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RESEARCH ARTICLE

ADVANCED IMAGING OF COLO-RECTAL CANCER: A REVIEW STUDY

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Abstract

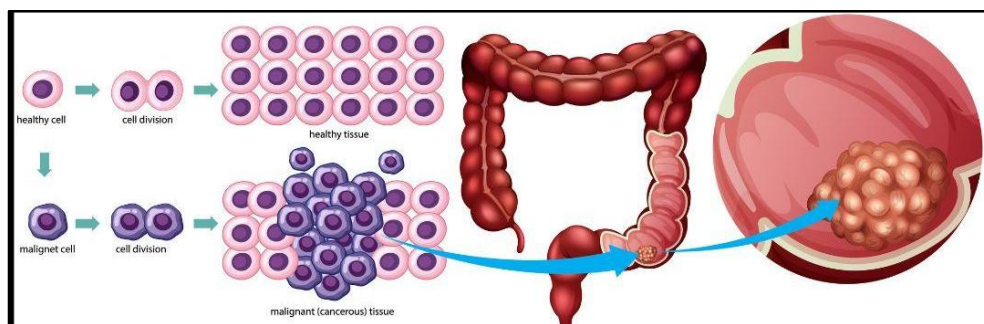
Colorectal cancer (CRC) is the third most frequent malignancy globally. Screening for CRC at a certain age is strongly encouraged for prompt earlier diagnosis owing to prognoses being greatly correlated with time of detection and cancer staging. This review aimed to elucidate the most recent advancements in the detection of CRC, with an emphasis on the latest innovations in diagnostics in conjunction with radiological imaging alongside stool-based tests for CRC screening. A comprehensive review of the literature was performed, focusing on specific terms in different electronic databases. Articles screened and evaluated were deemed relevant to the study aim and were presented in the medium of the English language. There have been several innovations in the diagnostics and identification of CRC. These generally comprise molecular biomarkers, currently being studied for suitability in disease detection.

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However, putting these strategies into reality is hampered by several issues. Progress in diagnostic technology alongside the identification of a few indicators suggested great promise for prompt detection and management of CRC.

Introduction:-

Colorectal cancer (CRC) is among the most frequently diagnosed cancers in the world. It is the second leading cause of cancer-related deaths in the West. In the last few years, the CRC mortality rate has dropped by 20% thanks to a multidisciplinary approach to the disease that includes the role of radiologists as well as the optimization of screening, biomarker and genomic analysis, imaging evaluation, surgical techniques, and therapies. WHO (2023); sung et al (2020) When it comes to assessing significant tumor characteristics, conventional imaging methods have obvious drawbacks. For instance, 9–10% of patients with liver and/or lung lesions that were computed tomography (CT)-indeterminate at the time of radiological staging of colorectal cancer (CRC) developed confirmed metastases. Markowitz et al (2009); Wm G et al (2015); Pino et al (2009) The evaluation of tumor-specific features using non-invasive imaging is also becoming more and more important. To overcome these restrictions, functional and molecular imaging (FMI) methods have been developed. The present function of sophisticated imaging modalities in the treatment of CRC patients is the main topic of this research. Gerstong et al (2020)



Source: <https://continentalhospitals.com/diseases/colorectal-cancer/>

Figure 1: Colorectal Cancer

Positron emission tomography (PET)/CT has made it easier to diagnose distant metastases and evaluate tumor physiology. Finally, improved tissue contrast has been made possible by the use of rectal magnetic resonance imaging (MRI) as a staging modality. Zhang et al (2023) In order to detect liver metastases, protocols have been improved using high-resolution T2-weighted sequences, diffusion restriction, PET/MR, and the creation of hepatobiliary MRI contrast agents. Tomida et al (2022) However, these methods have limits in terms of characterisation. These techniques are superior in re-evaluation after neoadjuvant treatment and metastatic resection, and they have directly increased completion rates of en bloc resection of the original tumor in both colon and rectal cancer. 1 and 2 Imaging approaches have continuously changed in response to the introduction of new, better, and more varied treatment strategies. Additionally, additional evidence has emerged to illustrate the advantages and disadvantages of imaging staging and restaging. Islam et al (2023)

