



**Mesorectal Excision Of Rectal Cancer: Oncological Outcome And  
Pelvic Nerve Preservation**

**Thesis**

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## LIST OF ABBREVIATION

	<b>Subject</b>	<b>Page</b>
<b>TME</b>	Total Mesorectal Excision	2
<b>PANP</b>	Pelvic Autonomic Nerve Plexus	2
<b>PBI</b>	Penile Brachial Index	27
<b>EMG</b>	Electromyography	28
<b>NCV</b>	Nerve Conduction Velocity	28
<b>FAP</b>	Familial Adenomatous polyposis	35
<b>HNPCC</b>	Hereditary Non Polyposis Colorectal Cancer	36
<b>APC</b>	Adenomatous Polyposis Coli	35
<b>hCG</b>	Human chorionic gonadotropin	46
<b>AIDS</b>	Aquired Immunity Deficiency Syndrome	47
<b>AJCC</b>	American Joint Committe on Cancer	52
<b>UICC</b>	International Union against Cancer	52
<b>FOBT</b>	Fecal Occult Blood Test	62
<b>DCBE</b>	Double Contrast Barium Enema	62
<b>LAR</b>	Low Anterior Resection	75
<b>APR</b>	Abdominoperineal resection	75
<b>ATZ</b>	Anal Tranzition Zone	67
<b>EEA</b>	End-End Anastmosis	69
<b>CAA</b>	Colo-Anal Anastmosis	71
<b>TEM</b>	Transanal Endoscopic Microsurgery	71
<b>5FU</b>	5 flourouracil	83
<b>NSAID</b>	Non Steroidal Anti-inflammatory Drugs	84
<b>CPS</b>	Cancer prevention Study	89

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## INTRODUCTION AND AIM OF THE WORK

The optimal operation for rectal cancer still remains controversial. Surgical management of rectal cancer has undergone a significant change during the past two decades, a new concept of total mesorectal excision (TME) was introduced, and its feasibility and efficacy had been confirmed by a series of clinical trials. Compared with conventional procedure, TME markedly improved both oncological and functional outcomes of rectal cancer, therefore, this procedure has been used as a golden standard for rectal cancer, (Zong et al., 2003).

In patients with advanced rectal cancer, it is difficult to preserve urinary and sexual function with the conventional surgical procedures which resect the mesorectum bluntly and blindly. In addition, the reported local recurrence rate is rather poor, ~20-30% . More recently, the local recurrence rate has declined to 5-8% owing to the introduction of the total mesorectal excision (TME) technique with/without adjuvant therapy. In Japan, lateral lymph node dissection was thought to be necessary to obtain good local control and pelvic autonomic nerves were sacrificed for patients with advanced-stage rectal cancer . Pelvic autonomic nerve preservation (PANP) surgery with lateral lymph node dissection has been tried from around 1987; the type of PANP varied and the indications were not established. In 1993, it was not commonly accepted to perform total PANP for patients who had a potential for stage II or III rectal cancer. They therefore started the study to examine the possibility of expanding the indications for total PANP, ( Ishikura et al.,1999).

Total mesorectal excision with pelvic autonomic nerve preservation has been reported to be an optimal surgery for rectal cancer. It minimizes local recurrence and sexual and urinary dysfunction. The aim of Kim study was to assess the safety of total mesorectal excision with pelvic autonomic nerve preservation in terms of voiding and sexual function in patients with rectal cancer, (Kim et al.,2005).

Sexual and urinary dysfunctions are recognized complications of resection for rectal cancer. The main cause of sexual dysfunction from surgical resection appears to be injury to the autonomic nerves in the pelvis along the distal aorta from blunt pelvic resection or undefined cutting. Incidence of genitourinary dysfunction depends on the type of surgery performed, i.e., the plane of dissection, the degree of preservation of the autonomic nerves, and the extent of pelvic dissection. Nerve injury can occur via direct injury, by vascular damage to the vasa nervosa, or where the blood supply to the nerves that enter laterally is disrupted with traction or devascularization, (Wein et al.,1999).

The neuroanatomy for sexual functioning requires an intact autonomic nervous system, which includes an interaction between the parasympathetic and sympathetic nervous systems. Erection

(parasympathetic-mediated response) is governed by impulses traveling along the nervi erigentes that arise from the second, third, and fourth sacral nerves, whereas ejaculation depends on sympathetic control. The sympathetic fibers originate from the lower thoracic and upper lumbar segments of the spinal cord. These fibers descend along the aorta, forming the superior hypogastric plexus near the aortic bifurcation. The plexus divides into 2 trunks, which enter the pelvis along its lateral walls as the hypogastric nerves. The parasympathetic fibers to the pelvis join the hypogastric nerves on each pelvic wall to form the pelvic plexuses. One study provided a more extensive review of the anatomy of the pelvic autonomic nerves and the relation of these nerves to the mesorectal fascial planes. Damage to the hypogastric (sympathetic) nerves or sacral splanchnic (parasympathetic) nerves, or both, during surgical resection are the most likely cause of urinary and sexual dysfunction. Pelvic plexus preservation is necessary to maintain erectile functioning, and both hypogastric nerve and pelvic plexus preservation are necessary to maintain ejaculate function and orgasm, (Havenga et al.,1996).

Postoperative retention can occur for a number of reasons. Nociceptive impulses can inhibit the irritation of reflex bladder contraction, perhaps through an opioid mediated mechanism or sympathetic mediated inhibition. Transient overdistention of the bladder can occur under anaesthesia or under the influence of analgesic medication. Purely neurologic injury during abdominal and pelvic surgery can occur, (Wein et al.,1999).

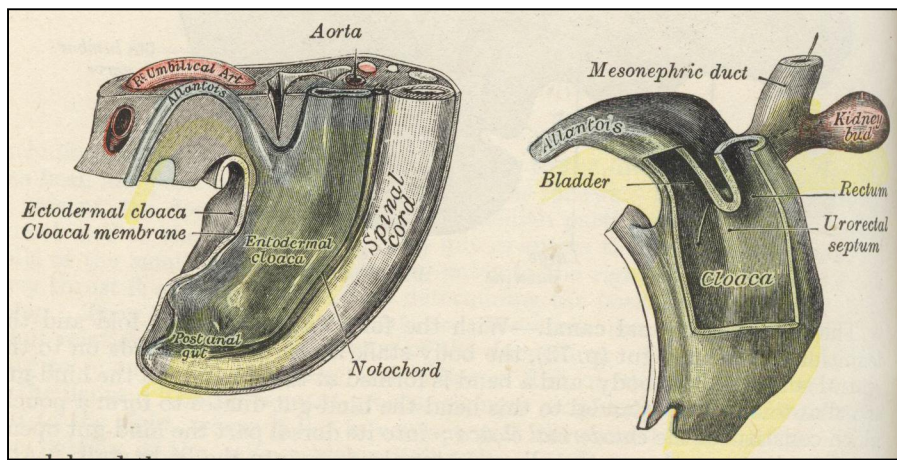
### **Aim of the work**

The aim of this research is to study the value of total mesorectal excision versus subtotal mesorectal excision in management of cancer rectum to reduce rate of local recurrence and pelvic nerve preservation to avoid postoperative urinary and sexual dysfunction.

## EMBRYOLOGY OF THE RECTUM

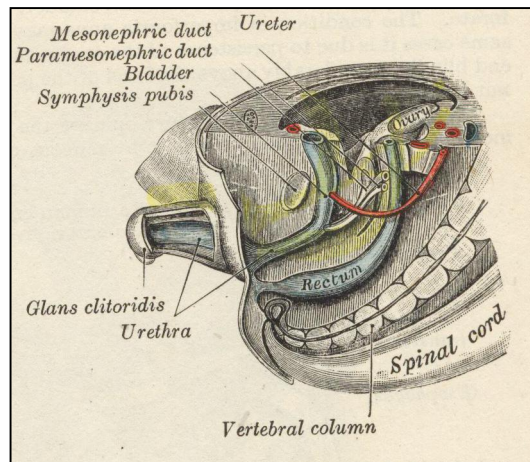
Some controversy still exists about the normal and abnormal development of the human anorectum. Therefore, a three-dimensional and histological study was performed on human embryos. In early anorectal development ( $\leq 49$  days postfertilization), the cloaca plays a crucial role, separated from the amniotic cavity by its cloacal membrane. In the cloaca, the yolk sac/primitive hindgut and allantois/primitive urogenital sinus enter. During the embryonic caudal folding process, incorporation of these structures occurs, including their surrounding extraembryonic mesoderm, which fuses to form the urorectal septum. Consequently, this septum does not grow in the direction of the cloacal membrane, and fusion of these structures is likewise never observed. The cloaca remains as such until the cloacal membrane ruptures by apoptotic cell death. The dorsal part of the cloaca then becomes part of the amniotic cavity, and is by no means involved in the development of the anorectum. The tip of the urorectal septum will become the perineal area. Soon after rupture of the cloacal membrane, during late anorectal development ( $\geq 49$  days postfertilization), a secondary occlusion of the anorectal canal occurs, first due to adhesion, followed by formation of an epithelial "plug" at the level of the anal orifice. Recanalization, by apoptotic cell death, of this secondary occluded anal orifice occurs later during development. Based on these embryological observations, congenital anorectal malformations with an abnormal communication to the exterior are best explained as early embryonic defects. The abnormal communications, usually called fistulae, should be regarded as ectopic anal orifices. Anorectal malformations with the anus in normal position are best explained as late embryonic defects. With the formation of the tail fold, definition of the hindgut, the body stalk is carried headwards on to the ventral surface of the body, and a bend is formed at the junction of the hindgut and allantoic canal. Caudal to this bend, the hindgut dilates to form a pouch, which constitutes the entodermal cloaca, into its dorsal part the hindgut opens, and from its ventral part the allantoic canal passes into the body stalk. At a later stage the mesonephric (Wolffian) and paramesonephric (Mullerian) ducts open into the ventral aspects of the cloaca, (Nievelstein et al.,1998).

Over the midventral wall of the cloaca, the endoderm comes into direct contact with the surface ectoderm without the interposition of mesoderm, and this area is termed the cloacal membrane. At first it extends on to the dorsal aspect of the connecting stalk but it undergoes real shortening and later the distance between it and the umbilicus gradually increases owing to the formation of the lower part of the abdominal wall, Fig. (1), (Heald et al.,1998).



**Fig. (1): Colorectal Development**

The cloacal membrane, in which the urogenital and anal orifices subsequently develop, lies in the line of the primitive stalk, which is carried round on to the ventral aspect of the body by the formation of the tail fold. By growth of the surrounding tissues the cloacal membrane comes to lie at the bottom of a depression, which is lined with ectoderm and named the ectodermal cloaca, Fig.(2), (Johnson et al.,2000).



**Fig. (2): The Tail – End Of A Human Embryo, 9 Weeks Old**

At the time when the mesonephric ducts enter the cloaca its ventral part is wider from side to side than its dorsal part, which remains very narrow. The mesoderm outside the line of union of these two parts grow rapidly and thrusts the endodermal epithelium inwards. As a result, the two walls come into apposition and fuse. This process commences opposite the connection of the allantoic canal with the cloaca and is continued caudally to form a septum, termed the urorectal septum, which separates the dorsal segment of the rectum from the ventral segment which forms the urinary bladder and the urogenital sinus, (George et al.,1997).

At its caudal end, the urorectal septum reaches the cloacal membrane and divides it into an anal and a urogenital membrane. For a time a of communication, named the cloacal duct, exists between the two parts of the cloaca caudal to the urorectal septum; this duct occasionally

persists as a passage between the rectum and the bladder or urethra, (George et al.,1997).

Anal tubercles form round the margin of the anal part of the cloacal membrane, thus comes to lie at the bottom of a depression, termed the proctodoeum. On the absorption and disappearance of this membrane, the rectum communicates with the exterior. The lower part of the anal canal is formed from the proctodaeum, but its upper part is endodermal in origin and is derived from the caudal end of the dorsal subdivision of the cloaca. The line of union corresponds with edges of the anal valves in the adult. A small part of the hindgut projects tailwards beyond the anal membrane; it is named the postanal gut and usually becomes obliterated and disappears, (Cecilia et al.,1997).

Embryologically, the mesorectum originates from a circular multilayer concentrate of mesenchymal cells, which form lamella of rectal adventitia that become filled fatty tissue during development. The outer lamella of rectal adventitia condense to form one or more fascial sheaths, (Fritsch et al., 1990). Usually, these sheaths are referred to as the visceral fascia of the mesorectum. Or the rectal fascia propria, (Hill et al., 1987).

## ANATOMY Of RECTUM

The rectum varies in length with age ,sex and body habits. It starts opposite the third sacral vertebra, but the surgeons describe it at the beginning of sacral promontory, (Fozard et al.,1996).

The length of the rectum varies from 12.5 -15 cm . It ends 2 to 3 cm in front and below the tip of coccyx backward . It passes through the levator muscles to form the anal canal which has an average length of 3 to 4 cm and terminates at the anal orifice or anus, (Goligher et al .,1984).

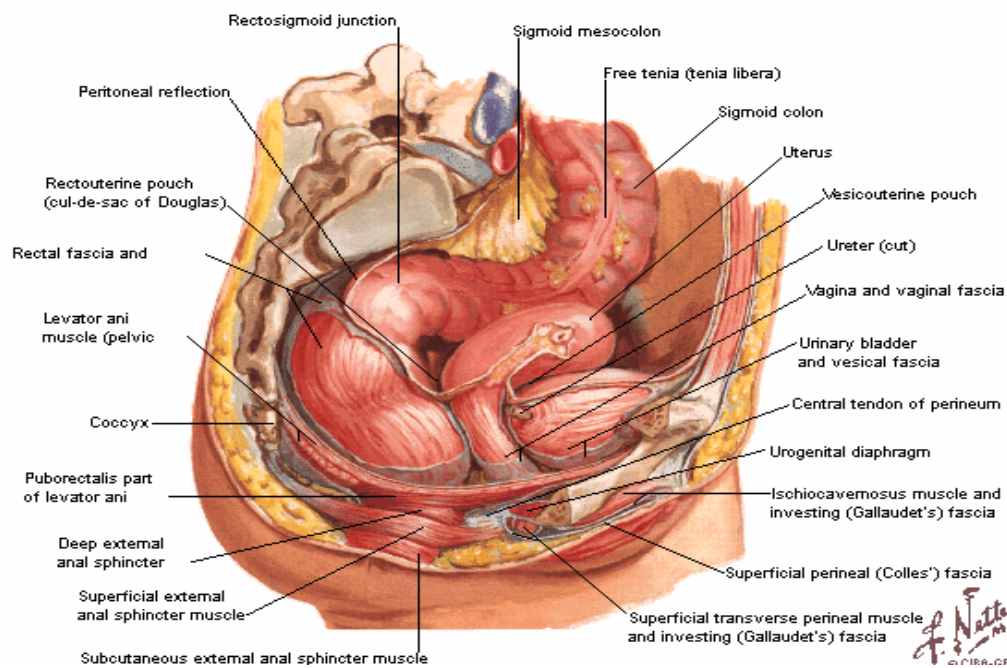
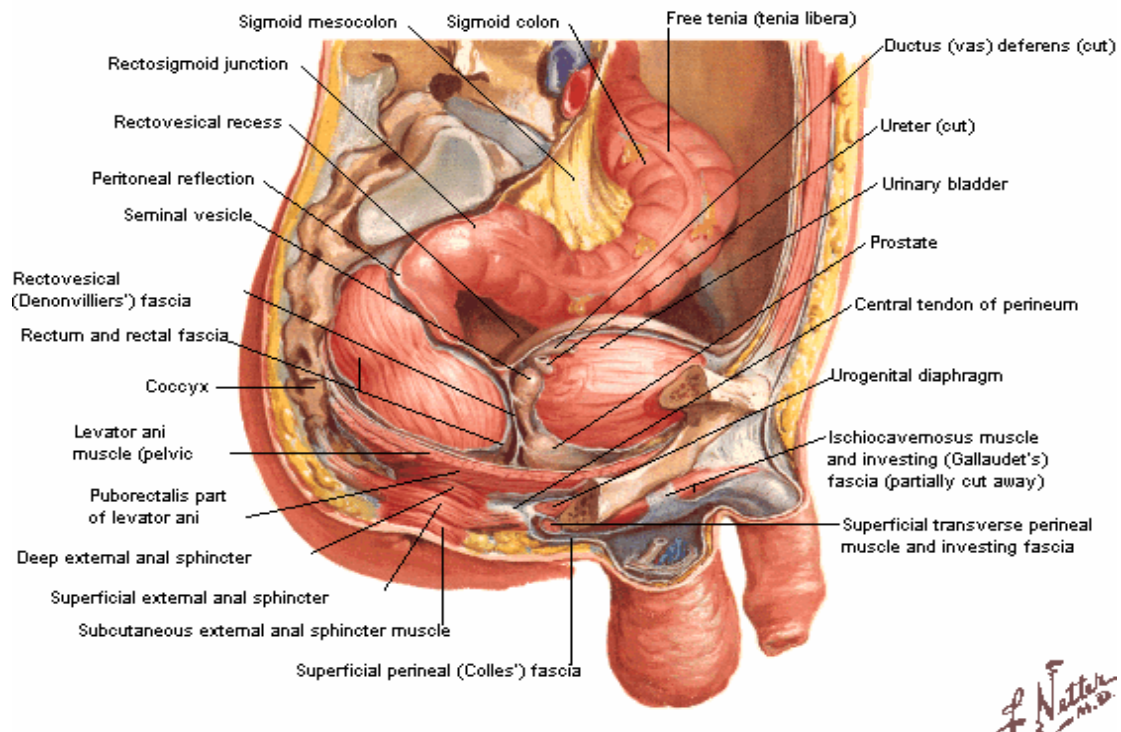
Posterior to the rectum in the median plane are the lower three sacral vertebrae, coccyx ,median sacral vessels and branches of superior rectal vessels. While on each side are the anterior rami of the lower three sacral and coccygeal nerves, sympathetic trunk, lower lateral sacral vessels and levator ani muscles. The rectum is attached to the sacrum along the lines of the anterior sacral foramina by fibro-areolar tissue enclosing the sacral nerve and pelvic splanchnic nerve from the anterior rami of the second to the fourth sacral nerves which join the pelvic plexus on the rectal wall, rami of superior rectal vessels, lymphatic vessels, lymph nodes and loose perirectal fat, (Williams et al.,1993).

Anteriorly in males and above the site of peritoneal reflection from the rectum, the upper part of the base of the bladder and of the seminal vesicle, the rectovesical pouch and its content [Terminal coils of ileum and sigmoid colon]. Below the reflection , the lower part of the ureters and prostate . In females above the reflection are the uterus, cervix, upper part of posterior vaginal wall, rectouterine pouch and its content [Terminal coils of ileum and sigmoid colon] while below the reflection lies the lower part of the vagina. Laterally the upper part of the rectum is related to the pararectal fossa while below the peritoneal reflection laterally are the pelvic sympathetic plexuses and levator ani and branches of superior rectal vessels, (Fig. 3 and 4 ), (William et al., 1993).

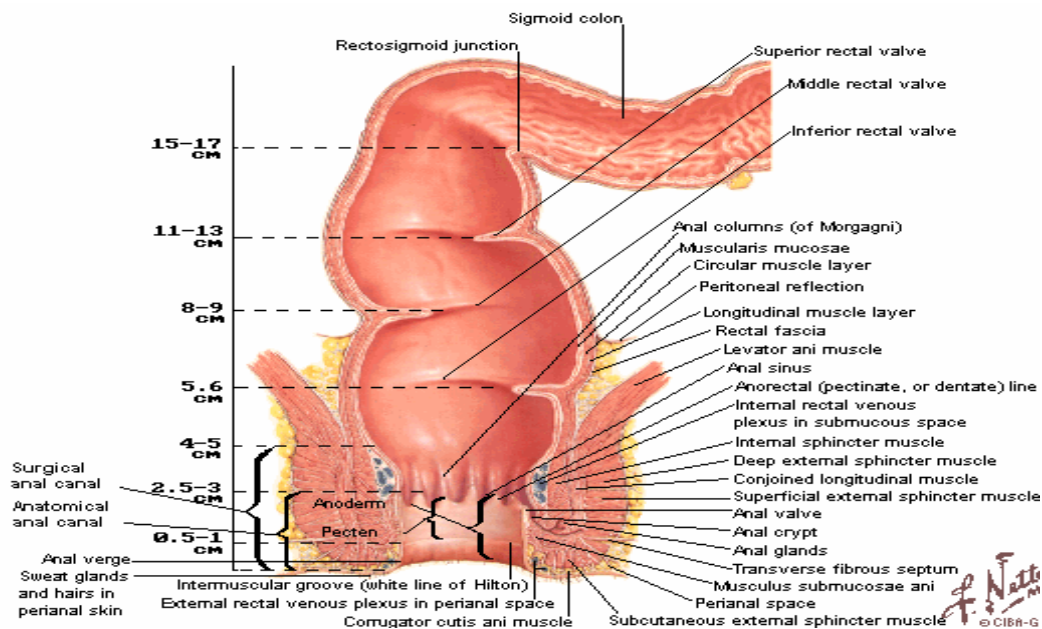
### **Curves of the rectum:**

Anteroposterior curves: As the rectum penetrates the pelvic diaphragm to become the anal canal it angles anteroposteriorly at approximately 90 degrees.Lateral curves. The lateral curves are usually three, the uppermost and the lowermost being both convex to the right while the middle one is convex to the left. The angulation of the bowel on the concave side of each of these curves is accentuated by infolding of the mucosa known as Houston valves. So there are upper and lower valves on the left side known as Kohlrausch fold. It is situated about the same level as the anterior peritoneal reflection. The part of the rectum lying a wider lumen than has the intraperitoneal part, this dilated lower portion is known as the ampulla of the rectum, (Fig.5), (Fleshman et al.,1997).





**Fig. (4) : Rectum Of Female In Situ**

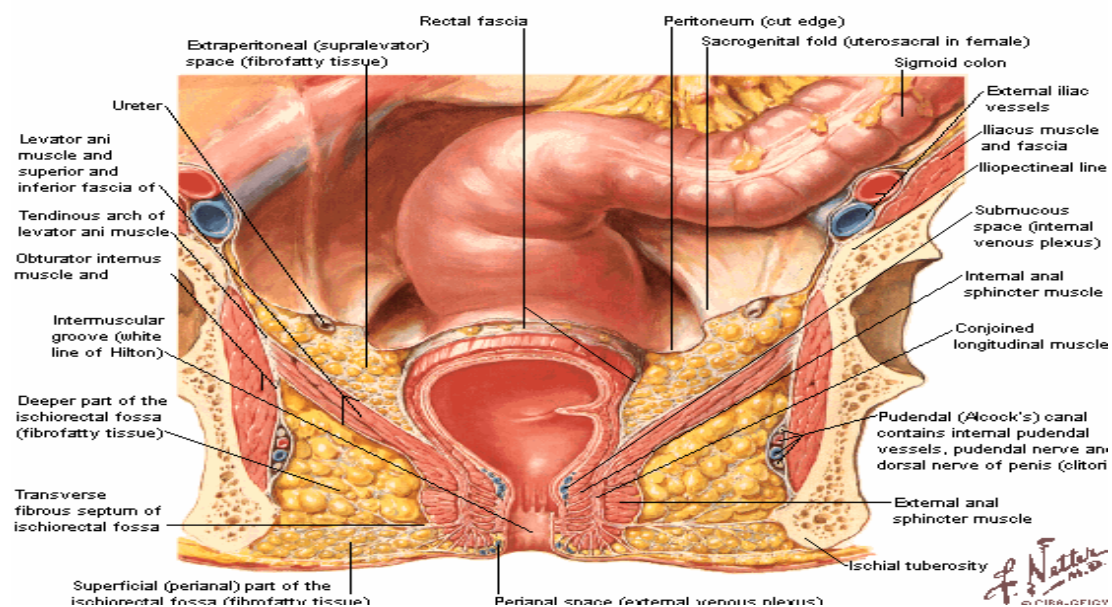


**Fig. (5) : Rectal Valves**

## **Perianal and pararectal spaces :**

### **Ischorectal fossa :**

The apex of this space is the origin of the levator ani muscles from the obturator fascia . The floor is the skin of the perineum. The space is bounded anteriorly by transverse muscles of the perineum. Posteriorly by the sacrotuberous ligaments and gluteus maximus muscles. Medially by the external anal sphincter and laterally by the obturator internus muscle and obturator fascia. The space contains inferior haemorrhoidal vessels, nerves and fat , Fig (6) , (Lindsey et al.,2000).



**Fig. (6) : Ischorectal Fossa**



### **Perianal space :**

It surrounds the anal verge and contains the caudal rim of the external anal sphincter and branches of inferior haemorrhoidal vessels.

### **Intersphincteric space :**

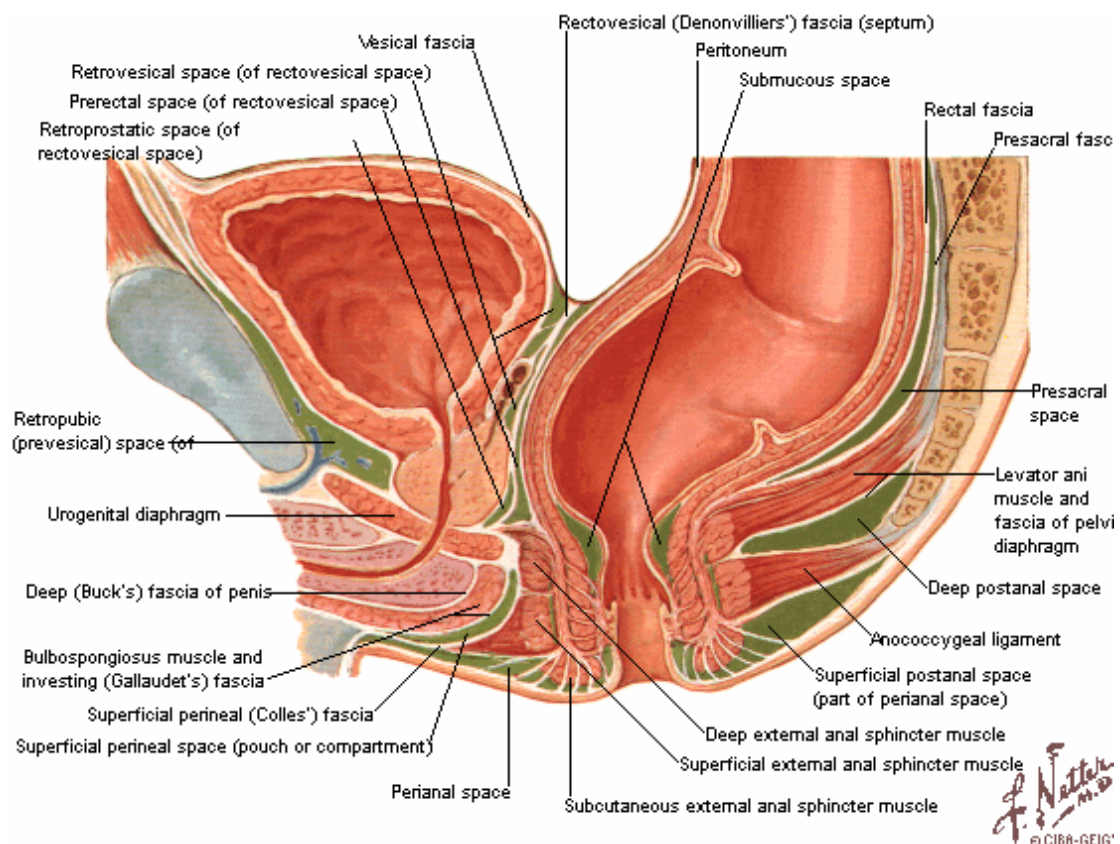
It is potential space between the internal and external sphincters.

### **Postanal spaces:**

The ischiorectal spaces communicate posteriorly through superficial and deep anal spaces. The superficial spaces run between the skin and the anococcygeal ligaments and the anococcygeal raphe of the levator ani muscles.

### **Retrorectal and supralelevator spaces:**

The rectal spaces begins cranial to Waldeyers fascia and extends upward between the fascia propria, the presacral fascia posteriorly, the pelvic fascia and peritoneum laterally and superiorly. At a deeper level between waldeyers fascia and the levator ani muscles is the supralelevator space, Fig. (7), (Fozard et al.,1997).



**Fig. (7) : Perineopelvic Spaces**

### **Blood supply of the rectum :**

The rectum receives its blood supply from : Fig. (8), (Keighley et al., 1993):

#### **1- The superior rectal [haemorrhoidal] artery:**

It is the continuation of the inferior mesenteric artery and descend inferiorly to the rectum. It bifurcates to supply the rectum and upper portion of the anal canal.

#### **2- The middle rectal [haemorrhoidal] arteries :**

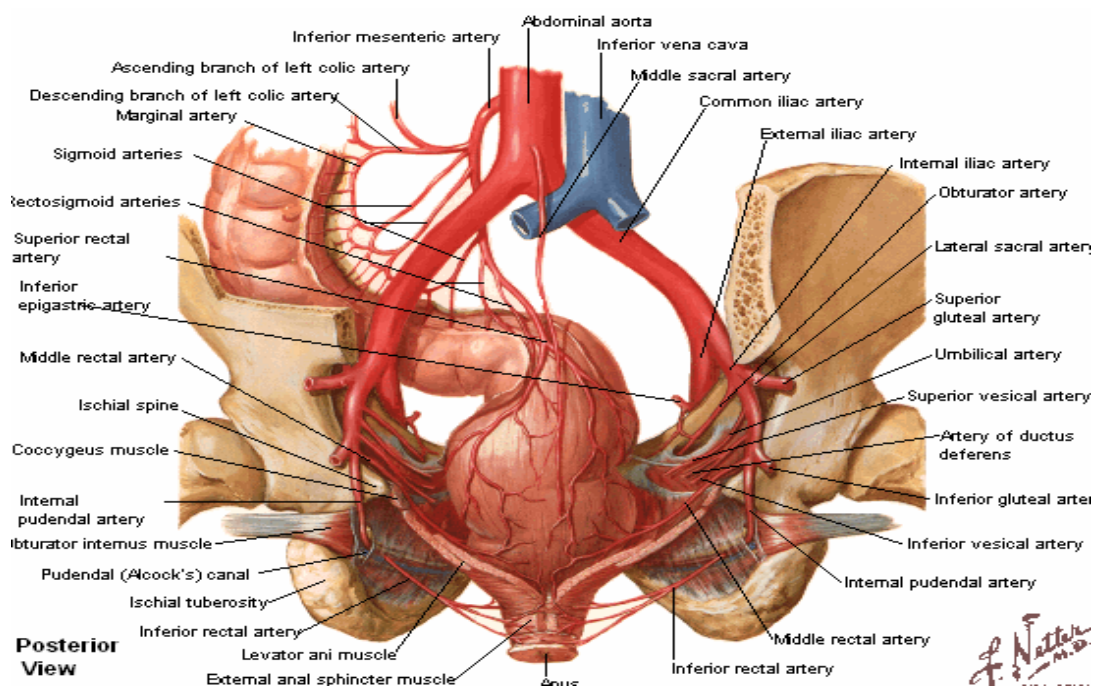
They arise from the anterior division of the internal iliac artery on each side and pass medially and forward below the pelvic peritoneum , in the tissue of the lateral ligament. They reach the rectal wall where they anastomose with the branches of the superior and inferior haemorrhoidal vessels. Their arrangement is very variable and may be absent.

#### **3- The inferior rectal [haemorrhoidal] artery :**

It arises indirectly from the internal iliac artery through its internal pudendal branch. It runs medially and slightly forward breaking up into branches which penetrate the external anal sphincters and reach the submucosa and subcutaneous part of the anal canal. They communicate with branches from the inferior haemorrhoidal artery of the opposite side.

#### **4- The median sacral artery :**

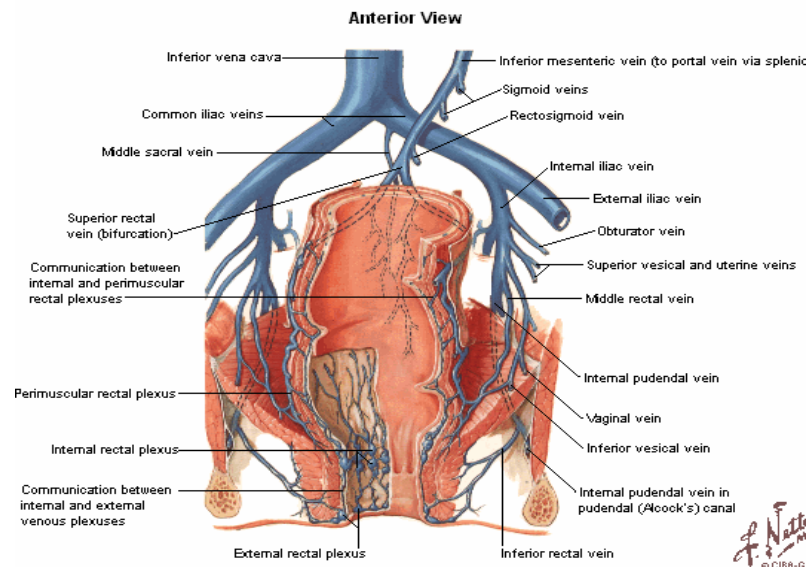
This artery arises from the back of the aorta about 1 cm above its bifurcation and runs downward in front of the last two lumbar vertebrae, the sacrum and coccyx. It provides an insignificant amount of blood to the rectum.



**Fig. (8) : Arteries Of Rectum And Anal Canal**

### **Venous drainage of the rectum:**

The veins of the rectum comprise: The superior haemorrhoidal [which drains into inferior mesenteric and portal system] and the middle and inferior haemorrhoidal [which enter the systemic venous circulation via the internal iliac veins]. The superior haemorrhoidal venous plexus lies in the submucosa of the upper part of the anal canal and the lower inch of the rectum. The middle haemorrhoidal vein is relatively unimportant. The inferior haemorrhoidal vein is more significant as it drains the external haemorrhoidal plexus of veins which lie under the skin of the anal orifice and the lower part of the anal canal, Fig. (9), (Thomas et al.,1988) .

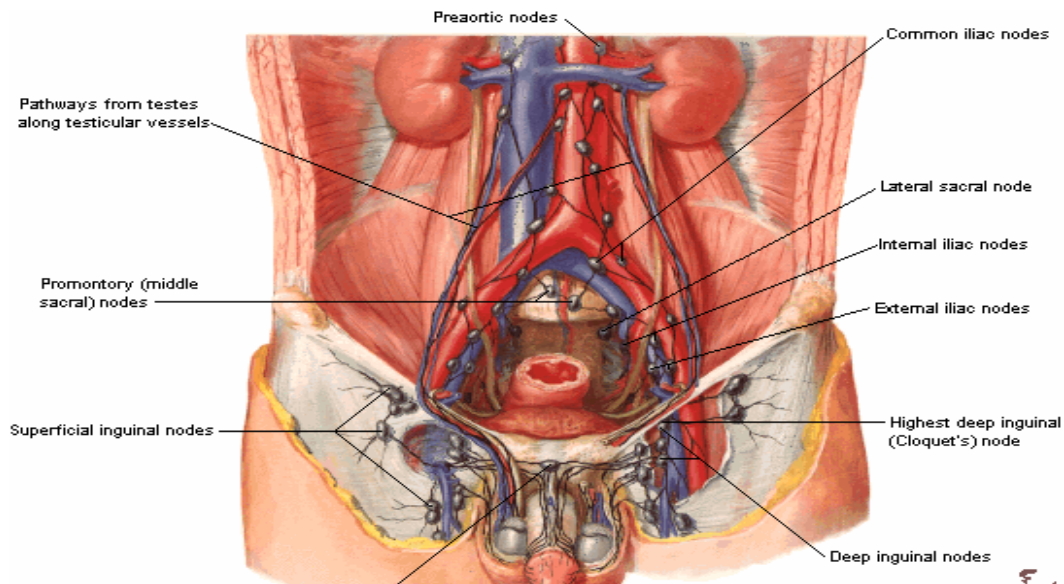


**Fig. (9) : Veins Of Rectum And Anal Canal**

### **Lymph drainage of the rectum :**

There are three main routes of lymphatic drainage:

- 1- Upwards: through the lymphatic and glands accompanying the superior haemorrhoidal and inferior mesenteric vessels essentially to inferior mesenteric glands. There may also be some drainage to the paracolic glands along the sigmoid colon but experience with spread of rectal carcinoma suggested that this latter route is rare , (Keshav et al.,2004).
- 2- Laterally: along the middle haemorrhoidal vessels to the internal iliac glands on the corresponding side wall of the pelvis. There may be some gland also in the course of these lymphatic channels on the upper surface of the levator ani muscles and in the substance of lateral ligaments but apparently the main collection is on the pelvic side wall (Williams et al.,1985).
- 3- Downwards: through pararectal lymph glands on the back of the rectum and along the lymphatic plexuses in the anal and perianal skin, the anal sphincters and ischiorectal fat to reach the inguinal lymph glands or the glands along the internal iliac vessels, Fig. (10), (Goligher et al.,1984).



**Fig. (10) : Lymph Drainage Of Rectum And Anal Canal**

### **Fascial relationship of the rectum:**

There are two fasciae, the visceral endopelvic fascia and the parietal endopelvic fascia, extending downward in the pelvis from the retroperitoneal space in the abdomen. The visceral endopelvic fascia essentially extends under the peritoneum and anterior to the aorta and vena cava. The parietal endopelvic fascia spreads under these vessels. In the pelvis, the parietal endopelvic fascia extends laterally along the whole pelvic wall, but the visceral endopelvic fascia is arranged to envelope the peritoneal cavity and the rectum with mesorectum. On the posterior side of the pelvis there is a space between two endopelvic fasciae. At the level of the peritoneal reflection, the visceral endopelvic fascia envelops Denonvillier's fascia on the anterior side, and the mesorectum, together with the rectum on the posterior side. It is important to recognize that the superior hypogastric nerve plexus and the hypogastric nerve fibres are situated close to the endopelvic fascia, (Welvaart et al.,1996).

A space filled with fibro-fatty tissue is seen on either side of the rectum. The fibrous elements in this tissue are a part of pelvic fascia that connects the parietal pelvic fascia on the side wall of the pelvis with the rectum. They are known as the lateral ligaments of the rectum. It has a triangular shape with the base on the side wall of the pelvis and the apex joining the side of the rectum, (Goligher et al.,1984).

The posterior aspect of the extra peritoneal rectum is loosely bound down to the front of the sacrum and coccyx by connective tissue which easily separated by blunt dissection. When this is done it is found that there is still a thin layer of fascia covering the fat, vessels, and lymph glands on the back of the rectum. This is called fascia propria or fascial capsule of the rectum and is a part of the visceral pelvic fascia,



(Goligher.,et al 1984).

The sacrum and coccyx are also still covered with a fascia , this is much stronger and tougher and is a specially thickened part of the parietal pelvic fascia which is known as the fascia of Waldeyer, (Schneck et al.,1990).

Anteriorly the extra peritoneal part of the rectum is covered with a layer of visceral pelvic fascia. It extends from the anterior peritoneal reflection above to the superior fascia of the urogenital diaphragm below. It is easily seen at operation of excision of the rectum and is known as Denonvillier's fascia. It intervenes between the rectum behind and prostate and seminal vesicles or vagina anteriorly, (Goligher et al., 1984).

### **Mesorectum:**

The transition between sigmoid colon and rectum is defined as the point where the sigmoid taenia spread into a uniform layer. The rectum is embedded in a layer of fatty tissue. Inside this perirectal fat , draining lymph nodes of the rectum are found. As well as the superior and middle rectal artery and vein. In surgical vocabulary, this layer has been referred to as the mesorectum, (Ryall et al., 1982).

Posterolaterally, the mesorectum lines the inner pelvic wall. Ventrally, to different degrees in men and women, the mesorectum may be covered with peritoneum. Distal to the peritoneal reflection, the mesorectum borders on the seminal vesicles and prostate in males and on the vagina in females, (Church et al.,1997).

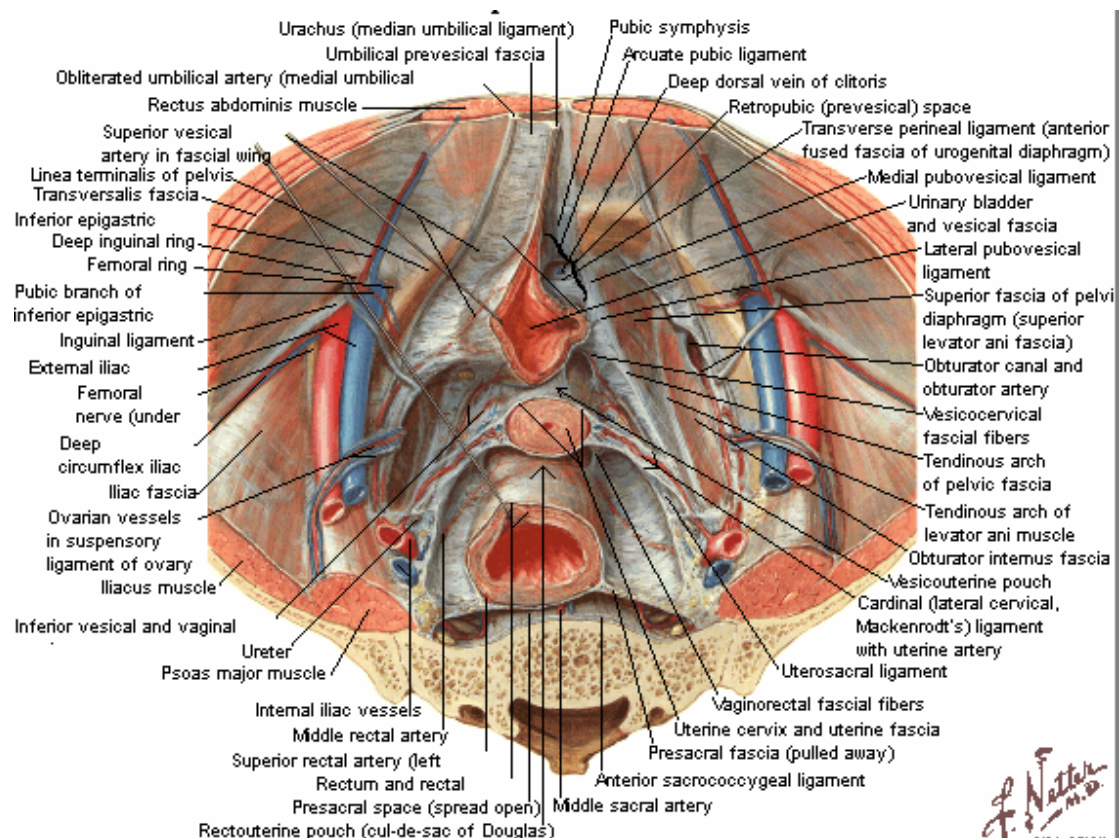
At the level of upper rectum, where the mesosigmoid shortens and disappears, the mesorectum has the shape of a half moon on a transverse cut. At the level of the seminal vesicles or upper vagina[ie, the midrectum, just under the peritoneal reflection ] the mesorectum is more or less a circle on a transverse cut, With the rectum eccentrically located anteriorly. Going down to the low rectum,entering the space between both the levator ani muscles, the mesorectum gets thinner and disappears at the junction with the anus, (Fritsch et al.,1990) .

### **Posterior attachments:**

The posterior pelvic wall consists of the piriformis, coccygeal, and levator ani muscles, the anterior surface of the sacrum and coccyx, and the anococcygeal ligament. The parietal fascia overlies these structures. The parietal fascia is identical to the muscle fascia it covers. On the bony surface, the parietal [presacral] fascia is in some places identical to the periosteum and difficult to demonstrate by dissection. The parietal fascia is continuous to the transversalis fascia in the abdomen, (Hinman et al.,1993).

Posterior or dorsal to the parietal fascia a presacral venous plexus is found, as are the spinal nerves. Posteriorly, the visceral and the parietal fascial layers are separated by a thin layer of loose connective tissue. This layer is easily entered and divided to open the retrorectal space. The

retrorectal space is bounded laterally in a line along the iliac artery, and , more caudally, the insertion of the levator ani muscle. Caudally, the retrorectal space ends at the anal sphincter. Cranially, the end of the retrorectal space is illdefined as the visceral fascia thins out over the sacral promontory and aorta. Some small branches of the internal iliac vein and presacral venous plexus cross the retrorectal space. At the level of the fourth sacral vertebra, the retrorectal space is interrupted with more or less a strong connection of fibres running in a craniocaudal direction from the parietal fascia to the visceral fascia. This fascia has been referred to as the rectosacral fascia, Fig. (11), (Enker et al., 1996).



**Fig. (11) : Anterior and posterior attachment of rectum**

### Anterior attachments:

Anterior to the rectum, Denonvillier's fascia divides the mesorectum from the seminal vesicles and the prostate. Recently, the anatomy and embryology of Denonvillier's fascia was reviewed in detail , (Warren et al 2000).

The fascia was originally described in males, but in females an equivalent, although thinner , rectovaginal fascia exist. Emryologically, Denonvillier's fascia is most likely a regression of the peritoneal reflection. Which extends to the pelvic floor in early development. Posterior to Denonvillier's fascia, the mesorectum is covered by the visceral fascia. Surgical planes exist anterior and posterior to

Denonvillier's fascia, (Noldus et al., 1999).

**Lateral attachments:**

Laterally the mesorectum is attached to the pelvis in a line along the iliac arteries, along the internal pudendal artery, and along the insertion of the levator ani muscle to the anus. At the upper mesorectum, the lateral attachment is formed by the connections of visceral fascia with parietal fascia, the peritoneum, and by fatty and connective tissue inbetween. At the sacral promontory these attachments are closer to the midline. The lateral attachment diverges laterally, reaching the widest distance from the midline at the peritoneal reflection [mid rectum], before coming down to the anus. The midrectum is attached to the pelvic side wall with a condensation of connective tissue. Within this condensation, rectal branches of the pelvic autonomic nerve plexus are found. As are the middle rectal vessels. In the absence of surgical dissection, the oval or circular mesorectum at this level is closely adherent to the lateral pelvic wall. When during surgical or anatomical dissection the retrorectal and presacral spaces are opened, the fibrous attachments of the mesorectum to the lateral pelvic wall resemble a ligament-like structure. Traditionally, these connections have been referred to as the lateral ligaments, (Goligher et al., 1984).

Lateral ligament has been regarded as a clinical or surgical term and not an anatomical one, (Dixon et al., 1986).

The lateral ligament as the medial segment is so-called identifying the inferior hypogastric plexus as the lateral segment, (Stato et al., 1991).

The medial segment, with its neurovascular attachments to the rectum, may be divided, while the lateral segment must be preserved if urinary and sexual function are to remain intact after total mesorectal excision, (Hill et al., 2000).

