Chapter One

Introduction

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Introduction

Varicocele was discovered nearly 2,000 years ago. It was the Roman physician Cornelius Celsus (42 BC–37 AC) who first observed a decreased testicular size with a correspondingly enlarged hemiscrotum caused by dilated scrotum veins. Varicocele is a collection of abnormally dilated, tortuous spermatic veins SV and is the most commonly seen and correctable cause of male factor infertility (Dubin and Amelar, 1971, Schlesinger, 1994). Although the link between varicocele and male infertility was identified in the 18th century, it was only in 1889 that Bennett described a case of bilateral varicoceles (BVAs) in which semen improved after ''one side had been cured'' by surgery (Bennett, 1889). Since then, various surgical techniques and types of percutaneous treatments have been devised, but discussions about treatment of this condition continue. The most hotly debated issues are: (1) frequency and bilaterality; (2) pathophysiology; (3) clinical diagnosis; (4) correlation with Infertileity; (5) selection of adult and pediatric patients; and (6) outcomes, recurrence, and complication rates of each surgical and percutaneous type of varicocelectomy.

Varicocele is dilation of the pampiniform venous plexus caused by pathological venous reflux resulting primarily from valve incontinence of the internal spermatic vein (WHO, 1992, Aso *et al*., 2005, Dogra *et al*., 2003). The pampiniform plexus (PP) of veins, which normally range from 0.5 to 1.5 mm in diameter, can become 2 mm or larger in diameter.

Incidence of Varicocele 1.2

Varicoceles have an incidence of 4.4%–22.6% in the general population, 21%–41% in men with primary infertility, and 75%–81% in men with secondary infertility (Saypol, 1981; Gorelick & Goldstein, 1993; Johnson *et al*., 1970; Cockett *et al*., 1979). A clinical varicocele is also found in about 15% of all adult males (Clarke, 1966) and 8–23% of young healthy male individuals (Meacham *et al*., 1994; Steeno *et al*., 1976). Varicocele considered left in 70–100% of cases, the right side in only 0–9% of cases and bilateral in 0–23% of cases (Meacham *et al*., 1994; Turner, 1983). While historically varicocele is considered as a left-sided phenomenon, recent published reports have found bilateral varicocele present in 42–77% of infertile males (Narayan *et al*., 1981; Gat *et al*., 2004; Formanek *et al*., 1981; Abdulmaaboud *et al*., 1998; Cockett *et al*., 1984; Trussell *et al*., 2003).

Based on the type of investigation, the incidence of bilateral varicocele is reported to be as high as 80% based on Ultrasound Doppler evaluation (Gat *et al*., 2004; Siegel *et al*., 2006; Trussell *et al*., 2003) whereas it is approximately 8–15% based on physical examination (Kadyrov *et al*., 2007; Nagler *et al*., 1997). When classified according to semen analysis results, 11.7% of infertile men with normal semen analyses and 25.4% of those with abnormal analyses were found to have clinical varicocele (WHO, 1992). Although varicoceles are almost always larger and more common on the left side (Dubin and Amelar, 1977), the incidence of bilateral varicoceles is in the range of 15–50% (Nagler *et al*., 1997; Zini *et al*., 1997; Pasqualotto *et al*., 2003).

Relationship between varicocele and infertility 1.3

Doubts that the varicocele should be considered as a possible cause or a contributing factor in male infertility have existed for centuries, but Tulloch's report of his

experience with surgical correction and subsequent improved sperm counts and postoperative fertility spawn significant research interest on the topic during the early 1950s. He reported that ligation of the spermatic vessels cured a 27-year-old azoospermic male with bilateral varicoceles. Within 3 months of the surgery, spermatozoa had returned to the seminal fluid, and within 9 months the patient's wife became pregnant (Tulloch, 1955). The first studies did not demonstrate any effect of varicocele treatment on fertility (Rodriguez-Rigau *et al*., 1978; Vermeulen *et al*., 1986). When clinical palpable varicocele coexists with impaired semen quality, surgical repair may potentially restore spermatogenesis and fertility.

Reports on varicocele and infertility issued by the Practice Committee of the American Society for Reproductive Medicine and the American Urological Association's Male Infertility Best Practice Policy Committee suggest that ''for infertile couples in which the female partner has no proven (or a potentially treatable) cause of infertility, repair of the male partner's varicocele should be considered if it is clinically palpable and he has abnormal semen parameters'' (PCASRM, 2008; MIBPPC, 2004).

However, the European Association of Urology's guidelines on male infertility cautioned that the issue of varicocele treatment with the aim of achieving pregnancy is controversial (Dohle *et al*., 2005). Meanwhile, the National Institute for Health and Clinical Excellence's clinical guideline on fertility states, ''men should not be offered surgery for varicocele as a form of fertility treatment because it does not improve pregnancy rates'' (NCCWCH, 2004).

In fact the issue of treating varicocele as an infertility disorder remains controversy. Part of the controversy lies in the fact that, despite considerable research, the exact

pathophysiologic mechanism by which varicocele can induce male factor infertility is not known. This is further complicated by the fact that most of the evidence suggesting a positive effect for varicocele repair on male fertility potential is based, to a great part, on retrospective or poorly controlled studies. Out of just four published randomized controlled trials (RCTs) that assess the effect of repairing a clinical varicocele in men with abnormal semen analysis on the couple's pregnancy rate, only two showed a benefit (Abdel-Meguid *et al.,* 2011; Madgar *et al.,* 1995; (Nieschlag *et al.,* 1998; Krause *et al.,* 2002).

Varicocele is the most frequent as well as correctable cause of male infertility. Fertility is decreased in 21–41% of cases of varicocele (Gorelick and Goldstein, 1993). Several hypotheses have been proposed to explain the link between varicocele and infertility. The most important factor is increased scrotal temperature (Turner, 1983; Ali *et al.,* 1990; Charny, 1962; Takihara *et al.,* 1991; Zorgniotti & Macleod, 1973). A testicular hypothermia device (THD) was created which when worn by "hard core" infertile males with varicocele, failed varicocelectomy, or "subclinical" varicocele resulted in lowering of temperature with improvement in semen in many. Pregnancies have resulted. The device is noninvasive and well tolerated (Zorgniotti and Sealfon, 1984).

Methods of diagnosis of varicocele 1.4

Physical examination 1.4.1

The term clinical varicocele refers to those detectable by physical examination, either by palpation or visual inspection. Significant interexaminer variability exists regarding the diagnosis of varicocele depending largely on the level of expertise (Kim *et al.,* 2015).

Physical examination has been the cornerstone of the varicocele evaluation. The scrotum may be warmed with a heating pad to achieve relaxation of the cremaster and dartos muscles, thereby facilitating examination. Scrotal examination should first be performed with the patient supine. The scrotum is visually inspected and the spermatic cord palpated to assess for dilatation of the pampiniform plexus. Each testis is palpated to determine its size (ideally with an orchidometer) and consistency. At this point, the examination is repeated with the patient standing, both prior to and during abdominal straining. Any dilatation or tortuosity of the pampiniform plexus that is visible or palpable in the standing position with or without abdominal straining is diagnostic of varicocele.

The condition is graded at the time of the initial physical examination from 1–3 (Dubin and Amelar grading system) (Dubin and Amelar, 1970).

Grade I varicoceles are detected by palpating an impulse in the spermatic cord veins felt during Valsalva maneuver without enlargement of the veins at rest. Cremaster and dartos muscular contractions elicited by abdominal straining must be carefully discerned from palpable venous impulses within the spermatic cord when assessing for a grade I varicocele.

Grade II varicoceles are palpable with the patient standing even without Valsalva maneuver, but are not visible.

Grade III varicoceles are easily visible through the scrotal skin during standing and classically appear like 'a bag of worms', (Cornud *et al*., 1999). Subclinical varicoceles, not palpable or visible at rest or during Valsalva maneuver.

Physical examination is limited by its inherent subjectivity and depends upon the experience of the examiner, the body habitus of the patient, and the contractile state of the scrotum. Significant interobserver and intraobserver variability in varicocele diagnosis is problematic, even when the physical examination is performed by experienced andrologists (Carlsen *et al*., 2000; Hargreave & Liakatas, 1991). Furthermore, physical examination only detects 50% of varicoceles that are detectable by venography and falsely identifies varicoceles that are venographically absent in 23% of cases (WHO, 1985).

1.4.2 Gray-Scale Ultrasound

The ultrasound appearance of varicocele consists of multiple, hypoechoic, serpiginous, tubular structures. The criteria for diagnosing a subclinical varicocele requires at least the presence of dilated veins with diameter >3.0 mm with concomitant reversal of flow after Valsalva (Lee *et al*., 2007), which usually best visualized superior and/or lateral to the testis. When large, a varicocele can extend posteriorly and inferiorly to the testis (Beddy *et al*., 2005; Dogra *et al*., 2003).

The size of dilated veins usually increases in the upright position and with a Valsalva's maneuver. Low-level internal echoes are often detected in the dilated veins (Fig. 1.1), consistent with slow flow

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(Dogra *et al*., 2003; Pearl and Hill, 2007). Echoes are mobile during respiratory movements, during manual compression, and with a Valsalva's maneuver.
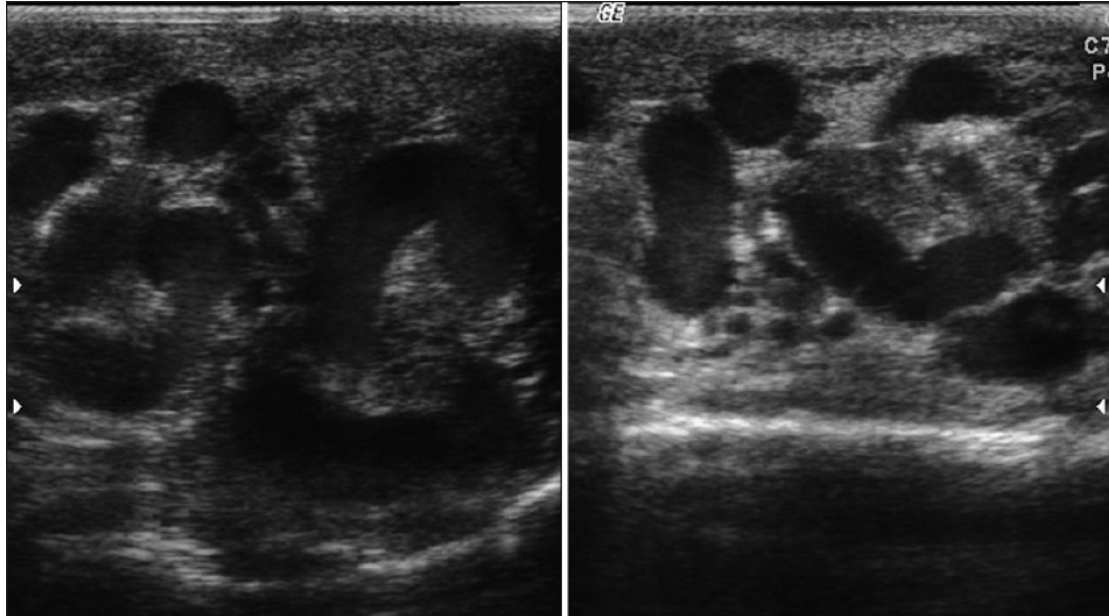

Figure.1.1. B-mode ultrasonography shows multiple serpiginous dilated veins of pampiniform plexus around testis. (Kishore Kumar *et al*., 2012).

Besides evaluation of varices, gray-scale ultrasound allows assessment of the testis as well. Accurate and objective measurement of testicular volume can be obtained more accurately than with physical examination or using an orchidometer. Studies showes strong association between clinical varicoceles and testicular damage was found, as reflected by testicular size (Jarow, 2001; Marks *et al*., 1986; Zini *et al*., 1997). Other studies, however, did not find a close relationship between testicular volume and subclinical varicocele (Sakamoto *et al*., 2008).

1.4.3 Color Doppler Ultrasound (CDUS)

Ultrasound technology has improved considerably in recent years. At present it allows the identification of minimal ectasia of the scrotal veins and minimal retrograde venous flow. Ultrasonography and particularly CDUS appear to be the most reliable and practical methods for diagnosing subclinical varicocele (Kim *et al.*, 2015). A widely accepted ultrasound criterion for diagnosis of varicocele is the existence of veins larger than 2 mm in diameter (Arslan *et al.*, 1998; Gonda *et al.*, 1987; Aydos *et al.*, 1993). CDUS can be used to measure the size of the pampiniform plexus and blood flow parameters of the spermatic vein (Fig. 1.2). Reflux is an important criterion for the diagnosis of varicocele. The change in color is subjective and unreliable for the diagnosis of reflux in CDUS examination and should be quantified with spectral Doppler analysis (Kim *et al.*, 2015).
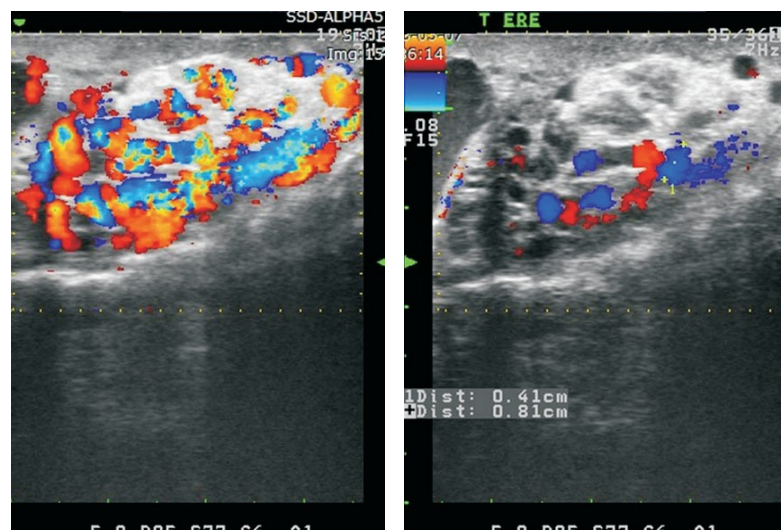

Figure.1.2. Color Doppler ultrasonography of varicocele. Maximal venous diameters in the pampiniform plexus were measured during resting (A) and during a Valsalva maneuver (B) in the standing position (Kim *et al.*, 2015).

