

L7-Colorectal Cancer (CRC)





Objectives :



Color Index: Slides & Raslan's (i) | Doctor's Notes | Extra Explanation | Additional

This work is based on doctor's Slides, Notes and Raslan's only (Does not include the book)

Mind Map



Introduction

Definitions

- **Colon** = large bowel = large intestine
- Rectum : terminal portion of the colon
- **Polyp:** is a descriptive term used to describe any mass of tissue that bulges or projects outwards . Colonic polyps are mostly benign outgrowths.
- Adenoma : type of polyp and has chance to develop cancer but not all.
- **Cancer** : malignant growth; invasive (invades the basement membrane)
- **Stage** is an estimate to determine how large has the tumor grown.
- **Primary** : the original tumor, where it started.
- Metastases : where the tumor has spread to.

Colon And Rectum Cancer Significance

- The management and the characteristics of colon and rectal cancers are completely different
- Cancer Development: Most cancers are acquired (sporadic), but some small percentage of cases arise from inherited diseases.
- Most cancers begin as adenomatous polyps , however only a tiny percentage of adenomas become cancers (1 – 9% become malignant)
- Colon differs from rectum histologically, that the latter lacks serosa so cancers invade easily in rectum.

Epidemiology

- 3rd most common malignancy worldwide.
- 1st most common in Saudi males.
- Second to lung cancer as a cause of cancer death
- 21,500 new cases, 8900 will die (2008)
- Risk of colorectal cancer women 1/16, men 1/14
- Median age of diagnosis was 60 according to the Saudi Cancer registry reports.

Age

- As seen on the graph, the incidence of colorectal cancer (CRC) increases tremendously after the age of 50.
- Colonoscopy is advised to be performed at the age of 50 for people with no significant risk factors, and should be performed at a younger age if the person has risk factors.
- Colonoscopy can detect and remove adenomas and thus prevent cancer occurrence.



POLYPS		
	POLYPS TYPES	
4		
Non-neoplastic polyps	Neoplastic polyps	Adenomatous Polyps (adenomas)
 The majority of polyps are non-neoplastic accounting for more than 90% of polyps are benign. These arise as a result of inflammation or improper maturation. These include: Hyperplastic polyps (most commonly seen) Hamartomatous polyps (Juvenile & Peutz-Jeghers polyps) Inflammatory polyps Lymphoid polyps 	 Account for less than 10% of polyps and these are dysplastic polyps that have malignant potential. (so removing polyps is highly clinically significant) Adenoma 	 Occur mainly in large bowel, Sporadic and familial , vary from small pedunculated to large sessile. Epithelium proliferation and dysplysia. Divided into: Tubular adenoma: less than 25% villous architecture Villous adenoma: villous architecture over 50% Tubulovillous adenoma: villous architecture between 25 and 50%.

Cancer Sequence

- The transformation from benign polyps to cancer takes from 7 10 years
- The transformation risk into cancer is based on:



• The transformation from normal mucosa to cancer undergoes some important steps as the following:

Adenoma to Carcinoma Pathway



Classification Of Colorectal Carcinoma

1. Adenocarcinoma <mark>(>95%)</mark>	2. Carcinoid	3. Lymphoma
4. Sarcoma	5. Squamous cell carcinoma	

Risk Factors

Medical and Family history:

- Hereditary colorectal cancer syndromes
- Personal history: previous polyps (relative risk of 3.5 to 6), occurrence of previous CRC (relative risk of 2 in the first two years)
- Family history: a first-degree family member doubles risk. Further detail to follow, so when a member of a family is diagnosed with colorectal cancer, it is recommended to screen other members at 10 years younger from their relative's age of diagnosis. (so if a father was diagnosed with CRC in his 50s, his sons and daughters should be screened in their 40s)
- Inflammatory bowel disease (mainly for cases of disease that extensively involve the colon and pancolitis, these conditions hold a (relative risk of around 2.6 – 2.8)
- Other: Diet (less vegetables and fibers and more carbs and fat), smoking, alcohol consumption

Hereditary colorectal cancer syndromes :

are a group of syndromes include hereditary nonpolyposis colorectal cancer (HNPCC) syndrome and Familial adenomatous polyposis (FAP). In typical FAP, numerous colonic adenomas appear during childhood. Symptoms appear at a very early age and colonic cancer occurs in 90 percent of untreated individuals by age 45. These patients will have to undergo prophylactic colectomy.