## PELVIC AUTONOMIC NERVE

Pelvic sympathetic nerve fibers originate from splanchnic branches from Th.12 through L.2 Through ganglia in the paravertebral sympathetic trunk, fibres contribute to the preaortic superior hypogastric plexus. The superior hypogastric plexus extends to the sacral promontory, distal to the aortic bifurcation. At this point the plexus condenses, usually in two hypogastric nerves. In some cases the hypogastric nerve may consist of a number of small branches. At the sacral promontory the hypogastric nerves are peripheral to or encased within the visceral fascia and are found approximately 1 cm from the midline. The superior hypogastric nerve extends distally and caudally, medial to the course of the ureter to the pelvic side wall, in the proximity of the lateral attachment of the upper mesorectum. The relation of the hypogastric nerve to the mesorectum and visceral fascia is disputed. Based on anatomical dissection, the hypogastric nerve has been described by Waldeyer to lie between the pelvic fascia and the peritoneum, Fig. (12), (Waldeyer et al., 1889).

Another minor sympathetic pathway is the sacral sympathetic trunk , a continuation of the paralumbar sympathetic trunk. The sacral sympathetic trunk is located posterior to the parietal fascia, close to the sacral foramina. It may give some small direct branches to the rectum that are divided when the retrorectal space is opened , Fig. (12).

Pelvic parasympathetic nerve fibres originate from the third and fourth sacral foramina, in some cases also from the second or fifth sacral foramina. These pelvic splanchnic nerves continue distally and caudally to the pelvic side wall. From their origin at the sacral foramina the pelvic splanchnic nerves are found peripheral to the parietal fascia. Three to four centimeters lateral to these foramina these nerves pierce the parietal fascia and continue in a double layer of visceral fascia. At the pelvic side wall, the pelvic splanchnic nerves join the hypogastric nerve to form the inferior hypogastric plexus. Because of its splanchnic parasympathetic as well as sympathetic makeup, it is referred to this structure as the pelvic autonomic nerve plexus , Fig. (12), (Enker et al., 1996).

From the inferior hypogastric plexus nerve fibres extend to the pelvic urogenital viscera. The middle rectal plexus arises from the upper part of the pelvic plexus , supplies the rectum and joins the branches of the superior rectal plexus , Fig. (12) , (Nano et al., 2000).

The vesical plexus arises from the fore parts of the pelvic plexuses. The nerves composing it are numerous and , as it is a mixed sympathetic and parasympathetic plexus, contain a large proportion of medullated preganglionic nerve fibres. They accompany the vesical arteries, and are distributed to the sides and fundus of the bladder. Numerous filaments also pass to the vesiculae seminalis and vasa deferentia ; those



accompanying the vasa deferentia join, on the spermatic cord, with branches from the testicular plexuses. The vesical sympathetic nerves convey motor fibres to the sphincter and inhibitory fibres to the muscular coats of the bladder, Fig. (12).

The prostatic plexus is continued from the lower parts of the pelvic plexuses. The nerves composing it are of large size. They are distributed to the prostate, vesiculae seminales, and the corpora cavernosa and corpus spongiosum of the penis. The nerves supplying the corpora cavernosa consist of two sets, the lesser and greater cavernous nerves, which arise from the fore part of the prostatic plexus, and, after joining the branches from the pudendal nerve, pass forwards below the pubic arch, Fig. (10).

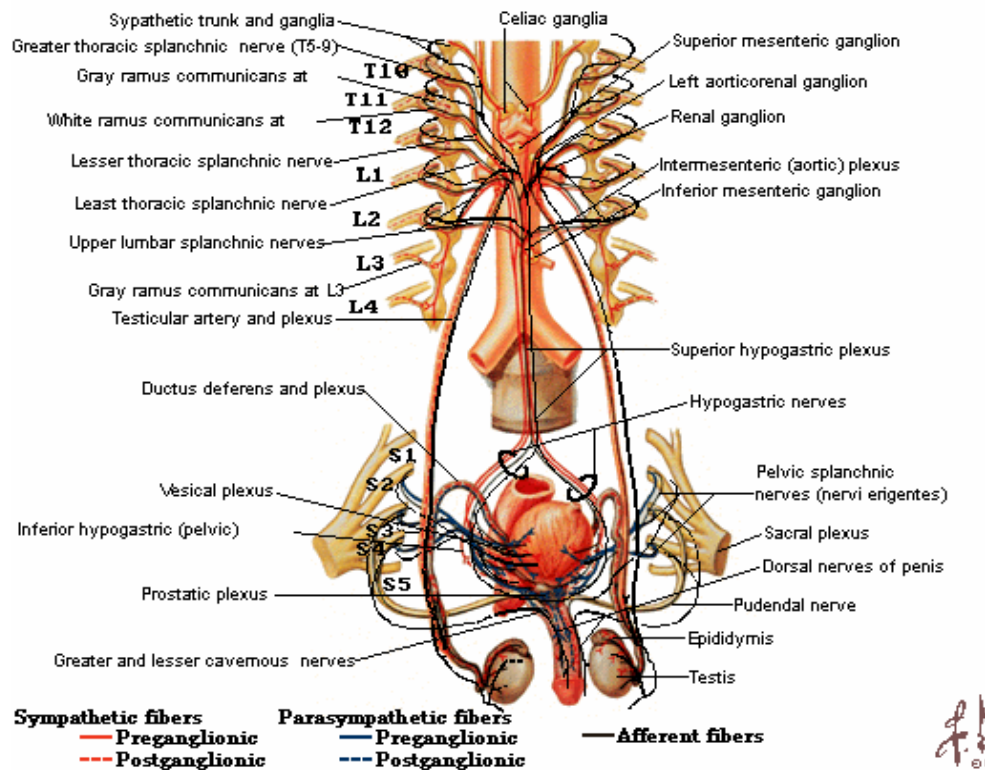
The lesser cavernous nerves perforate the fibres covering the penis, near its root, and are distributed to its erectile tissue. The greater cavernous nerve passes forwards along the dorsum of the penis, joins with the dorsal nerve of the penis, and is distributed to the corpora cavernosa, Fig. (12).

On anatomical dissections the hypogastric nerve is located between the endopelvic fascia and the peritoneum as well, (Lee et al., 1973). It lies anterior to the visceral fascia, on the posterior surface of the mesorectal fat, (Enker et al., 1996). This finding influences the surgical dissection, as recognition of the pathway of the nerve is essential to function preservation. Clinical studies have described the hypogastric nerve outside the fascia propria of the rectum, posterior to the visceral fascia, (Hill et al., 2000). According to Takahashi, the hypogastric nerve is situated within the visceral fascia [Takahashi et al., 2000]. This view may reflect the embryological multilamellar origin of the mesorectum and visceral fascia, Fig. (13), (Fritsch et al., 1990).

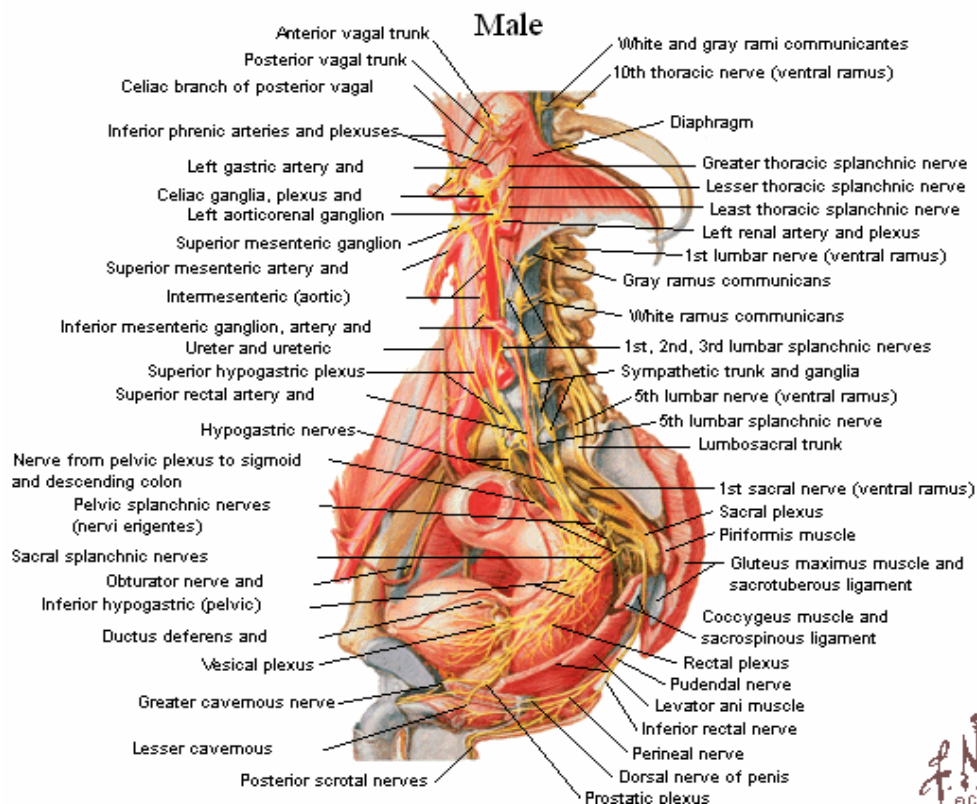
Median branches of the inferior hypogastric plexus toward the rectum form part of the lateral ligament of the rectum. They accompany the branches of the internal iliac artery, Fig. (13).

The vaginal plexus arises from the lower parts of the pelvic plexuses. It is distributed to the walls of the vagina and to the erectile tissue of the vestibule. The nerves composing this plexus contain, like the vesical, a large proportion of preganglionic parasympathetic nerve fibres, Fig. (14).

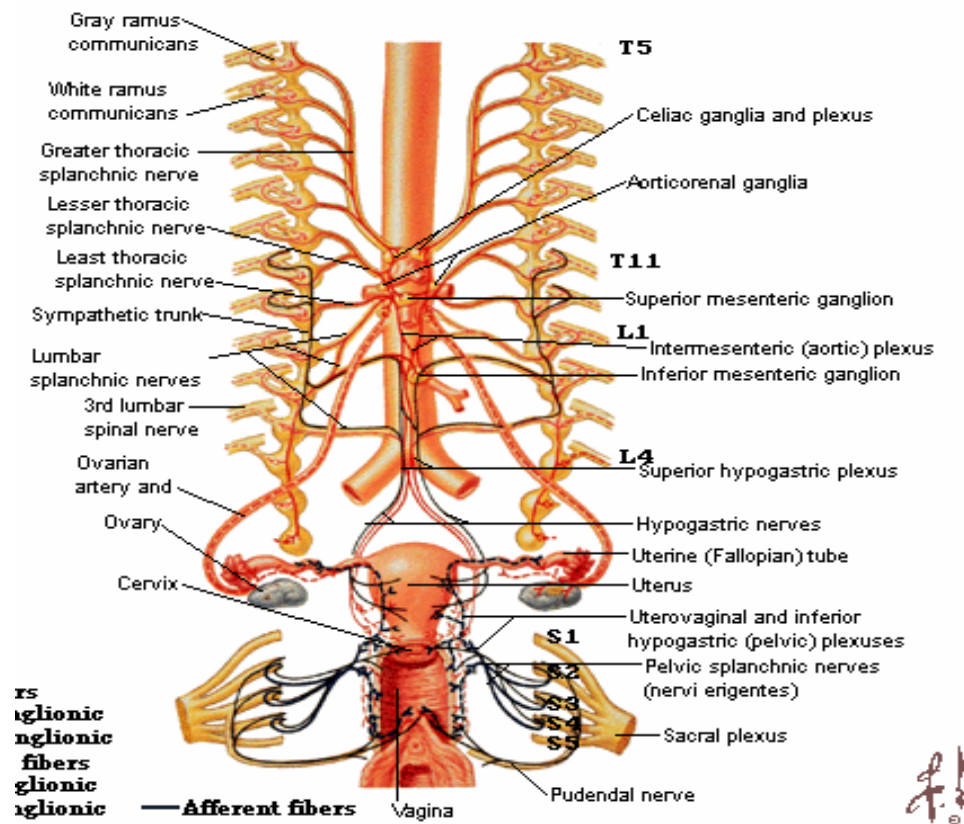
The uterine plexus accompanies the uterine artery along the side of the uterus, between the layers of the broad ligament, and communicates with the ovarian plexus. Its fibres are chiefly distributed to the neck, and the lower part of the body, of the uterus. A collection of small ganglia which together form the uterine cervical ganglion is situated at the side of the neck of the uterus, Fig. (14 and 15), (Hinman et al., 1993).



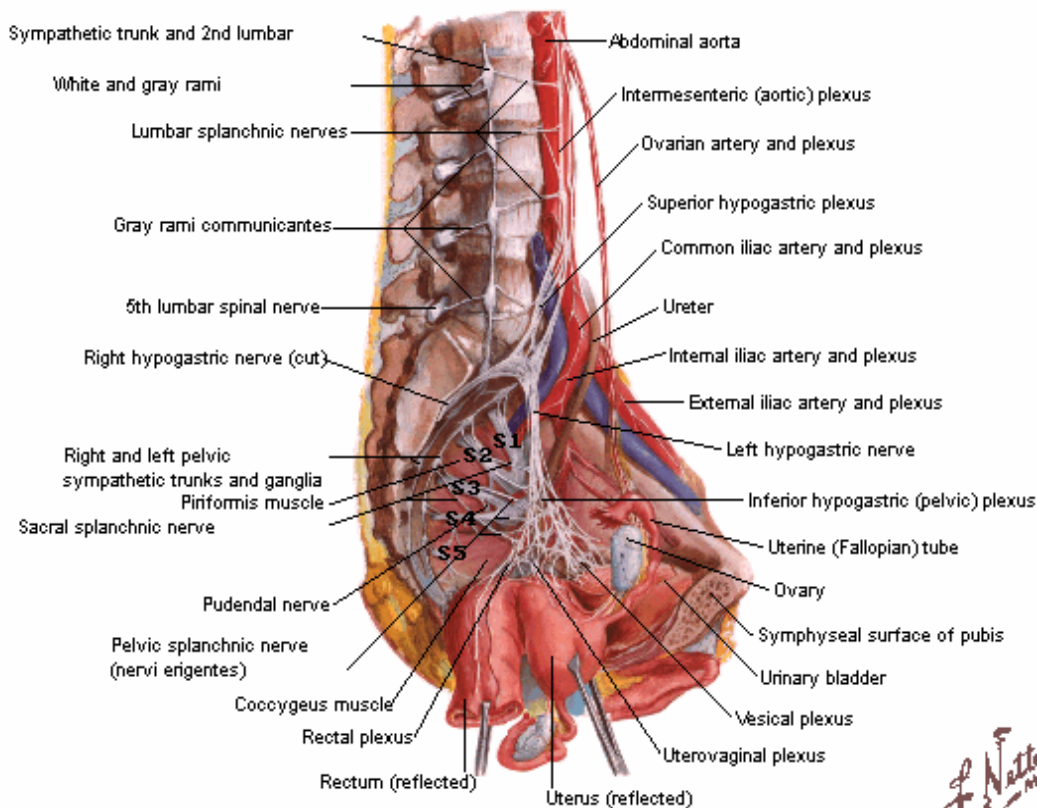
**Fig. (12) : Schema For Innervation Of Male Pelvic Organs**



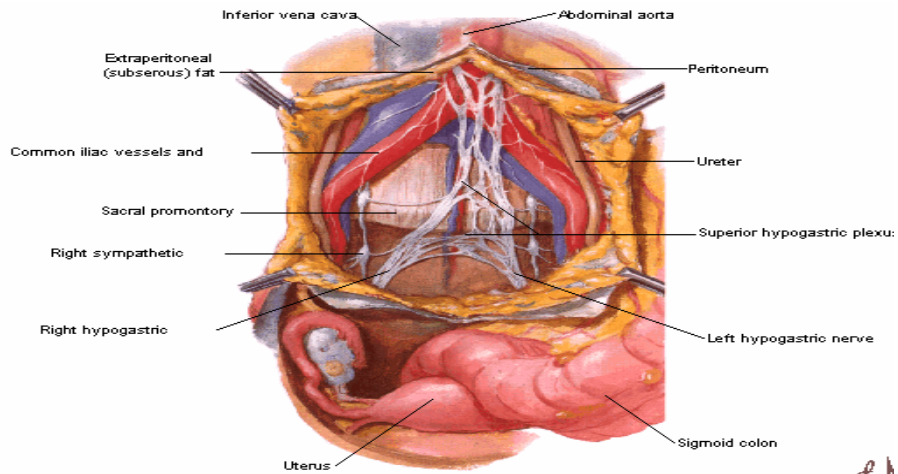
**Fig. (13) : Anatomic Location Of Pelvic Nerves In Male**



**Fig. (14) : Schema For Innervation Of Female Pelvic Organs**



**Fig. (15a) : Anatomic Location Of Pelvic Nerves In Female**



**Fig. (15b) : Anatomic Location Of Pelvic Nerves In male**

## **Pelvic nerve function test:**

### **1-Urodynamics:**

Urinary continence during bladder filling, urine storage in the bladder, and the efficiency of subsequent voiding all depend upon accurate coordination of the opposing forces of detrusor contractility and urethral closure pressure. Symptomatic evaluation of urinary tract dysfunction is difficult because the bladder often proves to be an unreliable witness, not only because of subjective bias, but also because there is considerable overlap between the symptoms for different disorders. Urodynamic techniques are objective investigations developed to clarify these symptoms. The term urodynamics encompasses a variety of complementary techniques of varying complexity, their use needs to be tailored to each individual case. Urinary tract infections are an uncommon cause of incontinence and should always be checked for before urodynamic investigation because it will aggravate any existing urinary symptoms and can invalidate the results of urodynamics. The filling cystometrogram may falsely demonstrate bladder instability and in some cases, loss of bladder compliance. The effects of asymptomatic bacteriuria on cystometry is unknown. Confirmation of recurrent urinary tract infections may alter the type and priority of investigations performed, (Christopher et al., 2000).

Volume voided charts are often overlooked as an important omission because it provides a natural volumetric urodynamic record of bladder function. The volume – frequency chart is a simple noninvasive tool used in the evaluation of patients who have voiding dysfunction, particularly those who have increased urinary frequency and incontinence as it helps to define the severity of symptoms and objective to history. Increased urinary frequency secondary to high urinary output can be readily diagnosed and differentiated from physiological nocturnal diuresis. A record of fluid intake helps in identifying an easily treatable cause of urinary frequency. The average maximum voided volume represents the

patient's functional capacity and knowing what this volume prevents overfilling of the bladder during cystometry. The normal bladder fills to a volume that approximates its functional capacity and the chart records a series of sizeable [300 – 500] and fairly consistent volumes and an unstable bladder contracts to a variable degrees of distension before full capacity, erroneously informing the patient that it is full, resulting in urinary frequency and low and varying voided volumes , (Abrams et al., et al.,1997).

Pad testing is a subjective assessment of incontinence and is often difficult to interpret and does not reliably indicate the degree of abnormality. Not all patients who complain of urinary incontinence are incontinent during a cystometric examination. Pad testing is a simple noninvasive objective method for detecting and quantifying urine leakage. To obtain a representative result, especially for those who have variable or intermittent urinary incontinence, the test period should be as long as possible in circumstances that approximate to those of everyday life and conducted in a standardized fashion, (Griffiths et al., 1998).

Flow rate is the simplest and often most useful investigation in the assessment of voiding dysfunction is measurement of a urinary flow rate. It is noninvasive and can often be used to confirm the presence of bladder outlet obstruction objectively and when combined with measurement of residual urine volume it is an excellent screening test for bladder outlet obstruction in patients who have benign prostatic hyperplasia and it is useful for identifying those patients who require more extensive urodynamic evaluation. Measured uroflow is dependent upon a number of factors including detrusor contractility, relaxation of the sphincter mechanisms and patency of the urethra. Flow rate can be normal in the early stages of obstruction due to a compensatory increase of detrusor contractility resulting in a high voiding pressure. This high pressure normal flow voiding more than 15 ml/s occurs in approximately 7 - 15 % of patients with bladder outflow obstruction secondary to benign prostatic hyperplasia. A low flow rate is not diagnostic of bladder outlet obstruction and may be due to obstruction or poor bladder contractility. They can be differentiated by simultaneous measurement of detrusor pressure and flow , (Anderson et al.,1999).

Cystometry is the method used to measure the pressure – volume relationships of the bladder. The term cystometry is usually taken to mean measurement of detrusor pressure during controlled bladderfilling and subsequent voiding with measurement of the synchronous flow rate [ filling and voiding cystometry ]. Cystometry helps to characterize detrusor function by assessing bladder compliance, sensation, stability and capacity. There are three methods of cystometry: simple cystometry in which the intravesical pressure is measured while the bladder is filled. It is not accurate because it assumes that the detrusor pressure approximates to the intravesical pressure. As the bladder is an intra



abdominal organ, the detrusor pressure is subjected to changes in intra abdominal pressure, which may lead to inaccurate diagnoses. Subtracted cystometry involves measurement of both the intravesical and intra abdominal pressure simultaneously. Electronic subtraction of the intra abdominal pressure from the intravesical pressure enables detrusor pressure measurement. Videocystometrography can be performed if there are radiological facilities as the bladder can be filled with contrast media to allow simultaneous screening of the bladder and outflow tract during filling and voiding. Most patients can be adequately investigated using simpler urodynamic techniques including simple cystometry for equivocal urological cases, (Mundy et al., 1994).

## **2- Doppler studies:**

The simplest and most common erectile function test to detect impaired hemodynamic blood flow parameters is the use of Doppler ultrasound techniques to record systolic occlusion pressure in the cavernosal arteries of the penis. A pediatric blood pressure cuff is placed around the base of the penis and inflated to a pressure above the brachial systolic pressure. As the cuff is slowly deflated, a Doppler ultrasound probe is used to detect the return of pulsation in the right and left cavernosal arteries. A penile systolic pressure less than 70 % of the brachial systolic pressure [ penile brachial index ( PBI ) :less than 0.7 ] is considered compatible with arterial vasculogenic impotence. It is important to note that study is inaccurate and difficult to reproduce. A decrease in PBI of more than 0.15 after exercise is suggestive of pelvic steal. This test is currently not commonly performed. Duplex ultrasound and pulsed Doppler analysis with and without intracavernosal vasoactive agent [papaverine and / or prostaglandin E 1] are very commonly used in many centers for evaluation of penile vascular insufficiency. After intracavernosal injection, venogenic impotence is ruled out by obtaining a rigid erection [ usually within 10 min ] that is sustained for half an hour. Following intracavernosal injection, Doppler wave form analysis is done with a 7.5 to 10 Mhz probe. Arterial insufficiency is diagnosed if the duplex scan shows an arterial diameter increase less than 25 percent and a peak systolic velocity of less than 25 cm / sec. Some people have used a criterion of end diastolic velocities of more than 5 cm / sec to represent venous leak. Duplex studies show reasonable correlation with arteriographic studies for arterial insufficiency, (Steers et al., 1999).

## **3- Electromyography and Nerve Conduction Velocity:**

Electromyography (EMG) and Nerve Conduction Velocity (NCV) are tests to evaluate the health and function of nerves and muscles in limbs and spine. It performed by inserting sterile pins that have a microscopic electrode on the tip into certain muscles of limbs or back and placing several electrodes on limb and applying a mild electric stimulus to the site. The physician will review the waveforms generated

by nerve input into muscle. There is a pinching sensation associated with this; the pin is usually in for approximately 30 seconds in each site. The NCV evaluates the speed of nerve function. This is performed by measuring how fast it takes for certain waves to form, (Harry et al.,1986).

If we suspect that urinary problem is related to nerve damage electromyography is done. This test measures the muscle activity in the urethral sphincter using sensors placed on the skin near the urethra and rectum. Sometimes the sensors are on the urethral or rectal catheter. Muscle activity is recorded on a machine. The patterns of the impulses will show whether the messages sent to the bladder and urethra are coordinated correctly, (Michael et al.,2004 and Washigton et al.,2004).

# EPIDEMIOLOGY OF RECTAL CANCER

## **General incidence:**

Colorectal cancer is the third cause of cancer related death in the world (Devesa et al.,1995). In Mexico, colorectal cancer is the second cause of mortality after cardiovascular diseases . Colorectal cancer accounts for 4 percent of all cancer deaths, (Direccion et al.,1994).

The average world wide incidence of colorectal cancer is 16.6 per 100.000, the lowest is recorded in Dakar (0.6/100.000) and the highest in Concutit (32.31/100.000), (Boyle et al.,1985).

## **Geographic distribution:**

The distribution correlates with the degree of industrialization, socioeconomic standard , educational level, and differences in exposures that are essentially dietary and environmentally imposed on a background of genetically determined susceptibility. So the highest incidence is in north America, West Europe and Australia, intermediate in Eastern Europe and lowest in Asia, Africa and South America. Also some of the differences may be related to delayed detection and the pain intolerance is high, (Kheighly et al., 1993).

The variation in incidence of colorectal cancer between countries may also reflect the influence of environmental factors, (Wagener et al.,1994).

## **Sex:**

The frequency of colon cancer is essentially the same among men and women, (Rose et al., 1986). Soybel et al,(1987) found cancer colon was 30% higher in women but cancer rectum is twice in males as females .

## **Race:**

Recent data demonstrate a decrease in incidence rates of colorectal carcinoma in whites since the mid 1980s, particularly for the distal colon and rectum. Proximal colon carcinoma rates in blacks are considerably higher than in whites and continue to increase, whereas rates in whites show signs of declining, (Potter et al.,1992).

## **Etiology:**

The essential element of the etiology of colorectal cancer is a process of genetic change in the epithelial cells of the colonic mucosa, (Vogelstein et al, 1988). Epidemiologic factors have provided initial evidence about the specific factors that initiate the process of carcinogenesis in the large bowel mucosa, (Winawer and Shike, 1992).

There is an interaction between mutagen exposure and genetic constitution. Metabolic pathways may be altered by polymorphisms in genes responsible for detoxifying mutagens, (Potter, 1999). Protection from the effects of mutagen-induced DNA damage is achieved by a range of detoxification enzymes, as reduced glutathione S-transferase (GSH transferase), DT-diaphorase, and N-acetyltransferase, (Gertig and Hunter, 1998).



Differences among individuals can account for susceptibility to mutagens from the diet, (Roberts-Thomson et al, 1996).

Chief among the factors that can initiate colorectal cancer development are predisposition to mutagen effect including : fecal mutagens, meat intake, bile acids, altered vitamin and mineral intake, and fecal pH .

### **1- Fecal Mutagens:**

Mutagenic compounds such as fecapentaenes, 3-ketosteroids, and heterocyclic amines in the stool may be produced by the interaction of digestion and food products. Intake of antioxidants reduces the mutagenicity of compounds in the stool. Changes in intestinal transit time owing to fiber intake affects the exposure of the mucosa to mutagens .In addition to mutagenic compounds, the presence of other products of digestion such as 3-ketosteroids, which are products of cholesterol metabolism, may act as tumor promoters or initiators , (Reddy et al, 1987) .

### **2-Meat Intake:**

Armstrong and Doll (1975) described the high correlation of meat intake and mortality from colorectal cancer. Among the risk factors are the intake of red meats and the compounds that result from cooking meats at high temperatures, (de Meester and Gerber , 1995) .

### **3- Bile Acids:**

Normal bile acids that are related to the digestion of fat can induce intestinal mucosal hyperproliferation, which acts as a marker for neoplasia risk, (Suzuki and Bruce, 1986). The presence of bile acids correlates with fat consumption, which is a known risk factor for colorectal cancer, (Minsky et al, 1995). Bile acids have been shown to activate AP-1, a transcription factor associated with the promotion of neoplastic transformation in colonic cells, (Glinghammar et al, 1999). They are also able to induce apoptosis, and variations in the epithelial apoptotic response to bile acids may correlate with risk, (Glinghammar et al, 1999) .

Cholecystectomy can result in high levels of bile acids in the cecum and ascending colon and appears to increase the frequency of right-sided carcinoma. It was found that levels of the secondary bile acid deoxycholic acid were higher than normal and that the ratio between deoxycholic acid and cholic acid may be an indicator of risk, (Kamano et al, 1999).

### **4- Vitamin and Mineral Intake:**

Calcium can alter colonic mucosal proliferation by binding fatty acids and bile acids in the stool, resulting in insoluble complexes that are less likely to affect the mucosa. It can also decrease proliferation of the mucosa directly, (Rozen et al, 1989). These effects of calcium may be site-specific within the colon, (Cats et al, 1995). The National Polyp Prevention Trial indicated that supplemental calcium intake reduced adenoma formation by 19%, (Baron et al, 1999).

Use of multivitamins has been shown to reduce the risk of adenoma formation in high-risk patients, (Whelan et al, 1999). Folate as a potentially protective agent has been demonstrated. Low folate intake has been implicated in increased colorectal cancer risk, especially when combined with alcohol and a low-protein diet, (Kato et al, 1999).

Populations with increased vitamin D intake have been noted to be at reduced risk for colon carcinoma, (Garland et al, 1989). A reduced risk of colon cancer is associated with the use of vitamin C, (Howe et al, 1992). Antioxidants such as vitamin E inducing some protection against colorectal cancer risks, (Newberne et al, 1990).

There is a weak association between high iron exposure and colorectal polyps, (Newberne et al, 1990). Low levels of selenium correlated with the presence of adenomas, whereas increased levels were associated with reduced risk of adenomas, (Russo et al, 1997).

### **5- Fecal pH:**

Alkaline environments in the stool support higher concentrations of free bile acids and other potential carcinogens. This pH may affect the solubility of bile acid and carcinogens and make them more damaging to the DNA of the intestinal mucosal cells, (McKeown-Eyssen and Bright, 1986).

### **Risk Factors:**

Risk factors include: (1) clinical risk factors (age, diet, alcohol and tobacco intake, energy intake, physical activity, and obesity). (2) Genetic risk factors (familial polyposis syndromes, hereditary nonpolyposis colon cancer, inherited colorectal cancer in ashkenazi jews, attenuated familial adenomatous polyposis syndrome, peutz-jeghers syndrome, juvenile polyposis and family history of colon carcinoma or polyps), and (3) Predisposing medical conditions (inflammatory bowel disease, granulomatous colitis, history of colorectal carcinoma or polyps, pelvic irradiation, previous non cancer surgery, bacterial infection, Diabetes Mellitus, hormone replacement in women, and laxative).

### **1- CLINICAL RISK FACTORS:**

#### **1- Age:**

Age is a well-known risk factor for colon cancer, and risk begins to rise in people older than 40 years. Age is a risk factor because a number of rare genetic alterations are believed to occur within the somatic cells of the colonic epithelium over years, ultimately leading to the development of colo-rectal cancer in older individuals. Individuals affected by one of the well-known familial predispositions to colon cancer are much more likely to develop cancer at a young age. For example, individuals with familial adenomatous polyposis have a 100% chance of developing colon cancer unless their colon is removed surgically, usually when they are aged 20-30 years, (Schoen et al., 2003).

There is a relative linear relationship for the incidence of colorectal cancer between the age 30 and age 70 years. Below 35 year of age the

incidence of colorectal cancer is higher than would expected based on this relationship. This perhaps is attributed to the inclusion of young patients with familial polyposis and bowel cancer syndromes who have developed malignancy. The incidence of large bowel malignancy is lower than expected in persons over 75 years of age, (Soybel et al., 1987).

The disease occurs more commonly over the age of sixty and most commonly in between 60 up to 69 years, (Cuschieri et al., 1995). Colorectal cancers account for approximately 1% of all childhood cancers, Fig. (16), (Goligher et al., 1984).



**Fig. (16): Incidence of colorectal cancer by age**

Open circle = General population.

Open square = hereditary nonpolyposis colon cancer.

Filled circle : Familial adenomatous polyposis population.

## **2 - Dietary factors:**

Several dietary components have been implicated in the aetiology of colorectal cancer e.g. fibers, animal fat, sugar, minerals deficiency or excess, and Soy food or Isoflavones, (Haskell et al., 1990).

### **A- High Fiber Diet:**

Burkitt in 1971 popularized his theory of high fiber diet reducing the intestinal transit time and producing bulky stool so the exposure of gut mucosa to carcinogens is reduced also the bulky stool dilutes the carcinogens (Burkitt et al., 1971). A strong negative association was reported between regional colonic cancer mortality and consumption of total dietary fibers. Also there are certain fibers that reduce the risk of colonic cancer development in populations consuming diet high in fat, (Bingham et al., 1985).

Thomson in 1981 hypothesized that acidification of the colon by dietary fibers may prevent the degradation of bile acids or cholesterol into co-carcinogens and so may contribute in the prevention of colorectal cancer, (Thomson et al., 1981). Low frequency of colon cancer is associated more with low fecal pH than with level of dietary fibers, (Walker et al., 1986).

### **B- High Animal Fat:**

Diet, and in particular fat content of diet, has been associated with

increased risk of colon cancer. Animal studies have found that dietary beef induces and dietary rye bran prevents formation of intestinal polyps. Obesity, rather than fat intake per se, predisposed to colon cancers induced in animals by exposure to the carcinogen azoxymethane. The animal fat favors the development of clostridia paraputrificum that dehydrogenates bile salts into carcinogenic compounds and increases the bile salts excretion so the animal fat effect is compounded (Hill et al., 1990).

### **C- High Sugar:**

An exploration of the relationship among obesity, energy intake, and insulin as a growth factor indicated an increased risk of colorectal cancer in the face of a high fasting glucose level, high insulin levels, and obesity, (Ma J et al, 1999) . Epidemiologic studies in the United States and Italy have shown a similar association between diabetes mellitus and colorectal cancer risk, (Willet et al, 1998).

### **D- Minerals Deficiency Or Excess:**

#### **i- Calcium deficiency:**

Calcium can bind intramurally with bile salts and fatty acid thus reducing their mitogenic effect, (Appleton et al.,1987). Newmark et al,(1984) found that calcium depletion produce colorectal cancer . Dietary supplementation with calcium reduces colonic crypt cells production rates in both normal and hyperplastic mucosa.

#### **ii- Selenium deficiency:**

Newmark et al (1984) found that selenium deficiency, produce colorectal cancer.

#### **iii- Zinc and fluoride excess:**

Newmark et al (1984) found that both zinc and fluoride excess produce colorectal cancer.

#### **iv- Bile salts excess:**

Newmark et al (1984) found that bile salts combination with cellular DNA leading to neoplastic change.

### **E- Low Soy Food Or Isoflavones:**

The evidence is weak that soy food or isoflavones in the diet protect a person from colon cancer, (Redy et al.,1981).

### **3- Alcohol And Tobacco Intake:**

Alcohol consumption is a risk factor for gastrointestinal cancer, including colon cancer. Daily alcohol intake has been associated with a twofold increase in colon carcinoma, (Giovannucci et al, 1995) . In addition, current and past smoking habits are independent factors that increase risk. Among Japanese men and women, it was found that long-term smoking predispose for adenoma formation, (Nagata et al, 1999).

### **4- Energy Intake, Physical Activity, and Obesity:**

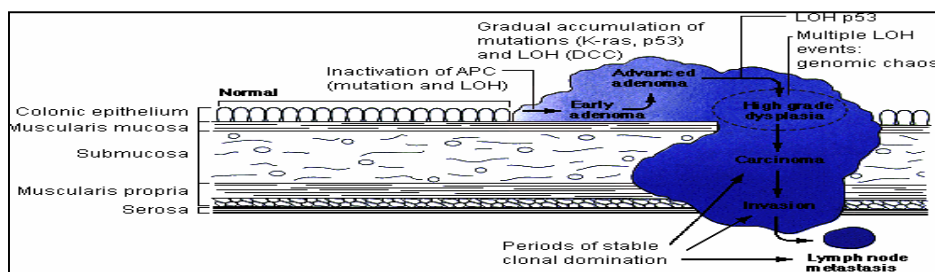
Multiple studies have correlated factors such as energy intake , physical activity, and other lifestyle factors with colorectal cancer risk, (Shike, 1999). In animal models, restricted energy intake has reduced the

development of colonic tumors, (Shike, 1999). The interaction between obesity and reduced physical activity was demonstrated by an alteration in intestinal prostaglandin activity, which can correlate with colon cancer risk, (Martinez et al, 1999). The Nurses' Health Study showed an inverse relationship between physical activity and adenomas. Excessive weight and abdominal obesity were found to be risk indicators in men and women, (Russo et al, 1998) .

## **II- GENETIC RISK FACTORS:**

### **A- Familial Polyposis Syndromes (FAP):**

FAP syndromes are a group of syndromes characterized by the early onset of multiple polyps and a virtually 100% risk of colorectal cancer development, (Bussey, 1990). It represent a small percentage of the overall number of colorectal cancer cases but confers very high risk. The risk of cancer rises progressively with age so that by 40 years nearly 80% of affected persons will have at least one adenocarcinoma (Bulow et al.,1984). These syndromes have autosomal dominant inheritance with high but variable penetrance, (Bresinger et al , 1998). Synchronous cancers are common in FAP patients. The basic genetic defect in FAP is a mutation in the APC gene. The genetic locus for the APC gene has been identified at 5q21, ( Kinzler et al, 1991). The most common abnormality is an alteration in the genetic sequence resulting in the generation of a stop codon, which in turn results in the production of a truncated nonfunctional protein, (Powell et al, 1993). This is the basis for a commonly used screening procedure in which the truncated protein is identified, Fig. (17), (Peltomaki and Chapelle, 1997).



**Fig. (17): Model Of Genetic Events Mediating Neoplastic Progression Of The Colon . LOH, Loss Of Heterozygosity**

### **B- Hereditary Nonpolyposis Colon Cancer (HNPCC Syndromes):**

Another predisposing condition is hereditary nonpolyposis colon cancer. It accounts for 1-5% of colon cancers, in which affected individuals inherit a mutation in one of several genes involved in DNA mismatch repair, including *MSH2*, *MLH1*, and *PMS2*. *ras* gene mutations have been detected in the stool of patients with colorectal cancer and may in the future be useful in early diagnosis. The inherited non polyposis colorectal cancer syndromes (lynch syndromes) include hereditary site specific non polyposis colorectal cancer (Lynch I) and cancer family syndrome (Lynch II).Lynch syndrome II is associated with extracolonic cancer particularly carcinoma of endometrium. These syndromes together

account for 5% of the colon cancer, (Canon et al., 1984).

### **C- Inherited Colorectal Cancer In Ashkenazi Jews:**

Israeli Jews of European birth have the highest colorectal cancer incidence of any Israeli ethnic group. There are reports of a missense mutation (I 1307 K) in the APC gene found in 6% of unselected Ashkenazi Jews and 28% of this population who have a family history of colorectal cancer, (Prior et al, 1999). This condition lacks the florid polyposis seen in FAP, so genetic testing in this population may be required to identify high-risk individuals for screening. This mutation appears to be unique to Ashkenazi Jews, (Rozen et al, 1999).

### **D- Attenuated Familial Adenomatous Polyposis Syndrome:**

Attenuated FAP syndrome is characterized by the development of flat adenomas that are precursor lesions to carcinoma, [Nagata et al, 1999]. Genetic linkage studies identify abnormalities on chromosome 5Q, and this may be a variant of FAP, with the mutation being more proximal or distal in the gene than common mutations with classic FAP. In patients with attenuated FAP syndrome, disease onset is later than usual for FAP, neoplasms appear in the proximal colon, and oligopolyposis is present, (Bresinger et al, 1998).

### **E- Peutz-Jeghers Syndrome:**

It is a polyposis of the alimentary tract associated with pigmented spots in the skin and buccal mucosa. There is a small chance of malignant changes (2-3%), (Goligher et al., 1984).

### **F- Gardner syndrome:**

Characterized by multiple adenomas of the large and small bowel with other mesenchymal abnormalities as desmoid tumor, lipomas, osteomas or fibromas, (Thun et al., 1992). It is characterized by colonic adenomatous polyposis associated with the presence of mesenteric or abdominal wall desmoid tumors, lipomas, and fibromas. The presence of a mesenteric desmoid tumor is a cause of great morbidity in these patients, (Arvanitis et al, 1990).

### **G- Turcot syndrome:**

Hamilton, 1995 has described the presence of two germline defects in Turcot's syndrome that are seen with both polyposis and HNPCC syndromes. There can often be considerable overlap between these adenomatous polyposis syndromes, and they are best characterized on the basis of their common genetic abnormality in the adenomatosis polyposis coli (APC) gene, (Bulow et al., 1984).

### **H- Oldfield syndrome :**

Winawer et al., 1993 described the presence of multiple dermoid cysts with the presence of multiple colorectal polyps.

### **I- Multiple neoplasm syndrome:**

Rose et al., 1986 found a close relationship between cancer of the breast, ovary, prostate, and colon.

## **I- Juvenile Polyposis:**

In which multiple hamartomatous polyps occur in the colorectum, although they may also be found in the small bowel and stomach. Jass et al (1988 ) defined this syndrome as the presence of more than five juvenile polyps, which differs from the solitary juvenile polyp seen in children. These investigators found colorectal cancer in 18 of 80 cases, (Jass et al, 1988). Neoplasia can occur in the index polyps or in a separate adenoma. Colonoscopic control of polyps appears appropriate, whereas colectomy may be used for large numbers of polyps, symptomatic polyps, or cancers, (Church, 19954). A subset of patients with juvenile polyposis has been identified to carry germline mutations in the SMAD4 gene, (Howe and Mitros, 1998). which causes a defect in growth factor control. The risk of colorectal cancer has been estimated at 38%. There is a 21% risk of upper GI cancers, (Howe et al, 1998).

## **J- Family History of Colon Carcinoma or Polyps:**

First degree relatives of patients with colorectal cancer have been noted to have approximately three times the risk of developing the disease than the normal population (Stubbs et al., 1983). Some of this increased familial risk is secondary to well defined inherited syndromes, inherited polyposis diseases. The inherited polyposis syndromes include Gardner syndrome, familial adenomatous polyposis and Turcot syndrome (Astrm et al.,1989).

## **III- PREDISPOSING MEDICAL CONDITIONS:**

### **A- Inflammatory Bowel Disease:**

#### **1- Ulcerative colitis:**

The incidence of colonic cancer in association with inflammatory bowel disease is higher and appears to be more marked in ulcerative colitis than in crohn's disease, (Schofield et al., 1990).

Occurrence of ulcerative colitis, the disease below the age of 30, stricture formation especially long standing one, proximal to the splenic flexure which causing obstruction, duration of the disease more than 10 years and the extent of the disease are risk factors, (Truelove et al., 1980). The risky factors are related also to extent of colites as greater incidence in right sided extended colitis, (Truelove et al., 1980) .

#### **2- Crohn's Disease (Granulomatous Colitis):**

Crohn's disease can affect the ileocolic area or may be limited to portions of the colon. In the absence of colonic involvement, there is no increased risk of colorectal cancer, (Ekbom et al , 1990). In addition to being at increased risk for large bowel cancer, all patients with Crohn's disease also have an increased risk of small bowel carcinomas, (Sigel et al, 1999). Seventy-three percent of the intestinal cancers in patients with Crohn's disease are found in the colon or rectum. Most carcinomas were found to be poorly differentiated. Dysplasia was found adjacent to carcinoma in 87% of the cases. Mucinous adenocarcinomas accounted for one-third of the carcinomas affecting Crohn's disease, (Rubio and

Befrits, 1997).

### **3- Schistomiasis:**

Bilharzial colonic infestation is not precursor of colonic cancer and the following support this fact:

- Low incidence of colorectal carcinoma in Egypt than Europe.
- Ratio of colorectal cancer specimen associated with bilharzial lesion is small, (Zaki et al., 1962). Also bilharzial polyps usually undergo shrinkage and bilharzial ulcer never precedes malignancy, (Elsebaei et al., 1961). In contrast bilharzial infestation by schistosoma japonicum lead to carcinoma of large bowel, (Chung et al., 1980).

### **4- Diverticulosis:**

Stewart et al. (1981) found no link between colorectal cancer, diverticulosis, tuberculosis, amoebiasis and syphilis.

### **B- History Of Colorectal Carcinoma Or Polyps:**

Patients with previous large bowel cancer are at greater risk of developing a second primary colorectal cancer. Clustering of breast and ovarian cancer in the same patient have been named cancer family syndrome lynch II, (Cohen et al., 1989).

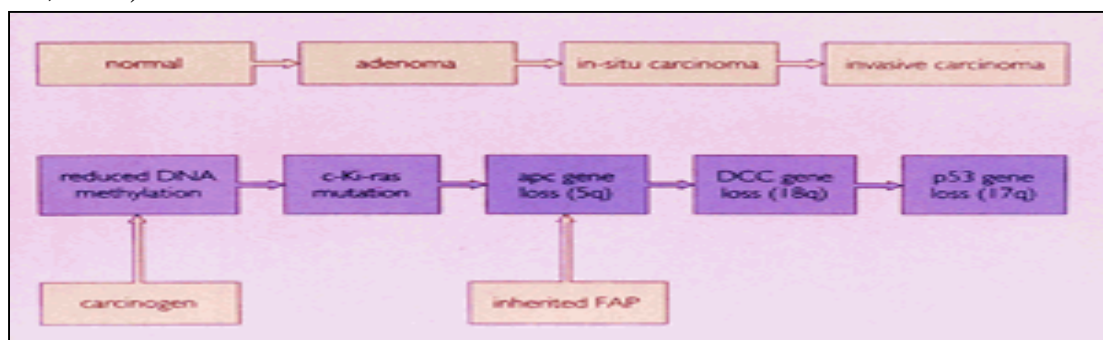
Colonic polyps, which occur with increasing age, represent a risk for colon cancer development. Recently concluded that adenomas probably are precursors of carcinomas, but the ultimate effect of removing polyps on reducing cancer incidence in the population remains unknown. The most direct support for this relation comes from the observation that foci of insitu and invasive carcinoma are commonly recognized in polyp, (Wilcox et al., 1986).

Villous papilloma is a soft sessile tumor with a coarsely granular or shaggy surface and ill defined edges. They -are pre cancerous lesions based on: (1) It's well known clinical phenomenon for villous papillomas to undergo carcinomatous changes. (2) Histological examination of the villous papillomas removed at operation often reveals presence of malignant foci, (Goligher et al., 1984).

Adenomas are tiny nodules in the mucous membrane have the size from a split pen to cherry. They may be sessile or pedunculated. Only 26% of cases with adenomatous polyps have multiple foci of malignancy , so adenomatous polyps tumors are pre-malignant lesion, (Goligher et al ., 1984). It is now agreed that the majority of colon cancer patients have a colonic adenocarcinoma arising from an adenomatous polyp. Polyps of 2 cm or greater have about 50% incidence of cancer, compared to 1% in adenomas of 1 cm or less. Adenomatous polyps are a premalignant condition, and their identification and removal before becoming malignant prevents the development of colon cancer. These polyps can arise anywhere in the colon, but they are more frequently seen in the left colon. The majority of polyps are completely asymptomatic, but the occurrence of occult bleeding does increase as they grow. Unfortunately, however, polyps can still be missed, even with occult blood testing of the

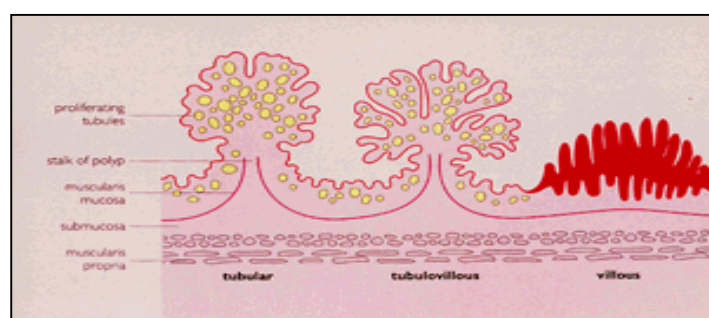


stool, since the blood loss may be intermittent ,Fig. (18) ), (Schoen et al.,2003).