Basic Imaging Techniques:-

Because they show how the tumor relates to surgical landmarks (such as the circumferential resection margin in the rectum), identify significant prognostic features, assess the tumor's response to treatment, and are helpful for post-treatment surveillance, conventional imaging techniques are crucial in colorectal cancer. Loktionov et al (2020) The most effective imaging method for assessing the primary factors influencing treatment and prognosis in cases of rectal cancer (RC) is magnetic resonance imaging (MRI). These factors include tumor length, distance from the anal verge, relationship to the peritoneal reflection, T-stage, depth of extramural tumor growth, lymph node (LN) status, vascular and neural invasion, invasion to adjacent structures, and distance to the mesorectal resection margin. Aboud et al (2013); Boriache et al (2018) Apart from this, achieving superior anatomical resolution has been the primary emphasis of medical imaging advancements. Imaging methods currently enable volumetric model reconstruction and image segmentation, with several clinical uses in colorectal cancer. Chen et al (2017); Hamid et al (2020)

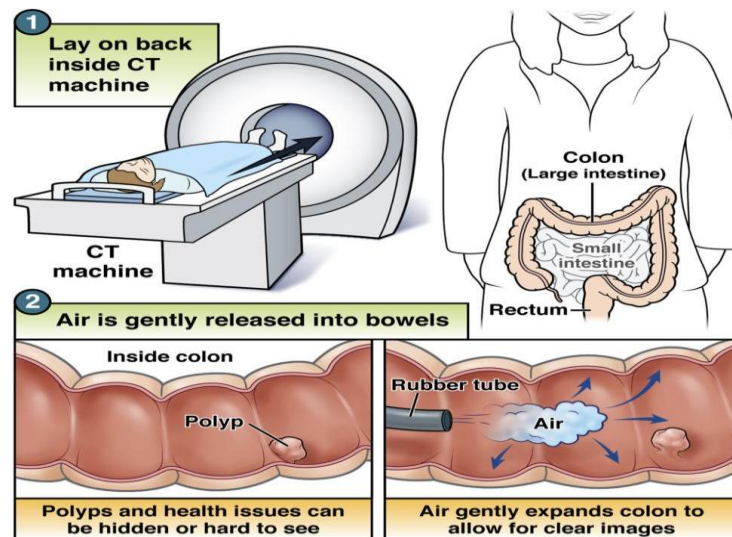
Computed tomographic colonography:-

Following air insufflation, computed tomographic colonography (CTC) creates two and three-dimensional (3D) images of the entire colon and rectum using a CT scanner. For detecting polyps and colorectal cancer, CTC is the most effective radiological diagnostic test. Its diagnostic performance for CRC detection has been demonstrated to be unquestionably better than that of a barium enema and comparable to that of a traditional colonoscopy. Zhan et al (2022); Phul et al (2021) CTC is also easier to execute and less intrusive than a traditional colonoscopy.

Scientific societies and solid evidence-based data have supported the emergence of several indications, such as:

1. incomplete, unsuccessful, or impractical conventional colonoscopy (for finding synchronous malignancies),
2. elderly and fragile patients (who are more prone to have a problematic colonoscopy), examination of diverticular disease and patients with colonic stoma;
3. tumor localization (particularly for laparoscopic surgery); and
4. warning signs suggestive of colorectal cancer.

Other indications include CRC screening and monitoring following polypectomy or CRC surgery, many of which are still up for dispute.



Source: <https://patient.gastro.org/ct-colonography/>

Figure 2: Computed tomographic colonography

Volumetry in CRC:-

For several types of tumors, tumor sizes and volumes have been shown to be significant prognostic indicators. Despite occasionally conflicting published findings, these traits were not found to be helpful in the TNM staging system for colorectal cancer or in forecasting the clinical outcome of patients. Volume can be measured simply using a variety of semi-automated approaches. Tosi et al (2017) T2-weighted volumetric-based tumor volume reduction rate (TVRR) after chemo-radiotherapy (CRTP) may be predictive in the case of RC. After preoperative CRTP, TVRR significantly correlates with the tumor pathological regression grade, and a volume reduction ratio greater than 75% is linked to a higher pathologic complete response rate. Sammoud et al (2012); Sui et al (2020) In the re-staging of RC after CRTP, T2-weighted images' primary drawback is their incapacity to discriminate between fibrosis and tiny tumor foci that remain, which adversely affects their sensitivity. Additionally, it can be challenging to determine which regions on T2-weighted images should be included in the volume measurements because they are still suspect for tumors. To differentiate between complete and non-complete responders, tumor volumetry based on the signal-intensity characteristics of dynamic contrast-enhanced (DCE) or diffusion-weighted (DW) images may be more accurate than traditional T2-weighted images (sensitivity, specificity, accuracy, and area under the curve (AUC) for DCE, DWI, and T2-weighted images, respectively, 86/64/86 %, 73/94/93 %, 79/76/93 %, and 0.76/0.81/0.90 respectively). These statistics must be carefully taken into account, though. Tumor segmentation on DWI may be inaccurate because to susceptibility artifacts and bright spots on high b-value images caused by the

