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Original Article

Role of Inflammatory and Prognostic Markers and Its Outcome Among Patients with Pre and Post-Operative Colorectal Carcinoma

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ABSTRACT

Colorectal carcinoma is a significant health concern, often presenting with symptoms like bleeding per rectum, mucous discharge, tenesmus, altered bowel habits, and weight loss. This study examines the influence of inflammatory and prognostic markers on the outcomes of patients undergoing per and post-operative treatment for colorectal carcinoma. **Objective:** To evaluate the role of inflammatory and prognostic markers on the outcomes of patients with per and post-operative colorectal carcinoma. **Methods:** This cross-sectional study included 112 patients aged 20-60 years, of either gender, with symptoms such as bleeding per rectum, mucous discharge, tenesmus, altered bowel habits, and weight loss for ≥1 month, diagnosed with colorectal cancer regardless of stage and grade. **Results:** The mean age of the patients was 45.16 ± 10.52 years, with 51.8% males and 48.2% females. Common symptoms included abdominal pain, per rectal bleeding, and weight loss, with 89.3% presenting with anemia. Tumors were located in the colon (84.8%) and rectum (28.6%). Pre-operative markers showed elevated WBC in 59.8%, CRP in 87.5%, decreased serum albumin in 77.7%, raised ESR in 61.6%, ferritin in 65.2%, and LDH in 60.7%. Post-operative markers indicated elevated WBC in 92.9%, CRP in 94.6%, decreased serum albumin in 82.1%, raised ESR in 68.8%, ferritin in 69.6%, and LDH in 73.2%. Complications included wound infection, pneumonia, sepsis, and prolonged hospital stays, with a mortality rate of 3.6%. **Conclusions:** Serum inflammatory markers significantly influence prognoses and predict adverse outcomes in patients undergoing surgical treatment for colorectal carcinoma.

INTRODUCTION

Colorectal cancer (CRC) is the third most common malignancy in men and the second in women worldwide [1]. Despite advancements in screening programs and treatment modalities reducing mortality rates in developed countries, approximately 20% of CRC patients present with synchronous metastasis at primary diagnosis, and more than half eventually succumb to the disease. The incidence of CRC in individuals under 50 years of age is notably increasing, highlighting the need for ongoing research and improved treatment strategies [2]. Patients with CRC often exhibit symptoms such as rectal bleeding, altered bowel habits, tenesmus, fatigue, and mucus discharge [3]. Diagnosis is confirmed through clinical evaluations, including digital rectal examination, proctoscopy, and colonoscopy with histopathological biopsy [4]. Staging of CRC involves methods such as ERUS, CT scans, MRI with localizing coils, and PET/CT [5]. There is emerging evidence that inflammation plays a critical role in the development and progression of CRC. Conditions like inflammatory bowel disease, characterized by localized inflammation, are linked to a higher risk of CRC. However, the role of systemic inflammation in colon carcinogenesis is less clear [6]. Systemic inflammation is known to promote cancer through the production of pro-inflammatory cytokines and reactive oxygen species, which activate tumor-promoting transcription factors [7]. In CRC, systemic inflammation often leads to increased production of proteins like CRP by the liver and manifests as fever, anemia, fatigue, and loss of appetite, eventually resulting in cachexia. Key inflammation markers, such as

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elevated CRP and decreased serum albumin, are recognized as significant in predicting outcomes in CRC [8]. Despite the established association of inflammatory markers with cancer progression and patient outcomes, data on their prognostic significance and related survival outcomes in specific populations, including the Pakistani population, remain limited. This study aims to address this gap by determining the significance of blood-based inflammatory biomarkers in prognostication and prediction of outcomes and survival among CRC patients in Sindh, Pakistan.