**Fig . (18) : Adenoma – Carcinoma Transformation**

Three histologic types of adenomatous polyps occur: tubular, tubulovillous and villous. The malignant potential is greatest in villous polyps (40%) and lowest in tubular polyps (5%), with an intermediate risk in tubulovillous polyps (22%). The malignant potential may also be described pathologically as the degree of “dysplasia”: the more severe the dysplasia, the greater the rate of malignancy. Since polyps precede cancer and removal of polyps “cures” the cancer, it has been hoped that screening colonoscopy may help reduce the incidence of cancer. Other polyps as well may be present at the initial or index colonoscopy, and polyps and cancer tend to recur. This sets the stage for the rationale for performing follow-up surveillance colonoscopies (colon cancer surveillance program). The best time interval for this surveillance is probably every three years; longer intervals between surveillance colonoscopies may be safe but have yet to be tested, Fig. (19) , (Schoen et al.,2003) .



**Fig. (19) : Types Of Adenomatous Polyps**

### **C- Pelvic Irradiation:**

Sundler et al,(1983) found that risk of colorectal cancer is 1 to 8 times as that of general population following radiotherapy for benign conditions and 2 to 6 times following radiotherapy for gynaecologic malignancy.

Black and Ackerman,(1985) established the criteria for tumor-induced irradiation as a lateral interval of 10 years, considerable irradiation dosage and tissue damage in the adjacent tissue.

## **D- Previous Non Cancer Surgery:**

### **1- Cholecystectomy:**

Lee et al,( 1989) found a significant increase in the relative risk of right- sided colonic cancer following cholecystectomy. The most sound theory is that alteration in the bile acid metabolism after cholecystectomy leads to more frequent turn over of the bile acid pool and proportional increase of secondary bile acid. Also the higher level of secondary bile acids and their metabolites are absorbed more proximally. Another theory, in cholecystectomized patients the bile instead of becoming neutral in pH by absorption of water and bicarbonate in the gall bladder, keeps into the intestinal tract an alkaline content which causes mucosal cellular damage and enhances mitotic activity . Also it was found in cystectomized patients the risk is greater in females than in males and is twice as high in patients with high colon cancer than those with left colon cancer, (Cohen et al.,1991). But Arbeit and associates, (1991) found that the effect is small may reflect sharing of common etiologic factors.

### **2- Vagotomy:**

Mullan et al,(1990) demonstrated that vagotomized patient develop more colorectal cancer than the control group .

### **3- Uretero Sigmoidostomy:**

Also there is a definite increased risk following uretero sigmoidostomy, the hypothesis for mechanism of carcinogenesis is conversion of urinary nitrate to an active carcinogen by the fecal bacteria and the colonic cells can further convert the carcinogen to more active form. for example : hydroxylate nitrosamine, whereas the urothelial cell 'don't convert it as colonic cells, (Gittes et al.,1991).

## **E- Bacterial infection:**

Anaerobic bacteria grow and metabolize cholesterol of animal origin to coprostanol whose increased concentration is related to the malignant transformation of colonic cells, (Peucharit et al.,1987).

The concentration of total bile acids in stool may not always be significantly increased in individuals with colorectal cancer. However the stool content of secondary bile acids, produced by bacterial degradation of primary bile adds appears related to an increase risk. Also the stool content of bacterial metabolites of lithocholic acid was found to be significantly increased in patients with colon carcinoma, (Hikasa et al.,1984).

A statistically significant association exists between *Helicobacter* exposure and colonic polyps, (Umar et al.,2002).

## **F- Diabetes Mellitus:**

Epidemiologic studies in the United States and Italy have shown an association between diabetes mellitus and colorectal cancer risk, (Will et al, 1998).

## **G- Hormone Replacement in Women:**

In the Nurses' Health Study, oral contraceptive use has been

implicated in reducing the risk of colorectal cancer development by 40% , (Martinez et al, 1997). A higher parity was found to increase risk in those women with a family history of colorectal cancer. The risk of colon cancer may be decreased among women who recently used postmenopausal hormone replacement therapy. Women who are postmenopausal and who have never used hormone replacement therapy have a higher risk of colon, but not rectal cancer than do women who are premenopausal and of the same age, sociocultural class, and dietary habits, (Platz et al, 1997).

#### **H- Laxative:**

Apparently, no association exists between frequency of bowel movement or laxative use and risk of colon cancer, (Gerhardson et al.,1990).

#### **Mortality/Morbidity:**

The overall 5-year survival rate from colo-rectal cancer is approximately 60%, and nearly 60,000 people die of the disease each year in the United States. The 5-year survival rate is different for each stage; the staging classification for colon cancer can predict prognosis well. For Dukes stage A tumors involving only the mucosa, the 5-year survival rate exceeds 90%, whereas for metastatic colon cancer, the 5-year survival rate is about 5%. For Dukes stage B colon cancers, the 5-year survival rate is greater than 70% and can be greater than 80% if the tumor does not penetrate the muscularis mucosa. Once the tumor has spread to the lymph nodes (i.e. Dukes stage C), the 5-year survival rate usually is less than 60%, (Winawer et al.,2000).

Mortality rates for women was greater than for men. It has been suggested that the difference in risk could be the result of hormonal effects in the composition of bile caused by the formation of secondary biliary acids that cause cancer. Also a possible relation between low fertility and increase mortality caused by this type of cancer and use of exogenous hormones, (Weisburger et al.,1991).

# **PATHOLOGY OF RECTAL CANCER**

## **Sites:**

Tumor of the large bowel can be located anywhere from the pouch of the caecum to anorectal junction. The majority of colorectal carcinomas are located distal to splenic flexure but the proportion in the proximal colon have been increased in recent years, (Bafil et al.,1990).

Deans et al, (1994) found 70% of colorectal carcinoma are rectosigmoid. In USA there is gradual increase of colonic cancer in relation to rectal cancer and rectal cancer is 21 % of colorectal cancer. Also the cancer rectum below the peritoneal reflection predominates and also the posterior lesions .

## **Macroscopic Appearance:**

### **1- Cauliflower carcinoma:**

It produces a large fungating mass which projects into the bowel lumen. It is not usually associated with much infiltration of intestinal wall. The protruding surface of the lesion may be fine or coarse nodular. But owing to rapid growth there is usually ulceration at some points. It represents 10 – 15 % of rectal cancer, (Goligher et al., 1984).

### **2- Ulcerative carcinoma:**

Ulcerative type typically as malignant ulcer. It may be roughly circular and confined to one aspect of the wall. But more often it is somewhat elongated in the transverse axis and may extend over two or more quadrants of the bowel circumference. As this type of growth tends to infiltrate the bowel wall deeply there may be considerable deformity and often some narrowing of the bowel and it is 40 – 45 % of rectal cancer, (Goligher et al.,1984).

### **3 Annular of stenosing carcinoma:**

It develops from an initially discrete malignant ulcers. This lesion gradually extends round the bowel wall and eventually forms a completely annular ulcerating tumor and occurs in the narrow parts of the rectum (upper and lower 1/3 rectum) not in the ampulla of the rectum and represents about 30 – 40 % of rectal cancer, (Kheighly et al.,1993).

### **4- Diffuse infiltrating carcinoma:**

It corresponds to linitis plastica of the stomach. It produces a diffuse thickening of intestinal wall usually extending for at least 5-8 cm and most of it is covered by intact mucosa. But there are usually ulcerations at some points. Sometimes this is found as an extension of one of the other gross types. It is also not infrequently the type that is found in ulcerative colitis, (Biasco et al., 1990).

### **5- Colloid carcinoma:**

It usually forms a bulky growth with a very gelatinous appearance. There may or may not be extensive ulceration and infiltration, (Spjut et al.,1984).

## **Microscopically:**

The majority in rectal cancer are adenocarcinoma and less commonly are adenosquamous, squamous and undifferentiated carcinoma (Spartt et al.,1989).

The major histologic type of cancer rectum is adenocarcinoma, other variants such as squamous cell carcinoma, undifferentiated carcinoma, and carcinoid tumors are less common. Sarcomas may account for 0.1% to 0.3% of all colorectal malignancies . These are chiefly leiomyosarcomas, (Kodner et al.,1997).

#### **(A) Adenocarcinoma:**

Adenocarcinoma of the rectum is defined as a malignant tumor of glandular epithelium that contains acinar or papillary forms. It represents 90% to 95% of all rectal tumors. Tumors can be further classified by grade and histologic subtypes. The vast majority of rectal cancers are moderately differentiated, gland-forming adenocarcinomas. Less common variants are classified on the basis of the predominance of an unusual pattern as compared with the usual adenocarcinoma of the rectum. Mucinous or colloid carcinomas exhibit the majority of tumor in mucin pools, which are often of low cellularity, (Minsky, 1990). This tumor elicits an inflammatory and desmoplastic reactions. Three grades are recognized:

a-Well differentiated (20%): when architecturally and cytologically the carcinoma resembles normal or only slightly dysplastic-epithelium.

b- Moderately differentiated: intermediate between A and C.

c- Poorly differentiated : when architecturally and cytologically the carcinoma poorly resembles the normal epithelium . In poorly differentiated cancers, features of neuroendocrine differentiation may appear, (Rosai et al.,1996).

#### **(B) Mucinous adenocarcinoma:**

It is a subtype of adenocarcinoma in which mucin forms 60% of the tumor mass and it is of two types:

##### **1. Primary Mucoïd Adenocarcinoma :**

About less than 1:1000 of cases and macroscopically there is dense infiltration of 5-8 cm so affected segment is rigid and called linitis plastica microscopically the cells are anaplastic, contain intracellular mucin resulting in displacement of nucleus with immature glandular formation, (Almargo et al.,1983). In spite of its very low incidence it carries bad prognosis. This type occurs in young age groups and more on the left, (kodner et al., 1997). Biologically the spread is mainly local, by lymphatics to the ovary, lymph nodes and implantation into the peritoneum. It has low incidence of hepatic metastasis. These often are associated with diffuse intramural spread beyond the obvious mucosal lesion, (Rosai et al.,1996).

It is of difficult diagnosis due to: Minimal symptoms. Rare tumor. and Radiographically it resembles an inflammatory process, (Bonello et al., 1990).

## 2-Secondary Mucinous Carcinoma:

It forms 10-15% of rectal carcinoma. There is abundant extracellular mucin and have little desmoplastic reaction, occurs in younger age groups (first four decades of life) and carries very poor prognosis, (Spjut et al., 1984).

### **(C) Adenosequamous carcinoma:**

This malignancy comprises distinct glandular component and malignant keratin producing squamous areas. The degree of differentiation assessed from the glandular component, (Ruabio et al., 1981).

This tumour was found to behave in a rather more aggressive way than pure adenocarcinoma. The origin of this squamous element is unknown, (Soybel et al., 1987).

### **(D) Squamous carcinoma:**

The tumor consists of sheets of squamous epithelial cells with intercellular prickles and keratin production. Metastatic squamous carcinoma in large intestine is even more rare than primary- tumor of this type, (Burgess et al., 1979).

They behave clinically in a very similar way to adenocarcinoma depending on the degree of differentiation and assessment from extent of keratinization. Squamous carcinoma in the lower rectum likely arise from the anal canal, (Rosai et al., 1996).

### **(E) Choriocarcinoma:**

Grossly it shows extensive hemorrhage and necrosis. Histologically it is a biphasic tumor composed of a central core of cytotrophoblasts surrounded by a covering of syncytiotrophoblasts. Immunohistochemically, the syncytiotrophoblasts stain for hCG. It doesn't show the dramatic response to chemotherapy as gestational choriocarcinoma due to absence of parenteral antigens, (Fearon et al., 1990).

### **(F) Medullary carcinoma:**

It is best remembered as pheochromocytoma-medullary carcinoma syndrome. It is genetically linked to germline mutation of RET proto-oncogene on chromosome 10 (10q 11.2). The pheochromocytoma associated with it may arise in extragonadal sites. The histopathology is characterized by solid groups of cells with amyloid in the stroma, (Cohen et al., 1995).

### **(G) Undifferentiated carcinoma:**

These are tumors with no feature of differentiation such as acini, keratin or melanin production. The cells arrange in cohesive sheets rather than loosely as in lymphoma. Distinct small cell and large cell types have been described:

#### 1. Small cell undifferentiated carcinoma:

There are sheets of tumor cells tightly packed together with trabecular arrangement. There is extensive confluent necrosis and a

tendency to perivascular pseudo rosetting. The tumor cells are small, oval or fusiform with little cytoplasm and elongated hyperchromatic nuclei with small nucleoli, (Mills et al.,1983).

## 2- Large cell undifferentiated carcinoma:

It is composed of sheets of large uniform cells and less compactly arranged than in small cell carcinoma. The tumor cells have large vesicular nuclei and prominent nucleoli, (Rosai et al.,1996). The tumor may resemble a malignant lymphoma but the diagnosis confirmed by electron microscopy when desmosomes and scanty neurosecretory granules are typically seen, (Rosai et al.,1989).

## **(H) Lymphoma:**

Colorectal lymphomas are rare and account for less than 0.5% of all colorectal malignancies. In most cases, widespread dissemination of lymphoma is documented and underscores the concept that lymphoma of the gastrointestinal tract is a systemic disease with tumor cells present in other organ sites,(El- Bolkainy et al., 1991).

They are almost exclusively of non Hodgkin's lymphoma with high incidence in middle east. It may be B cell lymphoma as in Burkitt's lymphoma, as well as, immunodeficiency lymphomas ( post-transplant and AIDS ). Or T cell lymphoma, as well as, celiac disease (gluten sensitive enteropathy), (Harris et al., 1994).

Because this disease is highly responsive to chemotherapy and radiation, surgery is not the primary mode of therapy. If the clinical workup reveals a focal site of disease in the large intestine, surgical resection may be considered. Usually, for localized, low-grade colorectal lymphomas, radiation therapy is considered first-line therapy. For intermediate- and high-grade lymphomas, chemotherapy, combined with radiation therapy, should be the primary treatment modality. The role of surgery for colorectal lymphomas has been primarily for diagnostic and staging purposes and for the management of treatment-related complications (ie, perforation or bleeding, (Reese et al., 2000).

## **(I) Carcinoid tumors:**

Carcinoid tumors are neoplasms derived from cells that are capable of synthesizing a wide variety of hormones. Most gastrointestinal tract carcinoids occur in the ileum and the appendix. The rectum is the next most common site, and occasionally carcinoid tumors occur in the colon. Tumor size is an extremely important prognostic factor. About 60% of rectal carcinoids present as asymptomatic submucosal nodules measuring less than 2 cm in diameter, (Mokhtar et al., 1991).

Williams and Sanders et al.,1963 classified carcinoids according to the site of origin, namely foregut, midgut and hindgut including colon and rectum. Carcinoids of hindgut are argentaffin reaction negative, non functional product, no carcinoid syndrome, and none per urine .13 % of carcinoids occur in the rectum. Malignant potential is seen almost exclusively in tumors larger than 2 cm, with 3 % bone metastasis



metastasis, (Rosai et al.,1996).

It spreads locally in the wall of the gut with lymph node spread 5 % in classic carcinoid and 70 % in anaplastic carcinoid. Transanal local excision suffices for definitive therapy, because small tumors rarely metastasize. More radical excisions of larger rectal lesions may be required for local control; however, the results of radical excisions for large rectal carcinoids are poor, because these tumors are prone to metastasize. They have unfavorable prognosis in males, tumor more than 2 cm in diameter and with metastasis, (El Bolkainy et al.,2000).

### **(J) Sarcomas:**

Rectal sarcomas are extremely rare and account for less than 0.1% of all large bowel malignancies. The most common histologic sarcoma subtype is leiomyosarcoma. With these tumors, the most significant prognostic indicator is tumor grade. Patients with high-grade tumors do poorly. These tumors usually metastasize to the liver and peritoneal surfaces, (Mokhtar et al.,1991).

Leiomyosarcoma has characteristic features as they are small in size (less than 2 cm) with absence of mitosis. They may be low grade or high grade based on the extent of mitotic activity and this classification was found to correlate significantly with prognosis, (Evans et al., 1995).

Recent immunohistochemical studies have revealed the complex structure of these tumors, particularly the presence of neural cellular elements, both neurilemmal and ganglionic (pacemaker cell of Cajal). For this reason the recent terminology has changed from leiomyosarcoma to gastrointestinal stromal tumor, (El Bolkainy et al., 2000).

If the tumors are clinically localized at initial presentation, a radical en bloc excision should be performed to obtain a margin of uninvolved normal tissue. Because of the rarity of this tumor, no studies have addressed whether adjuvant radiation therapy or chemotherapy is beneficial, (Ries et al., 2001).

### **Spread of rectal cancer:**

rectal cancer tends to be localized for long period of little chance direct invasion, of less lymphatic and intraperitoneal implantation and commonly haematogenous spread due to easy permeation of cancer cells into the small blood vessels, (Cuscheirie et al., 1995).

### **1-Local spread:**

Tumors may spread in three directions within the bowel wall: radially, longitudinally and circumferentially. The transverse spread is more frequent but slower and the bowel circumference invasion takes two years, (Miles et al.,1926).

Radial extension is perhaps the variable most strongly and independently correlated with the risk of lymphatic and haematogenous metastases, (Soybel et al., 1987).

The degree of mural extension directly correlates with the degree

of venous invasion in the primary specimen and with the incidence of distant metastases, (Talbot et al., 1980).

The frequency of lymph node metastases increased markedly from 15% when the tumor is confined to bowel wall to 50-60% when the tumor has extended beyond the bowel wall. The relationship of mural penetration to perineural invasion is not clearly defined, (Soybel et al., 1987).

Longitudinal spread of carcinoma cells beyond the gross boundaries of the tumor has been studied more carefully in carcinoma of distal colon and rectum. In most studies intra mural spread of rectal carcinoma was less than 1 cm in most cases, ( Kameda et al., 1990).

Annular spread of rectal carcinoma is more rapid than longitudinal spread owing to the circular distribution of lymphatics, (Sugarbaker et al., 1982).

Local spread from the rectum occurs posteriorly through the perirectal fat until reaches the Waldeyers fascia which represent an obstacle for further spread. After the initial mucosal growth tumor may progress in several directions but usually it protrudes first into the lumen. An additional pattern of local spread is perineural invasion which may reach as far as 10 cm from the primary tumor, (Goligher et al., 1984).

In advanced cases, it may involve the sacral plexus, sacrum and coccyx. The direct spread is more easy partially particularly if the tumor is situated in the extraperitoneal part of the rectum, anteriorly it spreads easily through the little perirectal fat and Denonvillier's fascia and the related viscera above the peritoneal reflection. Direct spread results in invasion of peritoneal coat and involvement of the nearby structure, (Sugarbaker et al., 1982).

### **2-lymphatic-spread:**

The tumor metastases first to the perirectal nodes at the level of primary tumor then to the chain accompanying the superior haemorrhoidal vessels. The pericolic lymph nodes along the mesenteric border of the pelvis usually are not involved by these rectal tumors unless there is extensive tumor with lymphatic blockage, (Cohen et al., 1993). The lymphatic spread takes place in three directions upwards, laterally and downwards. The upward lymphatic spread is the most frequent mode of spread from pararectal glands to the chain of superior haemorrhoidal and inferior mesenteric glands and eventually to the aortic glands. Retrograde lymphatic extramural spread was observed in only 1.6% this results from proximal lymphatic blockage by metastases, (Grinne et al., 1986).

Mediastinal lymph node metastases from colorectal carcinoma are very rare and the pathway of such spread is by reaching the lung by vascular spread that forms a parenchymal nodule (Janover et al., 1971). It may also reach the mediastinal lymph node from the liver metastases through lymphatic drainage of the liver to hepatic vein then to middle

diaphragmatic lymph nodes or falciform ligament and follow superior epigastric vessels to lower para sternal lymph nodes to mediastinal or retrograde lymphatic spread from thoracic duct to bronchomediastinal trunk to mediastinal lymph nodes, (Libso et al., 1987).

### **3-Haematogenous spread:**

The most common organ to be involved is the liver and the hepatic metastases about (13-25%). Also lung metastases occur in about 1-5% and generalized metastases in 10%, (Codemar et al., 1976).

Tumor located in the lower rectum metastasize to the lung and liver by dual pathway upward along the superior haemorrhoidal vein to the liver and laterally along the middle haemorrhoidal veins to lung, (Goligher et al., 1989).

Another route through Batson plexus of veins. The tumor emboli in this plexus affect the paravertebral vein resulting in spinal metastases, (Sugarbaker et al., 1982).

Osseous metastases are rare and indicate poor prognosis, (Bonnkeim et al., 1986).

Ovarian metastases occur in about 6% either microscopically or grossly, 20-50% have bilateral involvement, (Soybel et al., 1987).

### **4. Transcelomic spread:**

It is the most serious form of spread as it places the disease beyond the surgical cure. Then spread occurs all over the peritoneal cavity and the omentum producing malignant ascites, (Kheighly et al., 1993).

### **5- Local implantation:**

The shed viable cancer cells can lodge on raw surface to produce secondaries and thus explaining the transperitoneal spread, local recurrences either at the wound or the suture line, (Killingback et al., 1965). Other theories to explain suture line recurrence include metachronous carcinogenesis, (Dawson et al., 1987).

Retrograde lymphatic spread between healthy and tumor bearing areas, to and fro movement of lymphatics, (Healed et al., 1986). Also incomplete resection, or incomplete abdomino-iliac lymphadenectomy leads to local spread, (Drudey et al., 1987). Some studies disagree about the hypothesis of tumor implantation by demonstrating that shed cells are nonviable, not only when recovered from washing of the tumor surface in excised specimens but also when obtained from irrigative cytology, (Rosenberg et al., 1977).

Precautions to prevent tumor implantation during resection by mechanical measure as strong ligatures are applied to the rectum several centimeters, above and below the lesion before handling or mobilization of the rectum, (Cole et al., 1954). Also by irrigation of the rectum with cytotoxic solution just before anastomosis. Several chemicals are used e.g. mercury perchloride 1:500, sodium hypochlorate 0.5% and mustine hydrochloride 1-2 mg/100 ml in water, (Goligher et al., 1984).

## **6- Perineural spread :**

Is of little significance, and produces severe pelvic pain, (Cuschieri et al.,1995).

## **Staging Of rectal Carcinoma:**

Staging helps the clinician to plan the most appropriate treatment and assists in evaluation of different modalities of treatment. It provides some indications of prognosis for the patient. Staging facilitates the exchange of statistical informations among various institutes allover the world. Staging allows study of the natural history of cancer and permits evaluation of established cancer program, (Carr et al., 1983).

### **Duke's staging (1932):**

Duke (1932) altered this system by categorizing lymphatic involvement into class C , Fig. (18):

= Duke's A.: carcinoma is confined to the bowel wall and has not penetrated the muscularis propria

= Duke's B: carcinoma extends through the entire bowel wall and serosa if present.

= Duke's C: Duke's A or B with metastases to the lymph nodes.

In 1935 Duke further subdivided stage C into C1 & C2:

- C1 : Denoted lymph node involvement near the tumor but not to the nodes around inferior mesenteric artery pedicle.

- C2: Denoted spread of metastases to these nodes (Gabriel et al., 1935).

The British Empire cancer (1946) introduced a fourth stage D. This including distant metastases. Dealing with advanced cancer, it has been suggested a further subdivision of stage D into three subgroups which might be valuable in assessment of operability, resectability and prognosis:

- D1; Tumors directly involving a neighbouring structure or organ.

- D2; Tumors that had metastasized by blood stream or have lymph node metastases beyond the mesenteric group.

- D3; Tumors that had disseminated throughout the peritoneal cavity.

The value is in D1 cases, extended radical surgery may offer a cure (ElSebal et al .,1961).

## **Modified Astler-Coller Staging System :**

One of the more commonly used staging systems is the modified Astler-Coller system, (Fig. 18). According to this system:

= Stage A represents tumors that invade into the mucosa only.

= Stage B1 tumors invade into but not through the muscularis propria.

= Stage B2 lesions invade through the rectal wall without adjacent organ involvement, whereas stage.

= B3 tumors involve adjacent organs.

= Stage C tumors involve regional lymph nodes and are subgrouped into stages C1, C2, and C3, according to depth of intestinal wall penetration.

= Stage D represents evidence of distant organ involvement, (Wolmark et

al , 1986).

**Coller modification of Duke's classification (1954):**

- Stage A: Tumors confined to the mucosa; nodes are negative.
- Stage B1: Tumors into bowel wall but not through it, nodes are negative.
- Stage B2: Tumors extending through the bowel wall, nodes are negative.
- Stage C1: Tumors limited to the bowel wall, nodes are positive.
- Stage C2; tumors extended through the bowel wall, nodes are positive.

**Turn bull et al (1967) modification of Duke's staging:**

- Stage A: Tumors confined to the bowel wall.
- Stage B: Extension of tumor outside the serosa and/or into precolic/rectal fat.
- Stage C: Tumors with metastases to local lymph nodes..
- Stage D: Infiltrative growth in adjacent organs or distant metastases.

**TNM Classification (1979):**

The American Joint Committee on Cancer and the International Union Against Cancer (AJCC/UICC) have proposed an alternative staging system based on the extent of the primary tumor (T), regional node involvement (N), and metastasis (M) , Fig. (18). There are series of prefixes for T.N.M. which make it possible to identify different types of evaluating evidence.

c T.N.M: Clinical diagnostic staging.

s T.N.M: Surgical diagnostic staging.

p T.N.M: Post surgical-treatment pathological staging.

r T.N.M: Retreatment staging clinical diagnostic stage

a T.N.M: Autopsy staging, (Wood et al., 1979).

**Tumor (T):**

To : no evidence of primary tumor.

Tis: carcinoma in situ.

T1 : tumor confined to mucosa or submucosa.

T2 ; tumor limited to bowel wall but not beyond.

T2a : partial invasion of muscularis propria.

T2b : complete invasion of muscularis propria.

T3 : tumor invasion of all layers of bowel wall with or without invasion of adjacent or contiguous tissue, fistula may or may not be present.

T4 : tumor spread by direct extension beyond contiguous tissue or the immediately adjacent organs.

**Lymph node (N) :**

Nx : Minimal requirement to assess regional nodes cannot be met.

No : Nodes not involved

N1 : one to three regional nodes adjacent to primary lesion.

N2 : Lymph nodes around the tumor extending to the 1st line of resection or ligature of blood vessels.

N3 : nodes contain metastases location not identified.

**Distant metastases (M):**

Mx : Minimal requirement to assess presence of distant metastases cannot be met.

Mo : no metastases.

M1 : Evidence of distant metastases.

**T.N.M stages of disease:**

Stage 0 :Tis, No, Mo.

Stage I :Ia, T1, No, Mo.

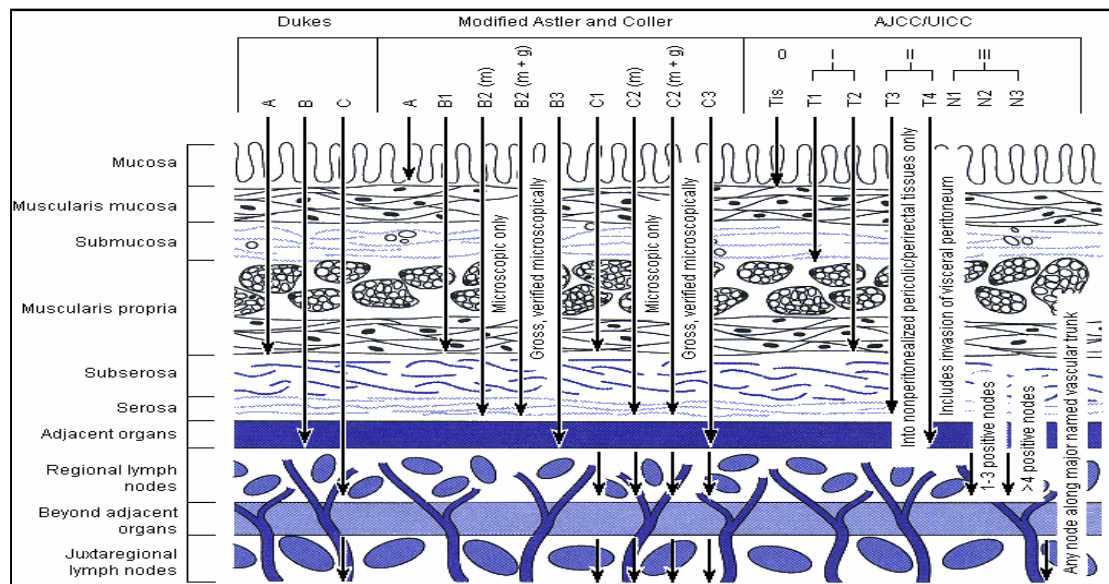
Ib, T2, No, Mo.

Stage II : T3, No, Mo.

Stage III: Any T,N1-N3,Mo.

T4, No, Mo.

Stage IV : Any, T, Any N, M1.



**Fig. (20): Schematic Description Of The Staging Systems With Respect To Depth Of Invasion**

There are some good reasons for adoption of the T.N.M system in resection setting which are:

- 1- Duke's system had been so changed, modified and consequently confused that it is difficult or impossible to know exactly to which A, B, C one refers.
- 2- More accurate staging of the primary tumor is required. The Duke's system puts all lesions from mucosa to muscularis propria into a single category.
- 3- Clinical data regarding involvement of adjacent structures (including peritoneal implants, perforation and fistula formation) should be considered.
- 4- Location of involved lymph nodes and the presence or absence and type (resectable or non-resectable) of metastases are required, (Sugarbaker et al., 1982).
- 5- Lastly the T.N.M. system assesses properly the data with significant prognostic influence namely depth of penetration of primary tumor (T) status of regional lymph nodes (N) and the presence of distant metastases (M), (Wood et al., 1979).

#### **Radiological Staging (1981):**

This staging was first described by (Thoeni et al, 1981). CT offered a new dimension in staging of rectal carcinoma because of its ability to evaluate extension of tumor into perirectal fat, adjacent organs and lymph node, this staging is classified into 4 stages:

- I: Intraluminal polypoid mass without thickening of the wall.
- II: thickening of the bowel wall > 0.5 cm invasion of surrounding tissue.
- IIIA: Invasion of surrounding tissue, muscle organs but no extension to the pelvic side wall.
- IIIB: Extension to the pelvic side walls.
- IV: pelvic tumor and distant metastases.

#### **Lackhart staging (1983):**

Lackhart (1983) was the first who defined classes for rectal tumor (A,B,C.) by defining extension of the lesion through the rectal wall and into the surrounding tissue and lymphatics.

#### **The Australian Clinio Pathological Staging system (A.C.P.S) , (Davis and Newland.1984).**

- A.C.P.S (0) : The carcinoma is confined to the submucosa in a patient who has undergone a bowel resection.
- A.C.P.S (A): The carcinoma has spread into bowel wall but not beyond the muscularis propria there are no lymph node metastases nor distant metastases.
- A.C.P.S (B): The carcinoma has spread beyond the muscularis propria into adjacent organs. There are no lymph node metastases nor distant metastases.
- A.C.P.S (C) : The carcinoma may have varying spread into or through the bowel wall but one or more lymph nodes contain cancer. There are no distant metastases.
- A.C.P.S (D) : This category is used when there is clinical or



microscopic evidence of any cancer remaining locally or at a distance whether there has been a (palliative resection), palliative operation, local excision or no operation because of the extent of the tumor.

- A.C.P.S (X) : is used when local excision or other local procedure are done, without lymphadenectomy it subdivided into:

- XO: When the tumor is confined to the mucosa.
  - XA: When the tumor does not spread beyond the muscularis propria.
  - XB: When the tumor spreads beyond the muscularis propria.
- Operation may be done with curative or palliative intent in this group.

- A.C.P.S (Y) : This category is used when the pathologic details are for some reason not known or are incomplete, (Davis et al., 1983).

A.C.P.S.-categories A,B, and C are identical with Duke's A, B, and C provided that only curative resection are considered, except that it allows for a category for disseminated or residual cancer (A.C.P.S category D), while Dukes does not, (Davis et al.,1984).

### **Extended Staging (E.S) (1985):**

Williams et al,(1985) introduced this sophisticated staging system. In this staging system, the patient is subjected to two staging systems:

#### **1- Initial Staging (I.S):**

A full clinical examination is performed including digital rectal examination and proctosigmoidoscopy using the rigid one. The patient's tumor was classified according to the following:

1-Palpable: The tumor is palpable in the conscious state and if not, it becomes palpable under anesthesia.

2-Degree of fixation: The tumor is assessed as absent, minimal, moderate or extensive if considered to be invading adjacent structure these are specified if possible.

3-Degree of dissemination: Based on clinical, haematological, biochemical and radiological investigation.

4-Degree of differentiation: the biopsies are graded routinely into well, moderate or poor differentiation.

#### **2- Extended Staging (E.S):**

The patient then underwent extended staging which consist of:

1- Computerized Tomography (CT) of liver and pelvis.

2- Ultrasound of the abdomen and liver.

3- Serum CEA and acute phase reactant proteins as CEA and APRPs might help to differentiate between fixation by malignancy and fixation by inflammation, and diagnosis of dissemination.

4- Flow cytometry of multiple biopsies.

The improved accuracy of E.S. would have altered both intra operative and clinical decision. It would have prevented some patients receiving inappropriate adjuvant therapy as well as selecting patients

more accurately for the correct treatment.

**Modified Duke's classification of Kivkiin (1991):**

Kiviklin et al (1991) cited the muscularis propria of the bowel wall as an anatomic landmark :

- Stage A: refers to growth that has not yet penetrated through the muscularis mucosa.
- Stage B1: Tumor extending into but not penetrating the muscularis propria.
- Stage B2: Tumors extending through the muscularis propria.
- Stage C: Either A, B1 or B2 with lymph node involvement.

## MANAGEMENT OF RECTAL CANCER

The diagnosis of rectal cancers can be made based on the evaluation of the symptomatic patient or through screening programs.

### **Symptoms :**

The symptoms of rectal cancer can be nonspecific, such as intermittent pain, bleeding, nausea, and vomiting. Bleeding may present as melena or as gross red blood which is associated more with rectal cancers. Lesser amounts of bleeding may be detected as part of a fecal occult blood test. Patients with chronic blood loss may develop iron-deficiency anemia associated with fatigue, (Chapman et al., 2000).

Malignant obstruction can result in abdominal pain with nausea and vomiting. In the presence of obstruction, there may be a perforation either at the site of the tumor or through the proximal uninvolved intestine. For rectal tumors, compromise of the rectal reservoir can cause a change in bowel habits, such as constipation or a decreased stool caliber. For locally advanced rectal cancers, symptoms of tenesmus, urgency, and perineal pain can occur, (Blumberg et al., 1998) .

### **Diagnostic Tests :**

A broad range of diagnostic studies can be employed in the evaluation of a suspected large bowel cancer:

#### 1- Digital examination:

The least expensive and potentially most informative study for rectal tumors is the digital examination. This permits the localization of distal rectal and anal neoplasms. In addition, stool can be obtained for evaluation of bleeding .

#### 2- Proctosigmoidoscopy:

Rigid sigmoidoscopy with a 25-cm instrument is comparatively inexpensive but is limited by the length of intestine that can be examined and by patient compliance. Flexible fiberoptic sigmoidoscopy has gained more acceptance. An examination of the sigmoid colon and rectum can usually be performed after cleansing enemas. Proctosigmoidoscopy should also be performed to exclude rectal lesions, because visualization of the rectum is inadequate on barium enema.

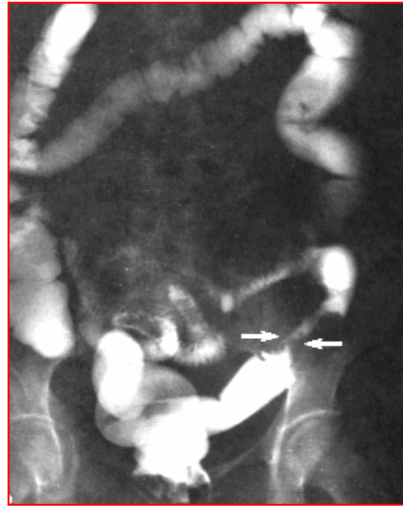
#### 3- Colonoscopy:

Colonoscopy with the 180-cm fiberoptic instrument is the most widely used diagnostic study to evaluate the colon. A valuable aspect of this procedure is the ability to obtain mucosal biopsy specimens and perform polypectomies. The incidence of severe complications that require surgical intervention (e.g. hemorrhage and perforation) is 0.1% to 0.3% .

#### 4- Barium enema:

The barium enema is the traditional study for the diagnosis of colorectal polyps and cancers. The double-contrast technique using air

insufflation is superior to the standard single-contrast barium enema to detect early polyps or cancers. The classic apple-core defect has been described for colorectal cancers . One advantage of barium enema over colonoscopy is the routine visualization of the right colon, which is not possible in 5% to 10% of colonoscopic examinations, (Fig. 21).



**Fig. (21):Barium Enema Examination Of An Invasive Sigmoid Carcinoma With Features Of The Apple-Core Defect (Arrows).**

#### 5- Fecal occult blood test:

Increasingly, the diagnosis of colorectal cancer is made on the evaluation of a positive fecal occult blood test. The most commonly employed test to detect occult blood uses guaiac-impregnated paper slides that change color in the presence of peroxidase activity from hemoglobin. Several factors affect the utility of this test. First, not all colorectal cancers or polyps are associated with bleeding, and even in those that are, bleeding is often intermittent in nature. Second, patients must be instructed to remain on low-peroxidase diets (no rare beef) before testing to avoid false-positive results. Third, certain medications, such as iron, cimetidine, antacids, and ascorbic acid, may interfere with the peroxidase reaction and may lead to a false-negative result, (Hardcastle et al, 1986) .

#### 6- Serum CEA level:

A preoperative serum CEA level is advisable in all patients to establish a baseline before surgical intervention. The dramatic decrease of circulating CEA level should be witnessed after operation and subsequent elevation is indicative of local recurrence, (Kikuchi et al.,1995).

#### 7- Intravenous urography and renal ultrasound:

The use of routine intravenous urography and renal ultrasound to demonstrate the invasion of the ureters does have some advocates but most commonly used selectively in patients with large tumors or in those with suspicious evidence of obstructive uropathy, (Kikuchi et al.,1995).

#### 8- Preoperative staging of rectal cancer:

Preoperative staging of rectal cancer is important and influence the treatment. Most agree that CT scan of the abdomen ( liver and tumor ) gives valuable information. Hepatic CT scanning is generally more sensitive than ultrasound scanning of the liver. For rectal tumors, the most detailed information on the tumor stage is obtained by endoluminal ultrasound scanning which can reliably establish the degree of involvement of rectal wall ( T stage ), the presence of extrarectal involvement and enlarged lymph nodes, although the nature of the enlarged lymph node ( secondary deposits or reactive hyperplasia ) cannot be ascertained by endoscopic ultrasound, (Chapman et al.,2000).

#### 9- Investigations for the patient's general condition:

There are no special investigations for the patient's general condition other than those which would normally be performed for patients with major abdominal operation . These include measurement of the full blood count, urea, creatinine and electrolytes, liver function tests, chest X ray and ECG, (Muto et al.,1991).

### **Screening :**

#### **Rationale for Screening :**

Screening is required for diseases with the following criteria: (Woelf et al., 1995).

1. It represent a high burden of suffering, in terms of morbidity, mortality, and loss of function.
2. A screening test that is sufficiently sensitive, specific, safe, convenient, and inexpensive.
3. Evidence that treating the condition when it is detected early, by screening, results in a better prognosis than treatment after it is detected because of symptoms.
4. Evidence on the extent to which screening test and treatment do harm.
5. The value judgment that the screening test does more good than harm.

Of these criteria, the first and second are satisfied in genetically determined colorectal cancer. Proof that early intervention results in better outcomes (criterion 3) is limited, but suggests benefit. The harms of screening (criterion 4), especially major complications of diagnostic colonoscopy (perforation and major bleeding) are also known, (Janvinen et al.,2000).

For screening purposes, asymptomatic patients can be divided into: (1) The general population and (2) Those in the high-risk category:

#### **1- The general population:**

In practical terms, knowing that a person is at increased risk of colorectal cancer because of a germline abnormality is most useful if the knowledge can be used to prevent the development of cancer or cancer-related morbidity and mortality once it has developed. While one can also use the information for family planning, decisions about work and

retirement, and other important life decisions, prevention is usually the central concern, (Muto et al., 1991).

At this time, the use of mutation testing to identify genetic susceptibility to colorectal cancer is not recommended as a screening measure in the general population. The rarity of mutations in the *APC*- and *HNPCC*-associated MMR genes, and the limited sensitivity of current testing strategies, render general population testing potentially misleading and not cost effective, (Janvinen et al., 2000).

Testing in the absence of symptoms for colorectal cancer and its precursors (i.e. adenomatous polyps) is to identify people with an increased probability of developing colorectal cancer.

In the asymptomatic general population, the efficacy of screening programs has been controversial. Testing for fecal occult blood is the most commonly used screening test as it is relatively inexpensive and simple. For the general population, the National Cancer Institute and the American Cancer Society advocate yearly fecal occult blood tests and flexible sigmoidoscopy every 3 to 5 years beginning at the age of 50 years. Those with abnormalities should undergo diagnostic testing to see if they have an occult cancer, followed by treatment if cancer or a precursor is found. Taken together, this set of activities is aimed at either preventing the development of colorectal cancer by finding and removing its precursor, the adenomatous polyp, or preventing complications by early detection and treatment, (Janvinen et al., 2000). Although these are reasonable guidelines, the cost-effectiveness of this program has yet to be ascertained, (Hardcastle et al., 1996).

## **2- People in the high-risk group:**

Clinical criteria may be used to identify persons who are candidates for genetic testing to determine whether an inherited susceptibility to colorectal cancer is present. These criteria include:

1. A strong family history of colorectal cancer and/or polyps.
2. Multiple primary cancers in a patient with colorectal cancer.
3. Existence of other cancers within the family consistent with known syndromes causing an inherited risk of colorectal cancer, such as endometrial cancer.
4. Early age at diagnosis of colorectal cancer.

First-degree relatives of patients with known hereditary colon cancer syndromes should undergo colonoscopy by age 20 and regularly thereafter. Patients who have had adenomatous polyps removed should have yearly colonoscopy until no further polyps are seen and then every 3 to 5 years thereafter. Patients with ulcerative colitis should have surveillance colonoscopy after 8 to 10 years of disease activity. Based on the findings, a subsequent surveillance program can be formulated .

Most public health organizations recommended the tests include:

- Fecal occult blood test (FOBT): The recommended screening interval is every year.

- Sigmoidoscopy: An exam of the rectum and lower colon. Recommended screening interval is every five years.
- Colonoscopy: The recommended screening interval is every 10 years.
- Double contrast barium enema (DCBE): The recommended screening interval is every five years.

### **State Of The Evidence Base :**

Currently there are no published randomized controlled trials of screening in people with genetically increased risk of colorectal cancer and few controlled comparisons. While a randomized trial with a no-screening arm is not feasible, there is a need for well-designed studies comparing various screening methods or differing periods of time between screening procedures. A published observational study that compared screened with unscreened “controls” evaluated a 15-year experience with 252 relatives at risk for hereditary nonpolyposis colorectal cancer, 119 of whom refused screening. Eight of 133 (6%) in the screened group developed colorectal cancer, compared with 19 in the unscreened group (16%,  $P = .014$ ), (Jarvinen et al.,2000).

In general, people with genetic risk have been excluded from the trials of colorectal cancer screening that have been published thus far, so it is not possible to estimate effectiveness by subgroup analyses. Therefore, prevention in these patients cannot be based on strong evidence of effectiveness. The kind ordinarily relied on recommendations by expert groups when they suggest guidelines. Given these considerations, clinical decisions are based by default on clinical judgment. These decisions take into account the biologic and clinical behavior of each kind of genetic condition, as well as possible parallels with patients at average risk, for whom screening is known to be effective. The evidence base for the effectiveness of screening in average-risk people (those without apparent genetic risk) is the benchmark for considering an approach to people at increased risk. In average-risk people, screening programs based on several different kinds of tests have been shown, with various degrees of persuasiveness, to prevent death from colorectal cancer, (Winawer et al.,2000).

Fecal occult blood testing (FOBT) is supported by 3 randomized controlled trials, (Winawer et al.,1990). Sigmoidoscopy screening is supported by 4 case-control studies, (Kavanagh et al.,1998). Colonoscopy has been shown to be effective in reducing the incidence of colorectal cancer in 2 cohort studies of patients with adenomatous polyps, (Citarda et al.,2001). Double-contrast barium enema may be effective, considering that it allows examination of the entire bowel, but has low sensitivity for large polyps and cancers, (Winawer et al.,2000).

The fact that screening of average-risk persons reduces the risk of dying from colorectal cancer forms the basis for recommending screening in persons at high increased genetic risk of colorectal cancer.



Randomized trials of screening have not been performed in this special population. Observational studies performed on families with HNPCC and FAP support the value of screening. These studies suggest a stage shift towards earlier stages and a probable reduction in colorectal cancer mortality among screen-detected cancers, (Woolf et al.,1995).

Preoperative radiotherapy is advisable in patients with large tumors which has broken through the muscularis propria into the perirectal fat. It is also indicated in patients in whom local excision of a small rectal cancer is contemplated ( usually T<sub>1</sub> and T<sub>2</sub> lesions in poor risk patients, (Bouvert et al.,1999).

# **TREATMENT OF CANCER RECTUM**

## **Neoplastic Polyps :**

With the availability of colonoscopy, endoscopic polypectomy has become the standard approach for the treatment of neoplastic polyps unless there are medical contraindications. The risk of this procedure is extremely low, with a complication rate of less than 1%. Almost all pedunculated polyps can be removed endoscopically with a snare. Sessile lesions can frequently be removed piecemeal but may require several sessions, (Nivatvongs et al., 1986).

A dilemma in treating colonic polyps occurs if a resected lesion contains a malignant focus. A decision must then be made about the need for a colectomy. If the lesion does not penetrate the muscularis mucosa, it should be considered an in situ malignancy that does not have the propensity to metastasize and, therefore, does not require further surgery. If the lesion penetrates the muscularis mucosa, it is an invasive cancer and may require surgery. In general, if there is evidence of invasion, colectomy with resection of paracolon lymph nodes is indicated, (Muto et al., 1991).

