Recent Concepts in the management of recurrent Colo-Rectal carcinoma

Essay

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List of Abbreviations

AAA : Abdominal aortic aneurysms.
ACG : American College of Gastroenterology.
ACS-MSTF : American Cancer Society, the United States Multi-Society Task Force on Colorectal Cancer.
AFAP : Attenuated Familial adenomatous polyposis.
AGA : American Gastroenterological Association.
AJCC : American Joint Committee on Cancer.
APC : Adenomatous polyposis coli gene
APR : Abdominal perineal resection.
ASCO : American Society of Clinical Oncology.
ASGE : The American Society for Gastrointestinal Endoscopy.
CA : carbohydrate antigen.
CEA : Carcinoembryonic antigen.
CI : Confidence interval.
CRC : Colorectal cancer.
CTC : Computed tomographic colonography.
DCBE : Double contrast barium enema.
DCC : Deleted in Colon Cancer gene.
DFS : Disease Free Survival.
DRE : Digital rectal examination.
EUS : Endorectal ultrasound.
EUS : Endoscopic ultrasound.
FAP : Familial adenomatous polyposis.
FIT : Fecal immunochemical tests.
FJP : Familial juvenile polyposis.
FNA : fine needle aspiration.
FOBT : Fecal occult blood testing.
gFOBT : Guaiac-based fecal occult blood test.
GIST : Gastrointestinal stromal tumor.
HNPCC : Hereditary nonpolyposis colorectal cancer.
IBD : Inflammatory Bowel Disease.
IMA : Inferior mesenteric artery.
LAR : low anterior resection.

LOH : loss of heterozygosity.
MBP : Mechanical Bowel preparation.
MMR : Mismatch repair genes.
NCCN : National Comprehensive Cancer Network of USA.
NCI : American National Cancer Institute.
pCR : pathologic complete response.
PCR : Polymerase chain reaction.
PET : Positron emition tomography.
PGD : preimplantation genetic diagnosis.
PJS : Peutz-Jeghers syndrome.
QOL : Quality of life.
RER : Replication error repair.
RT : Radiotherapy.
SEER : Surveillance, Epidemiology and End Results.
SIR : Standardized incidence ratio.
SLN : Sentinel node.
SMA : Superior mesenteric artery.
TME : Total mesorectal excision.
TRUS : Transrectal ultrasound.
USPSTF : United States Preventive Services Task Force.

Introduction

Colorectal cancer is a common malignancy in the developed world with a lifetime risk of 1 in 20. Around 20% of patients with colorectal cancer will have evidence of metastatic disease at presentation, and one third of patients undergoing surgical management with curative intent will subsequently relapse, resulting in significant morbidity, and the majority of these die of their disease. Relapse most often presents within 3 years, but rarely can occur up to 10 years after resection of primary disease. The most common sites of recurrence are the liver, the lungs, and the original site of resection ***(Jemal et al., 2006).***

The primary aim of surveillance in patients with colorectal cancer treated by curative intent surgery is to detect locoregional recurrence, metastases, or metachronous primary disease at an early asymptomatic stage. Detecting recurrent disease is only useful if early treatment leads to an improved prognosis ***(Manfredi et al., 2006).***

Although the majority of relapsing patients are incurable, around one third of patients with isolated distant or locoregional recurrence are alive at 5 years after treatment, and long-term survival is possible. Rates

of resection for isolated or limited disease recurrence have increased, and approximately 20% of patients with hepatic relapse are currently considered for surgery. Some additional patients may also have resectable disease after downstaging with chemotherapy. Long-term survival is also not uncommon after resection of pulmonary metastases, even after previous resection of recurrent hepatic disease. There is evidence that high risk (Stage II or III) patients with imaging-detected recurrence have better survival than those who relapse and present with symptoms, even after taking lead-time bias into account, most likely due to amenability to resection ***(Steven et al., 2007).***

Survivors of colorectal cancer are at increased risk of developing new primary tumours, and surveillance results in metachronous primary cancers being diagnosed at earlier stages than index tumours, with high rates of potentially curative resection ***(Steven et al., 2007).***

Tumour visualization is traditionally performed using anatomical imaging techniques such as computed tomography (CT), ultrasound (US) and magnetic resonance imaging (MRI). Functional imaging may be of additional value via visualization of metabolism with fluoro-deoxyglucose positron emission tomography (FDG-PET) is a valuable tool for detection of primary

and recurrent colorectal cancer. Tumour sites may be detected throughout the body with high contrast resolution. However, exact localization and demarcation of lesions with PET is hindered by its relatively low spatial resolution, and lack of anatomical reference ***(Ruers et al., 2002).***

