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CAUSES AND OUTCOMES OF EMERGENCY PRESENTATION OF COLORECTAL CANCER (ABOUT 203 CASES)

THESIS

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LIST OF ABBREVIATIONS

APC	: Adenomatous Polyposis Coli
CT	: Computed tomography
CRC	: Colorectal cancer
CTC	: Computed tomography colonography
ED	: Emergency department
FAP	: Familial adenomatous polyposis
GI	: Gastro intestinal
HNPCC	: Hereditary non-polyposis colorectal cancer
IBD	: Inflammatory bowel disease
IMA	: Inferior mesenteric artery
IMPACT	: International multicenter pooled analysis of colon cancer trials
MDC	: Moderately differentiated cancer
MMR	: Mismatch repair
MRI	: Magnetic resonance imaging
MSI	: Microsatellite instability
OR	: Odds ratio
PDC	: Poorly differentiated cancer
RR	: Relative risk
WDC	: Well differentiated cancer

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INTRODUCTION

Introduction

Colorectal cancer is a major problem for the public health. It represents the third and second most common cancer, respectively, in men and women worldwide. Mortality due to this type of cancer is increasing, and it is the fourth leading cause of cancer death in the world. [1]

It is infrequent before age 40, the incidence rises progressively afterwards to 3.7/1000 per year by age 80. The lifetime incidence for patients at average risk in the United States is 4.4 percent, with 90 percent of cases occurring after age 50. [2]

There is a higher incidence of this form of malignancy in developed countries and is thought to be mainly due to environmental factors. An improvement in survival of the patients has been obtained thanks to screening programs which enables diagnosis in the early stages and treatment options.

Emergency presentations of colorectal cancer are life-threatening conditions that occur often when a tumor developing in the inner wall of the colon causes a local complication. They are presentation or referral to our center through the ED (emergency department) with symptoms and clinical findings requiring admission and urgent surgical treatment. These presentations can be either bowel obstruction, perforation or hemorrhage

1. **bowel obstruction** is a significant mechanical impairment or complete arrest of the passage of contents through the intestine. Symptoms include cramping pain, vomiting, obstipation and lack of flatus. Diagnosis is clinical, confirmed by abdominal x-rays.

2. **perforation** also known as **ruptured bowel**, is a hole in the colon causing the bowel contents to spill freely into the abdominal cavity. The perforation may be at the site of the tumor or may occur secondarily at a proximal site, usually the caecum, in obstructing cancers. Symptoms include severe abdominal pain and tenderness. When the hole is in the stomach or early part of the small intestine the onset of pain is typically sudden while with a hole in the large intestine onset may be more gradual. Abdominal x-rays show free air under the right diaphragm.

3. **hemorrhage** is an abnormal and massive bleeding into the lumen of the colon or into the peritoneal space causing a hemodynamic instability

The age of patients presenting with these complications is generally advanced, a factor which contributes to a high post-operative mortality of patients. Malignant processes evolve over a longer period in order for these complications to be produced, which is why patients are usually found to be in advanced stages of oncologic evolution with peritoneal carcinomatosis or distant metastasis. Despite this fact, radical treatment for the complicated colorectal cancer is recommended whenever possible.

Invasive colorectal cancer is a preventable disease. Early detection through widely applied screening programs is the most important factor in the recent decline of colorectal cancer in developed countries

Colonoscopy is the most sensitive of available screening options at detecting cancer or polyps and is thus an acceptable modality; however, it is associated with the highest risk and cost.

Surgical resection remains the mainstay of treatment of cancers of the colon. since cancers spread locally, through the lymphatic nodes and hematogenously, the oncological principle of colon cancer surgery include resection of the tumor with adequate resection margins plus removal of all lymph node bearing tissue.

Surgical resection is the primary treatment modality for early stage CRC (stage I through III), and the most powerful tool for assessing prognosis following potentially curative surgery is pathologic analysis of the resected specimen. Although the parameters that determine pathologic stage are the strongest predictors of postoperative outcome, other clinical, molecular, and histologic features may influence prognosis independent of stage. Among patients with stage IV disease, prognosis is more closely tied to the location and extent of distant metastatic disease.

BACKGROUND

I–Anatomy[3],[4]

1–General Considerations

The colon is a capacious tube that roughly surrounds the loops of small intestine as an arch. Named from the Greek *koluein* (“to retard”), the colon is variable in length, averaging approximately 150 cm, which corresponds to one–quarter the length of the small intestine. Its diameter can be substantially augmented by distension; it gradually decreases from 7.5 cm at the cecum to 2.5 cm at the sigmoid.

Anatomic differences between the small and large intestines include position, caliber, degree of fixation, and, in the colon, the presence of three distinct characteristics: **the taeniae coli**, **the haustra**, and **the appendices epiploicae**.

- **The three taeniae coli**, anterior (taenia libera), posteromedial (taenia mesocolica), and posterolateral (taenia omentalis), represent bands of the outer longitudinal coat of muscle that traverse the colon from the base of the appendix to the rectosigmoid junction, where they merge. The muscular longitudinal layer is actually a complete coat around the colon, although it is considerably thicker at the taeniae.
- **The haustra** or haustral sacculations are outpouchings of bowel wall between the taeniae; they are caused by the relative shortness of the taeniae, about one–sixth shorter than the length of the bowel wall. The haustra are separated by the plicae semilunares or crescentic folds of the bowel wall, which give the colon its characteristic radiographic appearance when filled with air or barium.

- The appendices epiploicae are small appendages of fat that protrude from the serosal aspect of the colon.

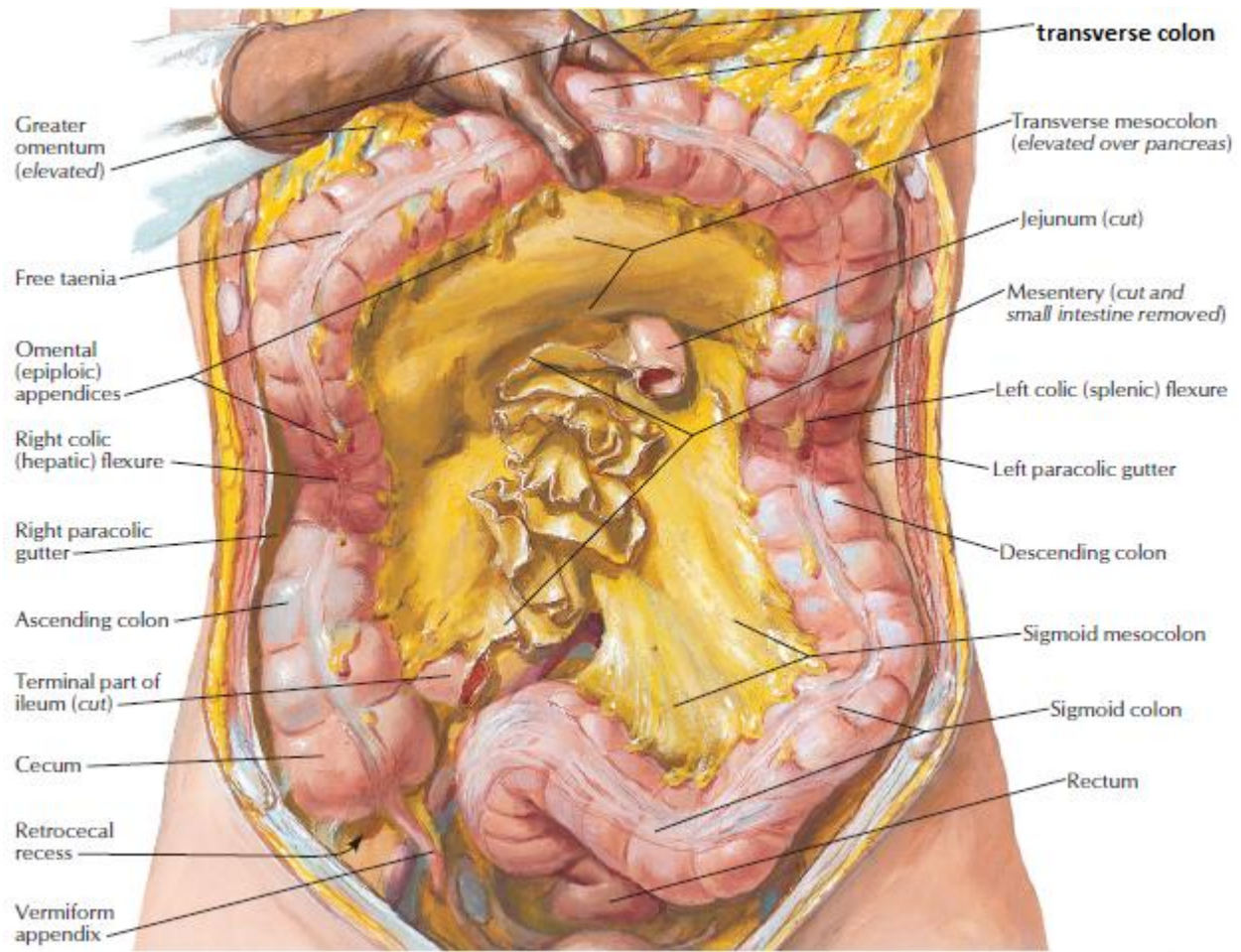


FIGURE 1:GENERAL VIEW OF THE LARGE INTESTINE

Mucosa and Musculature of Large Intestine

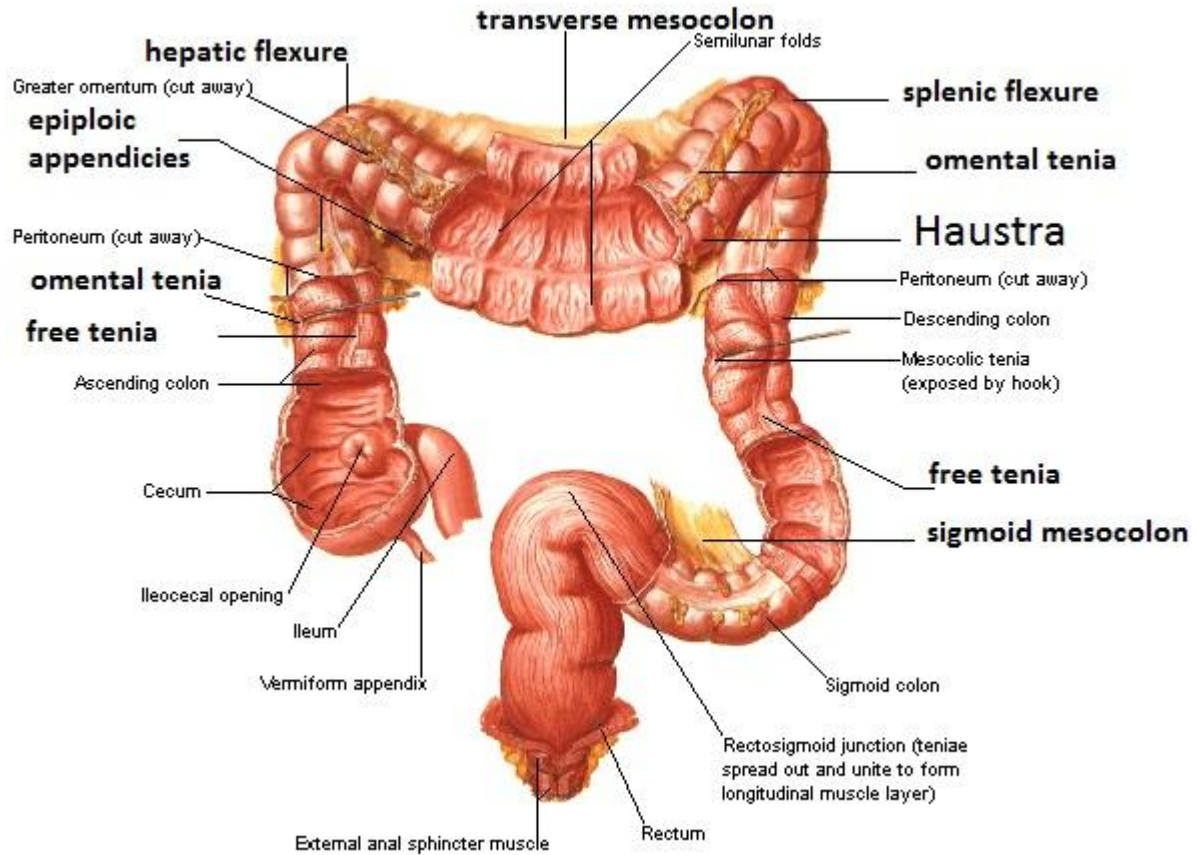


Figure 2: mucosa and musculature of the large intestine

2-Structure

The gastrointestinal wall surrounding the lumen of the large intestine is made up of four layers of specialized tissue from the lumen outwards:

Mucosa: Contains a glandular epithelium with goblet cells secreting mucus which lubricates the passage of food and protects it from digestive enzymes.

Submucosa: is a layer of loose connective tissue interposed between the mucosa toward the lumen and the outer muscle layer. The submucosa contains the nerves, blood vessels, lymphatics, and lymphoid follicles.

Muscular layer: Surrounding the mucosa and submucosa and comprises both longitudinal and circular smooth muscle. The muscle layer is responsible for the peristaltic movement of the luminal content of the large intestine. The outer longitudinal layer does not completely ensheath the circumference of the large intestine; it is formed into three bundles called the taeniae coli, which are spaced approximately equally around the circumference. The inner layer of circular muscle fiber contracts to give rise to sacculations of the colon, called the haustra.

Serosa: The serosa surrounds the large intestine as the external wrapping and is variable in its extent of wrapping, it is made up of loose connective tissue and coated in mucus so as to prevent any friction damage from the intestine rubbing against other tissue.

Holding all this in place are the mesenteries which suspend the intestine in the abdominal cavity and stop it being disturbed when a person is physically active. Since the serosa is rich in lymphatic vessels and is continuous with the serosal layer of the other organs in the abdomen, diseases that extend up to the serosal layer are usually prone to disseminate to other organs.

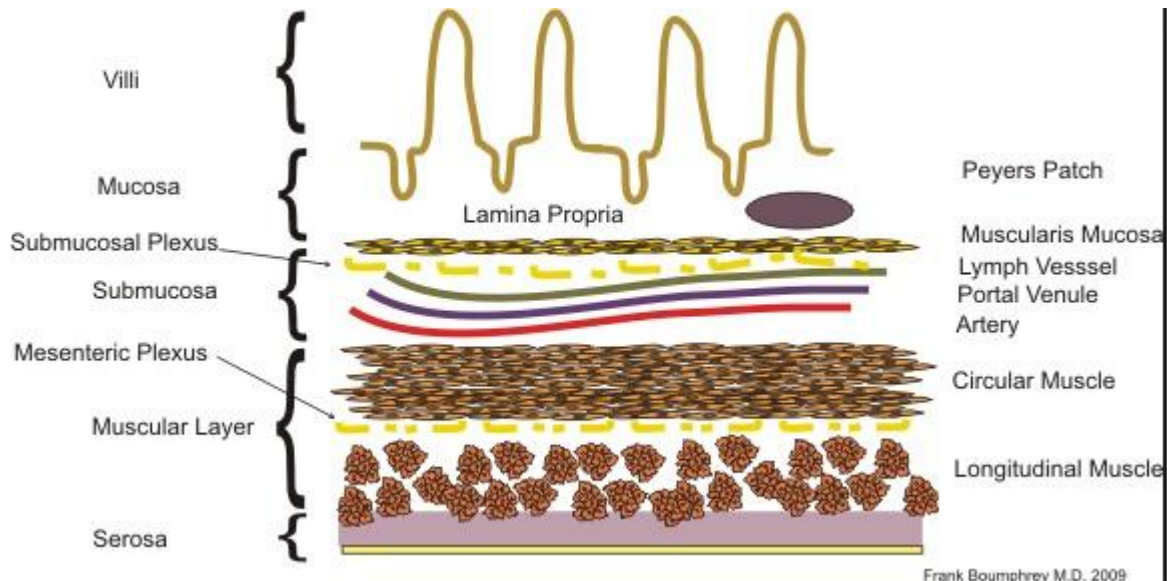


FIGURE 3: LAYERS OF THE COLON

3-Gross anatomy and support of the large intestine

3-1 Cecum

The cecum is the sacculated segment (Latin *caecus*, “blind”) of the large bowel that projects downward as a 6- to 8-cm blind pouch below the entrance of the ileum. Usually situated in the right iliac fossa, the cecum is almost entirely, or at least in its lower half, invested with peritoneum. However, its mobility is usually limited by a small **mesocecum**.

The ileum terminates in the posteromedial aspect of the cecum; the angulation between these two structures is maintained by the superior and inferior ileocecal ligaments. These ligaments, along with the mesentery of the appendix, form three pericecal recesses or fossae: superior ileocecal, inferior ileocecal, and retrocecal.

Viewed from the cecal lumen, the ileocecal junction is represented by a narrow, transversely situated, slit-like opening known as the ileocecal valve or **the valve de Bauhin**.

3-2 Appendix

The vermiform appendix is an elongated diverticulum that arises from the posteromedial aspect of the cecum about 3.0 cm below the ileocecal junction. Its length varies from 2 to 20 cm (mean, 8-10 cm), and it is approximately 5 mm in diameter.

Because of its great mobility, the appendix may occupy a variety of positions, possibly at different times in the same individual. It has been estimated that in 85% to 95% of cases, the appendix lies posteromedial on the cecum toward the ileum, but other positions include retrocecal, pelvic, subcecal, pre-ileal and retroileal. The confluence of the three taeniae is a useful guide in locating the base of the appendix. The mesoappendix, a triangular fold attached to the posterior leaf of the mesentery of the terminal ileum, usually contains the appendicular vessels close to its free edge.

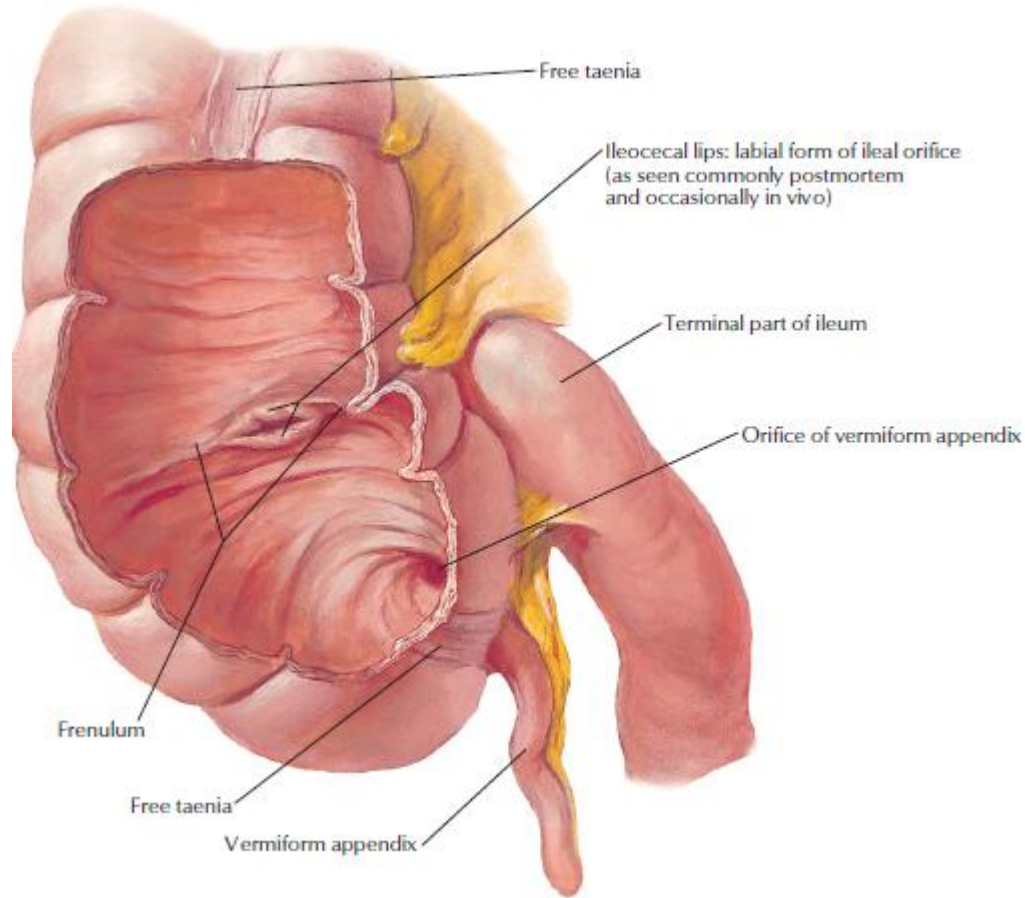


FIGURE 4: INTERIOR VIEW OF THE CAECUM

3-3 Ascending Colon

The ascending colon is approximately 15 cm long. It ascends, from the level of the ileocecal junction to the right colic or hepatic flexure, laterally to the psoas muscle and anteriorly to the iliacus, the quadratus lumborum, and the lower pole of the right kidney.

The ascending colon is covered with peritoneum anteriorly and on both sides. In addition, fragile adhesions between the right abdominal wall and its anterior aspect, known as **Jackson's membrane**, may be present. Like the descending colon on its

posterior surface, the ascending colon is devoid of peritoneum, which is instead replaced by an areolar tissue (fascia of Toldt) resulting from an embryologic process of fusion or coalescence of the mesentery to the posterior parietal peritoneum.

In the lateral peritoneal reflection, this process is represented by the white line of Toldt, which is more evident at the descending–sigmoid junction. This line serves as a guide for the surgeon when the ascending, descending, or sigmoid colon is mobilized. At the visceral surface of the right lobe of the liver and lateral to the gallbladder, the ascending colon turns sharply medially and slightly caudad and ventrally to form the right colic (hepatic) flexure. This flexure is supported by the nephrocolic ligament and lies immediately ventral to the lower part of the right kidney and over the descending duodenum.

3–4 Transverse Colon

The transverse colon is approximately 45 cm long, the longest segment of the large bowel. It crosses the abdomen, with an inferior curve immediately caudad (toward the tail) to the greater curvature of the stomach.

The transverse colon is relatively fixed at each flexure, and, in between, it is suspended by a 10– to 15–cm wide area which provides variable mobility; the nadir of the transverse colon may reach the hypogastrium. The transverse colon is completely invested with peritoneum, but the greater omentum is fused on its anterosuperior aspect.

The left colic or splenic flexure is situated beneath the lower angle of the spleen and firmly attached to the diaphragm by the phrenocolic ligament, which also forms a shelf to support the spleen. Because of the risk for hemorrhage, mobilization of the splenic flexure should be approached with great care, preceded by dissection upward along the descending colon and medially to laterally along the transverse colon toward the splenic flexure. This flexure, when compared with the hepatic flexure, is more acute, higher, and more deeply situated.

3-5 Descending Colon

The descending colon courses downward from the splenic flexure to the brim of the true pelvis, a distance of approximately 25 cm. Similarly, to the ascending colon, the descending colon is covered by peritoneum only on its anterior and lateral aspects.

Posteriorly, it rests directly against the left kidney and the quadratus lumborum and transversus abdominis muscles. However, the descending colon is narrower and more dorsally situated than the ascending colon.

3-6 Sigmoid Colon

The sigmoid colon is commonly a 35- to 40-cm-long, mobile, omega-shaped loop completely invested by peritoneum; however, it varies greatly in length and configuration.

The mesosigmoid is attached to the pelvic walls in an inverted V shape, resting in a recess known as the intersigmoid fossa. The left ureter lies immediately underneath this fossa and is crossed on its anterior surface by the spermatic, left colic, and

sigmoid vessels. Both the anatomy and function of the rectosigmoid junction have been matters of substantial controversy.

As early as 1833, it was postulated that the sigmoid could have a role in continence as the fecal reservoir, based on the observation that the rectum is usually emptied and contracted. Since then, a thickening of the circular muscular layer between the rectum and sigmoid has been described and diversely termed the sphincter ani tertius, rectosigmoid sphincter, and pylorus sigmoidorectalis, and it has probably been mistaken for one of the transverse folds of the rectum.

The rectosigmoid junction has been frequently regarded by surgeons as an indistinct zone, a region comprising the last 5–8 cm of sigmoid and the uppermost 5 cm of the rectum. However, others have considered it a clearly defined segment, because it is the narrowest portion of the large intestine; in fact, it is usually characterized endoscopically as a narrow and sharply angulated segment.

According to a study in human cadavers, the rectosigmoid junction, macroscopically identified as the point where the taenia libera and the taenia omentalis fuse to form a single anterior taenia and where both haustra and mesocolon terminate, is situated 6–7 cm below the sacral promontory. With microdissection, this segment is characterized by conspicuous strands of longitudinal muscle fibers and the presence of curved interconnecting fibers between the longitudinal and circular muscle layers, resulting in a delicate syncytium of smooth muscle that allows synergistic interplay between the two layers. The rectosigmoid does not fit the anatomic definition of a sphincter as “a band of thickened circular muscle that closes the lumen by contraction

and of a longitudinal muscle that dilates it”; however, this segment may be regarded as a functional sphincter because mechanisms of active dilation and passive “kinking” occlusion do exist.

3–7 Peritoneal attachments

- The transverse colon and sigmoid are completely peritonealized (the former being readily identified by its attachment to the greater omentum).
- The ascending and descending colon have no mesocolon but adhere directly to the posterior abdominal wall (although exceptionally the ascending colon has a mesocolon).
- The caecum may or may not be completely peritonealized, and the appendix, although usually free within its own mesentery, occasionally lies extraperitoneally behind caecum and ascending colon or adheres to the posterior wall of these structures.

3–8 Blood supply

The **superior** and **inferior mesenteric arteries** nourish the entire large intestine, and the limit between the two territories is the junction between the proximal two-thirds and the distal third of the transverse colon. This represents the embryologic division between the midgut and the hindgut.

The superior mesenteric artery originates from the aorta behind the superior border of the pancreas at L-1 and supplies the cecum, appendix, ascending colon, and

most of the transverse colon. After passing behind the neck of the pancreas and anteromedial to the uncinate process, the superior mesenteric artery crosses the third part of the duodenum and continues downward and to the right along the base of the mesentery.

From its left side arises a series of 12–20 jejunal and ileal branches. From its right side arises the colic branches: middle, right, and ileocolic arteries. The ileocolic, the most constant of these vessels, bifurcates into a superior or ascending branch, which communicates with the descending branch of the right colic artery, and an inferior or descending branch, which gives off the anterior cecal, posterior cecal, and appendicular and ileal divisions. The right colic artery may also arise from the ileocolic or middle colic arteries and is absent in 2% to 18% of specimens. It supplies the ascending colon and hepatic flexure through its ascending and descending branches, both of them joining with neighboring vessels to contribute to the marginal artery.

The middle colic artery is the highest of the three colic branches of the superior mesenteric artery, arising close to the inferior border of the pancreas. Its right branch supplies the right transverse colon and hepatic flexure, anastomosing with the ascending branch of the right colic artery. Its left branch supplies the distal half of the transverse colon.

The inferior mesenteric artery originates from the left anterior surface of the aorta, 3–4 cm above its bifurcation at the level of L2–3, and runs downward and to the left to enter the pelvis. Within the abdomen, the inferior mesenteric artery branches into the left colic artery and two to six sigmoidal arteries.

After crossing the left common iliac artery, it acquires the name superior hemorrhoidal artery (superior rectal artery). The left colic artery, the highest branch of the inferior mesenteric artery, bifurcates into an ascending branch, which runs upward to the splenic flexure to contribute to the arcade of Riolan, and a descending branch, which supplies most of the descending colon. The sigmoidal arteries form arcades within the sigmoid mesocolon, resembling the small-bowel vasculature, and anastomose with branches of the left colic artery proximally, and with the superior hemorrhoidal artery distally. The marginal artery terminates within the arcade of sigmoidal arteries.

The superior hemorrhoidal artery is the continuation of the inferior mesenteric artery, once it crosses the left iliac vessels. The artery descends in the sigmoid mesocolon to the level of S-3 and then to the posterior aspect of the rectum. In 80% of cases, it bifurcates into right and left terminal branches; multiple branches are present in 17%. These divisions, once within the submucosa of the rectum, run straight downward to supply the lower rectum and the anal canal.

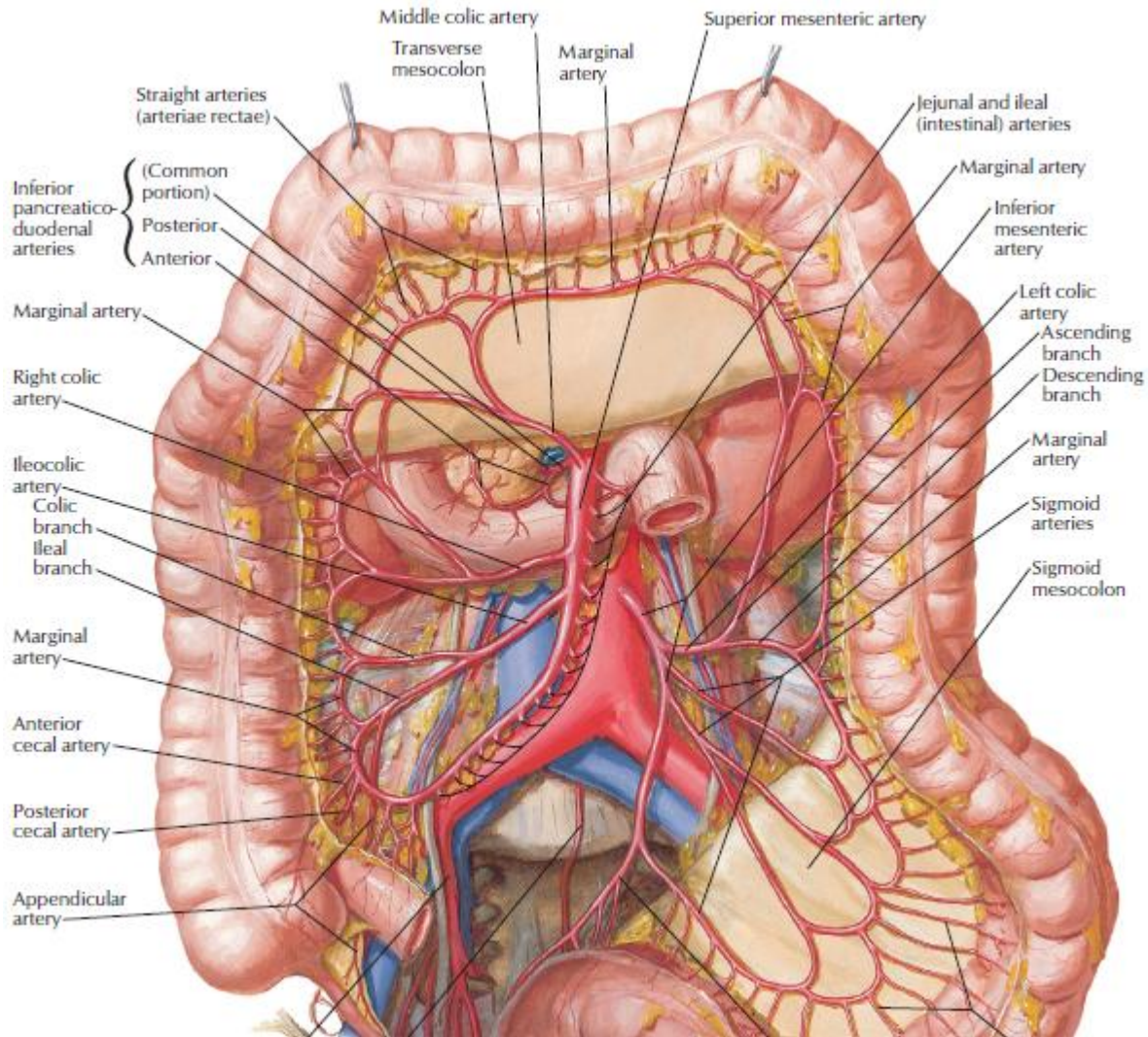


FIGURE 5: ARTERIES OF THE LARGE BOWL

The venous drainage of the large intestine basically follows its arterial supply. Blood from the right colon, via the **superior mesenteric vein**, and from left colon and rectum, via **the inferior mesenteric vein**, reaches the intrahepatic capillary bed through the portal vein.

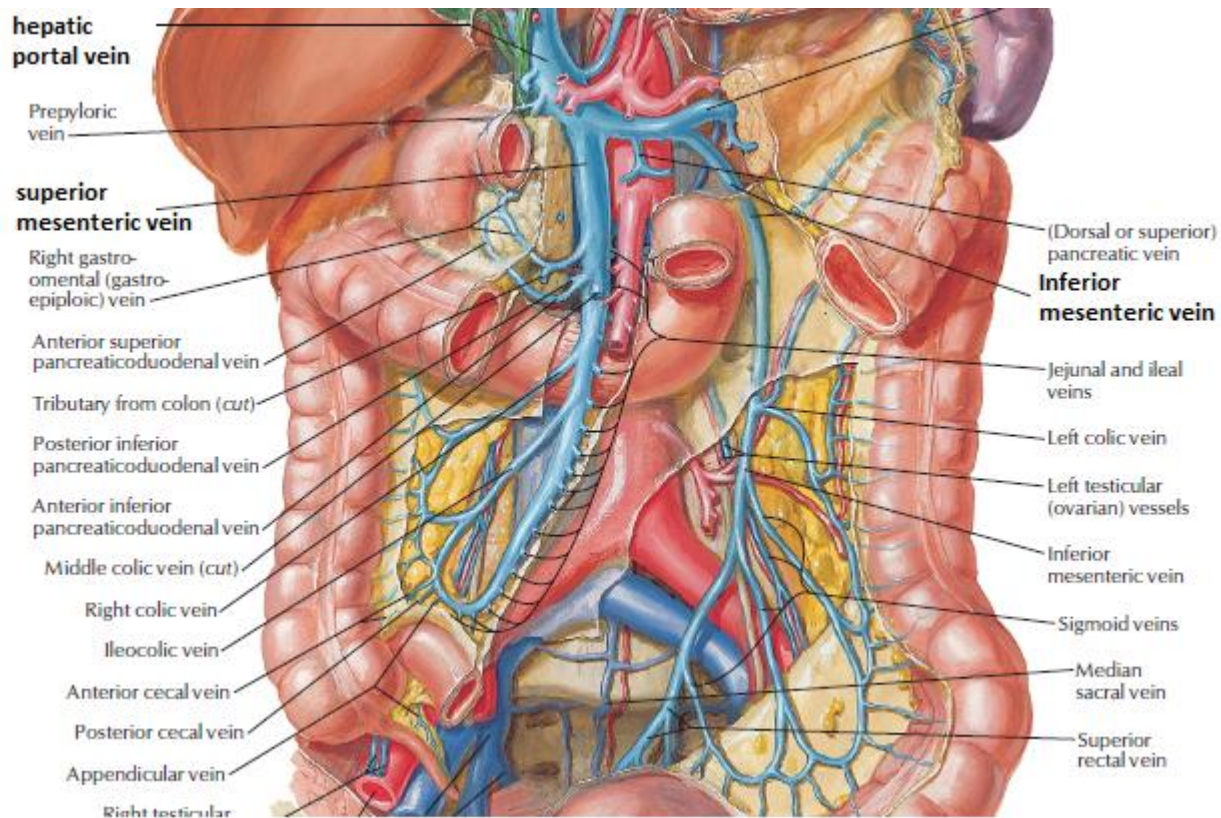


FIGURE 6: VEINS OF THE LARGE INTESTINE

3–9 Lymphatic drainage

The submucous and subserous layers of the colon and rectum have a rich network of lymphatic plexuses, which drain into an extramural system of lymph channels and follow their vascular supply. Colorectal lymph nodes are classically divided into four groups: *epiploic*, *paracolic*, *intermediate*, and *principal*.

- The **epiploic group** lies on the bowel wall under the peritoneum and in the appendices epiploicae; they are more numerous in the sigmoid and are known in the rectum as the nodules of Gerota. The lymphatic drainage from all parts of the colon follows its vascular supply.

- **The paracolic nodes** are situated along the marginal artery and on the arcades; they are considered to have the most numerous filters.

- **The intermediate nodes** are situated on the primary colic vessels, and the main or principal nodes on the superior and inferior mesenteric vessels. The lymph then drains to the cisterna chyli via the paraaortic chain of nodes. Colorectal carcinoma staging systems are based on the neoplastic involvement of these various lymph node groups.

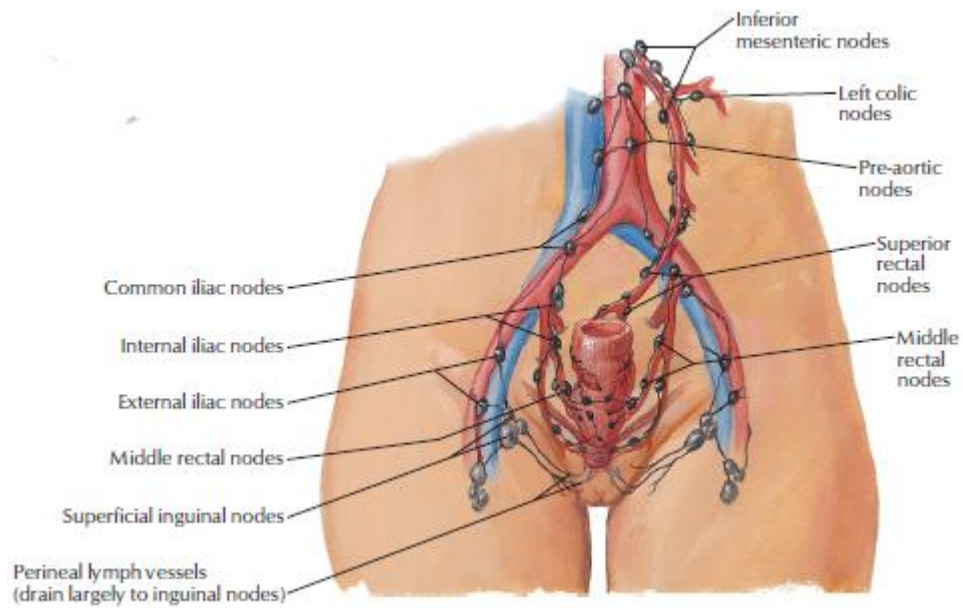
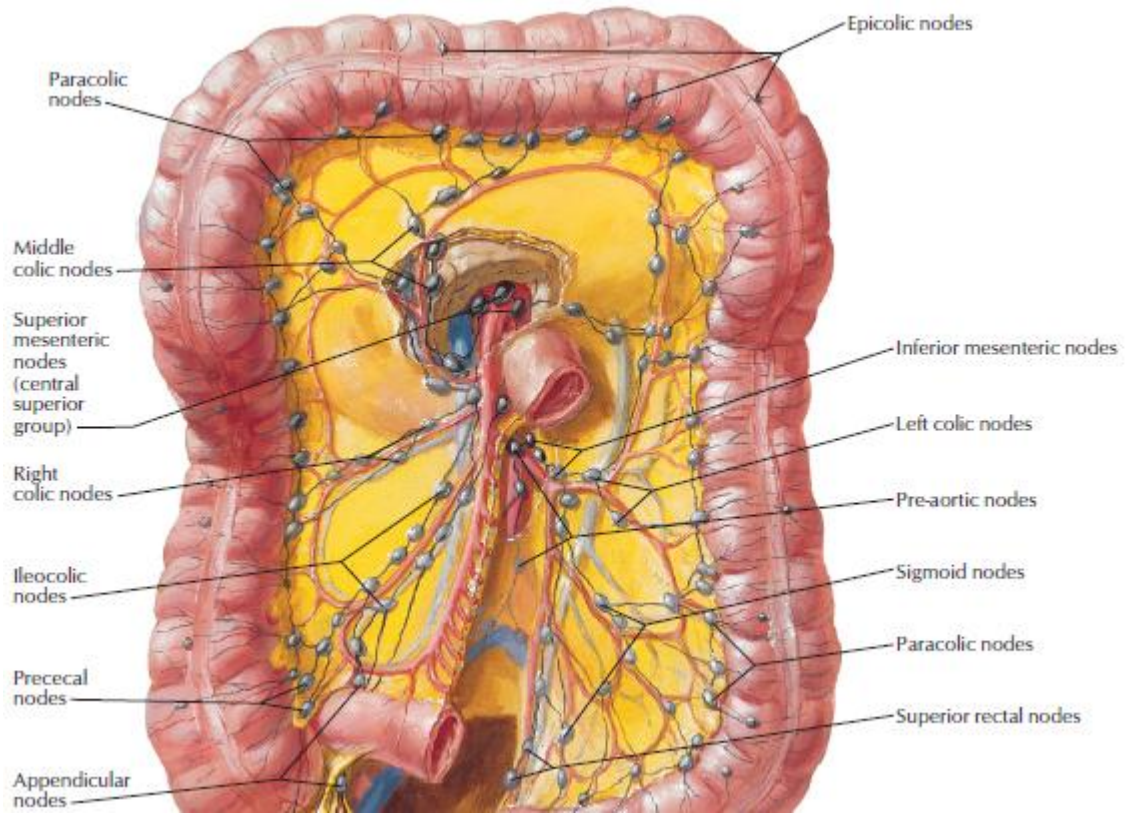


FIGURE 7 and 8: LYMPHATIC DRAINAGE OF THE LARGE INTESTIN

3-10 Innervation

The sympathetic and parasympathetic components of the autonomic innervation of the large intestine closely follow the blood supply.

The sympathetic supply of the right colon originates from the lower six thoracic segments. These thoracic splanchnic nerves reach the celiac, preaortic, and superior mesenteric ganglia, where they synapse. The postganglionic fibers then course along the superior mesenteric artery to the small bowel and right colon.

The parasympathetic supply comes from the right (posterior) vagus nerve and celiac plexus. The fibers travel along the superior mesenteric artery, and finally synapse with cells in the autonomic plexuses within the bowel wall.

The sympathetic supply of the left colon and rectum arises from L-1, L-2, and L-3. Preganglionic fibers, via lumbar sympathetic nerves, synapse in the preaortic plexus, and the postganglionic fibers follow the branches of the inferior mesenteric artery and superior rectal artery to the left colon and upper rectum.