In selected cases of pedunculated polyps, conservative management without colectomy may be undertaken if the lesion does not contain poorly differentiated tumor cells or evidence of vascular invasion and if a negative resection margin has been obtained at the level of the stalk. Lesions that are poorly differentiated or have evidence of vascular invasion, regardless of a negative surgical margin, should be treated by colectomy. Large villous tumors of the rectum can pose a challenge. Total excision is required to accurately assess the presence of invasive cancer. Transanal excision with sphincteric muscle and mucosal approximation is preferred; however, other approaches, such as low anterior resection, coloanal procedures, or abdominoperineal resection, may have to be employed to totally excise extensive benign rectal lesions. , (Blumberg et al., 1008).

## **Invasive Colorectal Cancers :**

### **I- Surgery:**

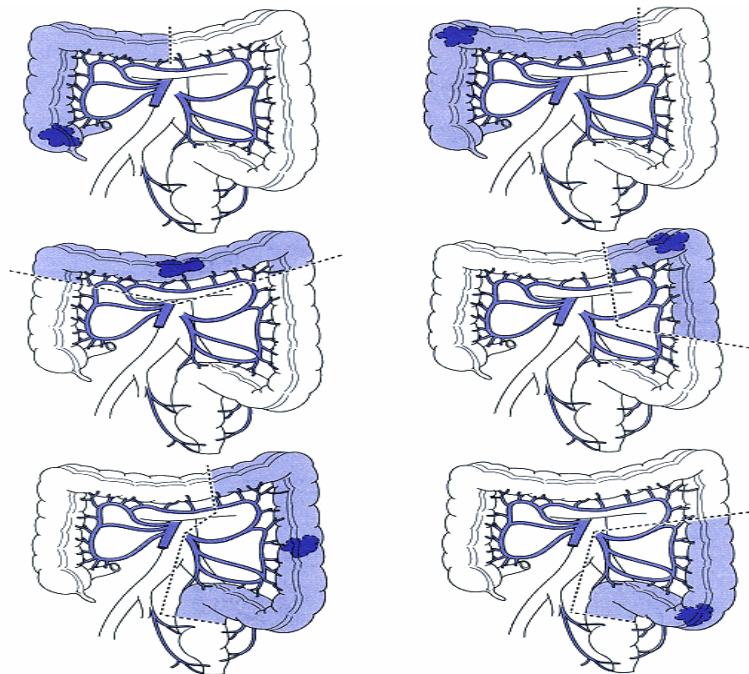
Surgical options for colorectal cancer depend on the location of the primary tumor. These surgical procedures are summarized as follows :

- 1- Intraperitoneal colon and upper third of the rectum :Resection and anastomosis.
- 2- Middle third of the rectum : Abdominoperineal resection , Low anterior resection , Abdominosacral resection , Coloanal resection , Local excision or fulguration , or Primary radiation therapy .
- 3- Lower third of the rectum : Abdominoperineal resection, Local excision or fulguration , or Primary radiation therapy .

Before surgical resection, the distance of the tumor from the anal

verge and its mobility are important in assessing resectability and type of operation required. Rectal ultrasound can be helpful in assessing extent of local invasion and the presence of enlarged lymph nodes within the mesorectum. The presence of metastatic disease may alter the planned surgical procedure; that is, a low rectal cancer with evidence of hepatic metastases may be better palliated with fulguration than with abdominoperineal resection. A full colonoscopy or air-contrast barium enema should be performed to rule out other primary colorectal polyps or cancers, (Maas et al., 1998).

The surgical goals in the resection of a primary colorectal cancer are to achieve an en bloc resection that encompasses an adequate amount of normal colon proximal and distal to the tumor, to obtain adequate lateral margins if the tumor is adherent to contiguous structures, and to remove regional lymph nodes. Accomplishment of these goals optimizes the chance of preventing locoregional recurrence of the disease. The extent of bowel resection has been the subject of numerous debates. From pathologic studies, tumor rarely extends intramurally more than 2 cm beyond the area of gross involvement. Traditionally, 5 cm of normal large intestine proximal and distal to the tumor has been advocated as a margin that is adequate to completely encompass intramural spread. The actual margin of intestine removed is often determined by the extent of the lymphadenectomy. The paracolic and intermediate draining lymph nodes should be removed as part of a curative resection (Fig. 22), (Heald et al., 1998).



**Fig. (22): Segmental Resections For Cancers Of The Colon And Upper Third Of The Rectum.**

Extensive resections of bowel along with more central or retroperitoneal lymph nodes are not indicated because they produce minimal additional oncologic benefit but substantially increase operative complications. At the time of surgical resection, a thorough investigation of the abdominal viscera, particularly the liver and peritoneal surfaces, should be performed. If evidence of disseminated disease is apparent, a less extensive resection of the primary lesion for palliation to avoid obstructive or bleeding complications may be indicated, (De hass et al., 1995).

### **Intraperitoneal Colon and Upper Third of the Rectum:**

Resection plus primary anastomosis is the surgical procedure of choice for cancers of the colon and for cancers of the upper third of the rectum. Whenever possible, a mechanical bowel preparation, along with oral antibiotics, should be instituted preoperatively to reduce infectious complications. The choice of anastomotic technique (staple or hand-sewn) depends on the surgeon's preference, (Harnsberger et al., 1994).

Rectosigmoid cancers and tumors confined to the upper third of the rectum are removed by an anterior resection. The upper third of the rectum is about 12 to 16 cm from the anal verge and is located above the peritoneal reflection (Fig. 23).

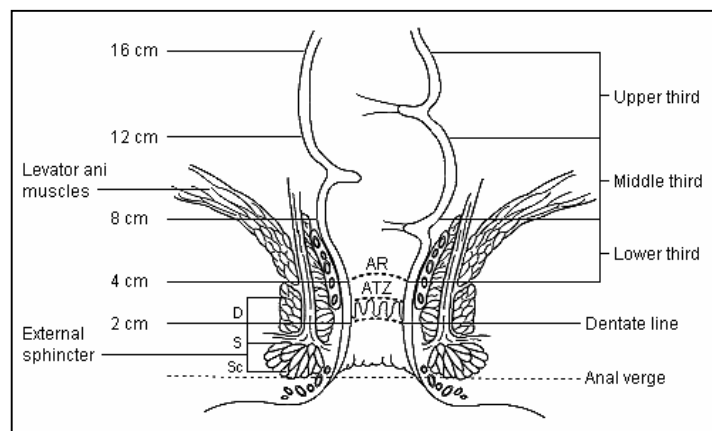


Fig. (23): Anorectal anatomy with important landmarks. Approximate measurements relative to the anal verge.

D = deep; S= superficial; Sc = subcutaneous; AR= anorectal ring; ATZ= anal transition zone.

The pelvic peritoneum is incised circumferentially around the rectum, and the intestine is mobilized from the presacral fascia. Laterally, the middle hemorrhoidal vessels are ligated, and anteriorly, the rectum is mobilized from the seminal vesicles and prostate or vagina. The mesenteric vessels are divided at the origin of the sigmoid artery or higher, at the origin of the inferior mesenteric artery, if further mobilization of the splenic flexure is required to obtain a tension-free anastomosis, (Harnsberger et al., 1994).

Recurrence patterns and cure rates for tumors in the upper third of rectum are similar to those for the colon. Advanced tumors in this location may involve the retroperitoneal structures (ureters, bladder, muscle) or major vessels. Extirpation of these tumors should include resection of the bowel segment containing the tumor along with the mesorectum to approximately 5 cm below the lower edge of the tumor. It is usually inappropriate to attempt local excision techniques in this area because of the relationship between the upper rectum and peritoneal cavity and because of the poor exposure due to the distance from the anal verge, (Lopez et al., 1998).

### **Middle Third of the Rectum:**

Cancer of the middle third of the rectum, between 8 and 12 cm from the anal verge (Fig. 23), can be managed by a variety of techniques. For these tumors, abdominoperineal resections do not yield superior results to other procedures that spare the anal sphincter. Therefore, an effort should be made to maintain intestinal continuity. Low anterior resection is a commonly used technique that involves resection of the middle rectum with primary anastomosis, (Dehni et al., 1998).

The introduction of the end-to-end anastomosis (EEA) stapler has increased the use of this sphincter-saving procedure (Fig. 25). If a transanal reconstruction with a stapler is contemplated, the patient should be placed in the lithotomy position. The initial stages of the operation, with complete mobilization of the rectum to the level of the pelvic floor, are identical to those for an abdominoperineal resection. After removal of the tumor, anastomosis can be end-to-end or end-to-side, and joined with sutures or staples. A temporary transverse colostomy should be employed if there is concern regarding the integrity of the anastomosis, (David et al., 2002).

Other sphincter-saving approaches have been described for middle rectal cancers. Abdominosacral resections were described in the 1940s and allowed surgeons more direct visualization of low, hand-sewn anastomoses. The rectum is mobilized through an abdominal approach, and a second incision is made above the anus, with resection of coccyx for visualization into the pelvis. A hand-sewn anastomosis is completed through the transsacral incision (Fig. 24). This procedure has largely been supplanted by the use of stapling devices. Coloanal anastomosis, another alternative, involves restoring bowel continuity by bringing the colon to the level of the anus and dentate line (Fig. 24) , (Yeatman and Bland, 1989).

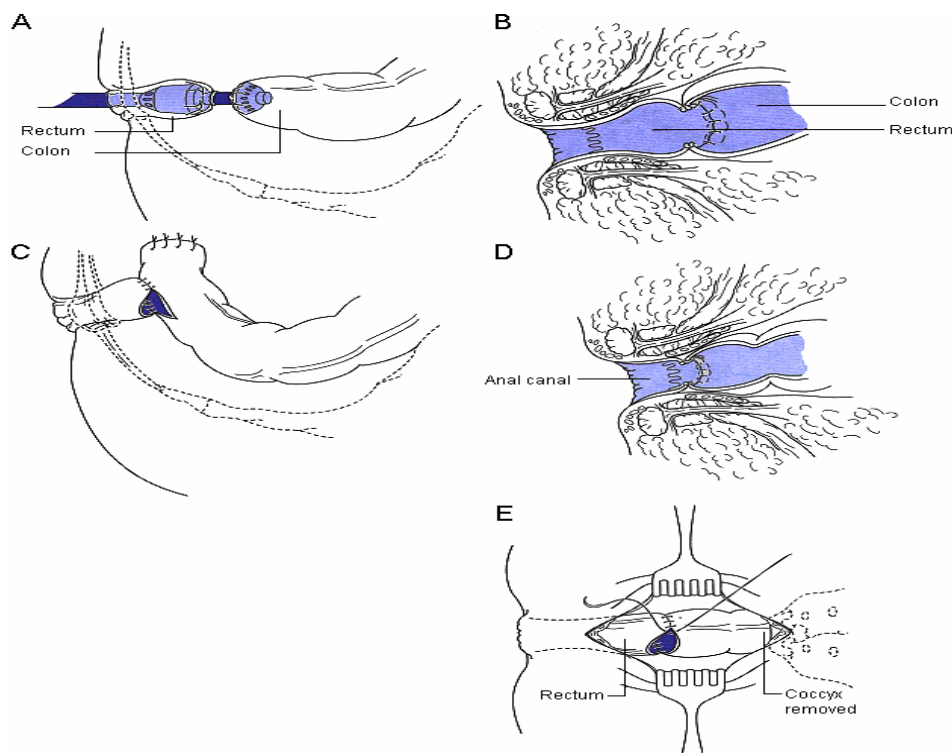


Fig. (24): Techniques for low anterior resections. (A) EEA stapler. (B) Single layer with sutures. (C) Side-to-end anastomosis. (D) Pull-through. (E) Transsacral resection.

One of the controversies concerning sphincter-saving procedures for rectal tumors is the length of adequate distal mucosal margin. The traditional dictum of 5 cm for a margin is not substantiated by any studies. Only 2.5% of patients have intramural spread beyond 2 cm from the palpable tumor, and these patients usually have dissemination of tumor despite aggressive local therapy. There is no correlation between local recurrence and the extent of distal margin when it is greater than 2 cm. Ideally, a surgical margin of 3 cm, measured on the fresh specimen, should be achieved. If the EEA stapler is used, then a margin of 2 cm plus the additional “doughnut” specimen obtained by the stapler should be adequate. If, in the surgeon’s judgment, this length of margin cannot be obtained, then abdominoperineal resection should be performed. The segment of rectum located between the tumor and the pelvic floor, determined preoperatively, can be lengthened as much as 4 cm after the rectum is mobilized from its pelvic attachments (Fig.25), (David et al., 2002).

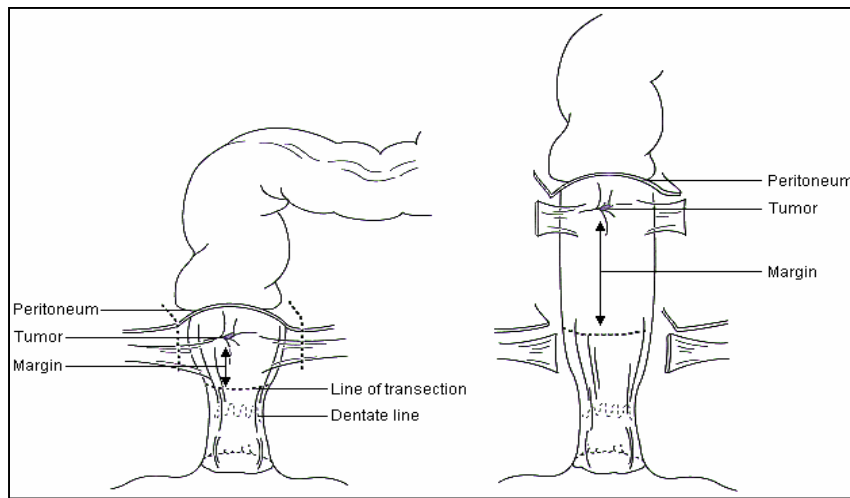


Fig. (25): Sphincter-saving procedure.

### **Lower Third Of The Rectum:**

Cancers located in the lower third of the rectum, between the anorectal ring and 7 to 8 cm from the anal verge, are reliably treated by abdominoperineal resection for adequate radial and distal margins. (Fig. 21). The procedure involves wide excision of the rectum to include the lateral attachments and pelvic mesocolon and establishment of a colostomy. The extent of surgery for an abdominoperineal resection is illustrated in Fig. 26, (Dehni et al., 1998).

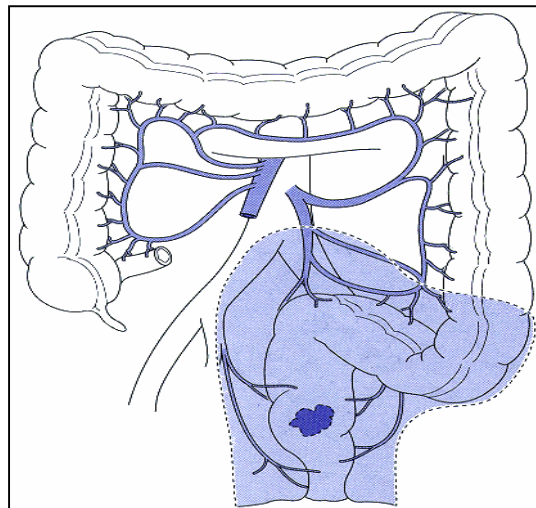


Fig. (26): Extent Of Surgery In Abdominoperineal Resection.

With the patient in a modified lithotomy position, the abdominal and perineal procedures can be performed simultaneously by two teams or sequentially by one team. Alternatively, the abdominal procedure can be completed with the patient in the supine position, and the perineal portion completed afterward, with the patient turned in the lateral position. On opening of the abdomen, evidence of intraabdominal spread is ascertained. The discovery of extensive disseminated disease may eliminate the need for an abdominoperineal resection, because a local excision or fulguration to preserve anal function may be more appropriate



for palliation. If an abdominoperineal resection is performed, ligation of the superior hemorrhoidal vessels at their origin from the left colic artery is required. Occasionally, if extensive nodal disease is present, higher arterial ligation may be necessary. The rectum is mobilized, with dissection down to the pelvic floor muscles, which are excised en bloc with the anus. An end sigmoid colostomy is brought out through the rectus sheath. Efforts to exclude small intestine from a future radiation field by use of the uterus, omentum, peritoneum, or absorbable mesh should be considered. Primary closure of the perineal wound over drains can usually be accomplished without complications, (Dehni et al., 1998) .

The entire mesorectum is included in this resection. Management of these tumors has been most clearly affected by multidisciplinary treatment strategies that allow for adequate oncologic resection and preservation of the anal canal. Important techniques have been proctectomy and coloanal anastomosis (CAA), as well as local excision, (Biggers et al., 1986). Both of these treatments are commonly combined with either preoperative or postoperative radiation therapy, ( Rosenthal et al., 1992).

The use of staplers has evolved to make an anastomosis easier when there is a short rectal stump deep within the pelvis. The double-staple technique of Knight and Griffin is most commonly used to restore intestinal continuity after resections in which a short rectal stump remains. Alternative forms of local therapy for low rectal cancers include transanal endoscopic microsurgery (TEM), endocavitary radiation, fulguration, and laser ablation. Surgical Issues in Resectable Rectal Cancer discusses the major issues that are common to surgical procedures for rectal cancer, (Griffin et al., 1990).

Local treatment options for middle and lower third rectal cancers were initially described for patients with advanced disease or medical contraindications to radical surgery. In addition, selected patients with small (less than 3 cm), well-differentiated tumors limited to the intestinal wall have been treated by local procedures with excellent results. These treatments include excision, ablation, and irradiation. Full-thickness bowel wall excisions can be performed by a transanal route with primary closure of the defect. If negative surgical margins are achieved, then consideration of adjuvant chemotherapy and radiation should be recommended to optimize locoregional tumor control. If the surgical margins are positive, then a more definitive procedure should be performed (i.e. low anterior resection or abdominoperineal resection). Alternatively, posterior approaches have been described, with removal of the coccyx, proctotomy, and closure, or posterior division of the anal sphincter, proctotomy, and closure with reconstruction of the anal sphincter muscles, (Paty et al., 1994).

Ablation by transanal electrofulguration of the tumor in multiple stages has been reported to be an acceptable treatment in patients who are

poor surgical candidates; however, this procedure cannot be employed for circumferential tumors, (Madden and Kandalf, 1983).

Endocavitary irradiation as primary curative therapy to treat early cancers has been reported with some success, (Saclarides et al., 1998).

In locally advanced colorectal tumors, the neodymium:yttrium aluminum garnet laser has been found to be effective in palliating obstructive or bleeding lesions, (Birnbau et al., 1999).

### **Mucosal Margins:**

Attaining tumor-free margins at the edges of a rectal cancer resection specimen is the hallmark of curative surgical therapy. The purpose of obtaining such a margin is to prevent local failure and effect cure. Spread beyond the lower edge of a rectal cancer may occur by submucosal spread in intramural lymphatics. Fewer than 5% of rectal cancers show distal mucosal spread beyond the edge of the tumor, and only 2.5% have histologic evidence of spread beyond 2 cm. These tumors commonly show aggressive biologic characteristics. Margins may need to be increased in locally aggressive tumors, such as those showing poor differentiation or vascular and lymphatic invasion. In these cases, the spread may be discontinuous. It does not appear that a mural mucosal margin of 5 cm is necessary to prevent local recurrence. Even margins of 1 cm have been demonstrated to provide adequate protection from local recurrence in the absence of aggressive histologic features, (Andreola et al 1997). Distal margins of more than 2 cm do not reduce the risk of anastomotic recurrence, (Hojo et al., 1986).

The impact of neoadjuvant therapies on the suitability of margins is unclear at this time. However, some have proposed that distal margins may be reduced in the face of preoperative chemoradiation. These concepts have allowed for an increase in sphincter-preserving procedures without detracting from local control and survival. However clinical response at the primary site can be misleading. Many patients have residual microscopic disease within the bowel wall, despite a complete response at the mucosal surface, (Meterissian et al 1994). Complete excision of the primary site with margins of normal tissue is recommended. The difference between margins reported in the literature and margins in situ at surgery can be significant. This fact is due to contraction of the specimen after its excision and the stretching of the rectal wall. Therefore, generous gross margins can be required to assure adequate resection. A microscopically involved margin is unacceptable for a curative resection and will not be salvaged by radiation and chemotherapy. The need for negative mural margins also applies to local excision specimens for which a 1-cm margin of grossly normal bowel wall around the tumor is recommended for satisfactory resection, (Nagle et al., 1996).

Adenopathy above the level of the inferior mesenteric artery is

frequently an indication of occult systemic spread that is not amenable to cure by surgery alone, (Drudey et al., 1987).

### **Total Mesorectal Excision:**

The mesentery of the rectum contains its blood supply and lymphatics in a bilobed fat packet situated immediately posterior and lateral to the thick-walled rectum. Both are contained in the visceral layer of the endopelvic fascia. The majority of resectable primary rectal tumors and involved lymph nodes in rectal cancer specimens are found within this structure. Nodes are involved in T1 cancers in 5.7% of cases; T2 tumors have positive nodes in 19.6%, and T3 and T4 cancers have positive nodes in 65% and 78% of cases, respectively, (Sitzler et al., 1997). Involvement of the radial or circumferential margin correlates with subsequent local recurrence and poor survival, (Hall et al., 1998).

Resection of the mesorectum should extend farther distally than the acceptable margin for rectal wall transection. Because the mesorectum tapers as it proceeds distally, it is totally excised for most middle and lower rectal cancers. More proximal rectal tumors can be treated by a mesorectal excision extending 5 cm beyond the lower tumor edge. Total mesorectal excision has been associated with a high rate of anastomotic leak when used for upper rectal tumors, (Hainsworth et al., 1997).

The work of Quirke and others (1986) has dramatically demonstrated the importance of lateral tumor spread in the local recurrence of resected rectal cancers. Among patients with local recurrence, tumor involvement at the circumferential margin of resection has been found in 85% of cases. Because of difficulty in obtaining adequate exposure in the low pelvis and the surrounding structures, circumferential margins around rectal cancer can be highly variable and minimal. Surgical experience and surgical technique have demonstrated their key role in the prevention of local recurrence by controlled sharp dissection done with attention to these margins, (Heald et al., 1995).

The mechanism for involvement of the circumferential margins can be direct spread, mesenteric implants, vascular or lymphatic invasion, or cancer-bearing lymph nodes. Up to 23% of patients can have mesorectal tumor implants aside from discrete nodes, (Reynolds et al., 1996). Tumor involvement of the circumferential margins of resection is frequently due to spread in the mesorectum distal to the tumor that can be violated by blunt dissection, (Scott et al., 1995). It has been implied that a positive circumferential margin after mesorectal excision is a prognostic factor for distant metastases also, (De hass et al., 1996).

Circumferential clearance of rectal tumors by total mesorectal excision has become the accepted surgical procedure for the management of most rectal cancer. Total mesorectal excision by full mobilization of the rectum along anatomic planes has been demonstrated to be effective in the surgical management of rectal cancer, (Enker et al., 1999).

Dissection is carried out along areolar planes that allow for hemostasis, identification of important nerves, and prevention of violation of the visceral fascia investing the mesorectum. This type of surgical resection for rectal cancer produces a negative surgical margin in more than 90% of resectable rectal cancers and reduces the possibility of local recurrence, (Havenga et al., 1999).

### **Lateral Pelvic Lymph Node Dissection:**

Lymphatic drainage of the rectum not only flows proximally along the inferior mesenteric vessels, but also follows the middle rectal vessels to the lateral pelvic sidewall and into internal iliac nodes. These nodes may be a source of recurrence. The incidence varies from 1% to 7% in resectable cases. Wide pelvic lymphadenectomy including lateral pelvic lymph nodes has been proposed for the treatment of rectal cancer. Although there is little doubt that the presence of metastases in such lymph nodes is a significant negative prognostic factor, no evidence supports a therapeutic benefit of the routine addition of extensive lymphadenectomy to standard locoregional procedures, (Moreira et al., 1994).

Gross disease can be resected when this procedure would provide a negative margin of resection. The morbidity of this procedure is significant, with the majority of patients developing urinary dysfunction and impotence, (Cohen et al., 1993).

### **Radical Surgical Treatment Options:**

Patients with stage II and III rectal cancer (60% to 80% of patients with rectal cancer) have tumors that are large and biologically aggressive. They are at higher risk of local and systemic recurrence after treatment. Accordingly, strategies have been developed to address these issues through locoregional resection and multimodality therapy, however, adequate surgical resection and technique are the most critical treatment factors determining patient outcome. The surgical management of stage II and III tumors is based on several issues: (1) the importance of the lateral spread of rectal cancer in local tumor recurrence; (2) the need for total mesorectal excision to minimize pelvic recurrence; (3) restoration of function by CAA after resection of low rectal cancers; and (4) optimization of bowel function and quality of life after low rectal anastomosis, (Goldberg et al., 1998).

### **Selection of Radical Excision Procedures:**

The surgical procedure chosen for radical excision is determined largely by tumor location. Three different operative procedures can be performed, all with adherence to the principles of total mesorectal excision: LAR, APR, and total proctectomy with CAA. For rectal cancer patients, a major component of quality of life is sphincter preservation.

This is simple to accomplish in middle and upper rectal cancers where LAR achieves adequate removal of the tumor and surrounding lymphatics and end-to-end anastomosis. In patients with low rectal cancers that do not involve the levators or sphincters, the anus may still be spared by proctectomy and CAA. Preoperative chemoradiation may facilitate this. However, patients with levator or sphincter involvement are best managed by APR and permanent colostomy, (Cohen et al., 1993).

### **Abdominoperineal Resection (APR):**

Preoperative planning of the stoma site and counseling about the consequences of a colostomy are critical to a successful outcome. Proper selection of a site must be planned preoperatively with attention to belt lines, scars, and body habitus. APR involves a combined transabdominal and perineal approach to complete resection of the rectum, mesorectum, levator muscles, and anus, with formation of a permanent colostomy. The rectum and mesorectum are mobilized via an abdominal approach down to the levator muscles. A perineal approach is used to widely resect the levator complex and anus along with an appropriate margin of perianal skin. A permanent end colostomy is done, (Laukhatt et al., 1983).

As sphincter preservation (LAR and proctectomy plus CAA) has advanced the overall proportion of rectal cancer patients undergoing APR has decreased, however, APR remains the only surgical option for some patients with rectal cancer, specifically in those patients with sphincter complex involvement or levator muscle involvement, (Dahlberg et al., 1999).

### **Low Anterior Resection (LAR):**

LAR involves the transabdominal resection of a portion of the rectum as well as the mesorectum. After complete mobilization of the rectum en bloc with the mesorectum, the rectum is divided at least 2 cm below the distal edge of the tumor. Although the length of mesorectal excision will exceed this, evidence indicates that total mesorectal excision is not required for upper rectal cancers. Reconstruction of the rectum is then carried out between the completely mobilized left colon and the remaining rectal stump. The use of LAR in midrectal and selected low rectal cancer has increased for two main reasons: (1) The double-stapled technique has permitted a simpler and lower anastomosis, with leak rates (clinical or radiographic) similar or better than with handsewn techniques. (2) Although 5 cm was previously felt to be the minimum acceptable distal margin, the acceptance of a 2-cm distal margin has enabled lower tumors to be resected by LAR, (Wolmark et al., 1986). The timing of sphincter-preserving surgery after preoperative radiation has been demonstrated to influence sphincter preservation. A 6- to 8-week interval increases the sphincter preservation rate from 68% for a 2-week interval to 76% , (Francois et al., 1999).

### **Proctectomy and Coloanal Anastomosis (CAA):**

Although LAR and APR are the traditional methods of locoregional resection in rectal cancer, proctectomy with CAA has emerged as a well-accepted surgical option in carefully selected patients. This procedure spares patients a permanent colostomy while obtaining good functional and cancer-related outcomes, (Cohen et al., 1993). A review of 117 patients from the Mayo and Cleveland Clinics provides a perspective on the current utility of proctectomy and CAA in patients with low rectal cancer, (Cavaliere et al., 1995).

The technique require complete mobilization of the rectum to the levators, transanal transection of the rectum, complete mobilization of the left colon, and endoanal anastomosis. Lateral ligaments are divided with attention to obtaining an adequate radial margin and to preserving the pelvic autonomic nerves. This dissection results in the complete exposure of the pelvic floor and complete excision of the mesorectum . The fully mobilized rectum can be amputated by a transanal technique or by transection at the upper end of the anal canal with a stapler. The reconstruction consists of delivering the mobilized left colon to the anal canal and performing an anastomosis. A hand-sewn anastomosis can be performed with full-thickness sutures through the colon and internal sphincter. Alternatively, a stapled anastomosis may be done. A diverting stoma is then usually created. The effectiveness of the procedure in preventing local recurrence was demonstrated by the low local recurrence rate of 7%. Fecal continence was satisfactory in 78%, and overall bowel function appeared to be improved in patients who had a colonic J pouch reservoir created for the CAA. No surgery-related deaths were reported. Early and late complications were related mainly to the anastomosis leaking and healing with a stricture, (Lazorthes et al., 1986).

Several groups have reported on patients who have a 6- to 10-cm colonic J pouch reservoir constructed with no additional risk or compromise of the anastomosis, (Lazorthes et al., 1986). The formation of the colonic pouch has been compared to the straight CAA in a randomized clinical trial. Hallbook and colleagues (1996) demonstrated a reduction in the frequency and urgency of bowel movements in the first year after pouch formation. Physiologic measures and short-term outcomes appear to be improved with the pouch, however, these differences may disappear with time, (Dehni et al., 1998). It has been suggested that lower leak rates with a colonic J pouch may be obtained because of improved vascular supply to the apex of the pouch and the side-to-end anastomosis, (Hallbook et al., 1996).

Postoperative problems after CAA are related to rectal capacitance and compliance. These manifest as the problems of urgency and frequency in bowel movements. This gradually improves over the 9 to 10 months after temporary stoma closure. Complete fecal continence usually is achieved in 85% to 100% of patients, (Drake et al., 1987).

## **Multivisceral Resection for Locally Advanced Rectal Cancer:**

Approximately 6% to 10% of rectal cancers are locally advanced and require extensive surgery for, complete tumor extirpation. Pelvic exenteration involving en bloc removal of the rectum, bladder, distal ureters, and other pelvic organs can be required to obtain negative margins of resection, (Cohen et al., 1990). A number of studies have demonstrated 5-year survival rates ranging from 33% to 50% for these selected patients with locally advanced rectal cancer. Despite the ability to achieve long-range survival rates in selected patients, the operation remains a formidable one, with significant morbidity and a mortality up to 6%, (Law et al., 2000). Patients who undergo such resections for primary tumors have better survival rates than those with recurrence. Meterissian et al.,(1994) reported a series of 40 patients undergoing pelvic exenteration for rectal carcinoma in which tumor-free margins were obtained. The 5-year overall survival rate was 49%, with a median survival of 56 months. Adjuvant chemoradiation appeared to provide a reduction in risk of recurrence. Long-term local control is obtained in approximately 70% of the patients who undergo resection with tumor-free margins. The results of such surgery cannot be separated from the benefits of adjuvant chemoradiation in this high-risk population, (Goldberg et al., 1998). This finding may be related to improvements in perioperative care, patient selection, and surgical techniques. Of major importance in the management of such patients, who are often heavily radiated, is the use of vascularized tissue flaps to accomplish healing of pelvic and perineal wound, (Dehass et al., 1995).

## **Complications Of Rectal Cancer Surgery:**

### **I- Peripheral Denervation Problems:**

#### **1- Disorders of the lower urinary tract:**

The clinical picture of peripheral denervation depends on the extent of denervation. Complete lesions decentralize the lower urinary tract and although ganglionic activity may persist, acontractile bladder will result with an inactive urethra. Subsequent continence is governed by the functional competence of the bladder neck mechanism. The urethra has a fixed resistance and bladder emptying depends upon abdominal straining or manual compression. Partial lesions often result in detrusor hyperreflexia, (Donker et al., 1986).

#### **2- Disorders of the lower urinary tract can best be subdivided into :**

A . Disorders of sensation.

B . Disorders of motor function.

Each of these may affect: The detrusor muscle and/or the sphincter active bladder outflow tract [ bladder neck mechanism, distal urethral sphincter, prostate ]. The detrusor muscle and the sphincter active bladder outflow tract may be normal, overactive, or underactive, (Abrams et al., 1997).

### **A- Disorders of sensation:**

These disorders represent an important poorly understood group of conditions where investigation is limited by limited knowledge about the structural and physiological basis for the perception of sensation in the lower urinary tract, and the subjective nature of sensation. Attempts to quantify sensation have included the use of objective or semi objective tests for sensory function such as evoked potentials and electrical threshold studies, (Donker et al.,1986).

Disorders of sensation are usually assessed by asking the patient about voiding pattern and any discomfort felt, based on clinical questioning or cystometry. In general terms, sensation can be subdivided as normal, hypersensitive, hyposensitive, and absent, (Ian et al.,2000).

### **B . Disorders of motor function:**

Detrusor function should be considered in the context of coexistent urethral function., but is often the primary cause of marked functional disruption. Cystometry is needed to assess the detrusor muscle efficiency and its capability to push urine. Detrusor function may be normal, overactive, underactive, or acontractile, (Griffiths et al., 1998).

### **3- Male sexual dysfunction:**

Reflexogenic erections are the result of local genital stimulation. This sets up a complex process. The impulses go to spinal erection centers and some reach the higher centers through ascending pathways to produce sensations. Others go to the autonomic ganglia and via cavernous nerves to the penis to produce erection. Injury to pelvic nerves abolishes reflexogenic erections, (Booth et al., 1993).

Emission refers to deposition of the following glandular secretions into the posterior urethra: periurethral glands, prostate, seminal vesicles, and contents of the distal vas. Emission and ejaculation are two reflexogenic phenomena that are closely related temporally occurring at the culmination of a sexually exciting situation. Each has the potential, in certain situations, to be independent of the other or even, independent of a penile erection. Although the exact nature of the afferent stimuli preceding is not clear, it appears as though both sensorial stimuli from the genitalia and cerebral stimuli are both involved. Cerebral control is such that emission may be halted voluntarily up to the sensation of inevitability caused by filling and distention of the posterior urethra. Efferent neural control emanates from the T10 to L2 sympathetic outflow. Sympathectomy can eliminate emission [ closure of the bladder neck is under sympathetic control], (Hallstorm et al.,1999 ).

Ejaculation is a complex phenomenon involving rhythmic contractions of the pelvic floor musculature with compression of the urethra, such that, under normal conditions, the semen is expelled in an ante grade direction through the urethra and out the penile meatus. The afferent stimulus seems to be the passage of semen from the posterior urethra into bulbous urethra. Little voluntary control exists after this



point. Although the control center for ejaculation appears to be located at the T11 to L2 level, outflow at the time of ejaculation also involves the sacral somatic nervous system [S 2-3-4]. A coordinated neural output controls both the smooth and striated muscles. The bladder neck remains tightly closed [sympathetic phenomenon], and rhythmic external sphincter relaxation allows semen to enter the bulbous urethra, where it is expelled by contractions of the bulbocavernosus and ischiocavernosus muscles [a somatic phenomenon], (Kirby et al., 1991).

Orgasm is a central nervous system phenomenon that relates genital experiences to whole body physiology. It can be described as an intense and profoundly satisfying cerebral sensation that represents the explosive discharge of accumulated neuromuscular tensions. Following orgasm, detumescence takes place and a refractory period ensues in which the male is unable to achieve full erection or repeat orgasm. Detumescence may be a sympathetic event secondary to vasoconstriction, (Evans et al., 1999).

## **II-Postoperative complications:**

### **1-Post-Operative Pain**

There are various methods for controlling pain. The common method of pain control is a PCA pump or patient controlled analgesia pump. This allows the patient to be given an intravenous dose of morphine or Demerol on demand. He will have a button to push that delivers the medication. Controls exist in the machine so that he cannot give himself too much. There are various types of injectable medications that can be used if the patient is allergic to morphine or Demerol, or find their side effects unacceptable. As soon as possible, the patient will be switched to oral medications. These will be given for the first week or two when he is at home. After that, it is unlikely that he will need to continue taking narcotic pain medications (Prior et al., 1982).

### **2-Blockage**

Blockage of the bowels is rare, but does occur. None of the signs of blockage are subtle, and they are often described as miserable. Those signs and symptoms include nausea and vomiting (for more than 24 hours), abdominal cramping, pain, bloating, and decrease in bowel activity. The patient will need to stop eating and drinking immediately with insertion of a Ryle tube with calculation of its content and blood electrolytes must be done to ensure if there is hypokalaemia or electrolyte disturbance. Although the patient may feel miserable, these blockages usually resolve themselves within 72 hours (Law et al., 2000).

### **3-Infection**

The major cause of infection in procedures in which reconstruction has been done is anastomotic leak. Anastomotic leaks can occur in 2% to 5% of cases, and they may result in subsequent stricture. The consequences of pelvic sepsis can be a major cause of mortality from resection of rectal

cancer. Use of a diverting stoma for a low rectal anastomosis will not prevent anastomotic leak, but it will reduce the clinical manifestations of sepsis, the need for reoperation, and mortality, (Dehni et al., 1998).

#### 4-Stoma complications

Creation of a stoma can produce complications requiring reoperation in 15% to 20% of patients such as stricture in the colostomy opening due to fibrosis or twisting of the diverted colon. The colostomy may be prolapsed or sunken inside the abdominal cavity due to its instability in the colostomy site. Reconstruction of the rectum avoids a permanent colostomy. However, bowel movements and urgency may be frequent because of the smaller neorectum (Dehni et al., 1998).

#### **Adjuvant Radiation Therapy :**

Radiation therapy combined with surgical resection for colorectal cancer has been demonstrated to reduce the incidence of local tumor recurrence. In general, the use of radiation therapy has been confined to rectal tumors in which the incidence of local recurrence is significant, including those extending through the intestinal wall or with lymph node involvement. Overall, for stage II (Dukes B2 and B3) rectal tumors, the incidence of local recurrence is about 30% to 35% but can be reduced to 5% with adjuvant radiation therapy. For stage III (Dukes C2 and C3) rectal cancers, the use of adjuvant radiation therapy decreases local recurrences from the range of 45% to 65% down to 10%. Despite improved local tumor control, the development of distant metastases still occurs, and no studies have documented an improved survival rate with adjuvant radiation therapy alone. Nevertheless, the use of this modality to improve local tumor control for rectal tumors invading the intestinal wall or involving lymph nodes is warranted to avoid the complications associated with tumor recurrence in the pelvis, (Kollmorgen et al., 1994) .

The technical aspects involving radiation therapy relate to dose and timing. The effectiveness of radiation therapy is directly proportional to the total dose. It appears that the most effective dose of radiation to eradicate microscopic disease is at least 5000 cGy. Adjuvant radiation therapy can be delivered preoperatively, postoperatively, or in combined sandwich approach, whereby small doses of preoperative treatment are followed by postoperative treatment to a high total cumulative dose. No studies clearly indicate that one approach is superior, (Swedish rectal cancer, 1997) .

Less experience has been reported for adjuvant radiation therapy of resected colon cancer. Adjuvant radiation therapy for colon cancer is associated with special problems of toxicity because of the large amount of small intestine that may lie in the treatment field. Nevertheless, several reports indicate that in high-risk cases, such as tumors involving adjacent viscera or perforated lesions, adjuvant radiation therapy can decrease local and regional recurrences, (Minsky et al., 1992).

### **Adjuvant Chemotherapy :**

Despite adequate local tumor control, patients who die from colorectal cancer do so from disseminated disease. About 25% of patients with stage II tumors, and 50% of those with stage III tumors, eventually die from growth of micrometastatic disease that was present at the time of primary tumor resection. Several randomized, prospective studies have demonstrated that postoperative adjuvant systemic chemotherapy benefits certain subgroups of patients, (Sugarbaker et al., 1995) .

A national cooperative intergroup study reported the results of 1296 patients with stage II or III colon cancer who were randomly assigned to receive either no chemotherapy, Levamisole alone, or 5-Fluorouracil (5FU) plus Levamisole therapy after resection. This study did not include rectal cancer patients. Patients with stage III disease had improved disease-free and overall survival rates if treated with the combination of 5FU and levamisole (Fig.27). The survival curve of patients treated with levamisole alone was similar to that of the control population. The results in patients with stage II tumors were equivocal and too preliminary to allow definitive conclusions. , (Moertel et al, 1990)

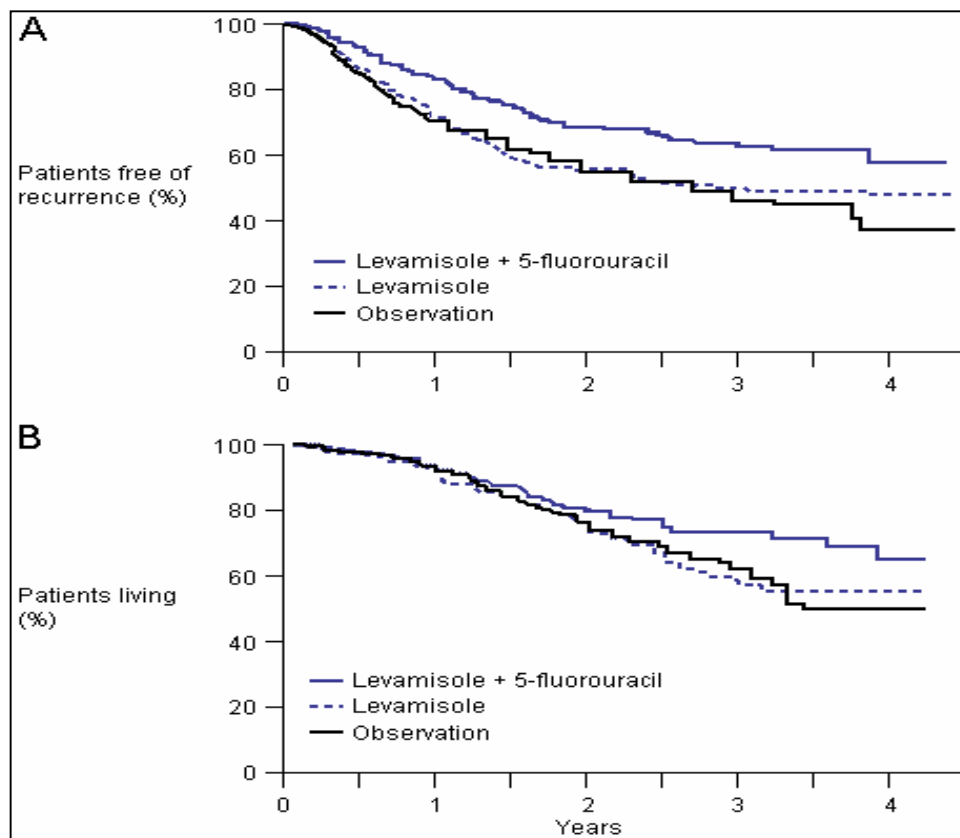


Fig. (27): Improved Disease-Free And Overall Survival In Patients With Colon Cancer Who Received Adjuvant Chemotherapy, (Moertel et al, 1990) .

In another study of 1166 patients with stage II and III colon cancers, the National Surgical Adjuvant Breast and Bowel Project (NSABP) reported an improved survival rate in patients randomly assigned to receive adjuvant chemotherapy (5FU, Semustine, and Vincristine), compared with those receiving no further treatment after resection, (Wolmark et al, 1988 ). In a follow-up study, the NSABP evaluated the efficacy of therapy with 5FU, Semustine, and Vincristine versus 5FU plus Leucovorin in stage II and III colon cancer patients, (Wolmark et al, 1993). Treatment with 5FU plus Leucovorin resulted in significantly improved survival rates and appeared to be the better combination of drugs. Semustine, which has been reported to have a leukemogenic effect, is no longer administered in this setting. Based on an evaluation of prospective, randomized studies, the National Institutes of Health recommended that patients with stage III colon cancer be offered adjuvant chemotherapy as standard treatment to improve the survival rate, (Steele et al, 1990) .

In colon cancer, local recurrence is infrequent; in rectal cancer, the use of adjuvant chemotherapy combined with radiation has proved effective in improving local control and increasing the survival rate. In rectal cancer, it is almost as important to prevent local failure and ensuing symptoms as it is to prevent death from distant failure. Radiation therapy is routinely recommended for patients with stage II or III rectal cancers. In a randomized, prospective study, 204 patients with stage II or III rectal cancers were randomly assigned to receive either postoperative radiation alone or radiation plus chemotherapy with 5FU and semustine, (Krook et al, 1991). The group that received chemotherapy had improved local tumor control and an increased overall survival rate (Fig. 28). In another prospective study, Semustine was found not to be an essential component for effective adjuvant therapy, (Gastrointestinal Tumor Study Group, 1992 ) . Based on these and other clinical studies, the National Institutes of Health has recommended that patients with stage II or III rectal cancers should receive postoperative chemotherapy and radiation as standard care, (Steele et al, 1990).

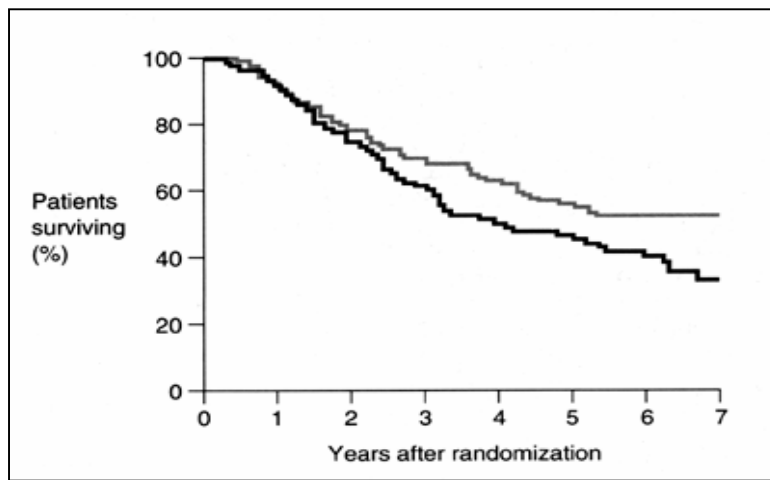


Fig. (28): Improved overall survival in patients with stage II or III rectal cancer who received adjuvant chemotherapy plus radiation (blue line) versus radiation alone (black line) postoperatively ( $P = .025$ ), ( Krook et al. 1991).

### **Adjuvant Portal Vein Chemotherapy:**

The liver is the most common site of metastatic disease for colorectal cancer. Metastasis is established by tumor cells embolized into the portal vein. From anatomic studies, it is known that micrometastases to the liver are initially fed by portal blood flow. These observations form the rationale for the administration of adjuvant intraportal 5FU chemotherapy in an attempt to decrease the incidence of liver metastasis. In an initial study, 244 patients who had resections of Dukes A, B, or C colorectal tumors were randomly assigned to receive or not receive continuous intraportal 5FU with heparin immediately after surgery, (Taylor et al, 1985) .

