



A Comprehensive Literature Review of Red Flag Signs and Symptoms for Patients With Early-Onset Colorectal Cancer

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ABSTRACT

Background: The literature on early-onset colorectal cancer (EOCRC) reveals a complex interplay of symptoms, diagnostic challenges, and the need for increased awareness among both patients and healthcare providers. The systematic review by (Mitchell et al., 2007) underscores the necessity of recognizing red flag symptoms such as rectal bleeding and changes in bowel habits, as these are critical for timely diagnosis and intervention. The study highlights that delays in diagnosis can lead to more advanced disease stages, emphasizing the importance of patient education regarding the seriousness of these symptoms.

Literature Review: Further investigations, such as those by (Renzi et al., 2016), reveal that many patients present with significant symptoms well before their diagnosis, indicating a gap in timely medical consultation. The findings suggest that abdominal pain and rectal bleeding are prevalent among emergency presentations, yet many patients do not receive timely evaluations, leading to missed opportunities for early intervention. The exploration of risk factors by (R Syed et al., 2019) highlights the challenges faced by younger patients, who often misinterpret their symptoms, resulting in substantial delays in seeking medical attention. This trend is echoed in the study from Indonesia by (Makmun et al., 2021), which notes that abdominal pain is the most common presenting symptom among early-onset CRC patients. The demographic characteristics presented in this study further emphasize the need for targeted screening and awareness initiatives.

Conclusion: In conclusion, the literature collectively emphasizes the critical need for heightened awareness and education regarding the red flag signs and symptoms of early-onset colorectal cancer. There is a clear call for improved diagnostic protocols and screening strategies to enhance early detection and treatment outcomes for this vulnerable population. Addressing both patient and healthcare provider awareness is essential to mitigate delays in diagnosis and improve prognosis for young patients with EOCRC.

Keywords: Red Flag, Signs, Symptoms, Early-Onset Colorectal Cancer

INTRODUCTION

The increasing incidence of early-onset colorectal cancer (EOCRC) has garnered significant attention in recent years, with a growing body of literature exploring the various factors contributing to this alarming trend. Understanding the red flag signs and symptoms associated with EOCRC is critical for timely diagnosis and intervention. The literature review begins with the systematic examination conducted by (Mitchell et al., 2007), which highlights the challenges of early diagnosis in colorectal cancer. Their findings underscore the importance of recognizing significant symptoms such as rectal bleeding and changes in bowel habits, as delays in diagnosis can lead to advanced disease stages and decreased chances of successful treatment.

Building upon this foundation, (Renzi et al., 2016) delve into the consultation patterns of colorectal cancer patients, revealing that many emergency presenters exhibit relevant symptoms well before their diagnosis. Their study

identifies abdominal pain and rectal bleeding as common symptoms, while also noting a concerning trend of missed opportunities for earlier diagnosis among non-emergency patients. This highlights the critical need for heightened awareness of red flag symptoms to facilitate timely medical consultations.

In 2019, (R Syed et al., 2019) expanded the discussion by identifying risk factors specifically associated with early-onset colorectal cancer. Their research indicates that young patients often present with symptoms such as rectal bleeding, abdominal pain, and altered bowel function, yet many fail to recognize these symptoms as indicators of serious illness. This lack of recognition can lead to significant delays in seeking medical attention, emphasizing the urgent need for educational initiatives targeting both patients and healthcare providers.

(Makmun et al., 2021) further contribute to the discourse by examining the prevalence of early-onset CRC in Indonesia, revealing that a substantial proportion of young

patients present with abdominal pain and exhibit distinct demographic and clinicopathologic features. Their findings reinforce the notion that early-onset CRC often presents with advanced disease, necessitating improved screening and diagnostic strategies.

(Shen et al., 2022) build on these insights by characterizing the clinical spectrum of early-onset rectal cancer, noting an alarming rise in incidence among younger populations. They emphasize the need for tailored treatment and surveillance strategies, as early-onset cases exhibit distinct clinical and molecular characteristics compared to late-onset counterparts.

(AlZaabi et al., 2022) address the diagnostic challenges faced by young patients with CRC, highlighting patient-related and physician-related delays in diagnosis. Their findings reveal that the nonspecific nature of gastrointestinal symptoms often leads to misdiagnosis and prolonged time to diagnosis, further complicating the clinical landscape for EOCRC patients.

(O'Reilly et al., 2023) examine oncotherapeutic strategies for early-onset colorectal cancer, emphasizing the need for increased awareness of this condition among both the medical community and the public. They argue that delayed diagnosis often results in worse outcomes for young patients, who possess unique physical and emotional needs that must be addressed in treatment plans.