4-Embryology

The distal colon, rectum, and the anal canal above the dentate line are all derived from the hindgut. Therefore, this segment is supplied by the hindgut (inferior mesenteric) artery, with corresponding venous and lymphatic drainage. Its parasympathetic outflow comes from S-2, S-3, and S-4 via splanchnic nerves.

The dentate line marks the fusion between endodermal and ectodermal tubes, where the terminal portion of the hindgut or cloaca fuses with the proctodeum, an ingrowth from the anal pit. The cloaca originates at the portion of the rectum below the pubococcygeal line, whereas the hindgut originates above it. Before the fifth week of development, the intestinal and urogenital tracts terminate in conjunction with the cloaca. During the sixth to eighth weeks of fetal life, the urorectal septum or fold of Tourneux migrates caudally and divides the cloacal closing plate into an anterior urogenital plate and a posterior anal plate. Any slight posterior shift in the position of the septum during its descent will reduce the size of the anal opening, giving rise to anorectal defects.

The cloacal part of the anal canal, which has both endodermal and ectodermal elements, forms the anal transitional zone after breakdown of the anal membrane. During the 10th week, the anal tubercles, a pair of ectodermal swellings around the proctodeal pit, fuse dorsally to form a horseshoeshaped structure and anteriorly to create the perineal body.

The cloacal sphincter is separated by the perineal body into urogenital and anal portions (external anal sphincter). The internal anal sphincter is formed later (6th to 12th week) from enlarging fibers of the circular layer of the rectum. In the female, the fused Müllerian ducts that will form the uterus and vagina move downward to reach the urogenital sinus about the sixteenth week. In the male, the site of the urogenital membrane will be obliterated by fusion of the genital folds and the sinus will become incorporated into the urethra. The sphincters apparently migrate during their

development; the external sphincter grows cephalad and the internal sphincter moves caudally. Concomitantly, the longitudinal muscle descends into the intersphincteric plane.

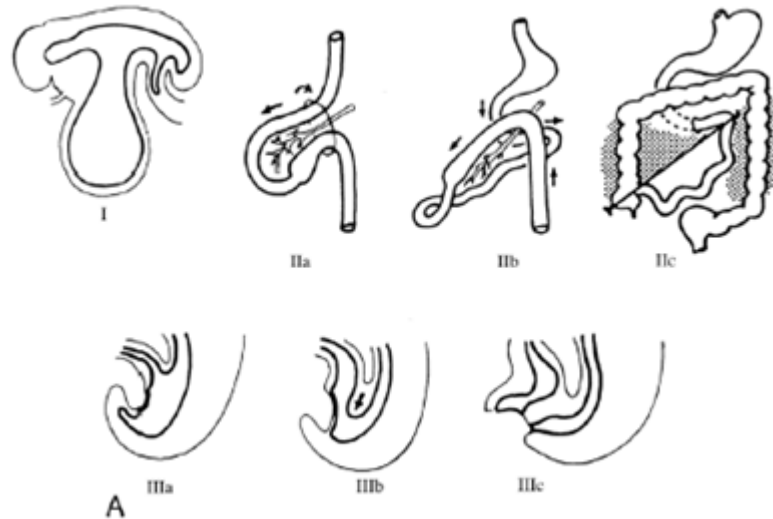


FIGURE 9: EMBRYOLOGY OF THE LARGE INTESTINE.

I. Sagittal section of early embryo with the primitive tube at the third week of development.

II. Normal development of intestine.

IIa: Midgut loop within the umbilical cord (physiologic herniation);

IIb: midgut rotation and return to the abdomen;

IIc: rotation complete with wide retroperitoneal fixation of small bowel mesentery as well as ascending and descending colon.

III. Development of the anus and rectum.

IIIa: The hindgut, tailgut, and the allantois form the cloaca;

IIIb: at the sixth week, the urogenital septum grows to separate the hindgut posteriorly and the allantois anteriorly;

IIIc: the rectum with the persistent anal membrane has been separated from the urogenital structures.

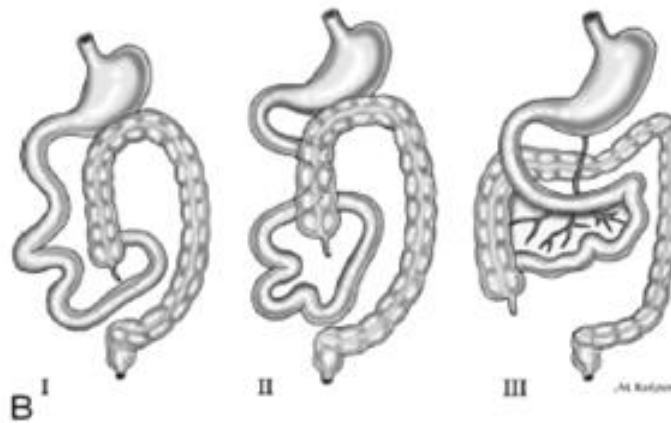


FIGURE 10: MALFORMATIONS OF THE DIGESTIVE SYSTEMS.

I, No rotation

II, incomplete rotation

III, reversed rotation.

5-Physiology of the large intestine

The colon has a limited role in digestion but is important for stool formation and storage. its main function is to absorb approximately 1.5 L of water daily from the stool (through a sodium transporter in exchange with potassium), to absorb chloride in exchange with bicarbonate, and to absorb vitamin K produced by the colonic flora.

As a result, severe colonic diarrhea leads to significant stool losses of potassium and bicarbonate resulting in hypokalemia and metabolic acidosis. Use of antibiotics can lead to eradication of the normal colonic flora and vitamin K deficiency in those with poor nutrition.

The colon displays two motility patterns: segmental mixing contractions with slow forward propulsion and high amplitude sweeping contractions occurring up to 10

times a day. These sweeping contractions typically occur in the morning and after meals caused by what is known as the gastrocolic reflex and produce the urge to defecate.

II-Epidemiology

1- Colorectal cancer incidence worldwide

There is almost a 10-fold variation in CRC incidence rates (proportion of newly diagnosed cases per year) worldwide for both sexes. CRC incidence rates are highest in Australia/New Zealand and Western Europe and lowest in Middle Africa and South-Central Asia.

In Canada, Colorectal cancer is the third most common cancer with an estimated 24,400 people diagnosed in 2014. Incidence is estimated at 59 per 100,000 in men, and 40 per 100,000 in women. It is the second leading cause of death from cancer in Canada.[5]

In the United States colorectal cancer is the second leading cause of cancer-related deaths and the third most common cancer in men and in women. [6]

136,119 people in the United States were diagnosed with colorectal cancer, including 71,099 men and 65,020 women in 2013, and over 51,813 people died from colorectal cancer, including 27,230 men and 24,583 women.[7]

Over 15000 CRC cases are registered in France per year, and the same country knew an increase of registered CRC from 24000 cases to 36000 in a 20-year period (1980-2000)

Although developed countries account for almost two-thirds of CRC cases (with the exception of a few countries in Eastern Europe, Eastern Asia, and Spain), the rates in developed countries have mostly remained stable or declined over time, whereas rates in developing countries are rising.

These differences may be attributable to changes in lifestyle and environmental factors as well as underlying genetic susceptibility. The rapid increase in the cancer burden in developing countries is possibly due to population growth and aging, and adverse lifestyle changes such as increased smoking, physical inactivity, and westernized diets.

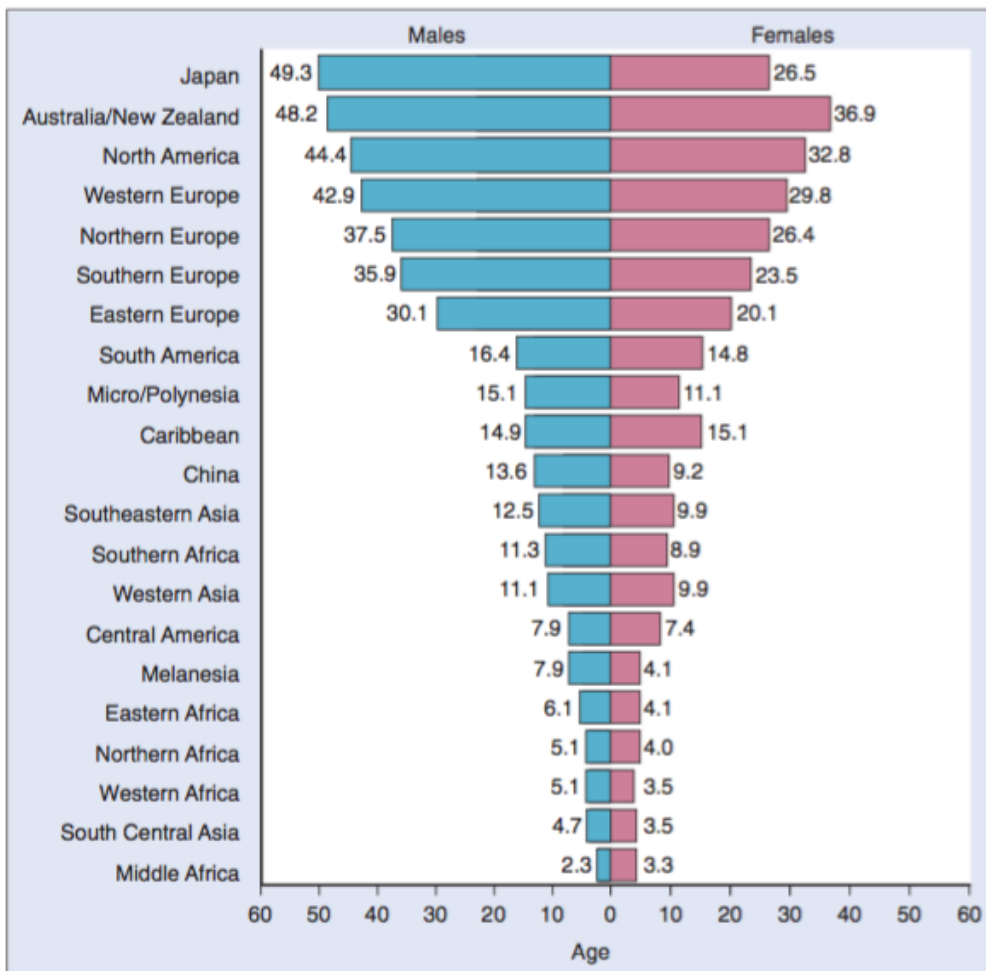


FIGURE 11: AGE STANDARDIZED RATES OF CRC FOR MALES BY GENDER IN DIFFERENT SITES[8]

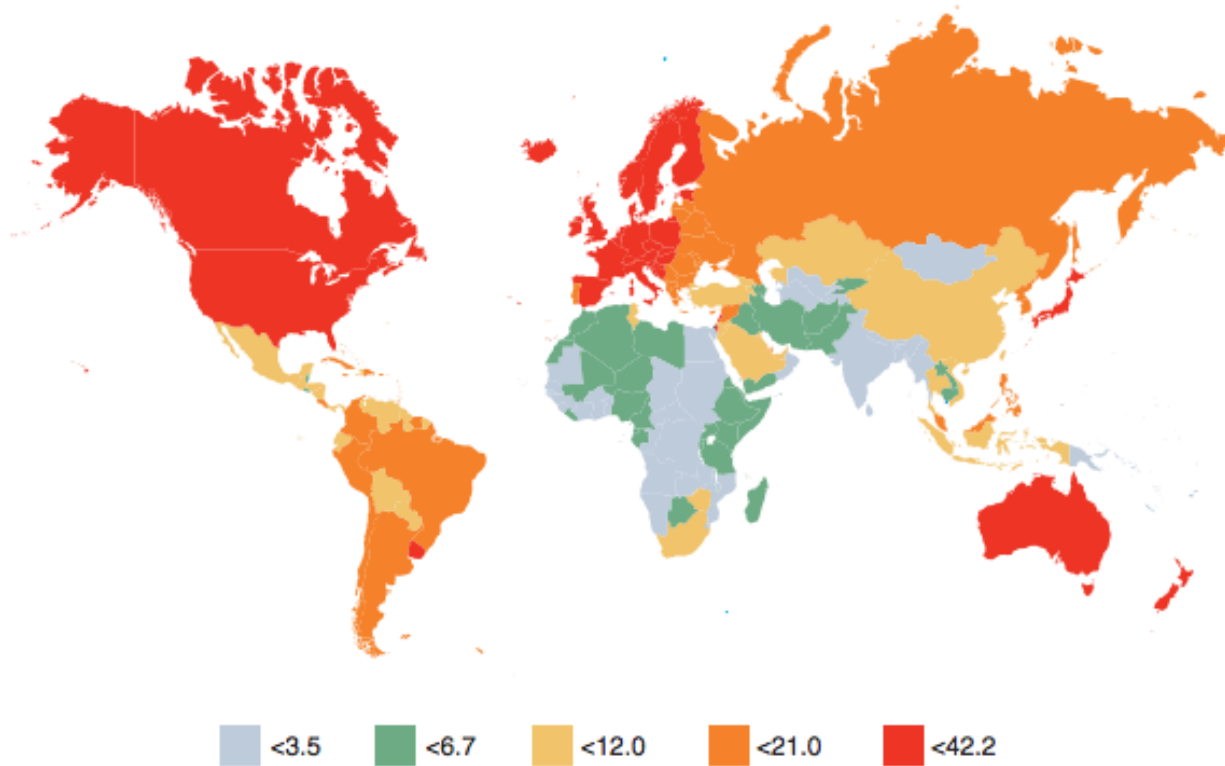


FIGURE 12: DISTRIBUTION OF COLON CANCER WORLDWIDE

2 –Colorectal cancer incidence in morocco according to local studies

The lack of epidemiological data makes it hard to appreciate precisely the incidence of colorectal cancer in morocco, however some local studies may give an overview of the frequency of this type of cancer in particular areas.

according to the register of cancers in Rabat 2005, colon cancer has the same incidence as the one found in other registers in the Maghreb countries except for Libya and still is lower than incidences observed in occidental countries, in Japan or China.[9]

half of colon cancer cases occur between ages 25 to 54 years; the average age of colon cancer patients is slightly higher in women (59,5) than men (53,6).

In Rabat, colon cancer incidence is two times more frequent in men and increases with age. and is diagnosed one quarter of the times in a metastatic stage, and half patients are treated for curative purposes.

	total	men	women
incidence for 100 000 people	2,5	3,3	1,8
standardized incidence on worldwide population	2,5 (1,2-3,7)	3,3 (1,2-5,4)	1,8 (0,3-3,2)
standardized incidence on Moroccan population	2,0 (1-3)	2,6 (1-4,2)	1,5 (0,3-2,7)
cumulative risk (%)	0,3	0,4	0,2

TABLE 1: INCIDENCE OF COLON CANCER IN RABAT

In Casablanca, and according to the register of Grand Casablanca, colon cancer represents an incidence higher in men than women and slightly increased for the last 3 years. [10]

The average ages in colon cancer cases are 57,2 and 56,8 years respectively for women and men.

	<u>2005</u>	<u>2006</u>	<u>2007</u>	<u>total</u>
<u>number of cases</u>	56	79	85	220
<u>gross incidence</u>	3,1	4,3	4,6	4
<u>cumulative incidence 0-74 years (%)</u>	0,47	0,66	0,64	0,59
<u>standardized incidence on the Moroccan population</u>	2,8	3,9	4,3	3,7
<u>standardized incidence on worldwide population</u>	3,7	5,2	5,3	4,7
<u>% regarding other cancers</u>	3,3	4,4	4,1	3,9

TABLE 2: INCIDENCE OF COLON CANCER IN MEN RCRC 2005 – 2007

	<u>2005</u>	<u>2006</u>	<u>2007</u>	<u>total</u>
<u>number of cases</u>	52	58	58	168
<u>gross incidence</u>	2,8	3,1	3	3
<u>cumulative incidence 0-74 years (%)</u>	0,36	0,42	0,35	0,38
<u>standardized incidence on the Moroccan population</u>	2,5	2,7	2,7	2,6
<u>standardized incidence on worldwide population</u>	3	3,4	3,2	3,2
<u>% regarding other cancers</u>	2,6	2,8	2,5	2,6

TABLE 3: INCIDENCE OF COLON CANCER IN WOMEN RCRC 2005 – 2007

In Fez, a study called COLOREC, examined 385 cases with colorectal cancer registered from 2010 to 2013 and reported a lower CRC incidence compared to western countries, placed between 2.5 and 3.3 cases per 100 000 people. average age is 56,9 years old with a minimal age of 16 and a maximum of 84.

3-Topographical distribution

In gathering clinical and population data, cancers of all parts of the large bowel are often considered as the same disease. The epithelium of the proximal colon is, however, subtly different in cellular composition and mucin histochemistry from that lining the distal colon and rectum.

The right colon is also usually exposed to a different luminal environment when compared with the distal bowel (rapid transit of fluid contents versus relatively stationary solid bulky stool respectively).

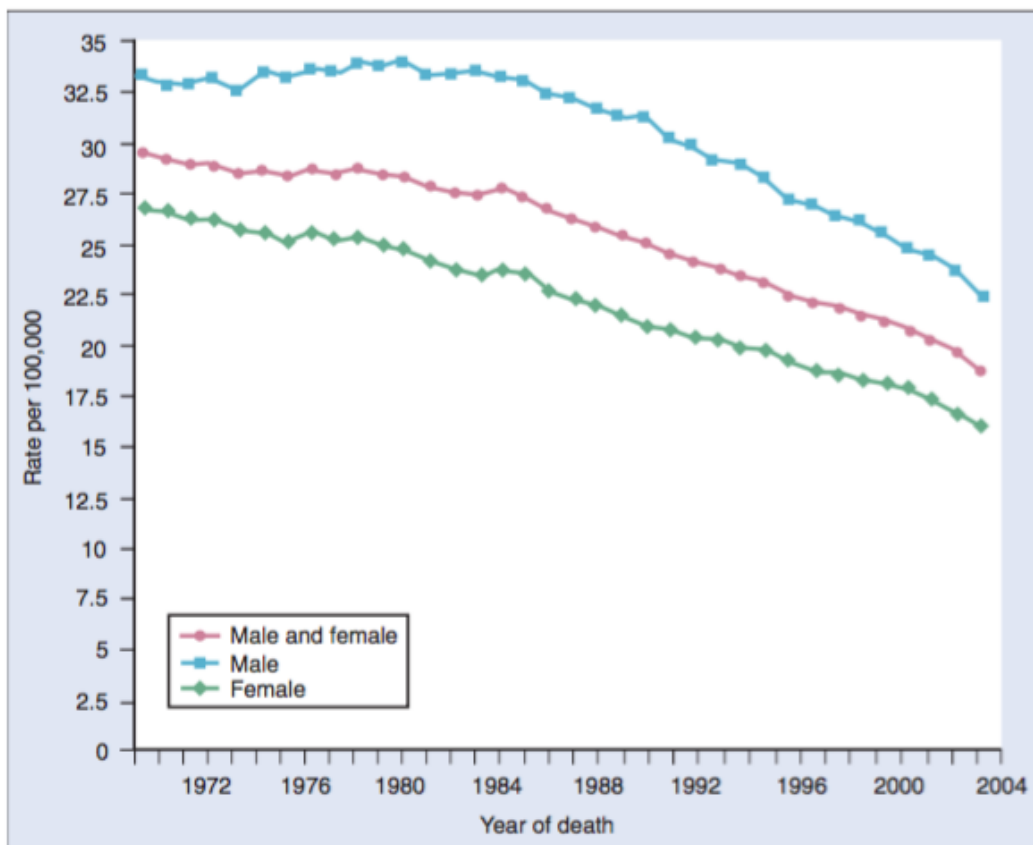
Proximal colonic cancers in general have a different biological profile. They tend to be chromosomally diploid and to have a relatively higher incidence of microsatellite instability (MSI). Right-sided cancers also become more common with advancing age and are relatively more frequent in women.[11]

In recent years, there has been a suggestion that right sided large bowel cancers have been increasing in incidence compared with more distal tumors. This area of study is complicated by differences in case ascertainment. (*Some populations, for example, have better access to colonoscopy services*). Development of colorectal cancer screening has also complicated this issue. Large-scale population based studies extending over several decades have tended to show, however, that there is no

fundamental anatomical shift that cannot be explained by age and gender differences.[12]

4- Mortality

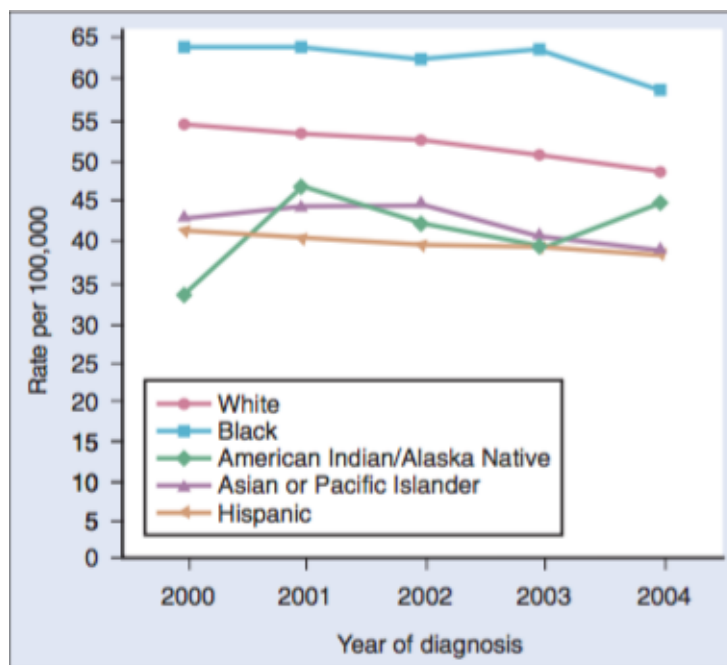
CRC is the third leading cause of cancer death in the United States. An estimated 49,920 individuals will die from CRC in 2008. This accounts for 9% of all cancer-related deaths. The 5-year survival rate is 64%. From 2000 to 2004, the median age at death for those with CRC was 75 years. CRC decreases life expectancy by an average of 13 years. Over the past 20 years, the mortality rate from CRC for both women and men has declined, especially in recent years, most likely as a result of significant advances in treatment modalities and improved screening.



**FIGURE 13: AGE-ADJUSTED MORTALITY RATES BY GENDER FOR COLON AND RECTAL
CANCER IN THE UNITED STATES, 1969-2004**

From 1985 to 2002, a 2% per year decrease occurred compared with a 5% per year decrease from 2002 to 2004. Men are more likely to die from CRC than women. This difference in survival has become less pronounced in recent years owing to a greater decline in mortality in men than in women.

Mortality for all racial and ethnic groups has declined except in American-Indian and Alaskan natives. Blacks have a worse prognosis after diagnosis than do whites



**FIGURE 14: AGE ADJUSTED INCIDENCE RATES BY RACE FOR COLON AND RECTAL
CANCER IN THE US 2000-2004**

III–Risk factors:

Epidemiologic studies have identified many factors that may increase or decrease risk of CRC. Some of these factors, such as a personal or family history of CRC or a history of inflammatory bowel disease, are non-modifiable, but many lifestyle risk factors, such as smoking, alcohol use, and lack of physical activity, are modifiable.

It was recently reported that following a healthy lifestyle that includes being physically active for at least 30 minutes per day, following a healthy diet, controlling abdominal adiposity, not smoking, and not drinking alcohol in excess could have prevented 23% of the CRC cases in a cohort of more than 50,000 people aged 50–64 years, who were cancer-free at baseline and followed up for an average of 10 years. Genetic susceptibility due to inherited germline mutations is the cause of CRC in about 5% of patients; however, most cases are sporadic, not familial.[8]

1– Age:

Age is a major risk factor influencing CRC incidence and death rate, because both rates increase with age. Over 90% of new CRC cases and deaths occur in people older than 50 years. However, CRC incidence rates in that age group have been steadily declining since the mid-1980s, whereas incidence rates in people younger than 50 years have consistently increased since the early 1990s.

Researchers are not sure what is causing the increase in younger adults, but a recent study found that young-onset CRC was more prevalent than later-onset CRC among patients of non-white race/ethnicity, and patients living in the Southern and Western US. Younger patients also had a more advanced stage at diagnosis, location

distal to the splenic flexure or in the rectum, a mucinous or signet ring histologic subtype, and poor or no cell differentiation.

2– Sex:

Worldwide, men are at greater risk for CRC than women, with a sex ratio of 1.5. but the reasons for the difference in CRC incidence and mortality rates by sex are not well understood.

The sex-specific differences may be related to hormonal risk factors, differences in screening and access to medical care, and sex-specific genetic and molecular interactions with environmental risk factors. Sex also affects the CRC site, men having a higher incidence of rectal cancers (31% of CRCs) than women (24%).[13]

3– Genetic predisposition:

Roughly 5% of CRC cases are attributable to a genetic predisposition. That is, inherited mutations in certain key genes result in a greatly increased lifetime risk of CRC. Several genetic susceptibility syndromes predispose people to CRC, the most common of which is:[14]

3-1 Lynch syndrome HNPCC

People with Lynch syndrome inherit germline mutations in one of the DNA mismatch repair genes, *MLH1*, *MSH2*, *MSH6*, or *PMS2*, and this predisposes them to cancers of the colorectum, endometrium, ovary, stomach, small intestine, hepatobiliary tract, urinary tract, brain, and skin.

These mutations have an autosomal dominant pattern of inheritance, so offsprings have a 50% probability of being affected. Other characteristics of CRC associated with genetic susceptibility include an earlier age at onset (the median age at CRC diagnosis is 45 years in patients with Lynch syndrome), multiple family members may be affected, and patients are susceptible to develop other primary cancers besides CRC.

Cancers are largely right-sided in patients with Lynch syndrome as compared to left-sided in sporadic CRC, and tumors in patients with Lynch syndrome display characteristic microsatellite instability.

Histologically, tumors in these patients exhibit poor differentiation, tumor infiltrating lymphocytes, and mucinous, signet ring, or cribriform histology.

Immunohistochemical staining of the tumors for loss of DNA mismatch repair protein, microsatellite instability testing, and family history are the hallmarks of screening for suspected Lynch syndrome mutation carriers prior to definitive mismatch repair gene mutation testing. Other, less common genetic susceptibility syndromes include: Familial adenomatous polyposis, Peutz-Jeghers syndrome, and mutY homolog (*MUTYH*)- associated polyposis.

3-2 Familial adenomatous polyposis:

FAP accounts for less than 1% of CRCs and is caused by mutations in the *APC* gene; its characteristic phenotype is early onset of multiple (up to thousands) adenomas, which lead to CRC if untreated. An attenuated form of familial adenomatous

polyposis with a less severe polyposis phenotype is due to mutations in *APC* at different sites.

3-3 Peutz-Jeghers syndrome:

Peutz-jeghers syndrome is another rare syndrome, caused by mutations in the *STK11* (alsocalled *LKB1*) gene. Patients with Peutz-Jeghers syndrome develop characteristic hyperpigmentation of the lips, fingers, and toes and are at increased risk of developing hamartomatous polyps in the digestive tract and of breast, colorectal, and other cancers.

3-4 MUTYH-associated polyposis:

Patients with *MUTYH*-associated polyposis present with multiple colorectal adenomas or CRC as a result of autosomal recessively inherited bi-allelic mutations in the base excision repair gene *MUTYH*.

4- Family history:

Family history is an important risk factor for CRC, even without the increased familial risk due to genetic predisposition syndromes. Familial risk is likely to be an interaction of genetic and environmental causes. Having a first-degree relative (parent, sibling, or child) with CRC increases CRC risk to almost double that of the general population, and CRC risk is increased further if two first-degree relatives are affected or if a family member is diagnosed with CRC at younger than 60 years. [14]

A family history of large (>1 cm) adenoma or histologically advanced adenoma is associated with roughly the same risk of CRC as a family history of CRC.

5- Personal medical history

A history of adenomas, prior CRC, and inflammatory bowel disease significantly increases the risk of CRC. Patients with a prior history of large (>1 cm) adenomatous polyps or villous or tubule-villous polyps, particularly a history of multiple polyps, are considered to be at increased risk of CRC.

Among CRC patients with a history of resection of a single CRC, 1.5–3% are likely to develop metachronous primary CRC during the first 5 years postoperatively.[15]

6- Obesity

Increasing rates of obesity worldwide and particularly in the US are of growing concern, because obesity has been linked to many types of cancer, including CRC. In a large prospective cohort of male health professionals, increasing body mass index (BMI) was associated with an increasing trend in risk for CRC. Furthermore, abdominal adiposity was also associated with risk of CRC, even after adjusting for BMI. Similarly, in an analysis of obesity and CRC risk among women in the Nurses' Health Study prospective cohort, compared with women of normal weight, obese women were 1.5 times more likely to develop CRC.

7- Diabetes mellitus

The association between diabetes mellitus and increased risk for CRC is becoming increasingly strong. [16] A recent meta-analysis concluded that there was a 38% increase in risk for colon cancer and a 20% increase in risk for rectal cancer in patients with diabetes compared with those without diabetes, and the association was evident even after controlling for other risk factors including smoking, obesity, and physical activity.

8- Physical activity

There is strong evidence linking physical activity with decreased risk of CRC. In a meta-analysis of 52 cohort and case-control studies, an inverse association between physical activity and colon cancer was found in both men and women. Regular leisure time and occupational physical activity are also associated with protection from CRC.

9- Diet

9-1 Fruits and vegetables:

The relationship between consumption of fruits and vegetables and CRC risk has been inconclusive. Some studies have found an inverse association between fruit and vegetable intake and CRC risk, comparing highest with lowest intakes of fruits and vegetables (RR 0.92; 95% CI 0.86-0.99), whereas other large cohort and pooled studies have shown a weak or no protective effect. The weak protective effect appears to be limited to distal colon cancers. Measurement of dietary exposures that depends on dietary recall can be challenging, and the imprecision of this measure may explain the heterogeneity in results.

9-2 Red meat consumption

Consumption of red meat or processed meat has been found to be associated with increased risk of CRC in many studies. A meta-analysis of prospective studies found a 22% (RR 1.22; 95% CI 1.11-1.34) increase in risk of CRC in the highest compared with the lowest intake of red and processed meat. In addition, there was a dose-response relationship: for every 100 g/day increase in consumption, the CRC risk increased by 14%, and the associations with CRC risk were similar for colon and rectal cancer.

9-3 Fiber:

Results from studies of dietary fiber and CRC risk have been inconsistent. In many studies, fiber was found to be associated with a decreased risk of adenomas and CRC, but others found no association or only a modest association.

The World Cancer Research Fund/American Institute for Cancer Research reported a meta-analysis showing strong evidence that consumption of foods containing dietary fiber, in particular fiber from cereals and whole grains, protects against CRC.

9-4 Calcium and dairy:

Dietary or supplemental calcium has been associated with a protective effect in CRC risk in several large cohort studies and pooled analyses, showing a 24-35% reduction in risk in the highest compared with the lowest levels of calcium intake.

9-5 Smoking:

Cigarette smoking is a preventable risk factor that is linked to many types of cancer, including CRC.

A large meta-analysis of more than 100 studies found an 18% increase in risk of developing CRC among smokers compared with non-smokers (RR 1.18; 95% CI 1.11-1.25).[17]

9-6 Alcohol:

Alcohol consumption has been associated with an increased risk of CRC. In a meta-analysis of alcohol drinking and CRC risk across 27 cohort and 34 case-control studies, risk was increased by 21% for moderate drinkers (2-3 drinks/day) and by 52% for heavy drinkers (≥ 4 drinks/day) compared with non-drinkers and occasional drinkers. Furthermore, in a dose-response analysis, RR increased with the amount of alcohol consumed, ranging from 7% in light drinkers (10 g/day) to 82% in those consuming 100 g/day.[18]

9-7 Drugs and supplements:

Many compounds such as aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs), COX-2 selective inhibitors, resistant starch, sulindac, hormones, bisphosphonates, statins, and supplements such as calcium, vitamin D, selenium, and folates may have a chemopreventive effect on colorectal adenomas and CRC. [19]

There is strong evidence that aspirin and COX-2 selective inhibitors such as celecoxib and rofecoxib reduce the risk of CRC. However, the harms, such as risk of bleeding and cardiovascular toxicity, outweigh the benefits. Therefore, the consensus statement from the US Preventive Services Task Force advises that these agents should not be used for the prevention of CRC in asymptomatic adults at average risk for CRC.

IV. Pathology of colorectal cancer

1 – General organization of the colonic wall

Under the scrutiny of light microscopy, colonic wall architecture recapitulates the general organization of the entire gastrointestinal tract as observed from proximal esophagus to anus: *mucosa* overlying *submucosa* that in turn is bounded by distinct inner circular and outer longitudinal smooth muscle layers (collectively known as the muscularis propria), the antagonistic actions of which serve to propel ingested material through proximal and distal regions.

Deep to this, a connective tissue sheath envelops the muscularis where the colon is bounded by visceral peritoneum, a loose connective tissue zone termed the 'subserosa', is covered by a thin layer of mesothelium, the serosa.

In partially or fully non-peritonealised colonic segments, such as the ascending colon and rectum, tissue identical to the subserosa is bounded by deeper fascial planes such as the anterior renal fascia of Gerota and the mesorectal fascia, respectively. Knowledge of such fascial planes is of critical importance, to both surgeons and pathologists, to ensure effective operative/postoperative patient management.

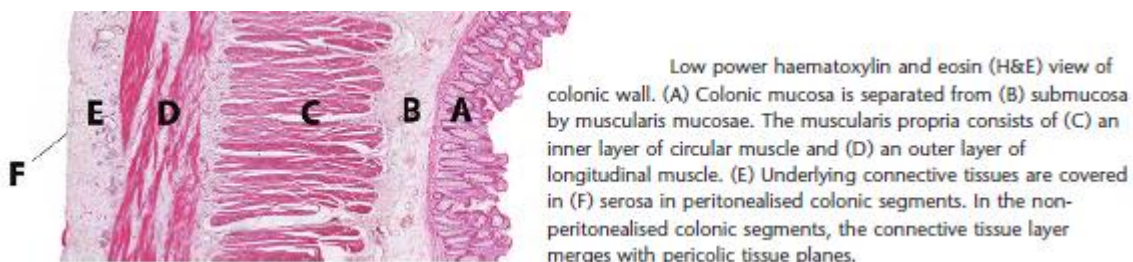


FIGURE 15: LAYERS OF THE COLONIC WALL

2- Pathways to colorectal adenocarcinoma development

Adenocarcinomas comprise the vast majority (95%) of colorectal malignancies. Colonic adenomas are precursor lesions, with about 5% eventually developing into adenocarcinomas, usually over 10–20 years. Rare colorectal cancers include carcinoid tumors, gastrointestinal (GI) stromal tumors (GISTs), lymphomas, and sarcomas.

The mechanism by which colorectal cancer arises is not completely understood, but it is believed to be multifactorial and involve a multistep process. At least three pathways are known to exist, as follows:

- Chromosomal instability
- Microsatellite instability
- CpG island methylator phenotype

Chromosomal changes in portions of chromosome 5q, 18q, and 17p have been implicated in the disease process, affecting genes such as *APC*, *TP53* and *DCC/MADH2/MADH4*, as well as mutations of the *KRAS* oncogene.

Several broad clinicopathological pathways that lead to the development of colorectal carcinoma are now recognized (Table below) FAP and HNPCC exemplify inherited pathways, whereas longstanding IBD is considered a separate pathway arising from repeated mucosal injury.

The remaining bulk of colorectal carcinoma, most often termed ‘sporadic’ to distinguish it from the other pathways, was at first considered a homogenous entity. Progression of adenoma to carcinoma, central to tumor development in FAP patients,

was identified by Morson as the most likely pathway for the pathogenesis of sporadic tumors too: the adenoma–carcinoma sequence.

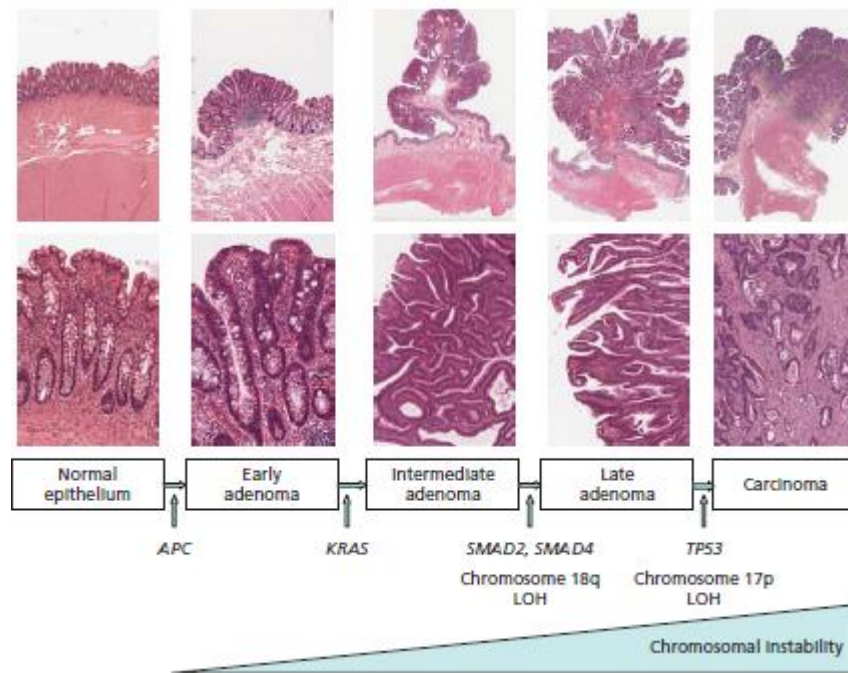


FIGURE 16: THE CLASSICAL ADENOMA–CARCINOMA SEQUENCE.

The initiation of tumorigenesis through *APC* gene mutation, followed by progressive accumulation of genetic and chromosomal damage, was related by Vogelstein and colleagues to progression from early adenoma to adenoma with high grade dysplasia and then to adenocarcinoma.

However, more recent clinico–pathological and molecular genetic studies have identified sporadic tumors that do not fit this classic model and are instead thought to arise along a novel pathway often termed the ‘serrated pathway’. Such tumors lack an initiating *APC* gene mutation, exhibit high levels of DNA methylation and MSI and demonstrate a serrated architecture on histopathological examination.

1. **Inherited pathways**
 - a. Familial adenomatous polyposis
 - b. Lynch syndrome (HNPCC)
 - c. *MYH*-associated polyposis
 - d. Serrated polyposis
 - e. Juvenile polyposis
2. **Sporadic pathways**
 - a. Conventional
 - b. Serrated
3. **Inflammatory bowel disease-associated pathway**

FIGURE 17: PATHWAYS TO COLORECTAL CARCINOMA

3– adenoma–carcroma sequence

Although a quarter century ago there was considerable controversy over the concept that a benign polyp is a precursor to cancer, the evidence from many fronts provides such strong support for the adenoma–carcinoma sequence that this concept is generally unquestioned today. It is naive to assume that all colorectal polyps are predestined to become cancerous, and there have been documented cases (especially in the Japanese literature) that occasionally large bowel cancers can arise directly from the mucosa without being associated with a benign precursor. Nevertheless, our understanding of the process of colorectal carcinogenesis assumes the fact that most cancers arise from benign polypoid precursors.

the incidence of both benign polyps and colon cancers increases with patients' age, with the polyps' rising incidence preceding that of the cancers' by about 7–10 years. This suggests a 7–10 year "dwell time" for benign polyp to acquire malignant characteristics.

4– Conventional adenoma

Conventional adenomas, well characterized and commonly seen in gastrointestinal pathology practice, are the precursor lesions for most colorectal adenocarcinomas. They are defined by the presence of dysplasia which, in turn, is defined as unequivocal intra-epithelial neoplastic change.

The ‘conventional’ adenomas – tubular, tubulo-villous and villous adenomas – are the best characterised of the colorectal adenomas, but more recently it has been recognized that other forms such as sessile serrated, traditional serrated and flat adenomas play an incompletely defined role in colonic carcinogenesis.

Endoscopic characteristics	Tubular adenoma (▣ 9.6)	Tubulovillous adenoma (▣ 9.7)	Villous adenoma (▣ 9.8)
Shape	Sessile or stalked	Sessile or stalked (thicker stalk than tubular adenoma), medium sized	Sessile, often > 3 cm
Surface	Normal to slightly erythematous	Erythematous	Pale yellow, irregular
Contour	Smooth to lobular	Nodular, lobular	Nodular, fingerlike processes, diffuse and tubular growth

FIGURE 18: ENDOSCOPIC CHARACTERISTICS OF HISTOLOGICALLY DIFFERENT ADENOMAS

<p>Epithelial</p> <p>Conventional adenoma</p> <ul style="list-style-type: none"> Tubular Tubulovillous Villous Flat adenoma <p>Serrated polyp</p> <ul style="list-style-type: none"> Hyperplastic (microvesicular, goblet cell, mucin poor) Sessile serrated adenoma Mixed polyp Traditional serrated adenoma <p>Polypoid adenocarcinoma</p> <p>Inflammatory</p> <p>Mucosal prolapse-associated polyp (includes polypoid prolapsing mucosal fold, inflammatory cloacogenic polyp, inflammatory myoglandular polyp, inflammatory cap polyp)</p> <p>Inflammatory pseudo-polyp</p> <p>Polypoid granulation tissue</p> <p>Infection-associated polyp (cytomegalovirus, schistosomiasis)</p> <p>Lymphoid</p> <p>Prominent lymphoid follicle/rectal tonsil</p> <p>Lymphomatous polyposis</p>	<p>Hamartomatous</p> <p>Peutz–Jeghers polyp</p> <p>Juvenile polyp</p> <p>Cowden syndrome and Bannayan–Riley–Ruvalcaba syndrome</p> <p>Cronkite–Canada syndrome</p> <p>Stromal</p> <p>Inflammatory fibroid polyp</p> <p>Fibroblastic polyp/peri-neurioma</p> <p>Schwann cell hamartoma</p> <p>Neurilemmoma and nerve sheath tumour variants</p> <p>Ganglio-neuroma</p> <p>Leiomyoma of muscularis mucosae</p> <p>Lipoma</p> <p>Lipohyperplasia of ileo-caecal valve</p> <p>Gastrointestinal stromal tumour</p> <p>Neurofibroma</p> <p>Granular cell tumour</p> <p>Endocrine</p> <p>Well differentiated endocrine (carcinoid) tumour</p>
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FIGURE 19: CLASSIFICATION OF COLORECTAL ADENOMAS



Large villous adenoma

FIGURE 20: LARGE VILLOUS ADENOMA

4-1 Macroscopic features

Macroscopically, several features of adenomas relate to their behavior. The size of the adenoma is important for several reasons. It is related to the likelihood of malignant transformation, and also to the risk of synchronous and metachronous adenomas. Diminutive polyps <5 mm only rarely (<2%) have advanced features, i.e. villous architecture or high grade dysplasia, and are not associated with carcinoma.