Patients with Dukes B and C tumors appeared to have an improved survival rate with intraportal 5FU and a decreased incidence of liver metastases. To confirm these results, the NSABP conducted a prospective, randomized study in which 1158 patients with Dukes A, B, or C colon carcinoma (rectal cancers were excluded) were randomly assigned to either observation or treatment with intraportal 5FU in the postoperative period. The study demonstrated an increased survival advantage in the group receiving intraportal 5FU compared with the control group; however, the incidence of hepatic metastasis was not different between the two groups. These results suggest that the intraportal 5FU conferred a systemic rather than a regional effect in reducing the incidence of metastatic disease; because the incidence of hepatic metastasis was not decreased by intraportal 5FU, the application of regional therapy in this setting does not appear to be justified, (Wolmark et al, 1990) .

### **Adjuvant Immunotherapy:**

An increasing interest in immunotherapy for cancer is based on animal studies that indicate tumor regression can be mediated by modulation of the host immune system. One approach has been the use of

bacillus Calmette-Guérin (BCG) as a nonspecific immunostimulatory agent, but randomized studies have demonstrated that adjuvant BCG therapy in patients with resected colorectal cancer does not improve the survival rate. Another approach has been active specific immunization with the use of autologous irradiated tumor cells admixed with BCG. This treatment was promising in a small, prospective clinical trial and is being evaluated in a larger multiinstitutional study; it should be considered investigational, (Hoover et al, 1993) .

### **Treatment Of Local Recurrence :**

Local recurrence of colon cancer occurs in about 20% of cases, and the local lesion is the only site of recurrence in about one third of these cases. If the recurrent tumor is isolated to the suture line, resection of this recurrence can be curative. Locoregional failure occurs in 30% to 65% of patients with transmural or node-positive rectal cancers. Often, pelvic recurrences of rectal cancer after a low anterior or abdominoperineal resection are diffuse and associated with disseminated disease. If pelvic recurrences are localized, they should be resected if negative surgical margins can be achieved. Surgical procedures necessary to accomplish this include en bloc partial sacrectomy or total pelvic exenteration, (Abulafi et al., 1994).

### **Treatment Of Disseminated Disease :**

Recurrent colorectal cancer is not usually localized to one site that is amenable to surgical resection. More commonly, colorectal cancer recurs in multiple sites. In these cases, systemic therapy may be considered. No studies have clearly documented that systemic therapies for disseminated colorectal cancer improve the survival rate; however, systemic treatment is commonly used for palliation, (Krook et al., 1991) .

The most commonly employed agent is 5FU. As a single agent, 5FU has an objective response rate of 10% to 20%. Promising studies have shown that the antitumor activity of 5FU can be enhanced by folinic acid (leucovorin). The tumor response rates of this combination of drugs have been in the range of 30% to 40%. 5FU combined with leucovorin is the first-line regimen for treatment of disseminated colorectal cancer. Biologic agents mediated through the action of natural host mechanisms or the administration of natural mammalian substances alone have not been found to be active in disseminated colorectal cancer. The biologic agent interferon- $\alpha$  has shown promising activity when combined with 5FU. Further studies to evaluate the efficacy of this combined therapy are needed, (Wolmark et al., 1993).

# **PREVENTION OF CANCER RECTUM**

## **Primary Prevention:**

Primary prevention of colorectal carcinoma is defined as the identification and eradication of etiologic factors responsible for this disease, including: (1) Dietary factors, (2) Lifestyle factors, (3) Alcohol consumption, (4) Cigarette Smoking, (5) Hormone use in women, (6) Nonsteroidal antiinflammatory drug (NSAID) use, (7) Bile Acids, (8) Calcium, and (9) Vitamines.

## **I- Dietary Factors:**

### **A- Dietary Fiber, Vegetables, and Fruit:**

The evidence on whether dietary fiber exerts a protective role in reducing the incidence of colorectal cancer is mixed. Most animal and epidemiologic studies show a protective effect of dietary fiber on colon carcinogenesis. The term fiber is used to describe a complex mixture of compounds, including insoluble fiber (typified by wheat bran and cellulose) and soluble fiber (usually dried beans). Ingestion of fiber could modify carcinogenesis in the large bowel by a number of potential mechanisms. These mechanisms include binding to bile acids, increasing fecal water and possibly diluting carcinogens, and decreasing transit time (not an obvious factor). Fiber may act as a substrate for bacterial fermentation with a resultant increase in bacterial mass and the production of short-chain fatty acids, typified by butyrate (Jacobs et al., 1988).

Butyrate has been shown to have anticarcinogenic effects in vitro and is regarded as an important fuel for the colonic epithelium. A meta-analysis of 13 case-control studies from 9 countries concluded that intake of fiber-rich foods is inversely related to cancers of both colon and rectum. The analysis did not include fiber supplements. The inverse association with fiber was observed in 12 of the 13 studies and was similar in magnitude for left-sided and right-sided colon and rectal cancers, men and women, and different age groups. It has been suggested that the inverse association with fiber may be reflective of some other closely associated dietary constituents, such as the anticarcinogens found in vegetables, fruits, legumes, nuts, and grains. These substances include phenolic compounds, sulfur-containing compounds, and flavones (Howe et al., 1992).

Many epidemiologic studies have examined the relationship between fruit and vegetable intake and the incidence of rectal cancer, with considerable variation in findings. Perhaps the most definitive analysis to date is a prospective study that examined dietary intake data based on food frequency questionnaires from 88,764 women in the Nurses' Health Study and 47,325 men in the Health Professionals Follow-up Study. The study included a total of 1,743,645 person-years of follow-

up, 937 cases of colon cancer, and 244 cases of rectal cancer. On the basis of analyses adjusted for numerous covariates, the authors found no association in women or men between overall fruit and vegetable consumption and risk of colon or rectal cancer. Neither were associations observed when the data were examined for subgroups of fruits or vegetables (with the exception of legumes, which were associated with an increased risk of colon cancer in women) or individual fruits or vegetables (with the exception of prunes, which were associated with an increased risk of colon cancer in men). Results did not change when data were examined by vitamin use status, smoking status, or family history of colorectal cancer, nor were elevated risks seen when individuals with very low levels of fruit and vegetable consumption were compared with those having the highest levels, (Michels et al.,2000).

High-fiber cereal supplements over a 3-year period did not result in a decrease in adenoma recurrence in a randomized controlled trial of 1,303 individuals. In a multicenter randomized controlled trial, a diet low in fat (20% of total calories) and high in fiber (18 g of dietary fiber/1,000 kcal) and fruits and vegetables (3.5 servings/1,000 kcal) was not associated with a reduction in risk of recurrence of colorectal adenomas (Schatzkin et al.,2000).

#### **B- Dietary Fat and Meat Intake :**

Rectal cancer rates are high in populations with high total fat intakes and are lower in those consuming less fat. On average, fat comprises 40% to 45% of total caloric intake in high-incidence of Western countries. In a prospective cohort study of a low-risk population of non-Hispanic white members of the Adventist Health Study, a positive association between meat (both red and white) intake and rectal cancer was observed. It has been hypothesized that the heterocyclic amines (HCAs) formed when meat and fish are cooked at high temperatures may contribute to the increased risk of rectal cancers associated with meat consumption that has been observed in epidemiologic studies (Singh et al.,1998).

#### **C- Energy Intake:**

In animal models, restricted energy intake has reduced the development of colonic tumors, (Lasko et al, 1999) .

#### **2- Lifestyle Factors:**

A sedentary lifestyle has been associated in some but not all studies with an increased risk of colorectal cancer. There are numerous observational studies that have examined the relationship between physical activity and colon cancer risk. Most of these studies have shown an inverse relationship between level of physical activity and colon cancer incidence. The average relative-risk reduction is reportedly 40% to 50%. It is not known, however, whether or to what degree the observed association is due to confusing variables such as diet or a genetic



predisposition to colon cancer. In a population-based case-control study of colorectal cancer among Chinese men and women in Western North America and China, colon and rectal cancer risk was elevated among men employed in sedentary occupations on both continents. Further, the association between colorectal cancer risk and saturated fat was stronger among the sedentary than among the active population. Perhaps related to physical activity, body mass was found to be correlated with rectal cancer in men in an Australian study and with colorectal cancer in men in Sweden. One study showed that physical activity in men, 2 hours or more per week, was more strongly associated with reduced risk for advanced adenomas (adenomas  $\geq 10.0$  mm in diameter, a villous adenoma, or an adenoma with high-grade dysplasia) versus nonadvanced adenomas. Obesity is associated with a 2-fold increase in the risk of colorectal cancer in premenopausal women, (Terry et al.,2002).

### **3- Alcohol Consumption:**

There is evidence of an association of colorectal cancer with alcoholic beverage consumption. In a meta-analysis, this association was weak. In another review, statistically significant elevations of risk were found in males, particularly as regard to beer consumption and rectal cancer. It is hypothesized that alcohol may act to stimulate mucosal cell proliferation, to activate intestinal procarcinogens and possibly provide a source of unabsorbed carcinogens that can reach the distal large bowel. Subsequently published case-control studies suggest a modest-to-strong positive relationship between alcohol consumption and large bowel cancers, (Meyer et al.,1993).

Five studies have reported a positive association between alcohol intake and colorectal adenomas. A case-control study of diet, genetic factors, and the adenoma-carcinoma sequence was conducted in Burgundy. It separated adenomas smaller than 10.0 mm in diameter from larger adenomas. A positive association between current alcohol intake and adenomas was found to be limited to the larger adenomas, suggesting that alcohol intake could act at the promotional phase of the adenoma-carcinoma sequence, (Boutron et al.,1998).

### **4- Cigarette Smoking :**

Most case-control studies of cigarette exposure and adenomas have found an elevated risk for smokers. In addition, a significantly increased risk of adenoma recurrence following polypectomy has been associated with smoking in both men and women. In the Cancer Prevention Study II (CPS II), a large nationwide cohort study, multivariate-adjusted colorectal cancer mortality rates were highest among current smokers, intermediate among former smokers, and lowest in never smokers, with increased risk observed after 20 or more years of smoking in men and women combined. On the basis of CPS II data, it was estimated that 12% of

colorectal cancer deaths in the U.S. population in 1997 were attributable to smoking. A large population-based cohort study of Swedish twins found that heavy smoking of 35 or more years duration was associated with a nearly 3-fold increased risk of developing colon cancer, although subsite analysis found a statistically significant effect only for rectal but not colon cancer. Another large population-based case-control study supports the view that current tobacco use and tobacco use within the last 10 years is associated with colon cancer. A 50% increase in risk was associated with smoking more than a pack a day relative to never smoking. However, a 28-year follow-up of 57,000 Finns showed no association between the development of colorectal cancer and baseline smoking status, although there was a 57% to 71% increased risk in persistent smokers. No relationship was found between cigarette smoking, even smoking of long duration, and recurrence of adenomas in a population followed for 4 years after initial colonoscopy, (Barron et al.,1998).

### **5- Postmenopausal Female Hormone Supplements:**

Several epidemiologic studies have suggested a decreased risk of colon cancer among users of postmenopausal female hormone supplements. For rectal cancer, most studies have observed no association or a slightly elevated risk. In the Women's Health Initiative Trial, 16,608 postmenopausal women aged 50 to 79 years were randomly assigned to a combination of conjugated equine estrogens (0.625 mg/day) plus medroxyprogesterone (2.5 mg/day) or placebo. There were 43 invasive colorectal cancers in the hormone group and 72 in the placebo group. The invasive colorectal cancers in the hormone group were similar in histologic features and grade to those in the placebo group but with a greater number of positive lymph nodes and were more advanced (regional or metastatic disease), (Chlebowski et al.,2004).

### **6- Nonsteroidal Anti-Inflammatory Drugs :**

The clinical utility of nonsteroidal anti-inflammatory drugs (NSAIDs) results from their ability to inhibit the activity of cyclooxygenase (COX). COX is important in the transformation of arachidonic acid into prostanoids, prostaglandins, and thromboxane A<sub>2</sub>. NSAIDs include not only aspirin, first-generation nonselective inhibitors of both COX-1 and COX-2, but newer second-generation drugs that inhibit primarily COX-2. The 2 functional isoforms of COX, termed COX-1 and COX-2, play important roles. Normally, COX-1 is expressed in most tissues and primarily plays a housekeeping role, e.g., gastrointestinal mucosal protection and platelet aggregation. COX-2 activity is crucial in stress responses and in mediating and propagating the pain and inflammation that are characteristic of arthritis, (Hinz et al.,2002).

In a randomized study of 635 patients with prior colorectal cancer (T1 to T2 N0 M0) who had undergone curative resection, aspirin intake at 325 mg/day was associated with a decrease in the adjusted RR of any recurrent adenoma as compared with the placebo group after a median duration of treatment of 31 months. The time to the detection of a first adenoma was longer in the aspirin group than in the placebo group. In a study of 1,121 patients with a recent history of colorectal adenomas, after a mean duration of treatment of 33 months, the unadjusted relative risks of any adenoma (as compared with the placebo group) were 0.81 in the 81-mg aspirin group and 0.96 in 325-mg aspirin group. For advanced neoplasms, the RRs were 0.59 in the 81-mg aspirin group and 0.83 in the 325-mg aspirin group, (Barron et al.,2003).

The potential for the use of NSAIDs as a primary prevention measure is being studied. There are, however, several unresolved issues that mitigate against making general recommendations for their use. These include a lack of knowledge about the proper dose and duration for these agents, and concern about whether the potential preventive benefits such as a reduction in the frequency or intensity of screening or surveillance could counterbalance long-term risks such as gastrointestinal ulceration and hemorrhagic stroke for the average-risk individual, (Imperial et al.,2003).

## **7- Bile Acids:**

A central effect of bile acids in the etiology and pathogenesis of rectal cancer has been claimed. An increased bile acid concentration in the intestinal tract accompanies a high-fat diet because bile acids are released from the gallbladder after fat ingestion. The concentration of bile acids in the colon is heavily influenced by the amount and type of fat in the diet. The potential mechanism of action of bile salts in colorectal carcinogenesis is unknown, although it has been suggested that it is mediated by diacylglycerol. The conversion of dietary phospholipids to diacylglycerol by intestinal bacteria is enhanced by a high-fat diet. It is proposed that diacylglycerol enters the cell directly, stimulating protein kinase C, which is involved in intracellular signal transduction, (Mosotoms et al.,1990).

## **8- Calcium:**

It has been hypothesized that orally ingested calcium lowers colon cancer risk by binding bile acids and fatty acids, thereby reducing exposure to toxic intraluminal compounds. Indirect effects on bile acid metabolism and a direct effect on colonic epithelial cells are also possible, (Wargovich et al.,1984).

Several but not all epidemiologic studies have observed an inverse relationship between calcium intake and cancer risk. Interpretation of these studies can be quite complex. The dose of calcium salt administered

may be important; the usual daily doses in trials have ranged from 1,250 to 2,000 mg of calcium, (slattery et al.,2003).

### **9- Vitamins:**

An inverse association between the risk of colon cancer and vitamin E intake was found. In a population-based case-control study, an inverse relationship between vitamin D intake and risk of colorectal cancer was found. A prospective cohort study observed that higher energy-adjusted folate intake in the form of multivitamins containing folic acid was related to a lower risk for colon cancer for intake of more than 400 µg/day compared with intake of 200 µg/day or less after controlling for age, family history of colorectal cancer, aspirin use, smoking, body mass, physical activity, and intakes of red meat, alcohol, methionine, and fibers, (Giovannuchi et al.,1998).

### **Secondary Prevention:**

Secondary prevention focuses on the identification of high-risk populations and interventions that can prevent the development of colorectal carcinoma. It involves identifying those persons at increased risk of death from colorectal cancer owing to the presence of premalignant lesions or early cancers. Secondary prevention strategies include screening for adenomas, treatment of adenomatous polyps by endoscopic polypectomy, or excision of the large bowel in FAP:

#### **1- Fecal Occult Blood Testing:**

The Minnesota randomized trial of fecal occult blood tests investigated reduction in incidence of colorectal cancer. Nearly 85% of subjects with a positive test underwent diagnostic procedures that included colonoscopy or double-contrast barium enema plus flexible sigmoidoscopy. After 18 years of follow-up, the incidence of colorectal cancer was reduced by 20% in the annually screened arm and 17% in the biennially screened arm, (Mandel et al.,2000).

#### **2- Polyp Removal:**

The National Polyp Study showed a greater than 75% reduction in the subsequent incidence of colorectal cancer after colonoscopic polypectomy compared with 3 nonconcurrent, external control groups, (Winawer et al.,1993).

# PROGNOSIS OF RECTAL CANCER

It is related to the following factors:

## **1) Patient's age:**

Colorectal cancer in very young and very old patients are associated with poor prognosis, (Graffin et al.,1987). In the first group, Lui et al,(1985) culminate the following factors, greater delay in diagnosis leading to more advanced disease, aggressive nature of tumors as signet cell and mucinous carcinoma. At the other end of spectrum older patients have a worse prognosis due to higher death rate of recurrent diseases and higher operative mortality rate, (Kheighly et al.,1993).

## **2) Patient's sex:**

McDennott et al, (1981) found the prognosis is significantly better for females than for males. This difference is explained by a higher incidence of more pathologically advanced tumors in the males compared with females.

## **3)Tumor-site :**

There has always been controversy over whether the site of the tumor in the colon has an influence on survival. Donaldson,(1974) found right side cancer of better prognosis than left sided cancer, but Pihl et al, (1980) found no difference in survival between left and right sided lesions. Umpleby et al,(1984) found left sided cancer is of better prognosis so, these conflicting reports define that if the anatomical site of the tumor does play a role in the survival it is not a major one. As regard cancer rectum, tumors of lower 1/3 are of poor prognosis Heald and Ryall,(1986) found this difference due to radial spread in the mesorectum which is difficult to remove in lower lesions.

## **4) Multiplicity of Tumors:**

It is of no significant important in prognosis as the survival rate for both metachronous and synchronous malignancy of colorectal carcinoma is similar to that for patients with solitary lesion, (Kaibara et al.,1984).

## **5) Tumor size:**

Steinberg et al, (1986) found a direct correlation between tumor size and the prognosis, but Stient and Coller, (1993) believed that tumor size is routinely regarded as being unimportant for prognosis of colorectal cancer.

## **6) Tumor shape:**

Tumors of exophytic shape are of better prognosis than those of infiltrative type, (Azaris et al., 1981).

## **7) Tumor extent:**

The tumors restricted to the mucosa and submucosa are of good prognosis than those invading muscles, serosa and adjacent structure, (Graffin et al.,1987).

## **8) Histopathologic grade:**

Poorly differentiated lesions are significantly worse than patients

with tumors of a degree of good differentiation however, the grading is a highly subjective parameter and of interobserver variations which tend to make classification is inaccurate and not uniform, (Kheighly et al., 1993).

#### **9) Histopathologic type:**

Mucinous carcinoma, signet cell carcinoma and small cell carcinoma have a worse prognosis than the ordinary adenocarcinoma, (Newland et al., 1981).

#### **10) Lymph-nodes-involvement:**

The greater the number of involved nodes the worse the prognosis and the vicinity of the tumor are involved, (Newland et al., 1987). Spart and Spajet, (1988) found that: if the number of L.N. below 6 lymph nodes, the 5 year survival is 10% and if above 6 all patients die within the 5 year.

#### **11) Pattern of lymph nodes reaction:**

Azaris et al, (1981) found that survival rate is better in patients whom L.N. show lymphocytes predominate in the cortex and the medulla, moderate when the L.N. show germinal center predominance (cortex only) and worse in lymphocytic depleted pattern.

#### **12) Tumor stromal reaction:**

The plasma cell lymphocytes and associated degenerative changes within the tumor have a better prognosis than those lacking these features, (Azaris et al, 1981). Also, esinophilic infiltration of the tumor stroma is associated with a markedly improved prognosis, (Pretlow et al., 1983).

#### **13) Vascular and perineural invasion :**

Vascular invasion specially in rectal cancer has a worse prognosis , (Talbat et al., 1980). Perineural invasion has the same adverse prognosis and is considered as a sign of advanced disease, (Williams et al., 1984).

#### **14) Mode of presentation:**

In emergent cases (Obstruction); Willet et al, (1984) found that the 5 year survival rate of patients undergoing curative resection for obstructing lesions was only half that of patients undergoing elective resection of apparent cure, owing to rapid intra-abdominal and systemic spread which suggested a peculiar biological behaviour of obstructing tumors.

With perforation: Ravoet al, (1984) similarly found the 5 year survival is reduced by 20% for those presented perforation. Moreover, Welch and Donaldson et al, (1990) stated that once free intraperitoneal perforation had occurred no cure could be expected in cases. Also the longer the history the better the prognosis, (Umpely et al., 1984).

#### **15) Duke's staging:**

This system (combine the items of local extent and L.N. involvement and it has been found 5 year survival is 90% for Duke's A, 50-56% for Duke's B and 15-25% form Duke's C , (Wolmark et al.,

1986).

#### **16) Blood transfusion:**

Benyon et al,(1989) found that preoperative blood transfusion was associated with poor prognosis due to its immunosuppressive action. March et al, (1990) suggest that immunosuppressive effect is due to plasma proteins rather than the cellular components.

#### **17) Extent of resection:**

Busuttil et al,(1977) found that : limited resection may be just as effective as a more radical resection. Also extended enblock resection is of no value above radical resection, (Pittam et al., 1984).

#### **18) Heat Shock protein 70:**

The local tumor hypoxia leads to the formation of heat shock protein 70 that covers the cancer cell membrane leading to poor antigen presentation resulting in poor antibody dependent cell mediated cytotoxicity, also that cover protects the cancer cell against tumor necrosis factor, (Jattella et al., 1993). Also, heat shock protein 70 reacts with antitumor antibodies inhibiting complement fixation resulting in poor complement mediated cytotoxicity and inhibit the monocytotoxic activity of natural killer cells, (lowe et al., 1989). Lastly they act a role in oncogenes complementations mainly P53. So their level correlated with high grade tumors, poor prognosis and advanced stages, (Lazaris et al., 1993).

The High Immune Antigene Degradation Products (HIADP) are epitopic antigens that play a role in antigen presentation of tumor cells resulting in effective antibody depenent cell mediated cytotoxicity, also they induce T helper cells producing the lymphokines and they activate the T cytotoxic cell having direct cytotoxic effect thus HIADP correlate with good prognosis, low grade and early stage, (Lazaris et al.,1993).

#### **19) Cell proliferation:**

Determination of S-shape fraction has shown a relation with survival rate, (Baur et al., 1987).

#### **20) Tumor margin and tissue reaction:**

Carcinoma having pushing margin and an inflammatory infiltrate at interphase between the tumor and the neighboring tissue mode up of plasma cells and lymphocytes and associated with degenerative change with the tumor have a better prognosis than those lacking this feature, (Naco poulou et al., 1981).

#### **21) Carcinoembryonic antigen:**

It has been observed that an increased level is related to higher risk for recurrence (Aabok et al., 1996). The preoperative value of carcino embryonic antigen used as a reference during follow up. Also a very high serum carcino embryonic antigen more than 5 times normal value detected preoperatively was related to a significantly worse survival rate but others as tissue plasminogen antigen and alkaline phosphatase did not predict outcome, (Rattoc et al., 1998).

## PATIENTS AND METHODS

A randomised prospective study was conducted at Surgical Oncology Unit - Mansoura University Hospital (MUH) and Oncology Centre - Mansoura University (OCMU) , during the period between June 2003 & June 2005 (total period 24 months). 40 patients with cancer rectum were enrolled in this study. Patients were of different stages. The age of the patients ranged from 22 to 70 years with a mean age of 43.65 years. 13 patients were males and 27 patients were females.

Patients were classified according to the operative procedure into 2 groups:

Group A (comparative group):

Included a retrospective studies of 20 patients subjected to subtotal mesorectal excision with conventional methods.

Group B:

Included a prospective studies of 20 patients subjected to total mesorectal excision and pelvic nerve preservation.

### Phases of The Work:

#### 1- First Phase (Diagnostic Phase):

- The aim of this phase was :
  - a) Confirm the diagnosis and exclude extrahepatic disease .
  - b) Stage the tumour.
  - c) Assess the underlying liver disease. and
  - d) Determine the general fitness of the patient.

All patients were submitted to:

1) Clinical history

Age, sex, presenting symptoms ( bleeding per Rectum, constipation, rectal mass or pain)

2)General examination

General, abdominal and per-rectal.

3)Routine preoperative laboratory investigations

Routine investigations for distant metastasis including liver function studies, and preoperative assessment of carcino embryonic antigen level to compare it with the normal level.

4)Radiologic studies

Chest X ray, Bone scan, Abdominal CT and Barium enema were done for



all patients. And according to the findings, the patients were divided according to the site of a rectal mass (upper, middle or lower third) which subjected to endoscopic biopsy from an actively growing portion of the tumor to confirm the presence of malignancy

According to the pathological examination of the postoperative biopsy, the patients were divided into Duke's A, B and C rectal cancer.

The patients were subjected to low anterior resection or abdominoperineal resection according to the site of the tumor.

Preoperative counseling

Bowel preparation

Correction of dehydration, anaemia, and nutritional deficits is essential. Mechanical reductions of the endogenous bacterial flora with enemas were required in addition to oral and parenteral antibiotics. Saline enemas were administered 2 to 3 days preoperatively..

Oral non absorbable antibiotics ( erythromycin ) in a period of 24 to 36 hours preoperatively further allowed a reduction of the colonic bacterial flora.

Third generation cephalosporin intravenously administered perioperatively and within the immediate postoperative period were determined to be of similar value as oral preparations for intestinal antisepsis.

stoma marking in patients who need permanent colostomy:

On the day before the proposed operation, the patient was assessed for his body habitus, clothing style, and any unusual deformities of the abdominal wall, such as scars, folds of fat, or unusual body contours.

The stoma site was chosen to conform best to the needs of each patient and was marked after the patient had been placed in erect, supine, sitting, and bending positions.

The stoma was through the rectus abdominis and not be deformed by proximity to the umbilicus, iliac crest, or costal margin.

The incision gave an easy access to the abdomen . The midline incision was preferred that veers to the right of the umbilicus so that potential encroachment on the colostomy site was avoided.

Surgical technique

Because the majority of rectal tumors and their eventual lymph node metastases are limited to the mesorectum, total mesorectal excision is an operation designed to resect the mesorectum intactly and completely. The operation requires direct visibility to remove the contents of the fascial envelope intact to prevent local recurrence. This requires a midline incision down to the symphysis pubis. A self retaining retractor is used to have an undisturbed view into the pelvis.

Visibility is improved if the uterus is elevated to the abdominal wall with a stitch. (occasionally, an ovary with cysts may hinder a good view and is

placed behind the retractor blades or resected) .

After mobilizing the sigmoid colon from its attachments to the lateral abdominal wall, the peritoneum around pouch of Douglas is incised.

At the level of the inferior mesenteric artery, or the sigmoid artery distal to the left colic branch, the mesenteric vessels are ligated and divided. Subsequently, the mesosigmoid and sigmoid (or descending colon with its mesentery ) are divided just proximal to the vascular pedicle.

Lifting up the sigmoid opens the retrorectal space. The retrorectal space is further opened by meticulous, precise, sharp ( scissors or electrocautery ) dissection under direct vision of exposed loose areolar tissues and small vessels between the visceral and parietal fascia allows a specimen oriented operation with an intact bilobed mesorectum avoiding any tearing or disruption of lymph vessels or nodes.

After dissection, it is possible to excise the mesorectum intact and leave a tube of rectal muscles for anastomosis at a sufficient level from anal verge preserving the anorectal ring (sphincter preservation).

The concept of total mesorectal excision can be associated with low anterior resection omitting a permanent stoma with colorectal anastomosis if the rectal tumor is above the area of differentiation between solid fecal matter and flatus ( 1 cm above the anococcygeal body posteriorly or perineal body anteriorly ) or can be associated with abdominoperineal resection with permanent colostomy.

Total mesorectal excision must be differentiated from the so called subtotal mesorectal excision which need only to remove the mesorectum to the level of 5 cm below the lower edge of the tumor (safety margin for excision of rectal tumor) in spite of it is sufficient to be total excision or not rather than anatomical mesorectum or incomplete lateral dissections.

The hypogastric nerves are identified at the sacral promontory or over the first sacral vertebra. As the hypogastric nerve is located in or above leaves of the visceral fascia, it may be lifted with the mesorectum.

Care has to be taken to divide any attachments between the hypogastric nerve and the mesorectum.

Some small branches coming medially of the main trunk of the hypogastric nerve and entering the mesorectum are to be divided.

As the hypogastric nerve is displaced laterally, the retrorectal space widens.

At the level of the fourth sacral vertebra, just under the anterior curve of the sacrum, the retrosacral ligament is divided sharply. At this point, on the inferior margin of the piriformis muscle, the pelvic splanchnic nerves are located under the parietal fascia.

When the retrorectal space is opened more laterally, these pelvic splanchnic nerves are identified where they pierce the parietal fascia, still covered, however, with sheaths of visceral fascia.

The prerectal space is opened between the rectum and either the seminal vesicle or posterior vaginal wall. Starting this dissection just above the

peritoneal reflection with posterior traction on the mesorectum is usually helpful in finding this plane.

The prerectal space is further opened by sharp dissection on Denonvillier's fascia.

Coming laterally, the mesorectum is now only attached to the pelvic wall by the so called lateral ligaments.

The dissection takes place just medial to the pelvic autonomic nerves plexus by dividing all transverse fibers ( autonomic nerve fibers to the rectum , connective tissue and blood vessels ) ( Wilch technique).

Division of the lateral ligaments may be performed by electrocautery, as the branches of the middle rectal artery and vein are small.

Pulling too hard on the mesorectum medially may tent the pelvic autonomic nerve plexus inward, putting this plexus at risk to surgical damage, especially by clamping or stapling.

When colostomy is indicated in abdominoperineal resection, a circle of skin is excised of a size that approximates the diameter of the proposed colostomy. The anterior rectus sheath is exposed by means of small retractors, and a cruciate incision in the sheath is performed. The abdomen is entered parallel to the muscle fibers after penetration of the anterior abdominal wall. The proximal bowel is drawn through the colostomy site after the abdominal wound is closed.

After the surgeon has determined that the patient will undergo an abdominoperineal resection, The anus is closed with a continuous encircling suture. Cutaneous incision is made with electrocautery and take the form of an ellipse surrounding the anus. The anterior extent of dissection should be in line with the deep transverse perineal muscles. The posterior dissection uses the tip of the coccyx as a landmark and a self retaining retractors permits dissection into the ischiorectal fossa. The anterior and posterior branches of the inferior rectal arteries are isolated , clamped and ligated bilaterally. The pelvis is entered in front of the coccyx, guided by the surgeon's fingers, which have been placed in the precoccygeal region. The dissection should be directed at the umbilicus to avoid stripping of the presacral fascia.

After abdominoperineal resection or low anterior resection, Foley catheter should be left in place for a minimum of 6 days. And a drain placed in the pelvis and led out through the anterior abdominal wall. Patients undergoing abdominoperineal resection have a drain brought out through the perineal wound. After low anterior resection, the abdominal drain is left in place for 10 days so that, leakage may occur from the anastomosis. After abdominoperineal resection, the perineal drain is left in place with wall suction for 4 days and then removed.

Perineal wound is closed in patients with abdominoperineal resection. In all patients the abdominal wall is closed in layers( peritoneum, linea alba, subcutaneous fat and skin). In deeper layers making sure not to pick up bowel or omentum. Generous bites with each stitch are taken and pulled

up not tightly , passing it to the assistant to maintain the tension while the next stitch is inserted. After placing 4-5 sutures and gently and evenly tightening them, a finger is inserted to confirm that the bowel is free.

Adjuvant treatment:

Patients were sent to deliver postoperative chemotherapy in the form of 5 fluorouracil and radiotherapy if suspected to be locally recurrent postoperatively.

Follow up

1) Local recurrence

Patients were followed up for a varying period with a mean period of one year considering history, physical examination, and measurement of Carcinoembryonic antigen (CEA) values done thrice yearly with chest radiograph and liver ultrasound every six months.

A follow up CT pelvis was also done at a year postoperatively.

2) Postoperative sequelae

Standard Questionnaire

Patients were asked to fill out a questionnaire with questions regarding preoperative and postoperative urinary and sexual function. The urinary symptoms are in the form of difficulty in bladder emptying, incomplete bladder emptying, abnormal feeling of bladder fullness, pain, burning or discomfort during urination; increased frequency; difficulty to start, continue or end urination; dribbling; leaking of urine; and urgency.

The sexual function : Five International Index of Erectile Function domain scores (erectile function, intercourse satisfaction, orgasmic function, sexual desire, and overall satisfaction).

**Urodynamic examination**

The duration between the operation and urodynamic examination varied from 6 months to 1 year with a mean duration of 9 months.

Urodynamics is the study of the different mechanical forces controlling urine formation and expulsion.

Urodynamics are primarily intended to study the lower tract , as the upper tract is difficult to access and they are an important investigative tool in neuropathic bladder disorders, bladder outlet obstruction, urinary incontinence and congenital anomalies as posterior urethral valve.

Urodynamic examination consisted of uroflowmetry and filling and voiding cystometry.

**Before the test:**

The patient will need to take the antibiotic that has been provided. Urine culture is collected prior to the examination to ensure sterility of urine.

Technique :

1) Medium : Types of filling media are used

Fluid as sterile saline or water is used as a filling medium

2) Filling rate : International Continence

Society ( ICS ) recommendations are

Slow fill ( $< 10$  ml/sec ).

Medium fill (  $10 - 100$  ml/sec).

Rapid fill ( $> 100$  ml/sec ).

3) Catheters : A transurethral double lumen catheter was passed with lubrication.

A uroflowmeter automatically measures the amount of urine and the flow rate (how fast the urine comes out). Commercially available flowmeters are either weight transducers which utilizes the voided volume as a measurement of weight or rotating disc transducer which depends on the mechanical impedance offered by urine flow to a rotating drum. The patient may be asked to urinate privately into a toilet that contains a collection device and scale. This equipment creates a graph that shows changes in flow rate from second to second. Results of this test will be abnormal if the bladder muscle is weak or urine flow is obstructed.

Most of the flowmeters available have an error within the range of  $1 - 8$  % for volume estimation and  $4 - 15$  % for flow rate estimation.

Reading of the flow curve :

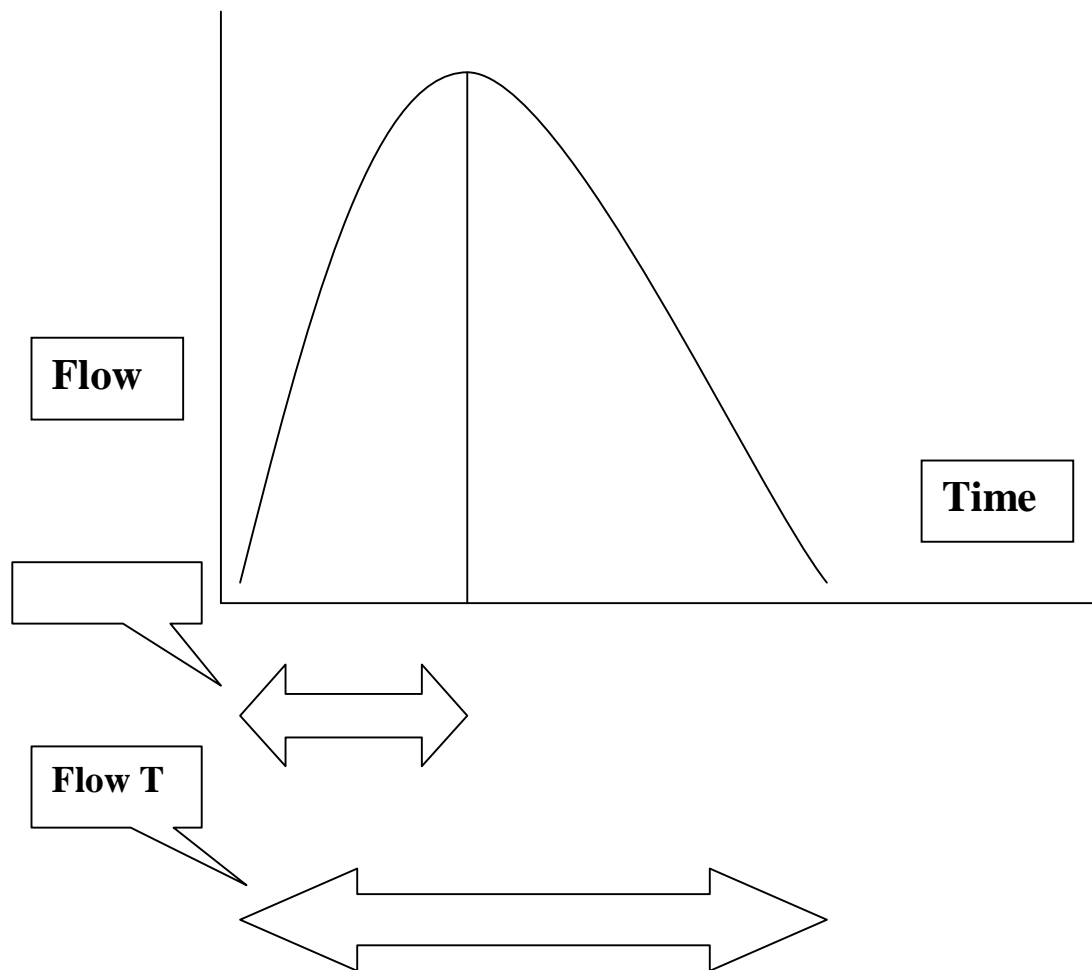
***Shape : a normal flow curve is characterized by being a bell-shaped curve ( like the normal distribution of most of the biological parameters ).***

***$Q_{max}$  : the maximum flow rate. Normal values for adult males:  $20 - 25$ , and for an adult female  $25 - 30$  ml/sec.***

***Time to  $Q_{max}$  : estimated to be  $1/3$  of the total flow time.***

***Flow time.***

## *Normal Flow Curve*

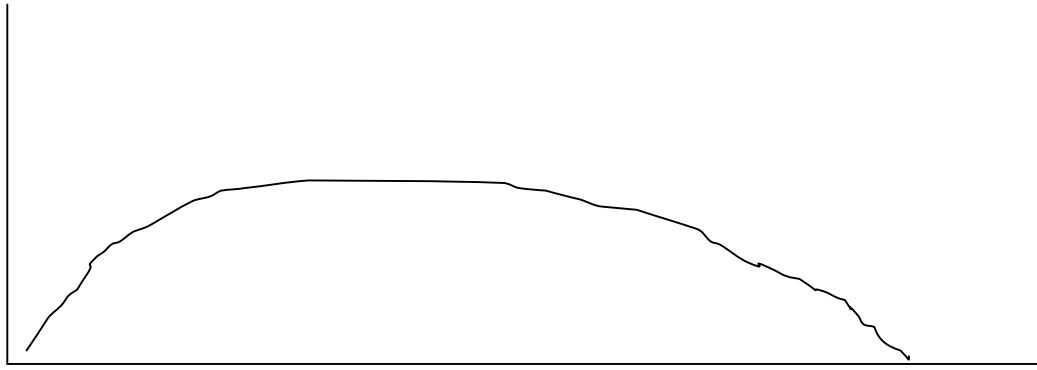


Normally  $Q_{\max}$  decreases by 1 – 2 ml/sec/5 years in adult males.  $Q_{\max} < 10$  ml/sec is considered abnormal while  $> 10$  ml/sec is normal. The voided volume is of crucial importance in the interpretation of the results of the flow curve. The minimal accepted volume is 100 – 150 ml. The value of  $Q_{\max}$  is directly proportional to the voided volume up to the value of 300 ml. After which the relation is no longer linear as no further increases of the  $Q_{\max}$  with increases of the volume.

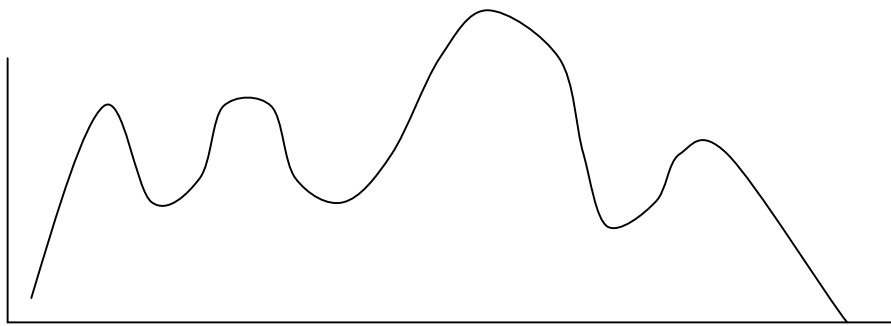
Flow curve patterns :

Normal : bell shaped with two points of inflection.

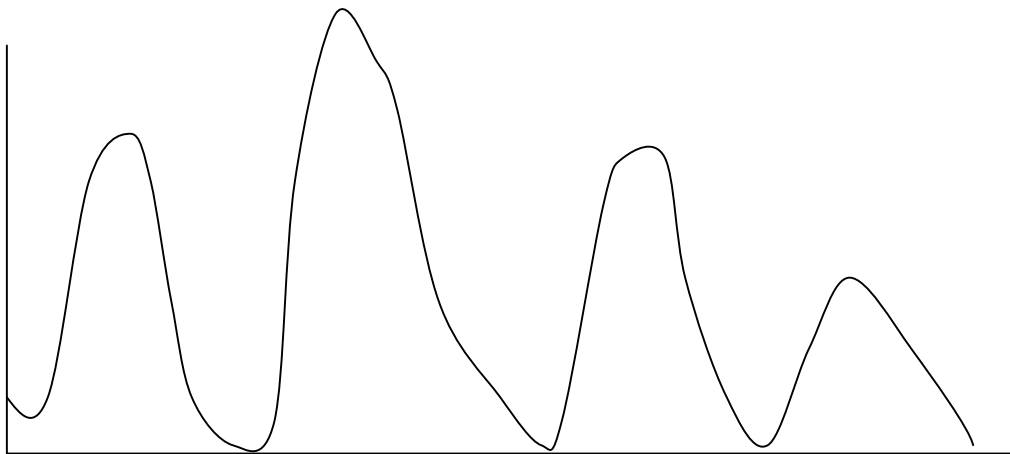
Prostatic curve : elongatened and flattened without spikes.



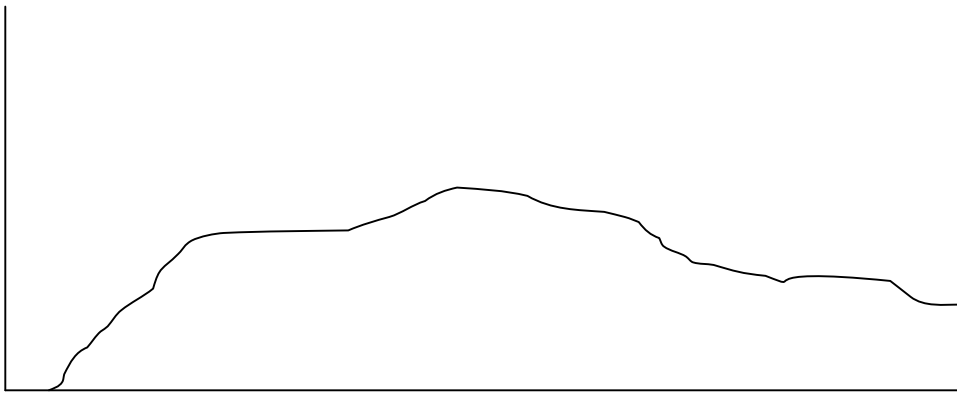
**Fluctuating** : multiple fluctuations but not reaching the baseline seen in abdominal voiding as in orthotopic reservoirs.



**Fractionated** : the flow drops to zero line repeatedly seen in interrupted flow as in neuropathic bladders and irritable patients.



**Plateau** : *prolonged and flattened, with a prolonged Qmax seen in poor detrusor function and in atypical prostatic enlargement.*



### **Postvoid residual**

After the patient have finished urinating, He may still has some urine, remaining in his bladder. To measure this urine, called a post-void residual, drain the urine and measure it. A post-void residual of more than 200 ml is a clear sign of a problem. Even 100 ml, about half a cup, may require further testing

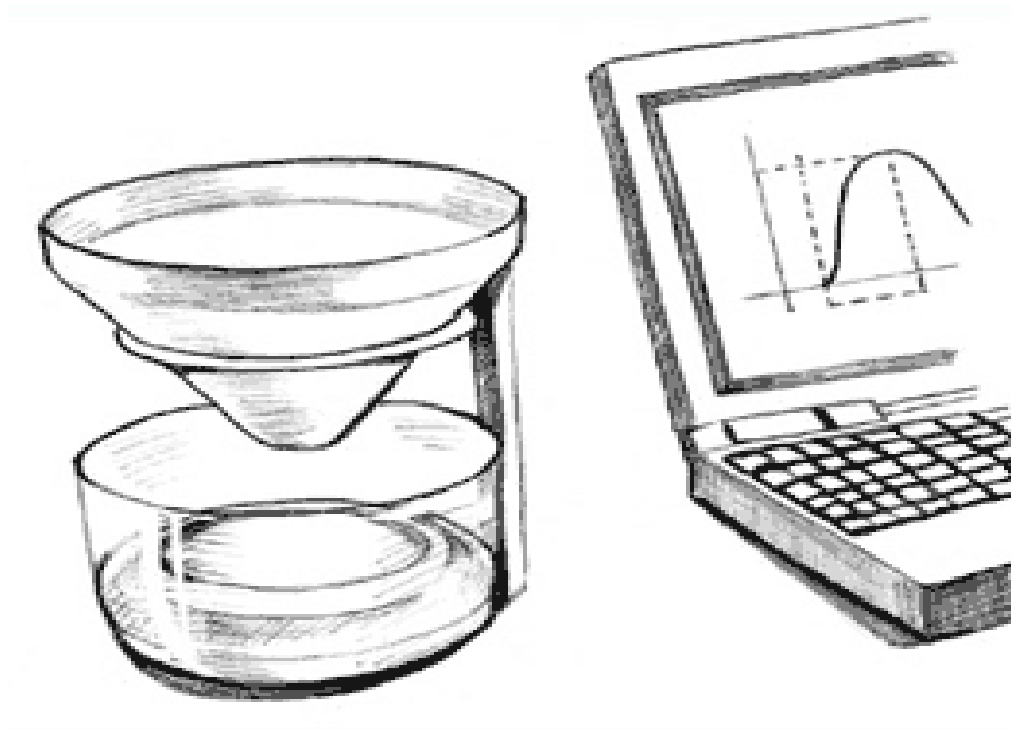
.  
Voiding phases were repeated 2 to 3 times in an attempt to minimize the effects of patient anxiety on the bladder behavior examination and reduce artifacts.

### **Doppler studies for penile function**

Male patients were subjected to Duplex ultrasound and pulsed Doppler analysis to detect impaired haemodynamic blood flow parameters to record systolic occlusion pressure in the cavernosal arteries of the penis. Doppler wave form analysis was done with a 7.5 to 10 Mhz probe. Arterial insufficiency was diagnosed if the duplex scan showed an arterial diameter less than 25 percent and a peak systolic velocity of less than 25cm/sec.