METHODS

The cross sectional study was conducted in the Department of Surgery, surgical unit-II, Liaquat University Hospital, Hyderabad/Jamshoro. It was carried out over six months following the approval of the synopsis, from January 2022 to June 2022. The non-probability consecutive sampling method was chosen due to the specific inclusion criteria and the need to enroll all eligible patients within the study period, ensuring a comprehensive assessment of the target population within the constraints of the study's timeframe and resources. Inflammatory and prognostic markers were measured using standardized laboratory procedures, with specific assays for each marker, ensuring accuracy and reliability in the obtained results. The sample size was determined to be 112 patients, calculated using the prevalence of raised inflammatory markers as 24.8%, with a margin of error of 8%, using the formula for sample size calculation [9]:

$$n = \frac{Z^2 \times P \times (1 - P)}{d^2}.$$

where: n is the sample size, Z value (1.96 for 95% confidence level), P is the prevalence (24.8% or 0.248), d is the margin of error (8% or 0.08). Patients included in the study were between 20 to 60 years old, of either gender, with a history of bleeding per rectum or mucous discharge, tenesmus, altered bowel habits, and weight loss for at least one month, and diagnosed with colorectal cancer through histopathological reports, regardless of stage and grade. Excluded from the study were elderly patients with ASA-3 and 4, known cases of other GI malignancies, cirrhosis, malabsorption syndrome, those already on corticosteroids, immunosuppressive therapy, albumin or antibiotic therapy, patients with chronic renal failure, nephrotic syndrome, pregnant and lactating women, vitally unstable patients due to intestinal obstruction or perforation, and those already on iron supplements and recurrent blood transfusions. Data were collected from patients admitted to the surgery ward after obtaining informed consent. A brief clinical history was taken, and relevant physical examinations were performed. Baseline investigations and specific investigations (colonoscopy and biopsy, CT scan of the chest, abdomen and pelvis, and transrectal ultrasound) were advised, and the history of associated co-morbidities was recorded. Diagnosed cases of colorectal cancer were further explored for inflammatory markers (white blood cell count, serum albumin, erythrocyte sedimentation rate, serum C-reactive protein, fibrinogen, and cytokines including interleukin-6 and tumor necrosis factor) and prognostic markers (serum LDH and ferritin). These were measured pre-operatively and post-operatively on the third day, and CEA levels were measured after one month by taking a 2-cc venous blood sample in a 5 cc disposable syringe and sending it to the laboratory for analysis. All maneuvers, including history taking, physical examination, sampling, and data collection, were conducted by the principal researcher. Data were collected using a pre-designed proforma, and the financial burden of the study was borne by the researcher. Biopsy specimens and biochemical analyses were performed by a senior pathologist with over five years of experience. Patients were kept in the ward for 5-7 days according to their status and the quantity of drainage, and were observed for in-hospital outcomes. The collected data were analyzed using SPSS version 21.0. The frequency and percentage of inflammatory markers, gender distribution, associated co-morbidities, and effect modifiers were computed. The mean and standard deviation were calculated for quantitative variables such as age, duration, WBC count, ESR, serum albumin, ferritin, LDH, and CRP levels. The study was conducted following ethical guidelines, and approval was obtained from the Research Ethics Committee, Liaquat University of Medical and Health Sciences, Jamshoro (LUMHS/REC/-203).

RESULTS

A total of 112 cases were studied with a mean age of 45.16±10.52 years (range: 25-67 years). The gender distribution was 51.8% males and 48.2% females. Most patients were urban residents (53.6%), while 36.4% were rural residents. The majority of patients presented with abdominal pain, per rectal bleeding, and weight loss (Table 1). According to comorbidities, 67.9% of the patients had hypertension, 44.6% were diabetics, 49.1% were smokers, 29.5% were obese, 24.1% had dyslipidemia, and 89.3% had anemia (Table 1).

Table 1: Socio-Demographic and Clinical Characteristics of Patients (n=112)

Variables	Frequency (%)
Age (Mean ± SD)	45.16 ± 10.52
Gender	
Male	58 (51.8)
Female	54 (48.2)
Residence	
Urban	60 (53.6)
Rural	52 (46.4)

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Presenting Complaints	
Abdominal Pain	112 (100.0)
Per Rectal Bleeding	112 (100.0)
Weight Loss	112 (100.0)
Comorbidities	
Hypertension	76 (67.9)
Diabetes	50 (44.6)
Smokers	55 (49.1)
Obesity	33 (29.5)
Dyslipidemia	27 (24.1)
Anemia	100 (89.3)

Tumor grading revealed that 58.0% had a tumor grade of T2N1M0, 37.5% had T2N0M0, 2.7% had T1N0M0, and 1.8% had T3N1M0 (Table 2). Surgical procedures included right hemicolectomy (23.2%), left hemicolectomy (11.6%), sigmoidectomy (11.6%), transverse colectomy (11.6%), high anterior resection (11.6%), low anterior resection (15.2%), abdomino-perineal resection (1.8%), and extended hemicolectomy (13.4%). Tumor locations were predominantly in the colon (71.4%) and rectum (28.6%). Surgical intent was curative in 84.8% of cases and palliative in 15.2% (Table 2).

