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Diagnostic and Therapeutic Insights into Colorectal Carcinoma

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Abstract

This review focuses on colorectal cancer (CRC), which ranks as the third most common cancer and the fourth leading cause of cancer-related mortality worldwide. Despite its prevalence in older adults, only 1% to 4% of cases are reported among individuals aged 25 to 30 years. Risk factors for CRC include a family history of colorectal cancer, dietary habits, alcohol use, smoking, and inflammatory bowel disease. A thorough literature search was conducted across databases such as Medline, PubMed, Embase, NCBI, and Cochrane to identify relevant studies, particularly those involving patients with non-alcoholic fatty liver disease. This review evaluates the incidence, causes, and current treatment strategies for CRC. While rare in children, adolescents, and young adults, the symptoms often mirror those seen in older patients—leading to delays in diagnosis. The research highlights that surgery remains the primary treatment option, and curative outcomes are uncommon in patients who are not eligible for surgical intervention.

Keywords: Colorectal cancer, Pediatrics, Young adults, Treatment guidelines, Inflammatory bowel disease, Polyps

Introduction

Colorectal carcinoma originates in the colon, whereas rectal cancer begins in the rectum—together, they are referred to as colorectal cancer (CRC) [1, 2]. Most colorectal cancers develop gradually from adenomatous (precancerous) polyps, which can transform into malignancies due to genetic mutations or cellular abnormalities over time [3]. Key risk factors include a family history of colorectal cancer, dietary habits, alcohol intake, smoking, and inflammatory bowel disease [3].

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Although CRC predominantly affects older adults, only about 1% to 4% of cases are diagnosed in individuals aged 25 to 30 years. Its symptoms in younger patients are often misattributed to less serious conditions, leading to delayed diagnosis. Due to its rarity in young populations, many pediatricians may encounter only one case, if any, throughout their careers [4].

Despite this, CRC remains the third most common cancer and the fourth leading cause of cancer-related death globally. The majority of cases occur in Western countries, where incidence rates continue to rise. An estimated 4% to 5% of the general population will develop colorectal cancer, with risk heightened by age, chronic illnesses, and lifestyle choices [5]. The disease results from mutations affecting oncogenes, tumor suppressor genes, and genes that regulate DNA repair.

Colorectal cancer can be categorized into three types based on mutation origin: sporadic (about 70%), familial (around 25%), and hereditary (approximately 5%). Its development follows one of three main molecular

pathways—chromosomal instability (CIN), microsatellite instability (MSI), or the CpG island methylator phenotype (CIMP) [5]. For example, in 2010, CRC affected approximately 142,000 people in the United States and led to 51,000 deaths [6]. However, fewer than 100 cases are diagnosed each year in children, adolescents, and young adults.

CRC is more prevalent in high-income countries, likely due to a combination of genetic, lifestyle, dietary, and environmental factors. Obesity, tobacco use, alcohol consumption, high-calorie diets, excessive red meat intake, and sedentary behavior have all been associated with increased CRC risk [7, 8]. These lifestyle patterns may help explain the higher prevalence of the disease in developed versus developing nations [9].

Although most adult CRC cases are sporadic, up to 30% may have a hereditary component, with around 5% involving well-defined genetic syndromes. Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer, accounts for 3% to 5% of all cases and is the most common hereditary form [10].

This review focuses on colorectal cancer (CRC), which ranks as the third most common cancer and the fourth leading cause of cancer-related mortality worldwide.

Materials and Methods

The PubMed database was utilized to select relevant articles using the following MeSH terms: ("Colorectal Carcinoma" [Mesh]) AND ("signs and symptoms" [Mesh]) OR ("Management" [Mesh]).

Inclusion criteria focused on studies that addressed key aspects of colorectal carcinoma, particularly its clinical features and management. Articles not centered on these topics were excluded.

From a pool of 1,202 indexed articles published over the past 20 years, approximately 90 publications were identified as most clinically significant. After a detailed review, 31 studies were selected for inclusion. Additional relevant resources were sourced from the reference lists of selected articles. Where applicable, expert consensus statements and commentaries were also incorporated to provide practical guidance for clinicians managing CRC.