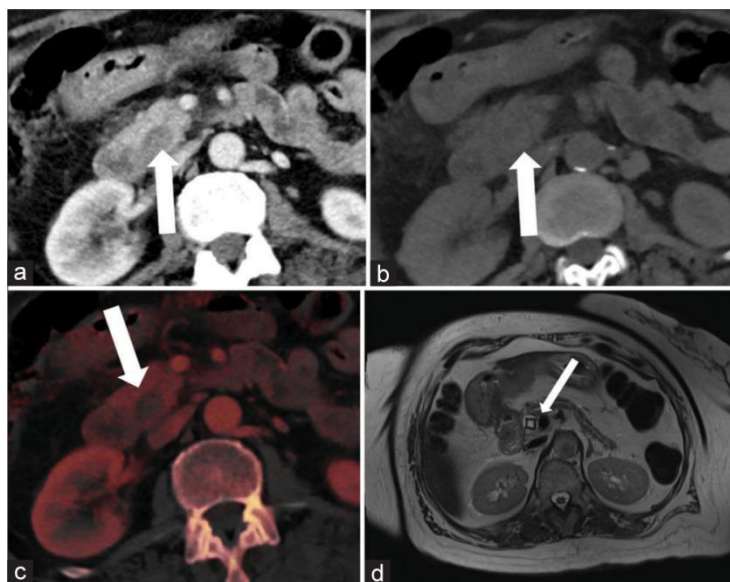
T2 shine-through phenomenon, as well as contrast uptake that may be more pronounced in inflammatory areas, changing DCE-based measures. Vitiello et al (2019); Moore et al (2020)

The survival rate of patients with metastatic colorectal cancer has increased with hepatic resection. About 25% of patients with colorectal cancer who receive a new diagnosis already have liver metastases, and another 25% will acquire liver metastases as the disease progresses. Yang et al (2022); Ao C et al (2020) When planning hepatic resection, there are a number of important factors to take into account, such as the quantity of remaining liver after resection, the number of segments affected, and the proximity of lesions to arterial and biliary structures. Nassar et al (2021); Massen et al (2022) Postoperative mortality and morbidity as well as procedural success are influenced by the size of the remaining liver. When a patient has underlying liver illness, such as fatty liver from hepatotoxic chemotherapy (CTP) in patients with colorectal cancer (CRC), this aspect is more crucial since the future hepatic residual needed must be greater than in people with normal livers. Koch et al (2018); Yue et al (2022); Mitchel et al (2014) A growing number of patients with colorectal cancer are undergoing imaging-based liver volumetry to acquire precise measurements for major hepatic resection planning. The primary basis for semi-automated computerized liver segmentation techniques is CT imaging, which employ liver attenuation to define the liver. However, MRI cannot measure attenuation. Stereology techniques have been employed for MRI evaluation with precise results in order to overcome this problem. Xie L et al (2018)

Present Techniques:-

Dual-energy computed tomography:-

Dual-energy computed tomography (DECT) is a novel technology that uses CT density measurements from two simultaneous CT acquisitions at different tube potentials in a single session to differentiate between different materials and tissues. García et al (2016); Kekelidze et al (2013); Mauri et al (2012) The greater photoelectric absorption of iodine at low tube voltages allows it to be differentiated from other materials. Tissue characterisation and material separation are enhanced by DECT. Data can be shown as a map of iodine concentrations, and the attenuation brought on by iodine on contrast-enhanced CT can be measured. Furthermore, it is possible to make virtual, non-enhanced photographs. Comparing the contrast-enhanced DECT with bowel preparation, the inclusion of iodine map evaluation may boost the diagnosis of colorectal cancers (CRCs) (accuracy 96.7% vs. 90%). Additionally, DECT can be helpful for tumor staging. The greatest capacity to differentiate LN metastases was exhibited by the iodine concentration (IC) in the portal phase (PP) (AUC 0.932). Cutsem et al (2016)