***Fig.29.***



***Uroflowmeter equipment***

## ***1 ) Clinical characters of patients***

The study included a retrospective study of 20 patients (Group A) and a prospective study of 20 patients (Group B).The clinical findings of the patients are:

### ***A ) Age of patients:***

Table (1) describes the age in years of the patients included in the study.

No. of patients	Group A		Group B		Total	
	No.	%	No.	%	No.	%
20 - 29	3	15	5	25	8	20
30 - 39	3	15	2	10	5	12.5
40 - 49	3	15	5	25	8	20
50 - 59	8	40	4	20	12	30
60 - 69	3	15	4	20	7	17.5

### ***B ) Sex of patients:***

Group A included 12 female patients ( 60 % ) and 8 male patients ( 40 % ).  
Group B included 15 female patients (75 % ) and 5 male patients ( 25 % ).  
Table (2) describes the sex of the patients.

Sex	Group A		Group B		Total	
	No.	%	No.	%	No.	%
Female	12	60	15	75	27	67.5
Male	8	40	5	25	13	32.5

### ***C ) Clinical presentation:***

Group A included 13 patients presented with bleeding per rectum ( 65 % ), 3 patients presented with constipation (15 % ), 2 patients with a rectal mass ( 10 % ) and 2 patients presented with pain on defecation ( 10 % ). Group B included 15 patients presented with bleeding per rectum ( 75 % ), 3 patients presented with a rectal mass ( 15 % ), 2 patients presented with pain on defecation ( 10 % ). Table (3) shows the details of these findings.

<b>Clinical picture</b>	<b>Group A</b>		<b>Group B</b>		<b>Total</b>	
	<b>No.</b>	<b>%</b>	<b>No.</b>	<b>%</b>	<b>No.</b>	<b>%</b>
Bleeding per rectum	13	65	15	75	28	70
Constipation	3	15	-	0	3	7.5
Rectal mass	2	10	3	15	5	12.5
Pain on defecation	2	10	2	10	4	10

### ***D ) Site distribution***

Group A included 9 patients with cancer upper 1/3 rectum ( 45 % ), 2 patients with cancer middle 1/3 rectum ( 10 % ) and 9 patients with cancer lower 1/3 rectum ( 45 % ). Group B included 5 patients with cancer upper 1/3 rectum ( 25 % ), 2 patients with cancer middle 1/3 rectum ( 10 % ) and 13 patients with cancer lower 1/3 rectum ( 65 % ) as shown in table (4).

<b>Site distribution</b>	<b>Group A</b>		<b>Group B</b>		<b>Total</b>	
	<b>No.</b>	<b>%</b>	<b>No.</b>	<b>%</b>	<b>No.</b>	<b>%</b>
Upper 1/3 rectum	9	45	5	25	14	35
Middle1/3 rectum	2	10	2	10	4	10
Lower 1/3 rectum	9	45	13	65	22	55

### ***2) Pathological characters***

#### ***a) Gross picture:***

Group A showed 9 patients with annular stenosing lesion ( 45 % ), 8 patients with ulcerative lesion ( 40 % ) and 3 patients with a cauliflower mass ( 15 % ). Group B showed 10 patients with annular stenosing lesion ( 50 % ), 8 patients with ulcerative lesion ( 40 % ) and 2 patients with a cauliflower mass ( 10 % ) as shown in table (5).

<b>Gross picture</b>	<b>Group A</b>		<b>Group B</b>		<b>Total</b>	
	<b>No.</b>	<b>%</b>	<b>No.</b>	<b>%</b>	<b>No.</b>	<b>%</b>
Annular stenosing	9	45	10	50	19	47.5
Ulcerative lesion	8	40	8	40	16	40
Cauliflower mass	3	15	2	10	5	12.5

### ***b) Microscopic examination:***

#### ***According to Crawford grading;***

Grade I : well differentiated adenocarcinoma

GradeII : moderate differentiated adenocarcinoma

GradeIII : poorly differentiated adenocarcinoma

GradeIV : mucinous adenocartcinoma

Grade V : signet ring cell carcinoma

Group A included 7 patients with grade I ( 35 % ), 6 patients with grade II ( 30 % ), 1 patient with grade III ( 5 % ), 5 patients with grade IV ( 25 % ) and 1 patient with grade V (5%)

Group B included 7 patients with grade I ( 35 % ), 8 patients with grade II ( 40 % ), 1 patient with grade III ( 5 % ), 1 patient with grade IV ( 5 % ) and 3 patients with grade V (15 % ) as shown in table (6).

Grade of tumor	Group A		Group B		Total	
	No.	%	No.	%	No.	%
Grade I	7	35	7	35	14	35
Grade II	6	30	8	40	14	35
Grade III	1	5	1	5	2	5
Grade IV	5	25	1	5	6	15
Grade V	1	5	3	15	4	10

### ***C ) Staging:***

Group A included 1 patient with stage Duke's A ( 5 % ), 2 patients with stage Duke's B<sub>1</sub> ( 10 % ), 8 patients with stage Duke's B<sub>2</sub> ( 40 % ), 2 patients with Duke's C<sub>1</sub> ( 10 % ) and 7 patients with Duke's C<sub>2</sub> ( 35 % ). Group B included 3 patients with stage A ( 15 % ), 5 patients with stage Duke's B<sub>1</sub> ( 25 % ), 4 patients with Duke's C<sub>1</sub> ( 20 % ) and 3 patients with stage Duke's C<sub>2</sub> as shown in table (7).

Stage of tumor	Group A		Group B		Total	
	No.	%	No.	%	No.	%
Duke's A	1	5	3	15	4	10
Duke's B <sub>1</sub>	2	10	5	25	7	17.5
Duke's B <sub>2</sub>	8	40	4	20	12	30
Duke's C <sub>1</sub>	2	10	5	25	7	17.5
Duke's C <sub>2</sub>	7	30	3	15	10	25

### ***3 ) Operative intervention:***

10 patients from Group A were subjected to low anterior resection with subtotal mesorectal excision and conventional method ( 50 % ) and the other 10 patients of the same group were subjected to abdominoperineal resection with subtotal mesorectal excision and conventional method (50 % ).

6 patients from Group B were subjected to low anterior resection with total mesorectal excision and pelvic nerve preservation ( 30 % ) and 14 patients were subjected to abdominoperineal resection with total mesorectal excision and pelvic nerve preservation. ( 70 % ) as shown in table (8).

<b>Operation</b>	<b>Group A</b>		<b>Group B</b>		<b>Total</b>	
	<b>No.</b>	<b>%</b>	<b>No.</b>	<b>%</b>	<b>No.</b>	<b>%</b>
L A R	10	50	6	30	16	40
A P R	10	50	14	70	24	60

### ***4) Recurrence***

Mean one year follow up of the patients by frequent clinical examination and radiological studies revealed;

#### ***Group A:***

2 patients presented with presacral recurrence.

2 patients presented with recurrence in the pelvic bottom.

1 patient presented with anastmosis recurrence

1 patient presented with recurrence in the perineum.

***Table (9) describes the criteria of patients in Group A presented with recurrence;***

<b>Case No.</b>	<b>Site</b>	<b>Stage</b>	<b>Grade</b>	<b>Surgery</b>	<b>Site of recurrence</b>
1	Middle1/3	C <sub>2</sub>	III	APR	Presacral
2	Middle1/3	C <sub>1</sub>	IV	APR	Presacral
3	Upper 1/3	C <sub>2</sub>	IV	LAR	Anastmosis
4	Lower 1/3	C <sub>2</sub>	IV	LAR	Pelvic bottom
5	Lower 1/3	B <sub>1</sub>	V	APR	Perineal
6	Lower 1/3	C <sub>2</sub>	IV	APR	Pelvic bottom

There were increases in serum CEA levels postoperatively in cases 2 and 4 four timesfold than the normal level and increase three timesfold than normal level in case 5 and two timesfold than normal level in cases 1,3 and 6.

***Group B:***

Among 20 patients included in that prospective study in which the patients subjected to total mesorectal excision, there was no patients reported to be presented with local nor distant recurrence ( 0 % ).

***Site of tumor and recurrence***

***Group A:***

Among 9 patients with cancer upper 1/3 rectum, only 1 patient presented with recurrence ( 11.1 % recurrence ) while among 2 patients with cancer middle 1/3 rectum, there was no recurrence ( 0 % ) and among 9 patients with cancer lower 1/3 rectum, there were 3 patients with recurrence ( 33.3 % ).

***Table (10) describes that relation***

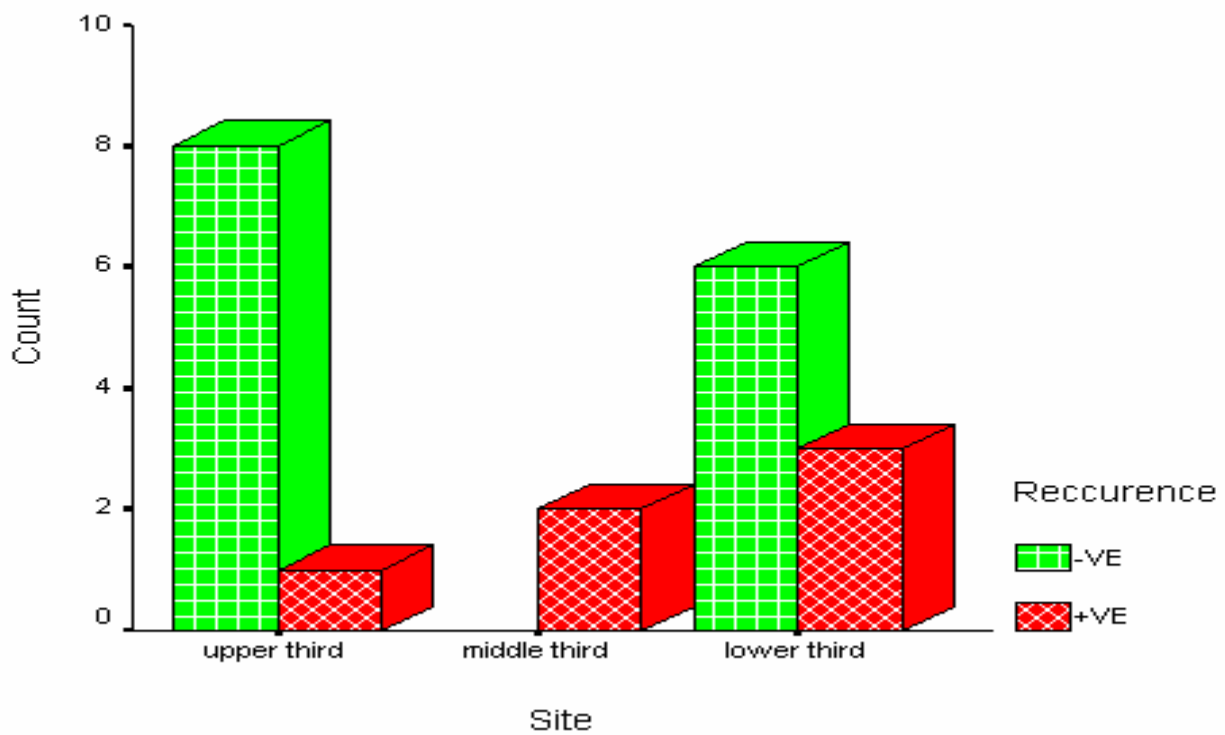
**Crosstab**

			RECURRENCE	
			+VE	-VE
SITE	upper third	Count	1	8
		% within SITE	11.1%	88.9%
	middle third	Count	2	.00
		% within SITE	100.0%	0 %
	lower third	Count	3	6
		% within SITE	33.3%	66.7%
Total	Count	6	14	
	% within SITE	30.0%	70.0%	

**Chi-Square Tests**

	Value	Asymp. Sig. (2-sided)
Pearson Chi-Square	6.243	.044





### ***Group B***

Among 5 patients with cancer upper 1/3 rectum and 2 patients with cancer middle 1/3 rectum and 13 patients with cancer lower 1/3 rectum, no patients presented with recurrence ( 0 % ).

### ***Stage of tumor and recurrence***

#### ***Group A***

There is increased recurrence with late stages as stage ( $C_1 + C_2$ ) than stage A or stage ( $B_1 + B_2$ ).

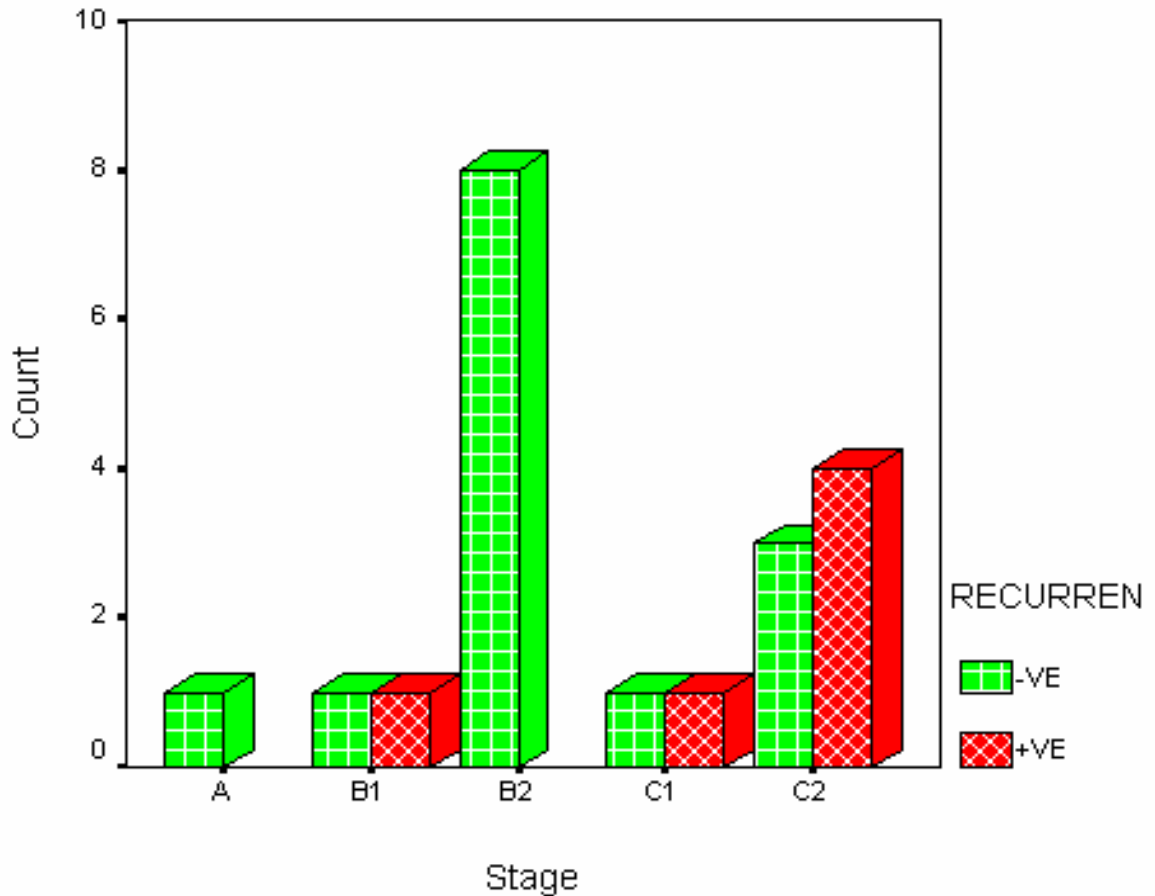
Table (11) describes the relation between grade of tumor and recurrence in Group A

### Crosstab

			RECURRENCE	
			+VE	-VE
STAGE	A	Count % within STAGE	.00	1 100.0%
	B1	Count % within STAGE	1 50.0%	1 50.0%
	B2	Count % within STAGE	.00	8 100.0%
	C1	Count % within STAGE	1 50.0%	1 50.0%
	C2	Count % within STAGE	4 57.1%	3 42.9%
Total		Count % within STAGE	6 30.0%	14 70.0%

### Chi-Square Tests

	Value	Asymp. Sig. (2-sided)
Pearson Chi-Square	7.075	.132



***Figure (31) describes the same relation.***

### ***Group B***

Stage A, B<sub>1</sub>, B<sub>2</sub>, C<sub>1</sub> and C<sub>2</sub> show no presented cases with recurrence ( 0 % ).

### ***Grade of tumor and recurrence***

#### ***Group A***

There is a highly significant relation between grade of tumor and recurrence as with grade I and grade II, there is no recurrence at all while there is increasing recurrence rate with high grade, 50 % in grade III and 100 % in grade IV and grade V. P value is 0.001.

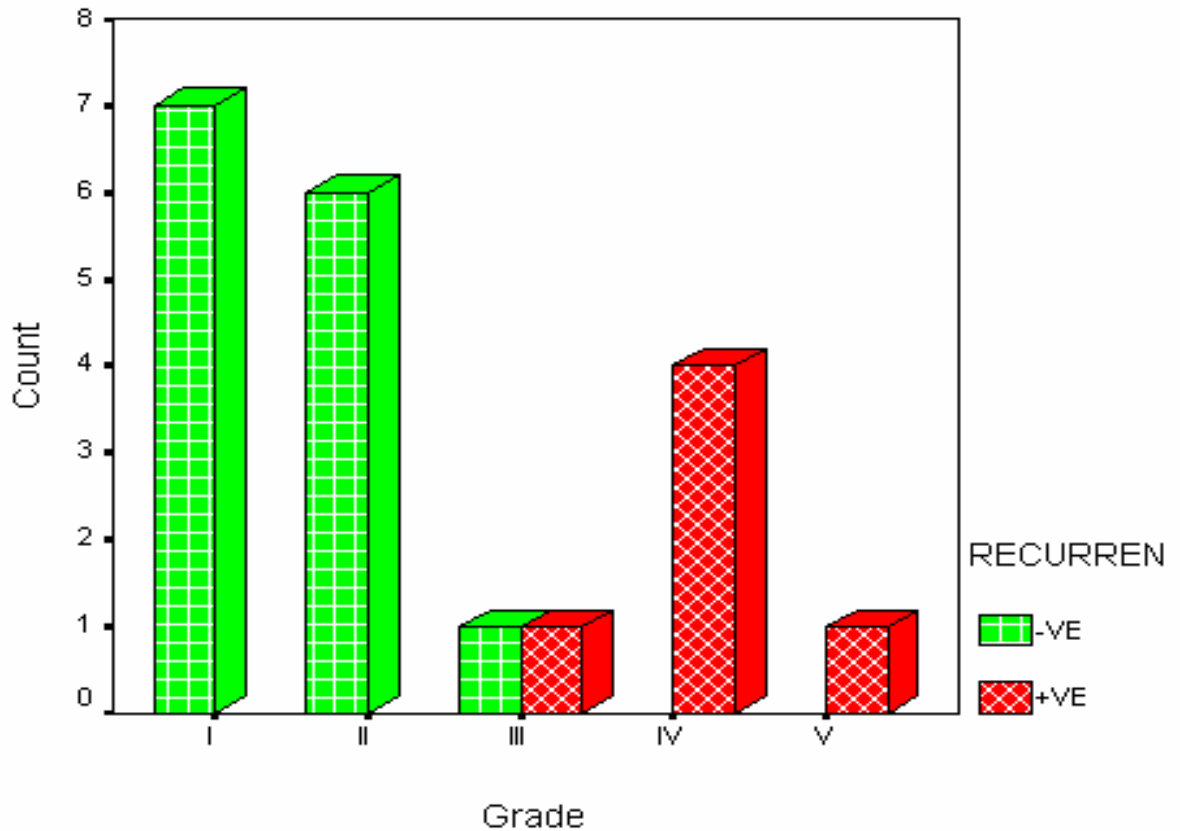
***Table (12) shows these findings.***

**Crosstab**

			RECURRENCE	
			+VE	-VE
GRADE	I	Count	.00	7
		% within GRADE		100.0%
	II	Count	.00	6
		% within GRADE		100.0%
	III	Count	1	1
		% within GRADE	50.0%	50.0%
	IV	Count	4	.00
		% within GRADE	100.0%	
	V	Count	1	.00
		% within GRADE	100.0%	
Total		Count	6	14
		% within GRADE	30.0%	70.0%

## Chi-Square Tests

	Value	Asymp. Sig. (2-sided)
Pearson Chi-Square	17.619	.001



***And Figure (32) describes that relation.***

### ***Group B***

Among all subjected grades of this study ( I, II, III, IV and V ), no cases presented with recurrence ( 0 % ).

### ***Recurrence in both groups ( A and B ):***

Table (13) shows the cross tabulation of recurrence in the 20 patients of group A and the other 20 patients of group B:

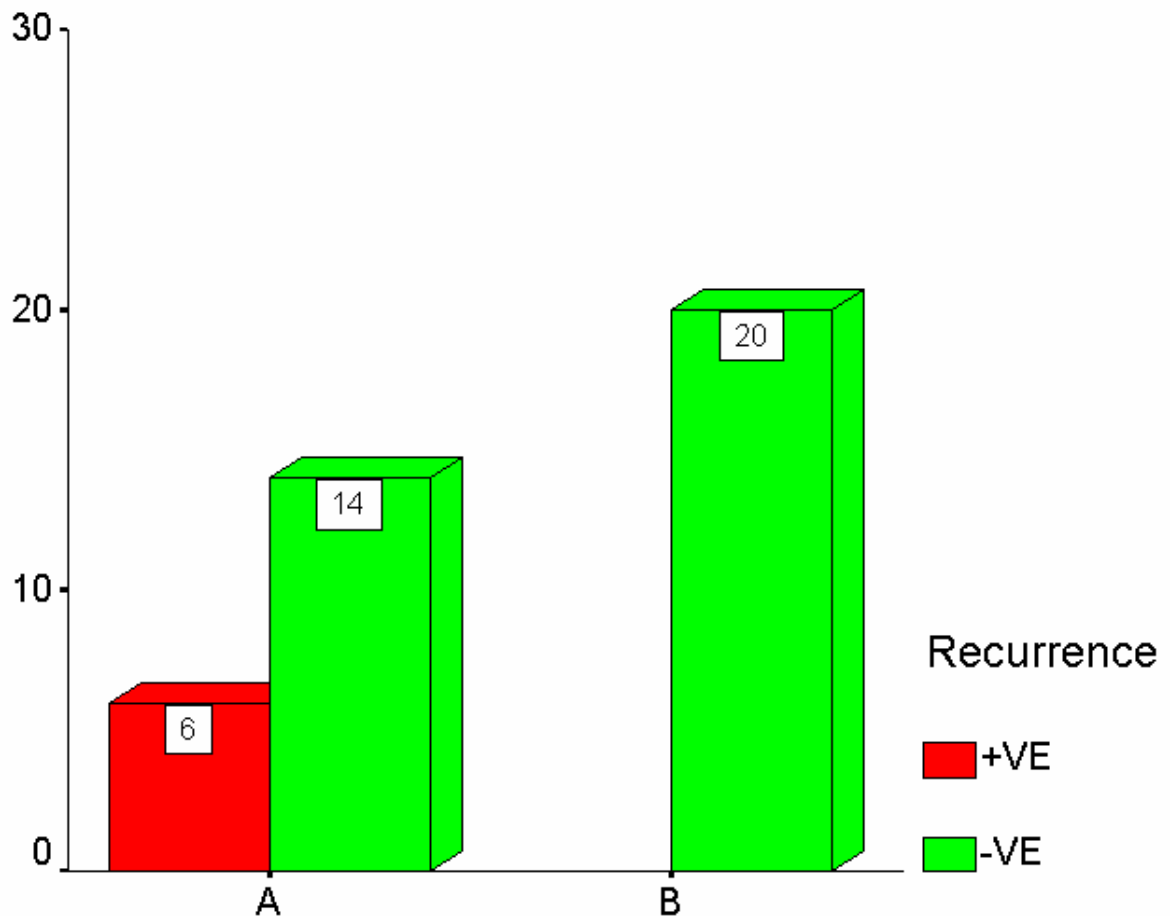
### RECURRENCE\* GROUP Crosstabulation

			GROUP	
			A	B
Recurrence	+VE	Count	6	.00
		% within GROUP	30.0%	0%
	-VE	Count	14	20
		% within GROUP	70.0%	100.0%
Total		Count	20	20
		% within GROUP	100.0%	100.0%

### Chi-Square Tests

	Value	Exact Sig. (1-sided)
Fisher's Exact Test	7.059	.010

That chi-square tests show the significant relation between total mesorectal excision versus subtotal mesorectal excision and recurrence as there is 6 cases of recurrence in group A versus no recurrence in group B. P value is 0.010.

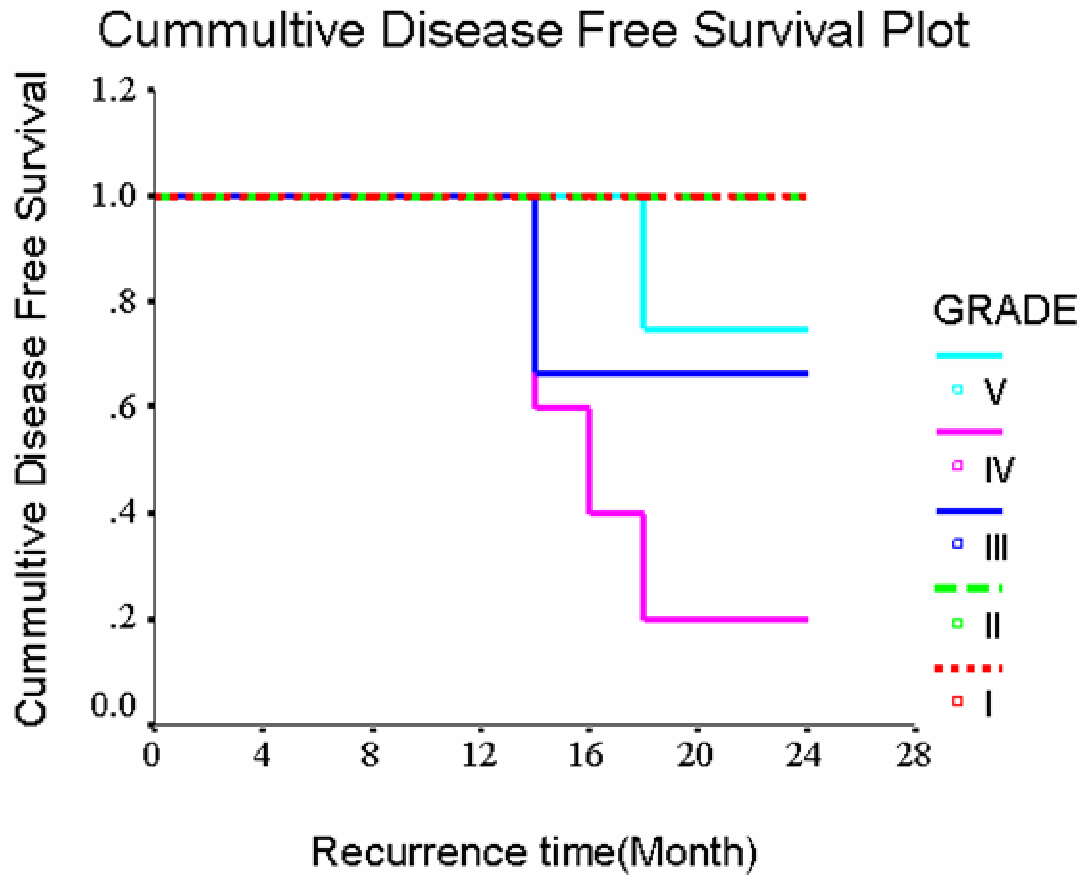


***And figure (33) describes that significant relation***

### ***Kaplan Meier's plots***

From Kaplan Meier's plots, disease free survival and various prognostic factors were studied.

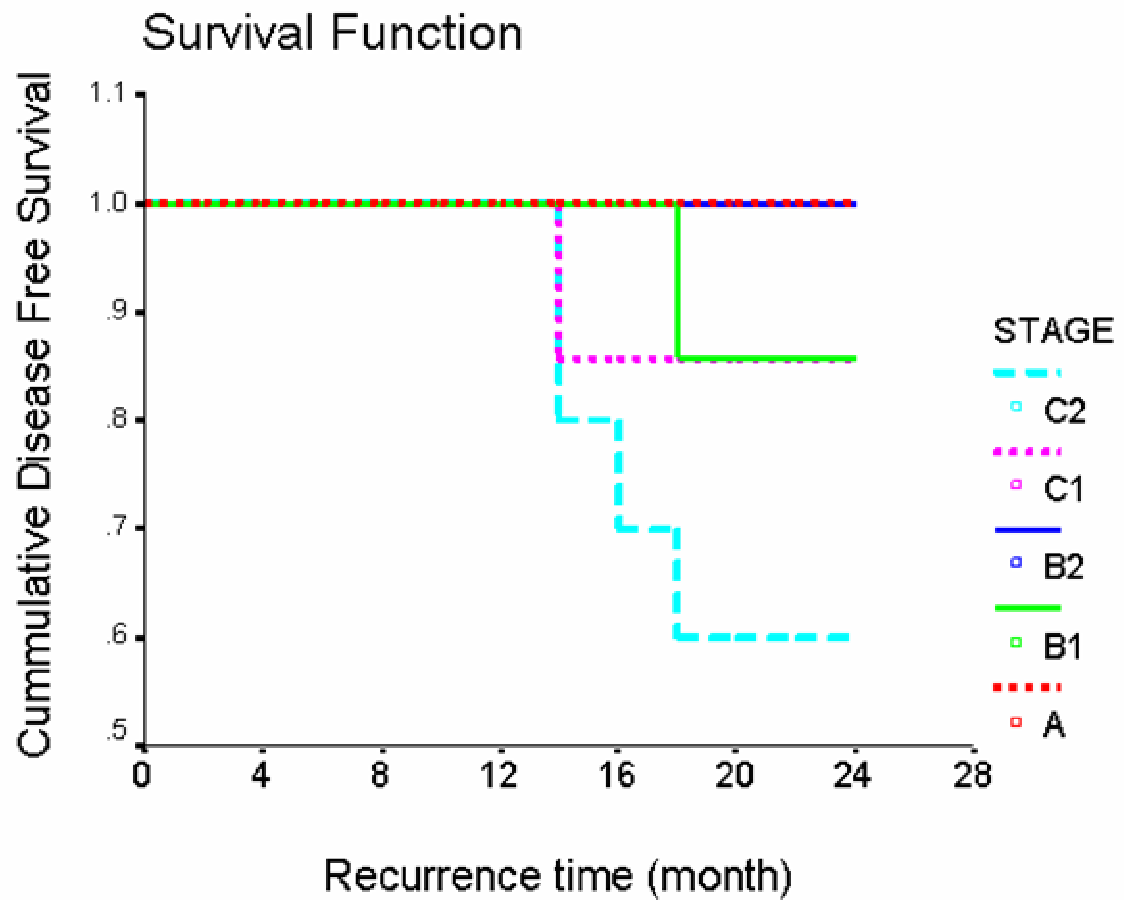
In Group A and B, low grade tumors had a significant and very high significant better disease free survival within the mean duration of one year than high grades (  $P = 0.001$  in Group A ) as in Fig.34.



***Fig.34***

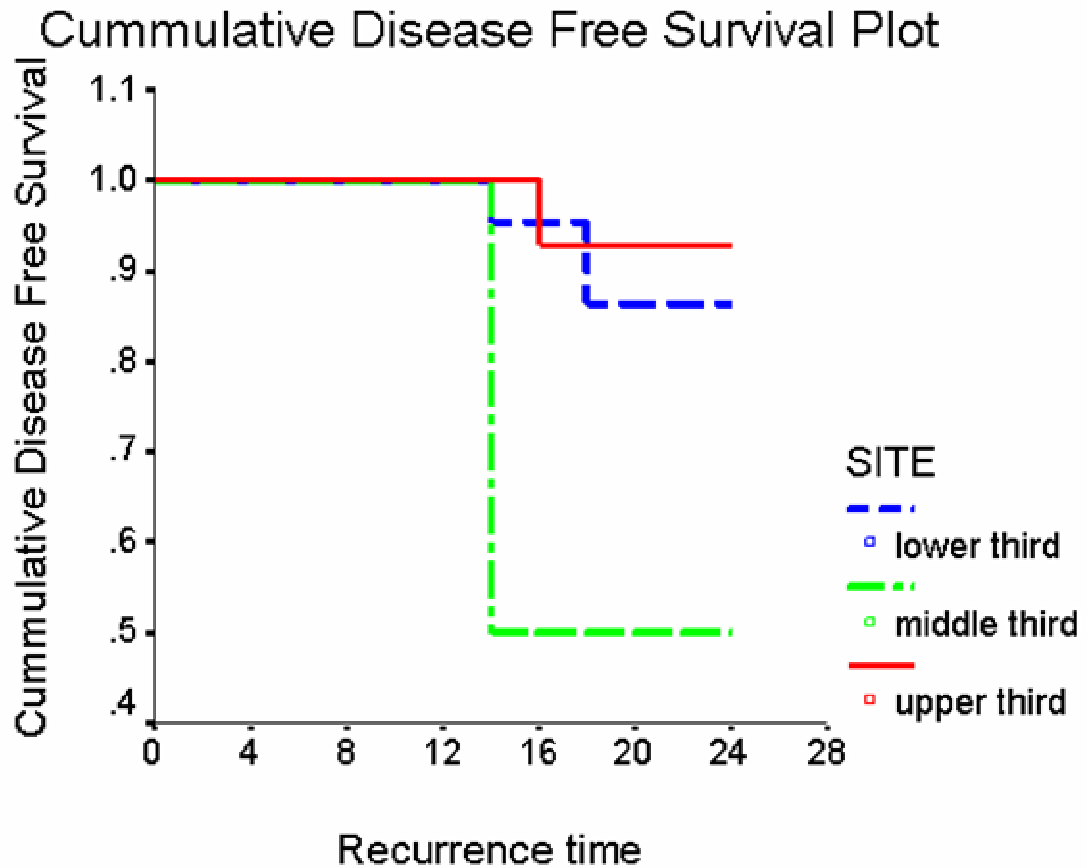
According to Duke's staging, the overall disease free survival as shown in fig.35 , Group A revealed better disease free survival with earlier stages (  $P = 0.132$  for Group A) which is insignificant.





**Fig.35**

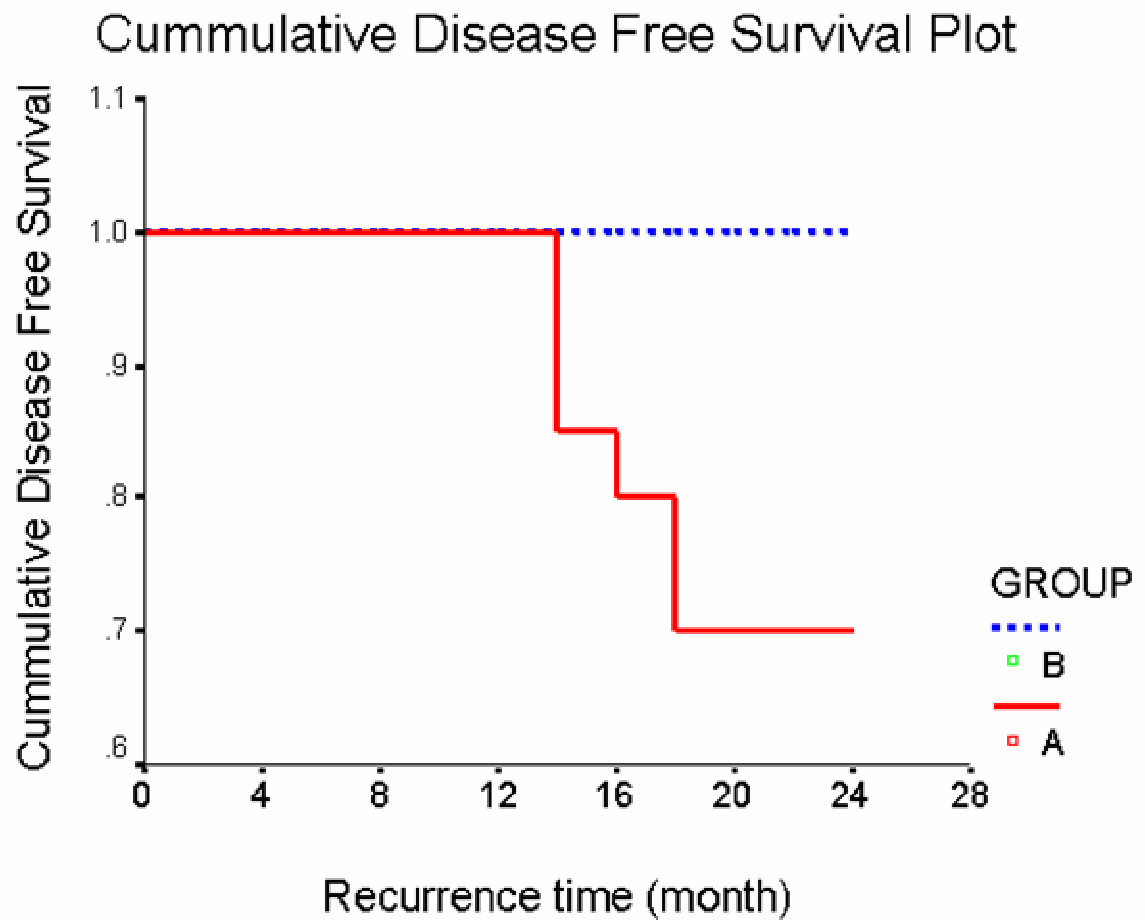
According to the relation between the site of the tumor and the disease free survival, there is significant relation between them in Group A as P value for Group A is 0.044 as in Fig.36.



**Fig.36**

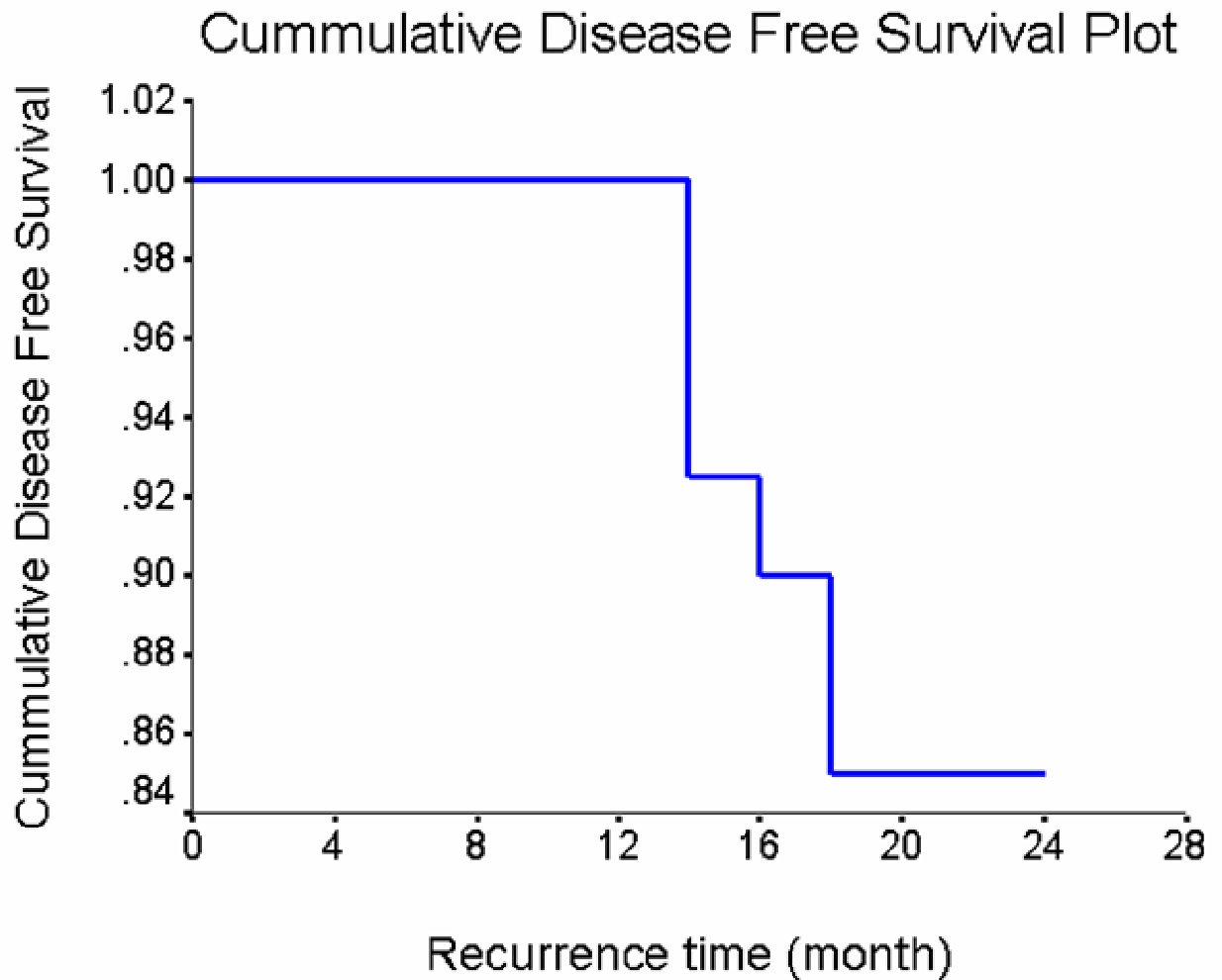
Among 20 patients subjected to subtotal mesorectal excision in Group A, 6 patients presented with recurrence ( 30 % ) while no patients presented with recurrence from 20 patients subjected to total mesorectal excision ( 0 % ).

According to the relation between both groups A and B, disease free survival plot in figure 9 showed the relation between them and recurrence.



***Fig.37***

***The cumulative disease free survival plot is shown in figure 38.***

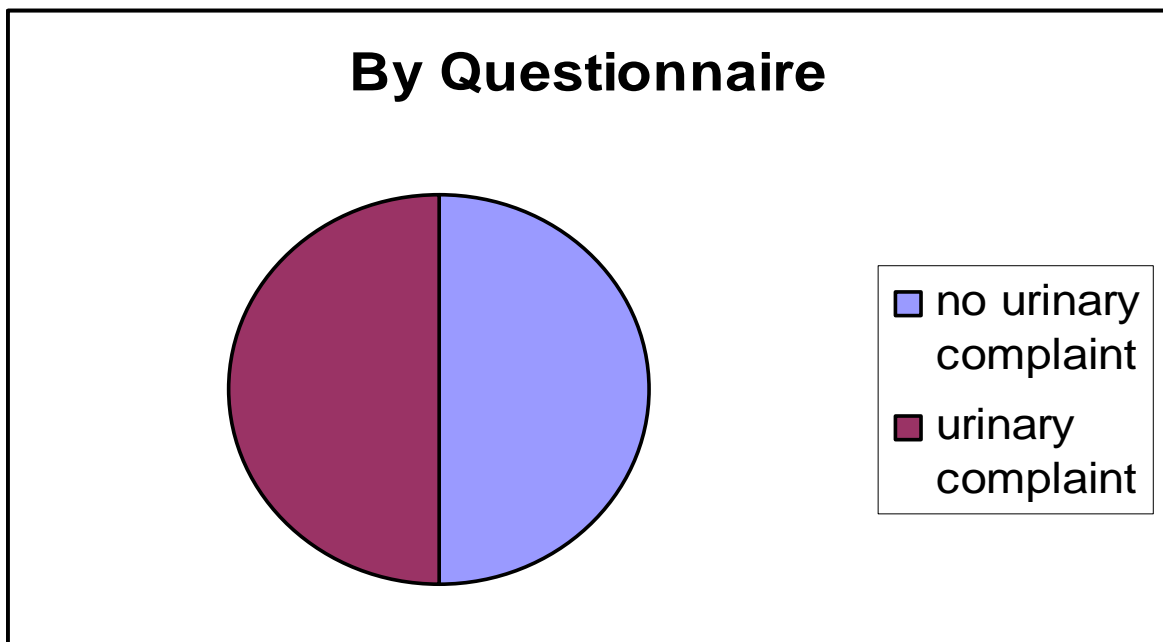


***Fig.38***

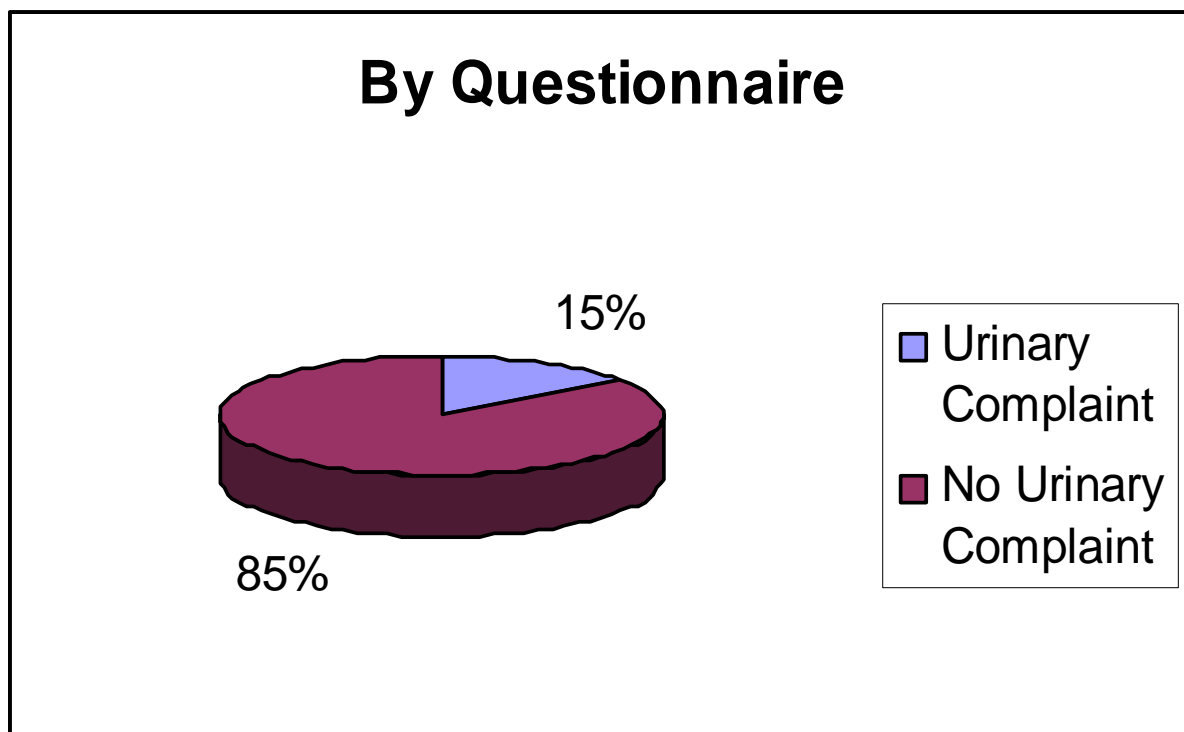
## ***5 ) Assessment of voiding function***

### ***a) Questionnaire:***

10 patients ( 50 % ) from 20 patients subjected to questionnaire after subtotal mesorectal excision with conventional method about any urinary complaint did not report any urinary complaint while the other 10 patients in the same group experienced one or more of the following early urinary symptoms; pain, burning, discomfort during urination or increased frequency. Fig.39 expresses these numbers.