Results and Discussion

Epidemiology

Colorectal cancer (CRC) is among the most common cancers globally, with 1 to 2 million new cases diagnosed annually. It is also the fourth leading cause of cancer-related mortality, responsible for around 700,000 deaths per year—trailing only lung, liver, and stomach cancers.

CRC is the second most common cancer in women (accounting for 9.2% of cases) and the third most common in men (10%) [11]. Between 1990 and 2012, annual CRC cases increased by more than 200,000. Although 55% of CRC cases occur in Western countries, the incidence is rising in developing nations due to socioeconomic and lifestyle shifts [12].

Improvements in healthcare access and the implementation of screening programs have reduced the proportion of global CRC deaths in Western countries to 33% as of 2010. Still, in 2016 alone, 134,490 new cases and 49,190 deaths were projected in the United States, reflecting ongoing public health concerns [12].

Risk factors

Globally, around 4%–5% of the population will develop colorectal cancer during their lifetime. Multiple non-modifiable and modifiable risk factors contribute to the development of CRC.

- Age remains the most significant risk factor, with CRC incidence rising markedly after age 50. Cases are rare before this age unless there is a hereditary predisposition [13].
- Inflammatory bowel diseases (IBD) like ulcerative colitis and Crohn's disease also elevate CRC risk—by 3.7% and 2.5%, respectively [14, 15]. Chronic inflammation in these conditions often leads to dysplasia, a precancerous change in cell structure that increases the likelihood of malignancy.
- Family history is another important factor. Individuals with first-degree relatives diagnosed with CRC, especially those under the age of 50 years, face a higher risk due to possible genetic mutations or shared environmental exposures [16].

Modifiable risk factors primarily relate to lifestyle choices.

- Sedentary behavior is associated with increased CRC risk, though the exact mechanism is unclear. However, regular physical activity is known to enhance metabolism, stimulate bowel movement, and reduce blood pressure—all of which contribute to a lower risk of cancer development [17].

• Alcohol and tobacco use also play a significant role. Ethanol's main metabolite, acetaldehyde, is a known carcinogen, especially in individuals with certain enzyme polymorphisms that affect alcohol metabolism [18]. Still, the exact relationship between alcohol and CRC remains under investigation.

Signs and symptoms

Colorectal tumors can sometimes develop silently, without causing any obvious symptoms. This makes routine screening tests crucial for early detection. Among the various screening tools available, colonoscopy is considered the most effective. Other methods include fecal occult blood tests, fecal DNA tests, flexible sigmoidoscopy, barium enemas, and CT colonography, also known as virtual colonoscopy. The decision on when to start screening and how often to repeat it depends on individual risk factors, particularly a family history of colorectal cancer [19-21].

Some of the more common signs of colorectal cancer include changes in bowel habits, such as constipation, diarrhea, or narrowing of the stool. These symptoms are often attributed to less serious conditions, but they can also be early indicators of colorectal cancer. The presence of blood on or in the stool is another significant warning sign. However, gastrointestinal bleeding can also be caused by hemorrhoids, anal fissures, ulcerative colitis, or Crohn's disease. In some cases, stool may appear discolored due to iron supplements or certain foods like beets, which can give a false impression of bleeding [18-22].

Unexplained anemia may also occur, as it involves a reduction in red blood cells that transport oxygen throughout the body. This can lead to symptoms like fatigue and shortness of breath that don't improve with rest. Abdominal or pelvic pain, unexplained weight loss, and vomiting are additional symptoms that may be observed.

Diagnosis

A definitive diagnosis of colorectal cancer requires the histopathological examination of tissue samples. The selection of the appropriate method for obtaining tissue should be made in consultation with surgical specialists and based on the patient's clinical condition. Since surgery plays a central role in successful treatment, this should be factored into the decision-making process for diagnostic procedures.

Patients suspected of having colorectal cancer should undergo a thorough diagnostic evaluation that includes chest X-rays, CT scans of the chest, abdomen, and pelvis, and sometimes bone scans. In some instances, a barium enema may be performed before the diagnosis is confirmed, as it can help detect problematic areas within the colon [19-23].

