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Long-Term Survival Outcomes of Colorectal Cancer Survivors: An In-Depth Exploration

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ABSTRACT

The survival rate for colorectal cancer has seen notable improvements thanks to advancements in early detection and treatment methods. As a result, the focus has increasingly shifted toward understanding the long-term health and well-being of survivors. This concern primarily revolves around three key areas: quality of life, psychological health, and financial burdens. In this article, we examine the quality of life of long-term colorectal cancer survivors, considering various treatment options such as surgery, radiation, chemotherapy, and watchful waiting. A particular emphasis is placed on sexual functioning, an aspect often overlooked in clinical settings, and its role in overall quality of life. In addition, this review examines the psychosocial challenges and financial pressures that survivors often encounter, delving into the factors that contribute to these issues. Survivors often experience persistent problems such as chemotherapy-induced peripheral neuropathy, dry mouth, hair loss, gastrointestinal problems resulting in frequent and urgent bowel movements, and incontinence. They may also face complications related to ostomy care, dissatisfaction with body image, sexual dysfunction, and an overall decline in life satisfaction. Psychosocial challenges such as anxiety, depression, and distress, along with the financial strain of treatment expenses and potential job loss, exacerbate their situation. Although these problems are not easily addressed, the review aims to provide a foundation for the development of targeted interventions, offering guidance for both researchers and healthcare providers in crafting effective support strategies to tackle these diverse challenges.

Keywords: Financial stress, Colorectal cancer, Quality of life, Long-term survivors, Psychological status

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Introduction

According to GLOBOCAN's global cancer statistics, colorectal cancer (CRC) was responsible for 10% of new cancer cases and 9.4% of cancer-related deaths in 2020, making it the third most common cancer in terms of incidence and the second leading cause of cancer mortality [1]. Although there has been a noticeable increase in cases of early-onset CRC, particularly in individuals under 50, the majority of survivors—approximately three-quarters—are over the age of 65, as reported by the American Cancer Society and the National Cancer Institute in 2022 [2].

The treatment landscape for CRC has evolved over the years, with surgery still being the most commonly used method. Other available options include chemotherapy, radiotherapy, immunotherapy, combination treatments, and a wait-and-watch strategy. The treatment decision is shaped by factors like the cancer stage, tumor type, and the patient-provider decision-making process [3]. For stage I and II colon cancers, surgery is generally performed without the need for chemotherapy or radiation [2]. Only patients with high-risk stage II colon cancer and those with stage III colon cancer typically receive adjuvant chemotherapy after surgery to reduce the risk of recurrence. In cases of stage I rectal cancer, over 60% undergo surgery, and about half of these patients also receive neoadjuvant chemotherapy or radiotherapy. For stage II and III rectal cancers, a combination of neoadjuvant chemotherapy, radiotherapy, and surgery is common. In the case of stage IV CRC, nearly half of colon cancer patients and 30% of rectal cancer patients undergo combined surgery, chemotherapy, and/or radiotherapy. Immunotherapy might be considered for patients whose tumors display certain molecular characteristics [4, 5]. The field has also seen innovations in surgical options, with a growing focus on organ preservation. Super minimally invasive surgery, enabled by digestive endoscopy, represents a major advancement over traditional and laparoscopic methods, prioritizing minimal disruption to the body's natural anatomical structure [6]. Further research is needed to assess the long-term benefits of these approaches on survivors' quality of life.

Thanks to advancements in early detection, surgery, chemotherapy, radiotherapy, and immunotherapy, survival outcomes for CRC patients have significantly improved. The American Cancer Society and the National Cancer Institute reported that the 5-year relative survival rate for CRC patients diagnosed between 2011 and 2017 reached 65%, an increase of roughly 15% compared to four decades ago [2]. As survival rates rise, there is a growing focus on understanding the long-term well-being of CRC survivors. This review aims to provide a comprehensive summary of research on aspects such as quality of life, financial burdens, psychological health, and more, to inform the development of interventions to address these long-term challenges.

Results and Discussion

Quality of life

The assessment of quality of life in colorectal cancer (CRC) patients typically relies on widely used scales, including the EORTC QLQ-C30, EORTC QLQ-CR29, and EORTC QLQ-CR38, along with the EuroQoL 5-dimension (EQ-5D-5L) and the SF-36, which all measure various aspects of health [7-11]. These instruments assess multiple areas such as bowel, urinary, and sexual functions, as well as physical, social, cognitive, and emotional well-being. Additionally, specialized scales like the LARS for intestinal function, IPSS for urinary issues, and IIEF and FSFI for sexual health evaluation are incorporated [7, 11]. The focus of these evaluations includes gastrointestinal health, the impact on daily physical activities, emotional well-being, social interactions, financial challenges, and general health.