Color Doppler ultrasound is the imaging modality of choice for detection and grading varicocele (Callea *et al*., 1997; Aydos *et al*., 1993; Chiou *et al*., 1997), it is more sensitive than clinical examination, and can detect up to 93% of the reflux subsequently confirmed by spermatic venography (Petros *et al*., 1991).

In order to obtain a suitable evaluation of flow changes in the spermatic veins, ultrasound should be performed in the supine and then the upright positions, with and without a Valsalva's maneuver (Fig. 1.3).
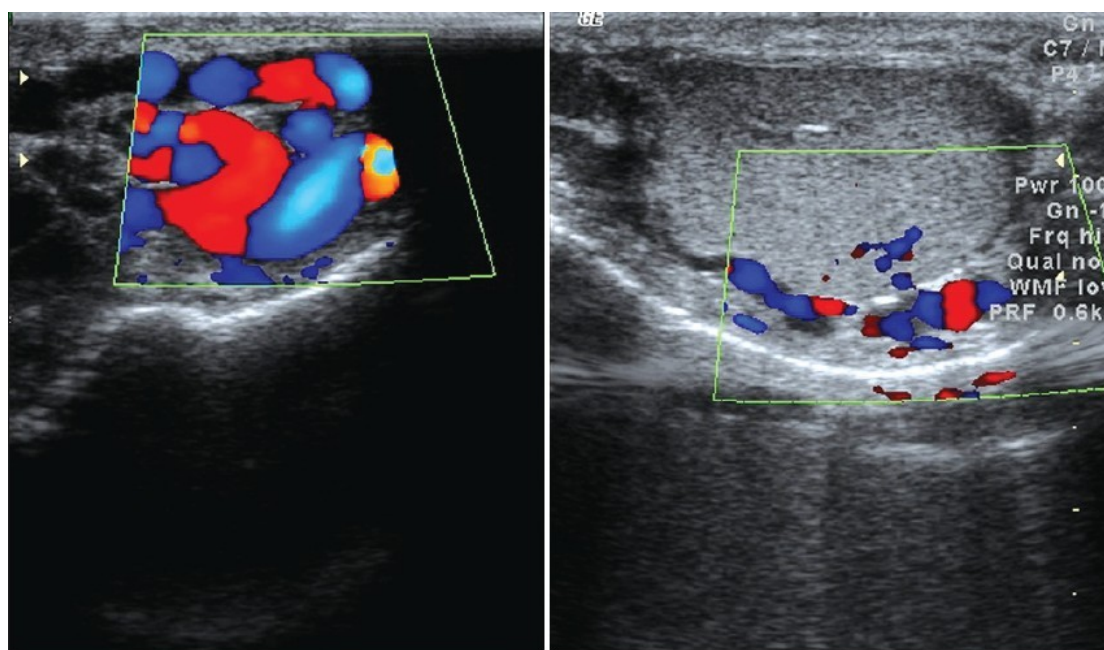
Figure. 1.3. Color Doppler study shows testicular varicocele. (Kishore Kumar *et al*., 2012).

Assessment for varicocele with Color Doppler Ultrasound (CDUS) is indicated when physical examination is indeterminate, such as when the scrotum is small, the patient is obese, or the patient has a history of prior scrotal surgery. It is suggested that the standing position and Valsalva maneuver during CDU could improve

diagnostic ability for varicocele. Resting-Valsalva ratio in the standing position could be a new diagnostic index for varicocele diagnosis using CDU (Kim *et al.*, 2015).

CDUS has significant advantages over physical examination. It is highly sensitive (97%) and specific (94%) (Trum *et al.*, 1996) and theoretically may enable more objective and reproducible assessment of varicoceles.

Most clinicians agree that the presence of multiple veins more than 3mm in diameter with retrograde flow during Valsalva maneuver is diagnostic of varicocele (Lee *et al.*, 2007). Reversal of flow as an indicator of varicocele is detectable in 94–100% of veins greater than 3.5mm in diameter (Bakirtas *et al.*, 2009; Kocakoc *et al.*, 2003; Hoekstra and Witt, 1995), suggesting that CDUS is not necessary to make the diagnosis of varicocele when vein diameter is greater than 3.5 mm.

In contrast, retrograde flow is detectable in 65–85% of veins 2.5–3.5mm in diameter (Bakirtas *et al.*, 2009; Hoekstra and Witt , 1995; Hussein, 2006), and in some cases, significant retrograde flow may be present in veins less than 2.5mm in diameter. In such cases when the maximum venous diameters are small (<3–3.5 mm), the presence or absence and duration of retrograde flow may help to establish the diagnosis of small or subclinical varicoceles.

Besides color Doppler ultrasound, several imaging techniques can be used in imaging varicocele. Scintigraphy and thermography have

been widely used in the past, but currently have no established clinical indications. Venography is currently indicated in selective cases only. MR imaging and CT are of limited clinical use for various reasons, including cost, availability, lack of randomized controlled studies, and lack of outcome data demonstrating that they are equally or more effective compared to venography and color

.(Doppler ultrasound (Geatti *et al*., 1991

Scintigraphy 1.4.4

Scintigraphy allows the noninvasive evaluation of reflux through the internal spermatic vein, which may be useful in planning therapy. Moreover, comparison of features obtained before and after therapeutic interventions allows to verify adequacy of treatment or

.(severity of recurrence (Liguori *et al*., 2011

Scintigraphy, however, is time consuming, and requires use of ionizing radiation. It has largely been superseded by color Doppler

.ultrasound

Venography 1.4.5

Venography shows, in real time, the direction of blood flow in the spermatic veins (Gat *et al.*, 2005), and is generally considered to be the best diagnostic test for varicocele. However, it is time consuming, it requires use of ionizing radiation, and it is an invasive procedure with risks. In patients with varicocele venography shows

enlarged internal spermatic vein with reflux into the abdominal, inguinal, scrotal, or pelvic portions (Fig. 1.4). Collaterals and anastomotic channels can be identified. Similar to color Doppler ultrasound, the degree of reflux can be classified in five degrees (Marsman, 1985).

Figure. 1.4. Varicocele with dilated, tortuous internal spermatic vein. Left and middle: selective; right: supraselective angiogram (Vajda, J *et al*., 1981).

CT and MRI 1.4.6

Varicocele can be identified incidentally in MRI and CT investigations performed for other purposes (Fig. 1.5). Published case reports describe the use of gadolinium-enhanced, three-dimensional, phasecontrast magnetic resonance angiography to evaluate recurrent varicoceles (von Heijne, 1997; Varma *et al*., 1998). This technique has been suggested as an alternative to spermatic venography, it is unlikely to achieve routine use.

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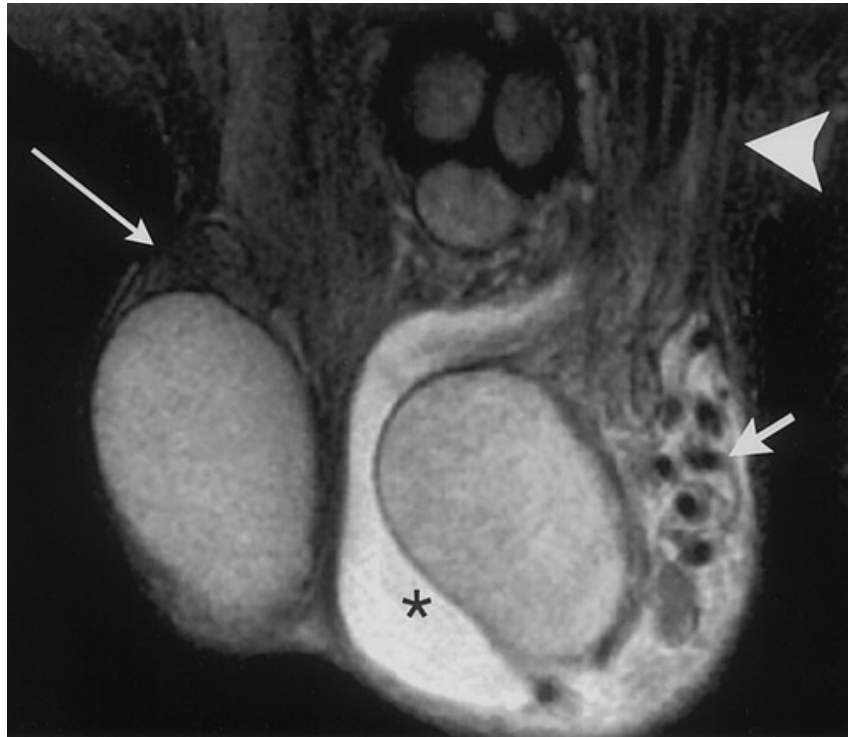
Figure.1.5. Coronal T2-weighted MR image of the scrotum shows the epididymis (long arrow) and the small left-sided hydrocele (*), spermatic cord (arrowhead), and varicocele (short arrow) .((Woodward *et al*., 2003

Thermography 1.4.7

Thermographic assessment of varicocele was first reported in 1979, and widely used for several years. Subsequent studies have found contact termography to be unreliable and to have little clinical utility (sensitivity 97%, specificity 9%) (Basile-Fasolo *et al*., 1986; Trum *et al*., 1996). As a consequence, this technique has largely been superseded by ultrasound. Some authors, however, claim use of thermography, combined with ultrasonography, to improve diagnosis of rightsided and bilateral varicocele (Gat *et al*., 2003; Gat *et al*., 2005).

Semen analysis 1.4.8

The Male Infertility Best Practice Policy Committee of the American Urological Association and the Practice Committee of the American Society for Reproductive Medicine recommended that a minimum of two semen analyses be performed for all men with varicocele associated subfertility (MIBPPC, 2004). Multiple semen analyses are considered essential by most clinicians because significant intraindividual variation in semen parameters is common (WHO, 1999).

Methods of treatment of varicocele 1.5

Understanding the approach taken for varicocele repair is critical for of relevant literature regarding subsequent improvements in end point parameters, as varying treatments are used depending on the severity of the varicocele and may help explain conflicting results.

Surgical treatment 1.5.1

A variety of operative and nonoperative approaches have been advocated for varicocele repair, including open surgical, radiologic, and laparoscopic approaches (Palomo, 1949; Ivanissevich, 1960; Nagler *et al.*, 1997; Cayan *et al.*, 1999; Cayan *et al.*, 2000; Cayan *et al.*, 2001; Cayan *et al.*, 2002; Tefekli *et al.*, 2001) and microsurgical (inguinal or subinguinal). The optimal procedure would be the one that ligates both the veins contributing to the varix at the time of repair and those that could

lead to a recurrence in the future. However, some veins clearly must be preserved so as to allow drainage of the blood from the testis and prevent vascular engorgement. In addition, the procedure should leave intact the testicular arteries, lymphatics, and vas deferens.

Agarwal et al. analyzed 17 studies reporting outcomes of microsurgical varicocelectomy and high ligation series for varicocele treatment in infertile men, and they demonstrated that surgical varicocelectomy significantly improves semen parameters in infertile men with palpable varicocele and abnormal semen analysis (Agarwal *et al*., 2007a).

There have been no randomized, controlled, prospective clinical studies that compare various techniques to describe the best method for the treatment of varicocele in infertile men. The best treatment modality for varicocele can be chosen only after comparing the spontaneous pregnancy outcomes and complication rates of these approaches (Cayan *et al*., 2008).

1.5.2 Interventional Radiology

Interventional radiology has also been employed for varicocele ligation. This is accomplished by percutaneous embolization of the spermatic veins, as identified by transfemoral venography. Embolization materials include balloons, coils, and dextrose (Shlansky-Goldberg *et al*., 1997). Sclerosing agents are commonly used for retrograde occlusion. Newer embolization techniques, employing more expensive materials such as detachable coils and occlusive balloons have been described (Sigmund *et al*., 1987).

Interventional radiology offer occlusion procedures (embolization, sclerotherapy) as minimally invasive outpatient options that have the advantage of venography to delineate anatomy more clearly. Although less invasive, this is the only approach that offers the potential for failure to ligate the varix. Radiointerventional Techniques include Retrograde Sclerotherapy, Acrylic Glue Embolization and Antegrade Sclerotherapy with inguinal or subinguinal Access (Kuroiwa *et al*., 1991).

In Retrograde Embolization -coil Embolization- several groups use stainless coils (Anderson *et al*., 1977), whereas other groups have started using detachable coils, (Coley and Jackson, 1998).

Acrylic Glue Embolization is frequently used in cases of persistent and recurrent postsurgical varicoceles (Sze *et al*., 2008).