Family History

Case	Chance to get CRC
General population " sporadic "	6%
One 1st degree CRC	2-3X* (12-18%)
Two 1st degree CRC	3-4X*
One 1st degree CRC < 50 y	3-4*
One 2nd or 3 rd degree CRC	1.5X
Two 2nd degree CRC	2-3X*
One first degree with polyp	2X*



Screening is effective in case of CRC

In healthy people with no risk factors ightarrow Start at 50 years old, every 10 years

If the screening was positive 🗲 surgery 🗲 screening every 5 years

- If +ve family history, start at 40 years old
- If +ve Hereditary disease, start in 20s

Clinical Presentation

- Bleeding (melena/hematochezia) gross, occult, anemia)
- Change in bowel habit diarrhea, constipation, alternating pattern (firstly constipation because the mass obstructing the lumen, stool accumulate then pass the mass causing diarrhea)
- Abdominal pain, Weight loss, Abdominal mass
- Obstruction
- Change in caliber *diameter* of the stools
- Some symptoms give clues on the location of the tumor:
 - Sigmoid colon: obstruction and change in bowel habits (Large bowel obstruction in old people is sigmoid cancer until proven otherwise)
 - ✓ Rectum: bleeding and tenesmus
 - ✓ Cecum: pain and melena
- Metastasis: weight loss
- Some people are asymptomatic

Notes on Clinical Presentation:

- Symptoms of CRC are typically due to growth of the tumor into the lumen or adjacent structures. As a result, symptomatic presentation is often a manifestation of relatively advanced CRC.
- In a series of Meta analyses: the previous first three symptoms were the most common upon presentation.
- Sensitivity of individual symptoms for the diagnosis of CRC was poor, but Dr.AlKhayal mentioned it in
- the lecture and I thought I should add it





Abdominal pains is caused by partial obstruction, peritoneal dissemination, or intestinal perforation leading to generalized peritonitis.

- Obstruction is more common with left sided lesions, 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.
- CRC is the most common cause of bowel obstruction in the elderly.



- General: Complete history and physical examination including a digital rectal examination (DRE)
- Endoscopic: (identify primary, synchronous lesions)
 - ✓ Flexible sigmoidoscopy
 - ✓ Colonoscopy " to rule out other lesions"

Bloodwork

- CBC, electrolytes and other function tests
- CEA (Carcino Embryonic Antigen) is a known protein molecule that is produced in high levels by CRC cells.
 - It is not a specific marker, and can be elevated in many benign conditions like smoking! and other malignant cases like pancreatic cancer; therefore, can never be used as a screening test. However, CEA maybe used as a prognostic factor for evaluation of CRC management. (high CEA indicate bad prognosis). In addition, for follow up (low means cure, and high mean recurrence)



Synchronous lesions: defined as two or more distinct primary tumors separated by normal bowel and not due to direct extension or metastasis. In other words: two or more cancers occurring at the same time. Colonoscopy " to rule out other lesions ": it is the most accurate diagnostic test in symptomatic individuals, since it can localize and biopsy lesions throughout the large bowel, detect synchronous neoplasms, and remove polyps.

Extra notes on Cancer spread:

- 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.
- Because the venous drainage of the intestinal tract is via the portal system, the first site of hematogenous dissemination is usually liver, followed by lungs, bone, and many other sites, including brain.
- 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.

Staging Very important



Staging of CRC is now achieved by using the TNM classification and not the modified Duke classification, as studies have shown that the 2010 modification of the TNM classification had better results.

Method Of Staging

- Endorectal ultrasound (rectal cancer)
- Chest x-ray (metastases)
- Liver ultrasound (metastases)
- Abdominal CT scan (metastases)
- Barium Enema: may show apple-core lesion as seen with this double contrast barium enema of the descending colon.
- When colorectal cancer is diagnosed, it is almost protocol to perform CT scans of the chest, abdomen and pelvis to detect or rule out any metastasis.
- We may use rectal MRI in case of rectal cancer



How far into the wall has it grown?

T stage	
Tis	invasion of mucosa only (in situ)
T1	Invasion of submucosa
Т2	Invasion of muscularis propria
Т3	Full thickness/perirectal fat/serosa
T4	Invasion into adjacent organs.

Is it growing in other places?

N stage: lymph node involvement	
N1	1-3 lymph nodes
N2	4 or more lymph nodes
N3	distant lymph nodes
M stage: presence of metastasis	
M1	Distant organ (mostly to the liver, lung)

Very Important

Take note that adjacent organs does not mean distant metastasis, as that is a different component in the score. Adjacent organs mean structures like: the urinary bladder, uterus, and even the abdominal wall.

