THE ROLE OF 18F-FDG PET/CT IN MONITORING RECURRENCE OF COLORECTAL CANCER IN PATIENTS WITH RISING CEA LEVELS

Essay submitted for Partial Fulfillment of the Master Degree in Radiodiagnosis

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2016

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µ MAP	Attenuation Map
18F-FDG	18F-FluroDeoxyGlucose
68Ge	Germanium-68
ACFs	Attenuation Correction Factors
AJCC	American Joint Commission on Cancer
APC	Adenomatous Polyposis Coli
ASCO	The American Scosiety of Clinical Oncology
BGO	Bismuth Germanate
CEA	Carcino Embryonic Antigen
Cm	Centimeter
CRC	Colorectal Cancer
CRCR	Colorectal Cancer Recurrence
CT	Computed Tomography
CTC	Computed Tomography Colonography
DNA	DeoxyriboNucleic Acid
DWI	Diffusion Weighted Image
EC	Electron Capture
EORTC	European Organization for Research and Treatment of Cancer
EUS	Endoscopic Ultrasound
FAPs	Familial Adenomatous Polyposis
FBP	Filtered Back Projection
FORE	Fourier rebinning algorithm
GISTs	Gastro Intestinal Stromal Tumors
GLUT	Glucose Transporter
GSO	gadolinium oxyorthosilicate
HNPCC	Hereditary Non-Polyposis Colorectal Cancer
HU	Hounsfeild Unit
IMA	Inferior Mesenteric Artery
IMV	Inferior Mesenteric Vein
IV	Intra Venous
KeV	Kilo electron Volt
KV	Kilo Volt
LNs	Lymph Nodes
LSO	lutetium oxyorthosilicate

MALT	Mucosa Associated Lymphoid Tissue
MDCT	Multi Detector Computed Tomography
MeV	Mega electron Volt
MIP	Maximum Intensity Projection
ML	Maximum-Liklehood
MMR	Mis Match Repair
MRI	Magnetic Resonance Imaging
MTV	Metabolic Tumor Volume
N	Neutron
NaI	Sodium Iodide
NPV	Negative Predictive Value
OSEM	ordered subset expectation maximization
P	Proton
PET	Positeron Emission Tomography
PMTs	Photo Multiplier tubes
PPV	Positive Predictive Value
ROC	Reciever Operator Curve
SMA	Superoir Mesenteric Artery
SMV	Superoir Mesenteric Vein
ß-	Electron
ß+	Positron
SSRB	single-slice rebinning algorithm
SUVmax	Maximum Standardized Uptake Value
SUVmean	Mean Standardized Uptake Value
TLG	Total Lesion Glycolysis
TNM	Tumor, Nodes, Metastases
UICC	Union International Center Cancer
γ	Photon

Abstract

Colorectal cancer (CRC) is the third most common cancer in the world. It is estimated that up to 40 % of patients will present with recurrence after surgical resection of the primary tumor, often within 2 years. Imaging plays an important role in the postoperative assessment of recurrence. Most guidelines recommend computed tomography (CT) at regular intervals (12 and 36 months postoperatively) as well as upon clinical suspicion

Assessment of therapeutic response to pre-operative chemotherapy is becoming fundamental practice in order to decide the best chemotherapy protocol or when to go for surgical treatment. Conventional CT and MRI only offer anatomical and morphological mapping of of the tumors with no information about the metabolic activity. Lately, PET imaging for tumor staging and monitoring therapy response has been introduced. PET imaging only provides physiologic information on glucose uptake and metabolism, the main downside to PET imaging in tumors is the lack of accurate anatomical landmarks which makes localizing the lesion hard.

Combined PET/CT provides both the anatomic and metabolic imaging at the same time. It also makes separating normal physiological uptake from pathological uptake more feasable. It has higher sensitivety and specificity and reduces false-positive and false-negative imaging studies.

The objective of the following Essay is to highlight the role of PET/CT in monitoring recurrence of colorectal cancer in patients with elevated CEA levels. In addition, an overview of current surveillance recommendations will be given.