In 1994, Tauber and Johnsen were the first to publish an article devoted to antegrade scrotal sclerotherapy (Tauber and Johnsen, 1994). They subsequently reported a success rate of 91% (Johnsen and Tauber, 1996) a better success rate can be obtained with a more accurate technique.

Statement of the problem 1.6

Varicocele embolization is performed in healthy young men with normal life expectancy. Therefore, it is essential that the radiation risks associated with the procedure are minimized. The estimated lifetime fatal cancer risk was of the order of 0.1% (Chalmers *et al*., 2000). During the procedures, patients are partially exposed to the radiation in testicles and other adjacent organs which are considered

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radiosensitive to the radiation. Therefore, stochastic effects (cancer or genetic

mutation are expected, no matter the dose).

In addition,   of adolescent and pediatric patients is based on the desire to prevent

testicular dysfunction and infertility that may be irreversible in adulthood. However,

the debate between microsurgery and interventional radiology is not determined yet.

The successful treatment depends on different factors: pathology and grade of

varicocele, experience of the team dealing with treatment procedures, low re-currency

rate, the pregnancy rate and recovery time.   Internationally, few studies were

performed regarding the treatment outcome and radiation risk. In Sudan, to the best of

our knowledge, no study was performed or published in the open literature.

1.7 Objectives of study

1.7.1 The main objective of the study

The main objective of this study is to: Evaluate the value of the Varicocele Catheter

Embolization versus the microsurgical varicocelectomy among our population in

terms of sperm quality.

1.7.2 The general objectives of the study are to

1-   Evaluate the feasibility of the methods of treatment of varicocele.

2-   Provide an overview of the indications and choices for treatment, as well as

highlight points of controversy in the literature.

3-   Estimate the radiation risks in the Varicocele Catheter Embolization.

4- Optimize the radiation dose to patients during the Varicocele Catheter Embolization procedures.

1.8 Thesis outlines:

This thesis is concerned with the evaluation of treatment methods of varicocele, either by varicocele catheter embolization or by varicocelectomy. Accordingly, it is divided into the following chapters:

Chapter one is the introduction to this thesis. This chapter presents the historical background, incidence, methods of diagnosis and treatment and radiation risks in varicocele, in addition to study problem, objectives and scope of the work. It also provides an outlines of the thesis.

Chapter two contains the background material for the thesis. Specifically it reviews the Anatomy and physiology of the scrotum, Pathophysiology of varicocele, types of treatment methods, and radiation doses in interventional radiolgy. This chapter also includes a summary of previous work performed in this field.

Chapter three describes the materials and methods that used in the evaluation of treatment methods of varicocele.

Chapter four presents the results of this study.

Chapter five presents the discussion, conclusion and recommendations of this thesis and presents the suggestions for future work.

Chapter Two

Theoretical Background

Chapter Two

Theoretical Background

Anatomy and physiology of the scrotum 2.1

Among the male reproductive system, the scrotum, a thin external sac of skin, contains the two testes, the epididymes and part of the spermatic cord. The scrotum is a cutaneous pouch divided in its surface into two lateral portions. It is derived from the labioscrotal folds, which under the influence of testosterone, swell and fuses to form twin scrotal sacs. The point of fusion is the median raphe,

which extends from the anus along the perineum to the ventral

surface of the penis (Larsen, 1993).

The testes, or testicles, are two glandular organs, which secrete the semen, and are suspended in the scrotum by the spermatic cords. Usually, the left testis hangs lower than its fellow. They normally, complete their descent into the scrotum from their point of origin on the back wall of the abdomen in the seventh month after conception. At an early period of fetal life the testes are contained in the abdominal cavity, behind the peritoneum. Before birth they descend into the inguinal canal with the spermatic cord, and then into the scrotum, becoming invested in their course by coverings derived from the serous, muscular, and fibrous layers of the abdominal walls, as well as by the scrotum. Testicular size depends on age and stage of sexual development. At birth, the testes measure approximately 1.5 cm in length and 1 cm in width. Before the age of 12 years testicular volume is around 1–2 cm^3. Clinically, a male individual is considered to have reached puberty once the testis achieves volume of 4 cm^3. On average, testes of adults are 3.8 cm long, 3 cm wide, and 2.5 cm deep and have a volume of 30 ml. The weight varies from 10.5 to 14 g (Leung *et al*., 1984).

Prepubertal testes ultrasound shows low to medium echogenicity, whereas pubertal and postpubertal testes are of medium homogeneous echogenicity, reflecting the development of germ cell elements and tubular maturation (Siegel, 1997). Each testis is enclosed in a fibrous inextensible sac, the tunica albuginea. This sac

is lined internally by the tunica vasculosa, which contains a network of blood vessels, held together by areolar tissue. The anterior border, lateral surfaces, and both extremities of the testis are convex, free, smooth, and invested by the visceral layer of the tunica vaginalis. The posterior border of the testis, to which the cord is attached, receives only a partial investment from that membrane and is covered by the epididymis on the lateral edge. The mediastinum testis (corpus highmori) is an invagination of the tunica albuginea, from which multiple septa (trabeculae) arise dividing the testis into multiple (250–400) lobules (Fig. 2.1a). The mediastinum extends from the upper to near the lower extremity of the gland, and supports the vessels and ducts of the testis in their passage to and from the parenchima of the gland.
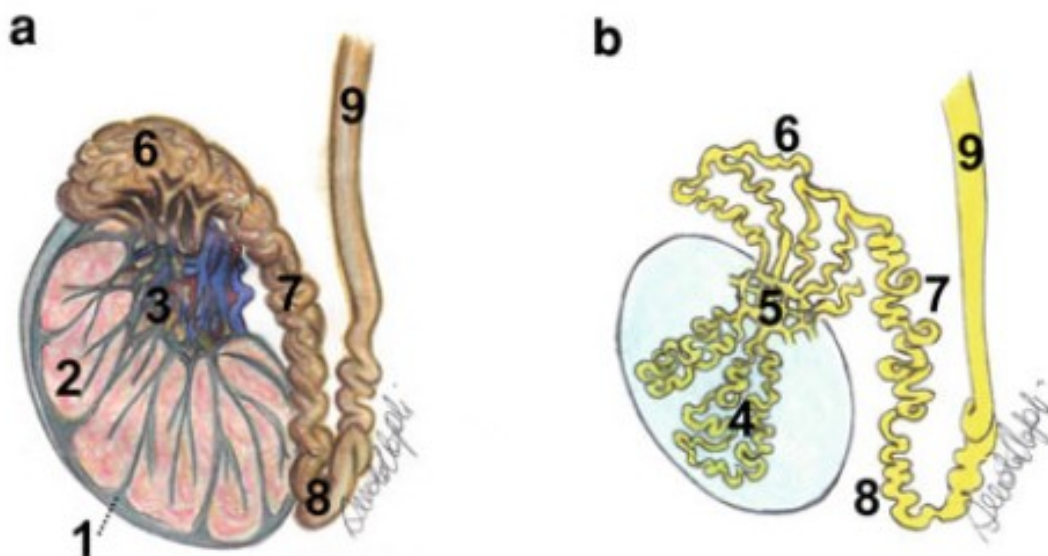
Figure. 2.1. Anatomy of the testis. 1- Tunica albuginea. 2- Lobules. 3- Mediastinum testis. 4- Seminiferous tubules. 5- Rete testis. 6- Head of the epididymis. 7- Body of the epididymis. 8- Tail of the epididymis. 9- Vas deferens (Liguori, G, 2012).

Structure of the Testis 2.1.1

The lobules are cone-shaped spaces that become narrower as they converge to the mediastinum and contains one to three convoluted seminiferous tubules (Fig. 2.1b). These are supported by loose connective tissue which contains somewhere groups of ''interstitial cells'' (Leydig cells) responsible for testosterone production. The total number of tubules is estimated at 840, and the average length of each is 70–80 cm. Their diameter range from 0.12 to 0.3 mm. Within the tubules spermatocytes and the supporting Sertoli cells give rise to sperm. The development of the spermatozoa begins around the inner extremities of the supporting cells.

Epididymis 2.1.2

Sperm cells produced in the testes are transported to the epididymes, where they mature and are stored. Each epididymis has three regions (Fig. 2.1a), called, respectively, the head (globus major), body, and tail (globus minor). Sperm cells mature primarily in the head and body of the epididymis and are stored in the tail (Bostwick, 1997).

In ultrasound of the testicles, the head of the epididymis is usually isoechoic to the testis, and its echotexture may be coarser than that of the testis (Bree and Hoang, 1996; Dambro *et al*., 1998). The narrow body of the epididymis (2–4 mm in diameter), when normal, is usually indistinguishable from the surrounding peritesticular tissue. The tail of the epididymis (globus minor) is approximately 2–5 mm in diameter and can be seen as a curved structure at the inferior pole

of the testis, where it becomes the proximal portion of the ductus

.deferens

Vascular Supply 2.1.3

The right and left spermatic arteries, branches of the abdominal aorta, arise just distal to the renal arteries and provide the primary vascular supply to the testes (Fig. 2.2). They enter the spermatic cord at the deep inguinal ring and divide into two main branches: testicular and epididymal artery. Testicular artery continues along the posterior surface of the testis, penetrating the tunica albuginea and building a vascular terminal system, made of capsular and

.intratesticular arteries, within the tunica vasculosa
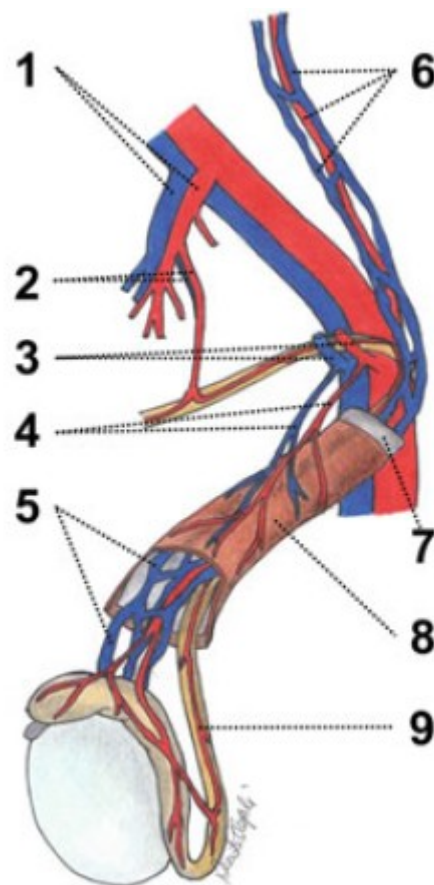
.**Figure**. 2.2. Vascular Anatomy of the testis

1- Internal iliac vessels. 2- Deferential vessels. 3- Inferior epigastrc vessels. 4- External spermatic vessels. 5- Pampiniform plexus. 6- Internal spermatic vessels. 7-Internal spermatic fascia. 8- Cremasteric muscle. 9- Deferential vessels.   (Liguori, G, 2012).

A transmediastinal arterial division of testicular artery is evident in approximately 50% of normal testes; it courses through the mediastinum to supply the capsular arteries and is usually accompanied by a large vein (Middleton and Bell, 1993). The deferential artery, a branch of the superior vesicle artery, and the cremasteric artery, a branch of the inferior epigastric artery, supply the epididymis, vas deferens, and peritesticular tissue (Siegel, 1994). The number and locations of anastomoses vary between the testicular artery and its branches and between the artery to the vas deferens and the cremasteric artery. Branches of the pudendal artery supply the scrotal wall.

2.1.4 Venous drainage

Venous anatomy of the scrotum is very complex (Dogra *et al*., 2003). The subcutaneous veins are divided into anterior and posterior scrotal veins. The former drain into the external pudendal veins drained themselves into the major saphenous or directly into the femoral vein. The latter drain into the internal pudendal vessels through the deep dorsal vein of the penis. The deep venous system originates as a plexus, anatomically schematized into anterior and posterior pampiniform plexuses. This plexus runs with a pattern of a decreasing number of constituents into the spermatic funicle forming three main groups; anterior group: including the spermatic

vein, intermediate group: including the ductus deferens vein (a layer of the internal spermatic fascia separate it from the anterior group); posterior group: including the cremasteric veins.

The anterior pampiniform plexus drains the blood coming from the testicle and the head of the epididymis. It is composed of 3–9 veins greatly connected with the deferential and cremasteric veins in a large amount of anastomoses. The normal size of these veins ranges from 0.5 to 1.5 mm in diameter, with the main draining vein being as large as 2 mm in diameter. Beyond the internal inguinal orifice, the spermatic vein turns back into the retroperitoneum; here this vein can be single, double, or even multiple. On the left side, the spermatic vein connects with the left renal vein, whereas on the right side it drains directly into the vena cava. It is a propulsive-type vein, as mostly happens below the diaphragm. Most of these veins that drain blood against gravity, contain semilunar valves, forming membranous pouches, in order not to allow blood reflow. It is highly discussed in the scientific literature whether semilunar valves are present within the spermatic vein or not. There is no clear evidence of a role of the semilunar valves on varicocele's pathogenesis (Wishahi, 1992).

The deferential, cremasteric, and external pudendal vein originate from the posterior pampiniform plexus and are highly connected with several anastomoses building a supplementary circulation system. Whereas the contribution of deferential and cremasteric veins to the total amount of blood drainage is low, both in healthy

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and varicocele-suffering men, on the contrary, the external pudendal vein plays an important role, especially after the treatment of varicocele (ligation or sclerotization of the internal spermatic veins). The deferential vein ascends with the deferential artery and duct within the spermatic cord and drains into the vesicoprosthatic plexus. Therefore, it is connected to the internal iliac vein: its preservation after varicocele correction prevents testicular congestion. The cremasteric vein (or external spermatic veins) runs into the posterior section of the deep venous system of the testis outside the funicle, and drains blood into the inferior epigastric or into the big saphenous vein to the external iliac vein.