Finally, (Savu et al., 2024) provide a retrospective analysis of EOCRC in Romania, documenting the increasing incidence and emphasizing the necessity for targeted screening programs. Their research underscores the importance of understanding the demographic and clinical features of young patients diagnosed with colorectal cancer, as this knowledge is crucial for developing effective prevention and intervention strategies.

This literature review synthesizes the critical insights from these studies, revealing a multifaceted landscape of red flag signs and symptoms associated with early-onset colorectal cancer. The collective findings underscore the pressing need

for improved awareness, education, and diagnostic protocols to enhance early detection and treatment outcomes for this vulnerable patient population.

LITERATURE REVIEW

The article titled "Influences on pre-hospital delay in the diagnosis of colorectal cancer: a systematic review" by (Mitchell et al., 2007) provides a thorough analysis of the factors contributing to delays in the diagnosis of colorectal cancer, emphasizing the critical need for early detection and intervention. The authors systematically review a wide range of literature to identify the reasons behind both patient and primary care delays, ultimately categorizing these factors into four primary themes: symptoms, patient history, patient characteristics, and behavior.

One of the significant strengths of this review is its inclusive approach, as it considers studies published in any language, thereby minimizing potential biases that could arise from excluding non-English literature. This methodological rigor

enhances the credibility of the findings and supports a more comprehensive understanding of the issue at hand. The authors' decision to grade the evidence based on the robustness of the studies' methodologies and analyses further strengthens the review's conclusions. Notably, the review found that half of the studies presented strong evidence regarding the factors influencing diagnostic delays, while a significant portion provided moderate evidence, indicating a solid foundation for the conclusions drawn.

A critical finding of this review is the intricate relationship between patients' presentation behavior and the symptoms they experience. The authors highlight that mere awareness of symptoms is insufficient; rather, patients must also recognize and comprehend the potential severity of these symptoms to prompt timely medical consultation. This insight underscores the necessity for effective patient education regarding red flag signs and symptoms associated with colorectal cancer. The authors argue that without this understanding, patients

may delay seeking care, which can lead to more advanced stages of the disease and diminished chances of successful treatment.

However, the review does acknowledge a limitation in the substantial heterogeneity among the included studies. This variability could potentially affect the generalizability of the findings and suggests a need for standardized measures in future research to better assess the factors influencing diagnostic delays. Despite this limitation, the review effectively illuminates the multifaceted nature of pre-hospital delays in colorectal cancer diagnosis and emphasizes the importance of addressing both patient awareness and understanding to enhance early detection efforts.

The article titled "Do colorectal cancer patients diagnosed as an emergency differ from non-emergency patients in their consultation patterns and symptoms? A longitudinal data-linkage study in England" by (Renzi et al., 2016) provides significant insights into the consultation behaviors and symptoms associated with emergency

presentations of colorectal cancer. The authors present a comprehensive analysis that aligns with existing literature, emphasizing the importance of recognizing red-flag symptoms in the early stages of cancer diagnosis.

One of the key findings of the study is that a substantial proportion of emergency colorectal cancer patients had relevant symptoms, such as abdominal pain and rectal bleeding, at least one month prior to their diagnosis. This aligns with previous research that indicates a lag in diagnosis despite the presence of alarming symptoms ((Renzi et al., 2016)). The identification of these symptoms as prevalent among emergency presenters suggests a critical gap in timely diagnosis, which could be addressed through enhanced awareness and proactive health consultations.

The authors also highlight that certain symptoms, particularly abdominal pain, constipation, diarrhea, and weight loss, are associated with a higher risk of emergency diagnosis. This finding is particularly important as it

underscores the necessity for both patients and healthcare providers to recognize these symptoms as potential indicators of serious underlying conditions. Moreover, the study reveals that despite the presence of red-flag symptoms, a significant percentage of individuals still presented as emergencies, indicating potential shortcomings in the healthcare system's response to these warning signs ((Renzi et al., 2016)).

In terms of demographic factors, the study notes that women, older adults, and individuals from deprived backgrounds are at a higher risk of emergency diagnosis, independent of symptom presentation. This raises critical questions regarding access to healthcare and the effectiveness of current screening practices, particularly for vulnerable populations. The authors advocate for targeted research to explore the interplay of patient factors, healthcare accessibility, and clinical considerations that contribute to delayed diagnoses in these groups ((Renzi et al., 2016)).