The use of fluorodeoxyglucose positron emission tomography (FDG-PET) scans in diagnosing colorectal cancer is still under evaluation. These scans appear to be less effective in detecting tumors with mucinous histology, which tend to be more common in children. Therefore, FDG-PET may not be as useful in pediatric cases.

Other diagnostic steps often include a full colonoscopy to check for additional lesions or polyps, a blood chemistry panel including liver enzyme tests, and a carcinoembryonic antigen (CEA) test. While CEA levels are frequently used to monitor disease progression or recurrence in adults, they are generally less useful in children [20-24].

Treatment

Treatment recommendations for children and adolescents with colorectal cancer (CRC) are largely based on clinical experience with adult patients. Among the available options, surgery remains the cornerstone of therapy and must be radical to achieve a potential cure. Complete surgical removal is essential, and in some cases, surgery may also be curative if liver or lung metastases can be resected. To prevent local recurrence at the site of anastomosis, surgeons must ensure resection margins of at least 5 cm of healthy bowel. Furthermore, accurate staging requires examination of a minimum of 12 negative lymph nodes. A thorough inspection of the peritoneal surface, including the renal fascia and diaphragm, is also necessary. Resection should include all peritoneal lymph nodes. If the initial surgery is deemed inadequate from an oncological perspective, a second exploratory surgery is recommended to reassess surgical margins and perform the required lymph node evaluation. It is also important to note that CRC is rarely considered an initial diagnosis in pediatric patients, which may delay treatment [18-21].

Adjuvant chemotherapy decisions depend on the stage of the disease at diagnosis, with guidelines typically

following adult protocols. For patients with early-stage disease, surgery alone may lead to a five-year survival rate of up to 90%, and additional treatment may not be necessary. In stage II cases, the benefit of chemotherapy is uncertain, with overall survival improving by no more than 5%. However, in pediatric patients, where stage II disease often carries poor prognostic features, chemotherapy should be considered. Chemotherapy is more clearly beneficial in stage III and IV disease, where there is lymph node involvement or distant metastasis [19-22].

Targeted therapies have also been explored, particularly in advanced-stage disease (stages III and IV). Drugs such as bevacizumab, pembrolizumab, cetuximab, panitumumab, bortezomib, and gefitinib have shown potential in selected patients. Their use is primarily reserved for those with more aggressive or refractory diseases.

Radiotherapy has a limited role in CRC treatment and is mainly applied in rectal cancer cases. It is typically used in combination with chemotherapy, especially 5-fluorouracil (5-FU), after surgery. In more advanced or complicated presentations, such as stage T4 tumors or cases involving perforation or obstruction, preoperative radiotherapy may be considered. This approach can reduce the likelihood of recurrence and make surgery more feasible or less invasive [20-24].

Conclusion

Colorectal cancer is rare in children, adolescents, and young adults, and its initial signs and symptoms are similar to those seen in older individuals. However, due to its infrequency in younger populations, CRC is often not considered during the early stages of clinical evaluation. Pediatric oncologists typically have limited experience with this malignancy, and clinical trials specifically targeting this age group are scarce. Most pediatric cases are diagnosed at an advanced stage and often present with histologic subtypes such as mucinous or signet-ring cell carcinomas—forms that occur in only about 5% to 15% of adult cases. Therefore, treatment protocols established for adults must be thoughtfully adapted to meet the needs of younger patients.

Surgery remains the most vital component of treatment. Unfortunately, patients who cannot undergo complete surgical resection have a low likelihood of being cured. As treatment strategies for adult CRC continue to evolve rapidly, it is essential to involve medical oncologists experienced in managing adult cases of CRC when planning the care of young patients.