2.1.5 Spermatic Cord

The vas deferens, testicular artery, cremasteric artery, deferential artery, pampiniform plexuses, genitofemoral nerve, and lymphatic vessels compose the spermatic cord, which begin at the deep inguinal ring and descends vertically into the scrotum. The spermatic cord or funicle is an organ of cylindrical shape surrounded by adipose tissue and enveloped within three fasciae: the external spermatic fascia, the cremasteric fascia and muscle, the spermatic cord should be evaluated in every scrotal ultrasound examination. It lies just below the skin but can sometimes be difficult to discriminate it from surrounding soft tissue (Woodward *et al*., 2003).

2.1.6 Lymphatic vessels

Lymph vessels are made of 4–8 collector ducts, that run aside to the spermatic vessels, and reach abdominoaortic lymph nodes along

aortic biforcation, until renal vessels. There is also a supplementary lymphatic pathway reaching the external iliac lymph nodes.

It is important to consider that urogenital anomalies are frequent and obviously associated with SV variations (Livera *et al*., 1989). Renal anomalies generate significant problems for renal vein and SV catheterization; therefore, renal ultrasound examination before percutaneous treatment is strongly recommended.

2.2 Pathophysiology of varicocele

The pathophysiology of varicocele has been attributed to one of three primary factors: increased venous pressure in the left renal vein or gonadal vein, reflux in the collateral veins, and incompetent ISV valves (Naughton *et al*., 2001). Varicocele may be primary (idiopathic) or secondary. Primary varicocele is considered to result from mesoaortic compression of the left renal vein (LRV) and is particularly evident when the patient is standing (''nutcracker syndrome'') (Mali *et al*., 1986, Verstoppen and Steeno, 1977).

Increased intrarenal and spermatic venous pressure, which creates venous reflux in the spermatic plexus, could also be related to anatomical variations of the LRV.

Secondary varicocele can be due to compression of the PP draining veins in cases of pelvic, abdominal and renal tumors, lymphomas (Roy and Steeno, 1989), and cecum cancer. Nontumor causes of secondary varicocele can be hydronephrosis and hydroureter (Dogra *et al*., 2003). A pseudoaneurysm consequent to an aortic graft can produce an RVA (Corlett *et al*., 1992). A high-flow arteriovenous

fistula caused by rupture of an aortic aneurysm in the LRV results in a secondary left varicocele (LVA) (Linsell *et al*., 1987). Varicocele may be also caused by a splenorenal shunt due to portal hypertension. Therefore, in secondary varicocele, the PP venous ectasia never disappears when the patient is in a supine position.

2.2.1 The pathophysiology of varicocele-related infertility

The classical theories of varicocele formation include theories concerning the mechanisms by which dilated scrotal veins impair spermatogenesis and cause infertility. The literature primarily includes studies on the progressive toxic effects of varicoceles, elevated temperature, adrenal hormone reflux, gonadotoxic metabolite reflux, altered testicular blood flow, antisperm antibody formation, alterations in the hypothalamic-pituitary-gonadal axis, and oxidative stress. Because the detrimental effects of varicoceles on spermatogenesis are apparently related to several factors that may act synergistically, it is difficult to explain the mechanism of action using only one theory. In healthy males, the scrotal temperature is 2 °C lower than the core body temperature. A testicular temperature that is identical to the core body temperature is associated with a decrease in the sperm count and sperm quality. Although the exact mechanism by which the temperature influences spermatogenesis is not clearly known, the most commonly accepted theory is thermal damage to the DNA and proteins in the nucleus of spermatic tubule cells and/or Leydig cells It has been reported that

men with varicoceles and impaired sperm quality have elevated scrotal temperatures and that varicocelectomy leads to a normal scrotal temperature (Naughton *et al*., 2001, Fujisawa *et al*., 1989). Venous hypertension, caused by the exertion of pressure on the gonadal venous valves by a hydrostatic column can cause chronic vasoconstriction of testicular arterioles, thereby reducing testicular function (Sofikitis and Miyagawa, 1993). This phenomenon leads to persistent hypoperfusion, stasis, hypoxia, and subsequent dysfunction of the spermatic epithelium (Marmar, 2001). Antisperm antibody formation is another theory for explaining varicocele-related male infertility. Infertile men have higher levels of testicular autoantibodies in their serum than fertile men. Currently, based on animal experiments, artificial varicocele induction does not cause rupture of the blood-testis barrier and is not correlated with an increase in antibody levels (Turner *et al*., 1996). Moreover, based on direct immunobead assays, varicoceles in infertile men do not alter the autoantibody level (Oshinsky *et al*., 1993). This theory has yet to accumulate sufficient evidence-based support. Another debatable pathophysiological theory of varicocele- related infertility is that varicoceles negatively affect the hypothalamic-pituitary-gonadal axis. Some patients with varicoceles were reported to have low testosterone levels and sperm quality, which were reversed via varicocelectomy (Cayan *et al*., 1999; Hurtado de Catalfo *et al*., 2007). The mechanism of effect of varicoceles on the hypothalamic-pituitary-gonadal axis is related to Leydig cell injury and an increase

in the heat-associated malfunction of intratesticular enzymes acting on spermatogenesis (Will *et al*., 2011). Oxidative stress secondary to elevated scrotal temperatures and the formation of reactive oxygen species (ROS) is another important theory for explaining the negative effects of varicoceles on testicular function; this explanation is gaining more support over time (Shiraishi *et al*., 2010, Agarwal *et al*., 2007b). In addition to other gonadotoxic factors associated with varicoceles, ROS also oxidize fatty acids in spermatozoa membranes and cause DNA damage and .(fragmentation of the sperm (Twigg *et al*., 1998

The etiology of varicocele was described in the past, and was shown to be accompanied by changes in blood supply (Shafik *et al*., 1972; Sayfan *et al*., 1984), hormones (Hudson *et al*., 1986; Nagao *et al*., 1986), and tissue metabolism (Comhaire and Vermeulen, 1974; Ito .(*et al*., 1982

The etiology and pathophysiology of varicocele appears complex and multifactorial. Evidence indicates that the phenomenon is age dependent, as the incidence in prepubertal boys is extremely rare and increases to about 15% in adolescents (Gorelick and Goldstein, 1993). In addition the effects of a varicocele on semen parameters, testicular size, and other indices of testicular function progress with time as men with a varicocele older than 30 years have lower sperm concentrations, impaired Leydig cell function, and lower Testosterone concentrations (WHO, 1992; Zini *et al*., 1997; Chehval and Purcell, 1992). However, significant variability exists in the

effect of varicocele on male fertility. Varicoceles have been observed in both fertile and infertile men. As a result, it seems that varicoceles may impair spermatogenesis, but with only clinical consequences in some men. Most varicoceles are left sided, possibly due to anatomical configuration with a more vertical inlet of the internal spermatic vein to the renal vein as opposed to a more oblique inlet on the right. As a result, the hydrostatic pressure in the left venous system is higher, whereas the tapering configuration on the right side may protect against venous reflux. Defective or missing venous valves also play an important role in the pathogenesis (Braedel *et al*., 1994). Other anatomical variants that lead to partial compression of the venous system, such the left renal vein between the aorta and the superior mesenteric vein (''nutcracker syndrome'') or extrinsic pressure from retroperitoneal processes on the internal spermatic vein, can also contribute secondarily to the development of a varicocele (Graif *et al*., 2000). Histologic studies of testicular biopsies of patients with varicocele indicate varying levels of dysfunction. Abdelrahim et al. studied bilateral testicular biopsies from 30 infertile patients with varicocele taken both during varicocelectomies and postoperativly. Compared with healthy control subjects, preoperative biopsies showed reduced spermatogenesis with maturation arrest, dead spermatogenic epithelium (Abdelrahim *et al*., 1993).

Despite ongoing extensive research on varicoceles, the exact mechanism(s) by which varicocele influences male fertility is not

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known. Regardless of specific mechanisms, it seems likely that the pathophysiology of varicocele is multifactorial and involves additional effects that inter-relatedly increase the detrimental effects on spermatogenesis. Differences in the incidence of these factors may, in part, explain the conflicting literature relating to varicocele-associated infertility.

2.3 Types of Embolization

2.3.1 Retrograde Embolization

Percutaneous embolization of the gonadal vein was originally described in the late 1970s (Iaccarino, 1977; Lima *et al*., 1978). It is an outpatient procedure, performed using mild intravenus sedation and local anesthesia, thus eliminating the risks associated with general anesthesia (Halden and White, 1987; Smith and Sewall, 2009; Zuckerman *et al*., 1994). It can be either retrograde or antegrade according to the direction of the sclerosing agent.

Standard Procedure Patients with congenital or acquired hemostatic disorders can undergo retrograde embolization only after prophylactic measures. Patients must be monitored and instructed how to perform the Valsalva maneuver. Retrograde embolization is usually performed in the outpatient clinic with the patient under local anesthesia, and if necessary, mild sedation. The angiographic catheter is introduced into the venous system either via the right femoral vein, the right jugular vein, or the basilic vein. The use of 4–5 F hydrophilic catheters and hydrophilic guidewires that do not cause venous spasms are recommended. In cases of difficult

spermatic vein catheterization e.g., of a continent subrenal valve, it is preferable to use a braided superior torque control catheter with appropriate tip configuration. The percutaneous vascular access is normally through the right common femoral vein, if spermatic vein catheterization is not possible, proximal brachial access is preferred, especially for right spermatic vein (Kuroiwa *et al*., 1991). Before retrograde embolization, diagnostic phlebography study of the spermatic vein is performed. Subsequently, hydrophilic guidewire are used to ensure that the catheter tip reaches the more distal part of the spermatic vein. Generally, the catheter tip must reach the lower edge of the ischiopubic ramus (Fig 2.3).
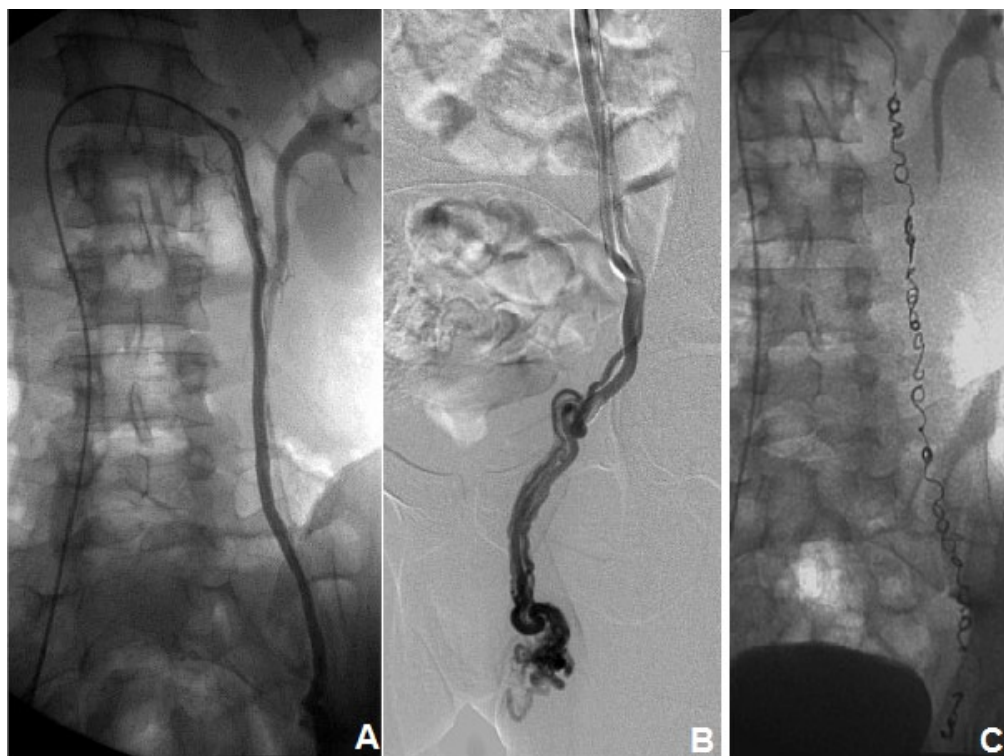

Figure. 2.3. Subsequent venograms (A-B) through a sheath show reflux into the scrotum. A parallel vein is present. (C) Image shows coil embolization from just above the inguinal ligament to a few centimeters from the renal vein (Bittles and Hoffer, 2008).

