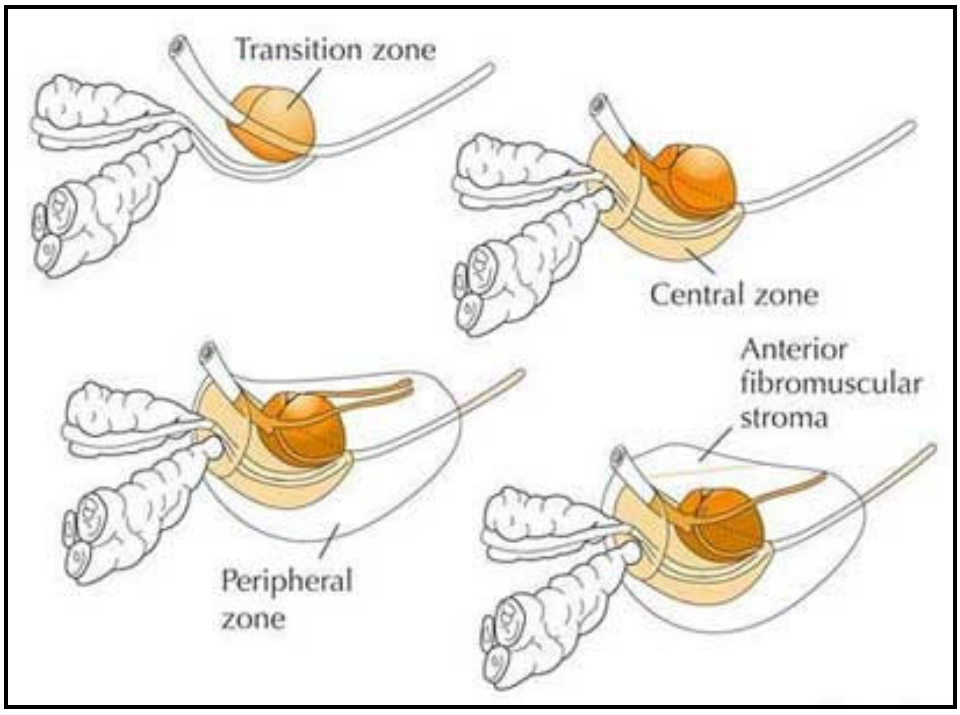

Fig. (2): Zonal anatomy of the prostate ***(Smith et al., 2012).***

Vascular Supply

Arterial supply:

Most commonly, the arterial supply to the prostate is carried by the prostatic artery which arises from the inferior vesical artery. As it approaches the gland, the prostatic artery (often several) divides into two main branches:

The urethral arteries penetrate the prostatovesical junction posterolaterally and travel inward, perpendicular to the urethra. They approach the bladder neck in the 1- to 5-o'clock and 7- to 11 -o'clock positions, with the largest branches located posteriorly. They then turn caudally, parallel to the urethra, to supply it, the periurethral glands, and the transition

zone. Thus, in BPH, these arteries provide the principal blood supply of the adenoma ***(Costello et al., 2004).***

When these glands are resected or enucleated, the most significant bleeding is commonly encountered at the bladder neck, particularly at the 4- and 8-o'clock positions ***(Stolzenburg et al., 2007).***

The capsular artery is the second main branch of the prostatic artery. This artery gives off a few small branches that pass anteriorly to ramify on the prostatic capsule. The bulk of this artery runs posterolateral to the prostate with the cavernous nerves within the NVBs and ends at the pelvic diaphragm. The capsular branches pierce the prostate at right angles and follow the reticular bands of stroma to supply the glandular tissues ***(Costello et al., 2004).***