17 patients ( 85 %) from 20 patients subjected to questionnaire after total mesorectal excision and pelvic nerve preservation about any urinary complaint did not report any urinary complaint. 3 patients experienced the early urinary symptoms described above. Fig.40 expresses these criteria.



***b) Flowmetry:***

***Table (14) shows the mean maximal urinary flow rate in ml/sec for patients of Group A included in that study.***

Mean max. flow rate	No. of patients	%
Less than 10	7	35
10 - 20	10	50
More than 20	3	15

***Table (15) describes the mean maximal urinary flow rate in ml/sec for patients of Group B included in that study.***

Mean max. flow rate	No. of patients	%
Less than 10	2	10
10 - 20	15	75
More than 20	3	15

***Table (16) describes the voided volume in ml for patients included in Group A.***

<b>Voided volume</b>	<b>No. of patients</b>	<b>%</b>
Less than 300	7	35
300 - 500	10	50
More than 500	3	15

***Table (17) describes the voided volume in ml for patients of Group B included in that study.***

<b>Voided volume</b>	<b>No. of patients</b>	<b>%</b>
Less than 300	2	10
300 - 500	15	75
More than 500	3	15

No patients revealed residual urine nor neurogenic bladder requiring catheterization in Group B while 4 patients revealed neurogenic bladder requiring catheterization in Group A.

## ***Flowmetry and site of tumor:***

Flowmetry showed normal maximal urinary flow rate and voided volume in 12 cases ( 38.7 % ) with cancer upper 1/3 rectum, 2 cases ( 6.5 % ) presented with cancer middle 1/3 rectum and 17 cases ( 54.8 % )with cancer lower 1/3 rectum.

It showed abnormal maximal urinary flow rate and voided volume in 2 ( 22.2 % ), 2 (22.2 % ) and 5 (55.6 % ) patients with cancer upper, middle and lower 1/3 rectum respectively.

Table (18) describes these criteria:

**Crosstab**

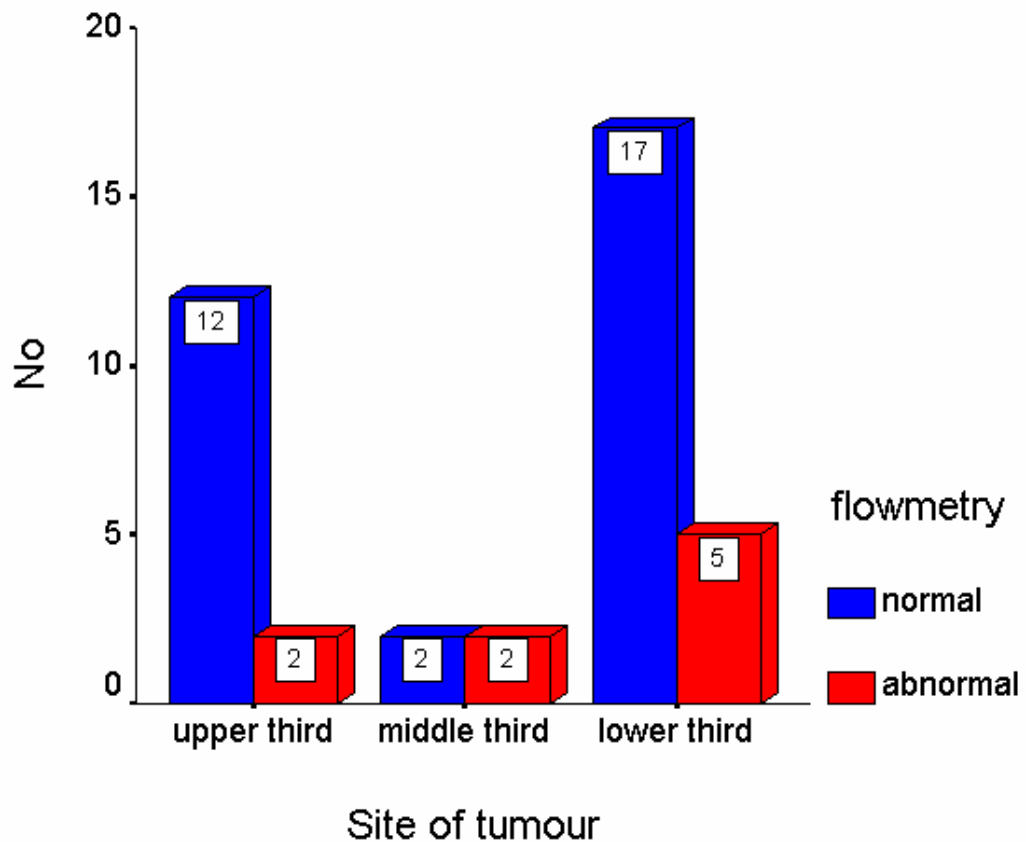
			flowmetry	
			normal urine flowmetry	abnormal urine flowmetry
SITE	upper third	Count	12	2
		% within flowmetry	38.7%	22.2%
	middle third	Count	2	2
		% within flowmetry	6.5%	22.2%
	lower third	Count	17	5
		% within flowmetry	54.8%	55.6%
Total	Count	31	9	
	% within flowmetry	100.0%	100.0%	

Chi-square tests show a significant relationship between the site of the tumor and abnormal flowmetry as there is increased abnormal flowmetry in lower tumors than upper tumors.

## **Chi-Square Tests**

	Value	Asymp. Sig. (2-sided)
Pearson Chi-Square	2.277	.320





***Fig.41 expresses the relation.***

### ***Flowmetry and type of surgery:***

Flowmetry expressed normal parameters in 14 ( 45.2 %) patients subjected to low anterior resection while it was abnormal in 2 (22.2 % ) cases subjected to the same operation.

But, it was normal in 17 ( 54.8 % ) patients subjected to abdominoperineal resection and abnormal in 7 (77.8) cases subjected to the same operation.

***Table (19) shows these criteria:***

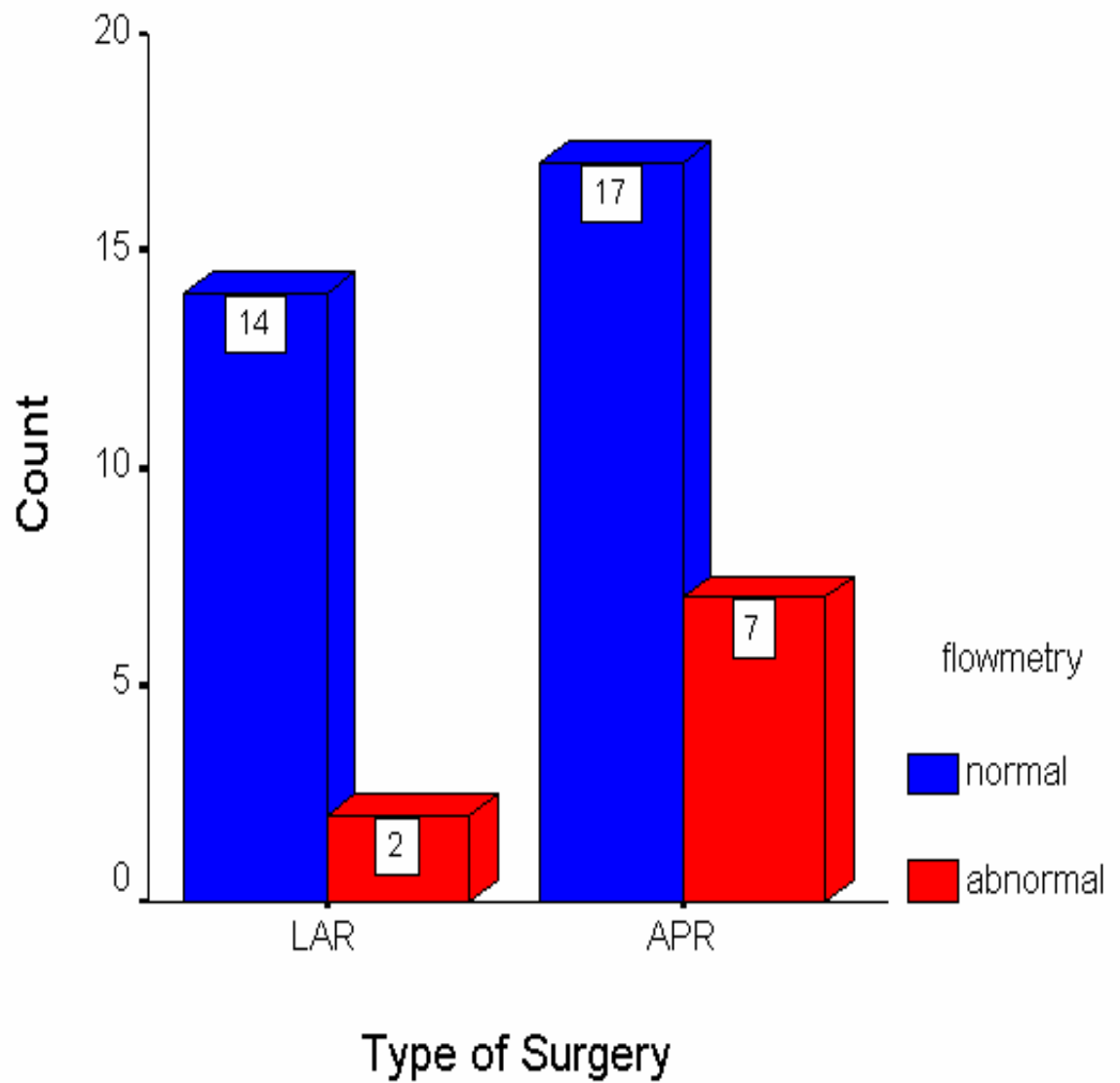
**Table.19.**

**Crosstab**

			flowmetry	
			normal urine flowmetry	abnormal urine flowmetry
SURGERY	LAR	Count	14	2
		% within flowmetry	45.2%	22.2%
	APR	Count	17	7
		% within flowmetry	54.8%	77.8%
Total		Count	31	9
		% within flowmetry	100.0%	100.0%

**Chi-Square Tests**

	Value	Exact Sig. (2-sided)
Fisher's Exact Test	1.529	.272



***Fig.42 describes this relation.***

## ***Flowmetry in both groups A and B:***

***Table (20) describes the Group-flowmetry crosstabulation in both groups A and B.***

***Table 20***

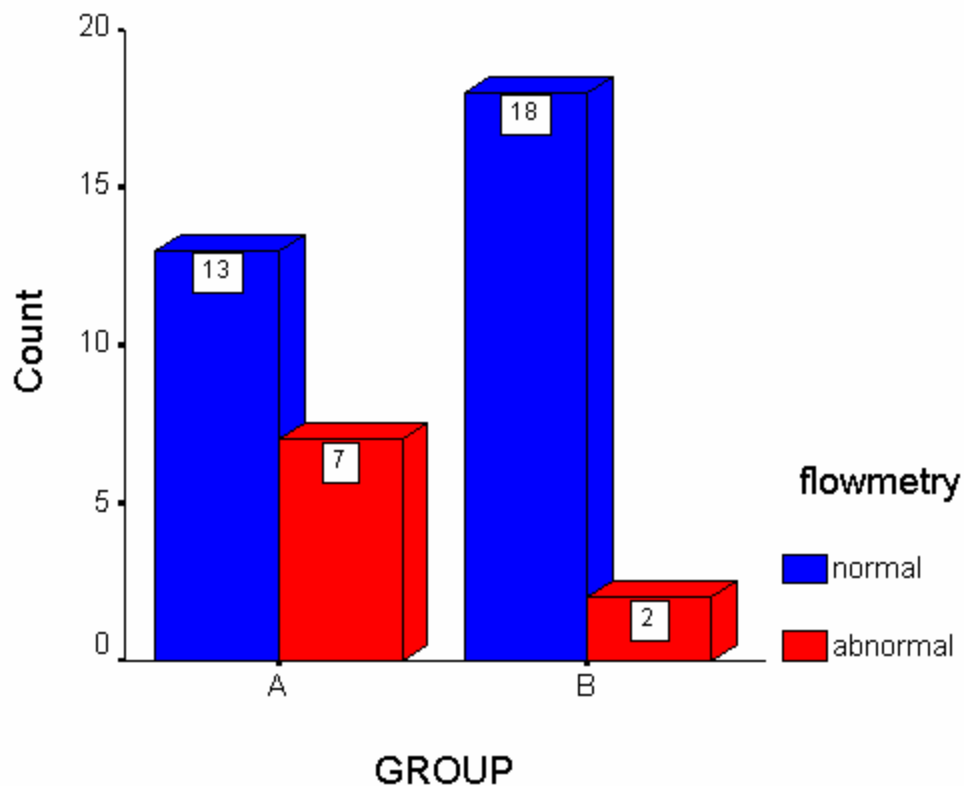
**GROUP \* flowmetry Crosstabulation**

			flowmetry		Total
			normal urine flowmetry	abnormal urine flowmetry	
GROUP	A	Count	13	7	20
		% within flowmetry	41.9%	77.8%	50.0%
	B	Count	18	2	20
		% within flowmetry	58.1%	22.2%	50.0%
Total		Count	31	9	40
		% within flowmetry	100.0%	100.0%	100.0%

## **Chi-Square Tests**

	Value	Exact Sig. (1-sided)
Fisher's Exact Test	3.584	.064

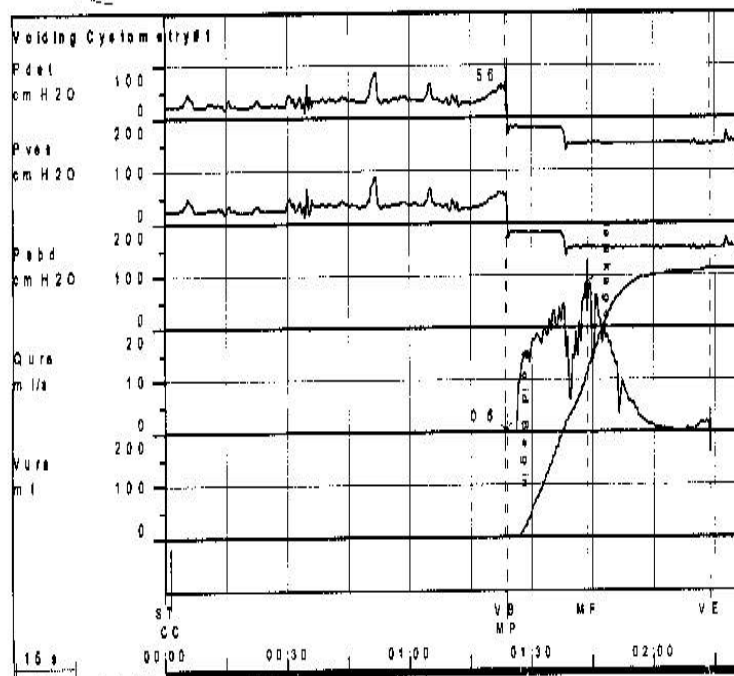
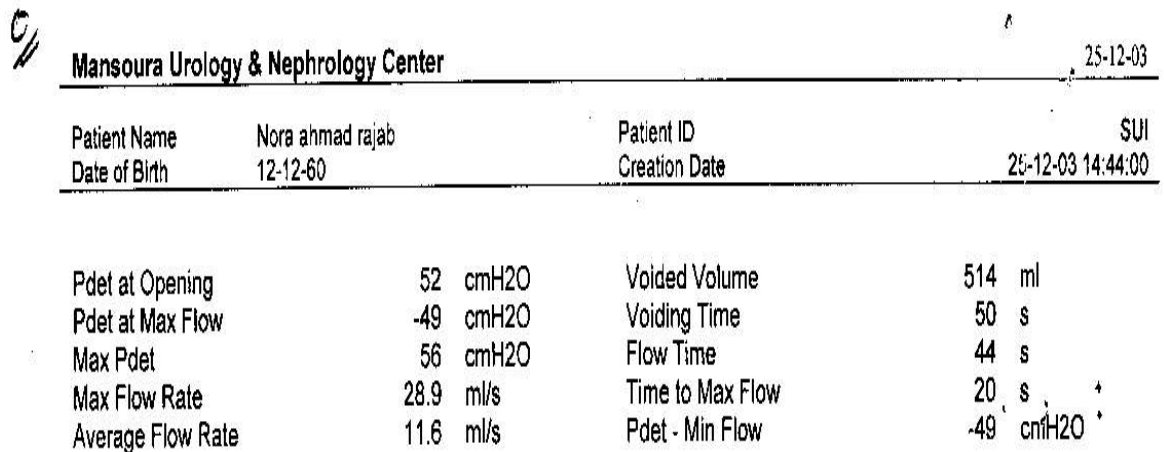
Chi square tests showed the significant relation between normal flowmetry and mesorectal excision with pelvic nerve preservation as there is only 2 (10 %) patients showed abnormal flowmetry among 20 patients subjected to total mesorectal excision with pelvic nerve preservation while there is 7 (35 %) expressed abnormal flowmetry among 20 patients subjected to subtotal mesorectal excision with conventional method.



***Fig.43 describes that significant relation***

**Fig.44:**

Flowmetry for a Female patient aged 44 years presented with cancer lower 1/3 rectum which is subjected to abdominoperineal resection with total mesorectal excision and pelvic nerve preservation.



**Fig.45:**

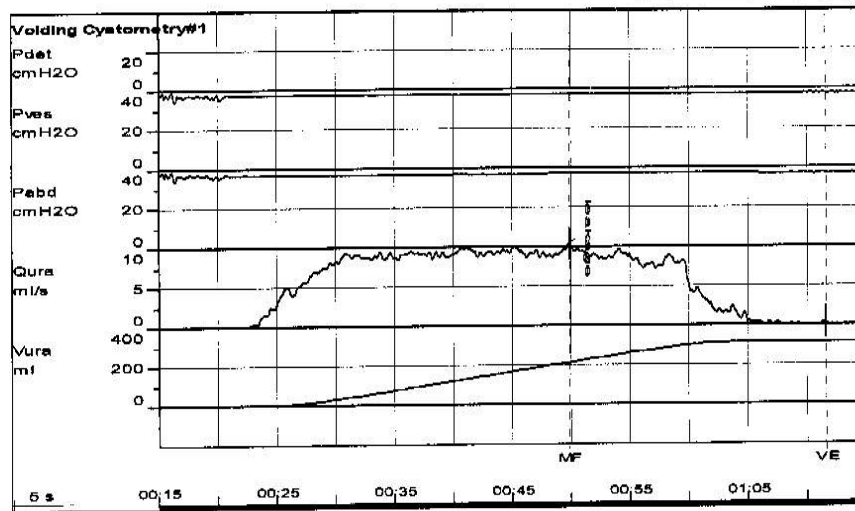
Flowmetry for another female patient aged 46 years presented with cancer lower 1/3 rectum which is subjected to abdominoperineal resection with total mesorectal excision and pelvic nerve preservation.

Patient Name dawlat abo al fotoh mohammed  
Date of Birth

Patient ID  
Creation Date

N.B  
02-01-03 11:47:16

Pdet at Opening	6 cmH2O	Voided Volume	317 ml
Pdet at Max Flow	-3 cmH2O	Voiding Time	70 s
Max Pdet	10 cmH2O	Flow Time	42 s
Max Flow Rate	10.4 ml/s	Time to Max Flow	48 s
Average Flow Rate	7.5 ml/s	Pdet - Min Flow	-2 cmH2O



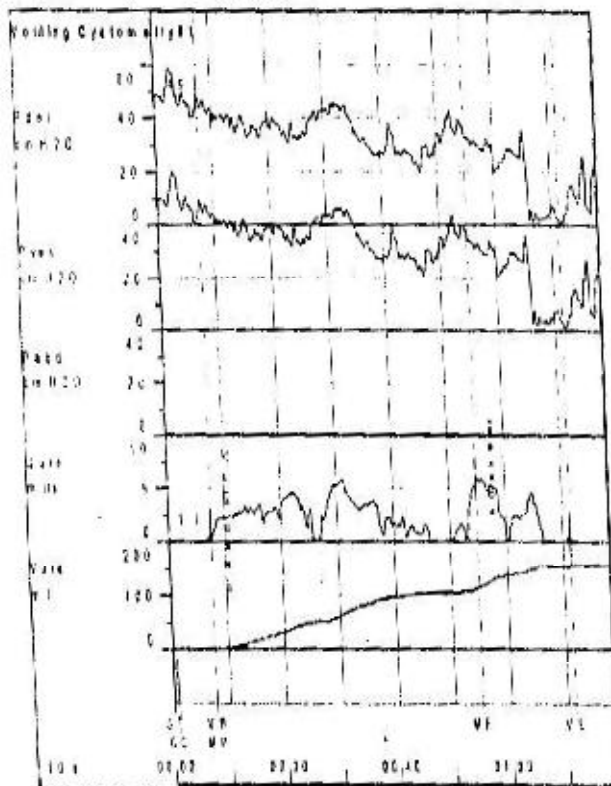
**Fig.46:**

Flowmetry for a male patient aged 26 years presented with cancer upper 1/3 rectum which is subjected to low anterior resection with subtotal mesorectal excision and conventional method.

//

Patient Name	Wael Ahmed Mohamed	Patient ID	NB
Date of Birth	30-06-79	Creation Date	27-07-04 10:10:28

Pdet at Opening	49 cmH2O	Voided Volume	157 ml
Pdet at Max Flow	36 cmH2O	Voiding Time	64 s
Max Pdet	49 cmH2O	Flow Time	53 s
Max Flow Rate	6.0 ml/s	Time to Max Flow	47 s
Average Flow Rate	3.0 ml/s	Pdet - Min Flow	29 cmH2O



## 6 ) Assessment of sexual function

### A ) Standard questionnaire

3,6,12 and 24 months after subtotal mesorectal excision with conventional method in Group A revealed that sexual activity was maintained by all 8 male patients at operation. Sexual activity was maintained by only 4 patients after operation.

Complete inability for erection and sexual intercourse was observed in 4 patients.

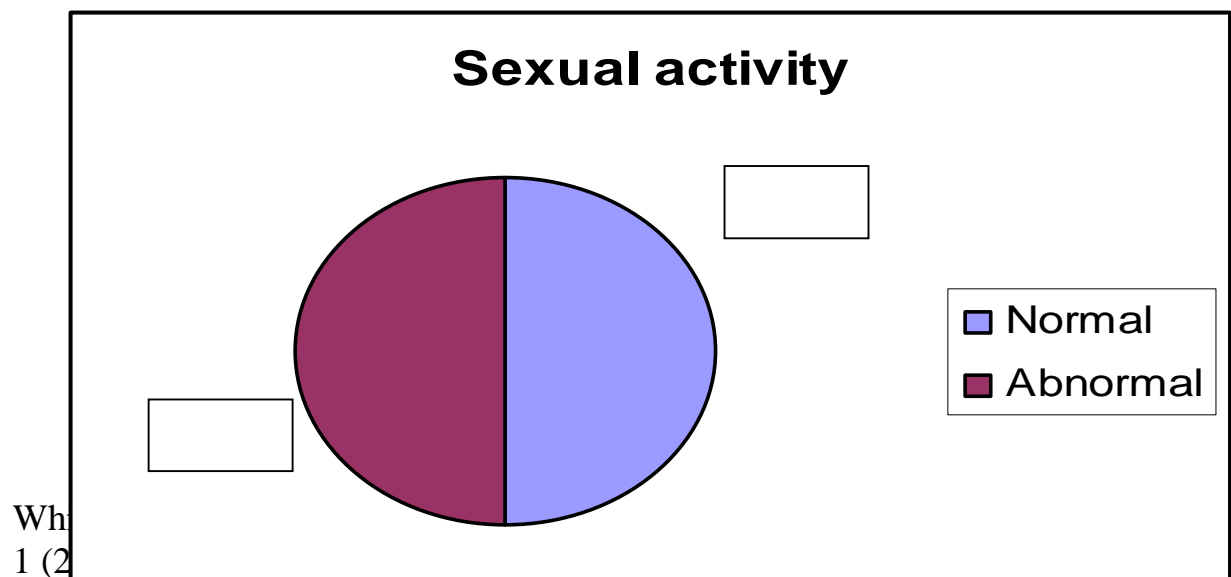


3,6,12 and 24 months after total mesorectal excision and pelvic nerve preservation in Group B, sexual activity was maintained by all five male patients at time of operation. Sexual activity was maintained by 4 patients after operation.

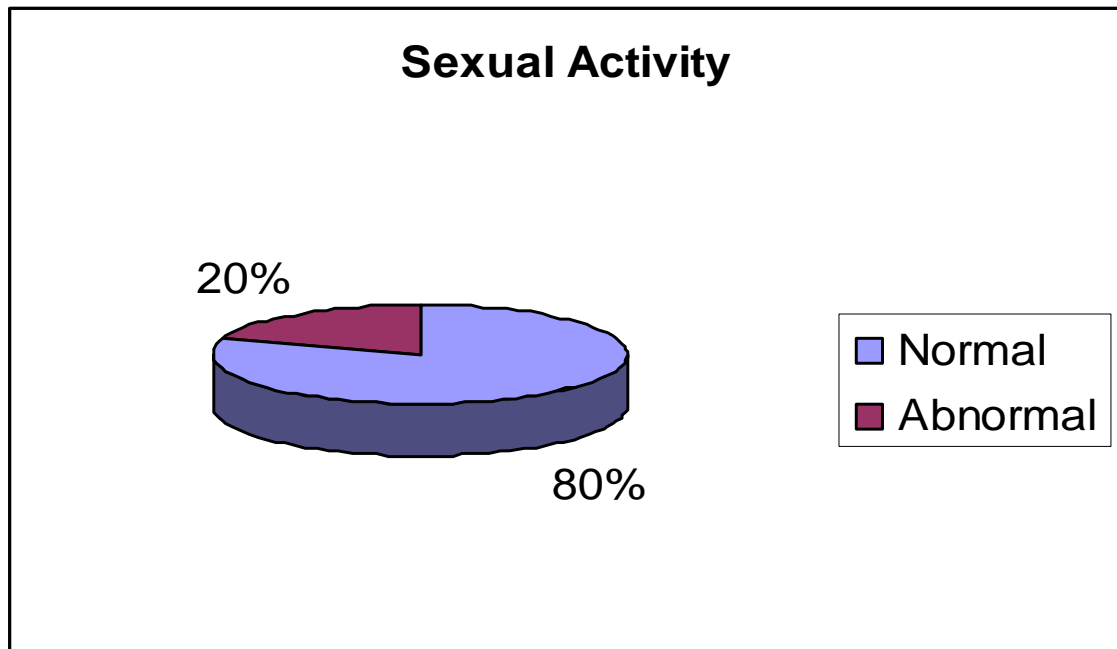
Complete inability for erection and sexual intercourse was observed in 1 patient.

### ***b)U.S color Doppler study:***

It showed normal biphasic arterial and venous flow within testicular vessels on both sides in 4 male patients (50 %) and abnormal in 4 male patients of Group A as shown in fig (47).



While U/s color Doppler was normal in 4 (80%) patients and abnormal in 1 (20%) of Group B(fig.48).



### ***Sexual activity and site of tumor:***

U/S Doppler showed normal biphasic arterial and venous flow in 3 ( 37.5 % ) cases with upper 1/3 cancer rectum, 1 ( 12.5 % ) patient with cancer middle 1/3 rectum and 4 ( 50 % ) patients with cancer lower 1/3 rectum.

While it was abnormal in 1 ( 20 % ), 1 ( 20 % ) and 3 (60 % ) in patients presented with cancer upper, middle and lower 1/3 rectum respectively.

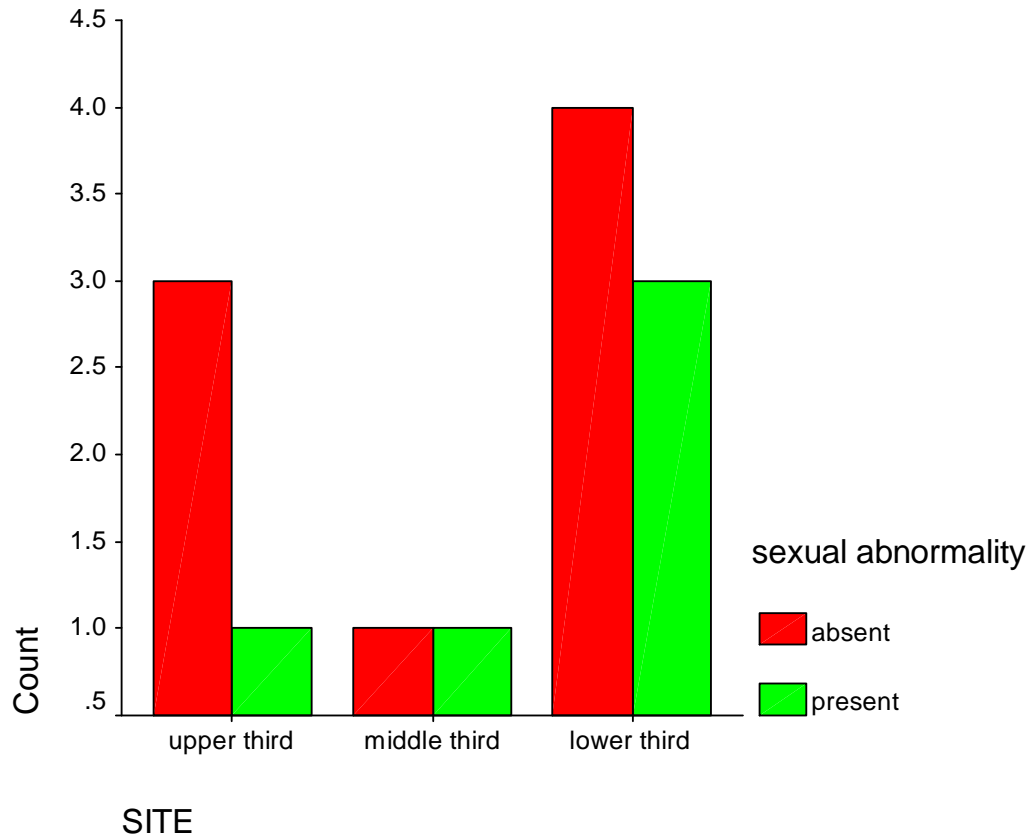
***Table (21) shows these figures:***

**Crosstab**

			sexual abnormality	
			no sexual abnormality	sexual abnormality
SITE	upper third	Count	3	1
		% within sexual abnormality	37.5%	20.0%
	middle third	Count	1	1
		% within sexual abnormality	12.5%	20.0%
	lower third	Count	4	3
		% within sexual abnormality	50.0%	60.0%
Total	Count	8	5	
	% within sexual abnormality	100.0%	100.0%	

## Chi-Square Tests

	Value	Asymp. Sig. (2-sided)
Pearson Chi-Square	.476	.788



***Fig (49) describes these figures:***

### ***Sexual activity and type of surgery:***

U/S color Doppler was normal in 5 ( 62.5 % ) patients subjected to low anterior resection and abnormal in 1 ( 20 % ) patient subjected to the same operation.

While it was normal in 3 ( 37.5 % ) patients subjected to abdominoperineal resection and abnormal in 4 ( 80 % ) patients subjected to the same operation.

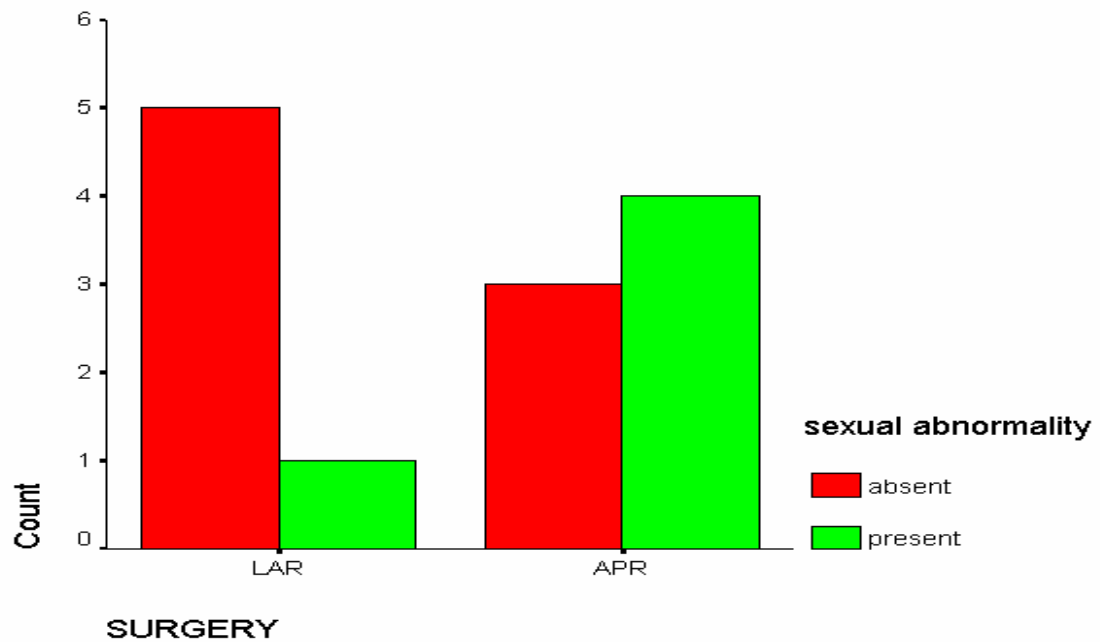
***Table (22) describes that relation***

**Crosstab**

			sexual abnormality	
			no sexual abnormality	sexual abnormality
SURGERY	LAR	Count % within sexual abnormality	5 62.5%	1 20.0%
	APR	Count % within sexual abnormality	3 37.5%	4 80.0%
Total		Count % within sexual abnormality	8 100.0%	5 100.0%

**Chi-Square Tests**

	Value	Exact Sig. (1-sided)
Fisher's Exact Test	2.236	.179



***Fig (50 ) describes these findings:***

***Sexual activity in both groups A and B:***

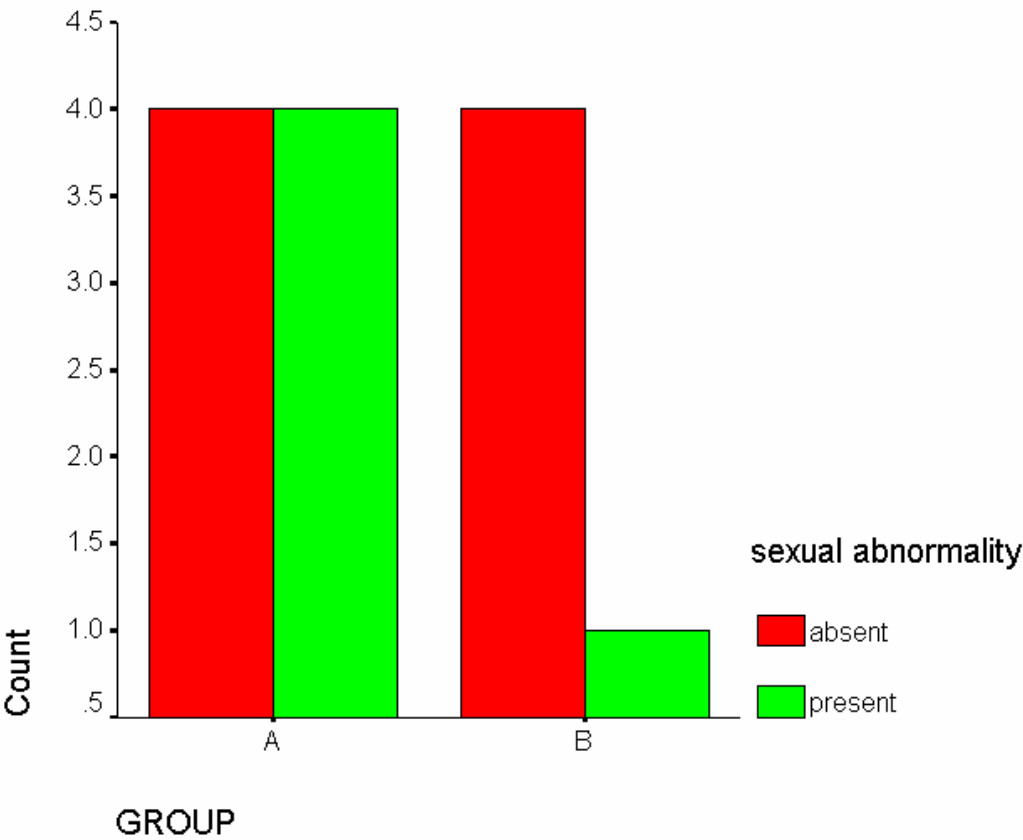
***Table (23) shows sexual activity-cross tabulation of both groups A and B.***

**Crosstab**

			sexual abnormality	
			no sexual abnormality	sexual abnormality
GROUP	A	Count	4	4
		% within sexual abnormality	50.0%	80.0%
	B	Count	4	1
		% within sexual abnormality	50.0%	20.0%
Total		Count	8	5
		% within sexual abnormality	100.0%	100.0%

Chi-Square Tests

	Value	Exact Sig. (1-sided)
Fisher's Exact Test	1.170	.315



*Fig (51) describes that relation.*

## **7) Postoperative complications**

The reported surgical complications were delayed wound healing in 3 patients and ileus in 1 patient.

***Table (24) shows the criteria of the patients presented with postoperative complications***

Case	Age	Sex	surgery	complication	Treatment
1	45	Female	LAR&TME	Wound infection	Mass closure
2	43	Female	LAR&conv.	Wound infection	Mass closure
3	65	Female	APR&TME	Wound infection	2ry closure
4	57	Female	LAR&conv	Ileus	conservative

2 cases subjected to low anterior resection, one of them for grade II adenocarcinoma stage B<sub>2</sub> cancer upper 1/3 rectum to whom total mesorectal excision was done and the other for grade IV stage C<sub>2</sub> cancer upper 1/3 rectum to whom conventional method was done presented with wound infection and burst abdomen on the 5<sup>th</sup> day after operation as there was seroma formation after closure of the abdomen.

Culture and sensitivity for a sample from the pus discharged from the wound was taken and revealed pseudomonas infection and treated with a specific antibiotic (cefobid in one case and piperacillin) in the other case. Then, on the tenth day, the 2 patients were subjected to debridement and mass closure of the wound.

while one case subjected to abdominoperineal resection for grade IV stage C<sub>1</sub> cancer lower 1/3 rectum to whom total mesorectal excision was done presented with fever 37.5 on the 3<sup>rd</sup> day postoperatively with throbbing pain in the middle of the wound with redness. Removal of three stitches was done with pus discharge from the wound which is subjected to culture and sensitivity for a sample from the discharging pus and revealed

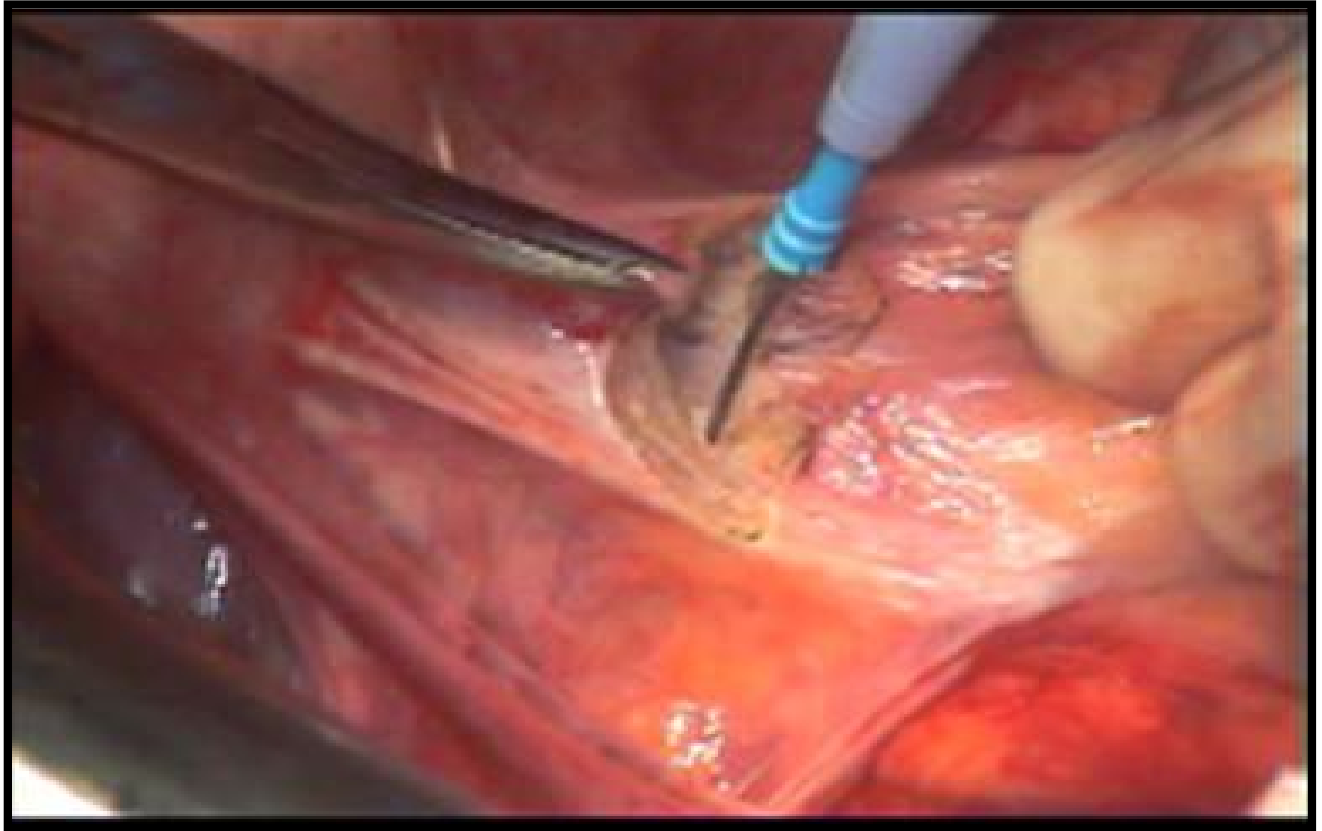


streptococcal infection treated with cephalosporins and after 10 days, the patient was subjected to 2ry closure of the wound.

One case presented with ileus and treated with conservative measures was subjected to low anterior resection for grade IV stage C<sub>2</sub> cancer upper 1/3 rectum to whom conventional procedure was done as the patient didn't pass flatus until the 7<sup>th</sup> day and subjected to plain X ray erect and supine which revealed multiple fluid levels in the erect position and distended colon in the supine position. Then, blood sample was taken from the patient for evaluation of blood Na and K which revealed hypokalaemia which is treated for 5 days with K supplementation in the form of kadlex and the patient passed flatus on the 12<sup>th</sup> day postoperative.

2 cases with total mesorectal excision presented with wound infection and one case with conventional operation was presented with wound infection and one patient with conservative measures presented with ileus.