In more complex cases, a road map must be obtained, and a microcatheter with a 0.018 inch hydrophilic guidewire is used. Once distal catheterization is obtained, a rubber band must be applied at the highest level of the scrotum and contrast media is immediately injected during a Valsalva maneuver to check that there is no reflux in the PP below the rubber band. Depending on the size of veins, it is recommended that 2–6 ml of 3% Na-tetradecyl-sulphate be injected in the anterior PP during the Valsalva maneuver and with the patient in the reverse Trendeleburg position. Scrotum elastic compression continues to be applied for 1 min and then is released with the patient in the Trendeleburg position to prevent posterior PP phlebitis. If sclerosant remains in the anterior PP, the procedure ends. Otherwise, embolization is repeated 10 min later, as described previously. Spasms and/or lacerations occur more frequently in children than in adults. In such cases, 1 ml aliquots of nitroglycerin (100 µg/ml) can be injected or the physician can wait several minutes before continuing the procedure. For cases of severe venous laceration, a microcatheter can be placed further downstream. In case of persistent contrast extravasations, the procedure should be postponed for 1 month. In case of a large spermatic vein, or in patients with bidirectional flow because of increased cardiac output in addition to distal barrage, a temporary proximal compliant balloon catheter of suitable diameter is also recommended to obtain a closed venous system with the double barrage. To ensure the sclerosant is always visible, 20% of contrast

media can be added to avoid occlusion of dangerous collateral anastomoses with mesenteric or splenic veins, which can open during double barrage. After inguinal barrage, inject 10–20 ml of CO_2 followed by sclerosant through a three-way stopcock (Fig 2.4). .This procedure results in much more effective and faster sclerosis
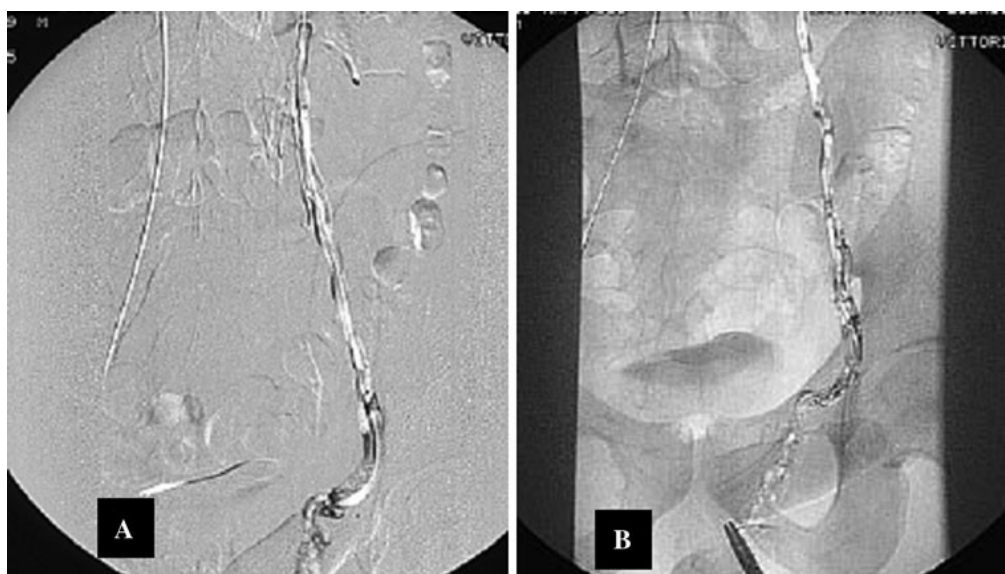
Figure. 2.4.   (A) CO_2 Digital subtraction angiography of a large LSV with a large collateral venous plexus, (B) The barrage was positioned at the ischiopubic level without visualization of CO_2 and .(sclerosant below the clamp (Iaccarino. and Venetucci, 2012

This procedure results in occlusion of all collateral veins, even those not visible at phlebography, but with time these veins may increase in size and generate recurrences. In contrast, recurrences will not occur when all of the anterior PP is occluded. Indeed, mechanical occlusion means or gluing agents can be considered equivalent to .surgical vascular ligation

Moderate hemoglobinuria occurred in a few cases in which the sclerosant exceeded 15 ml. This can happen with all sclerosant

agents and subsides after adequate hydration. Patients are usually discharged 2 h later with the following recommendations: resume normal activity after 48 h, avoid heavy physical activity for 7 days, assume a liquid diet for 3 days to prevent constipation, clinical check-up after 1 month, ultrasound Doppler examination after 3 months and semen analysis after 4–6 months. Several interventional radiologist use stainless coils (Anderson *et al*., 1977; Gianturco *et al*., 1975), whereas others have started using detachable coils (Coley and Jackson, 1998).

All coils are now magnetic resonance imaging (MRI)-compatible and are available in 0.035- and 0.038-inch sizes and in various lengths and diameters (3–12 mm). They have fibers to promote thrombosis. Venous embolization is safer and more accurate with these coils; moreover, they allow distal occlusion. A coil can be safely removed from the catheter before its detachment in case of inappropriate size or position (Coley and Jackson, 1998). Detachable microcoils are available for cases of more distal occlusion in the inguinal canal. These low-profile systems are equipped with a 0.014 inch guidewire, which allows more precise embolization. Selective catheterization of the left spermatic vein can be performed with the Left Vena Spermatica Coaxial Infusion Set AQ Hydrophilic Coating (Cook Medical) and the microcatheter directed, if possible, up to inguinal canal (Bechara *et al*., 2009). Another advantage of detachable microcoils is their hydrogel coating, which enables the coil to expand up to six times its original volume (Bui *et al*., 2006).

Standard coils were often used instead of the much cheaper external inguinal barrage to prevent sclerosant reflux in the PP, and many investigators still use them for scleroembolization. Traditional coils can be associated with several complications, which can be serious: coil migration, venous dissection, and venous perforation. In contrast, few technical complications have been associated with detachable coils, and these have been due to entangled fibers in the treated venous segments (Paul *et al*., 1996). The overall complication rate with detachable coils is 9.7%, and the recurrence rate is 4.8% (Bechara *et al*., 2009).

2.3.2 Acrylic Glue Embolization

Acrylic glue embolization was introduced in the 1980s. The technique is similar to coil embolization performed with a coaxial microcatheter to try to reach the inguinal canal. N-butyl cyanoacrylate (NBCA) glue (Trufill, Cordis, Miami, FL, USA) is normally mixed at a ratio of 1:3–4 per volume with Ethiodol (Savage Labs, Melville, NY, USA) or Lipiodol (Guerbet, Roissy, France) and slowly injected through the microcatheter. This kind of embolization is frequently used in cases of persistent and recurrent postsurgical varicoceles (Sze *et al*., 2008). Possible complications are glue migration into the pulmonary circulation, glued catheter, severe SV, or PP phlebitis.

2.3.3 Antegrade Sclerotherapy (AS)

Antegrade Sclerotherapy (AS) could be the solution to overcome difficulties in spermatic vein catheterization in complex anatomical cases, or when the percutaneous procedure was impossible in some surgical recurrences. (AS) started in the early 1980s. Figure 8 illustrates the procedure of left varicocele ascending sclerotherapy in a patient in whom retrograde catheterization of the left spermatic (vein was not possible. (Fig 2.5

Figure. 2.5. Left varicocele antegrade sclerotherapy in a patient whom retrograde catheterization of the left spermatic vein was not possible. (A) Ascending phlebography (black arrow). (B) Ascending phlebography shows 2 left spermatic veins (double asterisk). (C) Simultaneous left vasography (white arrows) performed after .(sclerotherapy (Iaccarino. and Venetucci, 2012

In 1994, Tauber and Johnsen were the first to publish an article devoted to antegrade scrotal sclerotherapy (Tauber. and Johnsen, 1994). They subsequently reported a success rate of 91% (Johnsen. and Tauber, 1996). However, an even better success rate can be .obtained with a more accurate technique

Advantages of Embolization 2.4

An attractive alternative to surgical varicocele repair is the selective catheterization and embolization of the gonadal veins using

sclerosing agents, tissue adhesives or detachable metallic coils. This radiologic approach is minimally invasive and has a quicker recovery time as well as several other advantages. Embolization can be performed under local anesthesia, thus eliminating the risks associated with general anesthesia; this approach also allows excellent real-time delineation of venous anatomy and confirmation of venous occlusion using venography at the time of varicocele repair. As embolization is purely intravascular it minimizes or eliminates the risks of arterial and deferential injury compared to surgical techniques, which has obvious implications in the management of the infertile male (Darby *et al.*, 2012).

Embolization has been demonstrated to pose no risk for postoperative hydrocele formation compared to the 8.24% rate in surgical approaches. Embolization is also not associated with testicular loss secondary to inadvertent arterial injury, which is a risk with the surgical approaches with a poorly described rate in the literature of 1% (Kumar and Gupta, 2003). The recovery period following varicocele embolization is typically 48 to 72 hours compared to 1 to 2 weeks following surgical repair (Storm *et al.*, 2010). It can be performed on an outpatient basis with less expense (Morag *et al.*, 1984). The improvements seen in semen parameters and fertility rates appear to be independent of the type of repair as long as the repair is technically successful. This makes success and failure rates of the individual techniques very important in the management of the infertile male. There is no large contemporary

series comparing these two approaches for varicocele management in the infertile male.

Radiation risk to health 2.5

Very soon after the discovery of X rays by Roentgen in 1895, and of radioactivity by Becquerel in 1896, harmful effects of the radiation were observed. Already within a year skin burns were reported and within 7 years skin cancer was reported. Over the following years and decades, much evidence accumulated of acute tissue damage and induction of malignant disease in humans exposed to radiation and of germ-line mutations in other biological systems. It has become conventional to classify the biological effects of radiation into two broad classes: stochastic effects and deterministic effects.

Stochastic effects occur as all or nothing consequences of exposure, with a probability that is dependent on the amount and nature of the radiation exposure but with severity independent of the exposure. Health effects in this category include cancer, inherited (germ-line) mutations and congenital abnormalities from in utero exposure. The underlying assumption is that such effects arise from chains of events triggered randomly by the radiation exposure.

Deterministic effects (previously called non-stochastic effects) occur in a predictable way, with severity dependent on the amount and nature of the radiation exposure. These effects are negligible or non-existent below their threshold doses and, above these doses, they increase in severity with increasing dose. Health effects conventionally put into this category include skin burns, cataracts in the eye, damage to (or failure of) individual organs receiving large exposures, cardiovascular disease

and death of an individual due to haemopoietic-system failure, gut damage or central nervous system damage after increasingly large acute exposures. The underlying assumption is that there are systematic increases in elementary damage with increasing radiation exposure, but that health effects become manifest only when a sufficiently large total amount of damage has accrued in the tissue or organ.

Radiation safety in imaging 2.6

Radiologists, medical physicists, registered radiologist assistants, radiologic technologists, and all supervising physicians have a responsibility for safety in the workplace by keeping radiation exposure to staff, and to society as a whole, "as low as reasonably achievable" (ALARA) and to assure that radiation doses to individual patients are appropriate, taking into account the possible risk from radiation exposure and the diagnostic image quality necessary to achieve the clinical objective. All personnel that work with ionizing radiation must understand the key principles of occupational and public radiation protection (justification, optimization of protection and application of dose limits) and the principles of proper management of radiation dose to patients.

The use of interventional procedures has gained tremendous popularity because of its inception in the 1960s (Mettler *et al.*, 2002). As an example of the number of procedures being performed, in 2003, there were an estimated 1,414,000 cardiac catheterizations and 664,000 percutaneous coronary interventions (Kim *et al*., 2008). With the increase in interventional procedures, the number of skin injuries reported has also increased according to Mettler et al. Since 1990s, incidences of erythema to necrosis and ulceration have increased and according to the authors, many of these injuries were avoidable. Skin injuries during interventional procedures can occur at doses as low as 2 Gy (Miller, 2003).

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In Interventional radiology and cardiology the establishment of dose reference level DRL values in is particularly difficult as these studies, by their very nature, are generally non-standard and therefore do not come within the definition of DRLs. Research programmes sponsored by the European Committee (EC) have been investigating the establishment of reference levels in these areas (IAEA, 2001), and have concluded that for complex procedures reference levels must include DAP values, fluoroscopy times and total number of images acquired. This approach, it is argued, will allow optimization and also minimize the incidence of skin injuries. For example, in a Spanish study (Vano *et al.*, 2001) the following values are indicated for the DRL for interventional cardiology:

DAP = 99 Gy.cm^2.

Fluoroscopy Time = 9.5 minutes.

Number of Images = 981.