Early detection of recurrent colorectal carcinoma has become more important in the past decade, as the treatment options for localized disease have improved significantly. However, aggressive locoregional interventions (e.g. partial liver resections, radiofrequency ablation (RFA) of liver metastases, resections of pulmonary metastases) are as of yet considered futile in the presence of metastases elsewhere. Therefore, detection of tumour sites throughout the body is needed with high sensitivity and specificity. For patient management with regard to invasive therapy, accurate information about the local extent of the tumour is also necessary ***(Wouter et al., 2005).***

The factors that predict the success of the surgery for LRRC remain controversial. Several parameters such as the type of initial surgery, tumor size, presence of severe symptoms and the serum CEA level before re-resection have been assessed as potential prognostic indicators ***(Lopez et al., 2001).***

Aim of the work

This research aims at better understanding of the patho-physiology of colo-rectal carcinoma, as well as the new modalities in the diagnosis of early recurrence. Also, to identify the recent concepts in surgical and non-surgical management of such condition.

Chapter (*I*)

Embryology and Anatomy of Colon and Rectum

(I) Embryology of Colon and Rectum:

The embryonic gastrointestinal tract begins developing during the fourth week of gestation. The primitive gut is derived from the endoderm and divided into three segments: foregut, midgut, and hindgut. Both midgut and hindgut contribute to the colon, rectum, and anus ***(Bullard and Rothenberge, 2007).***

The midgut develops into the small intestine, ascending colon, and proximal transverse colon, and receives blood supply from the superior mesenteric artery. During the sixth week of gestation, the midgut herniates out of the abdominal cavity, and then rotates 270 degrees counterclockwise around the superior mesenteric artery to return to its final position inside the abdominal cavity during the tenth week of gestation (figure 1) ***(Chang and Feig, 2006).***

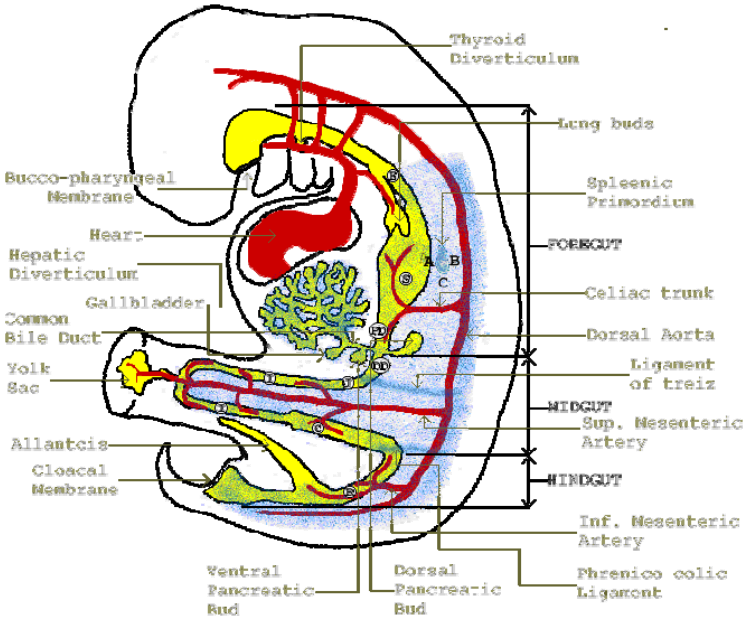

Fig. (1): Primitive gastrointestinal system ***(Hugo, 2004).***

The hindgut endoderm develops into the left 1/4 of the transverse colon, the descending colon, sigmoid colon and the rectum down to the ano-rectal line (the endoderm-ectoderm junction), all of which receive their blood supply from the inferior mesenteric artery. During the sixth week of gestation, the distal-most end of the hindgut, The cloaca divides into a dorsally placed rectum and a ventrally placed urogenital sinus(figure 2) ***(Hugo, 2004)***.