Table 2: Tumor Characteristics and Surgical Procedures (n=112)

Variables	Frequency (%)
Tumor Grade	
T2N0M0	42 (37.5)
T2N1M0	65 (58.0)
T1N0M0	3 (2.7)
T3N1M0	2 (1.8)
Surgical Procedures	
Right Hemicolectomy	26 (23.2)
Left Hemicolectomy	13 (11.6)
Sigmoidectomy	13 (11.6)
Transverse Colectomy	13 (11.6)
High Anterior Resection	13 (11.6)
Low Anterior Resection	17 (15.2)
Abdomino-perineal Resection	2 (1.8)
Extended Hemicolectomy	15 (13.4)
Tumor Location	
Colon	80 (71.4)
Rectum	32 (28.6)
Surgical Intent	
Curative	95 (84.8)
Palliative	17 (15.2)

Pre-operative inflammatory markers indicated raised WBC in 59.8% of cases, raised CRP in 87.5%, decreased serum albumin in 77.7%, raised ESR in 61.6%, raised ferritin in 65.2%, and raised LDH in 60.7%. Post-operatively, these markers showed a significant increase with raised WBC in 92.9% ($p < 0.001$), raised CRP in 94.6% ($p = 0.03$), decreased serum albumin in 82.1% ($p = 0.36$), raised ESR in 68.8% ($p = 0.24$), raised ferritin in 69.6% ($p = 0.48$), and raised LDH in 73.2% ($p = 0.04$) (Table 3).

Table 3: Pre-Operative and Post-Operative Inflammatory Markers (n=112)

Inflammatory Marker	Pre-Operative N (%)	Post-Operative N (%)	P-Value
Raised WBC	67 (59.8)	104 (92.9)	<0.001
Raised CRP	98 (87.5)	106 (94.6)	0.03
Decreased Albumin	87 (77.7)	92 (82.1)	0.36
Raised ESR	69 (61.6)	77 (68.8)	0.24
Raised Ferritin	73 (65.2)	78 (69.6)	0.48
Raised LDH	68 (60.7)	82 (73.2)	0.04

The hospital outcomes showed that 30.4% of patients had a normal recovery, while 18.8% experienced postoperative wound infections. Reoperation was required in 7.1% of cases, and 12.5% had sepsis, wound infection, and prolonged hospital stay. Mortality was 3.6% (Table 4).

Table 4: Hospital Outcomes and Mortality (n=112)

Hospital Outcomes	N (%)	P-Value
Normal	34 (30.4)	-
Reoperation	8 (7.1)	0.23
Pneumonia and Prolonged Stay	4 (3.6)	0.46
Pneumonia, Shock and Prolonged Stay	2 (1.8)	0.62
Pneumonia, Wound Infection and Prolonged Stay	8 (7.1)	0.23
Pneumonia	4 (3.6)	0.46
Sepsis, Wound Infection and Prolonged Stay	14 (12.5)	0.07
Sepsis and Prolonged Stay	4 (3.6)	0.46
Wound Infection and Prolonged Stay	11 (9.8)	0.13
Shock and Prolonged Stay	2 (1.8)	0.62
Postoperative Wound Infections	21 (18.8)	0.11
Mortality	4 (3.6)	-

DISCUSSION

This study investigated the socio-demographic characteristics, tumor grading, surgical procedures, inflammatory markers, and hospital outcomes of 112 patients with colorectal cancer at Liaquat University Hospital, Hyderabad/Jamshoro. The mean age of the patients was 45.16±10.52 years, with a slight predominance of males (51.8%). Elderly people with a high burden of coexisting disorders may be less likely to pay attention to cancer symptoms, may put off treating them, or may have other medical issues masking the warning signals of cancer (masked symptomatology not visible to patients or physicians). When it comes to the elderly, colon disruption is frequently thought to come with getting older [10-12]. The reason for this age related alteration in gut morphology night be due to the mitochondrial changes, oxidative stress, DNA damage and microbial damage in the intestinal ephithelium [10,12]. Most patients resided in urban areas (53.6%). The primary presenting complaints were abdominal pain, per rectal bleeding, and weight loss (Table 1). The prevalence of hypertension (67.9%), diabetes (44.6%), smoking (49.1%), obesity (29.5%), dyslipidemia