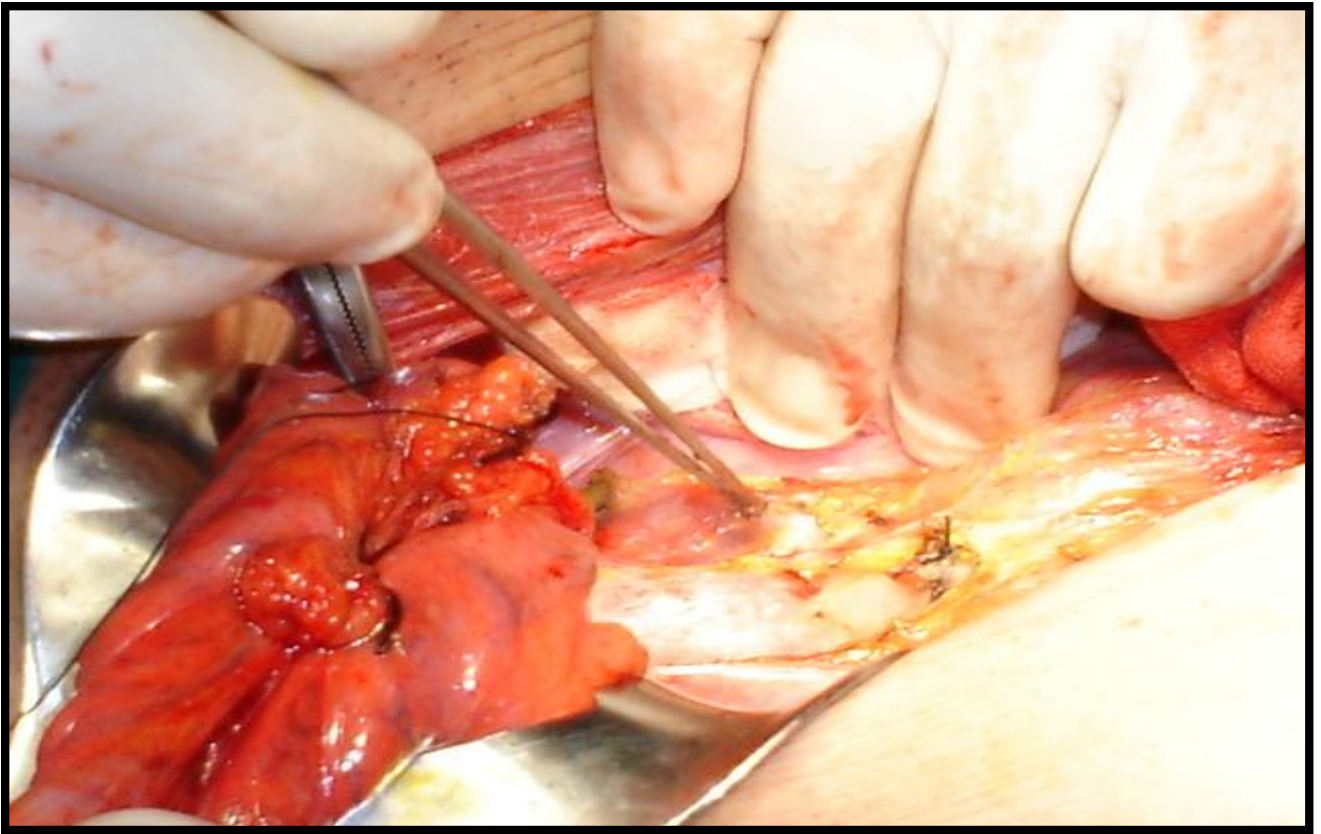
***Figure.52. Anterior dissection of the rectum.***



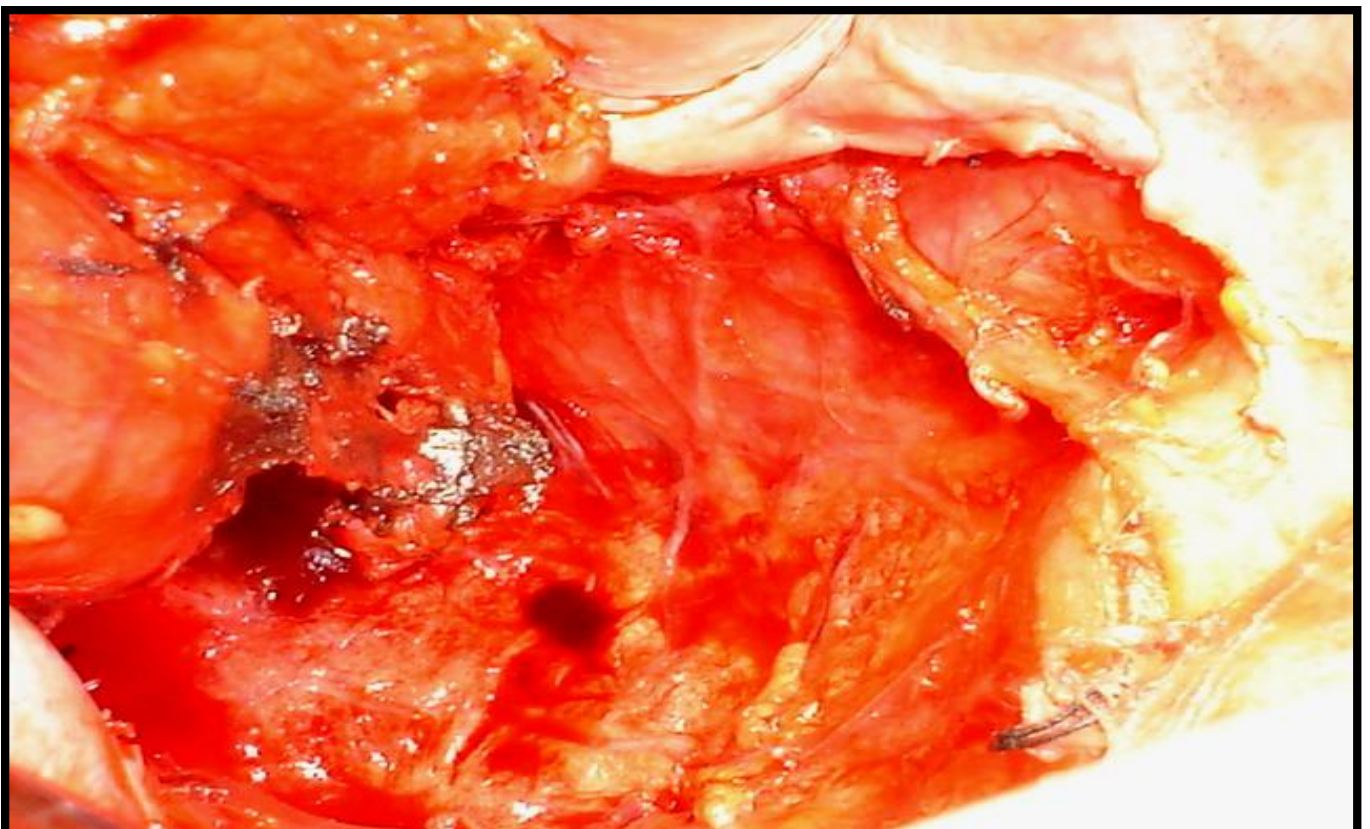
***Figure.53. Posterior mobilization of the rectum.***



***Figure.54. Posterior sharp dissection under direct vision.***

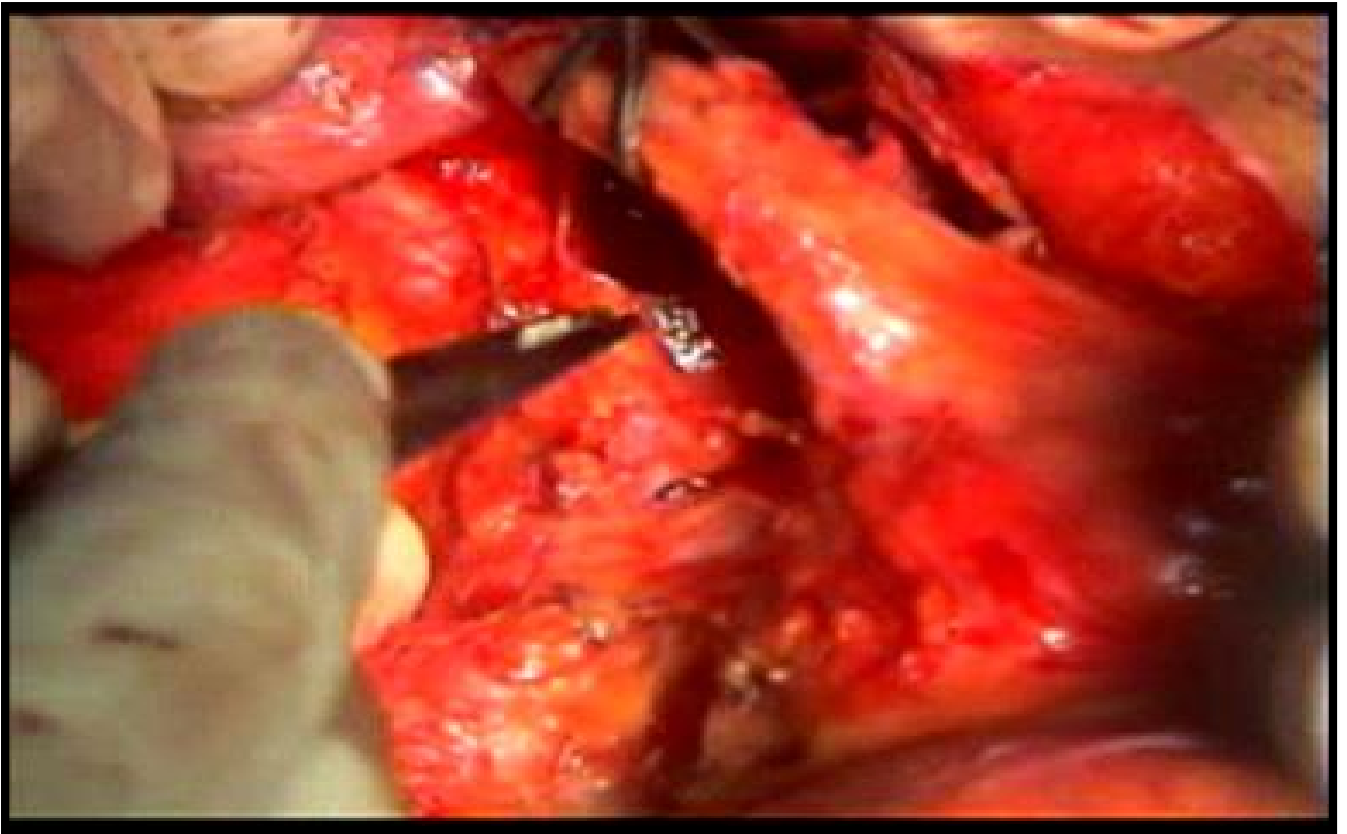


***Figure.55. Mobilization with total mesorectal excision.***

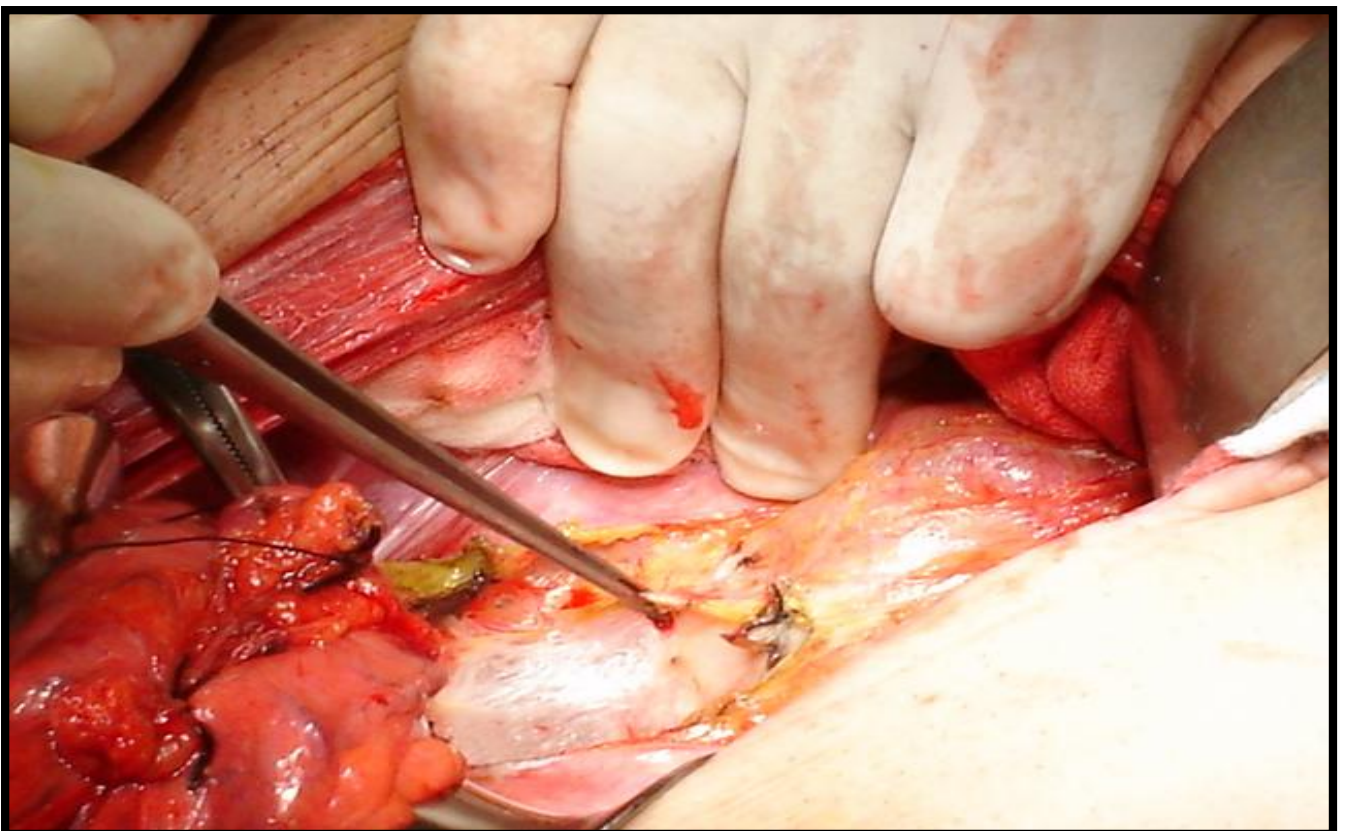




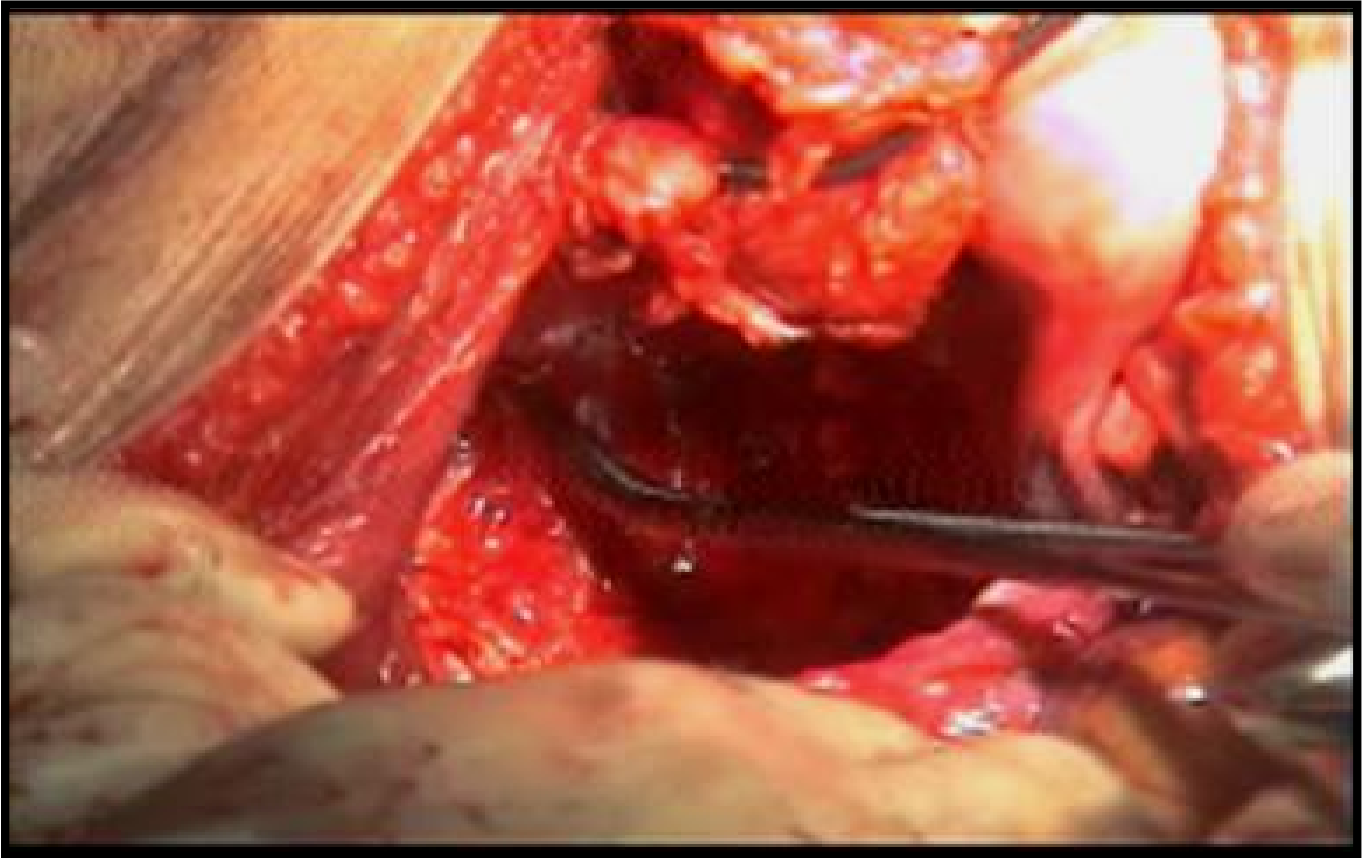
***Figure.56. Preservation of the sympathetic chain.***



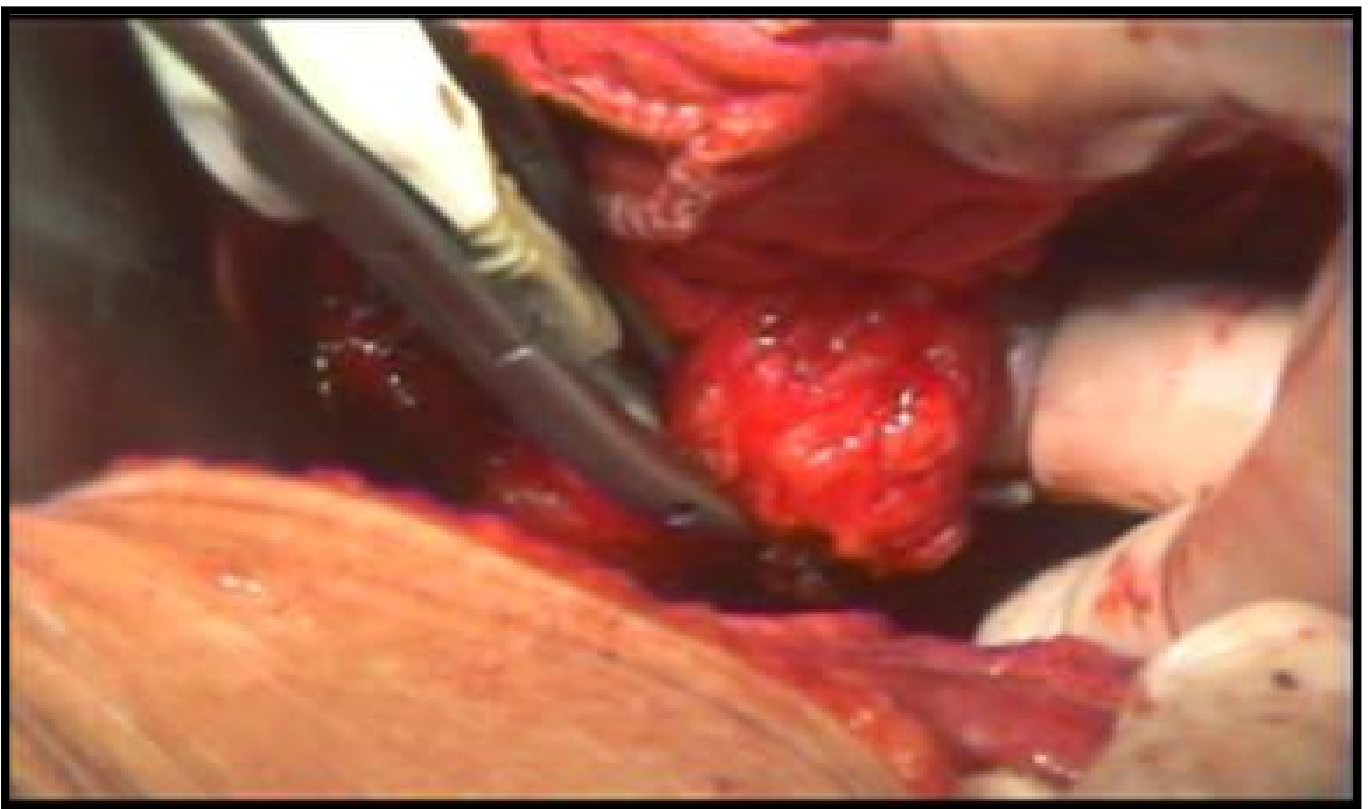
***Figure.57. Preservation of the hypogastric plexus.***



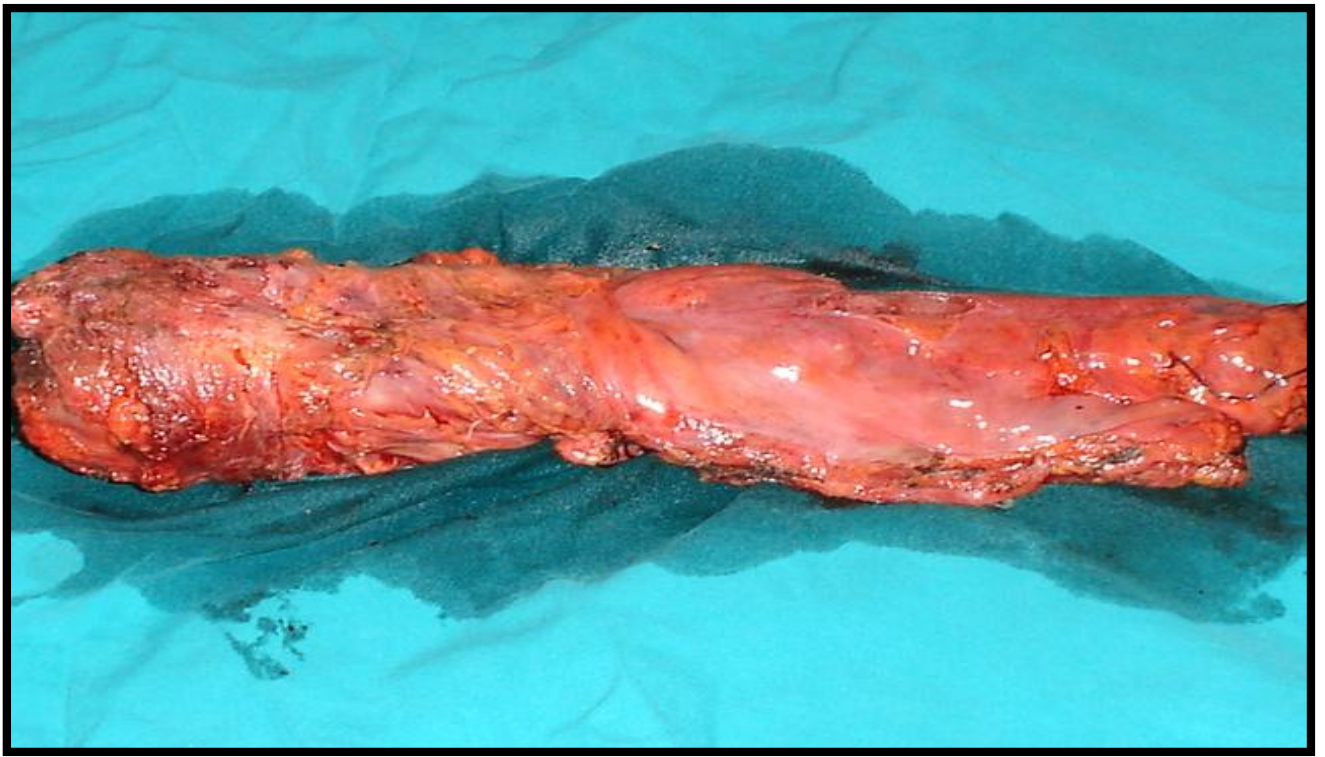
***Figure.58. Pelvic splanchnic nerves are intact.***



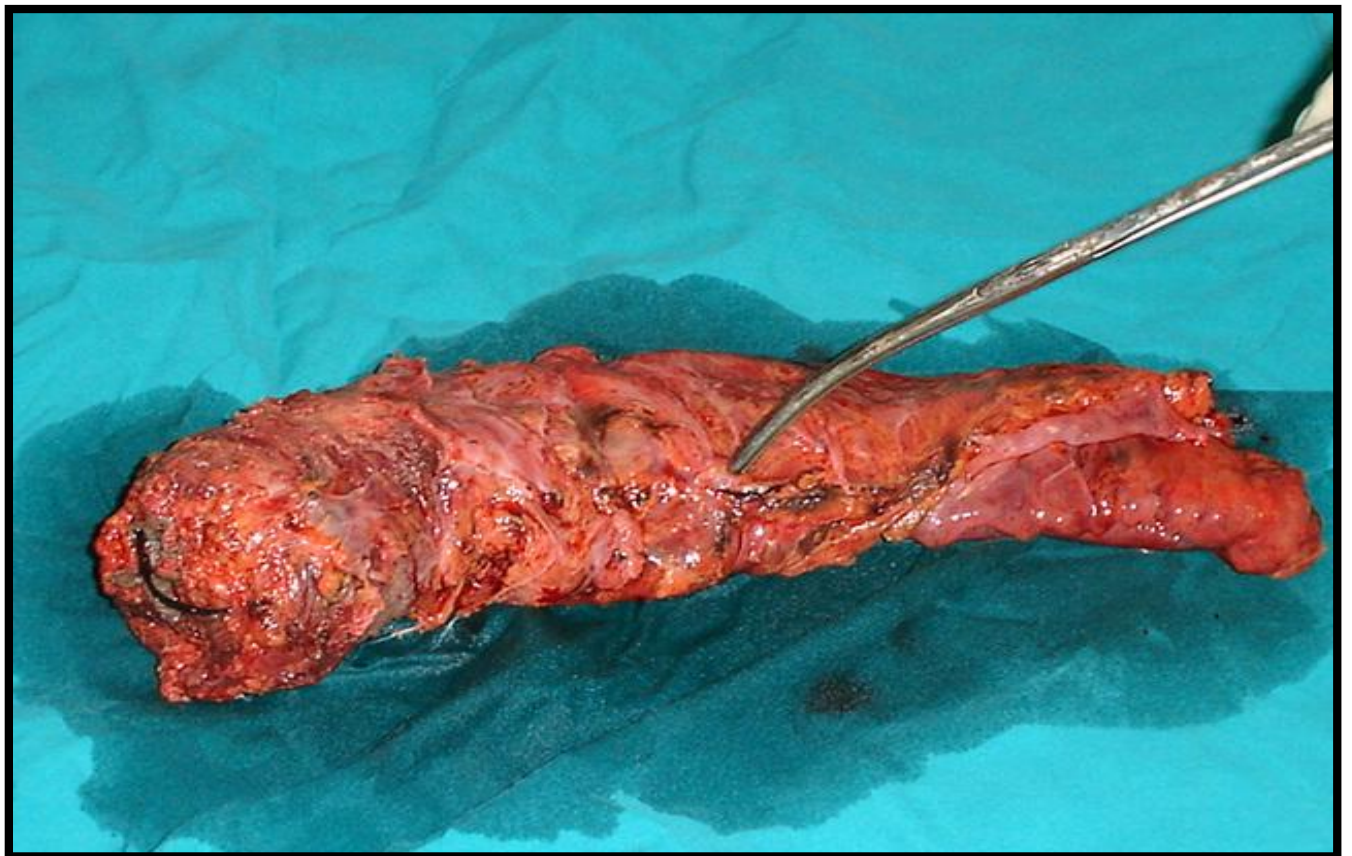
***Figure.59. ligation of lateral ligaments and middle rectal ves.***







***Figure.61. Rectal specimen showing the dorsal mesorectum***



## Discussion

For patients with rectal cancer, as with other malignancies, it is very important to preserve function without affecting oncological outcome ( Masui et al., 1996).

In recent decades, improvements have been made in the treatment of rectal cancer by the introduction of new surgical techniques and additional technicalities. However, the outcome after surgery for rectal cancer has differed markedly among patient series in both local recurrence rates and survival. A high incidence of local recurrence is associated with conventional, nonstandardized procedures ( Kapiteijin et al., 1998).

One of the common causes of local recurrence may be metastasis in the pelvis. The risk of residual positive lymph node metastasis is estimated to be from 17.5 to 36% (Sugihara et al., 1996).

In recent years, Heald described that local control and survival have been extensively improved by the introduction of TME technique ( Heald et al., 1992).

TME is accomplished by precise sharp dissection within the true pelvis around the integral mesentery under direct vision, enveloping the entire midrectum, with preservation of the hypogastric plexus. Besides better local control and survival, sharp TME dissection has been associated with a higher incidence of sphincter preservation and of pelvic autonomic and plexus preservation ( Maas et al., 1998). Study on the management of rectal cancer has progressed greatly in both clinical practice[Kapiteijin et al., 2001]. and basic research[Yang et al., 2000].

In recent years, Multiple clinical studies have demonstrated the correlation between pelvic recurrence with the degree of mesorectal excision as Shams recommended the introduction of TME as it led to a local recurrence rate of 5 % [Shams et al., 2000 ].

Residual mesorectum, especially inadequate excision of distal mesorectum (DMR), contributed to poor oncologic outcomes. Regarding DMR, histopathological evidence revealed a high metastasis rate in this region, and it was also found that patients with metastasis in tissues of mesorectum , LN, or both would experience a poor prognosis. This is why the principle of TME should be followed in the treatment of rectal cancer[Scott et al., 1995].

Since clinical application of TME, the local recurrence rate of the cancer has decreased dramatically to 5-7.1 % while that of conventional operative procedures remains 18.5 %.

Before the start of the TME trial, there were doubts whether the excellent results obtained by specialized surgeons could be repeated in a large trial (Aitken et al., 1996).

To investigate that, comparison was made between the outcome in Dutch patients of the TME trial with results from a randomized trial of the Cancer Recurrence And Blood Transfusion ( CRAB ) trial in which conventional, nonstandardized surgery was performed.(Houbiers et al., 1994).

This analysis showed that introduction of TME had led to a substantially lower local recurrence rate when only events within two years were analyzed : 16.3 % in the CRAB trial versus 8.6 % in the TME trial (Kapiteijin et al., 2002).

The reported results for the study focused on a preselected patient population with age ranging from 20 – 69 years. Below 40 years of age, the incidence of colorectal cancer is higher than expected and this is perhaps attributed to the inclusion of young patients with familial polyposis and bowel cancer syndrome who have developed malignancy. Similarly, we reported 13 cases under age of forty and this is similar to the reported cases in Egypt ( Khafagy et al., 2000).

Presented patients with symptoms investigated to be rectal cancer and staged by preoperative CT and endorectal ultrasound. Therefore, in this study, we considered two groups according to the operative interference: one group (Group A ) was subjected to subtotal mesorectal excision and the other ( Group B ) to TME. This group that can determine the value of TME.

The analysis showed that the introduction of TME had led to a local recurrence rate of 0 % which is comparable to Heald et al., 1986. and to those values previously reported. His series reported 2.7 % local recurrence rate while the local recurrence rate in the other group ( A ) was 30 % which is more than figures reported by Nymann et al., 1995. His series reported 21.1 % local recurrence rate. It is close to the reported result of Norstein et al., 1993. His series reported 29.5 % local recurrence rate.

Reported cases of recurrence in group B were managed according to each case. The case presented with anastomosis recurrence was reoperated and abdominoperineal resection was done with permanent colostomy. While other patients werw subjected to chemotherapy in the form of 5 flourouracil and radiotherapy.



Zedane and associates performed a study included 104 patients with middle and low rectal carcinoma who underwent potentially curative surgery . They observed the 55 median follow up local recurrence rate of 5.8% with no local recurrence in Dukes A nor Dukes B (Zedane et al.,1999).

Kapiteijin et al., 2002 performed a comparison between his study on 668 patients to whom curative conventional surgery was performed ( 36 % received postoperative radiotherapy ) and 661 patients to whom total mesorectal excision was performed. They reported 150 cases with local recurrence ( 22.5 % ) in patients subjected to conventional surgery and 57 cases with local recurrence ( 8.6 % ) in patients subjected to total mesorectal excision.

Hospital volume and specialization in the CRAP and TME trials were investigated. In the CRAP trial, higher hospital volume was associated with lower distant recurrence (  $p = 0.006$  ) and higher overall survival (  $p = 0.011$  ). This association between higher hospital volume and lower local recurrence risk was of borderline significance (  $p = 0.07$  ). In the TME trial, hospital volume and specialization did not have an effect on any long term outcome. There was no effect on presence of instructor surgeon ( 37 % of the operations were attended by these surgeons ) on outcomes either, indicating that non instructor surgeons were instructed well and had become familiar with the concept of TME surgery to reach outcomes equal to those achieved by instructor surgeons (Kapiteijin et al., 2002).

The criticism focused on patient case mix and analytical techniques (Isbister et al., 1990), unclarified selection process (Nelson et al., 1993), and incorrect use of definitions (Marsh et al., 1995).

The reported postoperative complications in our study were 3 cases presented with delayed wound healing and that was as a result of wound infection as there was seroma formation after closure of the abdomen. 2 cases of them had burst abdomen 5 days after operation. Culture and sensitivity for a sample from the pus discharged from the wound was taken and revealed pseudomonas infection and treated with a specific antibiotic ( cefobid in one case and piperacillin in the other case. Then , on the tenth day, the 2 patients were subjected to debridement and mass closure of the wound while the third case presented with fever (38.5) from the third day of operation and throbbing pain in the middle of the wound with redness. Removal of three stitches was done with pus discharge from the wound and subjected to culture and sensitivity for a sample from the discharging pus and revealed streptococcal infection treated with cephalosporins and after 10 days, the patient was subjected to 2ry closure of the wound.

One case presented with ileus as the patient didn't pass flatus until the 7<sup>th</sup> day and subjected to plain X ray erect and supine which revealed multiple fluid levels in the erect position and distended colon in the supine position. Then, blood sample was taken from the patient for evaluation of blood Na and K which revealed hypokalaemia which is treated for 5 days with K supplementation in the form of kadlex and the patient passed flatus on the 12<sup>th</sup> day postoperative.

Havenga et al.,1996 reported 3 cases of postoperative ileus on the 8<sup>th</sup> day postoperative and the patients were subjected to plain X ray erect and supine which revealed multiple fluid levels in the erect position and distended colon in the supine position and blood sample was taken from the patient for evaluation of blood Na and K which revealed hypokalaemia which is treated for 5 days with K supplementation in the form of kadlex and the patient passed flatus on the 13<sup>th</sup> day postoperative.

There was a reported case presented with anastmotic recurrence as the patient was subjected to low anterior resection for grade IV stage C<sub>2</sub> cancer upper 1/3 rectum and the patient complaint of gradual difficulty of defaecation starting from the 5<sup>th</sup> month of operation with inability to pass motion on the 11<sup>th</sup> month of operation, then the patient was subjected to virtual colonoscopy which revealed anastmotic recurrence which is treated with permanent colostomy with radiochemotherapy. There was no reported cases of deep seated pelvic pain. Postoperative pain detected in the patients of our study treated with analgesics ranging from non steroidal anti-inflammatory drugs to pethidine according to the severity of the pain.

Heald et al., 1986 reported high leak rates with TME surgery as compared with conventional procedures. The increased leak rates can be explained by the removal of the pain sensitive peritoneum or devascularisation of the anorectal stump during dissection of the distal mesorectum.

Maas et al., 1998 performed a prospective study on morbidity and functional outcome for radical and nerve preserving surgery for rectal cancer in the Netherlands revealing no reported complications including blood transfusion.

## Pelvic nerve preservation

Both sexual and urinary functions are complex, and patients undergoing surgery for rectal cancer may have differing baseline levels of function. Preexisting benign prostatic hypertrophy or stress incontinence are common physical conditions. Patients bring personal or cultural attitudes

to the subject of sexual function with advancing years, in a population with a median age in the mid sixties. Other health issues such as coronary artery or peripheral artery atherosclerotic disease, diabetes mellitus, smoking or alcohol intake, or the use of medications to treat these conditions, may influence sexual function ( Havenga et al., 2002).

Ishikura and associates between 1993 and 1997 evaluated urinary and sexual function using questionnaires. However, the fact that non of the patients had retention necessitating indwelling catheter was of good significance.

They observed the 3-year local recurrence rates of 0% and 27% for patients with stage II and III tumors, respectively. It means that their methods were fruitful for patients with stage II tumors, but unsatisfactory for stage III tumors. In their present study, four of six patients with local recurrence were found to have perineural invasion histologically and one was not assessed. Those findings suggest that preserving the pelvic nerve plexus does not influence the local control rate even for patients with stage III tumors. However, to improve local control, other methods of radiation delivery, such as PORT with chemotherapy, should be considered for patients with stage III tumors ( Ishikura et al., 1999 ).

Deliberate tracking and preservation of the autonomic nerves in conjunction with TME was introduced by Enker in 1991 (Enker et al., 1995).

Surgical training programs have spread the use of TME-ANP throughout Europe (Martling et al., 2000). Recently, efforts have been undertaken by the American College of Surgeons to set up a teaching program for TME in the United States (A.M. Cohen, personal communication, 2001).

In our study, in 20 patients with rectal cancer subjected to total mesorectal excision and pelvic nerve preservation, We reported 85 % of patients did not report any urinary complaint. The other patients ( 15 % ) experienced one or more of the early urinary symptoms such as pain, burning or discomfort during urination; or increased frequency. Postoperative urodynamics revealed normal mean maximal urinary flow rate and voided volume in 90 % of patients. 10 % of patients revealed mean maximal urinary flow rate less than 10 ml / sec and voided volume less than 300 ml. No patients revealed chronic retention requiring catheterization nor patients had significant residual urine.

Zedane and associates reported that patients with type III pelvic autonomic nerve preservation, 80.3 % maintained the ability to void spontaneously (Zedane et al.,1999).

While postoperative standard questionnaire and invasive urodynamics in 20 patients subjected to subtotal mesorectal excision with the conventional method reported 50 % of patients experienced early urinary symptoms and the other patients ( 50 % ) did not report any urinary complaint and normal mean maximal urinary flow rate and voided volume was reported in 65 % of patients. 35 % of patients revealed mean maximal urinary flow rate less than 10 ml/sec and voided volume less than 300 ml. 4 patients revealed chronic retention requiring catheterization.

Cross-tabulation between the two groups and chi square was approximately significant as P value is 0.064.

Havenga et al., 1996 reported on functional results in a group of 136 patients who underwent TME-ANP. Patients were asked to fill out standard questionnaire regarding preoperative and postoperative sexual and urinary function. 73 % of patients did not report any urinary complaint. The remaining patients experienced one or more of the following early symptoms: pain, burning or discomfort during urination, or increased frequency. No patient became incontinent or went on retention and requiring catheterization was not encountered.

Kim et al., 2002, performed urine flowmetry and a standard questionnaire before and after surgery in 68 males with rectal cancer. They reported significant differences in mean maximal urinary flow rate and voided volume were seen before and after surgery ( $18.9 \pm 5.7$  vs.  $13.7 \pm 7.0$ ,  $240 \pm 91.9$  vs.  $143 \pm 78$ ;  $< 0.05$ ,  $< 0.05$ , respectively) and the difference was statistically significant but no differences in residual volume before and after surgery were apparent ( $4.4 \pm 2.6$  vs.  $8.1 \pm 4.4$ ;  $> 0.05$ ).

Urinary complaints seemed more prevalent after abdominoperineal resection (Havenga et al., 2002).

Among 5 male patients with cancer rectum subjected to total mesorectal excision, by using a standard questionnaire, one patient only ( 20 % ) showed complete inability for erection and intercourse. Erection and penetration ability was possible in 4 patients ( 80 % ). Doppler US was performed in five male patients which revealed normal biphasic arterial and venous pulsations on both sides in 4 patients ( 80 % ) and abnormal in only one patient ( 20 % ).

While among 8 male patients in Group A with subtotal mesorectal excision with the conventional method, 4 patients (50 %) showed erection and penetration ability problems and the Doppler US ensured abnormality in those patients.

Abdominoperineal resection is associated with a high prevalence of sexual dysfunction. This may be related to inadvertent autonomic nerve damage

during the perineal resection or to altered pelvic floor anatomy after the operation.

Zedane and associates reported that with patients of type I pelvic autonomic nerve preservation, 65.5% maintained male sexual function and of patients with type II, 66.7 % were capable of erection and intercourse without normal ejaculation (Zedan et al., 1999).

Havenga et al., 1996 reported that male sexual function was related to age. The ability of erection was maintained by 86 % of patients younger than 60 years and 67 % of patients older than 60 years. Retrograde ejaculation was encountered in 20 % of patients.

Kim and associates reported that in their study erection was possible in 55 patients (80.9 percent), penetration ability was possible in 51 patients (75 percent). Complete inability for erection and intercourse was observed in three patients (5.5 percent). Retrograde ejaculation was noted in 9 patients (13.2 percent). The authors concluded that age older than 60 was a significant factor adversely affecting sexual function (Kim et al., 2002).

Kaname et al., 2005 performed a study to assess the long term voiding function and sexual function after pelvic nerve sparing radical surgery for rectal cancer. They reported that 52 patients subjected to an administered questionnaire and each patient was asked to record if there had been any changes in lower urinary tract symptoms after surgery. Sexual function was also investigated in men, 48 patients (92%) maintained voluntary voiding without catheterization in the long term. Clean intermittent self-catheterization was performed in only four patients with incomplete preservation because of persistent voiding dysfunction. Subjectively, approximately 60% of the patients remained unchanged in lower urinary tract symptoms after surgery. Despite the acceptable urinary status, 88% of men had some deterioration in the erectile function, regardless of type of surgical procedures. Overall, 64% of men were unsatisfied with the current sexual function.

Nesbakken et al., 2000 reported a reduced erectile function in 6 of 24 patients after total mesorectal excision . one patient became completely suffering from impotence.

Dr. Moriya of Tokyo conducted a study on 47 Dutch patients , all of them underwent total mesorectal excision with pelvic autonomic nerve preservation. 1 of 17 male patients experienced impotence problems (Maas et al 1998).

### Summary:

The main objectives of surgery for rectal cancer are cure and the prevention of local or pelvic recurrence. Preservation of pelvic autonomic functions are important associated goals that have influenced the design of the operation.

These changes began with modifications to the art of lateral pelvic lymphadenectomy, and with the introduction of sharp pelvic dissection along anatomical pelvic fascial planes for rectal cancer in the mid-1970s.

These changes evolved to include deliberate autonomic nerve preservation as a part of the operation that was ultimately reported as TME with ANP.

Dissection was generally directed to the widest possible pelvic margin medial to the autonomic nerves, as opposed to just peripheral to the mesorectum.

Both sexual and urinary functions are complex, and patients undergoing surgery for rectal cancer may have differing baselines levels of function.

The causes of impotence after surgery for rectal cancer are complex, and not all answers to the problem reside in autonomic nerve preservation.

Heald introduced the concept of total mesorectal excision at the North Hampshire Hospital by using sharp dissection under direct vision, a relatively bloodless plane is followed along the lipoma like outer surface of the mesorectum.

The sharp technique used in TME ensures a specimen with intact mesorectum with negative tumor margins in the majority of resectable mobile rectal cancers.

Furthermore, the sharp technique allows for preservation of the pelvic autonomic nerves, reducing sexual and urinary dysfunction.

Shams supported the use of total mesorectal excision with using sharp dissection under direct vision to ensure a large decline in local recurrence rate and improved overall survival with preservation of the urinary and sexual function and has become the new standard of operative management for rectal cancer, replacing conventional resection technique.

In our study, 40 patients presented with cancer rectum were divided into two groups, one group was subjected to total mesorectal excision and pelvic nerve preservation, And second group was subjected to subtotal mesorectal excision with conventional method.

All patients have undergone routine investigations and metastatic workup before operation.

Patients were followed up for at least 2 years considering history, physical examination, and measurement of Carcinoembryonic antigen (CEA) values done thrice yearly with chest radiograph and liver ultrasound every six months.

A follow up CT pelvis was also done at a year postoperatively.

All patients were asked to fill out a questionnaire with questions regarding urinary function and the male patients were asked to fill out a questionnaire with questions regarding sexual function.

All patients were subjected to urinary flowmetry to assess the urinary function and the male patients were subjected to U/S color Doppler to assess the male sexual function.

20 patients with total mesorectal excision showed no cumulative risk of local recurrence at two years while the other 20 patients with subtotal mesorectal excision and conventional method showed 30 % cumulative risk of local recurrence.

Our study reported that in patients subjected to total mesorectal excision with pelvic nerve preservation, 85 % of patients did not report any urinary complaint. The other patients ( 15 % ) experienced one or more of the early urinary symptoms such as pain, burning or discomfort during urination; or increased frequency. Postoperative flowmetry revealed normal mean maximal urinary flow rate and voided volume in 90 % of patients. 10 % of patients revealed mean maximal urinary flow rate less than 10 ml / sec and voided volume less than 300 ml. No patients revealed neurogenic bladder requiring catheterization nor patients revealed residual urine.

while in patients subjected to subtotal mesorectal excision with conventional method, 50 % only did not report any urinary complaint and the other 50 % reported urinary complaint. Postoperative flowmetry revealed normal menn maximal urinary flow rate and voided volume in 65 % of patients.4 patients revealed neurogenic bladder requiring catheterization.

Among 5 male patients subjected to total mesorectal excision and pelvic nerve preservation, by using a standard questionnaire, one patient only ( 20

% ) showed complete inability for erection and intercourse. Erection and penetration ability was possible in 4 patients ( 80 % ). Doppler US was performed to the five male patients which revealed normal biphasic arterial and venous pulsations on both sides in 4 patients ( 80 % ) and abnormal in only one patient ( 20 % ).

Among 8 male patients subjected to subtotal mesorectal excision with conventional method , by using a standard questionnaire, 4 patients ( 50 % ) showed abnormal sexuality. Doppler US revealed normal biphasic arterial and venous pulsations in both sides in 4 patients ( 50 % ) and abnormal in 4 patients ( 50 % ).

So, we conclude that the introduction of total mesorectal excision (TME) with pelvic nerve preservation (ANP) is one of the largest improvements in the outcome of rectal cancer.

We recommended TME –ANP to improve not only prognosis in terms of local recurrence, but also in terms of overall survival and preserving urinary and sexual activities.



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# المُلخَص العَرَبِي

كيفية استئصال سرطان المستقيم تمثل حجر الزاوية في علاج أورام المستقيم و المضاعفات الناتجة تختلف بين الجراحين. و تمثل مساريقا المستقيم السبب الرئيسي في الارتجاع الموضعي لأورام المستقيم و زيادة عدد الوفيات من بين المصابين بالمرض . و تمتد مساريقا المستقيم من تفرع شريان الأورطى حتى اتصال المستقيم بالشرج . و لذلك فان الاستئصال الكلى لمساريقا المستقيم مقترن بنقص الارتجاع الموضعي و زيادة فى نسبة الأحياء و كذلك انخفاض معدل المضاعفات الناتج عن الاستئصال الجزئى كالأحتباس البولى و ضعف النشاط الجنسى .

و يعتبر هيلد من اوائل الجراحين الذين اجروا عمليات الاستئصال الكلى لمساريقا المستقيم مع عدم ترك أي بقايا للورم فى معظم العمليات التى قد اجراها لحالات سرطان المستقيم و قد اتبرت المحافظة على العصب الحوضى من الأهداف الرئيسية مع الاستئصال الكلى لمساريقا المستقيم .

شملت هذه الدراسة تقييم الاستئصال الكلى لمساريقا المستقيم مع الحفاظ على العصب الحوضى فى 20 حالة سرطان مستقيم و دورة فى انخفاض معدل الارتجاع الموضعي و كذلك انتشار اورام المستقيم مع انخفاض معدل المضاعفات كالأحتباس البولى و ضعف النشاط الجنسى عن الاستئصال الجزئى بالطرق المعتادة فى 20 حالة سرطان مستقيم اخرى .

و قد تم عمل اختبار اسئلة حول الشكوى من التبول مع عمل اختبار لمعدل سريان البول لجميع الحالات بعد اجراء العملية . كما تم عمل اختبار اسئلة حول العملية الجنسية مع عمل دوبلر ملون على الاوعية الدموية للخصيتين بعد اجراء العملية.

و قد اتضح وجود 6 حالات ارتجاع موضعي فى الحوض من بين الحالات التى قد اجريت لهم عملية استئصال جزئى لمساريقا المستقيم بينما لم يحدث حالات ارتجاع موضعي من بين الحالات التى قد اجريت لهم عملية استئصال كلى لمساريقا المستقيم.

و مع عمل اختبار معدل سريان البول لجميع الحالات وجد طبيعيا فى 18 حاله من بين الحالات التى قد اجريت لهم عملية استئصال كلى لمساريقا المستقيم مع الحفاظ على العصب الحوضى بينما كان طبيعيا فى 13 حاله من بين الحالات التى قد اجريت لهم العملية التقليدية .

و مع عمل اختبارات سلامه العملية الجنسيه لحالات الذكور وجد 4 حالات من بين 5 لم يتاثرن بعد العملية و ذالك من بين الحالات التى اجريت لهم استئصال كلى لمساريقا المستقيم بينما وجد 4 حالات من بين 8 لم يتاثرن بعد العملية و ذلك من بين الحالات التى قد اجريت لهم العملية التقليدية .

و من هذه الدراسة يكون لنا القدرة على التوصل الى المحك الرئيسى فى الحكم على جراحة سرطان المستقيم و التوصل الى الطريقة المثلى فى استئصال سرطان المستقيم .



## رؤية جراحى الأورام فى استئصال مساريقا المستقيم فى حالات سرطان المستقيم مع الحفاظ على العصب الحوضى

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