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References

1. Bodnar P, Bodnar Y, Bodnar T, Soroka Y, Liudmyla B. Histological Changes in Muscles During the Lower Extremities Thrombosis in Individuals with Gastrointestinal Tract Cancer. Int J Pharm Res Allied Sci. 2021;10(3):15-9.
2. Abubaker SA, Abdelwadoud ME, Ali MM, Ahmad HA, Khlafalla AM, Elmahi OM, et al. Immunohistochemical Expression of Oestrogen and Epidermal Growth Factor Receptors in Endometrial Cancerous in Sudanese Patients. J Biochem Technol. 2021;12(1):58-62.
3. Colorectal Cancer Alliance. What colorectal cancer is, and where it starts. 2020. Available from: https://www.ccalliance.org/colorectal- cancer-information/what-is-colorectal-cancer
4. Kaplan MA, Isikdogan A, Gumus M, Arslan UY, Geredeli C, Ozdemir N, et al. Childhood, adolescents, and young adults (≤25 y) colorectal cancer: study of Anatolian Society of Medical Oncology. J Pediatr Hematol Oncol. 2013;35(2):83-9.
5. American Cancer Society. Cancer Facts and Figures 2010. Atlanta, GA: American Cancer Society. 2011.
6. Donohoe CL, Pidgeon GP, Lysaght J, Reynolds JV. Obesity and gastrointestinal cancer. Br J Surg. 2010;97(5):628-42.
7. Libutti SK, Saltz LB, Rustgi AK. Cancer of the colon. In: DeVita VT, Hellman S, Rosenberg SA, eds. Cancer Principles & Practice of Oncology. Vol 7th. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:1061-109.
8. Pappo AS, Rodriguez-Galindo C, Furman WL. Management of infrequent cancers of childhood. In: Pizzo PA, Poplack DG, eds. Principles and Practice of Pediatric Oncology. Vol 6th. Philadelphia, PA: Lippincott Williams & Wilkins; 2011:1098-123.

9. Grady WM. Genetic testing for high-risk colon cancer patients. Gastroenterology. 2003;124(6):1574-94.
10. Stewart Bernard W, Wild Christopher P. World Cancer Report 2014. Lyon: International Agency for Research on Cancer. World Health Organization. 2014.
11. Brody H. Colorectal cancer. Nature. 2015;521:S1. doi:10.1038/521S1a. 2015.
12. Levin B, Lieberman DA, McFarland B, Smith RA, Brooks D, Andrews KS, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. CA Cancer J Clin. 2008;58(3):130-60.
13. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut. 2001;48(4):526-35.
14. Canavan C, Abrams KR, Mayberry J. Meta-analysis: colorectal and small bowel cancer risk in patients with Crohn's disease. Aliment Pharmacol Ther. 2006;23(8):1097-104.
15. Johns LE, Houlston RS. A systematic review and meta-analysis of familial colorectal cancer risk. Am J Gastroenterol. 2001;96(10):2992- 3003.
16. Robertson DJ. ABC of colorectal cancer. Gastroenterology. 2012;143(3):868-9.
17. Pöschl G, Seitz HK. Alcohol and cancer. Alcohol Alcohol. 2004;39(3):155-65.
18. John SK, George S, Primrose JN, Fozard JB. Symptoms and signs in patients with colorectal cancer. Colorectal Dis. 2011;13(1):17-25.
19. Berger KL, Nicholson SA, Dehdashti F, Siegel BA. FDG PET evaluation of mucinous neoplasms: correlation of FDG uptake with histopathologic features. AJR Am J Roentgenol. 2000;174(4):1005-8.
20. Goldstein MJ, Mitchell EP. Carcinoembryonic antigen in the staging and follow-up of patients with colorectal cancer. Cancer Invest. 2005;23(4):338-51.
21. Indini A, Bisogno G, Cecchetto G, Vitellaro M, Signoroni S, Massimino M, et al. Gastrointestinal tract carcinoma in pediatric and adolescent age: The Italian TREP project experience. Pediatr Blood Cancer. 2017;64(12):1-8.
22. Goldberg J, Furman W. Management of colorectal carcinoma in children and young adults. J Pediatr Hematol Oncol. 2012; 34(Suppl 2):S76-9.
23. Negri FV, Wotherspoon A, Cunningham D, Norman AR, Chong G, Ross PJ. Mucinous histology predicts for reduced fluorouracil responsiveness and survival in advanced colorectal cancer. Ann Oncol. 2005;16(8):1305-10.
24. Cunningham D, Atkin W, Lenz HJ, Lynch HT, Minsky B, Nordlinger B, et al. Colorectal cancer. Lancet. 2010;375(9719):1030-47.