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(24.1%), and anemia (89.3%) among the patients is consistent with comorbidity patterns observed in other studies on colorectal cancer. These comorbidities can complicate treatment and affect prognosis, emphasizing the need for comprehensive management strategies [13]. For instance, the study by Yancik R et al., in 1998 highlights that comorbid conditions like hypertension and heart problems significantly increase early mortality risks in colon carcinoma patients [14,15]. Our findings similarly underscore the high prevalence of comorbid conditions, which necessitates careful consideration during treatment planning. Several studies report the presence of these comorbidities among CRC patients [16-20]. Tumor grading in our study showed that the majority of patients had T2N1M0 (58.0%) or T2N0M0 (37.5%) tumors, which is comparable to other studies reporting early-stage colorectal cancer as the most common diagnosis at initial presentation [21]. Surgical interventions were diverse, with right hemicolectomy being the most frequent procedure (23.2%), followed by left hemicolectomy, sigmoidectomy, and transverse colectomy (each 11.6%). The distribution of surgical procedures reflects standard practice in colorectal cancer management and is supported by existing literature. The study by Vissers PA et al., in 2016 suggests that lifestyle factors and BMI significantly affect health-related quality of life (HRQoL) in colorectal cancer patients [22]. Obesity is reported to be a common risk factor and affects prognosis in colorectal cancer. Obese patients displayed more comorbidities, more pain after cancer surgery, worse coping, and more depression and perceived less social support than nonobese patients [23]. This finding is relevant to our study, as we observed a high prevalence of obesity (29.5%) and smoking (49.1%), which are critical lifestyle factors influencing patient outcomes. The study by Abualkhair WH et al., in 2020 further supports our findings by demonstrating a significant increase in colorectal cancer incidence from ages 49 to 50, correlating with the onset of average-risk screening [24]. This steep increase indicates a high prevalence of undetected preclinical cases, suggesting that earlier screening could benefit those under 50. Our patient demographics reflect a need for heightened awareness and potential earlier screening interventions to detect colorectal cancer at more treatable stages. The study found significant pre-operative and post-operative elevations in inflammatory markers, such as WBC, CRP, ESR, ferritin, and LDH. Raised WBC (59.8% pre-operative, 92.9% post-operative, $p < 0.001$) and CRP (87.5% pre-operative, 94.6% post-operative, $p = 0.03$) were particularly notable. These markers are associated with systemic inflammation and have been linked to poorer prognosis in colorectal cancer patients. Elevated inflammatory markers may indicate a more aggressive disease course and a higher likelihood of complications, reinforcing the importance of monitoring these parameters during patient management. The study by Yancik et al., in 1998 also emphasizes that comorbidity and inflammation increase the complexity of cancer management and affect survival duration, which is consistent with our findings [14, 22]. Longitudinal studies with extended follow-up periods are necessary to evaluate the long-term prognostic significance of raised inflammatory markers in colorectal cancer. Additionally, investigating the potential therapeutic benefits of targeting inflammation in colorectal cancer could provide valuable insights into improving patient outcomes. Studies should also consider including detailed assessments of lifestyle factors and their interactions with comorbidities and inflammatory markers to develop more comprehensive treatment strategies.

CONCLUSIONS

The study demonstrates that serum inflammatory markers, both pre-operative and post-operative, play a significant role in influencing the prognosis and outcomes of patients with colorectal carcinoma. Elevated levels of markers such as WBC, CRP, ESR, ferritin, and LDH, along with decreased serum albumin, were associated with adverse surgical outcomes including wound infections, pneumonia, sepsis, and prolonged hospital stays. The mortality rate was noted to be 3.6%. These findings underscore the importance of monitoring inflammatory and prognostic markers in managing colorectal carcinoma to predict and potentially mitigate complications, ultimately improving patient outcomes.