Surgical treatment and quality of life

The type of surgical intervention plays a pivotal role in determining the long-term well-being of colorectal cancer (CRC) patients. Guren *et al*. [12] observed that patients who underwent abdominoperineal resection (APR) experienced a more considerable decline in their quality of life compared to those who had low anterior resection. Similarly, Koneru *et al*. [13] suggested that the presence of significant low anterior resection syndrome (LARS) post-surgery significantly contributed to this difference in quality of life. For patients with mild or no LARS, their quality of life was significantly better than those in the APR group, while those with severe LARS faced similar challenges in quality of life as APR patients. A study that compared various surgical options for rectal cancer found no significant differences in overall quality of life between groups. However, body image perception was notably worse in the APR group. Additionally, patients who underwent manual colorectal anastomosis had a substantially higher incidence of severe LARS compared to those with mechanical anastomosis (83.3% vs. 56.6%, $P = 0.002$) [14]. Female patients who had APR also faced an increased likelihood of experiencing dyspareunia (OR = 2.61, 95% CI = 1.00-6.85). In cases where low anterior resection caused intestinal dysfunction, there was an association with bladder storage issues (OR = 1.64, 95% CI = 1.01-2.65), urinary incontinence (OR = 2.17, 95% CI = 1.35-3.50), and decreased libido (OR = 2.69, 95% CI = 1.21-5.98) [15]. According to a meta-analysis, patients undergoing sphincter-preserving surgery for rectal cancer showed that intestinal dysfunction mainly affected social and emotional aspects of their quality of life, thereby diminishing their overall health status [16]. Long-term CRC survivors (≥ 15 years) reported quality of life levels similar to the control group in terms of fatigue, and urinary, physical, and emotional health. However, intestinal dysfunction continued to persist as a long-term concern for these patients [17].

In studies that focused on tumor location's impact on post-surgical quality of life, comparisons between colon and rectal cancer, as well as between right-sided and left-sided colon cancers, have been made. Keane *et al*. [18] found that almost 50% of rectal cancer patients who had low anterior resection experienced severe LARS, whereas only 25% of sigmoid colon cancer patients and 26% of non-cancer-matched controls faced the same issue. Despite these differences in LARS rates, no significant variations in overall quality of life were found across the groups.

Further analysis highlighted that factors such as the height of the anastomosis, the creation of a stoma, and radiotherapy were all linked to severe LARS in rectal cancer survivors [18]. Contrasting this, another study reported that both rectal and colon cancer patients faced significant gastrointestinal dysfunction after surgery, with severe LARS occurring in 21% of colon cancer patients and 55% of rectal cancer patients. In these patients, severe LARS had a marked negative impact on their quality of life [19]. A study comparing the outcomes of left-sided versus right-sided colon resections found a slight increase in severe LARS incidence in right-sided resections (20.6% vs. 15.6%). After adjusting for age and gender, the odds of severe LARS were higher in right-sided resection patients (OR 1.48, 95% CI 1.03-2.13; P = 0.035), and this was linked to reduced quality of life [20]. Severe LARS continued to be a major factor contributing to lower quality of life in these patients [20].

As for the surgical technique itself, a cohort study comparing laparoscopic and robotic-assisted surgeries found that patients who underwent robot-assisted or transanal surgery had a lower chance of requiring a permanent stoma after low anterior resection (OR = 0.39; 95% CI = 0.25-0.59, and OR = 0.35; 95% CI = 0.22-0.55, respectively) [21]. However, stoma-related complications were prevalent in 45.4% of stoma patients, including issues like high stoma output, skin irritation, and parastomal hernia. A follow-up study tracking CRC survivors over a decade revealed that while stoma patients faced more immediate complications, such as bleeding and infections, the incidence of long-term complications (including hernias, urinary retention, and intestinal obstruction) became similar for both stoma and non-stoma patients. Stomas were also associated with a higher likelihood of fistula formation (OR = 5.4; 95% CI = 1.4-21.2), which negatively impacted the health-related quality of life ($P < 0.05$) [22]. Newer studies suggest that permanent stomas, especially after low rectal cancer surgery, contribute to a decreased long-term quality of life, influencing daily activities and personal relationships [23]. However, this effect appears to be less significant in older patients. In research conducted by Orsini *et al.* [24], elderly patients (aged seventy and above) who had undergone total mesorectal excision (TME) showed minimal differences in their quality of life whether they had a stoma or not, based on assessments using the SF-36 and EORTC QLQ-C38 questionnaires.