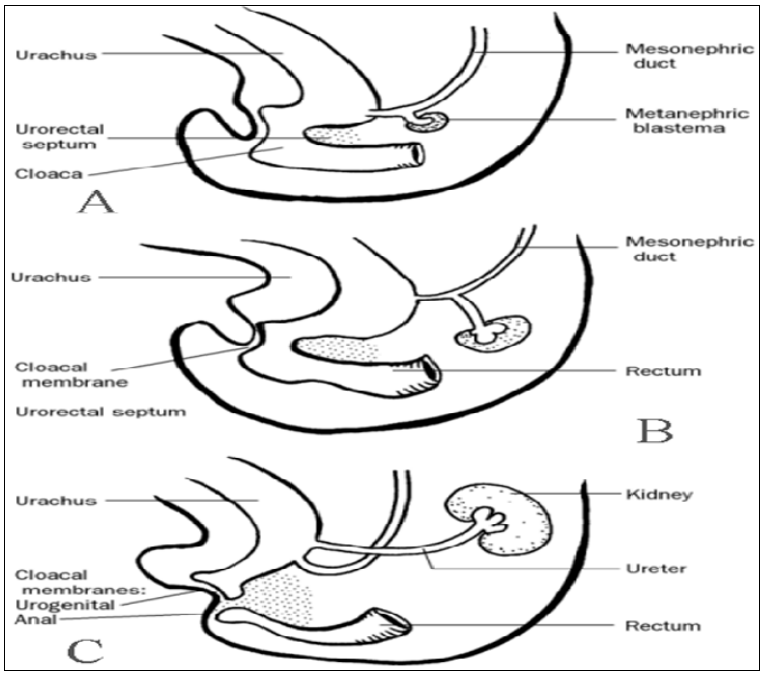

Fig. (2): Partitioning of the common cloaca ***(Bullard and Rothenberger, 2007).***

The distal anal canal is derived from ectoderm and receives its blood supply from the internal pudendal artery. The dentate line divides the endodermal hindgut from the ectodermal distal anal canal ***(Bullard and Rothenberger, 2007).***

(II) Anatomy of the colon, rectum and pelvic floor:

Although much of our fundamental understanding of the anatomy of the colon, rectum, and anus comes from the efforts of researchers of the 19th and early 20th centuries, comprehensive observations of this region had been made as early as 1543 by *Andreas Vesalius* through anatomic dissections. However, anatomy of this region, especially that of the rectum and anal canal, is so intrinsically related to its physiology that much can be appreciated only in the living. Thus, it is a region in which the surgeon has an advantage over the anatomist through in vivo dissection, physiologic investigation, and endoscopic examination. However, anatomy of the pelvis is also challenging to the surgeon: the pelvis is a narrow space, packed with intestinal, urologic, gynecologic, vascular, and neural structures, all confined within a rigid and deep osseous-muscular cage. Therefore, detailed anatomy of this region is difficult to learn in the setting of an operating room and it demands not only observations in vivo, but historical reviews, anatomy laboratory studies, including dissections of humans and animals, with in-depth descriptions and drawings and sometimes associated with physiologic evaluation ***(Yeatman and Bland, 1989).***

The colon extends from the end of the ileum to the rectum. The cecum, ascending colon, hepatic flexure, and proximal transverse colon comprise the right colon. The distal transverse colon, splenic flexure, descending colon, sigmoid

colon, and rectosigmoid comprise the left colon (figure 3) ***(Yeatman and Bland, 1989).***

The ascending and descending portions are fixed in the retroperitoneal space; the transverse colon and sigmoid colon are suspended in the peritoneal cavity by their mesocolons. The caliber of the lumen is greatest at the cecum and diminishes distally ***(George et al 2003)***.

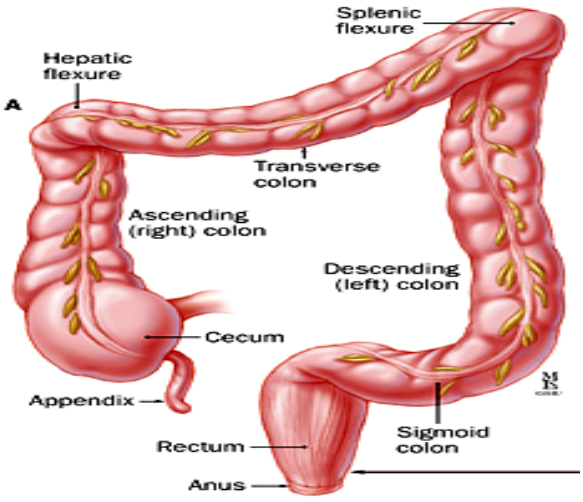

Fig (3): Anatomy of the colon ***(Yeatman and Bland, 1989).***

The colon and rectum constitute a tube of variable diameter about 150 cm in length. The terminal ileum empties into the cecum through a thickened, nipple-shaped invagination, the *ileocecal valve*. The cecum is a capacious sac-like segment of the proximal colon with an average diameter of 7.5 cm and length of 10 cm. (figure 4) ***(Wolff and Larson, 2007).***