Authors Contribution

Conceptualization: AIM

Methodology: SR, HK, N., SHI

Formal analysis: AIM

Writing, review and editing: AIM, AMB,

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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REFERENCES

[1] Wong MC, Huang J, Lok V, Wang J, Fung F, Ding H *et al.* Differences in incidence and mortality trends of colorectal cancer worldwide based on sex, age, and anatomic location. Clinical Gastroenterology and Hepatology. 2021 May; 19(5): 955-66. doi: 10.1016/j.cgh.2020.02.026.

DOI: https://doi.org/10.54393/pjhs.v5i07.1760

[2] Hossain MS, Karuniawati H, Jairoun AA, Urbi Z, Ooi DJ, John A *et al*. Colorectal cancer: a review of carcinogenesis, global epidemiology, current challenges, risk factors, preventive and treatment strategies. Cancers. 2022 Mar; 14(7): 1732. doi: 10.3390/cancers14071732.

[3] Haas S, Mikkelsen AH, Kronborg CJ, Oggesen BT, Møller PF, Fassov J *et al*. Management of treatment-related sequelae following colorectal cancer. Colorectal Disease. 2023 Mar; 25(3): 458-88. doi: 10.1111/codi.16299.

[4] Abbass MA and Abbas MA. Preoperative workup, staging, and treatment planning of colorectal cancer. Digestive Disease Interventions. 2023 Mar; 7(01): 003-9. doi: 10.1055/s-0043-1760733.

[5] Hayman AV and Vasilevsky CA. Colorectal Cancer: Preoperative Evaluation and Staging. The ASCRS Textbook of Colon and Rectal Surgery. 2022: 429-50. doi: 10.1007/978-3-030-66049-9_24.

[6] Piotrowski I, Kulcenty K, Suchorska W. Interplay between inflammation and cancer. Reports of Practical Oncology and Radiotherapy. 2020 Apr; 25(3): 422-7. doi: 10.1016/j.rpor.2020.04.004.

[7] Amin MN, Siddiqui SA, Ibrahim M, Hakim ML, Ahammed MS, Kabir A *et al*. Inflammatory cytokines in the pathogenesis of cardiovascular disease and cancer. SAGE Open Medicine. 2020 Oct; 8: 2050312120965752. doi: 10.1177/2050312120965752.

[8] Agharokh L, Mamola K, Yu AG, Medina AL, Gurram B, Fuller J *et al*. Cachexia, chorea, and pain in chronic nonbacterial osteitis and inflammatory bowel disease: a case report. Journal of Medical Case Reports. 2023 May; 17(1): 237. doi: 10.1186/s13256-023-03894-1.

[9] Sadiq IZ, Usman A, Muhammad A, Ahmad KH. Sample size calculation in biomedical, clinical and biological sciences research. Journal of Umm Al-Qura University for Applied Sciences. 2024 Jun: 1-9. doi: 10.1007/s43994-024-00153-x.

[10] Schneider AM, Özsoy M, Zimmermann FA, Feichtinger RG, Mayr JA, Kofler B, Sperl W, Weghuber D, Mörwald K. Age-Related Deterioration of Mitochondrial Function in the Intestine. Oxidative Medicine and Cellular Longevity. 2020;2020(1):4898217. https://doi.org/10.1155/2020/4898217

[11] Wang Z, Gong C, Zhang Y, Wang M, Chao C, Qian Y *et al*. Clinical Features, Treatment Modalities, and Outcomes of Elderly Thymoma Patients: A Propensity-Matched Study Based on the SEER Database. Oncology Research and Treatment. 2023 Dec; 46(12): 522-32. doi: 10.1159/000535020.

[12] Walrath T, Dyamenahalli KU, Hulsebus HJ, McCullough RL, Idrovo JP, Boe DM, McMahan RH, Kovacs EJ. Age-related changes in intestinal immunity and the microbiome. Journal of Leucocyte Biology. 2021 Jun;109(6):1045-61. https://doi.org/10.1002/JLB.3RI0620-405RR

[13] Hua H, Jiang Q, Sun P, Xu X. Risk factors for early-onset colorectal cancer: systematic review and meta-analysis. Frontiers in Oncology. 2023 May; 13: 1132306. doi: 10.3389/fonc.2023.1132306.