Small lesions 5–10 mm diameter have been shown to have advanced features in 10% and carcinoma in almost 1%, so they have a low but definite malignancy risk. The majority of adenomas removed, over 80–90%, are tubular adenomas <10 mm.

Adenomas >10 mm are regarded as advanced adenomas, but even some do not progress to invasive adenocarcinoma. In a follow-up study of barium enema-detected polyps >10 mm found before the routine use of colonoscopy, 37% of the polyps increased in size and 10% of patients developed carcinoma at the site of the polyp over a mean period of 108 months.

Importantly these polyps had not been biopsied and so the precise identification of the initial lesion is not known. In that study, actuarial analysis suggested an 8% carcinoma risk at 10 years and 25% at 20 years. In addition, 5% of patients developed a colorectal adenocarcinoma remote from the original polyp.

Macroscopically, adenomas have traditionally been described as pedunculated or sessile. More recently, this has been refined to include flat and depressed lesions.

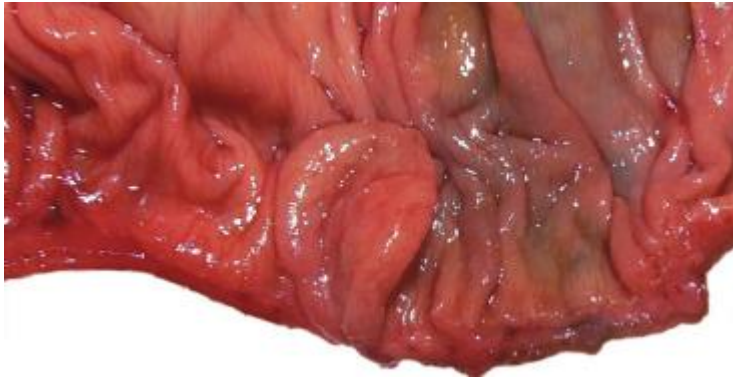


FIGURE 21: SESSILE SERRATED ADENOMA (LESION): THE LESION IS SLIGHTLY ELEVATED.

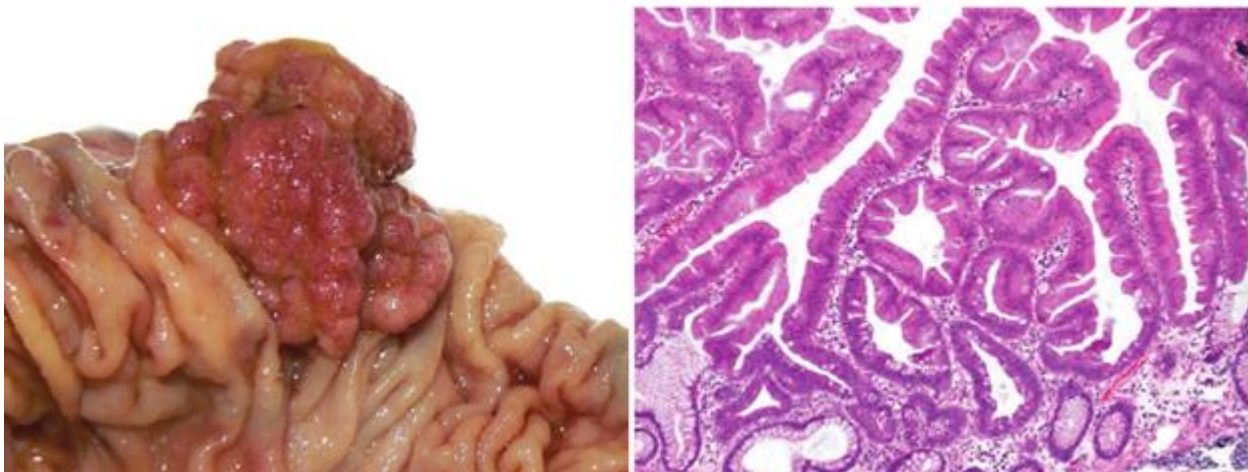


FIGURE 22: MACROSCOPY AND MICROSCOPY OF ADENOMA

Macroscopic: Traditional serrated adenoma with polypoid growth.

Microscopy: Traditional serrated adenoma with characteristic serration of crypt and abundant eosinophilic cytoplasm of the dysplastic epithelium.



FIGURE 23: FLAT ADENOMA WITH NO ELEVATION ABOVE THE SURROUNDING MUCOSA



FIGURE 24: SESSILE ADENOMA WITH LOBULATED APPEARANCE



FIGURE 25: FAMILIAL ADENOMATOUS POLYPOSIS

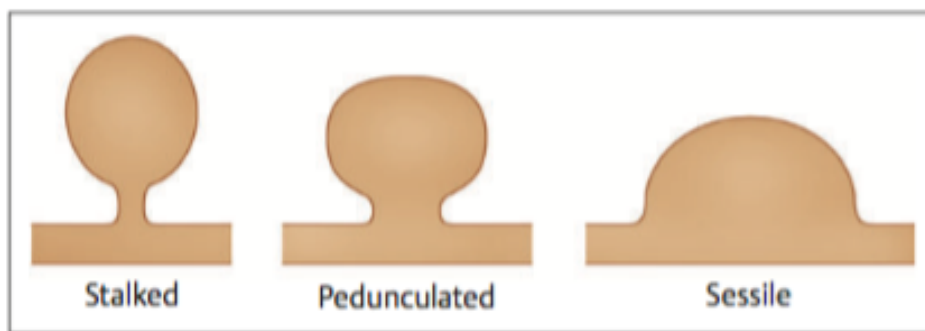


FIGURE 26: MACROSCOPIC GROWTH FORMS OF COLORECTAL ADENOMA.

4-2 Microscopic appearance

Microscopically, two key features are used to define and classify conventional adenomas: the architecture and the degree of dysplasia (intraepithelial neoplasia).

The architectural pattern assesses the proportion of tubular elements, characterised by epithelial glands surrounded by lamina propria, and villous elements in which the epithelial lining contains the lamina propria. Thus, the tubular and villous elements in an adenoma can be likened to the structure of crypts and villi in the small intestine.

Tubular adenoma is composed of tubular crypts, usually more closely packed than the adjacent normal mucosa, and by definition has less than 20% of villous elements using the World Health Organization (WHO) criteria.

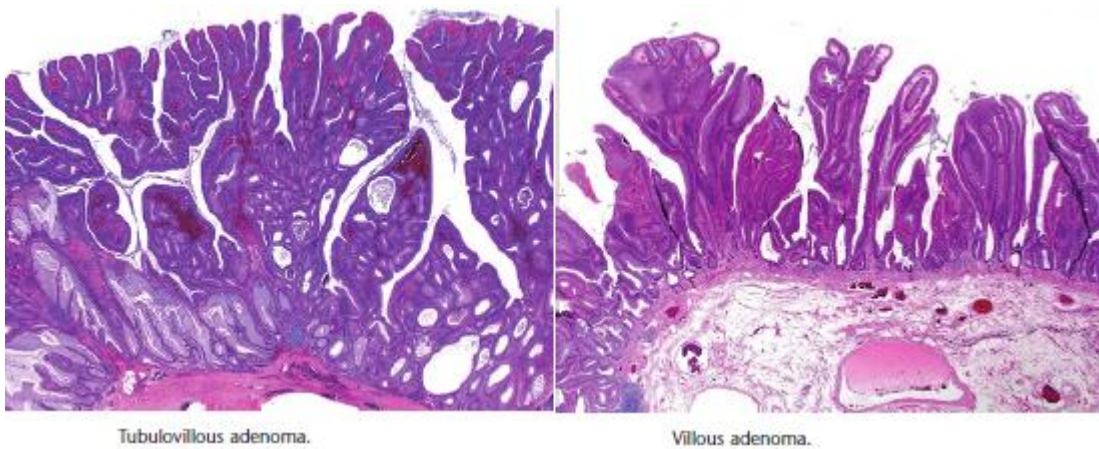


FIGURE 27: TUBULO-VILLOUS ADENOMA AND VILLOUS ADENOMA

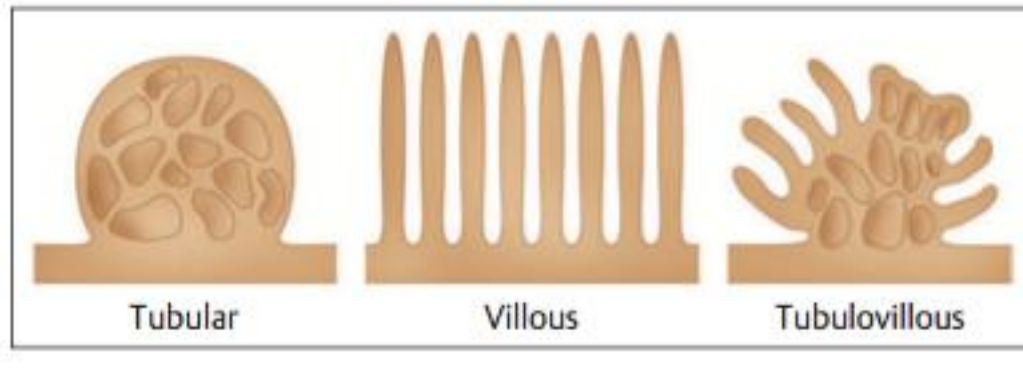


FIGURE 28: HISTOLOGICAL TYPES OF ADENOMA

Dysplasia (intra-epithelial neoplasia) is characterised by hypercellularity, nuclear enlargement with hyperchromasia and crowding. The nuclei show a variable degree of loss of polarity and stratification, are mitotically active and in most cases have a pencillate shape. More severely dysplastic nuclei may be oval and vesicular with a prominent nucleolus.

Some conventional adenomas have intensely eosinophilic cytoplasm. Mucin is variably reduced and atypical or dystrophic goblet cells may occur, often with reversed or 'upside-down' polarity. Previously graded as mild, moderate or severe, dysplasia in adenomas is now graded using a two-tier system of low grade and high grade.

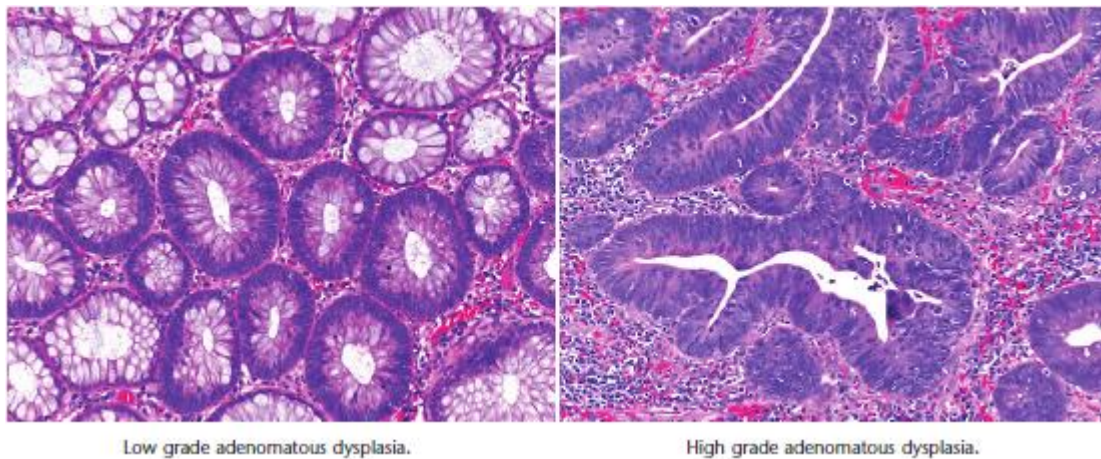


FIGURE 29: LOW AND HIGH GRADE ADENOMATOUS DYSPLASIA

- **In low grade dysplasia**, the nuclei are relatively uniform and pencillate, and mostly located in the basal half of the cell with cytoplasm on the luminal side. Invariably rare nuclei will extend into the apical half, but this is not prominent. Conversely.
- **high grade dysplasia** shows more marked stratification with nuclei extending prominently into the apical half of the cells and having greater nuclear pleomorphism.

5- colorectal adenocarcinoma

5-1 Macroscopic pathology

Carcinomas of the large bowel present in a range of macroscopic appearances. These vary somewhat with the anatomical site of origin within the colorectum.

Conventionally a number of distinct macroscopic forms of large bowel cancer have been recognized: polypoid, exophytic/fungating, ulcerating, circumferential, stenosing and diffusely infiltrating.

These morphological subtypes have been defined largely by pathologists who were looking at fully opened specimens. As current gross dissection protocols more commonly call for preservation of the intact tumor during fixation and subsequent examination in transverse sections.

Most colorectal cancers start as polyps and early carcinomas can be macroscopically indistinguishable from adenomas. These specimens are usually removed at endoscopy.

The earliest grossly visible changes include formation of depressed areas on the polyp surface. Eventually the carcinoma overwhelms the adenoma, leaving an ulcer with raised rolled edges. Sometimes the polypoid nature of the tumor is evident even in quite large lesions (figure below). Superficial ulceration and excavation in larger polyps will lead to an exophytic or fungating appearance.



Caecal carcinoma seen in transverse section as a macroscopically polypoid mass lesion filling much of the lumen. The tumour was invasive into the stalk but not beyond the submucosa.

FIGURE 30: CAECAL CARCINOMA

All of these bulkier macroscopic types are more frequently seen in the caecum and ascending colon, reflecting the fact that there is relatively more luminal space for growth in these parts of the large bowel.

As a tumor enlarges there is a tendency towards circumferential involvement of the bowel. Cancers arising in sessile or flat adenomas progress more rapidly to ulcerative, deeply invasive lesions. The classic ulcerated tumor plaque with raised rolled edges is most commonly seen in the rectum.

In the transverse colon, descending colon and sigmoid cancers often present as tightly stenosing lesions. On cross-section the normal bowel wall has 'disappeared' and been replaced by an infiltrative, scarred, tumor that can be surprisingly lacking in bulk.

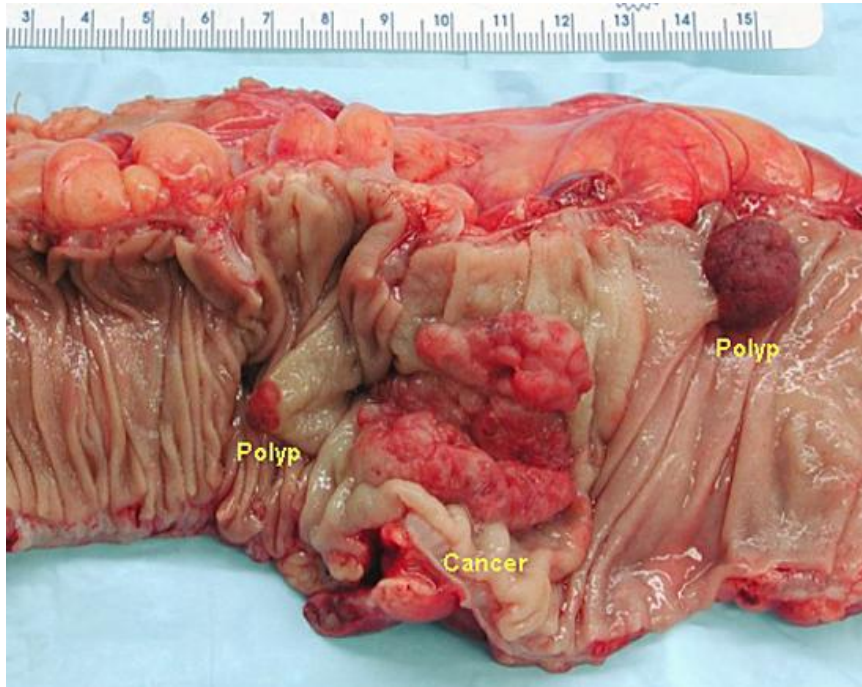


FIGURE 31: STENOSING COLON CARCINOMA

5-2 Microscopic pathology:

When compared with many other visceral carcinomas, colorectal cancers are remarkably homogeneous on microscopic examination with the great majority being moderately differentiated adenocarcinomas. As with other epithelial cancers differentiation is used as a pathological descriptor of variation from the norm in terms of glandular morphology.

Well differentiated cancers tend to show an ‘adenomalike’ morphology with recognisable tubular structures lined by columnar cells.

Moderately differentiated cancers show a lesser resemblance to adenomatous epithelium and often show accumulation of necrotic debris and acute inflammatory cells within the neoplastic glandular lumina.

Poorly differentiated cancers are best defined by a tendency to lose glandular architecture, with the Tumor being made up of sheets or discohesive clumps of neoplastic cells, often showing higher grade cytological atypia.

There are some morphological differences between right and left-sided cancers, mainly reflecting the higher proportion of right-sided tumors arising via the serrated and/or MMR(mismatch repair) pathway. Carcinomas arising via this route are more often poorly differentiated, more likely to have a Crohn’s disease-like inflammatory reaction and increased numbers of intra-epithelial lymphocytes, and to show mucinous differentiation.

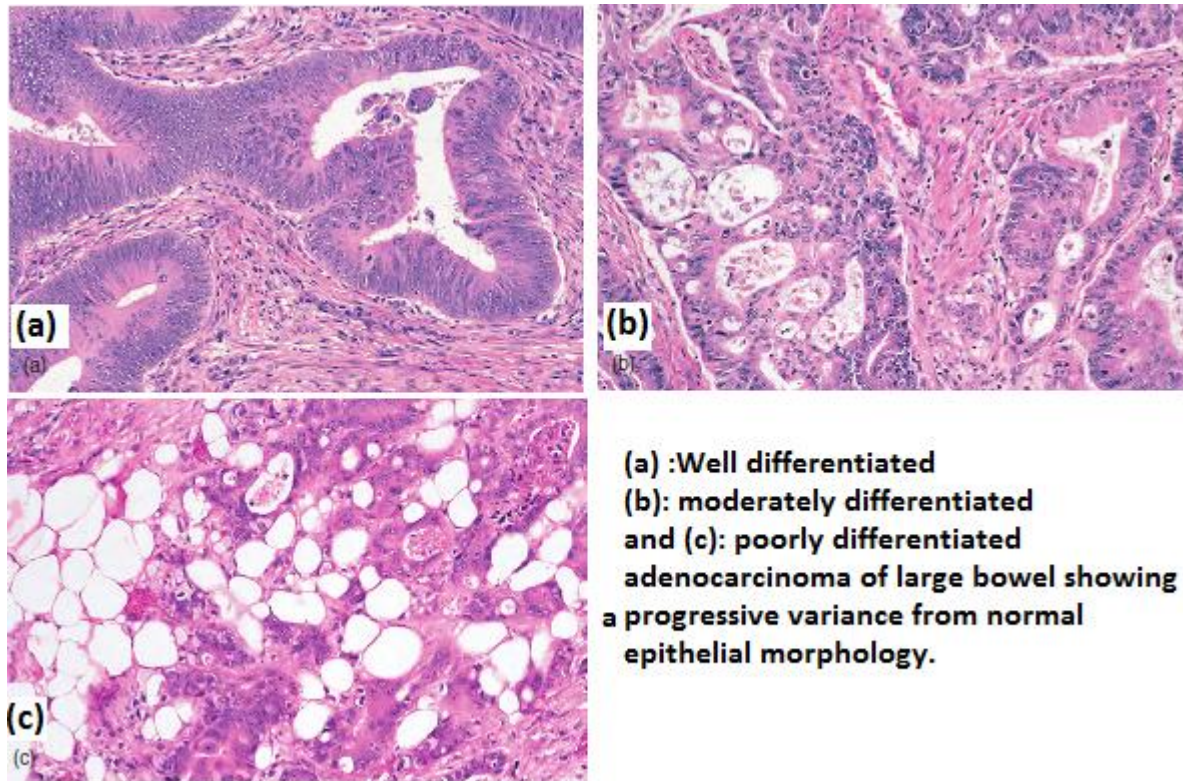


FIGURE 32: DIFFERENTIATION OF ADENOCARCINOMA

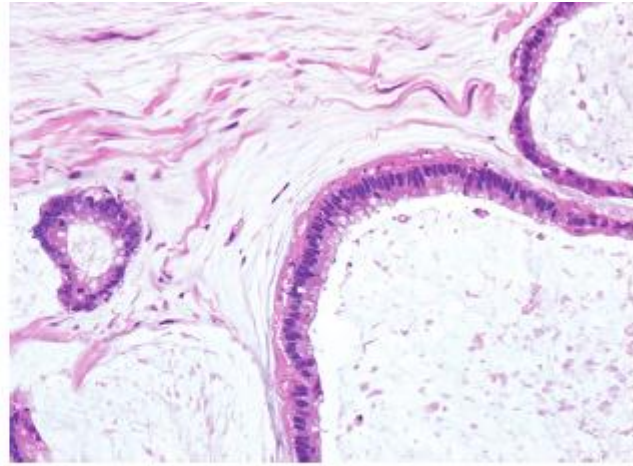
6-Mucinous tumors

Mucinous tumors account for approximately 10% of colorectal cancers. Focal mucin production is a very common feature in carcinoma and the term ‘mucinous carcinoma’ is reserved for cases where substantial extracellular deposits of mucus are seen in over 50% of the cut surface of the tumor.

This can often be appreciated on gross inspection of the tumor cut surface (figure below).



Mucinous carcinoma of the right colon arising in the vicinity of the ileo-caecal valve. The cut surface of the gross specimen shows abundant glistening mucus.



Microscopic section of a grossly obvious mucinous carcinoma (Figure 38.12) showing that the mucin is produced by a well differentiated carcinoma with an obviously mucinous epithelium.

FIGURE 33: MUCINOUS CARCINOMA OF THE RIGHT COLON

7-Synchronous colorectal cancers

In patients presenting with colorectal carcinoma a second (synchronous) carcinoma is identified in 1-5% of cases. This is more commonly seen in those with predisposing conditions such as familial cancer syndromes and IBD.

In many individuals, the presence of synchronous malignancy reflects a tendency to adenoma formation. A different phenomenon is evident in IBD where the presence of multiple neoplasms may be a reflection of 'field cancerization', a carcinogenic pathway more often seen in squamous epithelia of the head and neck and in Barrett's esophagus.

8-Spread of colorectal cancer

As with any carcinoma colorectal cancer can spread by direct local invasion, through lymphatics and blood vessels, and along nerve trunks.

Local invasion may involve adjacent viscera (other parts of intestine, urogenital tract), the anterior abdominal wall or the retroperitoneum. Direct involvement of the peritoneal (serosal) covering of the bowel is an important route of tumour spread. Once the serosa is penetrated malignant cells can readily cross the peritoneal cavity. Spread in this way quite commonly causes presentation as a large ovarian tumor mass and distinction from primary ovarian mucinous adenocarcinoma may prove difficult.

Lymphatic spread has long been recognised as a major prognostic parameter. It is very common to see clumps of tumor cells in thin-walled vessels in the wall of the colon (a feature that is, of itself, of clinical relevance only in localized resections for cancer). Detection of metastases in lymph nodes forms a major component of all prognostic systems. By the TNM/UICC convention this is defined as a nodal deposit seen on routine haematoxylin and eosin examination and measuring ≥ 0.2 mm in diameter. Smaller deposits are classified as either micro-metastases or isolated tumor cells, depending on whether or not they are aggregated into tumor cell clumps.

Spread of tumor through veins draining ultimately to the portal vein and liver is the primary route through which metastases in liver, lungs and ultimately other distant body sites may develop.

Detection of venous invasion in the primary tumor is a marker of propensity to spread in this fashion. Systematic studies have looked at the clinical implication of both intramural (within the wall of the bowel) and extramural venous invasion.

Prognostic studies have clearly shown that it is the presence of malignant cells in *muscular veins* that is of major clinical significance.

Perineural invasion by tumor is not uncommon, particularly in rectal cancers. There is evidence that this feature is an indicator of high risk of local recurrence and poor outcome.

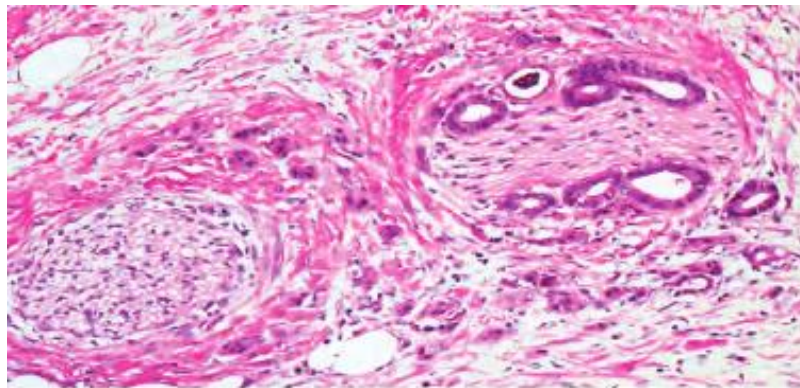


Figure Perineural invasion by carcinoma

FIGURE 34: PERINEURAL INVASION BY ADENOCARCINOMA

9- Pathological staging of colorectal cancer

9-1 TNM classification:

As with most visceral malignancies, the prognosis for a patient with colorectal carcinoma is heavily dependent on tumor stage.

Dukes' staging (originally described in rectal cancer in 1932) was the first attempt to combine some measure of local tumor invasion with spread to lymph nodes. The main problem with this classification is that most resected cancers are Dukes' B and better selection is needed to identify those in this group that are at most risk of progressive disease.

Modifications and developments of Dukes' approach, including those of Astler and Coller, have addressed some of the issues in the older classification.

The Astler–Coller system has advantages in that it defines a larger number of prognostically distinct groups but, as with many cancers, international opinion has now largely come to accept the TNM (tumour, node, metastasis) approach, which has the same advantages but avoids the confusing overlap in the 'ABC' nomenclature. The TNM classification (table below) is now in its seventh edition.

Table Staging of colorectal cancer

	TNM	Dukes	Astler–Coller
Direct spread			
Mucosa	Tis (TIE and TIM) ^a	–	A
Submucosa	T1	A	B1
Muscle coat	T2	A	B1
Beyond muscle	T3	B	B2
Transperitoneal (free surface)	T4A	B	B2
Involving adjacent organs	T4B	B	B2
Lymph node spread			
None	N0	(A/B)	(A/B1/B2)
1–3	N1	C1	C1/C2 ^b
>3	N2	C1	C1/C2 ^b
Apical node	N1/N2	C2	C1/C2 ^b
Residual local tumour (transection of tumour)	R1 ^c	d	d
Distant spread	M1 ^e	d	d

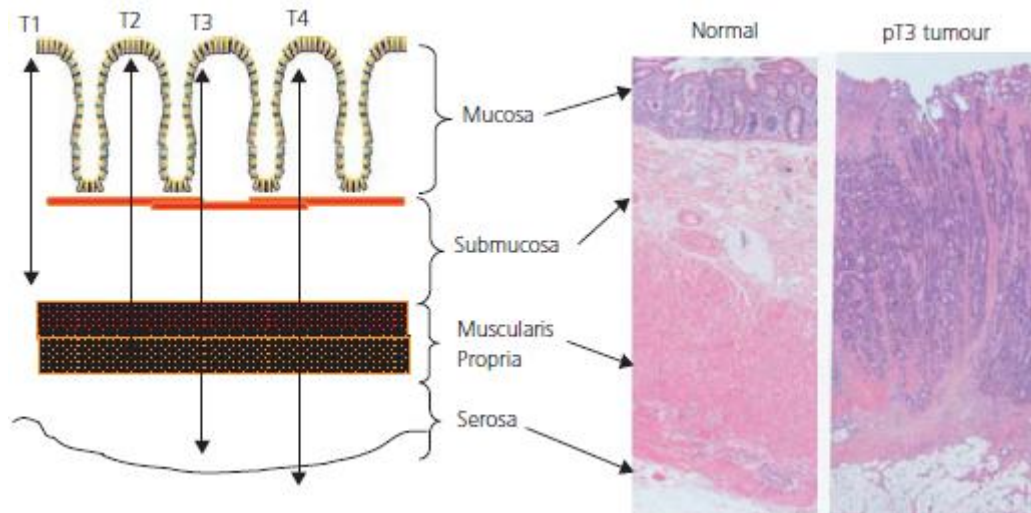
^aTIE, intra-epithelial; TIM, intramucosal.

^bC1, direct spread confined to wall; C2, spread beyond muscle coat.

^cR0, no residual tumour; R1, microscopic residual disease; R2, macroscopic residual disease.

^dAbsent, curative; present, palliative.

^eM0, no distant spread; M1, distant spread.

FIGURE 35: STAGING OF COLORECTAL CANCER**Figure 36: staging of colorectal cancer**

The TNM staging system has become the international standard for staging of colorectal cancer. It uses the following three descriptors:

- T for primary tumor
- N for lymph nodal involvement
- M for metastasis

Colon tumor categories are as follows: [20]

Tx: No description of the tumor's extent is possible because of incomplete information

Tis: In situ carcinoma; the tumor involves only the muscularis mucosa

T1: The cancer has grown through the muscularis mucosa and extends into the submucosa

T2: The cancer has grown through the submucosa and extends into the muscularis propria

T3: The cancer has grown through the muscularis propria and into the outermost layers of the colon but not through them; it has not reached any nearby organs or tissues.

T4a: The cancer has grown through the serosa (visceral peritoneum)

T4b: The cancer has grown through the wall of the colon and is attached to or invades nearby tissues or organs

Node categories are as follows:

Nx: No description of lymph node involvement is possible because of incomplete information

N0: No cancer in nearby lymph nodes

N1a: Cancer cells found in one nearby lymph node

N1b: Cancer cells found in two to three nearby lymph nodes

N1c: Small deposits of cancer cells found in areas of fat near lymph nodes, but not in the lymph nodes themselves.

N2a: Cancer cells found in four to six nearby lymph nodes

N2b: Cancer cells found in seven or more nearby lymph nodes

Metastasis categories are as follows:

M0: No distant spread seen

M1a: The cancer has spread to one distant organ or set of distant lymph nodes

M1b: The cancer has spread to more than one distant organ or set of distant lymph nodes, or has spread to distant parts of the peritoneum

stage	T	N	M	DUKES	ASTLER-COLLER
stage 0	Tis	N0	M0	"	"
stage I	T1	N0	M0	A	A
	T2	N0	M0	A	B1
stage II A	T3	N0	M0	B	B2
stage II B	T4	N0	M0	B	B3
stage III A	T1-T2	N1	M0	C	C1
stage III B	T3-T4	N1	M0	C	C2 C3
stage III C	any T	N2	M0	C	C1 C2 C3
stage IV	any T	N	M1	"	"
Union for International Cancer Control UICC classification					

TABLE 4: CANCER STAGING: TNM, DUKES AND ASTLER-COLLER**9-2 Poor prognostic features**

As well as tumor stage, other features of colorectal tumors have been identified which seem to be associated with a poor prognosis (Figure below). If these features are identified after histological examination, the patient may be considered for adjuvant chemotherapy.

In addition, the surgical margins will be assessed histologically. As with polyp cancers, the margin will be deemed involved by tumor (with the implication that resection is incomplete) if tumor cells are present either at the resection margin or within 1 mm of the resection margin. If there is margin involvement, then further therapy (such as radiotherapy) may be considered.

Table Prognostic features in colorectal cancer.

Poor prognostic features in colorectal cancer	Good prognostic features in colorectal cancer
pT4 (tumour perforation, breaching of serosal surface, invasion into surrounding organs)*	Microsatellite instability
Extramural vascular invasion*	Dense intra-tumoural lymphocytes
Poor differentiation (i.e. Grade 3)*	Pushing tumour edge
Involvement of resection margin*	
Recovery of small number of lymph nodes*	
Infiltrative tumour edge and tumour budding	
Peri-neural invasion	

FIGURE 37: PROGNOSTIC FEATURES IN COLORECTAL CANCER

V–Clinical presentation of colorectal cancer

1– patient’s history

A compassionately taken thorough history, complemented by a directed but gentle physical examination, is usually more revealing than a battery of sophisticated diagnostic tests in evaluating the patient with colorectal complaints. Disorders of this “unmentionable” part of the body are often embarrassing for the patient to discuss and require great tact on the part of the examiner.

The value of a carefully taken history cannot be overemphasized. It often uncovers pieces of the puzzle that allow for proper diagnosis. One of the rewards in medicine is finding on physical examination the problem that was suspected on taking the history.

1-1 Past medical history

A survey of the patient’s medical history should be included, with particular attention to prior colorectal problems, previous abdominal and anorectal operations, difficult labor or childbirth, and prior infections. Current prescription and over-the-counter medications must be reviewed. Laxative use or abuse is important to ascertain.

1-2 family history

A pertinent family history must be included in the patient interview. Familial adenomatous polyposis (FAP) is an inherited condition of colonic polyps that leads to early colorectal carcinoma. It is inherited in an autosomal dominant pattern.

Sporadic colorectal carcinomas (those without an inherited or identified cause) also show a familial tendency, especially for first-degree relatives (parents, siblings, or

children) When a positive family history involves multiple family members over two or more generations, the possibility of an inherited cancer syndrome must be considered.

2– Clinical presentation of a CRC patient

Patients with colorectal cancer may present in three ways:

- Suspicious symptoms and/or signs
- Asymptomatic individuals discovered by routine screening
- Emergency admission with intestinal obstruction, peritonitis, or rarely, an acute gastrointestinal (GI) bleed

There are no symptoms in the majority of patients with early stage colon cancer and these patients are diagnosed as a result of screening. Although the increasing uptake of CRC screening has led to more cases being diagnosed at an asymptomatic stage, most CRCs (70 to 90 percent in two contemporary series)[21]are diagnosed after the onset of symptoms. Symptoms of CRC are typically due to growth of the tumor into the lumen or adjacent structures, and as a result, symptomatic presentation usually reflects relatively advanced CRC.

2-1 Symptoms from the local tumor

Typical symptoms/signs associated with CRC include hematochezia (rectal bleed) or melena, abdominal pain, otherwise unexplained iron deficiency anemia, and/or a change in bowel habits. Less common presenting symptoms include abdominal distention, and/or nausea and vomiting, which may be indicators of obstruction.

Among symptomatic patients, clinical manifestations also differ depending on tumor location:

- **change in bowel habits** is a more common presenting symptom for left-sided than right-sided CRCs because fecal contents are liquid in the proximal colon and the lumen caliber is larger, and they are therefore less likely to be associated with obstructive symptoms.
- **rectal bleeding** (Hematochezia) is more often caused by rectosigmoid than right-sided colon cancer.
- **Iron deficiency anemia** from unrecognized blood loss is more common with right-sided CRCs. Caecal and ascending colon tumors have a fourfold higher mean daily blood loss (approximately 9 mL/day) than tumors at other colonic sites.
- **Abdominal pain** can occur with tumors arising at all sites; it can be caused by a partial obstruction, peritoneal dissemination, or intestinal perforation leading to generalized peritonitis.

2-2 Metastatic disease

Patients may also present with signs/symptoms of metastatic disease. Approximately 20 percent of patients in the United States have distant metastatic disease at the time of presentation.[22]CRC can spread by lymphatic and hematogenous dissemination, as well as by contiguous and transperitoneal routes.

The most common metastatic sites are the regional lymph nodes, liver, lungs, and peritoneum. Patients may present with signs or symptoms referable to any of these areas. The presence of right upper quadrant pain, abdominal distention, early satiety,

supraclavicular adenopathy, or periumbilical nodules usually signals advanced, often metastatic disease.

Because the venous drainage of the intestinal tract is via the portal system, the first site of hematogenous dissemination is usually the liver, followed by the lungs, bone, and many other sites, including the brain. However, tumors arising in the distal rectum may metastasize initially to the lungs because the inferior rectal vein drains into the inferior vena cava rather than into the portal venous system.

3- Impact of symptoms on prognosis

The presence of symptoms and their particular type provide some prognostic importance:

Patients who are symptomatic at diagnosis typically have more advanced disease and a worse prognosis. [23] In one study of 1071 patients with newly-diagnosed colon cancer, 217 of whom were diagnosed through screening, the patients not diagnosed through screening were at significantly higher risk for a more invasive tumor ($\geq T3$: relative risk [RR] 1.96), nodal involvement (RR 1.92), and metastatic disease on presentation (RR 3.37). In addition, patients not diagnosed through screening had significantly higher death rates (RR 3.02) and recurrence rates (RR 2.19) as well as shorter survival and disease-free intervals.

Obstruction and/or perforation, although uncommon, carry a poor prognosis, independent of stage. Among patients with node-negative colon cancer, obstruction or perforation are poor prognostic factors that may influence the decision to pursue adjuvant chemotherapy.

Tumors presenting with rectal bleeding (typically those involving the distal colon and rectum) have been thought to have a better prognosis because of their tendency to be diagnosed at an earlier stage; however, bleeding is not an independent predictor of outcome. Rectal bleeding is more commonly seen with distal tumors, and a larger proportion of distal colon cancers present as early-stage tumors as compared with proximal tumors.[24]

VI– DIAGNOSIS:

Colorectal cancer (CRC) may be suspected from one or more of the symptoms and signs described above or may be asymptomatic and discovered by routine screening of average and high-risk subjects. Once a CRC is suspected, the next test can be a colonoscopy, barium enema, or computed tomography colonography. However, examination of tissue is required to establish the diagnosis; this is usually accomplished by colonoscopy.

1 – Endoscopy:

Colonoscopy is the most accurate and versatile diagnostic test for CRC, since it can localize and biopsy lesions throughout the large bowel, detect synchronous neoplasms, and remove polyps.

Optical colonoscopy (OC) requires full laxative bowel preparation and sedation. It is expensive, occasionally causes bowel perforation, but has the advantage of immediate biopsy of detected lesions and can detect non-malignant process such as colitis. less invasive endoscopic methods are described below colonoscopy included.

1-1 Rigid proctosigmoidoscopy

Rigid proctosigmoidoscopic examination is anatomically limited by distal rectosigmoid angulations, and often will not negotiate the rectosigmoid junction. In practice, it detects about 25 – 30% of colorectal cancers, although a rate of 45% is theoretically possible based on recent UK data on distribution of cancers in the large bowel, if the rectosigmoid junction were always visualized. It is rarely used as the sole screening tool, and is much less comfortable than flexible sigmoidoscopy.

No special facilities are required, although training in technique and lesion recognition is essential. Because of the diagnostic limitations and discomfort associated with this examination, it is not used as a screening test.

1-2 Flexible sigmoidoscopy

Flexible sigmoidoscopy (video or fiber-optic) achieves more comprehensive views of the rectum and sigmoid colon than the rigid proctosigmoidoscope. While 30 cm and 60 cm instruments are available, the longer is the most commonly used. Its field of view is greater, with its size and flexibility allowing more comfortable insertion and manipulation around the rectosigmoid junction and sigmoid colon than the rigid sigmoidoscope. Significantly more neoplastic lesions are identified than with rigid sigmoidoscopy, and (with the 60 cm instrument) one-half to two-thirds of neoplasms are within its reach in practice.

This examination can be conducted without sedation and with enema preparation only, but the facilities required for instrument maintenance and disinfection are the same as those for colonoscopy. Instruments with a removable sheath have been developed that do not need disinfection.

1-3 Colonoscopy

Colonoscopy is the most accurate means of examining the colon. Combined with the ability to take biopsies and intervene therapeutically, it is the ideal diagnostic tool for follow-up after polypectomies²⁰. However, the need for vigorous bowel preparation and sedation of subjects, the time lost from employment, the need for trained personnel, limited availability in many countries, and the relatively high cost make it of questionable cost-effectiveness as the primary screening tool for the average-risk

subject. As with flexible sigmoidoscopy, appropriate training is essential, special facilities are necessary, and training in sedation is essential.

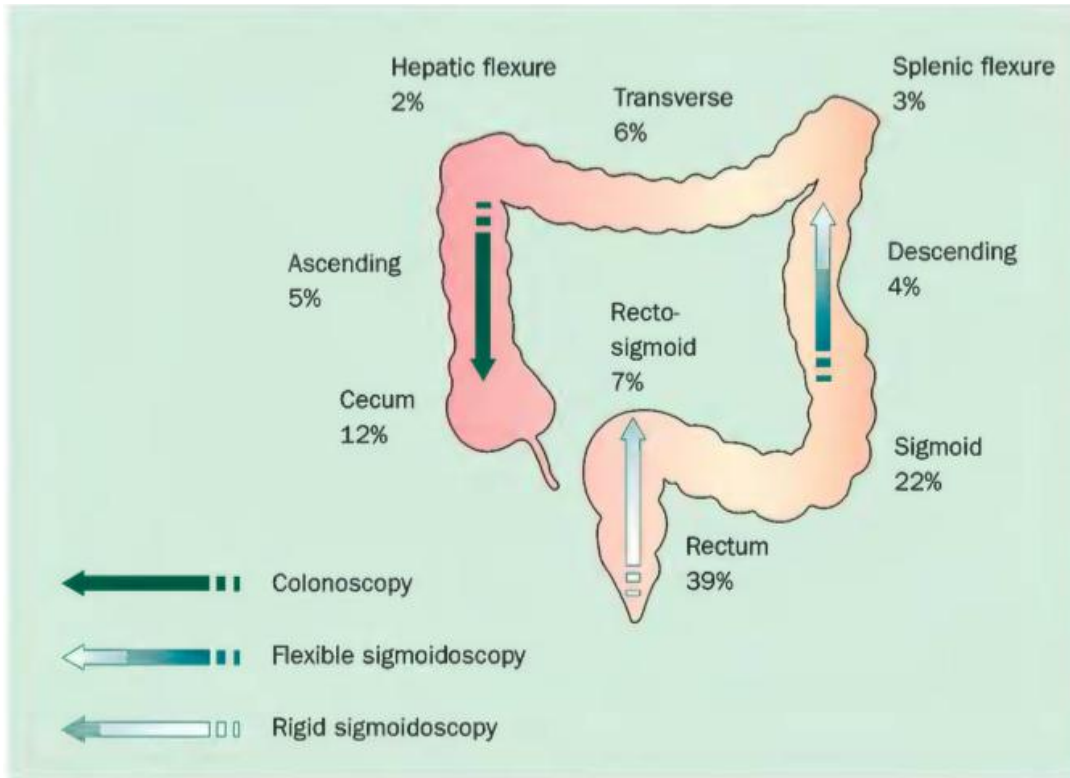
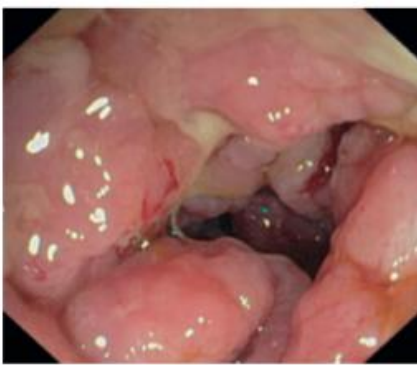


FIGURE 38: DIAGRAMMATIC REPRESENTATION OF THE OF THE VARIOUS ENDOSCOPIC METHODS

1. The proportions of colorectal cancers reached by rigid or flexible sigmoidoscopy or colonoscopy are limited by their reach into the colon.
2. While preparation for colonoscopy is complex, only an enema is required for flexible sigmoidoscopy. Inconvenience ranks similarly.
3. The facilities required for the flexible endoscopic procedures are substantial.
4. Training is necessary for all procedures, but is most complex for colonoscopy.