Source: Kocher et al (2021)

Figure 3: Example of DECT

The most effective predictor of metastatic LNs (AUC 0.933) was the IC in PP, even after excluding clinically evident metastatic LNs based on standard CT results. Shi Y et al (2022) The total accuracy of distinguishing metastatic from non-metastatic LNs in RC could be increased to 82.9% by combining normalized IC in PP with the

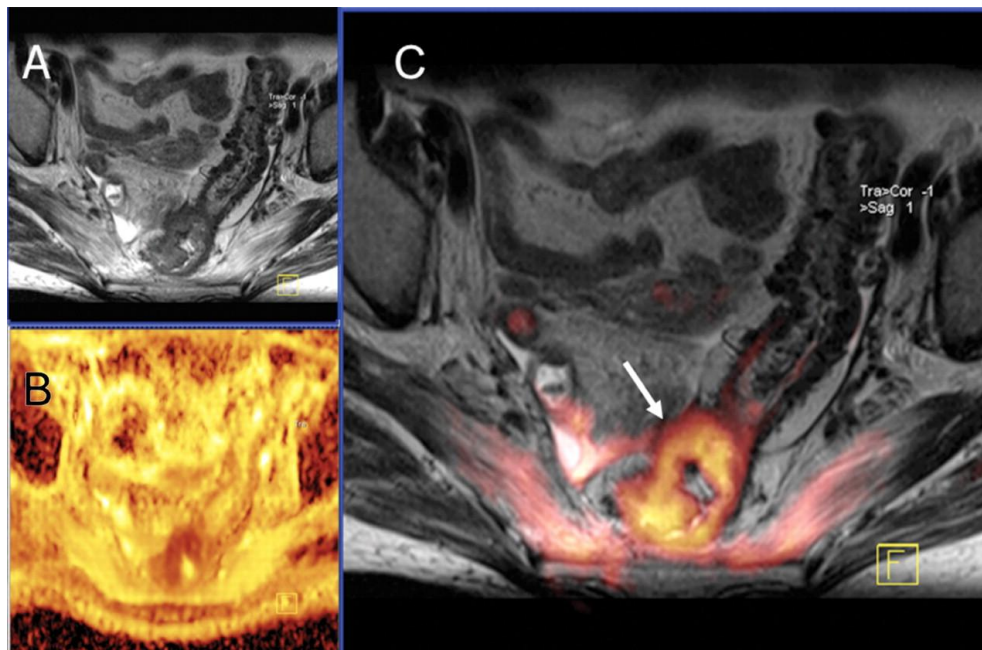
short axis diameter of LNs. However, these studies' drawbacks include a limited sample size, the exclusion of lymph nodes (LNs) smaller than 2 mm, and an insufficient one-to-one comparison between radiological and histology because not all of the LNs found during the pathologic examination were assessed on CT scans. Hetta et al (2020)

Texture analysis:-

The biology and behavior of malignant tumors exhibit significant geographical and temporal variability. On imaging, however, a large portion of the variability might be noise. In photos, texture analysis can improve biologic heterogeneity while lessening the impact of noise. The distribution and connections of grey-level values in pictures are the main subjects of texture analysis. In addition to producing a derived collection of sub-pictures, texture also allows the quantification of several metrics, such as entropy, kurtosis, and standard deviation of the pixel distribution histogram, by extracting fundamental components (i.e., spatial, frequency, etc.) from traditional images. Galem et al (2022); Takeda et al (2019)

Functional and molecular imaging:-

CRC frequently exhibits distinctive tumor phenotypic changes, which are signs of metabolic reprogramming and genetic modifications. These changes include changed metabolic pathways (such as an increased glycolytic capability), prolonged angiogenesis, and an infinite capacity for replication. It is possible that anatomic imaging methods are not sensitive enough to map the distribution of these tumor-specific features. In order to distinguish these characteristics for clinical decision-making, FMI-derived approaches might be useful. Andrei et al (2022); Kashihara et al (2017); Dickman et al (2013)