TNM Staging

Stage 0	Tis : invasion of mucosa only	
Stage 1	T1 - T2 and N0 : Invasion of submucosa or muscularis propria	
Stage 2	T3 - T4 and N0 : Invasion of full thickness or adjecent organ	
Stage 3	Any lymph node involvement	
Stage 4	Distant metastases	

Managment

- Surgery is the most important variable in the treatment of colorectal cancer
- Radiation and chemotherapy alone cannot cure any stage of colorectal cancer
- The site of tumor dictates the basic procedure

Treatment Indications For Different Stages

Stage I and II	High risk stage II and stage III	Stage IV
surgery	surgery + chemo/radiotherapy	chemotherapy ± Surgery depending on whether or not the tumor is resectable and on other factors.

Preoperative Preparation

- Evaluation of medical problems. This is important especially for patients who have cardiopulmonary disease, as these patients must be evaluated by concerned specialists.
- Mechanical bowel preparation (bowel cleansing by laxatives)
 - Colyte, Oral fleet
- IV antibiotics
- **DVT prevention**: Heparin shots, Compression stockings
- Foley catheter
- Epidural catheter

Principles Of Surgery

- Examine the entire abdomen
- Remove the appropriate segment of the colon with adequate margins
- Remove the corresponding lymph nodes: a minimum of 12 lymph nodes have to be removed in a proper colectomy.
- Open vs laparoscopic approach
- The types of colectomies can been seen on this figure:

Ostomy Insertion

- The intestine is brought out through a hole in the abdominal wall
- Colostomy (colon on the skin)
- Permanent when the rectum is removed
- Temporary when it is unsafe to make a join
- Ileostomy (ileum on the skin)
- Temporary when the join needs time to heal



Recovery

Surgery 2 to 4 hours

Hospital stay 4 to 10 days

- IV, urine catheter, compression stockings, intravenous pain killers, blood thinner
- Discharge when ambulating, eating, bowel function, good pain control
- Recovery 4 weeks

Follow Up

- Office visit every 3 months for two years then every 6 months for 3 years
 - Regular blood work (CEA)
 - Colonoscopy at year 1 and 4 and every 5 years
 - CT scan yearly

Some points on CEA:

- CEA is used to detect the prognosis: higher CEA levels indicate a worse prognosis.
- It is used to detect recurrence: (CEA levels are usually around 2.5 5 ng/ml).
- If CEA was 50, then after surgery it goes back to 5, then after some time it rises to 50 again. Here we suspect recurrence.

- If CEA was 100 and after a surgery it is still 100 it can indicates 2 things :
- A) There is another mass, i.e. metastasis and it hasn't been removed or
- B) the initial mass was not excised properly.

Who Gets Additional Therapy?

COLON

- All stage 3 patients (positive nodes) chemotherapy
- High risk stage 2 patients :
- These patients include: Cancers with the mucinous subtype, patients with bowl obstructions; perforation, and who have undergone resection with less than 12 resected nodes.

RECTUM

- All stage 2 and stage 3 patients should get radiation and chemotherapy.
- Note: in the rectum there are no serosa layer so the stage 2 patients should receive chemotherapy

Survival And TNM Staging:

STAGE	5-Year Survival	
1	90%	
2	80% (for T3N0)	
3	27-69% (depends on number of nodes involved)	
4	8%	

Summary

- ✓ Common Cancer.
- Most cancers begin as adenomatous polyps , however only a tiny percentage of adenomas become cancers.
- ✓ Can be prevented through screening and resection of polyps.
- \checkmark Colonoscopy is advised to be performed at the age of 50.
- ✓ Surgery is the primary treatment.
- \checkmark Slow but steady improvement in survival.
- ✓ CEA maybe used as a **prognostic** factor for evaluation of CRC management. (high CEA indicate bad prognosis).
- ✓ Staging of CRC is now achieved by using the TNM classification.





1) A definite increased risk of colon cancer is associated with:

- a) Diet high in fiber.
- b) Diet low in animal fat and protein.
- c) Diet low in fiber.
- d) Ulcerative Colitis
- e) Prior cholecystectomy.

2) A 52 year-old female diagnosed to have sigmoid cancer invading the uterus with no evidence of metastasis based on CT scan and colonoscopy, she underwent sigmoidoctomy and hysterectomy, the histopathology report revealed invasive moderately differentiated adenocarcinoma involving the entire bowel wall and invading the myometrium, perinuraln and lymphovascular invasion, 6 out of 15 lymph nodes were positive for

metastasis. The TNM classification for this patient will be:

- a) T3 N1 M0
- b) T3 N2 M1
- c) T4 N2 M0
- d) T4 N2 M1

3) Which one of the following factors is most likely to be associated with development of colorectal cancer?

- a) Increase Calcium intake
- b) Increase fat intake
- c) Smoking
- d) History of Colonic polyps

Thank You..

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