FIGURE 39: SUMMARY OF COLONOSCOPY PROCEDURES

1-4 pathological findings in colonoscopy



a



b



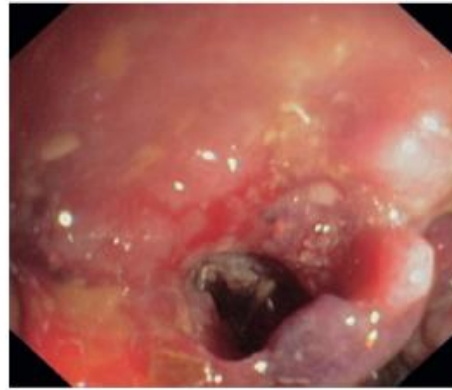
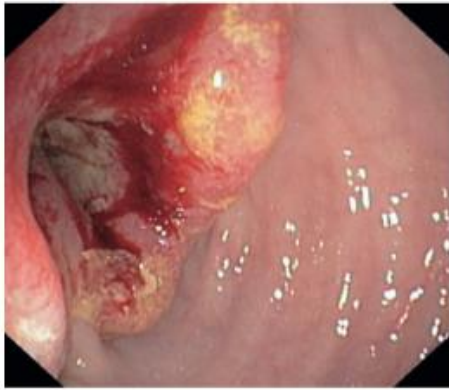
c



d

a,b sessile polypoid carcinoma,
nodular or lobular
c,d polypoid carcinoma with focal
erosions or ulcerated surface

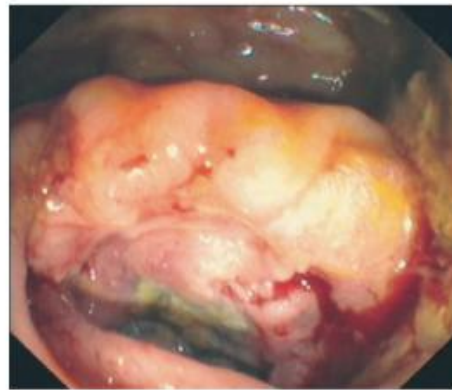
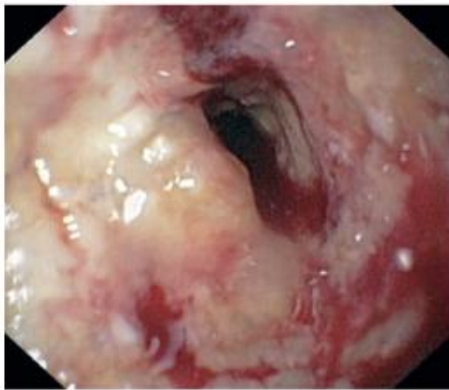
FIGURE 40: POLYPOID TUMOR



a,b circular ulcerated carcinoma

c,d stenosis caused by carcinoma, ulceration

a, b Circular ulcerated rectal carcinoma, stenosing.



d, e Circular ulcerated rectal carcinoma, stenosing.

FIGURE 41: ANNULAR TUMOR

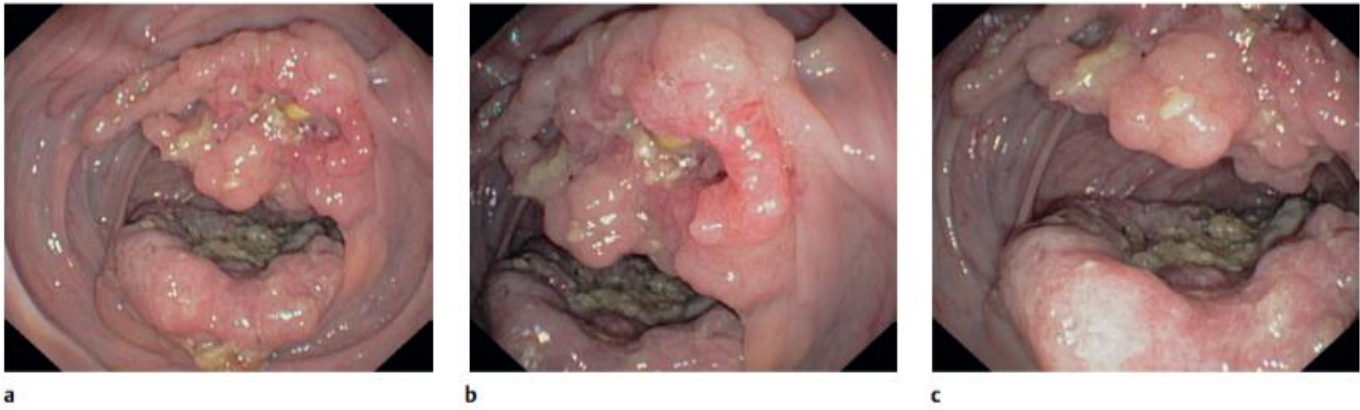


FIGURE 42: DOUBLE CARCINOMA IN CAECUM

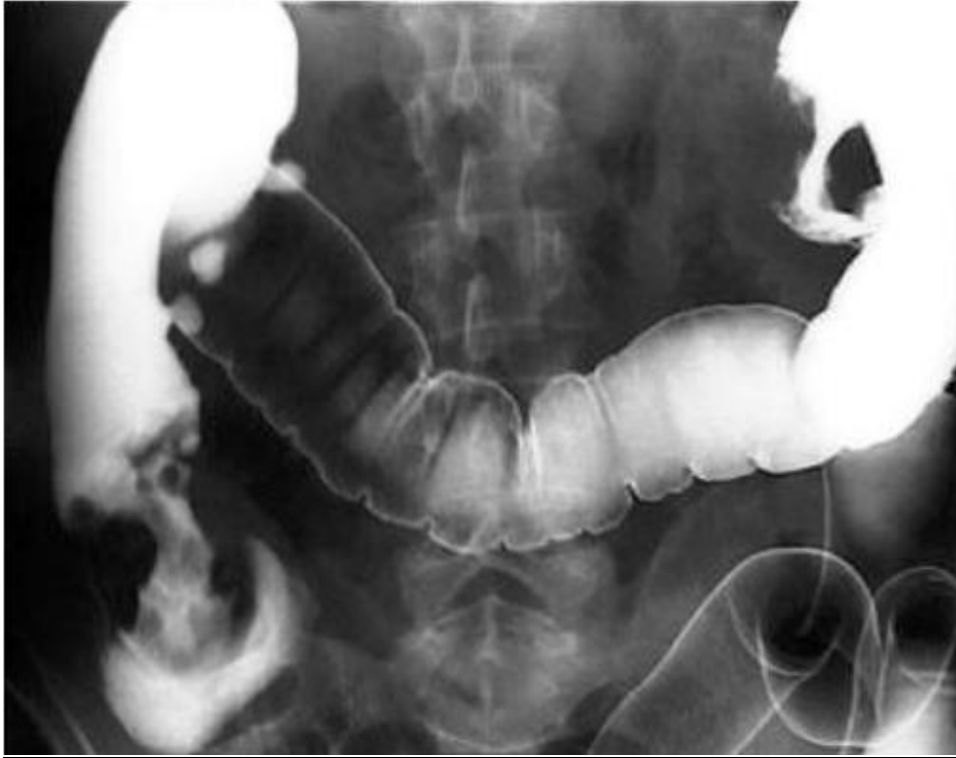
2- Barium enema

Enema is widely available and may be used to investigate patients with symptoms suggesting of CRC. However, the diagnostic yield of both double-contrast barium enema (DCBE) alone and the combination of DCBE plus flexible sigmoidoscopy is less than that of colonoscopy or CT colonography for the evaluation of lower tract symptoms.



FIGURE 43: DOUBLE-CONTRAST BARIUM ENEMA CECAL CARCINOMA.

A large polypoid cecal mass involves the ileocecal valve and causes small bowel obstruction.



**FIGURE 44: SYNCHRONOUS ANNULAR CARCINOMAS IN THE ASCENDING COLON AND
SPLENIC FLEXURE**

3- Computed tomography (CT):

Computed tomographic colonography (also virtual colonoscopy or CT colonography) provides a computer-simulated endoluminal perspective of the air-filled distended colon. The technique uses conventional spiral or helical CT scan images acquired as an uninterrupted volume of data and employs sophisticated post-processing software to generate images that allow the operator to evaluate a cleansed colon in any chosen direction.

CTC (computed tomography colonography) was first described using laxative bowel preparation, but techniques have been developed that use oral contrast agents for 24-48 hours and a modified diet instead. This technique is called faecal tagging;

faecal material that remains in the colon will be 'tagged' with oral contrast and so can easily be distinguished from pathology.

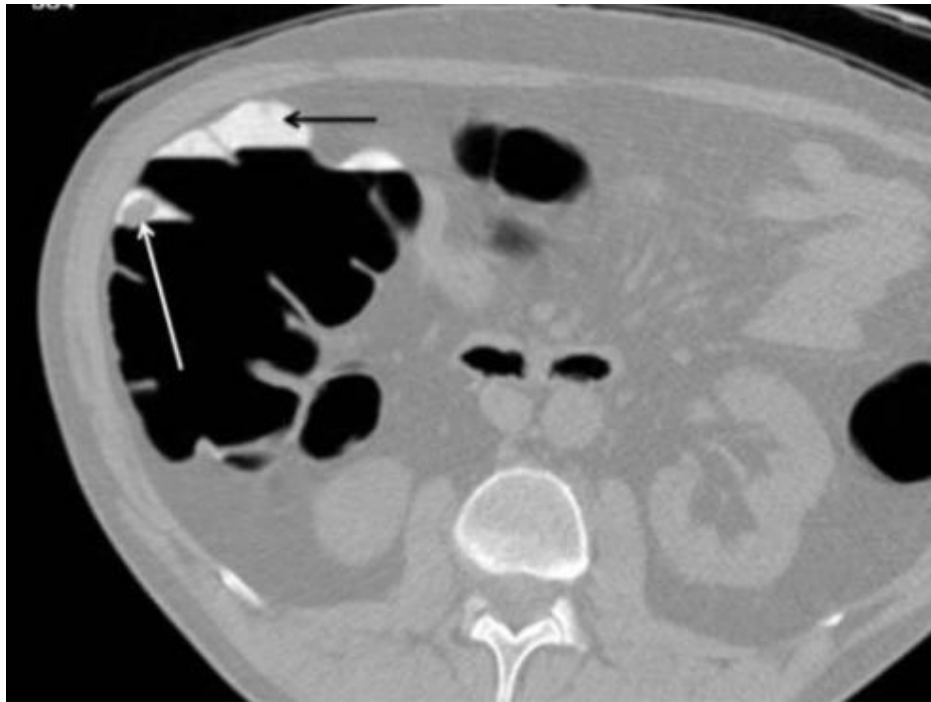


FIGURE 45: CT COLONOGRAPHY WITH FAECAL TAGGING

This axial CT image shows some residual faecal fluid within the colon, but this is high attenuation due to the tagging material (black arrow). A small polyp can be easily distinguished from this fluid (white arrow)

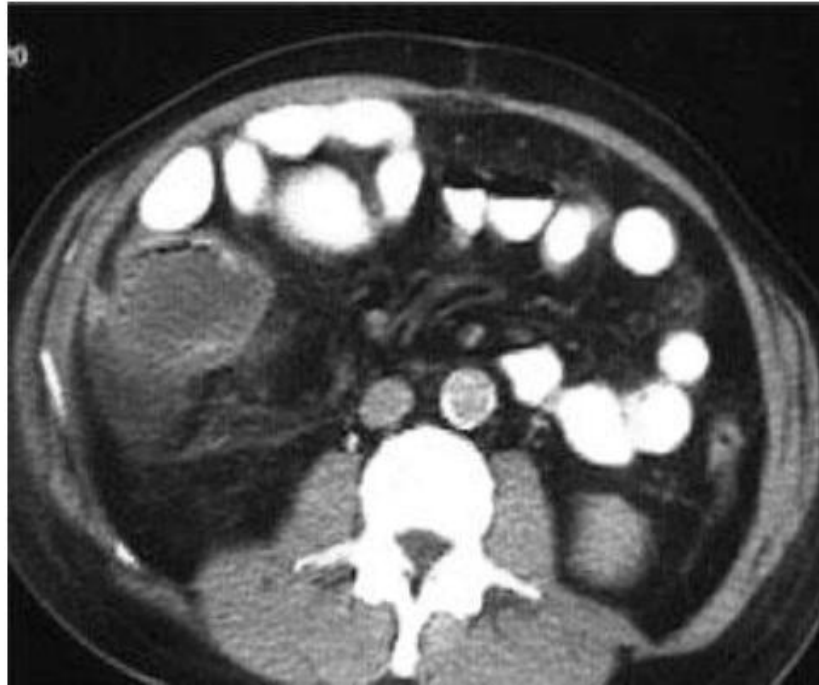


FIGURE 46: PREOPERATIVE CT: CECAL WALL THICKENING AND INFILTRATION OF THE PERICOLIC FAT

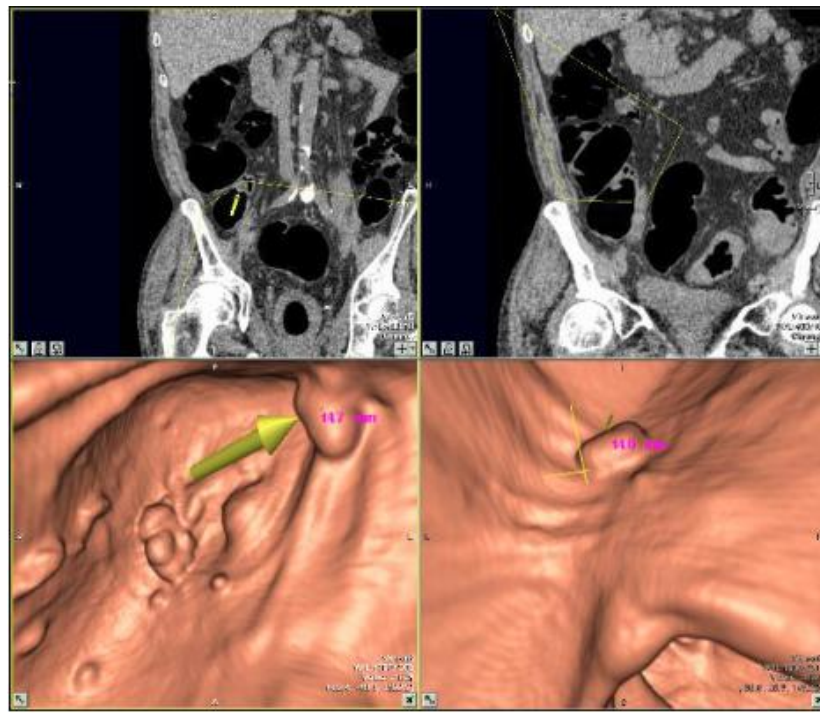


FIGURE 47: CT COLONOGRAPHY WITH 2- AND 3-DIMENSIONAL REFORMATTED IMAGES shows a 14-mm polypoid lesion close to the ileocecal valve (yellow arrow).

3-1 CT Staging of colorectal cancer

Colon cancer is staged by CT of the chest, abdomen and pelvis. Intravenous contrast is used, but bowel preparation is not required. The examination usually takes 15 minutes or less with the actual scan time being under a minute. Staging is by the TNM system.

CT cannot distinguish between T1 and T2, and is poor at nodal staging unless the nodes are grossly enlarged. CT is good at detecting T4 involvement of adjacent organs (Figure below), but is poor at detecting T4 involvement to the peritoneum.



FIGURE 48: AXIAL CT IMAGE OF A TUMOR OF THE SPLENIC FLEXURE

(white arrow) this abuts the spleen, and low attenuation within the spleen indicates tumor invasion (black arrow), making this t4.

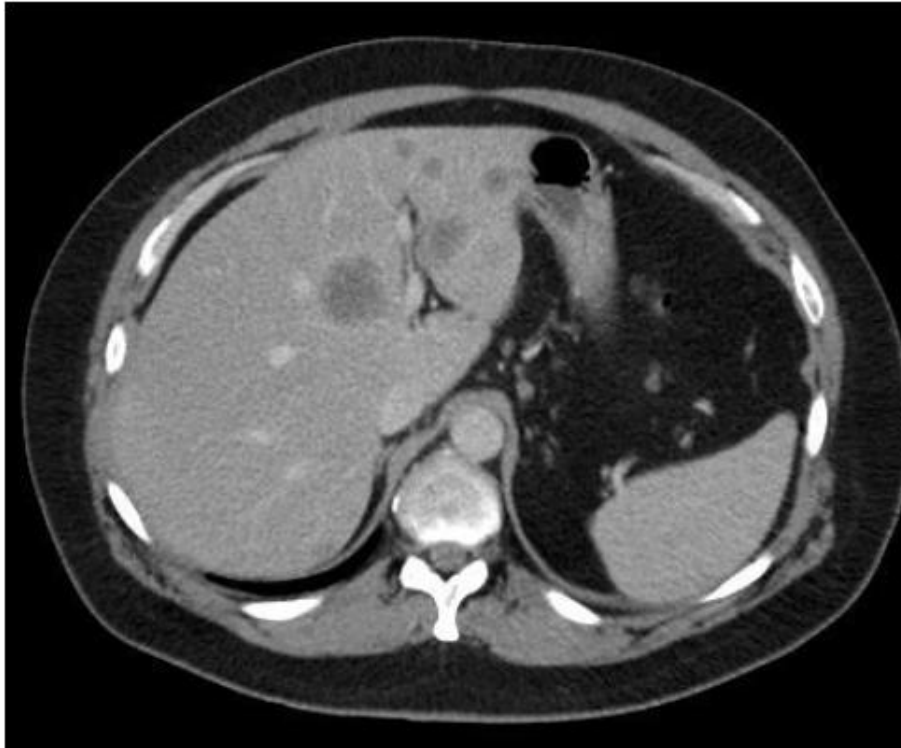


FIGURE 49: CONTRAST-ENHANCED CT SHOWING LIVER METASTASES. SEVERAL LOW-DENSITY METASTASES FROM THE COLON PRIMARY TUMOR INVOLVE BOTH LOBES OF THE LIVER.



FIGURE 50: CT SCAN IN PATIENT WITH COLON CARCINOMA AND LIVER METASTASES, SHOWING PULMONARY METASTASIS IN RIGHT LOWER LOBE.

3-2 Follow-up of metastatic disease

CT is the mainstay of follow-up of metastatic colorectal disease to monitor the response to chemotherapy. Radiofrequency ablation (RFA) of liver metastases involves placing a probe within the metastasis percutaneously under CT guidance, and applying a radiofrequency current that causes necrosis in the tumour cells. This is done under general anaesthetic.

It is now commonly used in combination with conventional hepatic surgery, and both can be curative if this is the only site of metastatic disease. Patients with advanced metastatic disease can develop bowel obstruction from growth of the primary tumor. This can be treated with a radiologically placed self-expanding metal stent, and this can obviate the need for surgery at all.

VII–Historical aspects of colorectal cancer surgery:

1– INTRODUCTION:

The advances in surgery of the colon since the 18th century attest to the extraordinary cunning and courage of early practitioners. Morbidity and mortality after procedures on the colon, however, remain unacceptably high, despite improvements in surgical instruments and technique, asepsis, anesthesia, antibiotics, and other areas of medicine and surgery. A review of the historical development of operations on the colon confirms that current clinical successes in colon operations depend in large measure on the application of those well-founded principles and techniques that have been introduced through the decades.

2– COLOSTOMY

The modern history of operations on the colon begins with **Alexis Littre**, who, in 1710, viewed an autopsy on a newborn with anal atresia and suggested that a deliberate colostomy might be done, bringing both ends out through an abdominal incision, with the proximal end a permanent anus. The French surgeon, Pillore of Rouen, in 1776, performed a cecostomy on an adult with a schirrous tumor of the rectum, but the patient died from gangrenous obstruction of the ileum because of mercury previously administered to induce a bowel movement. Duret, in 1793, attempting a perineal approach on a new born with an imperforate anus could not find the rectum, and so performed a sigmoid colostomy through an inguinal approach. The patient survived to age 45. Attempts at colostomy, inguinal or lumbar, over the next 50 years, were generally unsuccessful because of sepsis and high mortality.



Jean Amussat. (Photograph courtesy of the History Division, Portrait Collection, Biomedical Library, University of California, Los Angeles)

Jean Amussat, in 1839, successfully performed the first colostomy for obstructing carcinoma of the rectum. Amussat, without anesthesia, made a transverse incision above the iliac crest into the retroperitoneal space, punctured the sigmoid colon with a trocar, and released copious amounts of gas and feces. He then sutured the bowel to the skin at 4 points, establishing *un anus artificiel*.

Thomas Curling, in 1851, in his "Observations on diseases of the rectum," was the first to recommend colostomy for painful cancer of the rectum without obstruction. He contended that it was an injustice to the patient to reserve colostomy as a last resort. Although major advances in anesthesia and antisepsis during the second half of the 19th century made it relatively safe to enter the peritoneum, many surgeons preferred avoiding the risk of intraperitoneal contamination and infection.

John Deaver, whose surgical career in Philadelphia and at the University of Pennsylvania is legendary, strongly advocated the retroperitoneal (lumbar) colostomy over the intraperitoneal (iliac) approach. He cited, in addition to minimizing the chance

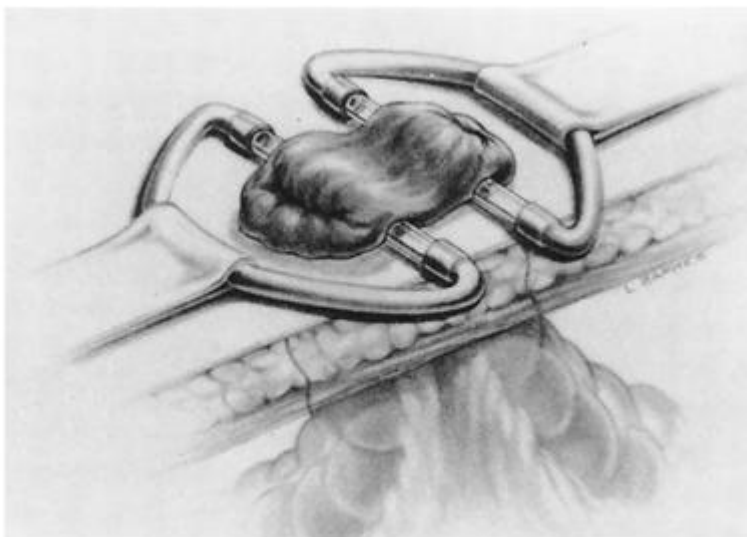
of peritoneal soiling, the ease in locating the distended sigmoid colon through the lumbar approach, and the comfort and convenience of the patient wearing only a small loin pad. Deaver advocated colostomy when the tumor could not be removed through the perineum, when the obstructed rectum could not be dilated from below, and when treating rectovaginal and rectovesicle fistulas. He believed colostomy should be performed before complete obstruction occurred, and hypothesized that peristalsis and the passage of stool over the carcinoma increased its rate of growth.

A rapid transition to the intraperitoneal approach to colostomy occurred once Lister's antiseptic technique gained acceptance. **Reeves**, in 1882, spearheaded the change from lumbar to inguinal or iliac colostomy. He readily entered the peritoneum and performed colostomy with minimal spillage. Surgeons, using this open technique, successfully managed most rectal and sigmoid obstructions with a left lower quadrant colostomy. They determined more easily the optimum site for the stoma and the resectability of the tumor. Efforts were then concentrated toward selecting an optimum time for the operation, choosing the best technique to open the colon, preventing stoma retraction, and managing the distal loop.

Allingham, in 1887, reported 6 patients with inguinal colostomy with outcomes superior to the retroperitoneal lumbar approach. Paul of Liverpool, in 1891, introduced his glass intestinal tubes. He performed an inguinal colostomy, divided the bowel completely, closed both ends, and dropped the distal end into the abdomen. He placed a flanged glass intestinal tube in the upper end, with a rubber tube connection to a bottle. He also performed double-barreled colostomies with a glass tube sutured into

each stoma, and he used the tube technique in his exteriorizing colectomy reported in 1895.

The first documented transverse colostomy was performed for an obstructing rectal carcinoma by Fine in Geneva in 1797. He brought out a loop of bowel and sutured the mesentery to the skin, thinking he was performing an ileostomy. Three months later, the patient died of the cancer and, at autopsy, was found to have had a right transverse colostomy. The transverse loop colostomy grew in popularity and, until the mid-20th century, was an often used component of a staged colon resection for obstructing carcinoma, inflammatory conditions of the left colon, and congenital and acquired anorectal disorders. Mechanical devices, reviewed by Corman and Odenheimer in their beautifully illustrated article, were utilized to prevent stoma retraction and to ensure effective spur formation. Maydl (1888) used a rubber rod or goose quill; any later apparatus was a modification of this. Hartmann (1900) inserted an iodoform gauze tampon through a hole in the colon mesentery. Glass rods and sections of rubber tubing were soon introduced. Kelsey (1889) used the “harelip pin,” which minimized apparatus bulk, allowing easier application of an appliance.



Owen Wangenstein (1947) created a device, which distracted the 2 stomas, promoting more effective fecal diversion (Fig. 2). Green's plasticbar and Aries's rotating device

(1971) were designed for easy insertion, ensuring against slippage, and easy removal. The Hollister appliance (1971), still used today, forms a butterfly shaped barrier to inadvertent removal.

Fred W. Rankin noted that the Maydl operation, which employed a glass rod or stiff rubber tubing to support the loop, caused pressure necrosis of the bowel when the loop was under tension, such as in an obese patient. He emphasized the importance of creating the loop “loosely and freely” in order to prevent compromise of the blood supply.

David Howard Patey’s “primary epithelial apposition” was a revolutionary concept. He noted the less-frequent occurrence of sepsis, retraction, and sloughing—3 factors that had prompted the traditional placement of the stoma at distance from the skin. Modern chemotherapy diminished the danger of sepsis, and creation of a tension-free colostomy with good blood supply, reduced retraction, and slough. He noted that suturing the edges of the stoma to the skin at the time the colostomy is created resulted in rapid healing and early function. This proved far superior to bringing the bowel out at a distance, and having to depend on granulation, fibrosis, and epithelial growth to mature the colostomy.

3-COLECTOMY

George Arnaud de Ronsil performed the first right hemicolectomy in 1732. The patient had an incarcerated scrotal hernia with scattered areas of gangrene of the ileum, cecum, and ascending colon. Because the bowel was densely adhered to the internal ring, he resected it, and left a double-barreled ileocolostomy that functioned

well. Early resections for carcinoma of the lower rectum were performed through a perineal or sacral incision. Although Faget reported the first successful excision of the rectum in 1739, his procedure was performed for devitalized rectum secondary to bilateral ischiorectal fossa abscess, and not for cancer.

Two Frenchmen, Lisfranc in 1826, and Maurin in 1831, and an Englishman, Herbert Mayo, about the same time, reported successful resection of the rectum for cancer. Sepsis remained a deterrent to widespread acceptance of resection for a half-century. The perineal approach was only practicable for resection of 4 in to 5 in of rectum, and carcinoma cure rates for this operation varied from 0% to 37%. Kraske, in 1885, gained better access to higher rectal lesions by resecting the coccyx and part of the sacrum. The idea occurred to Kraske while assisting Professor von Volkmann in removing a sarcoma of the sacrum.

Reybard of Lyon, in 1833, was the first to perform a 1-stage sigmoid colectomy.¹¹ His patient was 28 years old with a left lower quadrant abscess caused by perforation of a 6-cm carcinoma. He resected the lesion through an oblique incision, and sutured the bowel ends together with a continuous “furrier’s” suture of silk—the back row in 1 layer, and the front row in 2. Although his patient survived for a year, the case was rejected by the Royal Academy because the specimen had been lost, and Reybard’s efforts to duplicate the procedure in dogs for the commission were unsuccessful. Although Reybard’s report prompted further attempts at resection and primary closure, the operation remained unpopular because of high mortality caused by sepsis.

Martini of Hamburg, in 1879, resected a carcinoma of the sigmoid with involved mesenteric nodes, but could not bring the 2 ends of the bowel together. He closed the distal end and brought out the proximal end as a colostomy. Czerny of Heidelberg, in 1880, resected a tumor involving the sigmoid and transverse colon, and successfully performed a primary anastomosis. In 1892, Maunsell introduced the abdomino-anal approach, precursor to current “pull-through” procedures. The rectum and sigmoid were separated from the sacrum during the abdominal portion and then invaginated through the anus for resection.

Various modifications of the abdominoperineal and abdomino-sacral operation were performed between 1885 and 1900, with a mortality of only 20%, but with recurrence of tumor in over 80%. The report by Paul of Liverpool, in 1895, demonstrated his dedication to sharing experience in early colon resections, despite the results. He wrote, as he apologized for very poor outcome in 7 instances of colectomy, *“facts are always useful, and if none of them deserve to be regarded as guides to success, at least some have value as a warning against failure.”*

Ernest Miles reported 57 perineal excisions of the rectum for carcinoma, with a 95% recurrence rate of tumor within 6 months to 3 years. He determined that although the perineal operation reduced recurrence in the immediate vicinity of the tumor, it allowed metastasis in the *zone of upward spread*. He decided to bring the operation more in line with excision of the axillary lymphatics in breast cancer and Wertheim’s operation for uterine cancer. The essentials of Miles’ procedure were as follows:

1. *A permanent colostomy*
2. *Removal of the entire pelvic colon with its blood supply*
3. *Removal of the pelvic meso-colon below the point where it crosses the common iliac, together with a strip of peritoneum at least an inch wide on either side of it.*
4. *Removal of lymph nodes situated over the bifurcation of the common iliac artery*
5. *A wide perineal resection.*

Miles's resection is well described in his 1914 paper in the *British Journal of Surgery*. He resected the coccyx in every instance, and opened the sigmoid colostomy before the patient left the operating room. If Miles had to perform a preliminary colostomy for obstruction, he waited 2 weeks before doing the definitive resection. The Miles abdominoperineal resection, in the opinion of many, remains the best surgical procedure ever proposed for carcinoma of the rectum and rectosigmoid.



Johann von Mikulicz, in an address before the American Surgical Association in 1903, reported that colon resection with immediate suture was associated with a mortality rate of 30% to 50%, resulting from anastomotic breakdown and peritonitis. He attributed this complication to suturing nutritionally impaired,

dilated bowel. He reduced mortality to 15% using a 2-stage exteriorization procedure.

Mikulicz's classic report of his experience with 106 cases of intestinal carcinoma describes his operation in detail, discusses his results with tumors at various stages, and reports his transition from a 12- to 48-hour delay in removing the tumor-bearing portion of the bowel to immediate resection.

He obtained a 4-year survival of 35% to 40% despite the palliative nature of the operation.

Rankin recognized that although the "admirable features of the Mikulicz operation were theoretically and fundamentally sound," inherent problems were found with it.

Rankin noted auto-transplantation of tumor into the wound in 12% of cases; Mickulicz reported 8%. In addition, Rankin noted that necrosis and gangrene of the exteriorized bowel with peritoneal contamination sometimes occurred. Resection of the exteriorized loop was often necessary in the first 48 hours; it was problematical if it resulted in retraction and peritonitis. Rankin modified Mikulicz's procedure as published in his beautifully illustrated book in *Surgery of the Colon*.

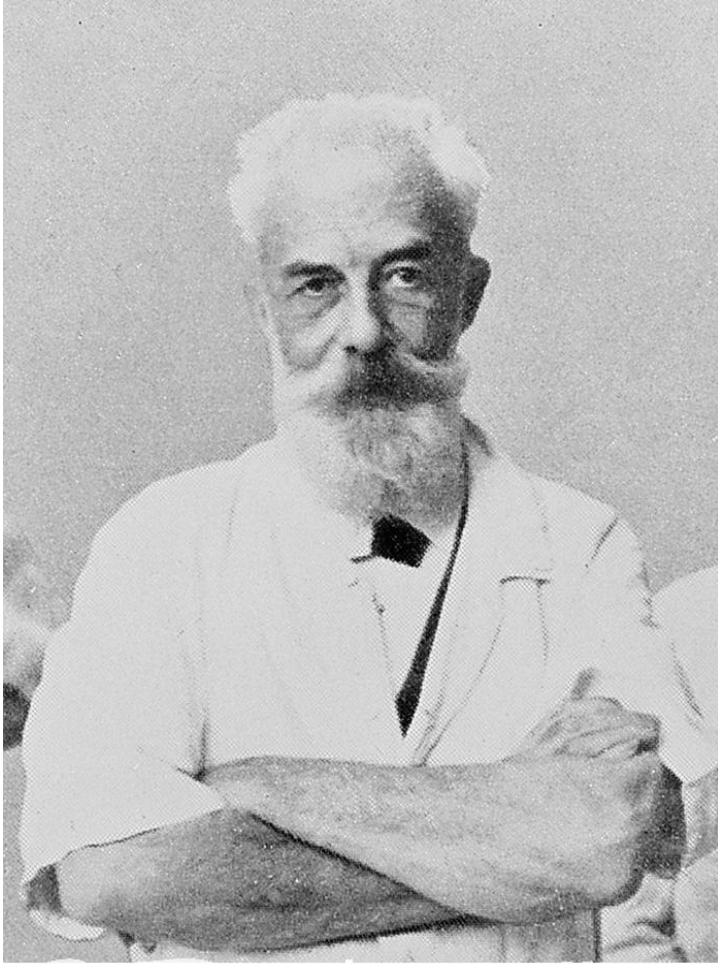


FIGURE 4: Henri Albert Hartmann(1860-1952)

The French surgeon, **Henri Hartmann**, born in 1860, performed over 30,000 operations, and published extensively in the areas of surgery and gynecology. Although the Hartmann operation, described in 1923, was performed for cancer, it is now used almost exclusively for acute diverticular disease of the rectosigmoid and sigmoid colon.

Hartmann performed a 2-stage operation on 2 patients with obstructing cancers of the pelvic colon. At the first procedure, he created a sigmoid

colostomy, and at the second, he resected the tumor-containing bowel, leaving the sigmoid colostomy, and closing the upper end of the rectum. He noted that, "Following the operation, both cases were as uneventful as an operation for a cold appendix." Hartmann never planned to reestablish intestinal continuity.

4-ILEOSTOMY

The wide acceptance of total colectomy in the treatment of inflammatory bowel disease and familial polyposis, followed successes in the creation and management of the ileostomy. Early, Rankin and his contemporaries believed that ileostomy alone, as described by John Young Brown, was the surgical treatment of choice in ulcerative

Mr. Bouimtarhan Youssef

colitis. It was easy to perform under local anesthesia, placed the large bowel at rest, and allowed irrigation of the intestine with medications.

Rankin admitted that the highly morbid colon resection was still necessary in patients in whom ileostomy failed to control the colitis, and in extensive polyposis of the colon with high malignant potential. Total colectomy and permanent ileostomy became almost commonplace by the early 1950s, prompting refinement in the creation and care of a permanent ileostomy.

Leland McKittrick and Richard Warren, in 1951, reported on functional stomal obstruction in 240 patients, and coined the term "ileostomy dysfunction."²⁰ McKittrick had already introduced 1-stage colectomy with diverting ileostomy for ulcerative colitis. Warren and McKittrick considered ileostomy dysfunction the result of edema of the everted stoma with associated rigidity and constriction of the serosa of the exteriorized ileum. The authors recommended longitudinal incisions through the indurated seromuscular layers to prevent this.

Bryan Brooke, in 1952, everted the stoma when the ileostomy was created, and sutured it to the skin, preventing ileostomy dysfunction. He condemned loop ileostomy, which interfered with a well-fitted appliance. Brooke made significant contributions in the prevention of skin excoriation and ileostomy prolapse.

Rupert Turnbull of the Cleveland Clinic played a similarly important role in improving ileostomy function. He emphasized careful selection of the stoma site with

immediate maturation, and he introduced Karaya powder for the prevention and treatment of skin irritation.

5-CONCLUSION

Progress in colon surgery continues into the 21st century. The intestinal stapler, introduced in 1908 by Hultl, has opened new horizons in gut surgery. Laparoscopic operations, now applied to virtually every surgical condition of the colon and small bowel, have reached unanticipated heights of technological advancement. Modern surgeons' innumerable options for resection, anastomosis, and repair of the large intestine result from the contributions of their predecessors who have met the enormous surgical challenges of the past 3 centuries.

VIII– treatment of colon cancer: [25], [26], [27], [28], [29]

When the overall survival rate for colorectal cancer is merely 40 per cent, for a potentially curable disease, it is essential that any treatments offer optimum prognosis. Surgical resection remains the mainstay of treatment of cancers of the colon. Since cancers spread locally, through the lymphatic nodes and hematogenously, the oncological principle of colon cancer surgery include resection of the tumor with adequate resection margins plus removal of all lymph node bearing tissue.

1–Principles of surgery [30]

Colorectal cancer is thought to spread in several ways, including direct growth, transperitoneal migration, lymphatic and haematogenous spread and implantation. The aim of surgical resection is to remove all cancerous tissue.

Involved margins and lymph nodes are associated with increased risk of recurrence and a worse prognosis. In cases of tumors involving spread to adjacent organs, an en–bloc resection may have to be undertaken to achieve a negative margin. Principles of Colorectal Cancer surgery can be summarized in four major points:

- isolation of the tumor
- removal of all tissue containing cancer cells with an adequate margin
- removal of regional lymph nodes
- maintenance of organ function

It is unusual for a tumor to extend distally more than 1 cm from the visible bulk of the tumor. Therefore, a minimum distal resection margin of 2 cm is usually sufficient. Radial extension may result in adhesion to adjacent tissues.

To achieve mesenteric nodal resection, the arterial trunk is ligated at its origin. Before mobilizing the tumor, the lymphovascular bundle is ligated early in order to minimise the release of circulating tumour cells.

Rectal cancer surgery is made more difficult due to the pelvic constraints, adjacent genitourinary organs and the presence of the sphincters. The aim is to remove the rectum with its mesorectum and an intact fascial envelope (TME, total mesorectal excision). Breaching this envelope runs the risk of shedding cancer cells into the pelvis.

2-Surgical planning

Surgery is considered to be the gold standard in order to achieve complete removal of tumors. Once a cancer is diagnosed, it is important to establish whether it is localised.

The presence of distant metastases influences any treatment strategy. Broadly speaking, surgery is the first option in colonic lesions. Factors such as the ability of the patient to manage a stoma also need to be considered prior to surgery.

3-Clinical assessment

It is important to evaluate the stage of the cancer and to exclude synchronous tumors. This will influence whether the tumor is suitable for local or segmental resection.

The presence of metastases will influence whether systemic therapy is considered.

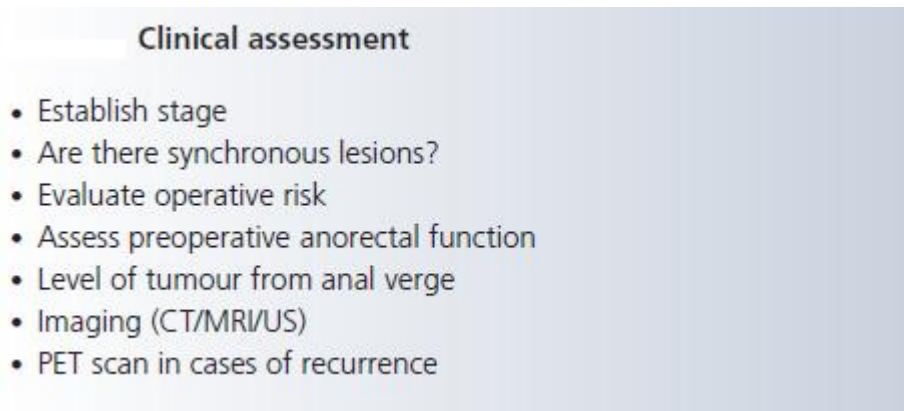


FIGURE 51: CLINICAL ASSESSMENT OF NEWLY DIAGNOSED COLORECTAL TUMOR

3-1 Preoperative evaluation

Imaging for preoperative staging is detailed under the Diagnosis chapter. Routine investigations include the use of blood tests (including FBC, renal function and liver function tests as well as serum CEA) ECG, CXR, chest function and the detection of metastases (CT, CT-PET and MRI).

3-2 Assessment of perioperative risk

A thorough preoperative evaluation in order to minimise the risk of death and morbidity is essential. Patients with chronic diseases such as ischaemic heart disease, congestive cardiac failure, hypertension, asthma and diabetes mellitus need to be optimised prior to surgery.

Warfarin, clopidogrel and aspirin need to be stopped and adequate DVT prophylaxis instituted.

3-3 Preoperative preparation

Standard practice is now to omit mechanical bowel preparation. Patients have oral dietary restriction to fluids only and a phosphate enema for rectal and left colonic operations.

DVT prophylaxis is important with the use of LMWH and graded compression stockings. Epidural anaesthesia is imperative for postoperative pain control in conventional open surgery.