Fluoroscopically guided medical procedures are an essential part of the contemporary practice of medicine. The risk of stochastic or deterministic injury as a result of radiation exposure during these procedures is low. Some fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. The majority of instances reported in the literature result from cardiac radiofrequency ablation or coronary angioplasty (Shope, 1996; Koenig *et al.*, 2001a). Some reported skin injuries were associated with transjugular intrahepatic portosystemic shunt (TIPS) creation, renal angioplasty, multiple hepatic/biliary procedures, or embolization (Shope, 1996; Koenig *et al.*, 2001a ; Huda, 1994; Lichtenstein, 1996; Vano *et al.*, 1998). The frequency of injury is unknown. The highest dose is to the skin at the entrance site of the radiation beam. Typical manifestations of radiation injury to the skin range from transient erythema at low doses to dermal necrosis or chronic

ulceration at very high doses (Koenig *et al.,* 2001b). Radiation-induced skin effects are deterministic. The threshold absorbed dose for transient skin erythema is typically estimated at 2 Gy (200 rad) (Wagner, 1994). Some patients may have more severe reactions at the same or lower doses because of biologic variation (Wagner, 1999). For most interventional radiology procedures, there is little or no published information on skin dose for either average dose or the frequency with which skin dose exceeds a given threshold (10). Much of the published data on radiation dose provides dose– area–product (DAP) data (Johnson, 2001; Marshall, 2000). This is a surrogate measure of skin dose and does not correlate well with skin dose (Castellano, 1995; Vehmas, 1997; Ruiz-Cruces, 1997; McParland, 1998; Vano, 2001; van de Putte, 2000). DAP is more reliable as an estimator of energy imparted to the patient, and

therefore of stochastic risk

Balter, 2001). In a Public Health Advisory of September 30, 1994, the FDA) recommended that "information permitting estimation of the absorbed dose to the skin be recorded in the patient's medical record" (FDA, 1994). No specific method of dose measurement or unit of dose was recommended. In a separate publication (FDA, 1995), the FDA recommended that dose information be collected and maintained for cardiac radiofrequency ablation, vascular embolization, transjugular intrahepatic portosystemic shunt (TIPS) creation, and percutaneous endovascular reconstruction (stents and stent-grafts). This recommendation was based on anecdotal re-ports of

.injuries rather than on published dose data for these procedures

2.7 Fluoroscopic Equipment

The recent angiographic equipment contains an integrated dosemeter. These systems are compliant with the dosimetry portion of the International Electrotechnical Commission (IEC) standard 60601–2–43 (IEC, 2000). The fluoroscopic unit

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performed exposure measurements automatically. Dosimetry information, including fluoroscopy time, DAP, and cumulative dose (CD) at the interventional reference point (IRP) were displayed directly on the console in the control room. Fluoroscopic dose rate and CD were displayed in the procedure room and were readily available to the operator during the procedure. The requirement for integrated ("built-in") dosimetry instrumentation was intended to ensure that there would be no increase in procedure time and no increase in dose to the patient. The use of data from integrated dosemeters also minimized the effort required for data collection and the potential for measurement errors. These units incorporate state-of-the-art dose reduction features, including modern image intensifier video systems, pulsed fluoroscopy, low-dose continuous fluoroscopy, spectral filtration, frame averaging, digital subtraction angiography without test exposures, variable-frame-rate digital subtraction angiography, last image hold, visualization of collimator and filter positioning without

.radiation, and real-time display of CD

Fluoroscopy time and the number of fluorographic images recorded during a procedure give an indication of the dose delivered by fluoroscopy and fluorography. These metrics do not include effects such as imaging system configuration, patient size, beam size, or beam position. CD indicates the total air kerma delivered to the IRP. It does not include effects such as beam size (collimator position) or beam position with respect to the patient (table position and gantry angulation). DAP indicates the total X.ray energy imparted to the patient. It does not include effects such as beam position with respect to the patient. None of these metrics directly

.(indicate peak skin dose (PSD) (Balter, 2001; Faulkner, 1999

Dose Measurement in Interventional radiology 2.8

Geise and O'Dea categorized the methods of dose measurement during interventional procedures as either direct measurement methods, in which the dose is determined by a direct measurement at or very near the skin during the procedure, or as indirect or calculation methods, in which the dose at the skin inferred from dose measurements at other locations or from other equipment parameters (Geise and O'Dea, 1999).

2.8.1 Post-Procedure Dose Results Methods

2.8.1.1 Thermoluminescent Dosemetry

A point measurement with a TLD chip requires advance knowledge as to the location of PSD on the patient. TLDs have several limitations as a method for determining patient dose from fluoroscopy: Information is not provided during the procedure. The variable locations of the x-ray beam make it difficult to place TLDs so that they will appropriately record the doses of interest. This is especially difficult if the maximum dose to the skin is the quantity of interest. In our study it is used to measure the gonad dose.

2.8.1.2 X-ray Film Dosemetry

Patient dosemetry for diagnostic and interventional x-ray procedures, using various types of film has been described by a number of investigators (Geise and Ansel, 1990; Fajardo, 1995; Vano *et al.,* 1997; Geise and O'Dea, 1999; Vano *et al.*, 2001). Dosemetry using film has the advantages of providing a detailed indication of the location of the skin dose, providing quantitative dose information with careful calibration and densitometry, and being used with any x-ray system. Certain films have a working range from 0.01 Gy to about 2 Gy. This is sufficient for many procedures, but too sensitive for very complex interventional procedures.

2.8.1.3 Radiochromic Film

A version of a radiochromic dosemetry film 2 can be used for quantitative mapping of patient skin dose during fluoroscopy. This is GAFCHROMIC® XR-Type R dosemetry media. This product's lower sensitivity makes it suitable for higher-dose fluoroscopy procedures. Giles and Murphy recently evaluated the characteristics of this material (Giles and Murphy, 2002).

2.8.2 Real-time Direct Dose Measurement Methods

There are several approaches to measuring dose during fluoroscopic procedures using geometrically small radiation detectors that provide immediate dose information via an electronic display. Hence, they can provide real-time feedback about relative dose magnitudes to the physician during the procedure to influence the conduct of the procedure. These systems have the advantages of providing immediate dose information but must be positioned, a priori, at exactly the right location on the patient if they are to record the PSD, the quantity of most interest.

2.8.2 1. MOSFET Radiation Sensors and Scintillation Dosimeters

The evaluation or use of a MOSFET radiation sensor has been described in several reports (Bower and Hintenlang, 1997; Peet and Pryor, 1999). Bower and Hintenlang evaluated the sensitivity, linearity, angular response, post exposure response, and physical characteristics. They anticipated that the system could find use in diagnostic radiology as a dosemetry tool if the directional sensitivity and post-exposure drift of response were accounted for.

2.8.3 Measurement of Dose at the Collimator Port

2.8.3.1 Dose-Area-Product Meters

Dose-Area-Product (DAP) meters are large-area, transmission ionization chambers and associated electronics. In use, the ionization chamber is placed perpendicular to

the beam central axis and in a location to completely intercept the entire area of the x-ray beam. The DAP, in combination with information on x-ray field size can be used to determine the average dose produced by the x-ray beam at any distance downstream in the x-ray beam from the location of the ionization chamber. A recent modification of the ionization chamber design used in a DAP meter has resulted in an instrument that measures both DAP and the dose delivered by the x-ray beam. This design effectively combines data from a small ionization chamber that is completely irradiated by the beam and independent of the collimator adjustments with the conventional DAP meter.

DAP is defined as the integral of dose across the X-ray beam. Therefore DAP includes field non-uniformity effects such as anode-heel-effect, and the use of semi-transparent beam-equalizing shutters (lung shutter). DAP is easy to measure. The simplest method is to place a transmission full-field ionization chamber in the beam between the final collimators and the patient. DAP may also be obtained by calculation. Data is accumulated during fluoroscopy, fluorography, and radiography. Assuming that the incident beam is totally confined to the patient, the recorded value essentially provides an upper limit on the X-ray energy absorbed by the patient (i.e. there is no transmission or scatter). DAP's ability to estimate stochastic risk is degraded because of the lack of dose distribution information within the patient. The best that one can do is to assume an average weighting factor for all the tissues at risk. This may lead to an over or under estimate of risk in certain cases. As an example, it does not account for the differential risk of breast cancer from an AP or a PA projection. DAP rate and cumulative DAP can easily be displayed in real-time. The primary utility of DAP rate is in a teaching situation. Scattered dose rate at any place in the lab is more or less proportional to DAP rate. The trainee can be shown that reducing DAP rate reduces

his or her personal exposure rate. The effect of different control options (e.g., collimation, zoom mode) on DAP rate can be demonstrated. Cumulative DAP does not provide a direct indication of the possibility of skin injury. The same DAP is observed with large fields and low skin doses as with small fields and high skin doses. Exceeding skin tolerance is more likely in the latter case. However, reasonable entrance field size estimates can be made for many procedures. These estimates are dependent on factors such as equipment configuration, patient size, and operator technique. Once known, the nominal field size can be used to obtain an estimate of skin dose. Rules-of-thumb can be established to make this conversion for typical procedures. DAP provides no information regarding the spatial distribution of the entrance beam around the patient's skin. It produces an overestimate of the possibility of exceeding the deterministic threshold when there is significant beam movement during the procedure.

Most non-interventional procedures and many interventional procedures do not approach deterministic dose levels. There is little need to monitor individual patients undergoing such procedures. Determining 'typical' doses and assuring appropriate equipment performance achieves adequate radiation monitoring. Radiation risks are accepted when the procedure is ordered and agreed to.

2.9 Patient's radiation dosage

Patient dosage is divided into two categories according to (Brusin, 2007): absorbed dose and effective dose.

2.9.1 The absorbed dose is measured in the unit Gray (Gy) and refers to the amount of ionizing radiation deposited in an organ or tissue. However, the author explained that the absorbed dose does not specify which organ or tissue received the radiation.

2.9.2 **The effective dose**, measured in Sieverts (Sv), is the dose that is specific to organs or tissues and measures the actual amount of radiation absorbed by the tissue. The International Council on Radiation Protection established specific effective dose limits for specific parts of the body, including skin, eyes, and whole body dose. For health care workers using ionizing radiation, it is important to understand that the amount of radiation being emitted by the unit is not necessarily the amount deposited in tissues, and is not the amount of radiation actually absorbed by the tissue.

As a global average, the natural background radiation in terms of effective dose is 2.4 mSv/year (UNSCEAR, 2010). In some countries, typical background radiation is approximately 1 mSv/year, and in other countries, it is approximately 3 mSv/year. There are some areas in the world, (e.g. India, Brazil, Iran) where the population is exposed to background radiation levels in terms of effective dose of 5–15 mSv/year.

Cancer risks are estimated on the basis of probability, and are derived mainly from the survivors of Hiroshima and Nagasaki. Therefore, these risks are estimated risks. With the current state of knowledge, carcinogenic effects are more likely for organ doses of >100 mGy. For example, a chest CT scan that yields approximately 8 mSv effective dose can deliver approximately 20 mGy dose to the breast; five CT scans will therefore deliver approximately 100 mGy. There may be controversies about cancer risk at the radiation dose from one or a few CT scans, but the doses encountered from five to 15 CT scans approach the exposure levels where risks have been documented. As radiation doses to patients from fluoroscopic procedures vary greatly, one must determine the dose to get an approximate idea of the cancer risk. It must be mentioned that cancer risk estimates are based on models of a nominal standard human, and cannot be considered to be valid for a specific individual person.

As stochastic risks have no threshold, and the Commission considers that the linear no-threshold relationship of dose effect is valid down to any level of radiation exposure, the risk, however small, is assumed to remain even at very low doses. The best way to achieve protection is to optimize exposures, keeping radiation exposure as low as reasonably achievable, commensurate with clinically useful images as advised by International Commission on Radiological Protection (ICRP, 2010).

2.10 Individual differences in radiosensitivity

It is well known that different tissues and organs have different radiosensitivities, and that females are generally more radiosensitive than males to cancer induction. The same is true for young patients (increased radiosensitivity) compared with older patients. For example, the lifetime attributable risk of lung cancer for a woman after an exposure of 0.1 Gy at 60 years of age is estimated to be 126% higher than that for a man exposed to the same dose at the same age (BEIR, 1998). If a man is exposed to radiation at 40 years of age, his risk of lung cancer is estimated to be 17% higher than if he was exposed to the same radiation dose at 60 years of age. These general aspects of radiosensitivity should be taken into account in the process of justification and optimization of radiological protection in fluoroscopically guided procedures because, in some cases, the radiation dose level may be relatively high for several organs. There are also individual genetic differences in susceptibility to radiation induced cancer, and these should be considered in specific cases involving higher doses based on family and clinical history (ICRP, 1999).

2.11 Previous studies

The influence of varicocele on male fertility has been discussed earlier in the literature since the end of the 19th century; Baker et al. reviewed infertility in a large group of patients: 214 men who had a varicocele operated on and 243 men who did

not undergo treatment. The cumulative conception rates in the female partners of both groups were nearly identical, resulting in about 30% in 12 months and about 45% in 24 months, and concluded: Our results suggest that ligation of a varicocele is not effective with respect to future fertility. (Baker *et al*., 1985). Okuyama et al. found 15 pregnancies in a group of 83 patients with uncorrected varicoceles (18.1%) and 43 pregnancies in a group of 141 patients with corrected varicoceles (30.6%) (Okuyama *et al*., 1988). A meta-analyses have suggested that varicocele repair has a beneficial effect on fertility status in infertile men with palpable varicocele, Ficarra *et al*. reviewed randomized clinical trials for varicocele repair and found a significant increase in pregnancy rate in patients who underwent varicocele treatment (36.4%) compared with patients having no treatment (20%) (Ficarra *et al*., 2006). Marmar et al. reported a 33% pregnancy rate in patients who underwent surgical varicocelectomy and a 15.5% pregnancy in the control group receiving no treatment (Marmar *et al*., 2007). A nonrandomized studies have suggested that repairing a clinically palpable varicocele in the presence of an abnormal semen analysis results in improvements in semen parameters and pregnancy rates, Daitch et al. studied 58 infertile couples, of whom the women had normal evaluations and men had abnormal semen analyses and a history of varicocele, and found that the pregnancy rates were significantly higher in patients in whom varicocele was treated than in those without varicocele treatment

.((11.8% versus 6.3%) respectively (Daitch *et al.*, 2001

Unlike Daitch et al., Rageth et al. studied 89 patients with varicocele and a median duration of infertility of 36 months,   postoperative sperm examinations have shown a significant improvement in sperm count and morphology, but not in motility.

Pregnancy rates were 42% (23 out of 55, 1 patient lost to follow-up) in the operated group and 45% (14 out of 31, 2 patients lost to follow-up) in the nonoperated group and concluded that pregnancy rates in the nonoperated group are relatively high despite present varicocele, and the operated group achieved practically the same high pregnancy rate when monitored over a longer period of time (6 years) (Rageth et al., 1992). There are few randomized controlled studies supported the fact that varicocele impairs fertility, and treatment improves semen parameters and pregnancy rates. Abdel-Meguid et al. prospectively studied 145 patients diagnosed with varicocele factor infertility (72 not treated, control and 73 treated) and reported that spontaneous pregnancy was achieved in 13.9% of the control group versus 32.9% in the treated group, and concluded ''there is an evidence of the superiority of varicocelectomy over observation in infertile men with palpable varicoceles and impaired semen quality after one year follow-up'' (Abdel-Meguid *et al.,* 2011).