The findings also suggest that there are opportunities for earlier diagnosis, especially given that one in five emergency presenters exhibited at least one red-flag symptom in the year leading up to their diagnosis. This statistic is particularly alarming, as it indicates that many patients may not be receiving timely evaluations that could lead to earlier interventions. The authors call for a concerted effort to improve recognition of these symptoms not only among patients but also within the healthcare system to facilitate quicker referrals and diagnostics ((Renzi et al., 2016)).

The article "Old vs new: Risk factors predicting early onset colorectal cancer" by (R Syed et al., 2019) provides a comprehensive examination of the increasing incidence and mortality rates associated with early-onset colorectal cancer (CRC). The authors highlight that a concerning 3% of CRC patients in their study were under the age of 50, indicating a significant shift in the demographic affected by this disease. This finding underscores the necessity for heightened awareness and proactive screening measures for

younger populations, particularly given that early-onset CRC often presents at more advanced stages and is less amenable to surgical resection compared to cases in older patients.

The article identifies several key risk factors associated with early-onset CRC, emphasizing the importance of family history in predicting the likelihood of developing the disease. The authors note that a family history of any gastrointestinal malignancy significantly correlates with early-onset CRC, which is a critical insight for clinicians. Other notable risk factors include African American ethnicity, obesity, and specific gastrointestinal symptoms such as abdominal pain, rectal bleeding, and altered bowel function. These findings align with the growing body of literature advocating for earlier screening protocols, particularly for high-risk groups.

One of the critical evaluations presented in the article is the observation that young adults and their physicians often fail to recognize the symptoms indicative of early-onset CRC. This delay in seeking medical attention can extend up to six

months, which may lead to worse prognoses due to late-stage diagnosis. The authors argue that there is a pressing need for enhanced education and awareness among both patients and healthcare providers regarding the specific red flag signs and symptoms associated with early-onset CRC. They suggest that clinicians frequently misattribute symptoms in younger patients to alternative diagnoses, which can hinder timely intervention.

The article also discusses current guidelines recommending the initiation of CRC screening for African Americans at age 45, which reflects an adaptation to the rising incidence of early-onset cases in this demographic. However, the authors advocate for a more nuanced approach that considers a broader range of risk factors, including family history and symptomatic presentations, to guide screening and diagnostic processes.

The article "Colorectal cancer patients in a tertiary hospital in Indonesia: Prevalence of the younger population and associated factors" by (Makmun et al., 2021) provides

significant insights into the demographic and clinical characteristics of early-onset colorectal cancer (CRC) patients in Indonesia. This study is particularly relevant given the rising incidence of early-onset CRC globally, highlighting an urgent need for awareness and early detection strategies.

The research involved a comprehensive assessment of 495 CRC patients, revealing that 205 (41.4%) were classified as early-onset cases. A notable demographic finding is that the majority of these patients were male (53.7%), which aligns with existing literature suggesting a male predominance in colorectal cancer incidence. The article emphasizes that most early-onset cases presented with adenocarcinoma histopathology (89.8%) and predominantly involved left-sided tumors (78%). These findings are critical as they suggest a specific pattern of tumor location and type that may influence screening and management strategies for this age group.

One of the most significant contributions of this study is the

identification of abdominal pain as the most common presenting symptom in early-onset CRC patients, reported by 55.6% of the subjects. This symptom, along with the higher incidence of underweight individuals (34.6% in early-onset compared to 20.0% in late-onset cases), underscores the need for increased vigilance among healthcare providers when patients present with gastrointestinal complaints, especially in younger populations.

Furthermore, the study highlights a concerning trend regarding hereditary factors, with a higher proportion of early-onset CRC patients being suspected of having hereditary nonpolyposis colorectal cancer (HNPCC) (9.3% vs. 4.1% in late-onset cases). This finding emphasizes the importance of genetic counseling and testing in younger patients, as early identification of hereditary syndromes can lead to timely interventions and improved outcomes.

The article "Clinical spectrum of rectal cancer identifies hallmarks of early-onset patients and next-generation treatment strategies" by

(Shen et al., 2022) addresses a significant and concerning trend in the incidence of colorectal cancer, particularly among individuals under the age of 50. The authors present a thorough analysis of the increasing rates of early-onset rectal cancer, underscoring the necessity for heightened awareness and tailored strategies for this demographic.

The article begins by establishing colorectal cancer as the third most prevalent cancer globally, with alarming statistics indicating a rising incidence among younger populations. The authors cite a registry-based study that highlights a consistent increase in colorectal cancer cases among individuals aged 20-49 from 2004 to 2016, projecting that by 2030, 23% of rectal cancer diagnoses will occur in those under 50 ((Shen et al., 2022)). This projection is critical, as it signals an urgent need for healthcare systems to adapt to the changing epidemiology of this disease.