Radiotherapy and its influence on post-treatment quality of life

Radiotherapy is a critical component in the treatment of rectal cancer, and while effective, it has been associated with an increased likelihood of bowel complications. Both preoperative (neoadjuvant) and postoperative (adjuvant) radiotherapy have been found to exacerbate bowel dysfunction in survivors. According to Guren *et al.* [12], those undergoing radiotherapy reported significantly worse symptoms, including irregular bowel movements, urgency, and fecal incontinence. Similarly, Bruheim *et al.* [25] in their cohort study found notable differences between irradiated and non-irradiated patients, showing that those who received radiotherapy had higher incidences of frequent bowel movements, fecal incontinence (49% versus 15%, $P < 0.001$), and dependency on sanitary pads (52% versus 13%, $P < 0.001$), as well as an increased rate of urinary incontinence (9% versus 2%, P = 0.001), and poorer social function. Additionally, preoperative radiotherapy has been associated with a range of sexual and urinary dysfunctions, including dyspareunia (OR = 2.76, 95% CI = 1.12-6.79), reduced libido (OR = 2.22, 95% CI = 1.09-4.53), and challenges in sexual activity (OR = 0.55, 95% CI = 0.30 - 0.98) [15]. Chronic proctitis, a consequence of pelvic radiotherapy, is another complication that significantly impacts survivors' well-being, leading to persistent pain, which in turn affects their functional capacity and quality of life [3].

Chemotherapy and long-term quality of life in CRC survivors

Chemotherapy remains a cornerstone in treating colorectal cancer (CRC), but it has significant long-term effects on quality of life, especially among younger survivors. In a cohort of 562 CRC patients, chemotherapy was linked to worsened quality of life after five years, particularly among those under 70 years old. The treatment often induces issues such as anorexia, taste disturbances, and alopecia, affecting the patient's physical and cognitive abilities. Among survivors over 70 years of age, chemotherapy led to dry mouth and hair loss [26]. A study by Vardy *et al.* [27] reported that nearly half of the patients diagnosed with localized CRC had cognitive impairments within two years of treatment, compared to just 13%-19% in the general population ($P < 0.001$). However, long-term follow-up revealed no major differences between the cognitive status of long-term CRC survivors and healthy controls (16% vs. 8%) [28]. Furthermore, multiple studies suggest that chemotherapy's influence on cognitive function in CRC survivors is relatively minimal [27, 29-31].

A known side effect of chemotherapy, particularly with oxaliplatin, is neurotoxicity, often presenting as numbness in the extremities, with the severity depending on the dosage. A meta-analysis revealed that the rates of peripheral neuropathy in patients were 58%, 45%, 32%, and 24% at six months, one year, two years, and three years post-treatment, respectively [32]. While chemotherapy often causes diarrhea, it typically resolves spontaneously and does not seem to affect long-term quality of life [33].

Wait-and-see strategy and survivors' quality of life

The "wait-and-see" strategy, a newer approach that avoids surgery in favor of strict monitoring, has garnered increasing attention for its potential impact on survival and quality of life outcomes. In a study of 880 rectal cancer patients, those who followed the wait-and-see approach after achieving a clinically complete response exhibited a local recurrence rate of 25.2% at two years. At five years, the overall survival rate was 85%, and disease-specific survival reached 94% [34, 35]. In another study tracking 278 patients who had a complete or near-complete response to neoadjuvant treatment, 80% chose the wait-and-see strategy, with 6% opting for local resection and 14% receiving total mesorectal excision (TME). Interestingly, while a significant portion of patients in the wait-and-see group experienced severe intestinal dysfunction and sexual dysfunction (especially in males), overall, those who chose this approach reported a higher quality of life compared to those undergoing further surgery [11].