Keywords

PET/CT, Colorectal cancer, Colon cancer recurrence

Introduction

Colorectal cancer (CRC) is the third most common cancer in the world. It is estimated that up to 40 % of patients will present with recurrence after surgical resection of the primary tumor, often within 2 years. Imaging plays an important role in the postoperative assessment of recurrence. Most guidelines recommend computed tomography (CT) at regular intervals (12 and 36 months postoperatively) as well as upon clinical suspicion **(Gade et al., 2015).**

Computed tomography (CT) and positron emission tomography (PET) are both well-established methods for the evaluation of patients with suspected CRC recurrence (CRCR). The results of CT depend on the site of recurrence and the size and morphological appearance of the lesion. Because of the well-known high uptake of 18F-fluorodeoxyglucose (FDG) in primary colorectal carcinomas and their recurrences, FDG-PET provides accurate information about changes in glucose metabolism; however, it is of limited value for anatomical localization and morphological depiction. Integrated imaging using both modalities improves the detection of CRCR even when the recurrent tumor is small, with good anatomical and structural delineation of the tumor and adjacent structures. In addition, integrated imaging has the potential to differentiate between tumor recurrence and changes attributable to previous surgery and radiotherapy, a task which often presents a challenge to investigators **(Votrubova et al., 2006).**

Relapse after initial surgery for CRC is responsible for significant morbidity and mortality also it impairs the quality of life. In contrast to other malignancies, both local recurrence and metastatic spread from CRC can be addressed by curative-intent surgery. However, only 20–30% of patients with local relapse detected during follow-up have tumors that are deemed resectable at the time of diagnosis. Aggressive surgical approaches for CRC recurrence confined to a single organ are associated with a 5-year survival rate of up to 30% in selected patient populations. Thus, early diagnosis of local recurrence and small volume metastases are two of the primary goals of surveillance strategies because salvage surgery clearly has a higher chance of success in the asymptomatic patient with limited disease. Consequently, surveillance should enhance the proportion of resectable cases to increase survival. In rectal cancer the majority of local recurrences originate from the tumor bed, which underlines the importance to directly visualize the perirectal tissues as part of postoperative follow-up **(Schaefer and Langer, 2007).**

Aim of the work

The objective of the following Essay is to highlight the role of PET/CT in monitoring recurrence of colorectal cancer in patients with elevated CEA levels. In addition, an overview of current surveillance recommendations will be given.

Colorectal anatomy

The large intestine runs from the ilocecal junction to the anal verge. In the adult, it measures around 1-1.5 meters long (Fig.1). It is differentiated from the small intestine by having a greater caliber with a more fixed position, and in having certain appendages to its external coat (the appendices epiploicae). Furthermore, its longitudinal muscular fibers are arranged in three longitudinal bands rather than forming a continuous layer around the gut. The large intestine is divided into the cecum, colon, rectum, and anal canal **(Stringer, 2016).**