In laparoscopic surgery, a reduction in analgesic requirements has been seen which enables a more rapid recovery programme. Preoperative preparation is outlined in Box below:

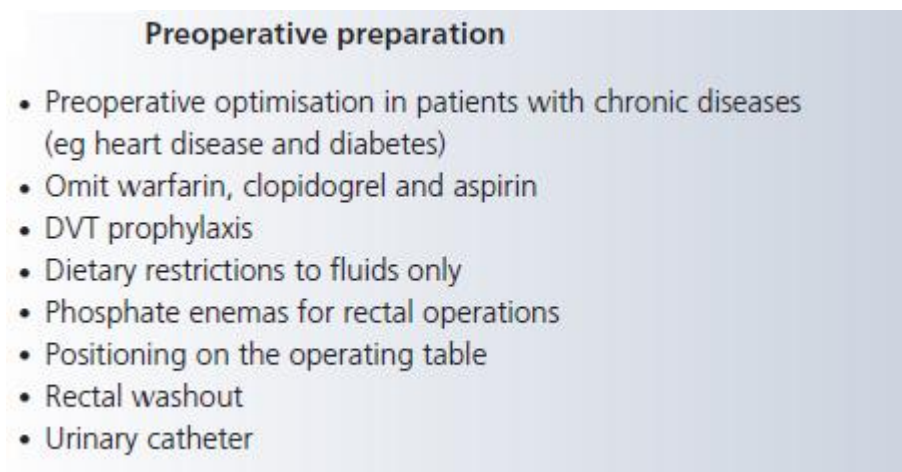
- 
- Preoperative preparation**
- Preoperative optimisation in patients with chronic diseases (eg heart disease and diabetes)
 - Omit warfarin, clopidogrel and aspirin
 - DVT prophylaxis
 - Dietary restrictions to fluids only
 - Phosphate enemas for rectal operations
 - Positioning on the operating table
 - Rectal washout
 - Urinary catheter

FIGURE 52: preoperative preparation for colorectal surgery

Positioning of the patient is dependent on the site of the colorectal lesion. For right and proximal transverse colon tumors, patients are placed in the supine position. Those with left colonic cancers are placed in the Lloyd–Davis position.

Rectal irrigation can be carried out in those with rectal tumors. This is done with 0.3% chlorhexidine solution, which has some anti–microbial and tumoricidal properties. A urinary catheter is placed for perioperative monitoring of kidney function.

3–4 Operative access: conventional approach

The incision is placed in order to gain best access to the bowel tumor. A midline incision is most often used. However, transverse incisions, particularly for right colonic cancers, are associated with less pain, improved ventilation of lung bases and better cosmesis postoperatively.

Irrespective of the type of incision, a complete laparotomy is performed paying attention to the mobility of the tumor as well as the liver, small bowel, lateral peritoneal spaces and the pelvis.

When a limited access abdominal incision has been made it is not possible to check the whole abdomen for other pathology, but those areas which are accessible can still be examined. For example, after the removal of a normal appendix it is usually possible to check at least the terminal ileum and the right ovary for an alternative pathology, without enlarging the incision.

Laparoscopic surgery has the advantage of allowing a full inspection of the abdomen, but without the benefit of palpation. When a major abdominal incision has been made, the opportunity to check for another obvious intra–abdominal pathology

should not be missed. It is a good discipline to do this immediately on opening the abdomen or it may be forgotten later.

3-5 Laparoscopic surgery

The first reports of laparoscopic colectomy for cancer were made in the early 1990s. Initial observations of port site metastases were concerning. However, recent meta-analyses (consisting of COST, MRC-CLASSIC and COLOR trials) have shown that laparoscopic colorectal surgery is as safe and efficacious as the conventional open approach with no difference in overall and disease-free survival.

In addition, laparoscopic resection was associated with reductions in peri-operative blood loss, postoperative pain, length of incision and length of hospital stay (2 days) when compared with open surgery.

4-Colon cancer: surgical procedures (stomas)

4-1 Formation of stomas

An enterocutaneous stoma is a controlled iatrogenic fistula. A stoma may be fashioned as an alternative outlet to the gastrointestinal tract after the excision of all distal bowel, or when restoration of continuity after a resection is contraindicated. Stomas are also used as a temporary or permanent diversion of the faecal stream from distal pathology or a healing anastomosis. A temporary stoma is commonly a loop stoma which can be closed without a major laparotomy when it is no longer required.

An end stoma is preferable when permanence is anticipated. A loop stoma may be left as a permanent stoma, but is more prone to complications. An *end stoma* has a

single opening into the proximal bowel, and the epithelial continuity is between the skin and the whole circumference of the bowel mucosa.

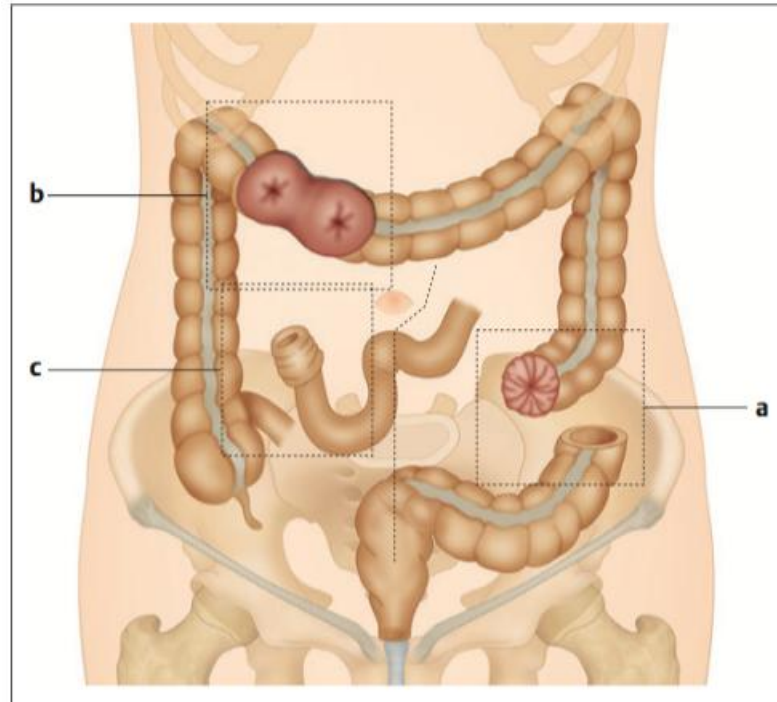


FIGURE 53: SCHEMATIC ILLUSTRATION OF VARIOUS STOMAS

a: end colostomy

b: double-barreled colostomy

c: end ileostomy

4-2 Left iliac fossa end colostomy

This stoma is formed after a resection which leaves no distal bowel to which an anastomosis can be made, or when a restorative procedure is contraindicated. It is therefore the final step in an abdominoperineal resection, or a Hartmann's operation. An end left iliac fossa colostomy may also be used as a permanent diversion of a rectum irretrievably damaged by tumour, inflammation or trauma, and as a final solution for faecal incontinence or a rectovaginal fistula.

4-3 Left iliac fossa loop colostomy:

This is the appropriate stoma when there is a rectosigmoid obstruction and no resection is planned as it can also decompress the distal colon immediately above the obstruction. If, however, a later resection is planned a more proximal colonic stoma may be preferable. The pelvic colon is mobilized, as for the formation of an end colostomy. The bowel is not divided but brought out as a loop in a similar manner to the fashioning of a transverse loop colostomy.

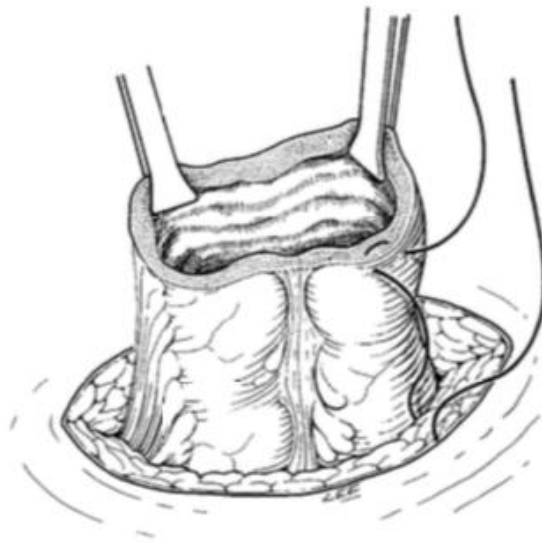


FIGURE 54: AN END COLOSTOMY. THE CLOSED END OF COLON HAS BEEN BROUGHT THROUGH THE ABDOMINAL WALL AND TRIMMED

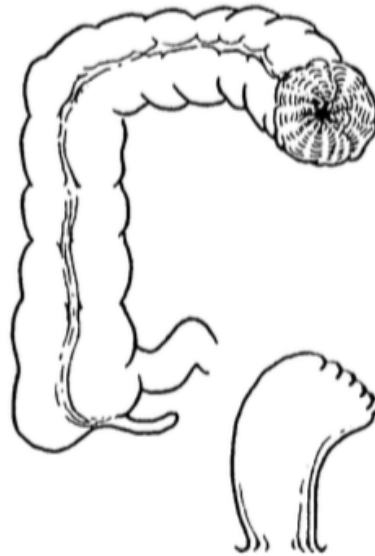


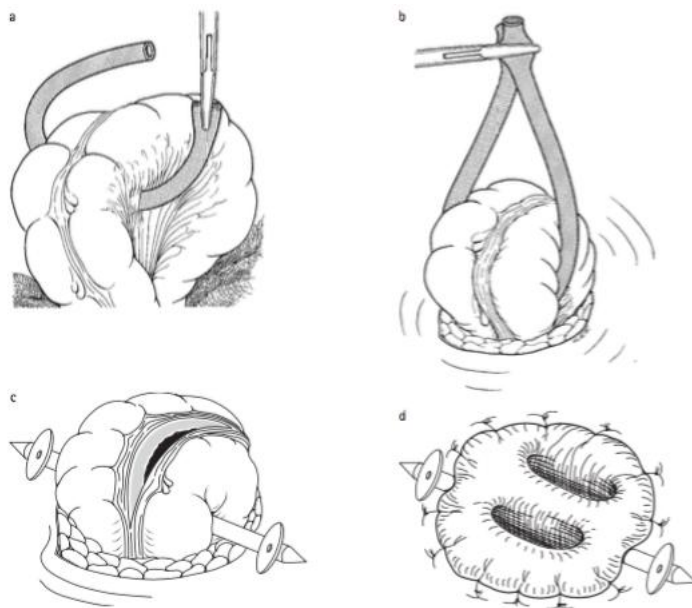
FIGURE 55: A TERMINAL COLOSTOMY. AN END STOMA HAS BEEN FORMED AND THE RECTUM HAS BEEN CLOSED AND LEFT IN SITU

This is a satisfactory solution when there is no distal obstruction. When there is a distal obstruction, either a loop stoma should be formed or the distal end brought out as a separate mucous fistula.

4-3 Transverse loop colostomy:

This is a temporary stoma, and was traditionally the standard emergency treatment of a left colon obstruction. It may still have a place in this situation, but a primary resection is now the preferred option. The defunctioning loop colostomy is most often indicated as a temporary diversion to protect a left colon anastomosis.

Coloanal anastomoses are particularly vulnerable to anastomotic leakage, and some surgeons routinely defunction with a loop stoma. Surgeons are divided in their preference for either a loop transverse colostomy or a loop ileostomy as a temporary measure. The colostomy is less pleasant for the patient to manage, and is probably associated with more wound infections and incisional herniae after closure.



(a) An artery forceps has been passed through a mesenteric window close to the bowel and is now drawing a catheter through. (b) An artery forceps has been passed into the abdomen through the prepared stoma site and the ends of the catheter grasped. The bowel is gently delivered to the exterior. (c) The colostomy bar has been guided through the mesenteric window by its insertion into the open catheter end. A longitudinal incision is made in the colon. (d) The bowel edges are folded back to the skin edges and skin- mucosal apposition is achieved with interrupted sutures, except where the stoma bar emerges.

FIGURE 56: A LOOP COLOSTOMY ILLUSTRATED WITH A COLOSTOMY BAR

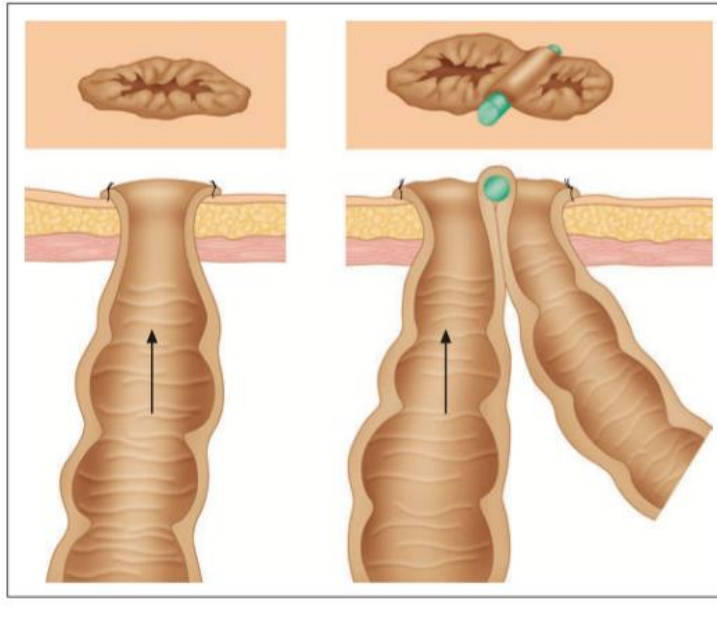


FIGURE 57: SCHEMATIC ILLUSTRATION OF AN END COLOSTOMY (LEFT) AND DOUBLE BARRELED COLOSTOMY(RIGHT)

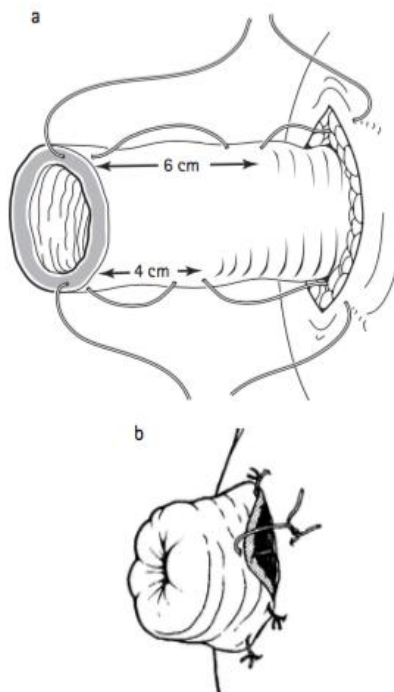


FIGURE 58: NORMAL SMOOTH COLOSTOMY WITH NORMAL WIDE OPENING.

4-4 End ileostomy:

This is the stoma created at the completion of a total colectomy. The optimal stoma site, high in the right iliac fossa, should have been marked preoperatively. At

surgery, a disc of skin is excised, and an incision made through the abdominal wall as described for an end colostomy. The terminal ileal stump is then drawn through the abdominal wall in a similar manner, with care being taken to avoid rotation. There will inevitably be some mesentery drawn through with the ileum, as complete division of this from the bowel will result in an ischaemic stoma.



(a) Lateral view of the stoma as the everting sutures are inserted. These sutures include a seromuscular bite of the ileal wall between the bites of skin and bowel edge. To produce a 2.5-cm spout, facing slightly downwards, these seromuscular bites should be 6 cm from the end of the ileum superiorly and 4 cm inferiorly. Laterally, they should be at 5 cm.

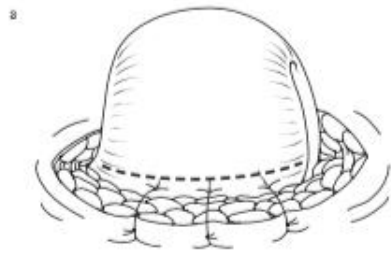
(b) The everting sutures are tied, the spout is formed, and skin mucosal apposition is completed with additional sutures.

FIGURE 59: AN END ILEOSTOMY

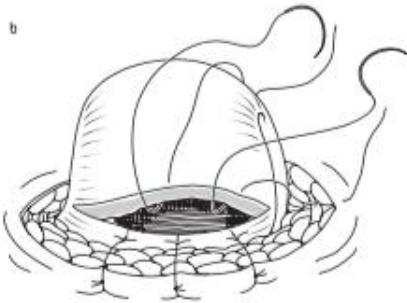
4-5 Loop ileostomy:

This stoma is most frequently used to defunction an empty colon to protect a vulnerable distal anastomosis. The abdomen is already open, and the terminal loop of ileum is drawn through the prepared stoma site. Few surgeons use a stoma rod for a loop ileostomy, and it is therefore preferable not to use a catheter through a

mesenteric window as described for the delivery of a loop of colon. A Babcock forceps passed through the stoma incision is usually sufficient to guide the loop through.



(a) Three sutures are placed between the skin edge and the seromuscular coat of the distal limb prior to closure of the main wound. This manoeuvre prevents any rotation of the loop and confusion as to which is the proximal and which the distal limb.

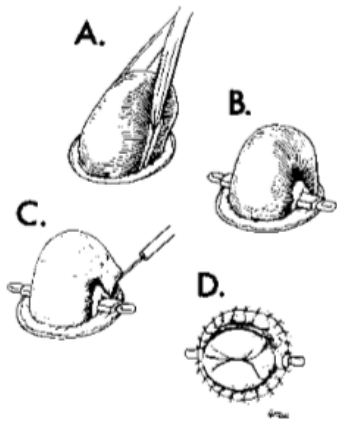


(b) An incision has been made a few millimetres above the three seromuscular skin apposition sutures. The superior and the first lateral eversion sutures are in place but untied.



(c) As the sutures are tied, the stoma everts as a spout. Viewed from below, the distal bowel opening is visible, flush with the skin.

FIGURE 60: A LOOP ILEOSTOMY



Loop ileostomy:

(A) loop brought through the abdominal wall with a Penrose drain or umbilical tape;

(B) loop secured with a plastic ileostomy rod;

(C) incision made at the skin level through the distal (cephalad) aspect of loop;

(D) matured stoma

FIGURE 61: LOOP ILEOSTOMY

4-6 Stoma complications:

Some patients have a trouble-free stoma, while others have recurrent problems for which they may need further surgery. most comon stoma complications are listed below:

- **Retraction and stricture:** Retraction of a stoma in the first 2 weeks is often in conjunction with separation of the skin to mucosa suture line. It is most commonly caused by excessive tension on the afferent bowel, and therefore no local operation on the stoma will be helpful.
- **prolapse:** Prolapse of an end colostomy can be dealt with locally by a circumferential skin incision. After minimal dissection the redundant bowel is drawn out and amputated. The new end is sewn to the skin edges. Unfortunately, recurrence is com- mon. A prolapse is sometimes associated with an incisional hernia, and is then best managed by re-siting of the stoma
- **parastomal hernia:** Parastomal herniae are difficult to treat, but strangulation, although possible, is fortunately uncommon. Surgeons are therefore often reluctant to advise any action, especially if the hernia is easily reducible. Patients, however, are often trou- bled with both the difficulty in securing the appliance, and the prominence of the device showing through their clothes when it is secured to the summit of a protruding hernia. Patients may also complain of abdominal wall discomfort on exertion, or colic from small bowel loops within the sac. Occasionally, a specially fitted corset will be of value.

4-7 CLOSURE OF LOOP STOMAS:

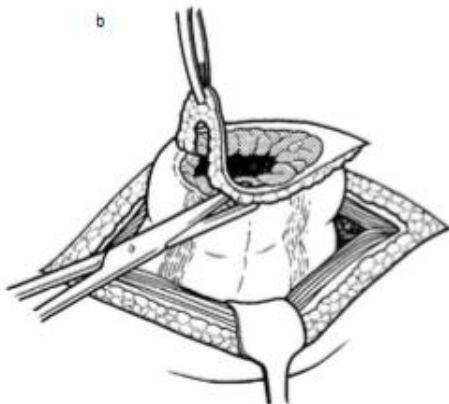
A temporary stoma, which has protected an anastomosis, may be closed as soon as the anastomosis is soundly healed. Early closure, at around 2 weeks, is practised by some surgeons but is technically more difficult at this stage.

A delay of 6-8 weeks allows the stoma to mature and the planes around the stoma to become better defined. The additional wait will also allow the patient to regain nutritional and immunological status after a major operation, and will also reduce the risk of thromboembolic complications. However, the patient has to learn to manage the stoma in order to return home.

Bowel preparation is normally only necessary before closure of a sigmoid loop colostomy, which has formed stool. An elliptical incision allows linear closure of the skin (figure (a) below), but some surgeons prefer a circular skin incision which cicatrices to a circular scar.



(a) *Elliptical skin incision.*



(b) *After full mobilization of the stoma, the mucocutaneous junction of the colostomy is excised.*

(c) *The bowel is then closed transversely*



FIGURE 62: CLOSURE OF A LOOP STOMA

5-Colon cancer: surgical procedures: (radical resection):

5-1 Right hemi-colectomy:

Carcinoma of the caecum or right side of the colon is usually managed by right hemicolectomy. The operation, via a right transverse or midline incision, consists of resection from the terminal ileum, past the hepatic flexure along to the mid-transverse colon, preserving the middle colic vessels with end-to-end or stapled side-to-side anastomosis and removal of its regional lymphatic drainage.

In this surgical procedure, as with all other colonic resections, the abdomen is explored to determine respectability and to search for synchronous tumors, distant metastases and associated abdominal disease. The small intestinal mesentery and the transverse mesocolon are divided on a line parallel to the superior mesenteric and middle colic arteries, and most of the greater omentum is removed in the resection specimen.

The blood vessels are divided and ligated early in the operation, again to avoid dissemination of tumor cells into the portal circulation or the lymphatics. When the carcinoma is near the ileocaecal valve a substantial segment of the terminal ileum (10-12 cm) with its mesentery should be removed because of the lymphatics along the ileocolic vessels.

When the lesion is in the hepatic flexure or mid-transverse colon, less ileum is removed, although careful dissection of the mesentery to the root of the mid-colic from the superior mesenteric is necessary.

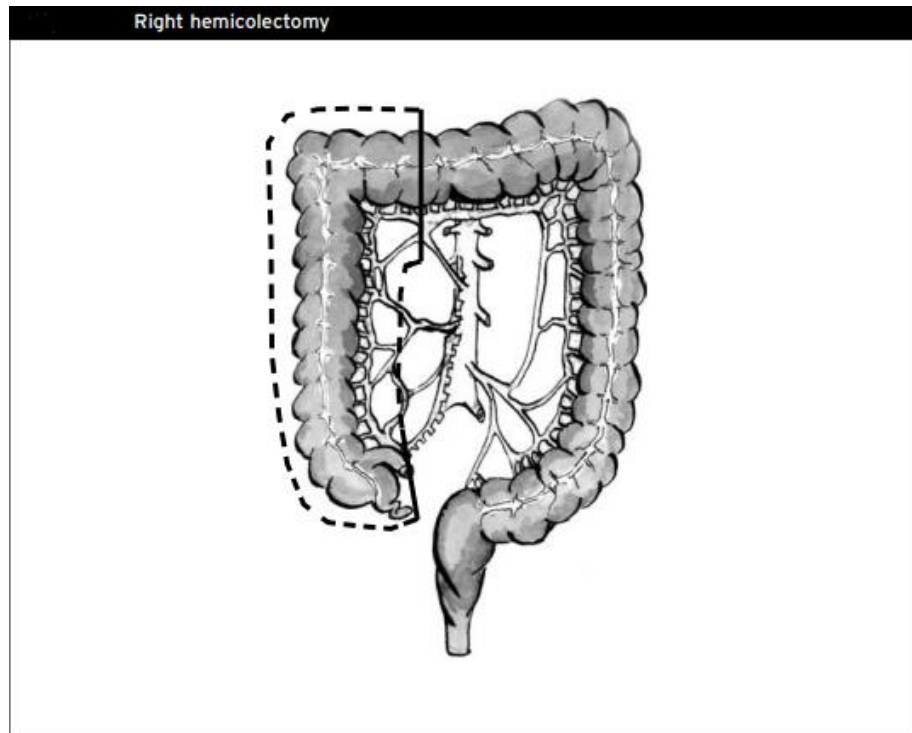
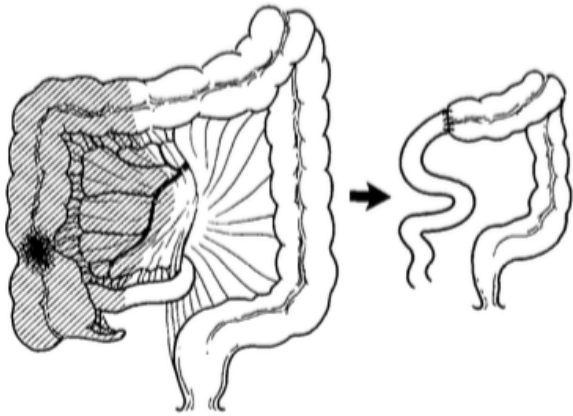


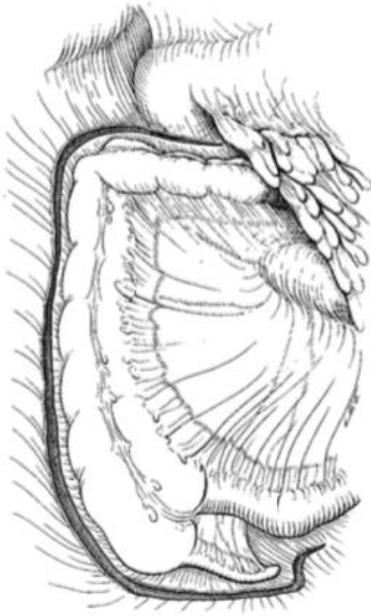
FIGURE 63: SCHEMATIC ILLUSTRATION OF A RIGHT HEMICOLECTOMY

A primary tumor on the right side of the colon is usually resected even if distant metastases have occurred, because prevention of obstruction or anaemia may offer best palliation. If a patient has an unresectable carcinoma, the obstruction may be bypassed by carrying out a palliative side-to-side anastomosis between the ileum and the transverse colon.



The right colic and ileocolic vessels are divided, and the tumour excised en bloc with the lymphatic drainage alongside these arteries. The bowel supplied by these arteries is excised, and continuity restored by an ileocolic anastomosis to the proximal transverse colon. A right hemicolectomy for a caecal pole tumour should include in the resection specimen the lymphatic channels alongside the terminal arcade of the mesenteric root, and a longer segment of terminal ileum may have to be sacrificed.

FIGURE 64: A RIGHT HEMICOLECTOMY



lateral peritoneal incision this is the first step in mobilizing the right colon with its retroperitoneal mesentery. Note the relationship to the second part of the duodenum.

FIGURE 65: THE LATERAL PERITONEAL INCISION

5-2 Extended right hemicolectomy

Tumors of the transverse colon and splenic flexure were traditionally managed by segmental resection; however, extended right hemicolectomy is now accepted as a safer option.

The procedure is excision of the right colon and a variable length of transverse and descending colon, sacrificing the colic vessels but preserving the inferior mesenteric vessels with ileocolic anastomosis.

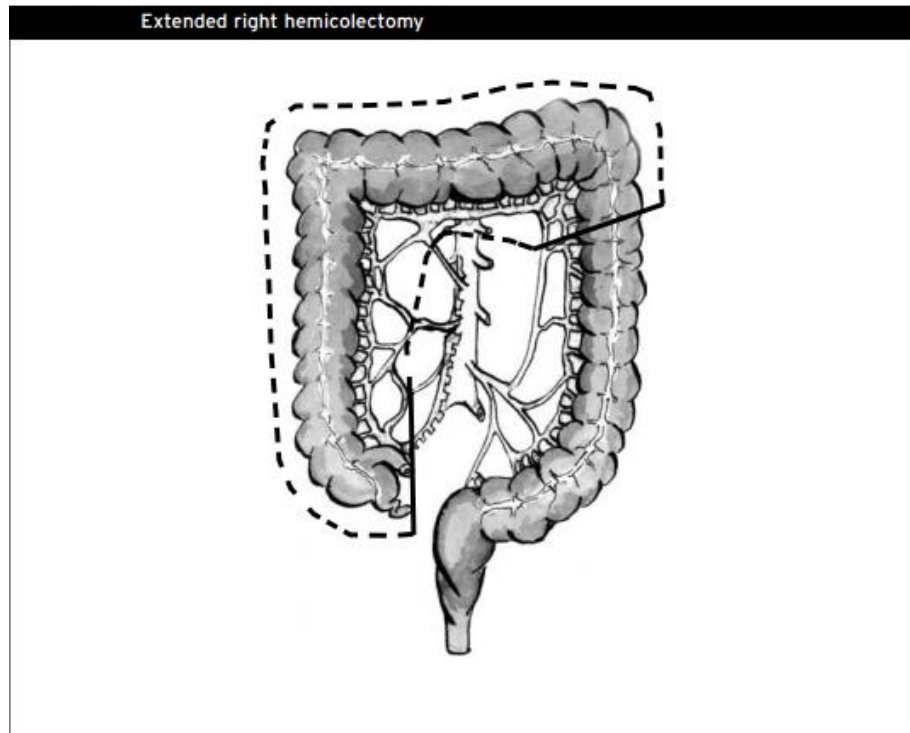


FIGURE 66: SCHEMATIC ILLUSTRATION OF EXTENDED RIGHT HEMICOLECTOMY

5-3 Left hemicolectomy

When no intestinal obstruction is present, the treatment of choice for carcinoma of the descending colon is usually managed by left hemicolectomy.

Resection, via a midline excision, extends from the middle of the transverse colon to below the sigmoid colon near the origin of the left branch of the middle colic artery. The resection also incorporates excision of a large proportion of the greater omentum and all of the colic mesentery, the left colic artery, the sigmoid vessels and the superior haemorrhoidal artery that supplies the resected bowel.

Primary anastomosis is usually performed. Even when liver metastases are present, this surgery is justified because it gives best palliation. Trepine colostomy

formation has little value and has obvious implications regarding body image, quality of life and management/dependency issues.

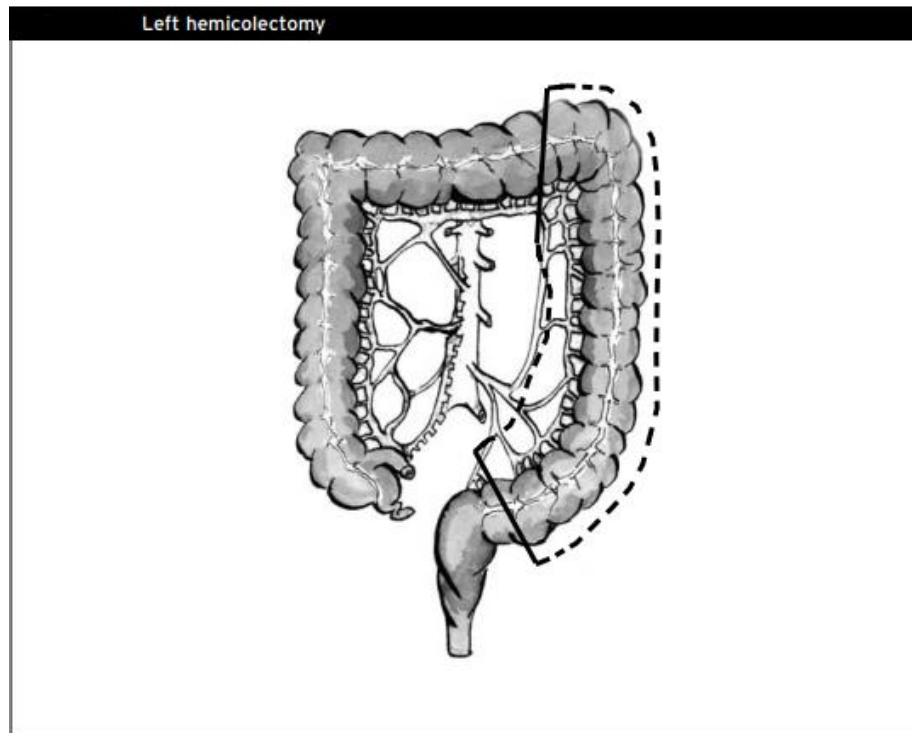


FIGURE 67: SCHEMATIC ILLUSTRATION OF LEFT HEMICOLECTOMY

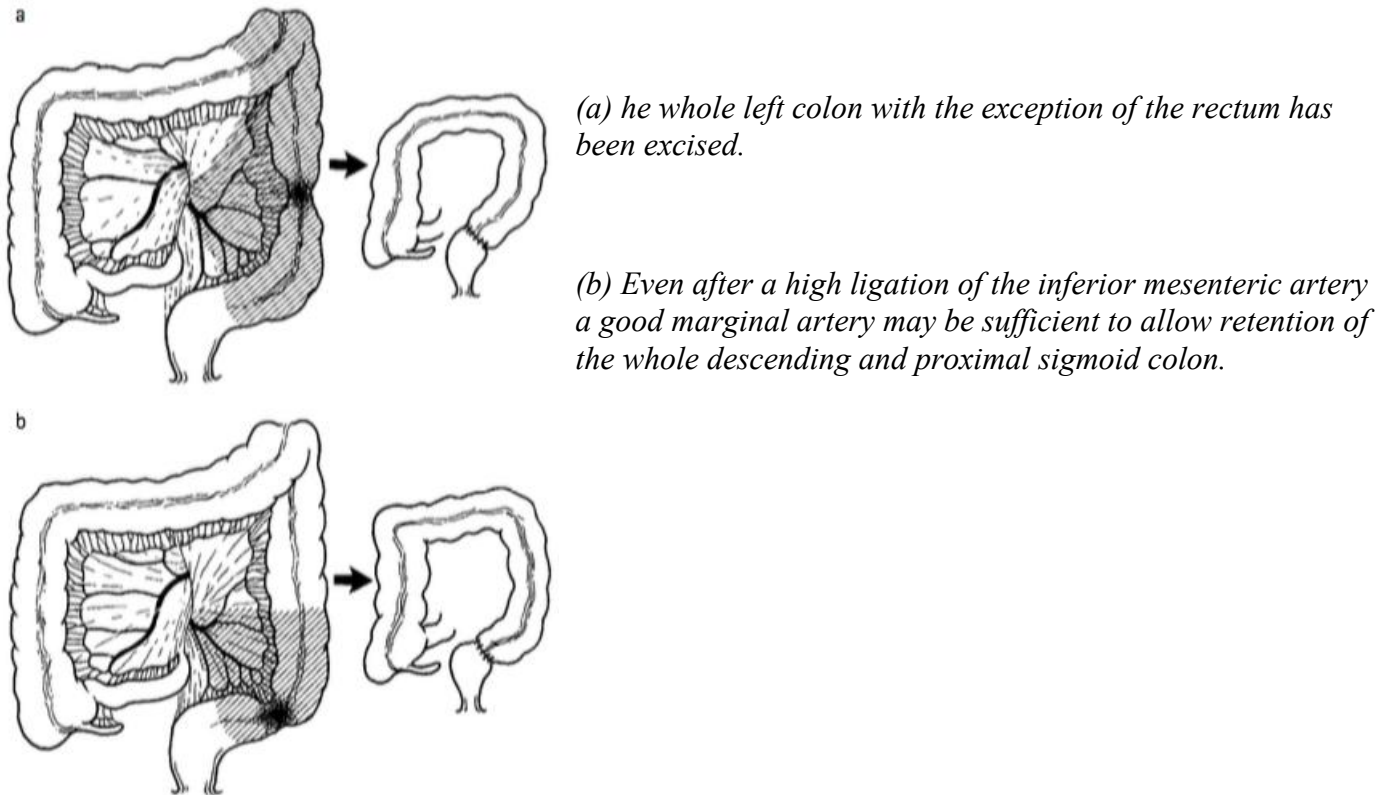


FIGURE 68: LEFT HEMI-COLECTOMY BASED ON LYMPHATIC DRAINAGE AROUND THE IMA

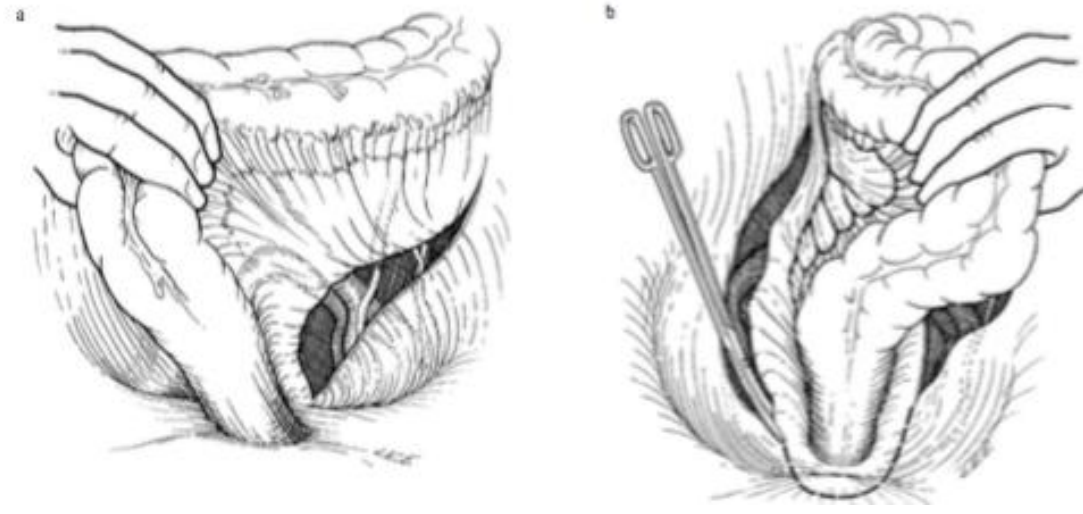


FIGURE 69: LEFT HEMI-COLECTOMY(MOBILIZATION)

(a) The descending and sigmoid colon mobilization starts on the left, and the ureter must be identified early.

(b) When the dissection from the left has reached the midline, the colon is swung to the left. The right leaf of the peritoneum is incised to form a window in front of the aorta and behind the mesenteric package which contains the inferior mesenteric artery, its branches and the lymphatic drainage of the hind gut. The inferior mesenteric artery is then ligated and divided close to its origin. The anterior and lateral peritoneal incisions around the rectum allow it to be drawn up to make an anastomosis easier.

5-4 Sigmoid colectomy:

Carcinoma of the sigmoid colon is occasionally managed by sigmoid colectomy with primary anastomosis of the descending colon to the rectum, although more frequently anterior resection or left hemicolectomy is the surgical option of choice.

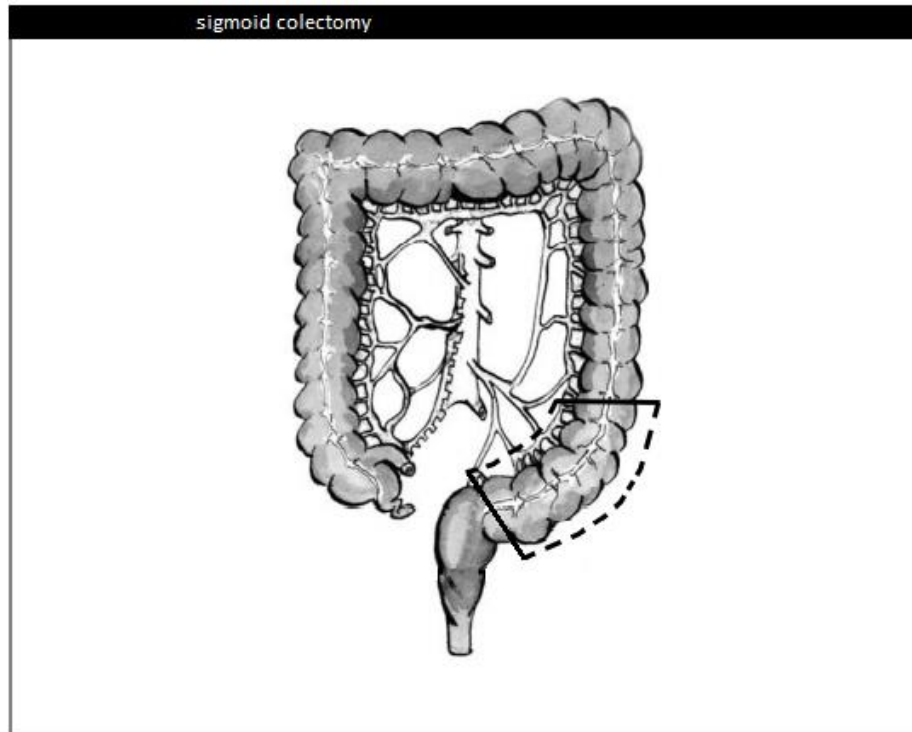


FIGURE 70: SIGMOID COLECTOMY

Tumor Location	Procedure
Cecum and ascending colon	Right hemicolectomy. Resect distal ileum to mid transverse colon with ileocolic, right and middle colic with mesentery
Left transverse colon to splenic flexure	Extended right hemicolectomy or transverse colectomy. Resect transverse and proximal descending colon with middle and left colic arteries
Descending and sigmoid colon	Left hemicolectomy or sigmoid colectomy. Resect from splenic flexure to rectosigmoid with left colic and sigmoidal arteries
Proximal third of rectum 5-10 cm from anal verge	Anterior resection, low anterior resection or abdominal-sacral resection
Distal third of rectum	Abdominoperineal resection (Miles procedure) with sigmoid colostomy. Low anterior resection with reanastomosis if >4 cm of rectal tissue remains. Sphincter saving operations are gaining popularity

FIGURE 71: SURGICAL PROCEDURES BASED ON CANCER LOCATION

6-Surgery in emergency settings

6-1 Obstructing cancer

Cancers are the most common cause of large bowel obstruction. Left-sided cancers are more likely to cause obstruction, but obstruction may be caused by cancers at virtually any location. Obstructing cancers tend to be large and are usually associated with poor prognosis with many already having distant metastases.

Treatment will depend to some extent on whether the patient is partially obstructed or completely obstructed. If possible, it is always worthwhile to delay surgery to allow the obstruction to resolve. However, if the patient is completely obstructed, emergency surgery may be necessary. For patients with right-sided obstructing lesions a right hemicolectomy with a primary anastomosis can usually be performed unless there are extenuating circumstances. A defunctioning stoma is not necessary.