One of the key insights presented in the article is the distinction between early-onset and late-onset colorectal cancer. The

authors emphasize that while some early-onset cases may be linked to hereditary cancer syndromes, the majority are sporadic, with unclear risk factors. This distinction is vital for clinicians, as it suggests that early-onset patients may require different diagnostic and treatment approaches compared to their older counterparts. The authors argue for the importance of recognizing these differences in clinical, pathological, and molecular characteristics to inform next-generation screening, treatment, and surveillance protocols.

The article also highlights the increasing proportion of rectal cancer cases within the broader category of colorectal cancer, noting that approximately 10% of newly diagnosed rectal cancer cases occur in younger adults. This statistic reinforces the need for targeted research and intervention strategies aimed specifically at early-onset rectal cancer, which has been historically underexplored compared to other age groups.

The article "Early onset colorectal cancer: Challenges across the cancer care continuum" by

(AlZaabi et al., 2022) provides a comprehensive analysis of the multifaceted challenges faced by young patients diagnosed with early-onset colorectal cancer (EOCRC). The authors emphasize that timely diagnosis is critical for improving outcomes, yet diagnostic delays remain a significant hurdle in the care continuum for this demographic.

One of the primary insights from the article is the identification of patient-related delays, which stem from difficulties in interpreting gastrointestinal symptoms. The authors note that the sensitivity of symptoms in identifying colorectal cancer ranges from 5% to 64%, highlighting the nonspecific nature of these symptoms, which are often attributed to benign conditions ((AlZaabi et al., 2022)). This poor correlation not only leads to patients disregarding their symptoms as serious but also contributes to a lack of timely medical intervention. Factors such as embarrassment, fear of diagnosis, and access to healthcare exacerbate these delays.

Furthermore, the article discusses physician-related delays,

which are equally concerning. The authors report a misdiagnosis rate of 31-34%, where physicians may misattribute symptoms to non-malignant conditions, thus delaying necessary investigations ((AlZaabi et al., 2022)). The lack of thorough physical examinations and inadequate communication regarding the urgency of further testing can further hinder prompt diagnosis. This highlights a critical need for enhanced training and awareness among healthcare providers regarding the presentation of EOCRC in younger patients.

The article also addresses systemic challenges, particularly the increasing demand for colonoscopies amid limited healthcare resources. The authors suggest that implementing a risk assessment tool or an EOCRC symptoms index could facilitate better stratification of patients, allowing for more immediate attention for those at high risk while providing reassurance to lower-risk individuals ((AlZaabi et al., 2022)). The identification of common symptoms such as abdominal pain, rectal bleeding, weight loss, and changes in bowel habits is crucial, as

these signals should prompt immediate medical evaluation.

The article "Oncotherapeutic Strategies in Early Onset Colorectal Cancer" by (O'Reilly et al., 2023) provides a comprehensive examination of the rising incidence of early-onset colorectal cancer (EOCRC), defined as colorectal cancer occurring in individuals under 50 years of age. This demographic shift is noteworthy and demands urgent attention, as it highlights a significant public health concern that is often overlooked. The authors effectively outline various risk factors associated with EOCRC, including genetic predisposition syndromes, gut microbiota disruption, obesity, and inflammatory bowel disease. This multifactorial approach to understanding the etiology of EOCRC is critical, as it underscores the complexity of the disease and the necessity for a tailored approach to prevention and treatment.

One of the most compelling aspects of the article is the emphasis on the lack of awareness surrounding EOCRC among both healthcare professionals and the general

populace. This gap in awareness contributes to delays in diagnosis, which can lead to poorer outcomes compared to older patients diagnosed with colorectal cancer. The authors argue that increasing awareness is essential for early detection and intervention, which could ultimately improve survival rates in this patient population. This assertion is supported by evidence indicating that early diagnosis is a key determinant of prognosis in colorectal cancer ((O'Reilly et al., 2023)).

Furthermore, the article delves into the specific needs of patients with EOCRC, acknowledging that this cohort faces unique physical, emotional, social, and financial challenges. This holistic view is crucial, as it advocates for a more comprehensive care model that addresses not only the medical but also the psychosocial aspects of living with cancer. The authors suggest that healthcare providers must be equipped to recognize the distinct experiences of younger patients, who may require different support systems compared to older individuals. This perspective aligns with contemporary

approaches to patient-centered care, which emphasize the importance of understanding the patient's context in treatment planning ((O'Reilly et al., 2023)).