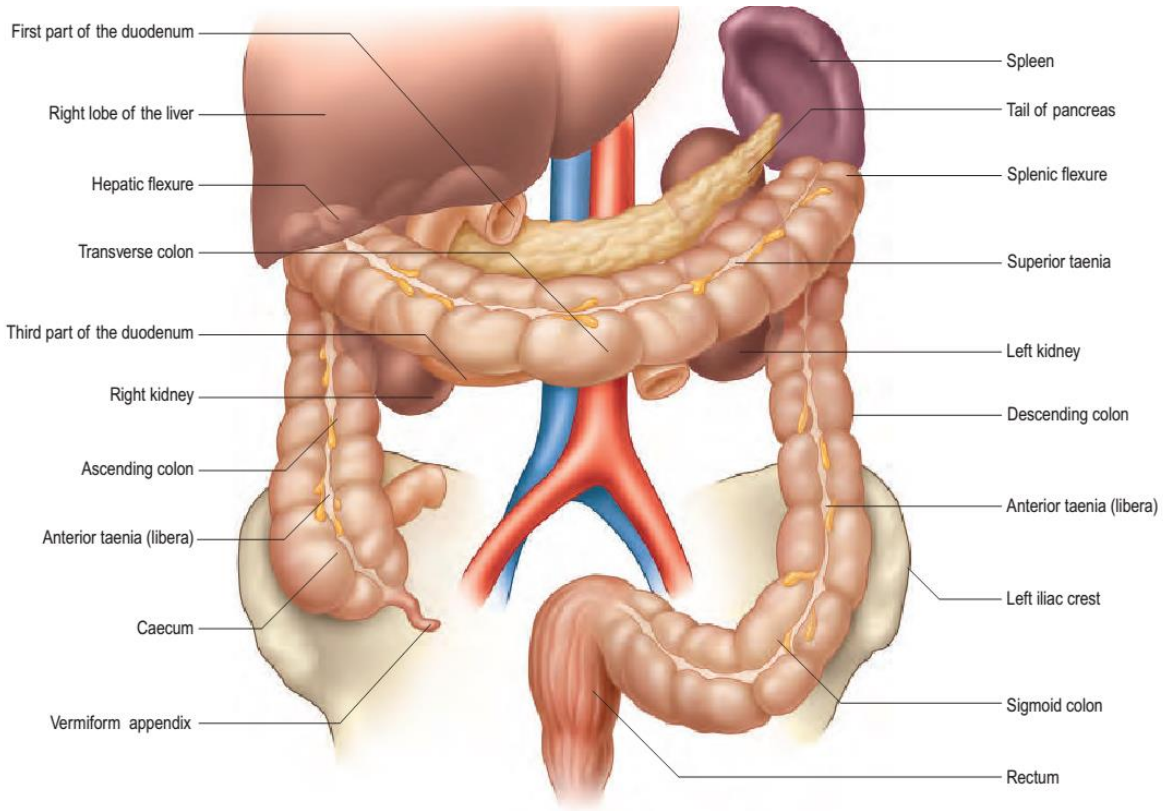

Fig. 1: An overveiw of the colon and it's realations **(Stringer, 2016)**.

I-The Cecum:

It is connected to the ileum and extends around two and half inches below it. The adult cecum is usually adherent to the posterior wall of the peritoneal cavity with a serosal cover on its anterior wall only. The cecum also forms a blind pouch from which the appendix projects. It varies in size according to different authors, but on average it reaches around 6.25 cm in length and 7.5 cm in width. It rests on the iliacus & psoas major muscles, usually in contact with the anterior abdominal wall **(Stringer, 2016).**

II-The colon:

The colon functions as a reservoir, moving its contents in the caudal direction towards the anal canal. It is divided into four parts from proximal to distal; the ascending colon, the transverse colon, the descending colon, and lastly the sigmoid colon **(Fenoglio et al., 1999).**

1. Ascending colon:

It reaches about 15-20 cm long and passes upwards from the ileo-cecal valve to the hepatic flexure. Its upper portion lies posterior to the right lobe of the liver, in front of the anterior surface of the right kidney and lies in a retroperitoneal position against the right posterior abdominal wall. The hepatic flexure forms the junction between the ascending colon and the transverese colon, it has a less acute angle than the splenic flexure **(Stringer, 2016).**

2. Transverse colon:

It comprises the longest segment of the large intestine. It reaches nearly 20 inches long, beginning at the hepatic flexure and ending at the splenic flexure. It lies inferior to

the stomach and is attached to the transverse mesocolon **(Young et al, 2011).**

It is attached to the stomach by the gastro-colic ligament while contacting the second part of the duodenum, the pancreas, and the spleen. The position of the transverse colon varies as it is suspended by the mesocolon and it is a free moving part of the large intestine. The omentum attaches to its anterior surface **(Fenoglio et al., 1999).**

The splenic or left colic flexure is present at the junction of the transverse and descending parts of the colon, related to the lower end of the spleen and the tail of the pancreas; the flexure is so acute that the end of the transverse colon usually lies in contact with the front of the descending colon. It is situated at a higher level than the right colic (hepatic) flexure, and it attaches to the diaphragm, opposite the 10^{th} and 11^{th} ribs, by a peritoneal fold, called the phrenico-colic ligament **(Stringer, 2016).**

3. **Descending colon:**

The descending colon extends downwards from the splenic flexure to the level of the iliac crest and reaches around 25-30 cm long. In most adults it is retroperitonial **(Stringer, 2016).**

4. **Sigmoid colon:**

The remaining part of the colon crosses the pelvic rim into the pelvic cavity and lies partly in the abdomen and partly in the pelvis. It then forms an S-shaped curve in the pelvis terminating in the rectum at the level of the third segment of the sacral vertebrae **(Young et al., 2011).**

The sigmoid colon lies inside the peritoneal cavity and it has a mesentery that is sometimes called the mesosigmoid