Madgar et al. also studied 20 couples, the men with abnormal semen analysis because of varicocele only, the couples were treated and observed for 3 years, they concluded that ''in a population of infertile men presenting varicocele as the only demonstrable factor of infertility, the varicocele is clearly associated with infertility and reduced testicular function, and its correction by ligation improves sperm parameters and fertility rate. Furthermore, the highest PR in both groups occurred during the 1st year postoperation'' (Madgar *et al.,* 1995).

In the 1970s, with the advent of smaller vascular catheters and improved imaging techniques, percutaneous transcatheter embolization has become a valuable adjunct to varicocelectomy for the treatment of patients with varicocele. Thus a new debate arises whether to treat varicoceles with surgery or embolization to improve seminal parameters and pregnancy rates. Sayfan et al. prospectively studied a randomized trial

of 3 methods including surgical ligation and percutaneous embolization and found no statistical difference in pregnancy rates (Sayfan *et al.*, 1992). E. Nieschlag et al. prospectively studied 71 patients with varicocele, 38 treated with surgical ligation and 33 treated with angiographic embolization and concluded both treatment modalities appear equivalent, whereby embolization has the advantage that it can be performed on an outpatient basis. (Nieschlag *et al.*, 1992). Shlansky-Goldberg et al. retrospectively reviewed 346 men who underwent correction of their varicocele for infertility (surgical ligation 149 and embolization 197) and found that there is no significant statistical difference in seminal values or pregnancy outcome between the two techniques (Shlansky-Goldberg *et al.*, 1997). The old Cochrane database suggested no benefit of varicocele treatment on a couple's chances of conception compared with control subjects. However, this meta-analysis included men with subclinical varicoceles or normal semen analyses (Evers *et al*., 2001; Evers and Collins, 2004; Evers *et al*., 2008; Evers *et al*., 2009). A recent Cochrane database reported an analysis of ten randomized control trails (RCTs), found that there is evidence suggesting that treatment of a varicocele in men from couples with otherwise unexplained subfertility may improve a couple's chance of pregnancy (Kroese *et al*., 2012; Freire, 2013; Kroese *et al*., 2014)).

Chapter Three

Material and Methods

Chapter Three

Material and Methods

Material and methods 3.1

From June 2012 to June 2015, a total of one hundred and nineteen patients aged 23–48 years (mean age 35.56 years) referred to the division of andrology in King Faisal specialist Hospital in Riyadh Kingdom of Saudi Arabia for infertility were diagnosed with varicocele both clinically and by ultrasound B-mode and Doppler of the testis and spermatic cord. The indication for the treatment was clinical evidence, as observed by the andrologist, of grade II and III varicocele, according to Dubin–Amelar classification (Dubin and Amelar, 1971).

Inclusion criteria 3.1.1

1. Men with palpable unilateral varicocele.

2. History of primary or secondary infertility.

3. Varicocele as the only demonstrable factor of infertility.

4. Female partner has no proven cause of infertility.

Exclusion criteria 3.1.2

1. Men with obstructive azoospermia.

2. Subclinical varicocele.

3. Follow-up of less than 12 months.

4. Associated urogenital disorders.

5. Endocrine and internal disorders.

All patients were assessed on entry and one year later. Semen analysis was performed for three times before treatment with 3-days abstinence from sexual intercourse before semen collection. A minimum interval between all the analyses was at least 2 weeks. Postoperative evaluation included serial semen analyses with 3-months intervals in the first year after treatment according to the hospital protocol, and then multiple readings are averaged for the pre and post-treatment separately. Seminal examinations were carried out in accordance with the World Health Organisation (WHO) criteria (WHO, 2010). Patients were divided into two groups according to the method of treatment: Group (A) 66 patients treated by varicocele catheter embolization and group (B) 53 patients treated by microsurgical varicocelectomy. Infertility was the indication for treatment in both groups.

3.2 Group (A) Retrospective and prospective varicocele embolization

In Group (A) a 15 consecutive patients attending for varicocele embolization were optimized prospectively by reducing fluoroscopy time, tube current, beam collimation, number of images in fluorography and number of exposures in radiography. In a retrospective of departmental records of previous 35 patients the

dose was estimated from the dose reports. In 16 patients the dose reports were lost and their records used only in seminal aspect of the study. All cases in the embolization group treated by selective catheterization of the spermatic vein performed with a right transfemoral approach. The angiographic catheter is introduced into the venous system via the right femoral vein, then a 4–5 French hydrophilic catheters and hydrophilic guidewires is used to avoid venous spasms. A diagnostic phlebography study of the spermatic vein is performed. When the catheter tip reaches the more distal part of the spermatic vein (the ischiopubic ramus), then a rubber band is applied at the highest level of the scrotum and contrast media is immediately injected during a Valsalva maneuver to check that there is no reflux in the PP below the rubber band. Then a 0.014 inch guidewire is used to allow for the use of detachable coils to insure distal embolization of spermatic vein. Sclerosing agents is then injected via the catheter. Scrotum elastic compression continues to be applied for 1 min and then is released with the patient in the Trendeleburg position to prevent posterior PP phlebitis. If sclerosant remains in the anterior PP, the procedure ends. Otherwise, sclerotherapy is repeated 10 minutes later, as described previously. The catheter then removed and hemostasis achieved.

Postprocedural care included bed rest with routine pulse and blood pressure monitoring and punctures site observation, followed by mobilization after 2 hours. Patients were sent home with nonsteroidal anti-inflammatory analgesics for 3 days.

3.2.1 Prospective

Fifteen patients aged 23-44 years (mean age 33.4 years) underwent percutaneous embolization of the left spermatic vein. The procedures were carried out using fluoroscopy (Artis Zee. Siemens. Erlangen. Germany 2009), a low dose protocol is used to reduce the dose to the patient. A built-in DAP meter was used to measure the

dose area product (DAP) (field size 140x140 mm^2). The chamber was positioned at the X-ray tube window during the procedures. Three thermo luminescent dosimeters, type GR200A LiF, were positioned on the upper inner thighs adjacent to the scrotum to directly measure gonad dose. Dosimeter calibrations and readings were carried out by expert medical physist, the values were expressed in terms of air kerma free-in-air and were converted into gonad dose equivalent using the appropriate conversion coefficient (ICRP, 1995). Considering that the mean working current 75.8 kV for the device used corresponds to a mean energy of 44KeV. A Monte Carlo program, PCXMX (ICRP, 1995), were used to estimate effective dose from recorded DAP. By referring to standard projections modeled in the software, the approximation to the field sizes and positions used was a posterior-anterior kidneys corresponding to a femoral approach with a deliberate inclusion of the gonad from the primary beam. Informed consent was obtained by the interventional radiologist in charge of the procedure, explaining to both the patient and his co-patients the indications of the procedure, its technique and possible complications.

3.2.2 Retrospective

Records of 35 patients underwent varicocele embolization using the same machine in the prospective series, were reviewed for seminal and dose concerns, effective doses for each patient in this series were corrected by comparing the calculated testes doses with those directly measured with TLD in the prospective series. The total cancer risk was made by combining the effective doses with a risk factor of 5.5 x 10^{-2} Gy^{-2} for a reproductive population (NRPB, 1993). Semen analysis was reviewed before treatment and one year after treatment. Seminal data were collected from records in terms of spermogram: volume (ml), concentration (sperm 10^6 /ml), motility (% motile), morphology (% normal forms) and total motile sperm count TMSC (sperm 10^6 /ejaculate) only.

3.3 Group (B) surgery

In group (B) 53 patients underwent microsurgical varicocelectomy. An operating microscope is incorporated into either the traditional inguinal or subinguinal approach to allow for the more reliable identification and preservation of the testicular artery or arteries, cremasteric artery or arteries, and lymphatic channels. Enhanced visualization also aids in the identification of all possible routes of venous return contributing to the varix, including external spermatic, cremasteric, and gubernacular veins. The success and pregnancy rates after the procedure are calculated and determined. The seminal records were reviewed before treatment and one year after treatment. Open varicocelectomy was performed under local anesthesia (bupivacaine and lidocaine 1%), with a short (4 to 5 cm) oblique incision made over the internal inguinal ring. After incision of the muscular layer, the funiculum was carefully exposed. The elements of the funiculum and spermatic veins are identified using magnifying lenses (3.53) to obtain magnification and to preserve the spermatic artery. The spermatic veins were closed and sectioned in the upper part of the funiculum, where they usually flow together in 2 to 3 major branches. At the end of these procedures a careful inspection of the inguinal channel is performed, looking for extrafunicular vessels.

A data collection sheet is used to collect the data, containing patient information, clinical history, exposure factors for fluoroscopy and radiography, semen analysis and technical information for both groups.

A record of the post-treatment semen parameters was made at 3, and 6 months after the procedures. If the semen analysis did not show any improvement, a subsequent semen analysis was obtained at 9 and 12 months. An average of all the semen analyses during the post-treatment period for each patient and for each parameter was taken for comparison. The statistical significance of any change in the semen

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parameters after embolization was tested using the SPSS version 22.0 (SPSS Inc., Chicago, IL, USA), Paired t-test. Patients were followed up to discover the success rate of the procedure, pregnancy rates and any complications for both groups.

Chapter Four

Results

Chapter Four

Results

Introduction 4.1

From June 2012 to 2015, one hundred nineteen patients with left side varicocele underwent varicocele correction by either varicocele embolization or varicocelectomy. All varicoceles were clinically palpable and discovered on routine physical examination or ultrasound.

The mean age was 36.5 (range 26-48 years) and 33.4 (range 23-44 years) for group (A) and Group (B) respectively. Varicocele was grade II in 45 cases (37.82%) and grade III in 74(62.18%), according to Dubin–Amelar classification (Dubin and Amelar, 1971).

Clinical results 4.2

During one year follow-up Group (A) Varicocele embolization was successful in 63/66 (95.45%), one patient develop phlebitis and two

recurrences. Group (B) varicocelectomy was successful in 45/53 (84.90%), two patients developed hydrocele, four recurrences, one developed phlebitis and one testicular atrophy (artery not preserved). Seminal results (as shown in Table. 4.1- Table.4.10) (Fig. 4.1- Fig. 4.4) which taken from the successful procedures in both groups shows slightly significant increase in the volume of ejaculate in Group (A) (P. value = 0.0.0172) while not changed in Group (B) (P. values = 0.460), an extremely significant increase in the concentration, motility, morphology and TMSC (P. values < 0.0001) for all these semen parameters except in morphology in Group (B) (P. values = 0.0004). Pregnancies were achieved in 23/66 (34.85%) .(in Group (A), while 19/53 (35.85%) in Group (B) (P. Value = 0.6221

Dosimetry results 4.3

The mean value of X-ray tube voltage was 78.5 (range 65-85 kV) and 75.4 (range 65-85kV) in fluoroscopy mode in the prospective and retrospective series respectively, and 75.8 kV (range 64-90 kV) and 76.14 kV (range 65-88 kV) in radiography mode the same series respectively. The mean value of tube current was 4.7 mA (range 3-8.2 mA) and 5.3 mA (range 4-9.6 mA) in fluoroscopy mode in the prospective and retrospective series respectively, 545 mA (range 385-704 mA) and 556.05 mA (range 412-800 mA) in radiography .mode in the same series respectively

The mean value of screening time of fluoroscopy was 8.95 min (range 6- 12.6 min) and 13.33 min (range 5.5- 27.7 min) for the prospective and retrospective series respectively, and the mean

number of fluoroscopic images was 65.67 (range 22-168) and 84.11 (range 23-210) for the prospective and retrospective series respectively. The mean number of the radiographic exposures was 6.8 (range 4-11) and 7.97 (range 3-14) for the prospective and retrospective series respectively, the mean value of the total DAP during fluoroscopy and radiography was 18.32 Gy.m2 (range 5.72-34.85 Gy.m2) and 29.79 Gy.m2 (range 4.97-105.34 Gy.m2) in the same series respectively.

The mean value of the effective dose was 5.32 mSv (range 1.66-10.11) and 8.64 mSv (range 1.44-30.54) in the same series respectively. The mean value of the estimated fatal cancer risk was 292.4×10^{-6} (range 91.3×10^{-6} -5559×10^{-6}) and 478.1×10^{-6} (range 79.3×10^{-6} -1670.1×10^{-6}) in the prospective and retrospective series respectively.

P. values of all these differences was (P<0.0001) except for number of exposures (P= 0.0178), total DAP for radiographic exposure and fluoroscopy (P= 0.0012), Effective dose (P= 0.0306) and the estimated fatal cancer risk (P= 0.0227) as shown in Table 4.11, this significant differences indicate the great reduction in the patient dose in the prospective series.

4.4 Tables and figures

Table 4.1. Semen volume (ml) before treatment (Pre) and 12 months (Post) following Embolization.

	Pre	Post
Mean	2.825	3.071
SD	0.730	0.390
Range	5 - 1.5	4.5 – 2

65

		P. value
S 0.0172 =		
63	63	N

Table 4.2. Sperm concentration (10^6ml^{-1}) before treatment (Pre) and 12 months (Post) following Embolization.