Treatment options for obstructing lesions of the left colon include the following: Hartmann procedure, subtotal colectomy and ileorectal or ileosigmoid anastomosis or a washout procedure followed by resection and anastomosis. In rare circumstances, a defunctioning colostomy alone may be the preferred option but it should probably be reserved for patients with significant comorbidities or who are systemically unstable or as a palliative procedure. Each of the other procedures has both advantages and disadvantages. The Hartmann procedure is the standard operation and is probably the most straightforward procedure. Mobilization of the splenic flexure, which might be difficult if the bowel is greatly distended, is not required. It is the preferred option for

unstable patients or those in whom it might be safe to perform an anastomosis. The disadvantage of a Hartmann procedure is that second operation is required.

In fact, reconstruction is never performed in a large proportion of patients who are elderly or have comorbidities. Colectomy and ileorectal or ileosigmoid anastomosis eliminates the need for a second operation. Furthermore, it eliminates stoma problems and deals with synchronous cancer if present and unsuspected. It, however, should not be performed if the resection line is below the sacral promontory or in elderly patients as functional results might be suboptimal. In younger patients, it's is probably the procedure of choice. It may also be required if there are ischemic changes or tearing of the caecal serosa due to the obstruction.

Theoretically, colonic washout followed by segmental resection and anastomosis is the best option. However, surgery for obstructing cancers is usually performed in the middle of the night and the washout tends to be tedious and fraught with mishaps so this technique has not gained popularity with many surgeons. If undertaken, the resection is performed in the usual way. Intravenous tubing is then threaded into the appendix and anesthetic tubing is inserted into the bowel at the proximal resection margin. An umbilical tape is used to fasten securely the tubing. The distal end of the anesthetic tubing is placed in a bucket. the splenic flexure needs to be mobilized so one can assist with the passage of the fluid and stool. several liters of saline are required to wash out the colon but once complete, an anastomosis is performed.

The operative morbidity and mortality following emergency or urgent surgery for obstructing cancers is higher than following elective surgery and vary widely depending on the site of the tumor and the type of procedure performed as well as the status of the patient. Furthermore, obstructing cancers tend to be more advanced than non

obstructing cancers and there for curative operation may be possible in only half of them.

6-2 Perforation

Perforation is an uncommon complication but portends a poor prognosis. The perforation may be at the site of the tumor or may occur secondarily at a proximal site, usually the caecum, in obstructing cancers. there may be invasion of other structures and organs. Primary resection is the preferred treatment and if there is a contained perforation, it may be possible to undertake a primary anastomosis. Otherwise, a colostomy or an anastomosis with a defunctioning stoma may be necessary. If the perforation is in the right colon due to an obstructing left sided lesions, a subtotal colectomy is required.

7- surgery complications:

7-1 Operative mortality and morbidity:

Operative morbidity is affected by:

- preoperative health status of the patient
- elective or emergency procedure
- age
- pre-existing health problems of the patient.

Where possible, all colorectal surgery should be performed in the daytime when the full compliment of the colorectal specialty is available. The preoperative anaesthetic assessment is essential, as this directly translates morbidity risk and assists in the preparation for intensive care or high-dependency input.

7-2 General early complications of colonic surgery:

- Cardiorespiratory:
 - deep vein thrombosis
 - pulmonary embolism
 - chest infection
- Anastomotic leakage
 - more prevalent in left-sided resections
- Sepsis and wound infection
- Urinary retention and infection
- Impotence
- Accidental damage to other organs, e.g. ureters
- Intra-abdominal abscess.

Operative mortality and morbidity are greatly increased with emergency surgery, and when perforation occurs this increases the possibility of:

- wound infections (caused by possible faecal contamination)
- dehiscence
- intraperitoneal abscess
- anastomotic leak
- generalized peritonitis
- systemic sepsis and multi-organ failure

7-3 Late complications:

- Anastomotic stricture
- Small bowel or colonic obstruction caused by adhesions
- Tumor recurrence.

The Association of Coloproctology indicates an acceptable mortality rate of between 3 and 7 per cent for elective surgery and between 1 and 25 per cent for emergency procedures. Wound infections should be less than 10 per cent, and anastomotic leak rate should be less than 4 per cent.

8-Systemic therapy for colon cancer[31] [32] [33] [34] [35] [36]

The fluoropyrimidine analog fluorouracil (5-FU) first developed by Heidelberger and coworkers in 1957 was the only first-line chemotherapeutic option for patients with advanced colorectal cancer until the late 1990s. As such, 5-FU underwent extensive dose and schedule optimizations and combinations with different modulators to improve response and survival rates. Median survival beyond 12 months, however, was rarely attainable.

Over the past 10 years, considerable investigational work has resulted in new drugs and more innovative combination strategies for treating colon cancer. The new landscape of systemic therapy for colon cancer has seen the addition of irinotecan, oxaliplatin, and capecitabine as cytotoxic agents. In addition, targeted therapies, such as the first monoclonal antibody against the vascular endothelial growth factor (VEGF), bevacizumab (Avastin), was approved in 2004 for first-line therapy for metastatic colorectal cancer.

Two monoclonal antibodies against the epidermal growth factor receptor (EGFR), cetuximab and more recently panitumumab, have been approved for chemotherapy-refractory colorectal cancer. *K-ras* codon 12/13 testing has revolutionized the way in which EGFR-targeting antibodies are used in the clinic.

8-1 Fluorouracil and Leucovorin

The benefit of systemic therapy in the management of metastatic colorectal cancer was initially established in the 1980s and 1990s. Several phase III randomized trials showed improvement in the quality of life and overall responses despite low objective response rates (RR 10%–20%) with the use of 5-FU and leucovorin (LV).

According to a meta-analysis of 13 such trials, systemic chemotherapy significantly improved overall survival compared with best supportive care. Fluorouracil forms the back-bone of systemic therapy for advanced colorectal cancer, and the survival of these patients nearly doubled with the advent of new chemo-therapeutic and targeted agents.

Fluorouracil and leucovorin are administered intravenously in a variety of dosing schedules. In the loading bolus schedules, 5-FU and leucovorin are administered daily in bolus for 5 consecutive days and repeated every 28 days (Mayo Clinic Protocol); alternatively, in the weekly bolus schedule, 5-FU and leucovorin are given weekly for 6 of every 8 weeks (Roswell Park regimen).

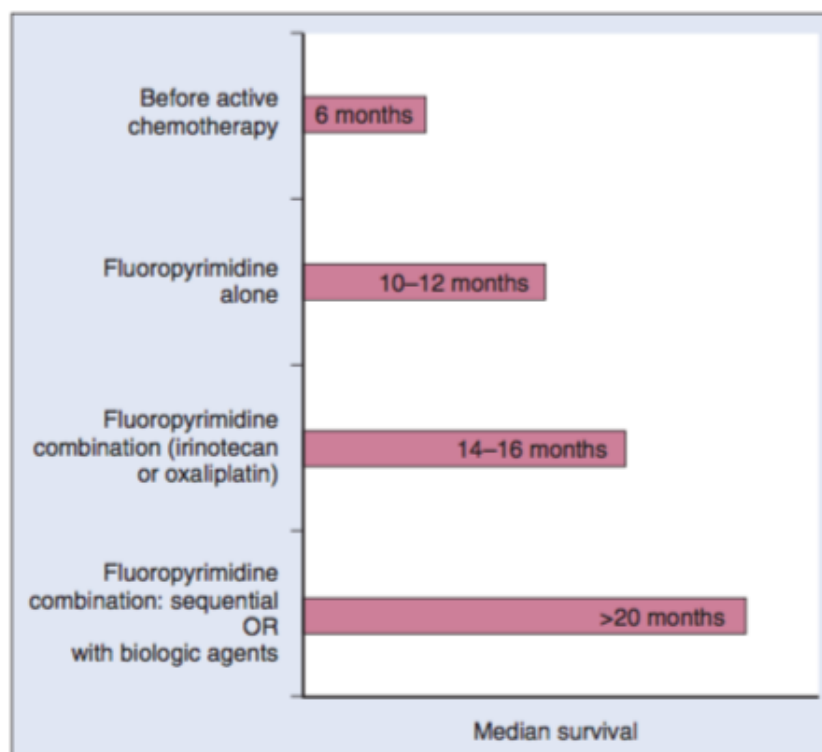


FIGURE 72: MEDIAN SURVIVAL OF PATIENTS WITH ADVANCED COLONRECTAL CANCER

8-2 Irinotecan

The advent of a number of active agents allowed the use of combination chemotherapy (Box below). The earliest combination regimens used irinotecan with various schedules of 5-FU/LV in first-line therapy of metastatic colorectal cancer.¹⁷⁻¹⁹ Irinotecan (alsoknown as CPT-11) is a semisynthetic derivative of the natural alkaloid camptotecin and exerts its cytotoxic effects by inhibiting topoisomerase I, which is necessary for the proper uncoiling of DNA for replication and transcription.

Box 15-1. Selected Agents with Proven Efficacy in Metastatic Colorectal Cancer	
Cytotoxic Agents	
Fluoropyrimidines	
5-Fluorouracil (+ folinic acid/leucovorin modulation)	
Capecitabine	
Tegafur/uracil	
S-1	
Irinotecan	
Oxaliplatin	
Biologic/Targeted Agents	
Bevacizumab	
Cetuximab	
Panitumumab	

FIGURE 73: SELECTED AGENTS WITH PROVEN EFFICACY IN METASTATIC COLON CANCER

In first-line advanced colorectal cancer therapy, irinotecan improved median survival by about 2 months and almost doubled the response rate when combined with 5-FU and leucovorin in two randomized trials.

8-3 Oxaliplatin

Oxaliplatin is a third-generation diaminocyclohexane-containing platinum compound that forms bulky DNA adducts and induces cellular apoptosis. Unlike

previous generations of platinum compounds, oxaliplatin showed promising activity against human colorectal cell lines in preclinical studies. In clinical studies, oxaliplatin had limited single-agent efficacy but was highly synergistic with fluoropyrimidines in first- and second-line therapy for metastatic colorectal cancers. A possible mechanism was downregulation of thymidylate synthase by oxaliplatin.

8-4 Oral Fluoropyrimidines

The oral fluoropyrimidine that has been studied the most is capecitabine. Having been designed to recapitulate the pharmacokinetics of continuous infusion 5-FU via oral administration, capecitabine was compared with the Mayo Clinic regimen of bolus 5-FU/LV in a phase III trial. It was found to have superior response rates, equivalent PFS and overall survival, and a favorable toxicity profile.⁴⁸ These observations led to studies exploring capecitabine as an alternative to infusional 5-FU in combination with oxaliplatin or irinotecan.

8-5 Adjuvant systemic therapy

8-5-1 The Fluoropyrimidines

In 1995, the results of the IMPACT (International Multicentre Pooled Analysis of Colon Cancer Trials) study were published. In this pivotal study, data were pooled from 1526 patients with resected Dukes' B and C colon cancer enrolled in three independent international trials. All the patients were randomized to either observation alone or 6 monthly cycles of 5-FU/LV. There was a significant 22% reduction in the risk of death in the 5-FU/LV arm with 3-year overall survival increasing by 5% (83% versus 78%) in the treated group. Subsequent subgroup analysis showed that the benefit was limited to patients with node-positive disease. Subsequently, a flurry of randomized studies trying to optimize this therapy was performed.

A number of important observations emerged from these trials. First, administering 5-FU/LV for 6 months was equally effective as it was for 12 months. Second, 5-FU administered with high-dose leucovorin (200-500 mg/m²) is equivalent to low-dose leucovorin (20 mg/m²). Finally, no significant difference was found between the two most widely used regimens for administering bolus 5-FU/ LV, namely, the Mayo Clinic and the Roswell Park regimens.

Furthermore, despite the significant survival advantage and lower hematologic toxicity with continuous infusion 5-FU over bolus regimens in advanced colorectal cancer, this observation did not pan out in the adjuvant setting. In at least three studies comparing continuous infusion to bolus 5-FU in adjuvant treatment of colon cancer, no statistically significant differences were observed in either disease-free survival or overall survival.

5-8-2 Combination Adjuvant Chemotherapy (Oxaliplatin and Irinotecan)

The significant impact of oxaliplatin and irinotecan in metastatic colorectal cancer provided the rationale for their evaluation in the adjuvant setting. Two major trials evaluated the combination of 5-FU/LV with oxaliplatin.

The MOSAIC trial randomized 2200 patients, of whom 60% had stage III and 40% had stage II colon cancer, to either infusional 5-FU/LV or the same regimen combined with oxaliplatin (FOLFOX4). With a median follow-up of 3 years, there was a statistically significant 5% improvement in PFS for the oxaliplatin-containing regimen. The overall survival benefit reached statistical significance in only the stage III patients (68.3 vs. 72.9% probability of survival at 6 years), whereas there was no difference in overall survival for the stage II patients.

Material and methods

I– Objectives:

The overall aim of this thesis is to verify whether patients diagnosed with colon cancer in an emergency setting differ from scheduled elective surgery in terms of presentation characteristics, surgical stay outcomes and survival.

II– Patients and methods:

1– Study framework

Clinical, operative and follow up data have been collected from both general surgery department "A" and "B" of the University hospital Hassan II in Fez: a teaching hospital with a capacity of 1050 beds located in the northeaster part of the country.

This study is a descriptive, retrospective, comparative analysis involving cases who underwent colon cancer surgery in the university hospital CHU Hassan II, Fes between 2012 and 2015.

2– Material:

All colon cancer patients admitted for colon cancer at the departments of general surgery A and B at the university hospital Hassan II, Fes, from January 1st 2011 to December 31st 2015, (n= 203) were eligible.

Patients admitted through the emergency room, operated on within three days of admission, and with an emergency condition (obstruction, perforation or bleeding) confirmed at surgery were classified as colon cancer emergencies.

Also patients who presented with symptoms indicating colon cancer and confirmed in the same hospital or referrals to the surgery services A and B after being diagnosed with colon cancer

3- Data extraction

- A non computerized research using:

admission and follow up registers from both services A and B: patients admitted for colon cancer or presented as an emergency that could have an underline colon cancer (bowl obstruction, perforation, GI bleed, abscess)

we also used medical charts archived in both services, operative reports, pathology reports and hospital stay reports.

- A computer search of cases with colon cancer on the data collection system "HOSIX" using patient's identification

4- Population studied

4-1 Inclusion criteria:

All cases of colon cancer (>12 cm from the anal margin) admitted to the university hospital Hassan II through the Emergency department or appointments were included in this study.

4-2 Exclusion criteria:

- Patients with colon cancer at less than 12cm from the anal margin.
- Patients whose files were lost or incomplete.

5- Statistical analysis:

All patients' data were coded and imported into MS Excel® worksheets and posteriorly analyzed by epidemiology specialists using IBM SPSS Statistics in 3 steps.

we compared percentages using Khi-square and Fisher test, and we used student's test to determine the significance of each test.

A 2-tailed P value below 0.05 was considered statistically significant. We compared dichotomous outcomes among emergency and elective patients using the chi-square test and a relative risk (RR) calculation, while a 1-way analysis of variance or a univariate linear regression, with the unstandardized B regression coefficient as a point estimate, was used for continuous outcomes. Multivariate analysis was performed to control the findings for any potentially significant confounders found during univariate analysis.

1- We performed a descriptive analysis of data collected. The results were presented as a percentage and mean \pm standard deviation.

2- Univariate analysis for comparing averages and percentages using statistical tests Student and khi 2 and fisher.

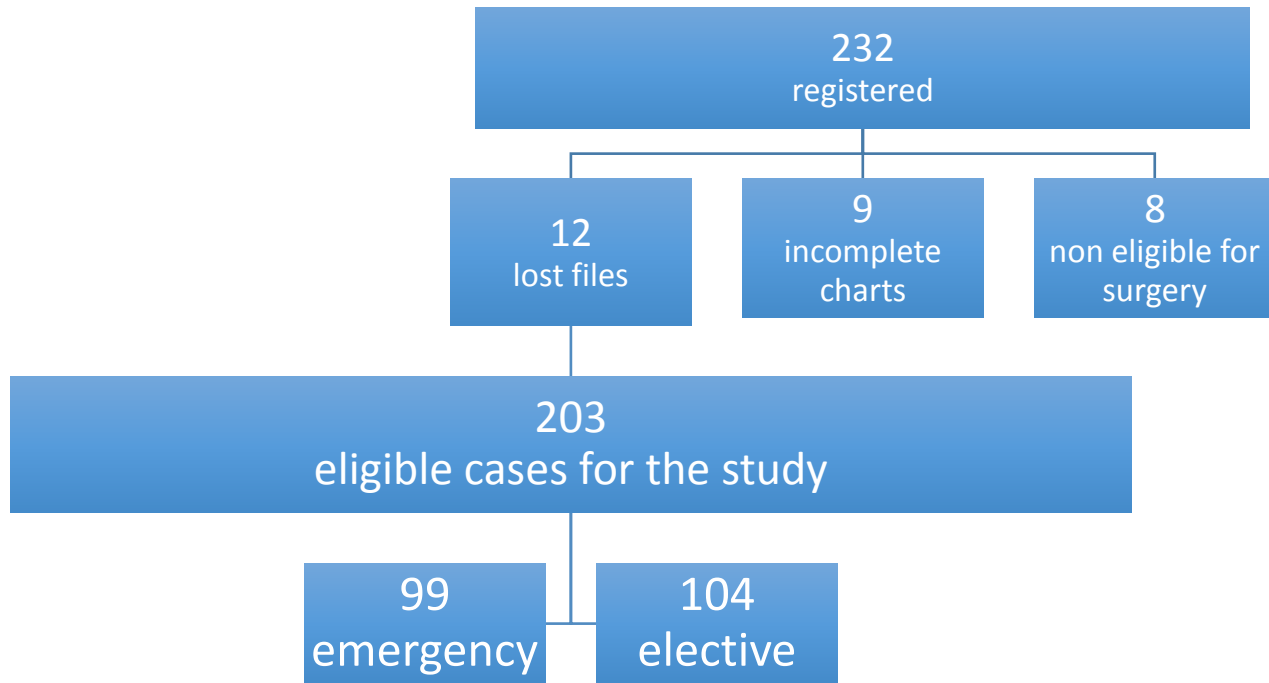
3- Multivariate analysis by logistic stepping down regression. The results are reported in graphs and tables commented. A $p < 0.05$ was considered significant.

6- Study design

we initially gathered 232 cases registered in the departments' registers.

- 8 weren't eligible for surgery.
- 12 files were lost in the archive and couldn't be traced on the system.
- 9 patients' charts were judged very incomplete.

203 patients were eligible for our study represented in the following chart.



Statistical

results

I– Epidemiological data

1– Patients' recruitment per year

From January 2012 to December 2015, 203 patients were diagnosed with colon cancer (>12 cm of the anal margin).

12 files were lost in storage and 9 were incomplete to be included in the study.

203 patients were studied in a 4–year period, with an average of 50 patients per year (4 to 5 patients per month) with a minimum of 37 and a maximum of 62 patients per year.

two hundred and four patients form the overall sample of our study.

TABLE 5: ANNUAL DISTRIBUTION OF PATIENTS' ADMISSION

<u>year</u>	<u>patients (n=203)</u>	<u>percentage</u>
2012	61	30,4 %
2013	50	24,5 %
2014	55	27,0 %
2015	37	18,1 %
total	203	100%

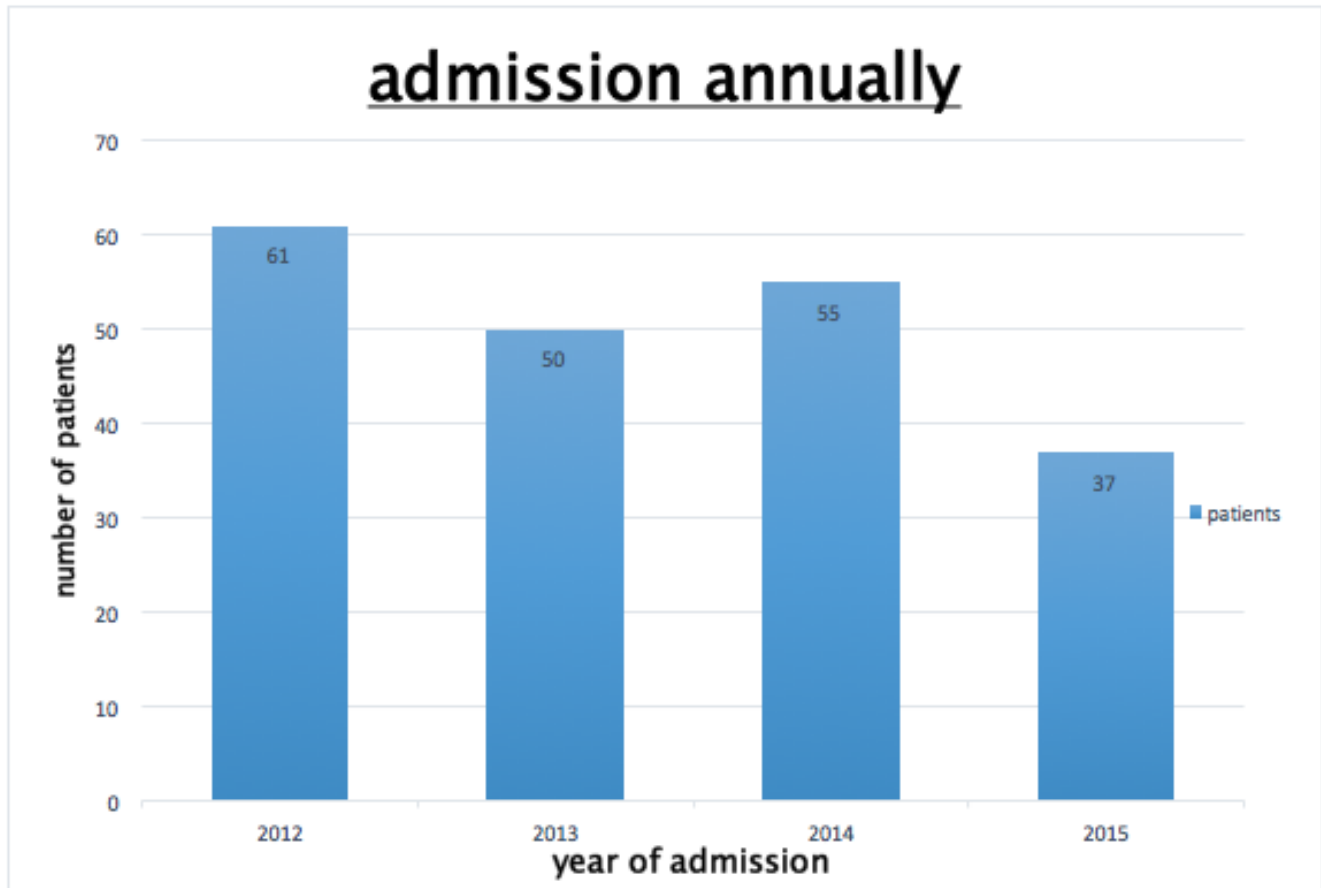


FIGURE 74: ADMISSION PER YEAR

2- Distribution by age

We documented a mean age of 57 years ranging from 20 to 97, with a median of 59 years.

TABLE 6: DISTRIBUTION OF PATIENTS BY AGE

number	minimum	maximum	median	standard deviation
203	20	97	59,36	14,731

TABLE 7: PATIENTS' DISTRIBUTION BY AGE GROUPS

age (years)	number	percentage
<50	58	28,5 %
50-70	109	53,7 %
>70	36	17,8 %

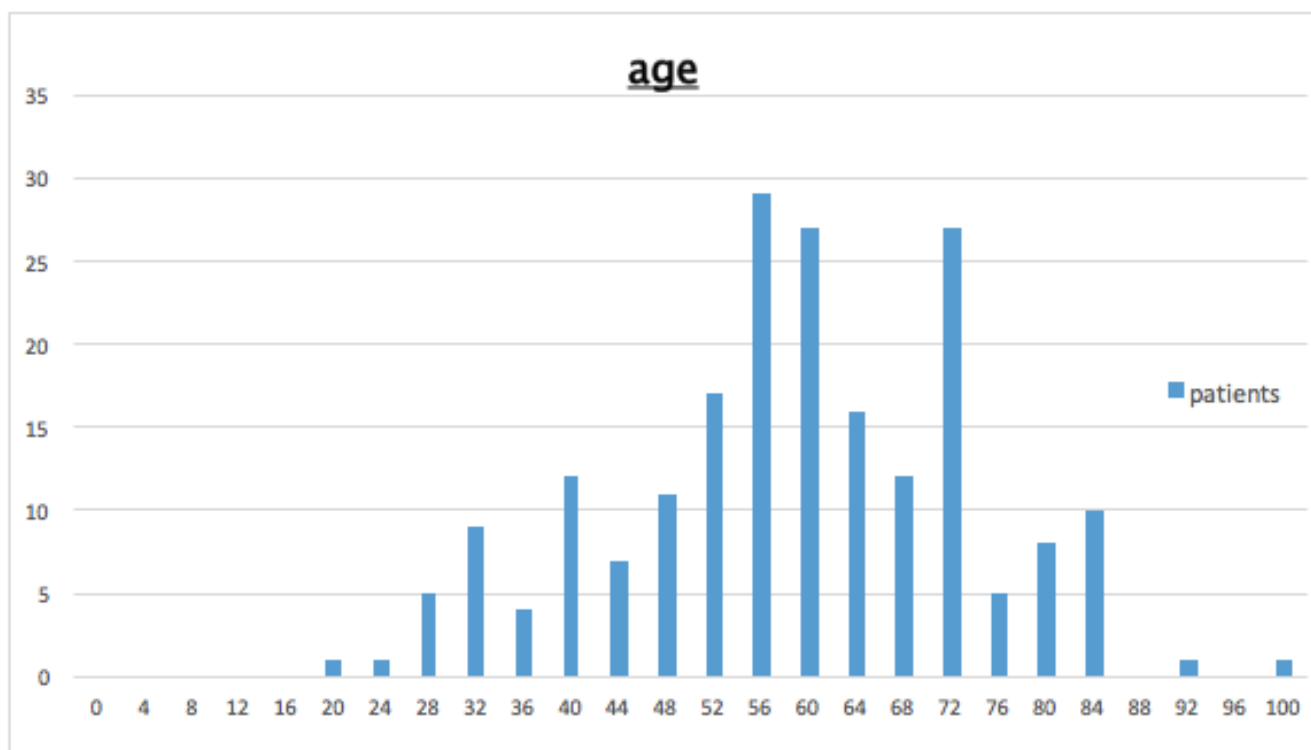


FIGURE 75: PATIENTS' DISTRIBUTION BY AGE

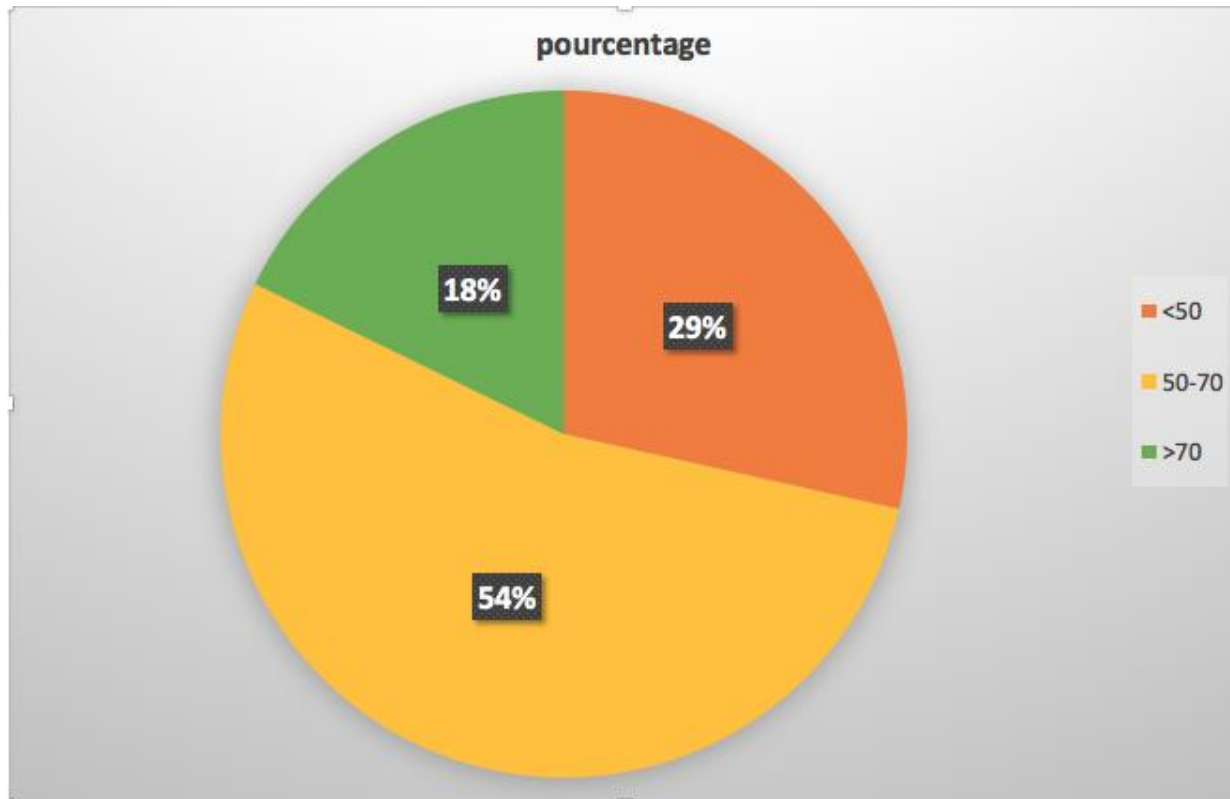


FIGURE 76: PERCENTAGE OF PATIENTS BY AGE CATEGORY

3- Gender distribution

We noticed a slight predominance of males over women on our study, 114 males and 89 females with a sex ratio of $M/F = 1.2$

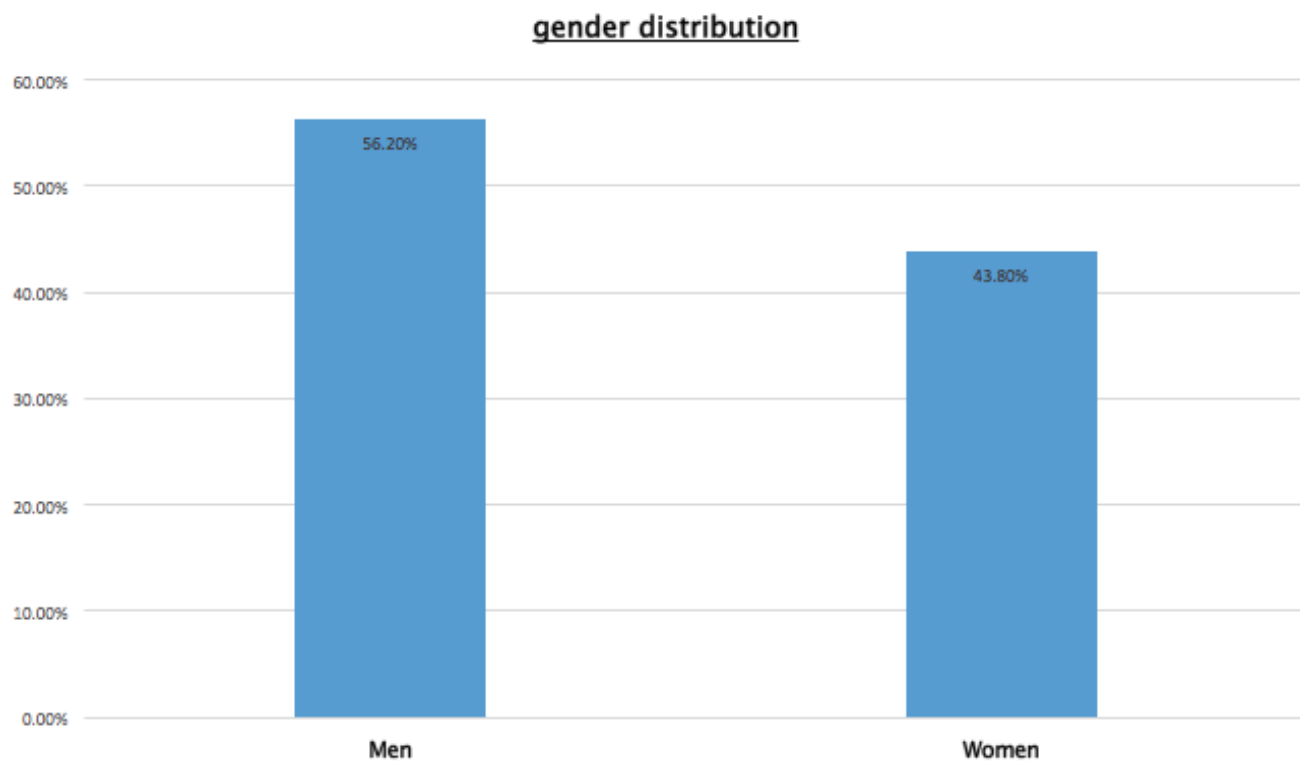


FIGURE 77: GENDER DISTRIBUTION

4- Distribution by area of origin

138 cases in our sample are originally from an urban area while only 65 patients were referral from rural zones.

TABLE 8: DISTRIBUTION OF PATIENTS BY ORIGIN

origin	patients	percentage
urban	138	68%
rural	65	32%
total	203	100%

II- Clinical study

1- Consultation period

Emergency presentation patients took an average of 5 days before consultation but elective surgery patients averaged 4.5 months after first symptoms

2- Personal history

We didn't note any particular medical or surgical history for 140 of the patients which represent 69% of the overall studied sample, whereas 83 (31%) of them presented with a positive history for a surgical or a medical condition.

2-1 Medical history

48 patients 23.5% of our sample had a concomitant disease distributed as following on the table bellow.

TABLE 9: MEDICAL HISTORY

<u>medical history</u>	<u>patients</u>	<u>percentage</u>
High blood pressure	16	33%
Diabetes	19	39.50%
Cardiopathy	5	10.50%
Nephropathy	3	6%
Asthma	2	4%
Tuberculosis	3	6%
Total	48	100%

2-2 Surgical history

35 cases of our sample presented with surgical history, represented in the table following:

TABLE 10: SURGICAL HISTORY

<u>Surgical history</u>	<u>patients</u>	<u>percentage</u>
Cholecystectomy	12	35%
Hernia	7	20%
Myomectomy	3	8.50%
C- section	8	23%
Appendectomy	4	11.50%
Valve replacement	1	2%
total	35	100%

3- Family history of cancer

Patients with family history of cancer represent 6.9 % (n=14 cases) of our sample.

TABLE 11: FAMILY HISTORY OF COLORECTAL CANCER

	<u>patients</u>	<u>percentage</u>
History of CRC	14	6.90%
No history of CRC	189	93.1%
Total	203	100%

4 patients have a history of familial adenomatous polyposis (FAP) with a percentage of 2%.

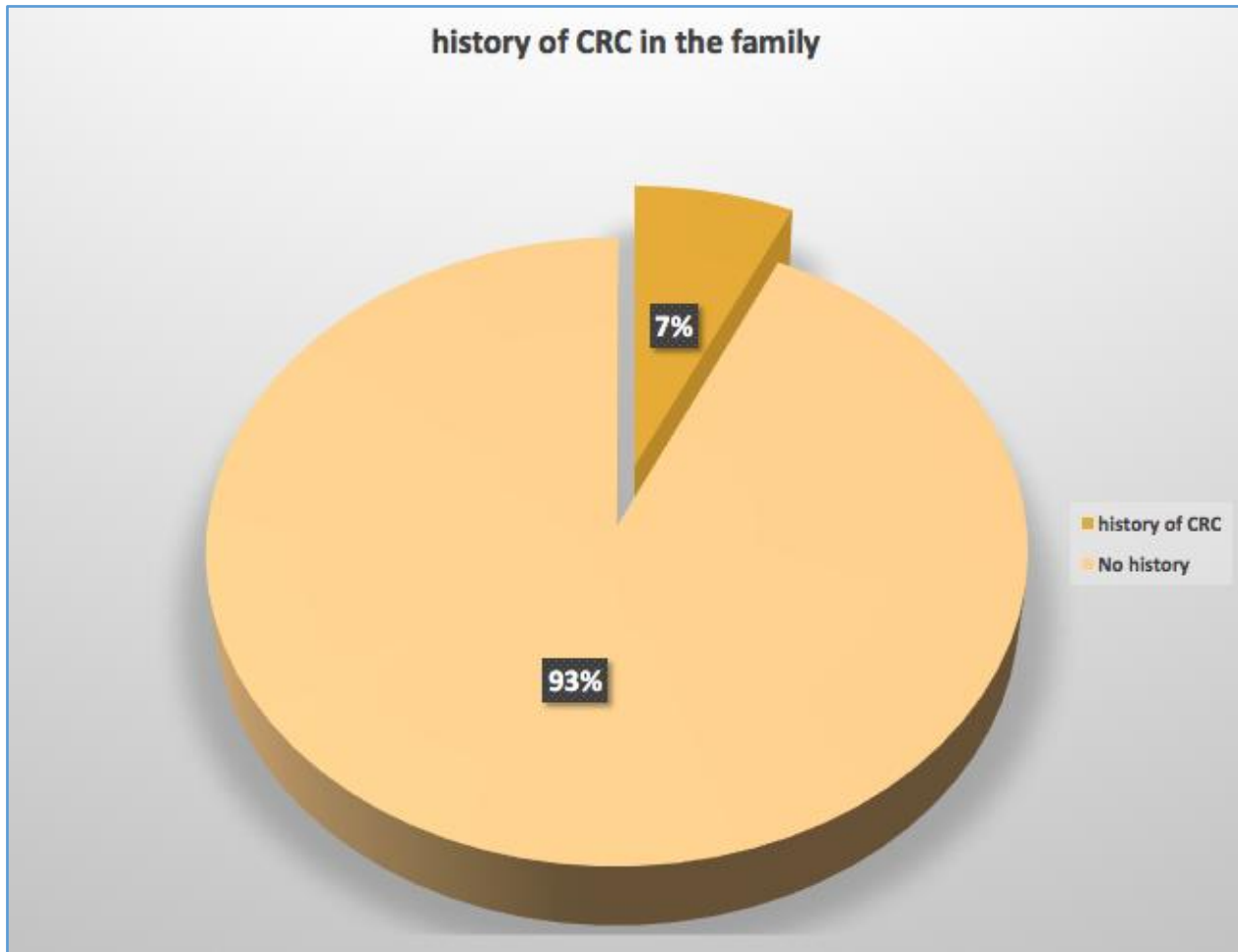


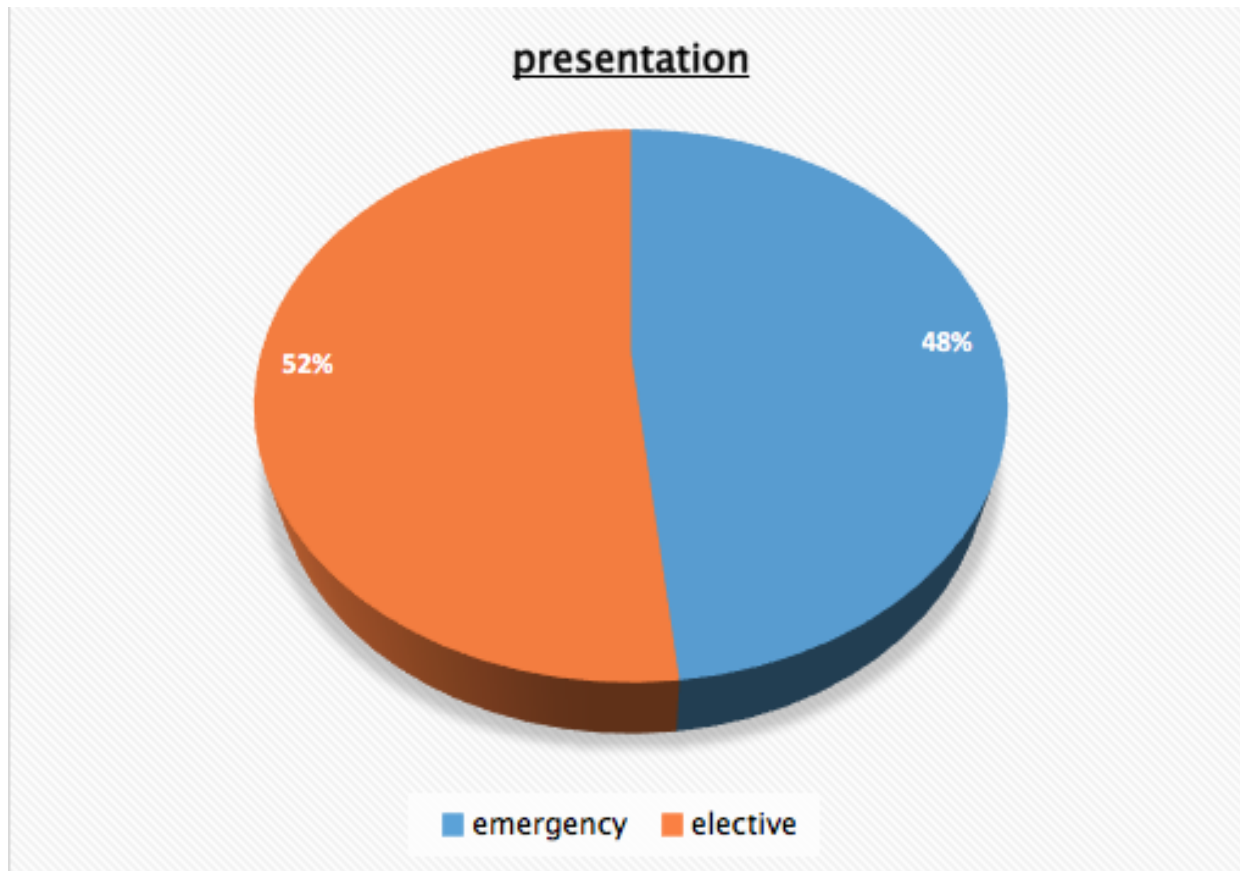
FIGURE 78: HISTORY OF COLORECTAL CANCER IN THE FAMILY

4- Type of presentation

104 cases presented with colon cancer symptoms and were diagnosed after work up while 99 cases presented initially with emergencies revealing an underline tumor of the colon

TABLE 12: TYPE OF PRESENTATION

presentation	patients	percentage
emergency	99	48.80%
elective	104	52.20%
total	203	100%

**FIGURE 79: TYPE OF PRESENTATION****5- Type of emergency**

We recorded 99 cases with emergency presentation of CRC 85 of which are bowel obstruction alone, 11 cases of perforation, 1 case of abscess, 1 case of abscess with perforation, and 1 case of abscess with bowel obstruction.