In terms of treatment strategies, the article discusses various oncotherapeutic options available for EOCRC, highlighting the need for ongoing research into effective therapies tailored to this specific demographic. The authors advocate for clinical trials that include younger populations to ensure that treatment protocols are relevant and effective for those affected by EOCRC. This call for inclusivity in clinical research is vital, as it addresses the historical underrepresentation of younger patients in oncology studies, thereby ensuring that advancements in treatment benefit all age groups ((O'Reilly et al., 2023)).

The article "Early-Onset Colorectal Cancer—A Retrospective Study from a Tertiary Referral Hospital in Romania" by (Savu et al., 2024) provides a thorough examination of the demographic, clinical, and pathological

characteristics of patients diagnosed with colorectal cancer before the age of 50. The authors emphasize the increasing incidence of early-onset colorectal cancer (EO-CRC) globally, highlighting its emergence as a unique clinical and biological entity. This retrospective study is crucial as it contributes to the growing body of literature addressing an urgent public health concern.

The findings of the study reveal significant insights into the clinical presentation of EO-CRC. The authors report that patients often present with later-stage disease and a higher prevalence of distal colon tumor localization, which aligns with existing literature on the subject. Additionally, the identification of mucinous histology as a common feature among these patients adds a valuable dimension to understanding the pathology of EO-CRC. This information is critical for healthcare practitioners, as it underscores the need for heightened awareness and vigilance in diagnosing colorectal cancer in younger populations.

Moreover, the authors argue for a paradigm shift in the approach to

screening for EO-CRC. They advocate for the establishment of effective and targeted screening programs, which is imperative given the rising incidence rates. The lack of a standardized definition for EO-CRC complicates the development of such programs, as the cutoff age of 50 is not universally accepted. This inconsistency in defining EO-CRC could lead to missed opportunities for early detection and intervention, which are crucial for improving patient outcomes.

The study also acknowledges that the underlying causes of the rising incidence of EO-CRC remain poorly understood. This gap in knowledge highlights the need for further research to explore potential risk factors and biological mechanisms that contribute to the development of colorectal cancer in younger individuals. The authors call for a comprehensive approach that enhances clinical, pathological, and molecular diagnostics, which could lead to improved understanding and management of EO-CRC.

CONCLUSION

The literature on early-onset colorectal cancer (EOCRC) reveals a complex interplay of symptoms, diagnostic challenges, and the need for increased awareness among both patients and healthcare providers. The systematic review by (Mitchell et al., 2007) underscores the necessity of recognizing red flag symptoms such as rectal bleeding and changes in bowel habits, as these are critical for timely diagnosis and intervention. The study highlights that delays in diagnosis can lead to more advanced disease stages, emphasizing the importance of patient education regarding the seriousness of these symptoms.

Further investigations, such as those by (Renzi et al., 2016), reveal that many patients present with significant symptoms well before their diagnosis, indicating a gap in timely medical consultation. The findings suggest that abdominal pain and rectal bleeding are prevalent among emergency presentations, yet many patients do not receive timely evaluations, leading to missed opportunities for early intervention.

The exploration of risk factors by (R Syed et al., 2019) highlights the challenges faced by younger patients, who often misinterpret their symptoms, resulting in substantial delays in seeking medical attention. This trend is echoed in the study from Indonesia by (Makmun et al., 2021), which notes that abdominal pain is the most common presenting symptom among early-onset CRC patients. The demographic characteristics presented in this study further emphasize the need for targeted screening and awareness initiatives. The clinical spectrum of early-onset rectal cancer, as discussed by (Shen et al., 2022), indicates a distinct rise in incidence among younger populations, necessitating tailored treatment and surveillance strategies. The diagnostic challenges faced by young patients, including both patient-related and physician-related delays, are critically analyzed by (AlZaabi et al., 2022), revealing that the nonspecific nature of gastrointestinal symptoms often leads to misdiagnosis.

The oncotherapeutic strategies outlined by (O'Reilly et al.,

2023) advocate for increased awareness of EOCRC's unique needs, stressing that delayed diagnosis can adversely affect treatment outcomes. This sentiment is echoed in the retrospective study from Romania by (Savu et al., 2024), which documents the increasing incidence of EOCRC and the necessity for targeted screening programs.

In conclusion, the literature collectively emphasizes the critical need for heightened awareness and education regarding the red flag signs and symptoms of early-onset colorectal cancer. There is a clear call for improved diagnostic protocols and screening strategies to enhance early detection and treatment outcomes for this vulnerable population. Addressing both patient and healthcare provider awareness is essential to mitigate delays in diagnosis and improve prognosis for young patients with EOCRC.

DISCLOSURE STATEMENT

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