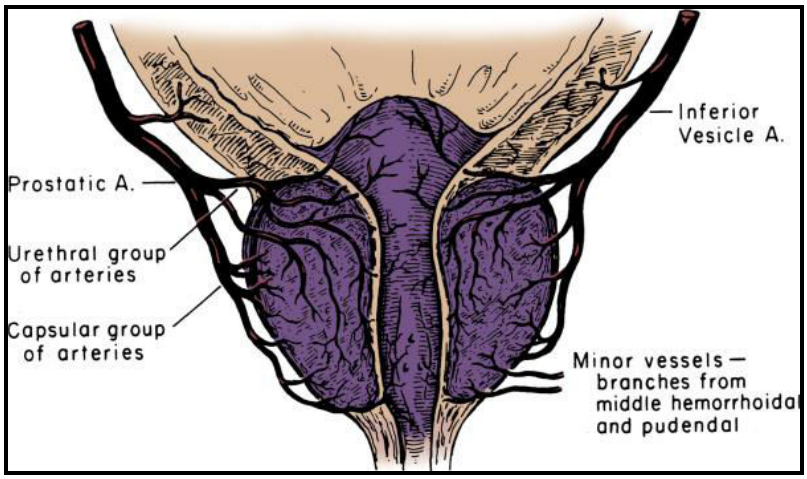

Fig. (3): Arterial supply of the prostate ***(Smith et al., 2012).***

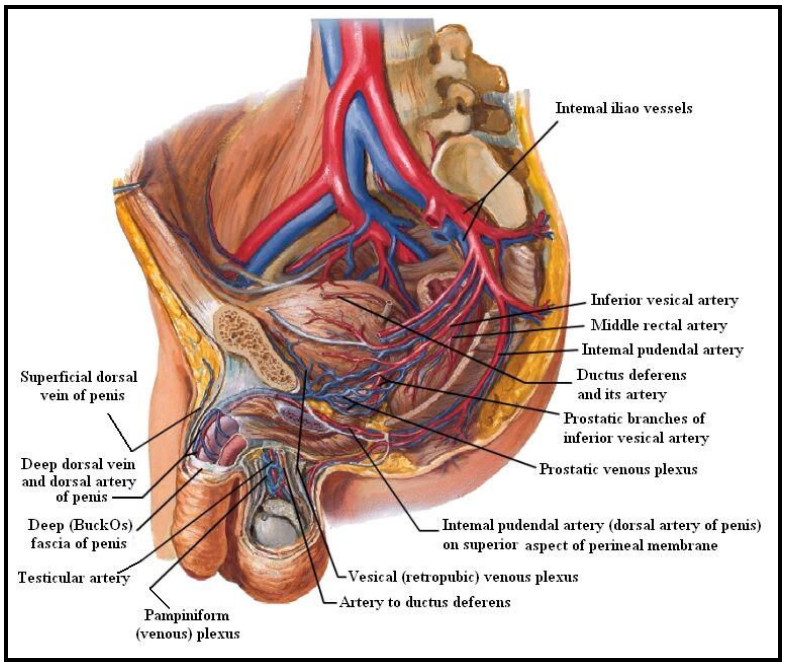

Fig. (4): Arterial supply of the prostate ***(Smith et al., 2012).***

Venous drainage:

The deep dorsal vein leaves the penis penetrates the urogenital diaphragm passes between the inferior pubic arch and the striated urinary sphincter to reach the pelvis, where, dividing into three major branches: the superficial branch and the right and left lateral venous plexuses ***(Walz et al., 2010).***

The superficial branch, which travels between the puboprostatic ligaments, is the centrally located vein overlying the bladder neck and prostate. The superficial branch lies outside the anterior prostatic fascia so this vein is easily visualized early in retropubic operations ***(Wimpissinger et al., 2003).***

The lateral venous plexuses are covered and concealed by the prostatic and endopelvic fascia. The lateral venous

plexuses traverse posterolaterally and communicate freely with the pudendal, obturator, and vesical plexuses. Near the puboprostatic ligaments, small branches from the lateral plexus often penetrate the pelvic sidewall musculature and communicate with the internal pudendal vein. The lateral plexus interconnects with other venous systems to form the inferior vesical vein, which empties into the internal iliac vein. So any laceration of these rather friable structures can lead to considerable blood loss ***(Walz et al., 2010).***

Part of this complex runs within the anterior and lateral wall of the striated sphincter; thus, care must be taken not to injure the sphincter when securing hemostasis ***(Walz et al., 2010).***

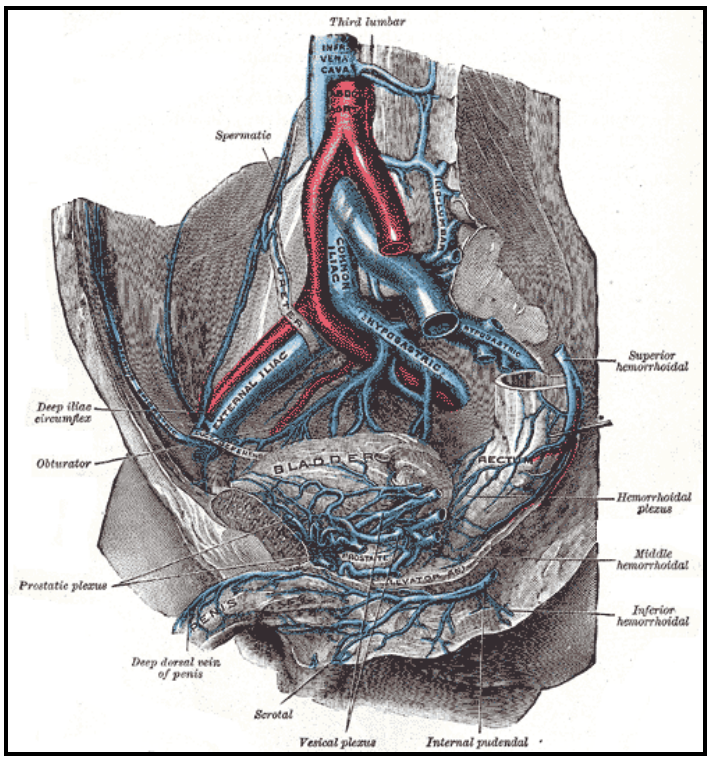

Fig. (5): The veins of the right half of the male pelvis ***(Smith et al., 2012).***