TABLE 13: TYPES OF EMERGENCIES

<u>emergency</u>	<u>patients</u>	<u>percentage</u>
bowel obstruction	85	85%
perforation	11	11.50%
abscess	3	4.50%

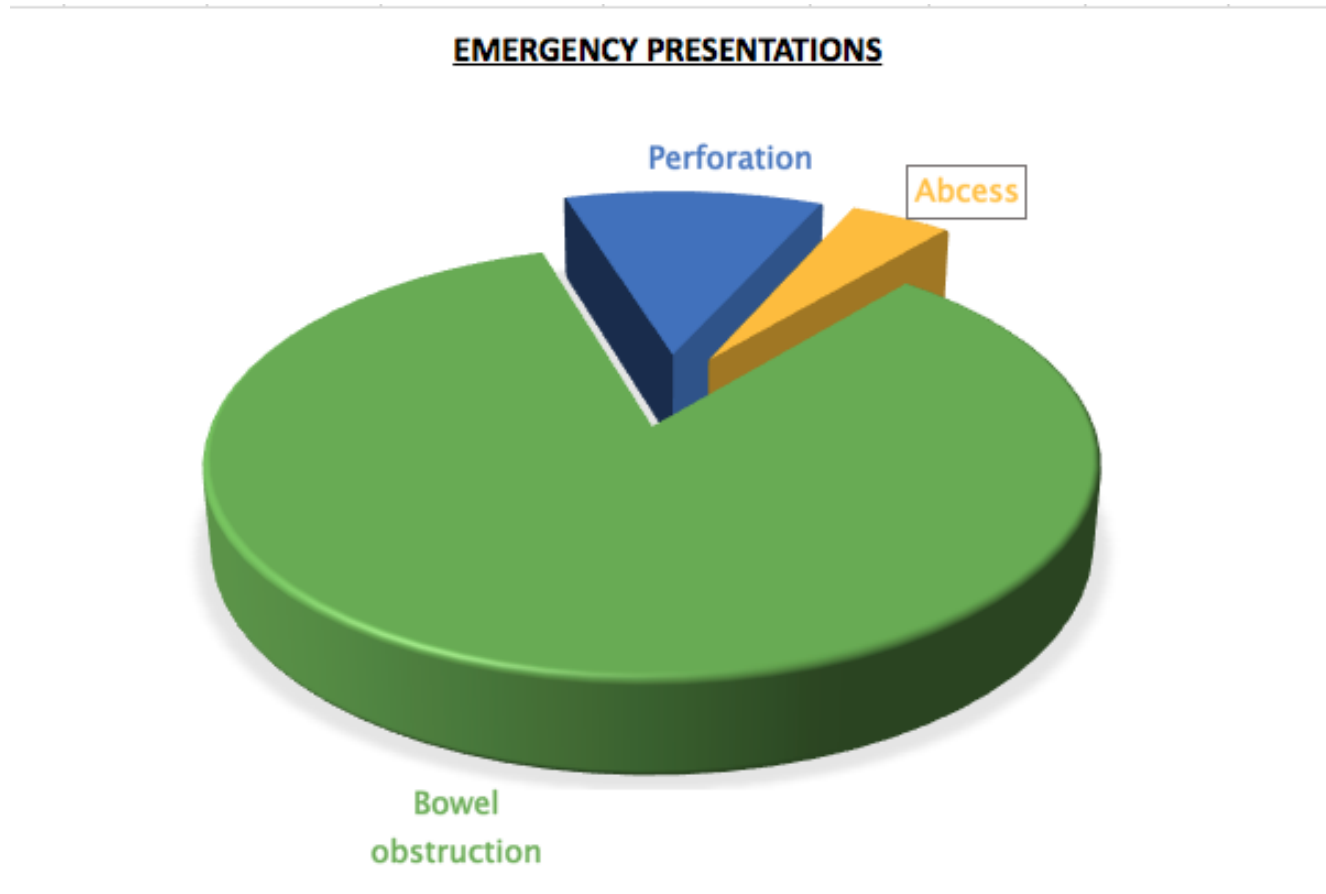


FIGURE 80: PRESENTATION OF TYPE OF EMERGENCIES

Of all our cancer patients Bowel obstruction represents 42.4%, perforation 6% and abscess 1.5%.

6- Tumor site

We recorded a most frequent tumor site to be the left colon with 138 cases (68%) second is the right colon with 55 patients (27%) and the less frequent site is the transverse colon with only 10 patients (5%).

TABLE 14: TUMOR SITES

tumor site	number of patients	percentage
right colon	55	27.00%
transverse	10	4.90%
left colon	138	68%
total	203	100%

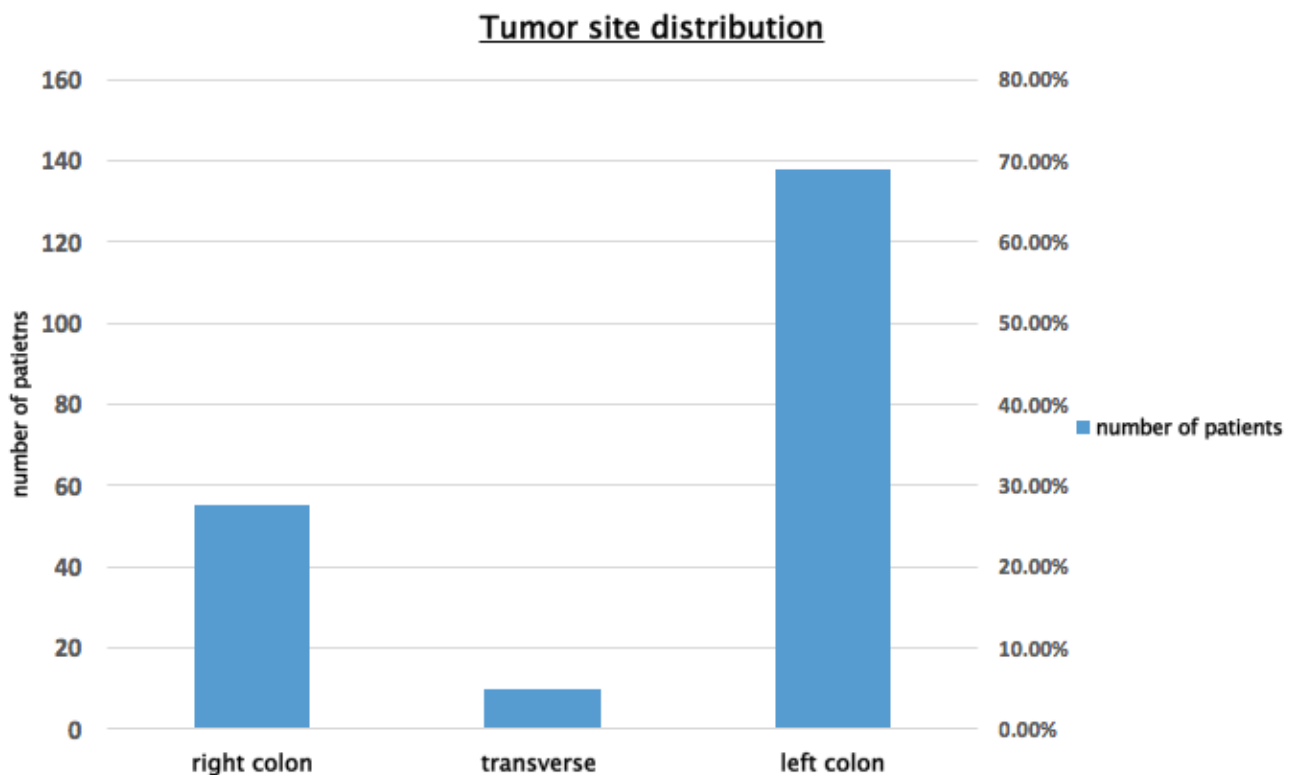


FIGURE 81: TUMOR SITE DISTRIBUTION

III– Treatment statistics

1– Type of surgery

195 cases of our sample received a surgical treatment 21 of which palliative stoma (10%), 47 cases a right colectomy (23%), 112 left colectomy (56%), 11 cases total colectomy (5%), and 8 cases with multivisceral resection (4%).

TABLE 15: TYPE OF SURGERY

Type of surgery	patients n=	percentage
Palliative stoma	22	10,8 %
Right colectomy	47	23,2 %
Left colectomy	115	56,6 %
Total colectomy	11	5,5 %
Multivisceral resection	8	3,9 %
Motal	203	100.00%

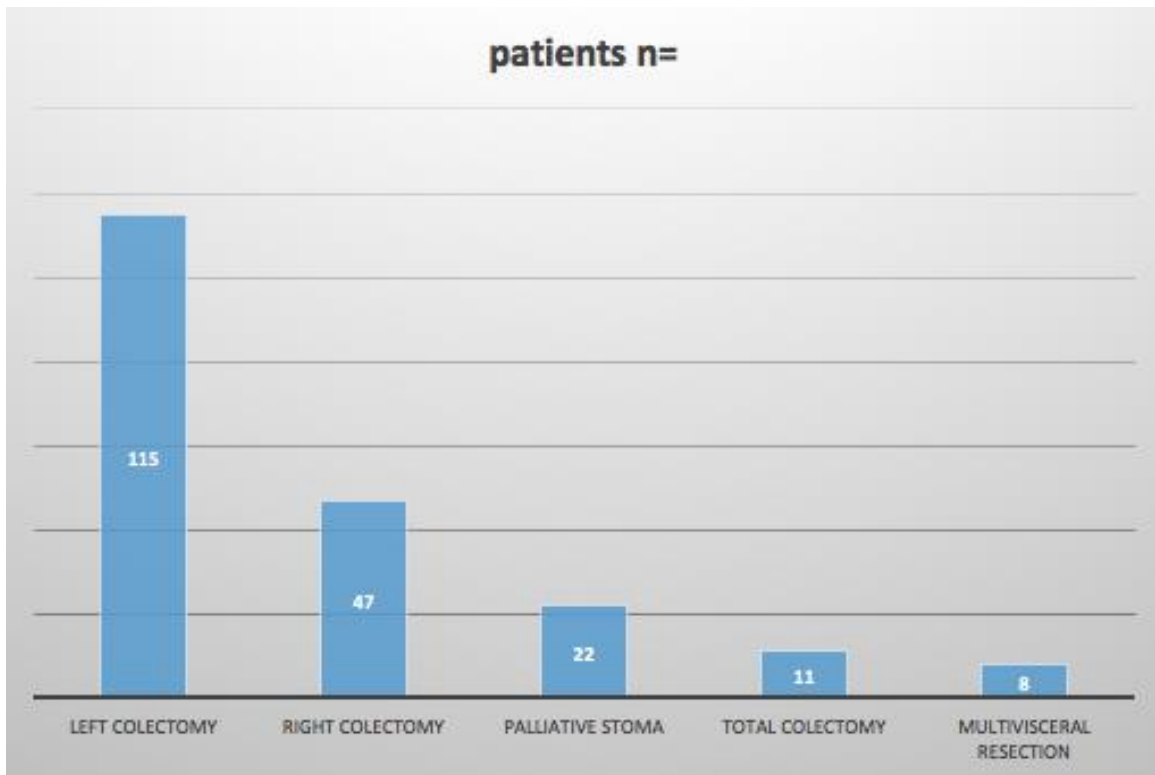


FIGURE 82: TYPE OF SURGERY PERFORMED

2- One stage surgery and two stage surgery

we recorded 133 cases who underwent one stage surgery (66%) and 70 patients who received a two stage surgery (34%).

TABLE 16: ONE STAGE VERSUS TWO STAGE SURGERY

	patients	percentage
one stage surgery	133	66%
two stage surgery	70	34%
total	203	100%

3- Surgical pathology statistics

2-1 Degree of differentiation

Our pathology findings showed a predominance of well differentiated adenocarcinoma with a percentage of (57%), moderately differentiated adenocarcinoma (34%), poorly differentiated ADK 1%, mucous colloid ADK 7%, and Independent cell carcinoma 0.5%.

We couldn't have pathology reports for 35 of our patients 21 of them underwent palliative stoma and 14 reports couldn't be traced, which leaves us with 168 reliable pathology reports of which the results are displayed in table below:

TABLE 17: DEGREE OF DIFFERENTIATION

<u>pathology</u>	<u>patients n=</u>	<u>percentage</u>
Well differentiated adenocarcinoma	96	57.50%
Moderately differentiated adenocarcinoma	57	34%
Poorly differentiated adenocarcinoma	2	1%
Mucous colloid adenocarcinoma	12	7%
Independent cell carcinoma signet cell carcinoma	1	0.50%
Total	168	100%

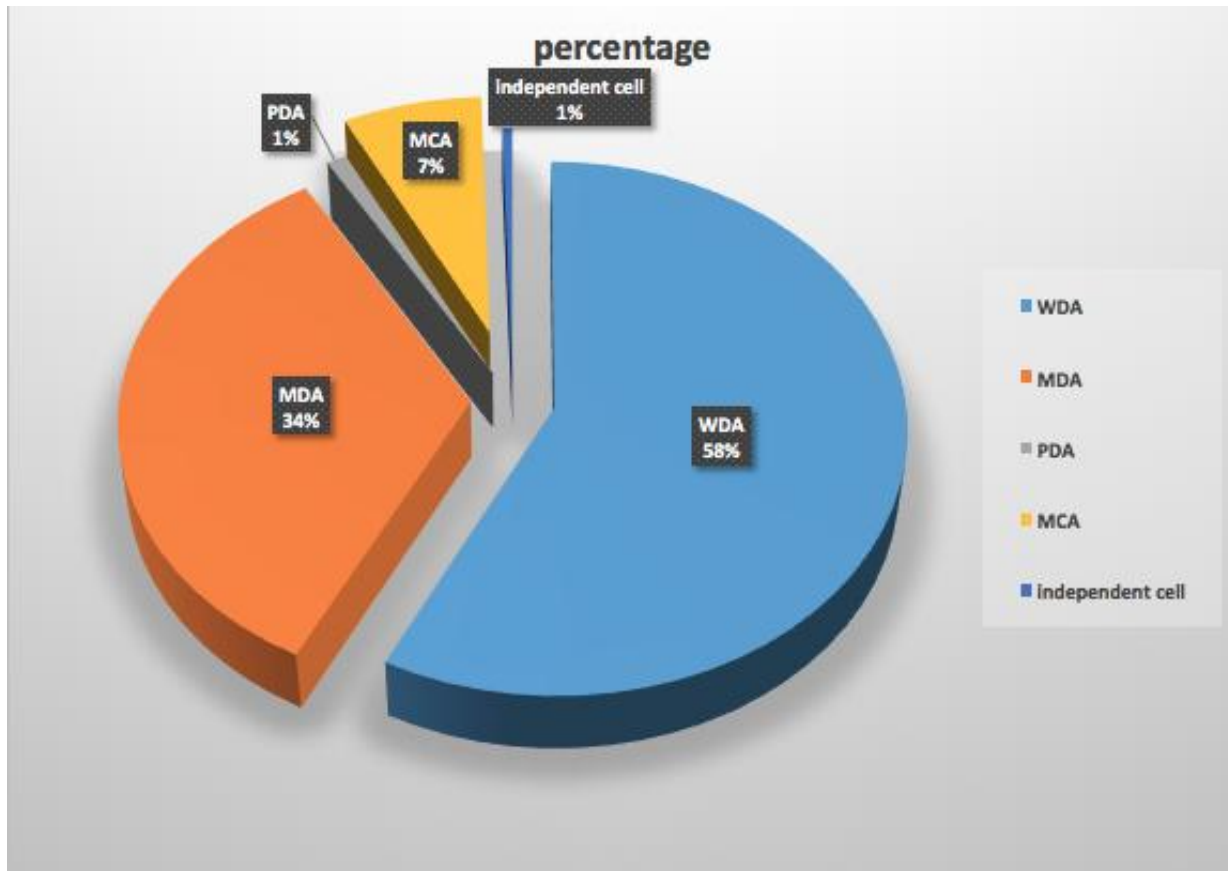


FIGURE 83: PERCENTAGE OF CANCER DIFFERENTIATION

2-2 TNM staging

Tumor invasion study showed a predominance of T3 with 63% followed by T4 with 20%, whereas T1 and T2 counts respectively for 0.5% and 16%.

The number of regional lymph nodes which were dissected was greater than or equal to 12 in 71% of patients undergoing resection of the tumor. Node positive disease (N greater than or equal 1) counts for 71 patients (35%).

M1 stage pathology was found in 10 cases with a percentage of 6%.

TABLE 18: TNM CLASSIFICATION STATISTICS:

	TNM	patients n=	percentage
pT	T1	1	0.50%
	T2	27	16%
	T3	107	63.50%
	T4	33	20%
pN	N0	97	57.70%
	N1	54	32%
	N2	17	10.30%
M	M0	158	94%
	M1	10	6%

3- Post operative complications

Table below shows the rates of major postoperative complications. there was 14% of our patients (n=30) who had post op complications. Most of them are site infection with a percentage of 10%. peritonitis was recorded in 9 cases 4,4 %, and anastomotic leaks in 1 case.

1 case of leakage that was complicated later the same day into peritonitis.

TABLE 19: POST OPERATIVE COMPLICATIONS

	patients(n=)	percentage
site infection	20	10 %
peritonitis	9	4,4 %
Leakage	2	1%
Total complications	30	14.5 %

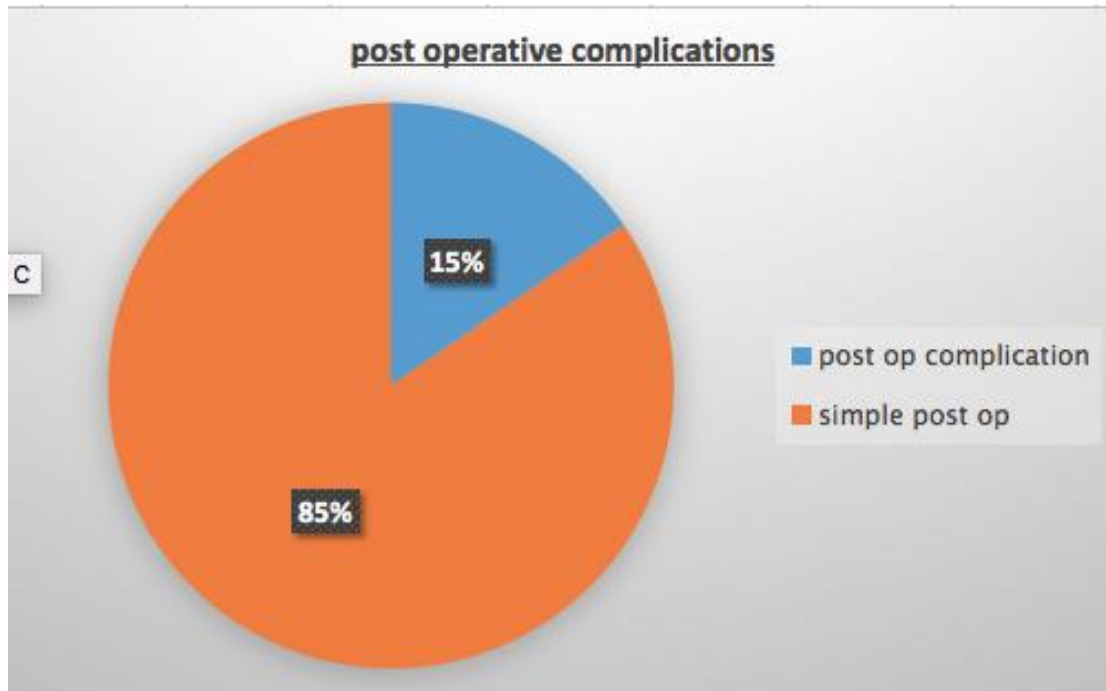


FIGURE 84: POST OPERATIVE COMPLICATION

4- Post operative mortality

Of all included patients, 7 (3.4%) died within 30 days postoperatively

5- Post operative stay outcomes

A hospital stay average of 11 days was recorded in our sample.

TABLE 20: POST OPERATIVE STAY

hospital stay duration	patients n=	percentage
0 to 5 days	29	14%
5 to 10	81	40%
10 to 15	29	14%
15 to 20	46	23%
20 to 25	8	4%
25 to 30	10	5%
total	203	100%

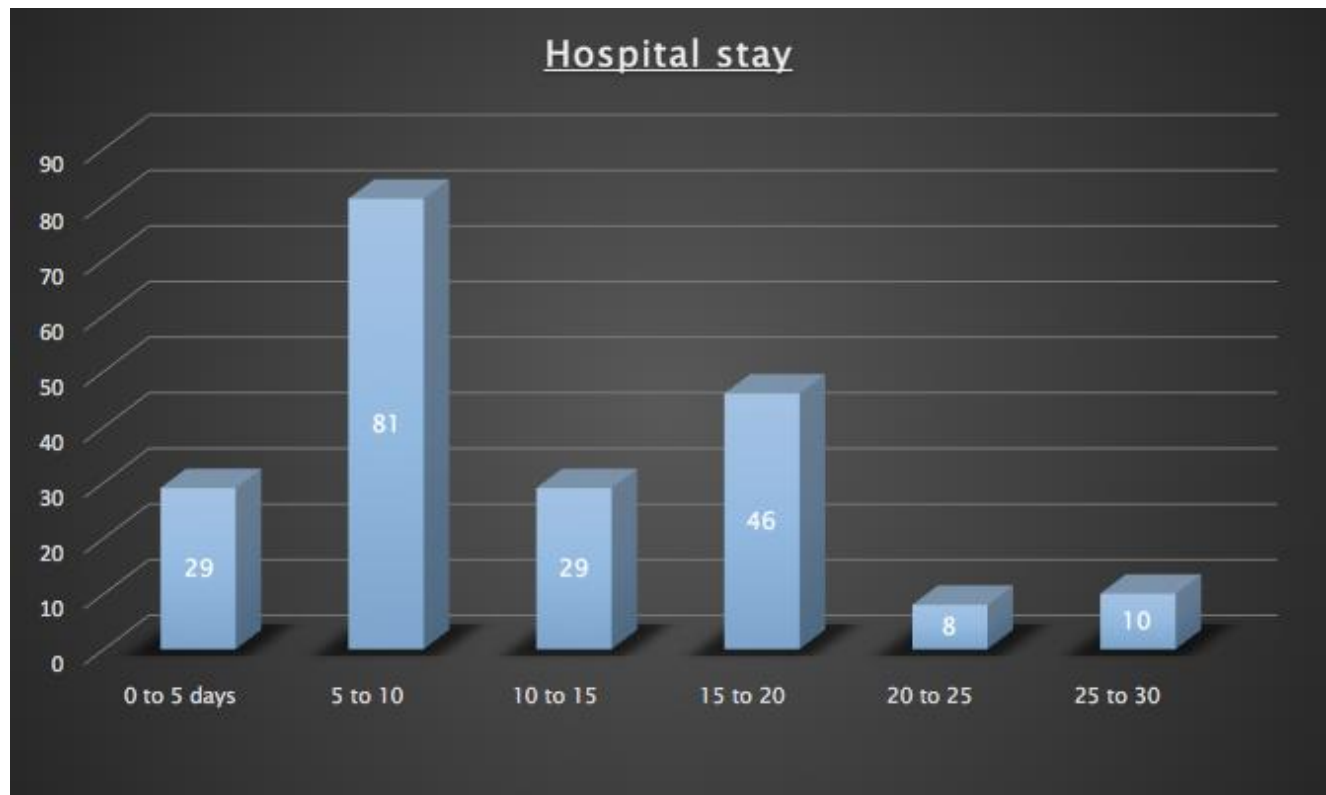


FIGURE 85: POST OPERATIVE STAY

III– Oncological results

1– Synchronous metastasis

45 of our colon cancer patients were diagnosed with synchronous metastasis which represents 22% of our sample.

TABLE 21: SYNCHRONOUS METASTASIS

	patients	percentage
Metastasis	45	22.20%
No metastasis	158	77.80%
Total	203	100%

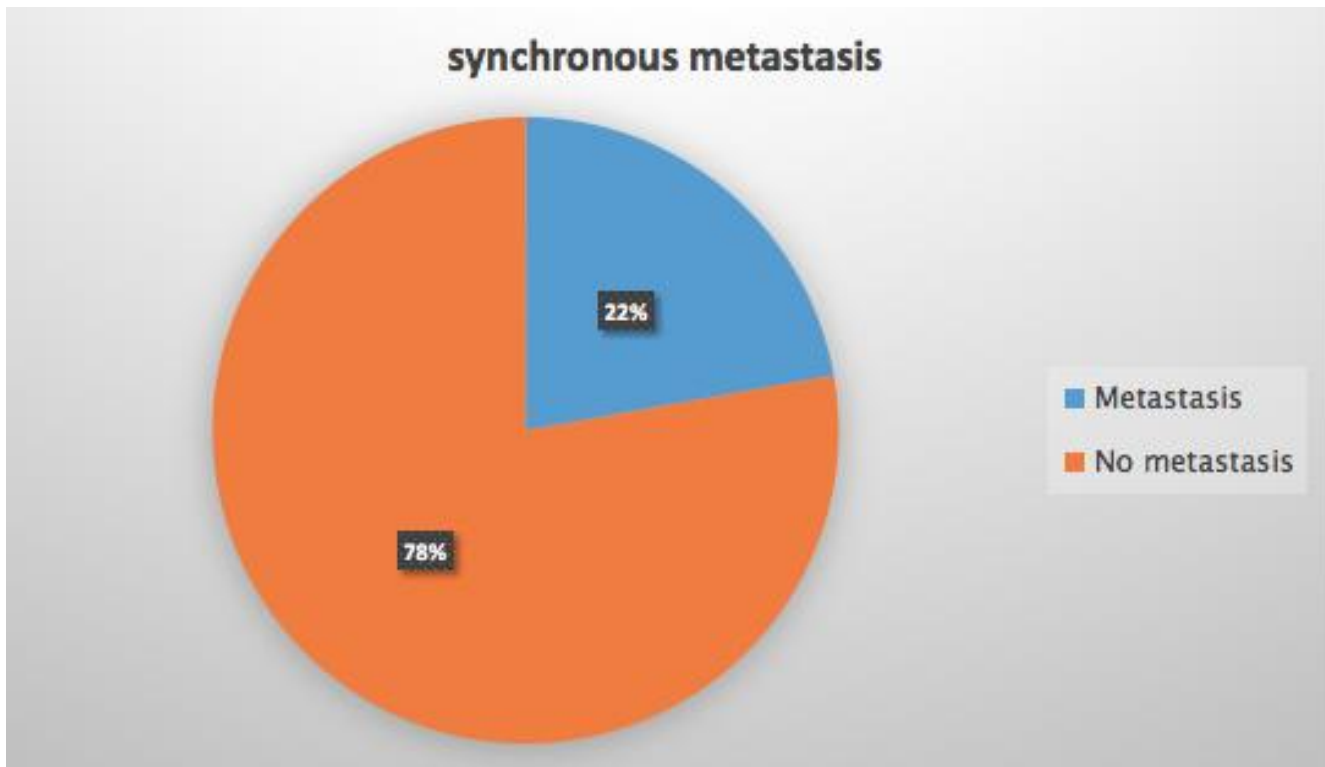


FIGURE 86: SYNCHRONOUS METASTASIS

2– Cancer recurrence

We documented 10 recurrences over our sample of 203 patients (5%). 6 of them (3%) were new metastatic disease while only 4 patients (2%) presented with local recurrence.

TABLE 22: CANCER RECURRENCE

<u>Recurrence</u>	<u>patients (n=)</u>	<u>percentage</u>
Local recurrence	4	40%
Metachronous metastasis	6	60%
Total	10	100%

3– Chemotherapy

153 patients received chemotherapy 75.3%, 21 were afterpalliative stoma (13,7 %)and 132(86,3%) received adjuvant chemotherapy after surgery.

TABLE 23: POST OPERATIVE CHEMOTHERAPY

	<u>patients (n=)</u>	<u>percentage</u>
palliative chemo	21	13,7 %
post op adjuvant chemo	132	86,3 %
total	153	100%

4- Survival

survival was calculated after 6 months, 2 years, 3 years, and 5 years.

at 6 months the survival rate was 79.1%

at 2 years, survival rate was 52.7%

at 3 years, survival rate was 40%

at 5 years, survival rate was 21.4%

overall survival was 21.4%

the mean survival was 878 days (125.4 weeks) +/- 48.4 days.

the median was 660 days (94.2 weeks)

TABLE 24: SURVIVAL MEAN AND MEDIAN

mean				median		
estimation	Std error	confidence interval at 95%		estimation	Std error	CI at 95%
		inferior limit	superior limit			inferior limit
878,85	48,48	783,83	973,87	825,00	83,79	660,77

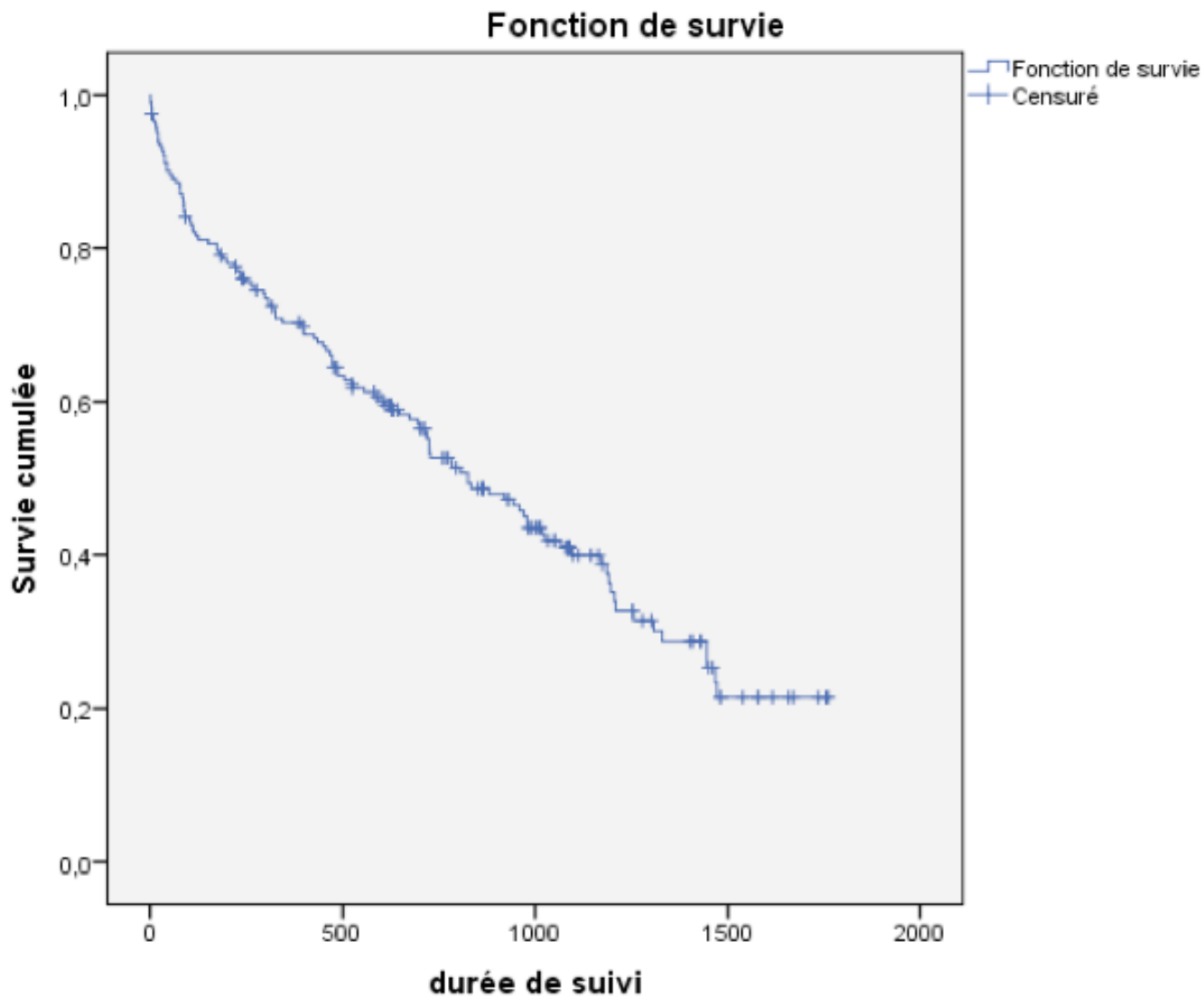


FIGURE 87: SURVIVAL FUNCTION

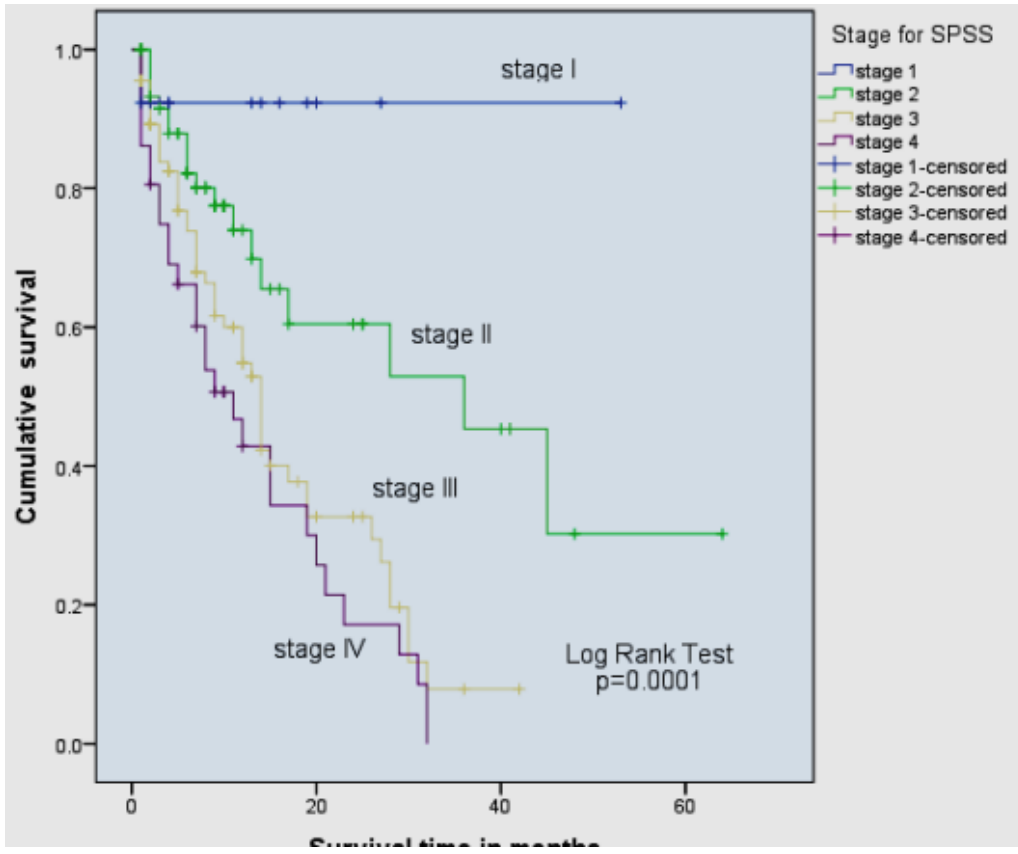


figure 88: survival curves for different stages of colorectal cancer

COMPARATIVE STUDY

This part of the study is a comparison between patients who were presented as emergencies and those who underwent elective surgery for colon cancer in terms of:

- baseline characteristics (age, sex, urban or rural origin, family history of colorectal cancer, tumor site when it was first diagnosed).
- surgical pathology (TNM and pathology)
- surgical stay characteristics (surgical procedures, surgical stay, post op complications).
- long term outcomes (recurrence, post operative chemotherapy, new metastatic disease, survival)

I– Baseline characteristics

Baseline characteristics are displayed in table bellow. there were no significant differences in general characteristics. patients with emergency presentation were slightly younger than elective surgery patients, with a relative male overrepresentation (64% vs 48% $P=0.023$).

The mean age of emergency surgery patients is 55.8 years old vs 58.8 for the remainder group with a standard derivation respectively of 13.24 and 16.07 years ($P=0.190$).

Origin of the patients urban or rural, and family history of cancer and tumor site recorded no significant difference (P equals respectively 0.654, 0.88, and 1).

the difference in tumor sites showed no significance for right, transverse or left colon with a (P value respectively of 0.753, 0.333 and 0.879).

there were no differences in regards of synchronous metastasis in the two groups but emergency presentations had higher rates of metastasis presentation at diagnosis 24% emergency group vs 20% elective group ($P= 0.504$).

table 25: baseline characteristics at presentation

	emergency	elective	OR (95% CI)	<i>P</i> value
n(%)	99 (48.7%)	104 (52.2%)		
Age (mean)	55,87	58,79		0.190
Sex(%male)	64% (n=64)	48% (n=50)	1.97 (1.12–3.47)	0.023
females	35% (n=35)	52% (n=54)		
Origin				
Urban	65% (n=65)	69% (n=72)	0.85 (0.47–1.52)	0.654
Rural	34% (n=34)	30% (n=32)	1.09 (0.60–1.97)	0.88
History of cancer	7% (n=7)	6% (n=7)	1.05 (0.35–3.12)	1
Tumor site				
Right colon	28% (n=28)	25% (n=27)	1.12 (0.60–2.08)	0.753
Transverse colon	3% (n=3)	6% (n=7)	0.43 (0.11–2.56)	0.333
Left colon	70% (n=70)	69% (n=72)	1.07 (0.58–1.95)	0.879
Metastasis	24% (n=24)	20% (n=21)	1.26 (0.65–2.45)	0.504

II- Surgical pathology characteristics

1- Tumor invasion

T2 stage of tumor invasion is significantly higher in elective surgery patients than emergency group (18% elective vs 7% emergency) with a p value of 0.021. on the other hand, there was no difference between the two groups regarding T3 and T4)

T3 (56% emergency group vs 51% elective group P=306).

T4 (18% emergency vs 14% elective P=438).

2- Node positive disease

emergency group counts for 45% of negative node disease whereas elective group 33% with P=0.521

N1 emergency patients count for 28% vs 23% elective group P=0.239.

N2 emergency and elective respectively (7% vs 8%) P=0.761

N \geq 1 (35% emergency vs 31% elective) P=0.347

emergency surgery patients had a slightly higher rate of metastasis M1 24% vs 20% for elective group P=0.400.

3- Stages

stage I are dominated by elective group 14% vs only 4% for emergency group P=0.01.

stage II (38% emergency vs 33% elective) P=0.443.

stage III (34% emergency vs 26 elective) P=0.186.

stage IV (24% emergency vs 20 elective) p=0.289.

4- Pathology

Histological analysis of the degree of cellular differentiation of the resected specimens revealed: well differentiated adenocarcinoma counts for 51% in emergency group vs 43% in elective group with a P value of 0.31. moderately differentiated carcinoma counts for 25% emergency vs 32% elective with P=0.444.

only one case in emergency group presented a poorly differentiated carcinoma vs 0 cases in elective group with a percentage of (1% vs 0%) P=0.498.

mucinous tumors count for 6% in emergency vs 5% elective P=1.

TABLE 26: SURGICAL PATHOLOGY CHARACTERISTICS

	emergency	elective	OR (95% CI)	<i>P</i> value
T1	0% (n=0)	0.5% (n=1)	0.51 (0.44-0.59)	0.333
T2	7% (n=7)	18% (n=19)	3.34 (0.13-0.88)	0.021
T3	56% (n=56)	51% (n=53)	2.05 (1.7-2.5)	0.306
T4	18% (n=18)	14% (n=15)	1.42 (0.66-3.06)	0.438
N0	45% (n=45)	33% (n=35)	0.52 (0.44-1.51)	0.521
N1	28% (n=28)	23% (n=24)	0.24 (0.77-2.85)	0.239
N2	7% (n=7)	8% (n=9)	0.76 (0.30-2.40)	0.761
N \geq 1	35% (n=35)	31% (n=33)	1.34 (0.72-2.48)	0.347
M=1	10% (n=10)	14% (n=15)	0.68 (0.29-1.61)	0.4
stages				
stage I	4% (n=4)	14% (n=15)	0.24 (0.78-0.76)	0.01
stage II	38% (n=38)	33% (n=35)	1.26 (0.95-2.29)	0.443
stage III	34% (n=34)	26% (n=27)	1.52 (0.81-2.83)	0.186
stageIV	24% (n=24)	20% (n=21)	0.62 (0.25-1.5)	0.289
pathology				
well diff ADK	51% (n=51)	43% (n=45)	1.38 (0.78-2.4)	0.31
moder. diff ADK	25% (n=25)	31% (n=32)	0.78 (0.42-1.4)	0.444
poorly diff ADK	1% (n=1)	0% (n=0)	0.5 (0.45-0.59)	0.498
mucinous tumor	6% (n=6)	5% (n=6)	1.1 (0.34-3.56)	1

III– Surgical stay characteristics:

We found a significant difference in one stage surgery versus two stage surgery. Elective surgery group had a higher percentage of one stage surgery with 89% vs 39% in emergency group (P=0.001).

Two stage surgery counts for 63% in emergency group vs 2% only in elective (P=0.001).

Palliative stoma was higher in emergency group with 19% vs 1% in elective group P=0.001.

Emergency patients required longer hospital stay with an average of 15.08 days (SD=6.45) vs 8.75 days (SD=5.55) for elective surgery group with a B coefficient of 0.043 (P=0.540).

Complications occurred with a percentage of 17% emergency vs 12% elective P=0.431.

Intestinal leakage occurred in 2 elective surgery cases 1% vs 0% emergency P=0,498.

Site infection counts for 12% emergency vs 7 elective P=0.351.

Peritonitis 6% emergency vs 2% elective (P=324).

The postoperative mortality rate (death within 30 days) was of all included patients 7 (3,4%). 2 deaths (1%) in patients who underwent potentially curative resection as an elective procedure and 5 deaths (5%) in those who presented as an emergency (P=0.271).