Source: <https://doi.org/10.2214/AJR.10.4422>

Figure 4: Functional Imaging of Colorectal Cancer

Imaging tumour proliferation:-

Since both benign and malignant nodes exhibit high DWI signals with increasing b-values and the ADC values of malignant nodes have been shown to be only slightly lower than those of benign nodes—not enough to allow for their discrimination—uncontrolled cell proliferation is a fundamental feature of cancer that typically results in a higher cell density in tumor lesions. Cutse et al (2016); Hur K et al (2017); Yin et al (2014)

Imaging oxygenation and hypoxia:-

In colorectal cancer, hypoxia is thought to be a significant modulator of the evolution of malignant disease, influencing patient prognosis and survival as well as determining how well a patient would respond to radiation therapy. To the best of our knowledge, there hasn't been any published research on imaging assessment of hypoxia in CRC. By using endogenous deoxyhemoglobin as a contrast agent, blood oxygenation level-dependent (BOLD)-

MRI may offer a non-invasive way to evaluate in-vivo tumor oxygenation. Nonetheless, there are a number of BOLD-MRI constraints to take into account. Initially, there is no known association between hypoxia indicators and BOLD-MRI data in colorectal cancer. Second, this method necessitates the concurrent evaluation of tumor vascular functionality and is more likely to represent acute tissue hypoxia (perfusion-related and frequently temporary) than chronic hypoxia (induced by increasing oxygen diffusion distances due to tumor expansion). Third, the clinical use of BOLD-MRI in colorectal cancer is restricted by motion and susceptibility artifacts. Additionally, there is a lack of experience with the use of hypoxia-related radiotracers in CRC for the PET evaluation of hypoxia. Zygulska et al (2022); Niu et al (2017); Ghafouri et al (2021)

Functional imaging of lymph nodes:-

In RC patients, nodal metastases are among the most important predictors of local recurrence and cancer-specific death. They also have an impact on the choice of adjuvant and surgical therapies. Normanno et al (2018) The sensitivity and specificity of CT, MRI, and endorectal ultrasound were insufficient to detect metastatic LNs, with a range of 55% to 78%. In addition, histological data indicate that up to 45% of nodal metastases in RC are ≤ 4 mm, making it more challenging to accurately characterize LNs. The introduction of contrast agents using ultra-small iron oxide particles (USPIO) made MR lymphography (MRL) possible. The macrophages in normally functioning nodes exhibit a particular cellular absorption of the contrast agent. Mizutan et al (2018); Brown et al (2022); Moon et al (2018)

Multi-parametric evaluation of CRC:-

The combination of functional (like DWI and DCE imaging) and molecular (like PET) techniques with the anatomical resolution of imaging may provide more information about the treatment of tumor microenvironments in various clinical scenarios, such as staging, tumor characterization, treatment response prediction, and response examination. Normannod et al (2019); Tsai et al (2018) The quantitative assessment of tumor phenotype, including post-therapy modifications in tumor biology, is made possible by the application of these approaches. The multi-parametric/multi-modality technique has seen very little application in CRC. Most of these investigations have been conducted in single-center settings with tiny patient populations, and they are primarily limited to experimental settings. Tumor biological properties may be explained by the relationship between various parameters. Vascular endothelial growth factor (VEGF) expression was higher in CRC with a low-flow/high-metabolism phenotype in this context, which may indicate a more aggressive and angiogenic nature. According to Fischer et al. (2022), using a cut-off value of -75% , changes in the flow-metabolic phenotype (blood flow \times maximum standardized uptake values (SUV)) of RC following CRT demonstrated high accuracy for the prediction of histopathology response to CRT (AUC 0.955, 95% CI 0.833-1.000). Hui et al (2023); Kowal et al (2014)

Conclusion:-

To sum up, there are a lot of chances for evaluating patients with colorectal cancer using modern imaging techniques. The evaluation of tumor hallmarks and tumor heterogeneity made possible by the advent of functional and molecular imaging techniques into clinical practice may alter patient therapy and, therefore, prognosis. A better knowledge of the regulatory mechanisms controlling cancer-specific epigenetic changes has made it feasible to look more closely at prospective clinical implications as diagnostic or therapeutic targets in CRC. In terms of prognosis, response to therapy prediction, or early CRC stage identification, the diagnostic performance of stated molecular biomarkers still has to be improved. Modern imaging technologies are the basis of most treatments developed to support the identification and follow-up of all phases of treatment in all forms of malignancies, including solid tumors, as they may reduce the need for traditional biopsy-based procedures.

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