Sexual health and its impact on quality of life

In a research study conducted in the Netherlands, utilizing the sexual function subscale of the EORTC QLQ-CR38, a sample of 1,371 CRC survivors was assessed, out of which 1,359 had undergone surgery. This study revealed that male survivors of rectal cancer faced significantly higher rates of erectile dysfunction (54% vs. 25%, $P < 0.0001$) and ejaculation issues (68% vs. 47%, $P < 0.001$) compared to those with colon cancer. Moreover, the occurrence of sexual pain was notably higher in female survivors of rectal cancer (30%) than in those with colon cancer (9%), both of which were far greater than in the general population (0%, $P = 0.001$) [36]. A study by Bregendahl *et al*. [15] found that 72% of female rectal cancer survivors reported experiencing vaginal dryness, 53% experienced sexual pain, and 69% indicated a reduction or complete loss of sexual interest. Despite the commonality of sexual health issues among CRC survivors, conversations regarding sexual function between patients and healthcare providers are often insufficient [37, 38]. Barriers such as time constraints and insufficient knowledge regarding treatment options for sexual dysfunction may hinder effective communication. Increasing proactive discussions and better utilization of referral resources could be key to addressing these concerns [38]. Although it is well-documented that CRC patients face sexual health challenges during and after treatment, there is still a lack of sufficient long-term studies and interventional strategies to address these issues and enhance quality of life [39].

Psychological health challenges

Many survivors of CRC report difficulty returning to their normal lives following treatment, with the anxiety of potential recurrence significantly contributing to mental health challenges [2, 40]. Studies examining psychological distress in CRC survivors show considerable variation in the prevalence of anxiety, depression, and distress, likely due to differences in research methods and assessment tools. In one prospective study of 1,966 CRC survivors, 42% reported psychological distress five years after diagnosis, including anxiety, depression, or somatic complaints [41]. Another report by Chambers *et al*. [42] indicated that only 5% of individuals reported severe mental health issues five years after diagnosis. Despite limited research, existing findings highlight that a significant portion of long-term CRC survivors experience psychological distress, particularly anxiety and depression [43].

Dunn *et al*. [41] observed that male survivors had a higher likelihood of mental health struggles compared to their female counterparts ($P < 0.001$). The study suggested that younger men, particularly those with low educational attainment and limited social support, may benefit from targeted interventions. In a five-year longitudinal study of rectal cancer patients, mental health scores on the SF-36 scale showed no significant gender differences, although women's mental health improved over time, while men's remained relatively unchanged [44]. Furthermore, an 11-year follow-up study on rectal cancer survivors revealed that those with permanent stomas had worse mental health outcomes compared to those without stomas [45]. Survivors who undergo permanent stoma surgery often face psychological difficulties, primarily linked to post-surgical adjustment and coping with bodily changes. To improve the quality of life for these individuals, it is crucial to address aspects such as emotional support, social integration, and a sense of belonging [46].

Economic strain and its effects on quality of life

Economic challenges are a significant issue for approximately 40% of CRC survivors, with estimates ranging from 7% to 80%. Economic strain related to CRC has been shown to negatively affect the quality of life (OR = 2.54, 95% CI = 1.62-3.99) [47-49]. Mo *et al.* [50] reported that over half of survivors with stage I-III CRC experience considerable financial pressure. Factors such as younger age, lower family income, unemployment, chemotherapy treatment, and lack of social support are strongly associated with economic burden ($P < 0.05$). Financial strain can lead to decreased adherence to treatment plans, which in turn affects both survival rates and overall quality of life [51].

Conclusion

In the current landscape of personalized medicine, which emphasizes multidisciplinary and precise treatments, we must consider not just the survival rates but also the long-term well-being of colorectal cancer (CRC) survivors. Those who survive CRC may experience a range of complications that go beyond the physical—such as chemotherapy-related neuropathy, dry mouth, and hair loss—but they also face ongoing issues like bowel dysfunction (including frequent bowel movements, urgency, and fecal incontinence). Survivors can struggle with colostomy management, body image concerns, and sexual health challenges, all of which significantly affect their quality of life. Additionally, psychological burdens such as anxiety, depression, and stress are common, as are financial strains resulting from treatment expenses and potential job loss. This review has outlined various perspectives on the long-term health status of CRC survivors, discussing the impacts of different treatment modalities (including surgery, radiation, chemotherapy, and wait-and-see approaches) on survivors' quality of life and mental health, while also considering how gender, age and the presence of a colostomy influence these outcomes. While immediate solutions may be difficult to implement, this work offers valuable directions for future research and clinical practice.

The treatment and survival of cancer undoubtedly leave a lasting mark on the health and daily functioning of CRC survivors. As a result, it is critical to offer them comprehensive, coordinated follow-up care that addresses not only their physical recovery but also their emotional and social challenges. Tailoring care to meet the individual needs of each patient based on their treatment history is essential. Although clinical follow-up care is still evolving, the need to educate CRC survivors on effective health management has become increasingly recognized. For example, the American Cancer Society has developed guidelines to support survivors in minimizing the negative impacts of long-term cancer survival [3]. Moving forward, further strategies to improve CRC survivors' long-term health outcomes will likely emerge, guiding efforts to improve their overall quality of life.

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