[14] Yancik R, Wesley MN, Ries LA, Havlik RJ, Long S, Edwards BK *et al*. Comorbidity and age as predictors of risk for early mortality of male and female colon carcinoma patients: a population-based study. Cancer: Interdisciplinary International Journal of the American Cancer Society. 1998 Jun; 82(11): 2123-34. doi: 10.1002/(SICI)1097-0142(19980601)82:11<2123::AID-CNCR6>3.0.CO;2-W.

[15] Chen H, Zheng X, Zong X, Li Z, Li N, Hur J, Fritz CD, Chapman Jr W, Nickel KB, Tipping A, Colditz GA. Metabolic syndrome, metabolic comorbid conditions and risk of early-onset colorectal cancer. Gut. 2021 Jun 1;70(6):1147-54. https://doi.org/10.1136/gutjnl-2020-321661

[16] Lee SF, Yip PL, Vellayappan BA, Chee CE, Wong LC, Wan EY *et al*. Incident Cardiovascular Diseases Among Survivors of High-Risk Stage II-III Colorectal Cancer: A Cluster-Wide Cohort Study. Journal of the National Comprehensive Cancer Network. 2022 Oct; 20(10): 1125-33. Doi: 10.6004/jnccn.2022.7042.

[17] Zhang X, Wong VW, Yip TC, Tse YK, Liang LY, Hui VW *et al*. Colonoscopy and risk of colorectal cancer in patients with nonalcoholic fatty liver disease: a retrospective territory-wide cohort study. Hepatology Communications. 2021 Jul; 5(7): 1212-23. doi: 10.1002/hep4.1705.

[18] Fowler H, Belot A, Ellis L, Maringe C, Luque-Fernandez MA, Njagi EN *et al*. Comorbidity prevalence among cancer patients: a population-based cohort study of four cancers. BioMed Central Cancer. 2020 Dec; 20: 1-5. doi: 10.1186/s12885-019-6472-9.

[19] Ottaiano A, Santorsola M, Circelli L, Perri F, Cascella M, Sabbatino F *et al*. Hypertension, type 2 diabetes, obesity, and p53 mutations negatively correlate with metastatic colorectal cancer patients' survival. Frontiers in Medicine. 2023 Jan; 10: 1091634. doi: 10.3389/fmed.2023.1091634.

[20] Gausman V, Dornblaser D, Anand S, Hayes RB, O'Connell K, Du M *et al*. Risk factors associated with early-onset colorectal cancer. Clinical Gastroenterology and Hepatology. 2020 Nov; 18(12): 2752-9. doi: 10.1016/j.cgh.2019.10.009.

DOI: https://doi.org/10.54393/pjhs.v5i07.1760

[21] Low EE, Demb J, Liu L, Earles A, Bustamante R, Williams CD *et al.* Risk factors for early-onset colorectal cancer. Gastroenterology. 2020 Aug; 159(2): 492-501. doi: 10.1053/j.gastro.2020.01.004.

[22] Vissers PA, Thong MS, Pouwer F, Creemers GJ, Slooter GD, van de Poll-Franse LV. Prospectively measured lifestyle factors and BMI explain differences in health-related quality of life between colorectal cancer patients with and without comorbid diabetes. Supportive Care in Cancer. 2016 Jun; 24: 2591-601. doi: 10.1007/s00520-015-3052-7.

[23] Gomez D, Jimenez-Fonseca P, Fernández AM, Castellanos PC, Arbizu MV, Cabañes RM, Estellés DL, Ferreira E, Del Rio J, García TG, Carmona-Bayonas A. Impact of obesity on quality of life, psychological distress, and coping on patients with colon cancer. The oncologist. 2021 May 1;26(5):e874-82. https://doi.org/10.1002/onco.13687

[24] Abualkhair WH, Zhou M, Ahnen D, Yu Q, Wu XC, Karlitz JJ. Trends in incidence of early-onset colorectal cancer in the United States among those approaching screening age. Journal of the American Medical Association Network Open. 2020 Jan; 3(1): e1920407-. doi: 10.1001/jamanetworkopen.2019.20407.