Post	Pre	
69.49	48.59	Mean
43.50	46.38	SD
184 - 14	172 - 8	Range
Less 0.0001		P. value
63	63	N

Table 4.3. Sperm motility (%) before treatment (Pre) and 12 months (Post) following Embolization.

Post	Pre	
43.35	31.52	Mean
13.50	13.88	SD
75 - 16	67 - 7	Range
Less 0.0001		P. value
63	63	N

Table 4.4. Sperm morphology (%) before treatment (Pre) and 12 months (Post) following Embolization.

Post	Pre	
50.40	26.19	Mean
17.37	13.22	SD
85- 10	60 - 5	Range
Less 0.0001		P. value
63	63	N

Table 4.5. Total motile sperm count (TMSC) (10^6) before treatment (Pre) and 12 months (Post) following Embolization.

Post	Pre	
9369.810	4732.079	Mean
6439.693	5576.254	SD
811.325	702.542	Range
0.0001		P. value
63	63	N

Figure. 4.1. Spermogram (Volume, concentration, motility and morphology) pre-treatment and 12 months following Embolization.

Figure. 4.2. Total motile sperm count (TMSC) (10^6) before treatment (Pre) and 12 months (Post) following Embolization.

Table 4.6. Semen volume (ml) before treatment (Pre) and 12 months (Post) following surgery.

Post	Pre	
2.8433	2.9833	Mean
1.0327	1.6412	SD
1-6	0.5-7.5	Range
NS 0.4603 =		P. value
45	45	N

Table 4.7. Sperm concentration (10^6ml^{-1}) before treatment (Pre) and 12 months (Post) following surgery.

Post	Pre	
82.740	35.640	Mean
48.357	30.235	SD
255 - 0.3	121 - 0.1	Range
Less 0.0001		P. value
45	45	N

Table 4.8. Sperm motility (%) before treatment (Pre) and 12 months (Post) following surgery.

Post	Pre	
38.29	24.33	**Mean**
18.37	13.97	**SD**
10-77	3-60	**Range**
Less 0.0001 ES		**P. value**
45	45	**N**

Table 4.9. Sperm morphology (%) before treatment (Pre) and 12 months (Post) following surgery.

Post	Pre	
41.69	29.00	**Mean**
20.57	19.55	**SD**
10-90	5-90	**Range**
ES 0.0004 =		**P. value**
45	45	**N**

Table 4.10. Total motile sperm count (TMSC) (10^6) before treatment (Pre) and 12 months (Post) following surgery.

Post	Pre	
8000.5380	3156.7293	**Mean**
8823.2637	5259.4462	**SD**
24948 - 16.5	21360 - 4	**Range**
Less 0.0001		**P. value**
45	45	**N**

Figure. 4.3. Spermogram (Volume, concentration, motility and morphology) pre-treatment and 12 months following Surgery.

Figure. 4.4. Total motile sperm count (TMSC) (10^6) before treatment (Pre) and 12 months (Post) following surgery.

Table 4.11. Exposure parameters of the prospective and retrospective series, effective dose and fatal cancer risk.

P. Value	Retrospective			Prospective			
	Range	SD	Mean	Range	SD	Mean	
> 0.0001	65-88	6.29$\pm$	76.14	64-90	8.86$\pm$	75.8	Tube potential (kV) Exposure
> 0.0001	65-85	5.5$\pm$	75.4	65-85	7.2$\pm$	78.5	Tube potential (kV) Fluroscopy
> 0.0001	412-800	$\pm$ 102.09	556.05	385-704	$\pm$ 105.59	525	Tube current mA Exposure
> 0.0001	4.5-9.6	2.2$\pm$	5.3	3-8.2	1.7$\pm$	4.7	Tube current mA Fluoroscopy
> 0.0001	5.5-27.7	4.93$\pm$	13.33	6-12.6	1.87$\pm$	8.95	Screening time (Min)
> 0.0001	23-210	$\pm$ 46.69	84.11	22-168	$\pm$ 41.66	65.67	No of fluro images

No of Exposures	6.8	2.11±	4-11	7.97	3.03±	3-14	= 0.0178
Total DAP (Flu + Expo) Gym^2	18.32	8.44+	5.72-34.85	29.79	± 24.33	4.97-105.34	= 0.0012
Effective dose mSv	5.32	2.45±	1.66-10.11	8.64	7.06±	-1.44 30.54	= 0.0306
Fatal cancer (risk $\times (10^{-6}$	292.4	± 134.6	91.3-555.9	478.1	± 388.1	79.3-1670.1	= 0.0227

Chapter Five

Discussion and conclusion

Varicocele is an abnormal dilation of the pampiniform plexus of veins, usually caused by reflux of the internal spermatic vein. The incidence of varicocele is greater in the infertile male population, and a correlation between semen quality impairment and varicocele has been reported in previous studies (WHO, 1992; Baker *et al.*, 1985). The Debate regarding the role of intervention in the management of varicocele has been considerable. Although some series (Baker *et al.*, 1985) have reported no or minimal changes in the semen quality or pregnancy rate after surgical ligation, others have reported significant improvement in semen quality and an increased pregnancy rate (Ferguson *et al.*, 1985). The present study showed a significant increase in semen parameters: concentration, motility, morphology and TMSC p. values ($P <$ 0.05) in both groups thus prove that the correction of varicocele improves semen quality regardless the method of treatment. The best evidence-based answer would be from a randomized prospective controlled trial, this may be difficult to achieve in clinical practice. A strong desire to achieve parenthood, no convincing evidence-based support in published studies, a lack of motivation to recruit controls, and poor compliance are some of the difficulties faced in conducting controlled studies. Mark et al. observed that 70% of the patients were lost to follow-up in a large controlled study of 480 patients (Mark *et al.*, 1986). In the present study, it was possible to obtain questionnaire-based assessment in patients with successful treatment only

.107/119 (89.9%) for both groups

The management of varicocele basically involves interruption of reflux in the spermatic vein. This can be achieved by ligation at various levels either by an open or laparoscopic approach. There has been a continuous endeavor to improve the surgical techniques to decrease the morbidity, such as hydrocele, testicular atrophy, and

recurrence, since its introduction by Palomo (Palomo, 1949). The recently introduced microsurgical technique (Goldstein *et al*., 1992; Marmar and Kim, 1994) carried out in dedicated centers has been reported with the least morbidity and minimal complications. In the present study, retrograde embolization was performed under local anesthesia, with a minimal requirement for analgesics and minimal morbidity. The possible reasons for the minimal morbidity in embolization of varicocele include precise definition of the anatomy on venography, a lack of perivenous dissection or disruption of the lymphatic supply, and a lack of potential danger to the testicular blood supply (Marsman, 1985). Recent improvements in angioembolization techniques include: the use of better contrast media, the availability of better thrombogenic coils, the use of hydrophilic catheters and guide wires and the growing expertise in this area have improved the technical success rate. In the present study, it

was possible to achieve a high successful rate 63/66 (95.45%).

The partners of 23/66 (34.85%) in group (A) and 19/53 (35.85%) in group (B)   achieved pregnancy at a follow-up period of 1 year, clinically no significant differences between the two procedures in terms of pregnancy rate. Improvement in semen quality could increase the pregnancy rates.

Varicocele embolization is performed in healthy young men with normal life expectancy; therefore every effort must be made to minimize radiation exposure, thus preventing the patient from radiation cancer risk (Chalmers *et al*., 2000). As reported by Dudley, cancer, in general, is assumed to develop through a slow multistage process during which a normal cell, through its progeny, undergoes

a series of mutational and/or epigenetic changes, which may be broadly described as initiation, promotion, transformation and progression. This series of changes takes the cell from a normal state through clonal expansion, immortality and growth independence, to develop into a fully malignant invasive tumor. Radiation is conventionally assumed to act predominantly at the early 'initiation' stage, by inducing in one of the exposed cells a key rate limiting mutation. This stochastic occurrence gives the cell a growth, or other advantage, which increases the chance of a cancer developing if the other multistage changes happen to take place as in spontaneous carcinogenesis. The radiation protection paradigm used by the ICRP assumes that the dose–response for cancer induction is linear at low doses and that there is no threshold below which effects do not occur. This ICRP approach accords broadly with the above radiobiological and carcinogenesis paradigms, whereby the key rate-limiting radiation step in radiation carcinogenesis is a mutation, induced stochastically by the radiation with a linear-quadratic dose–response without threshold (Goodhead, 2009).

In interventional radiological techniques, patient doses are noted because sometimes they can be high. In this study, dose area product DAP during varicocele embolization were measured; these results were then used to estimate the effective dose which used to estimate the fatal cancer risk. A carful reduction in exposure parameters in both fluoroscopy and radiography during the procedure led to a considerable reduction in patient's doses. Doses

obtained were within the range of other diagnostic procedures, such

as computed tomography and nuclear medicine.

Exposure times and effective dose values were comparable with average lower values reported in the literature (Miller *et al.*, 2003; Chamlers *et al.*,2000; Gioppo *et al.*, 2014; Gazzera *et al.*, 2006) as shown in Table 5.1. Similar remarks apply to effective dose values. In this study we report the effective dose as a weighted average of man equivalent organ doses designed to reflect the stochastic risk of a gender averaged reference person. The total fatal cancer risk mean result in a minor risk descriptor and in a moderate benefit required to justify the procedure Table 5.2.

To optimize exposure during the varicocele embolization procedure, adequate field-limiting measures, limited fluoroscopy time to a maximum of 10 minutes and the use of fluoroscopy images instead of radiographic images as hard copies. This will make the dose as low as reasonably achievable (ALARA). More training and education to the staff are required to be aware of radiation doses incurred by fluoroscopy guided procedures.

Table 5.1 Comparison of present and previous studies. Exposure times and effective dose values were comparable with average lower values reported in the literature.

Fatal cancer risk		Effective dose		DAP		No of images		Fluoroscopy time		No of pt	
Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean		
91.3-	292.	1.66-	5.32	5.72-	18.3	22-	65.67	6-12.6	8.95	15	Present

555.9	4	10.11		34.85	2						study
-	-	-	-	7.4-19.05	5.1	6-127	31	6.4-40.5	17	14	Miller *et al.*, 2003) (
99-198	135	0.61-1.55	0.7	4.95-12.5	5.56	-	-	4.9-6.9	5.2	10	Chalmers) *et al.*, 2000) (
54-1100	280	0.47-8.4	2.15	1.88-41-32	10.08	-	-	2.4-18.7	6.5	21	Gioppo) *et al.*, 2014) (
		3.8-6.9	5.2	28.1-52.5	38.40	-	-	5-8.5	6.3	206	Gazzera) *et al.*, 2006) (

Table 5.2 Radiation Risk descriptors

Benefit required to justify exposure	Risk Descriptor	Effective Dose Range mSv
Describable	Negligible	0.1 >
Miner	Minimal	1 – 0.1
Moderate	Miner	10 – 1
Substantial	Low	100 – 10
Very substantial	Acceptable in context of benefit.	100 <

.

Correction of varicocele improves semen quality regardless the method of treatment. Percutaneous varicocele embolization is a reliable, with high successful rate, effective, minimally invasive and economically viable technique that can be performed on an outpatient basis with advantages over surgical ligation which require hospitalization and general anaesthesia. However, due to radiation protection issues, this procedure should be performed using fluoroscopy only and limiting exposure time. Varicocele embolization may be the preferred approach in men with unilateral left-sided varicoceles as this approach offers many benefits in terms of patient safety and morbidity. With careful attention to the technique, substantial reduction in radiation dose can be achieved.

Recommendation 5.3

Clear justification of percutaneous varicocele embolization is highly recommended, unless it is symptomatic, or impact the male fertility no need for varicocele correction. Also continuous follow-up must be performed periodically to assess for recurrences and to follow the changes in semen parameters. More training and education to the radiology department staff is required, to be aware of radiation doses incurred by fluoroscopy guided procedures.

Suggestions for further studies 5.4

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Future studies should be done to optimize the radiation dose incurred in percutaneous varicocele embolization with greater number of patient and more attention to the radiation doses.

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Appendixes

(Appendix (1

Data Collection Sheet

EVALUATION OF MICROSURGICAL VARICOCELECTOMY VERSUS VARICOCELE CATHETER EMBOLIZATION

A- Pt Information

Pt ID	Age	Clinical Indication	Varicocele Side

:B- Fluoroscopy Factops

Tube Potential ((KV	Tube Current ((mA	Fluoroscopy .Time (Min)	Projection AP/PA	DAP Gy.m^2

:C- Exposure Factops

Tube Potential ((KV	Tube Current ((mA	Fluoroscopy .Time (Min)	Projection AP/PA	DAP Gy.m^2

:D- Semen Parameter (Spermogram) Before Treatment

Volume (ml)	Concentration (Sperm 10^6/ml)	Motility (motile %)	Morphology (normal forms %)	TMC ((Sperm10^6/ejac

:E- Semen Parameter (Spermogram) After Treatment

Volume (ml)	Concentration (Sperm10^6/ml)	Motility (motile %)	Morphology (normal forms %)	TMC ((Sperm10^6/ejac

Embolization Technique Trans-jugular/Trans-femoral	
Type of X-ray Machine	
Type of Catheter	
Size of Catheter	
Any Other Medication Used	
Contrast media Used	
Sclerosing Agent Used	
Coil Used	
Technical Success	
Complications	
Recurrence	

(Appendix (2

Publication

http://saspublisher.com/wp-content/uploads/2015/07/SJAMS-34A1669-1673.pdf