The most commonly performed surgical resections within the emergency group were left colectomy (50%), and right colectomy with 22%. for the elective group 59% left colectomy and 22% right hemi-colectomy.

Total colectomy was performed for 19% of the emergency group versus 2 % for the elective group.

we recorded a higher use of palliative stoma in emergency sitting patients with a percentage of 19% and only 1% in elective surgery group.

Multivisceral resection was also higher in emergency group 4% versus 2%.

TABLE 27: SURGICAL STAY CHARACTERISTICS

	emergency	elective	OR (95% CI)	<i>P</i> value
one stage surgery	39% (n=39)	89% (n=93)	0.11 (0.56-0.216)	0.001
two stage surgery	63% (n=63)	2% (n=4)	36.87 (12.5-108,2)	0.001
procedure type				
right colectomy	22% (n=22)	22% (n=23)	0.98 (0.50-1.90)	1
left colectomy	50% (n=50)	59% (n=62)	0.69 (0.39-1.12)	0.256
total colectomy	7% (n=7)	2% (n=3)	2.56 (0.64-10.19)	0.205
MVR	4% (n=4)	2% (n=3)	1.404 (0.30-6.43)	0.714
palliative stoma	19% (n=19)	1% (n=2)	12.11 (2.7-53,5)	0.001
	emergency	elective	<i>B</i> coefficient	<i>P</i> value
post operative hospital stay (SD)	15.08 (SD 6.45)	8.75 (5.55)	0.043 (-6,8-12,9)	0.540
	emergency	elective	OR (95% CI)	<i>P</i> value
complications	17% (n=17)	12% (n=13)	1.43 (0.65-3.13)	0.431
fistula	0% (n=0)	1% (n=2)	0.50 (0.44-0.57)	0.498
peritonitis	6% (n=6)	2% (n=3)	2.15 (0.52-8.84)	0.324
site infection	12% (n=12)	7% (n=8)	1.63 (0.63-0.19)	0.351
post op mortality	5% (n=5)	1% (n=2)	2.71 (0.54-14.31)	0.271

IV– Long-term outcomes

Our study noted no significant difference in terms of long term outcomes regarding post operative chemotherapy, recurrence rates new metastatic disease and overall metastatic rates.

Post operative chemotherapy counts for 77% in emergency group vs 73% elective with a p value of 0.515.

Recurrence rates were slightly higher in elective surgery group with 6% vs 3% for emergency patients (P=0.333).

New metastatic disease cases were the same on both groups 3 cases each, with a percentage of 3% emergency vs 2% elective (P=1).

overall metastatic rates were higher in emergency group with 27% vs 9% in elective group (P=0.636).

emergency presentation cases had a shorter median disease-free survival 78.6 weeks' vs 104 weeks for elective patients (P=0.058).

global survival duration was higher in elective group with 106.8 weeks vs 80.7 for emergency group (P=0.061).

TABLE 28: LONG TERM OUTCOMES

	emergency	elective	OR (95% CI)	<i>P</i> value
post op chemo	77% (n=77)	73% (n=76)	1.28 (0.67–2.45)	0.515
recurrence	3% (n=3)	6% (n=7)	0.43 (0.10–1.72)	0.333
new meta disease	3% (n=3)	2% (n=3)	1.05 (0.20–5.34)	1
overall meta rates	27% (n=27)	9% (n=10)	1.30 (0.20–2.75)	0.636
	emergency	elective	<i>B</i> coefficient	<i>P</i> value
disease free survival (weeks)	78.6	104.1	9.71 (6.9–44.0)	0.058
survival duration (weeks)	80.7	106.8	9.48 (7.3–44.7)	0.061

V- Multivariate assessment of outcomes

Table below shows the outcomes of multivariate analysis. After adjusting the survival curves for age at surgery, comorbidity and procedure done on patients in multivariate Cox regression still indicated a clear increase in risk of death and shorter survival (HR=0.683; P=0.037).

Similarly, adjusting disease-free survival for baseline staging still indicated a significantly higher hazard for recurrence and hence shorter disease-free survival (hazard ratio=0.683; P=0.037).

TABLE 29: MULTIVARIATE ASSESSMENT OF OUTCOMES

	khi-square	HR (95% CI)	P value
cox regression			
survival	4.343	0.683 (0.476–0.98)	0.037
disease free survival	4.328	0.683 (0.476–0.98)	0.037

Survival analysis by the Kaplan–Meier method demonstrated a significant survival advantage for patients treated electively compared with those treated emergently. The median survival time for patients treated electively was 106 weeks in comparison to 80 weeks for those treated on an emergency basis.

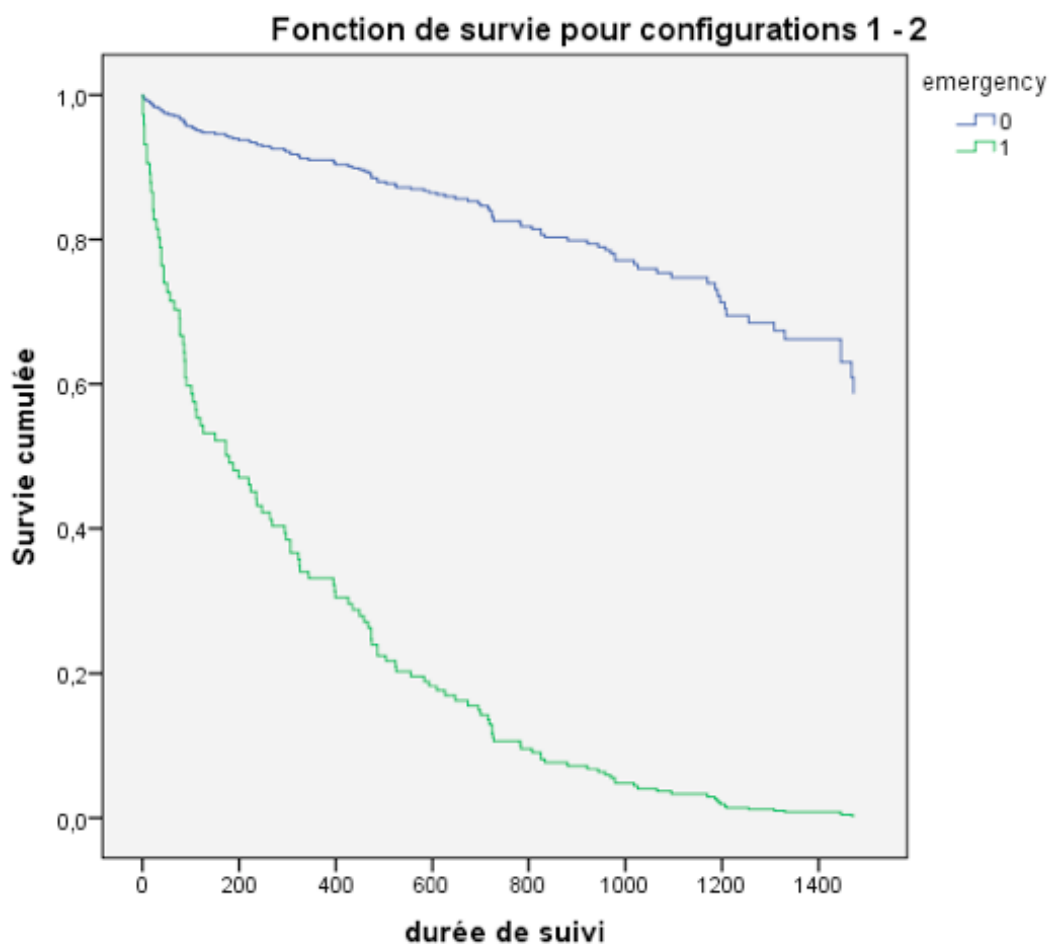


FIGURE 89 : MULTIVARIATE SURVIVAL COX REGRESSION (KHI2=4.343 ; P=0.037)

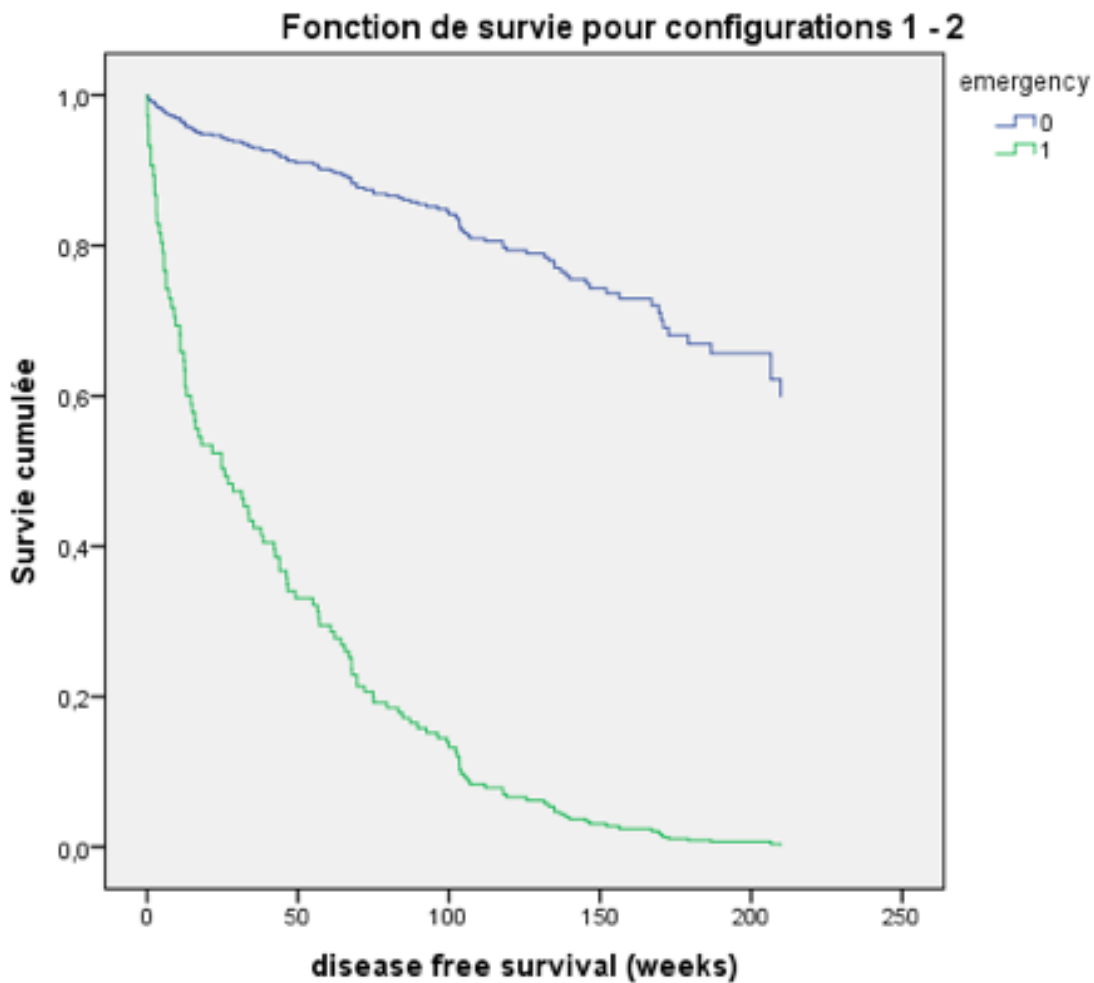


FIGURE 90: MULTIVARIATEDISEASE FREE SURVIVAL COX REGRESSION (KHI-2=4.328 ;

P=0.03)

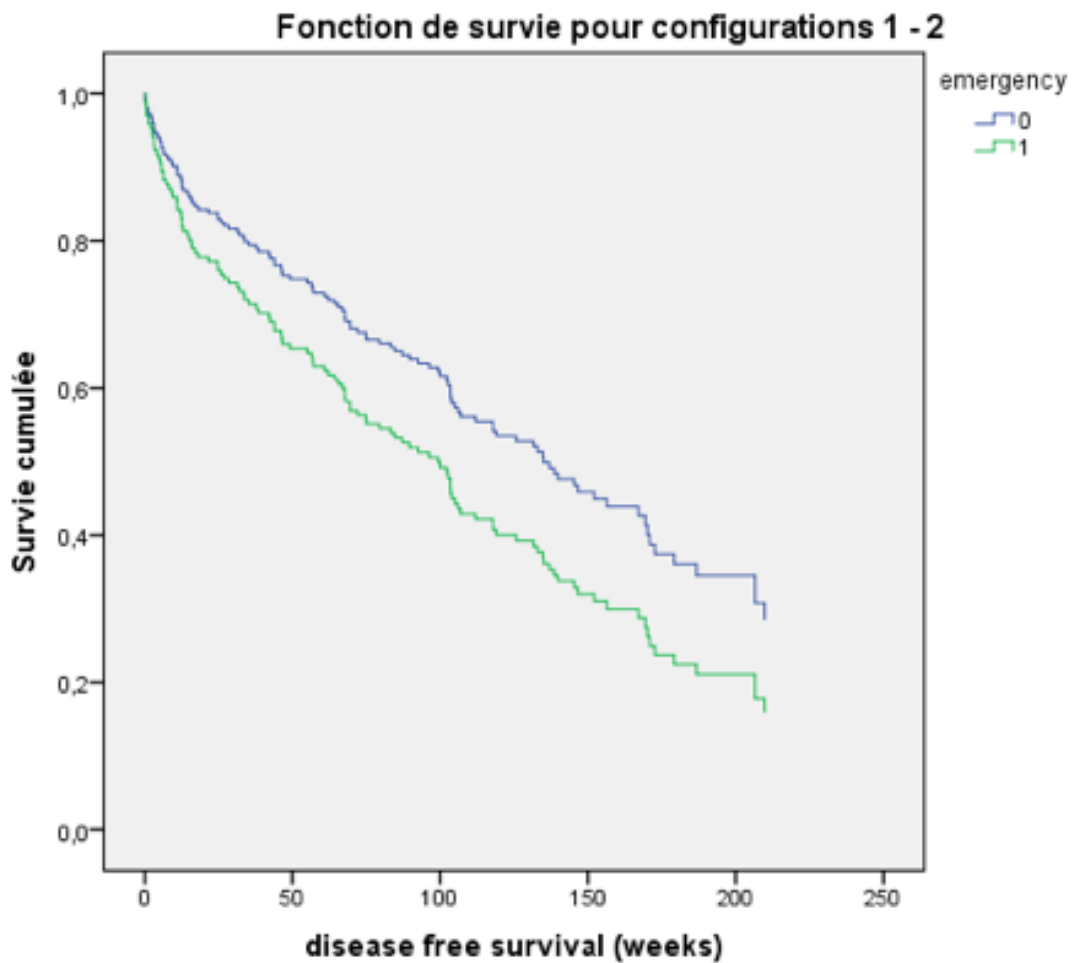


FIGURE 91: UNIVARIATE DISEASE FREE SURVIVAL Cox regression

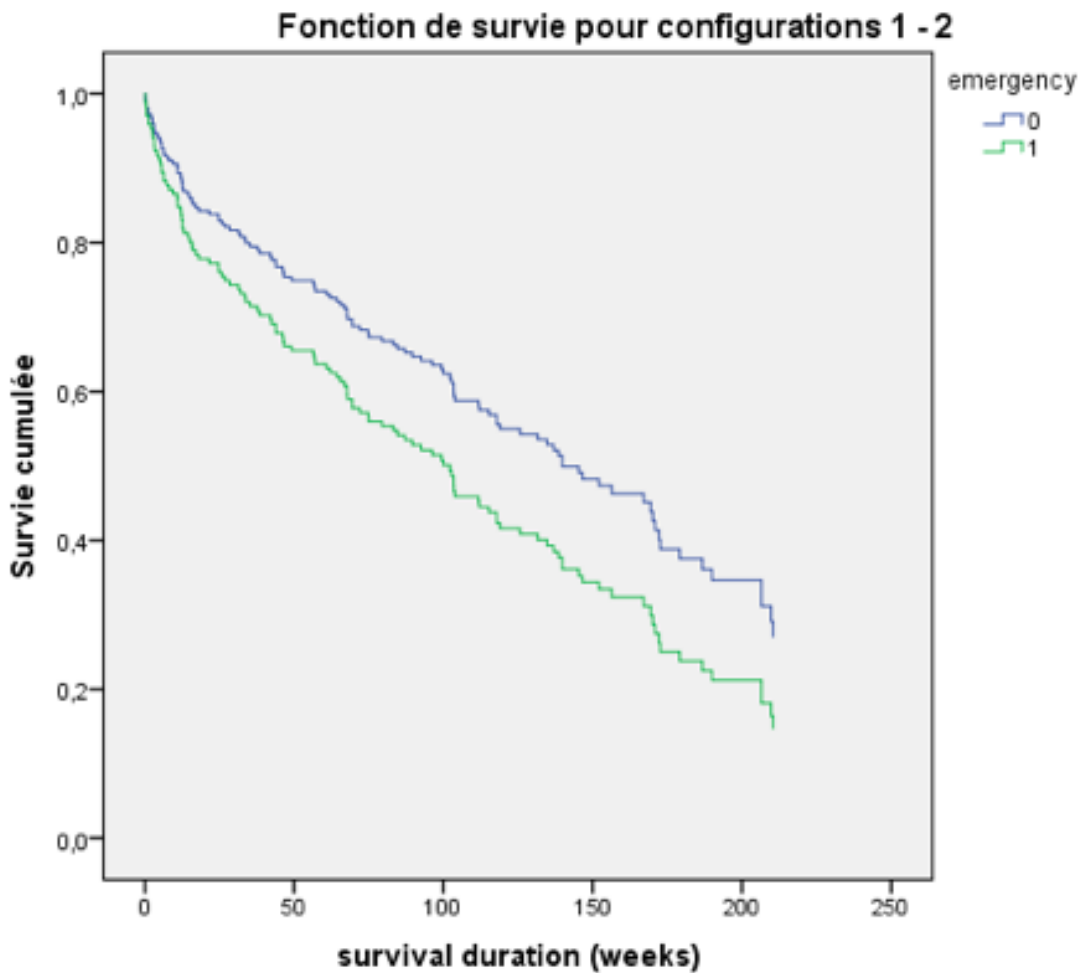


Figure 92: UNIVARIATE SURVIVAL Cox regression

Discussion

I- Demographic

1- Incidence

A study in Spain by Sebastiano Biondo and his team in the Department of Surgery, Hospital Universitario de Bellvitge conducted on 266 patients with colon cancer 59 emergency surgeries and 207 elective.[37]

Massimo Chiarugi and his team in University of Pisa, General and Emergency Surgery Unit, Pisa, Italy studied 499 colon cancer patients 121 emergency and 378 elective surgeries.[38]

Division of General and Gastrointestinal Surgery, Massachusetts General Hospital lead by Ramzi Amri conducted a study on 1071 colon carcinoma patients 102 emergency presentations and 969 elective surgeries.[39]

Much larger studies than the previous ones were conducted:

A. M. Ingraham et al. gathered more than 30 000 colon cancer patients from 142 hospitals around the US.[40]

A. Askari et al. Department of Surgery, St Mary's Hospital, London, United Kingdom studied 286,591 colon cancer patients over a period of 15 years.[41]

2- Age

Age is an important risk factor for CRC. its prevalence increases with advancing age. More than 90% of CRC patients are diagnosed after the age of 50. [42]

table below compares the mean age in different studies done on colon cancer patients.

TABLE 30: MEAN AGE FROM DIFFERENT STUDIES

references	year	country	sample	mean age (range)	
				emergency	elective
N.A. Scott et al. [43]	1994	U.K	905	74 (37-101)	72 (32-101)
Biondo et al.[37]	2004	Spain	266	67,2 (30-100)	67 (30-92)
Chiarugi et al. [38]	2007	Italy	499	73,2 (38-97)	70,7 (35-99)
A. Hussein et al.[44]	2011	Egypt	98	59,27	60,58
Ramzi Amri et al.[39]	2014	USA	1071	69	67
our study	2016	Morocco	203	55,8	58,8

In our study the median age for emergency patients and elective group are respectively 55,8 and 58,8 years. compared to the other studies, our series has a lower median age but still in line with them in both elective and emergency groups.

3- Gender

Overall incidence and mortality rates for colorectal cancer showed decreasing trends over the years especially for females, and both continue to be substantially higher for males than for females.

In spite of the lower rates for women, the absolute number of cases for the two sexes is more similar than one might expect. This is due to the fact that colorectal cancer is most common for the older age groups in which women outnumber men. A surprising finding was that males and females showed such differences in the distribution of subsites. For example, males had the highest rates for rectal cancer, which was only the third highest for women at just above half the male rates.

The most common subsite for females was right colon cancer, still somewhat lower than the male equivalent. Subsite-specific incidence rates for females showed declines or remained level with the possible exception of right colon cancer, which showed a slight increase in recent years.[45]

the following findings displayed in the table bellow comparing sex ratio for these studies is coherent with the literature.

table 31: sex ration

references	year	country	sex ratio (M/W)	
			emergency	elective
N.A. Scott et al.[43]	1994	U.K	134/138	329/304
Biondo et al.[37]	2004	Spain	36/23	132/75
Chiarugi et al.[38]	2007	Italy	55/66	199/179
A.H Abdelrazek[44]	2011	Egypt	38/21	33/26
H. Gunnarsson [46]	2013	Sweden	1354/1502	4634/4803
Ramzi Amri et al.[39]	2014	USA	49/53	499/470
our study	2016	Morocco	64/35	50/54

4- History of colorectal cancer

TABLE 32: FAMILY HISTORY OF COLORECTAL CANCER

references	year	country	History of CRC	
			emergency	elective
N.A. Scott et al.[43]	1994	U.K	10%	13%
Chiarugi et al.[38]	2007	Italy	3%	2%
Ramzi Amri et al.[44]	2014	USA	1%	2.7%
our study	2016	Morocco	7%	6%

5– Tumor site

Many studies showed a greater predominance in left colon as a tumor site than right or transverse colon in both emergency and elective groups, our series fall in line with these studies with a percentage of 70% left colon versus 28% right and 3% transverse for emergency patients, and 69% left colon, 25% right colon and 6% transverse for the elective group. table below displays the results of different studies.

TABLE 33: TUMOR DISTRIBUTION BY SITE

references	emergency group			elective group		
	right	transverse	left	right	transverse	left
Biondo et al.[37]	42%	---	57%	43%	---	56%
A. Askari et al.[41]	36%	---	21%	63%	---	79%
Chiarugi et al [38]	29%	10%	58%	33%	4%	60%
J. H. Anderson et al.[47]	22%	8%	47%	17%	6%	33%
our series	28%	3%	70%	25%	6%	69%

6– Type of emergency

TABLE 34: TYPE OF EMERGENCY

references	type of emergency		
	bowel obstruction	colonic perforation	GI bleeding
A.H Abdelrazek[44]	91.50%	3.4%	1.7%
R. Amri et al.[39]	87%	15%	---
S. Biondo et al.[37]	76.30%	22%	1.7%
our study	85%	11.5%	---

Our series falls in line with the other series regarding the predominance of bowel obstruction as a number one emergency occurring in emergency colorectal cancer patients followed by perforation. other studies A. H Abdelrazek et al. and S. Biondo et al. both recorded 1.7% of GI bleed as a third most common emergency presentation.

7– Metastasis at presentation

TABLE 35: METASTASIS AT PRESENTATION

references	country	year	sample	metastasis at presentation	
				emergency	elective
A. Ingrahalm et al.[40]	USA	2007	30 793	5.40%	5.20%
H. Gunnarsson et al.[46]	Sweden	2006	12 293	29%	16%
R. Amri et al.[39]	USA	2014	1071	28.40%	13.30%
Biondo et al.[37]	Spain	2004	266	10.20%	6.30%
our study	Morocco	2016	203	24%	20%

Metastasis at presentation were higher in both Spanish and American studies Biondo et al. and R. Amri et al. respectively with 10% and 28% for emergency groups versus 6 % and 13% for elective groups.

H. Gunnarsson et al. and our series similarly showed higher percentage of metastasis at presentation for emergency patients versus elective group.

II- Surgical analysis

1- Tumor invasion

TABLE 36: TUMOR INVASION STAGING PT

references	pT	emergency	elective
S. biondo et al.[37]	T1	5,1%	13%
	T2	3,4%	17,4%
	T3	81,4%	63,3%
	T4	10,2	6,3%
G. Bass et al.[48]	T1	1%	7%
	T2	6%	23%
	T3	54%	60%
	T4	38%	13%
R. Amri et al.[39]	T4	45%	20%
our study	T1	0%	0,5%
	T2	7%	18%
	T3	56%	51%
	T4	18%	14%

The incidence of T1 or T2 stage tumors in electively resected specimens was higher, compared to emergency resections in all of the series we studied including ours. On the other hand, T3 and T4 tumors are fewer in elective resection cases than emergency resection cases.

the proportion of later stage tumors was greater in emergency resection compared with those performed electively in all of the studies.

2- Lymph nodes

table 37: Lymph node invasion

references	pN	emergency	elective
G. Bass et al.[48]	N0	41%	61%
	N1	41%	27%
	N2	17%	11%
	N \geq 1	58%	38%
R. Amri et al.[39]	N \geq 1	56%	38,6%
our study	N0	45%	33%
	N1	28%	23%
	N2	7%	8%
	N \geq 1	35%	31%

G. Bass et al. reported in their study that: in patients who underwent elective resection, 39 percent (75/195) of lymph nodes were involved by tumor (N1 or N2), compared with 59 percent (54/92) of nodes harvested from emergency patients (P = 0.002).

R. Amri et al. argues that Pathological characteristics are indicative of considerably more advanced and aggressive disease, with worse TNM staging in all levels, including tumor invasion (45.1% T4 disease vs 20.9% in other patients; P=0.001), node- positive disease (56.6% vs 38.6%; P=0.001).

our study counts for tumors N \geq 1 35% emergency vs 31% elective (P=0.347) which compares favorably with that reported in the literature.

3- Cancer stage

table 38: cancer staging

references	group	stage I	stage II	stage III	stage IV
S. Biondo et al.[37]	emergency	5,1%	44,1%	50,8%	---
	elective	13%	57,5%	29,5%	---
Chiarugi et al.[38]	emergency	----	----	62%	
	elective	----	----	48%	
H. Gannarsson.[46]	emergency	3%	32%	33%	29%
	elective	14%	39%	27%	16%
J.H. Anderson et al. [47]	emergency	1%	26%	28%	31%
	elective	4%	32%	28%	6%
our series	emergency	4%	38%	33%	24%
	elective	14%	33%	26%	20%

A higher proportion of advanced cancer was observed among patients with complicated cancer treated by curative surgery when compared with elective patients in all the series including ours.

Certainly, the unequal distribution of cancer stage (too few T1 or stage I patients for valid comparisons) must have influenced the outcome of complicated patients regarding survival and recurrence rates which was shown also in all of the studies above.

4– Histologic characteristics

Histologic grade of tumors is important for the evaluation of tumor behavior, prognosis and treatment selection. Adenocarcinomas are graded according to the tumor cell's organization similarity to normal epithelial cells. When the degree of tumor differentiation was evaluated between the two groups, poor differentiation was significantly greater in the group who underwent emergency intervention in many studies. These same studies showing that the degree of differentiation and histologic grade of the tumor affect prognosis.[56]

TABLE 39: DEGREE OF DIFFERENTIATION OF DIFFERENT SERIES

references	differentiation	Emergency	Elective
G. Bass et al. [48]	well differentiated	95%	96%
	moderately diff		
	poorly diff	5%	4%
S. Biondo et al. [37]	well differentiated	5,3%	3,6%
	moderately diff	89,5%	88,1%
	undifferentiated	5,3%	8,3%
B. Bayar et al.[49]	in situ	1,1%	3%
	well differentiated	5,6%	18,2%
	moderately diff	58,8%	71,4%
	poorly diff	35,6%	10,4
	mucinous cell	5,6%	6,1%
our series	in situ carcinoma	0%	0%
	well differentiated	52%	47%
	moderately diff	27%	33%
	poorly diff	1%	0%
	mucinous cell	6%	5%

4- Surgical procedures

TABLE 40: TYPE OF SURGERY PERFORMED ON PATIENTS

references	procedure type	Emergency	Elective
R. Amri et al.[39]	segmental	69%	79,6%
	extended segmental	18,6%	12,8%
	total colectomy	8,8%	6,3%
chiarugi et al.[38]	resection + stoma	23,1%	2,9%
	resection + anastomosis	76,9%	97,1%
G. Ming-gao [50]	resection + stoma	30,6%	9,6%
	resection + anastomosis	41,2%	80,1
	palliative surgery	15,3%	10,3%
	palliative stoma	11,8%	6,5%
	palliative bypass	3,5%	3,8%
A.H Abdelrazek [44]	Hartman's	32,2%	0%
	right hemicolectomy	6,8%	6,8%
	anterior resection	22%	83,1%
	total colectomy	18,6%	0%
	palliative stoma	20,3%	10,2%
B. Bayar [49]	Hartman's	18,9%	1,7%
	right hemicolectomy	16,7%	23%
	left hemicolectomy	31,2%	19,7%
	palliative stoma	21,1%	1,7%
G. Bass [48]	right hemicolectomy	19,3%	28%
	left hemicolectomy	17,3%	24%
	total colectomy	3,5%	21%
our series	right hemicolectomy	22%	22%
	left hemicolectomy	49%	56%
	total colectomy	7%	2%
	palliative stoma	19%	1%

5- Post operative hospital stay

TABLE 41: POST OPERATIVE HOSPITAL STAY

references	length of hospital stay (days)	
	emergency	elective
R. Amir et al.[39]	8	5
S. Biondo et al.[37]	13	10
B. Bayar et al.[49]	18	10
S. Kumar et al.[51]	18	9
our series	15	8

G. Bass et al. and G. Ming-Gao recorded respectively 4 and 9 days longer length of stay emergency groups than elective surgery group.

6- Post operative mortality

TABLE 42: POST OPERATIVE MORTALITY

references	post operative mortality	
	emergency	elective
S. Biondo et al.[37]	15,3%	4,8%
R. Amir et al.[39]	7,8%	0,8%
M. Chiarugi et al.[38]	8,2%	0,8%
J. H Anderson al.[47]	22,9%	8,7%
our series	5%	1%

post operative mortality rate was higher in patients presented with emergency sittings in each of the studies we viewed to discuss our results. our series recorded a 5% mortality for the emergent group versus 1% elective group.

7- Post operative complications

One of the most feared major complications of colorectal surgery is anastomotic leakage. It leads to an increase in post-operative morbidity, length of hospital stay, and surgical site infection as well as adversely affecting mortality rate.

It is generally accepted that the risk of anastomotic leakage after intra-pelvic surgery should be kept below 10%, and in recent series this risk has been reported at even lower levels (<3%).[52]

The rate of anastomotic leakage varies in different series from 0.5% to 30%, and its rate is higher in emergent surgery than in elective surgery *. In our study, colorectal anastomotic leakage rate was 0% in the group with emergency surgery, and was less as compared to the group with elective surgery. The anastomotic leak rate in the elective surgery group was detected to be 1%, and was at an acceptable level based on the literature.

Colorectal surgery patients are at high risk for surgical site infections (SSI).[53] The rates of SSI in large series has been reported as approximately 1.5 to 3.9% for clean wounds, 3-4% for clean-contaminated wounds, 8.5 to 15.2% for contaminated wounds, and 21.3 to 41% for dirty wounds.[54]

In our series, the SSI rate in the elective surgery group was found as 7% while in the emergency surgery group, the SSI rate was 12 % which is similar to other studies, It is stated in the literature that the SSI rate increases 1.69 times for malignant neoplasms and 1.9-2.65 times for emergency procedures.

TABLE 43: POST OPERATIVE COMPLICATIONS:

references	complications	emergency	elective
M. Chiarugi et al.[38]	overall	22,3%	13,4%
R. Amri et al.[39]	overall	16,7%	13,8%
	anastomotic leakage	2,9%	1,8%
	site infection	4,9%	7,1%
	sepsis	4,9%	1,1%
A.H.Abdel Razek [44]	overall	27%	10%
	anastomotic leakage	5,1%	3,4%
	site infection	8,5%	5,1%
our series	overall	17%	12%
	anastomotic leakage	0%	1%
	site infection	12%	7%
	peritonitis	6%	2%

The analysis of pooled patients' data described in table above, shows that emergency CRC patients are more likely to experience post-operative adverse events compared to their elective counterparts.

8- Post operative chemotherapy

Postoperatively, all patients were discussed at the multidisciplinary team meeting for each study displayed bellow, Patients with stage III tumors were generally advised to have adjuvant chemotherapy. For those with stage II tumors, adjuvant therapy was recommended if poor histopathologic features (such as lymphovascular invasion, high-grade tumor, or serosal involvement) were present. In patients with stage IV tumors, potentially resectable metastatic lesions were discussed with the appropriate specialists. Patients with diffuse metastatic disease were offered

palliative chemotherapy.

TABLE 44: POST OPERATIVE CHEMOTHERAPY

references	post operative chemotherapy	
	emergency	elective
R. Amri et al. [39]	38,2%	36%
B. Weixler et al[55]	39,3%	31,5%
our series	77%	73%

9– Recurrence and new metastatic disease

Differences existed between the type of recurrence, with distant metastasis being more frequent among patients with complicated cancer than in elective patients. Only one study reported disease recurrence rates in emergency and elective groups. Biondo and his group reported disease recurrence rates of 30.5% and 29% in emergency and elective groups, respectively (OR= 0.371, 95% CI, P= 0.006).

tables below display different results of the study compared to ours.

our current series showed a higher percentage of recurrence for the elective group with 6% versus only 3% for emergency group.

TABLE 45: DISEASE RECURRENCE RATES

references	tumor recurrence	
	emergency	elective
S. Biondo et al. [37]	30,5%	14%
our series	3%	6%

TABLE 46: NEW METASTATIC DISEASE

references	new metastatic disease	
	emergency	elective
R. Amri et al. [39]	21,9%	12,9%
S. Biondo et al.[37]	27,1%	11,6%
our series	3%	2%

10– Survival

TABLE 47: OVERALL SURVIVAL

references	overall survival (median in weeks)	
	emergency	elective
G. Bass et al. [48]	252	351
Guo Ming–gao [45]	109	135
R. Amri et al. [39]	90	187
our series	80	106

The highest median survival found in the series we compared our study to was G. Bass et al. department of surgery Wexford, Ireland with a survival time for patients treated electively 82 months (351 weeks) in comparison to 59 months (252 weeks) for those treated on an emergency basis.

all of the studies showed a greater median overall survival for elective groups compared to emergency patients.

Conclusion

Conclusion

Colorectal cancer is of a great importance both because it is the third most common cancer among all cancers and because of the increase in its frequency. The biggest risk factor for sporadic CRC is age, and the disease is characterized by an increase in incidence with age. Being diagnosed at advanced stages adversely affects several parameters such as the type of surgery, period of hospitalization, complications, and patient survival.

Despite screening programs for colorectal cancer, emergency admissions and surgical procedures in emergency conditions remain high. Surgical operations for patients with impaired metabolic status due to mechanical obstruction do not only carry risks for patients but also yield inadequate results. In our study comparing the postoperative treatment results of patients with emergency and elective surgery for CRC, post-operative morbidities were more frequent in patients with emergency surgery.

It is observed that the disease remains asymptomatic for a long period and patients remain undiagnosed. The treatments performed under emergency conditions should be evaluated not only for the associated risks but also in terms of their effect on health related costs.

From the clinician's point of view, early diagnosis of patients by effectively adopting screening programs particularly to risk groups will positively affect treatment efficacy and survival results.

Results of our study didn't show significant differences in terms of post-operative outcomes, recurrence rates and survival between the emergency and elective colon surgery. Prospective with large Cohort studies are needed for the better assessment of these results.

Summary

Summary

Introduction: Colon cancer is the most common type of gastrointestinal cancer. It is a multifactorial disease process, with etiology encompassing genetic factors, environmental exposures (including diet), and inflammatory conditions of the digestive tract. Despite advances in perioperative care and operative techniques, urgent colorectal operations are still associated with higher mortality and morbidity than elective surgery.

Aim: The overall aim of this thesis is to verify whether patients diagnosed with colon cancer in an emergency setting differ from scheduled elective surgery in terms of presentation characteristics, surgical stay outcomes and survival.

Material and methods: This is a retrospective comparative study performed at the department of surgery at the University Hospital Hassan II of Fez from January 1st, 2012 to December 31st 2015. The study includes 203 consecutive patients operated for colonic carcinoma. 104 underwent elective surgery, while 99 patients underwent emergency surgery.

Results: The two groups are comparable in term of age, sex, comorbidity and tumor stage. Palliative stoma (19% vs 1% $P=0.001$), two stage surgery (63% vs 2%) was significantly higher in emergency group. Recurrence rate (3% emergency vs 6% elective $P=0.333$), post-operative complications (17% emergency vs 12% elective $P=0.431$) and mortality rate (5% emergency vs 1% elective $P=0.271$) are comparable in the two groups. Free disease survival (80 weeks emergency vs 104 weeks elective $P=0.058$) and overall survival (80 weeks emergency vs 106 weeks elective $P=0.061$) are higher in elective surgery group.

Conclusion: Results of our study didn't show significant differences in terms of post-operative outcomes, recurrence rates and survival between the emergency and elective colon surgery. Prospective with large Cohort studies are needed for the better assessment of these results.

Résumé

Introduction : Le cancer du côlon est le type le plus fréquent des cancer gastro-intestinaux. C'est un processus de maladie multifactorielle, avec une étiologie englobant les facteurs génétiques, les expositions environnementales (y compris l'alimentation) et les états inflammatoires du tube digestif. Malgré les progrès dans les soins péri-opératoires et les techniques opératoires, les opérations colorectales urgentes sont encore associées à une mortalité et une morbidité plus élevées que la chirurgie élective.

Objectif : L'objectif général de cette thèse est de vérifier si les patients diagnostiqués avec un cancer du côlon dans un milieu d'urgence diffèrent de la chirurgie élective programmée en termes de caractéristiques de présentation, des résultats du séjour chirurgical et de survie.

Matériel et méthodes: Il s'agit d'une étude comparative rétrospective effectuée au département de chirurgie à l'hôpital universitaire Hassan II de Fès du 1er janvier 2012 au 31 décembre 2015. L'étude comprend 203 patients consécutifs opérés pour le carcinome colique. 104 ont subi une chirurgie élective, tandis que 99 patients ont subi une intervention chirurgicale d'urgence.

Résultats: les deux groupes sont comparables en terme d'âge, de sexe, de comorbidité et de stade tumoral. La stomie palliative (19% vs 1% $P = 0,001$), la chirurgie en deux temps (63% contre 2%) était significativement plus élevée dans le groupe d'urgence. Le taux de récurrence (3% d'urgence contre 6% $P = 0,333$), les complications post-opératoires (17% d'urgence contre 12% $P = 0,431$) et le taux de mortalité (5% d'urgence contre 1% $P = 0,271$ électif) sont comparables dans les deux groupes. La survie sans

maladies (période de transmission de 80 semaines contre 104 semaines $P = 0,058$) et la survie globale (période d'urgence de 80 semaines contre 106 semaines $P = 0,061$) sont plus élevées dans le groupe de chirurgie élective.

Conclusion: Les résultats de notre étude n'ont pas montré de différences significatives en termes de résultats post-opératoires, de taux de récurrence et de survie entre l'urgence et la chirurgie élective du côlon. Des études prospectives et de grandes études de cohorte sont nécessaires pour une meilleure évaluation de ces résultats

ملخص

مقدمة: سرطان القولون هو النوع الأكثر شيوعاً من سرطانات الجهاز الهضمي. بله عملية المرض متعددة العوامل، مع المسببات تشمل العوامل الوراثية، والتعرض البيئي (بما في ذلك النظام الغذائي)، والظروف الالتهابية في الجهاز الهضمي. على الرغم من التقدم في الرعاية المحيطة بالجراحة وتقنيات الجراحة، لا تزال العمليات القولونية المستقيمة العاجلة مرتبطة بارتفاع معدل الوفيات والاعتلال مقارنة بالجراحة الاختيارية.

الهدف:

الهدف العام من هذا الأورحة هو التحقق مما إذا كان المرض الذي يتم تشخيصه مسرطاناً القولون في حالة الطوارئ تختلف عن راحة الاختيارية المقررة من حيث خصائص العرض، نتائج البقاء الجراحية والبقاء على قيد الحياة.

المواد والأساليب:

هذه دراسة مقارنة بأثر رجعي أجريت في قسم الجراحة في مستشفى جامعة الحسن الثاني بمدينة فاس من 1 يناير 2012 إلى 31 ديسمبر 2015. وتشمل الدراسة 203 مريضاً تم تأليينهم خضوعاً لعمليات سرطان القولون. خضع 104 لعملية جراحية اختيارية، في حين خضع 99 مريضاً لعملية جراحية طارئة.

النتائج:

المجموعتين قابلتان للمقارنة في العمر، الجنس، الاعتلال المشترك ومرحلة الورم. كان معدل الجراحة الملطفة (19% مقابل 1% $P = 0.001$)، وجراحة في مرحلتين (63% مقابل 2%) أعلى بكثير في مجموعة الطوارئ. معدل التكرار (3% الطوارئ مقابل 6% اختياري $P = 0.333$)، مضاعفات ما بعد الجراحة (17% الطوارئ مقابل 12% اختياري $P = 0.431$) ومعدل الوفيات (5% الطوارئ مقابل 1% اختياري $P = 0.271$) قابلة للمقارنة في مجموعتين. البقاء على قيد الحياة بدون مرض (80 أسبوعاً الطوارئ مقابل 104 أسبوعاً اختياري $P = 0.058$) والبقاء على قيد الحياة عموماً (80 أسبوعاً الطوارئ مقابل 106 أسبوعاً اختياري $P = 0.061$) هي أعلى في مجموعة الجراحة الاختيارية.

الخلاصة:

أظهرت نتائج دراستنا عدم وجود فروق ذات دلالة إحصائية في نتائج ما بعد الجراحة، ومعدلات التكرار، والبقاء بين جراحة الطوارئ والجراحة الاختيارية. هناك حاجة إلى دراسات مستقبلية ودراسات كبيرة متطالعة بالوراء لتقييم هذه النتائج بشكل أفضل.

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