

REVIEWS

Quality of life in patients with colorectal cancer: a review

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Abstract

Quality of life is a concept that must be approached in a multidimensional way, related to the physical, mental, social and functional health of an individual. Colorectal cancer is one of the most common malignancies in the world and a major cause of death. We conducted a literature review in order to present the existing knowledge regarding the quality of life in patients with colorectal cancer. Although the cause of colorectal cancer is currently unknown, we identified a number of risk factors that need to be considered, such as unchanged hereditary risk factors: age and aging, family and personal history, gender, genetic risk, as well as modifiable, non-hereditary risk factors: diet, obesity, sedentary lifestyle, diabetes, smoking, alcohol, air pollutants.

Colorectal cancer can contribute to the deterioration of quality of life through the direct consequences of the disease, through the effects of surgical treatment (colorectal cancer operated and / or with colostomy), long-term complications and metastases. Comorbidities, obesity, smoking, old age, poor education are associated with a low quality of life and risk of death.

Keywords: quality of life, colorectal cancer, risk factors.

Premises and objectives

The purpose of this review is to investigate how the quality of life dimension is reported through various assessment tools for colorectal cancer patients and to examine the sociodemographic and clinical factors associated with average and low quality of life scores.

Colorectal cancer, general considerations

Colorectal cancer (CRC) is one of the most common malignancies and a major cause of mortality and morbidity (Ferlay et al., 2015; Hamidreza et al., 2017). In the EU-27 area, in 2020, colorectal cancer was estimated to be the third malignant localization in men (after prostate and lung) and the second localization in women (after breast). CRC is the second cause of cancer death in men (after lung cancer) and the third one in women (after breast and lung cancers). Epidemiological studies have shown major variations in the geographical distribution of CRC, with a significantly higher risk in developed countries associated with diet and lifestyle, but also with different levels of quality of screening, diagnosis, and treatment as a result of healthcare expenditure (1).

In Romania, the reported incidence of CRC was approximately 8.23 / 100,000 inhabitants in 2005, the

diagnosis being often in advanced stages, due to late onset of clinical signs and the lack of systematic screening tests (Vasile, 2010). Other data indicated an incidence of 10.1 / 100,000 inhabitants for men and 7.3 / 100,000 inhabitants for women (Toma, 2018). Based on data reported by the North-Western Cancer Registry it was estimated that in Romania, in 2017, there were 4912 new cases of colorectal cancer in males and 3860 new cases of colorectal cancer in women (Coza et al., 2019).

Globally, the trends show an increase of the incidence and a decrease of mortality, which is a consequence of the large scale screening programs adopted by more and more countries, but also of the progress in the treatment of this type of cancer. These trends also have the effect of improving the quality of life of colorectal cancer patients (Ferlay et al., 2015).

Colorectal cancer is characterized by:

- increased risk after 50 years, as a sporadic disease;
- localization in the terminal part of the colon (last 20 cm) or in the rectum;
- slow progressive evolution, in terms of years or decades;
- onset of colorectal polyps in the epithelium of the colon and rectum, as a predisposing hereditary cause;
- predisposing risk factors, probable and possible:

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lifestyle, diet, sedentary lifestyle, environmental factors, family and personal history;

- hereditary or non-hereditary character (acquired);
- treatment may include surgery, radiation therapy and chemotherapy;
- the consequences of the disease and the treatment concern the quality of life both from a medical point of view through complications and metastases, as well as psychological, affective, volitional and social.

Risk factors

Risk factors in CRC can be unchangeable, hereditary and modifiable, non-hereditary; they may have a cumulative action.

To date, the cause of the CRC is unknown. Some people have risk factors but will never develop CRC, while others who do not have risk factors will develop the disease.

a) Unchangeable factors

- *Aging*: with age, the risk of CRC increases.
- *Family history*: It is estimated that 20% of colorectal cancers occur in the family context, with common environmental factors or genetic inheritance being risk factors.
- *Gender*: Men are generally more affected than women, in a ratio of 3:2.
- *Personal history*

A number of personal backgrounds may favor the evolution towards colorectal cancer:

- colorectal polyps, considered as precancerous lesions, because they can evolve over time in CRC;
- history of CRC, in case of tumor removal there is a risk of developing over time a new tumor in another location in the colon or rectum area;
- history of other cancers: lymphoma, testicular cancer, endometrial cancer;
- hereditary syndromes of colonic adenomatous polyposis (familial adenomatous polyposis, Gardner syndrome, Turcot syndrome, attenuated colonic adenomatous polyposis);
- Lynch syndrome (hereditary nonneoplastic CRC);
- Crohn's intestinal inflammatory diseases (ulcerative colitis) can cause long-term inflammation of the large intestine followed by dysplasia and progression to CRC in 2/3 of cases.

CCR is associated with elevated levels of inflammatory (IL-4) and proinflammatory cytokines (IL-6, IL-17, TNF, IL-23, IL-12, IL-8; IL-10 have a protective effect on CRC (Szyllberg et al., 2015; Mariani et al., 2014)

- Genetic risk

The role of heredity and acquired mutations was highlighted by disorders in signal proliferation (KRAS, evelin D1, WNT, MYC, RB, TP53, PTEN, APC), elution of cell apoptosis angiogenesis (VEGF, PG6F, THBS1), local metastatic invasion (E-cadherin), genetic instability (CIN, MSI, NER, BER) (Szyllberg et al., 2015; Kanwal & Ghias, 2016).

Defects of the MLH1, MLH2, MLH6 or PMS2 genes associated with the microsatellite instability biomarker (MSI) have been found in Lynch syndrome and sporadic CR tumors (Murcia et al., 2016).

b) Modifiable factors (Simon, 2016; Giovannuci,

2002)

The diet, especially the western type, is considered the most important risk factor for CRC, due to the increased caloric intake and the qualitative content:

- increased protein intake, red meat (beef, lamb, pork) and processed meat (sausages, pressed meat, sausages);
- high lipid content;
- low selenium content;
- low content of folic acid and methionine;
- high content of aromatic hydrocarbs in burnt and smoked foods (meat and fried fish);
- low dietary fiber content;
- low content of vegetables, especially crucifers: garlic, onion, citrus;
- reduced intake of vitamins (A, C, E) and minerals (Ca).

Obesity

Overweight - BMI over 25 increases the risk of CRC.

Sedentarism

Low physical activity, regardless of weight, is a risk factor for CRC.

Type 2 *diabetes* increases the risk, regardless of weight.

Smoking is a risk factor by favoring the development of large colorectal polyps, as precancerous lesions.

Alcohol, consumed in excess, especially beer, is a risk factor, being frequently associated with smoking and drug use.

Organic and inorganic *air pollutants* also have carcinogenic potential.

The modifiable protective factors are:

- physical activity (Brown et al., 2012)
- dietary factors: increased intake of calcium, folic acid, dietary fiber, polyunsaturated fish oil.

General considerations on the quality of life

The interest in the quality of life (QoL) increased considerably after World War II, with the rise of awareness and recognition of social inequalities. In the medical literature, the term was introduced in the 1960s and has become a key word in databases since 1975.

Another root of the concept of QoL may be related to the definition of health formulated by the World Health Organization (WHO) in 1947 as "complete state of physical, mental and social well-being, and not only in the absence of disease and infirmity" (***, 1947). Subsequently, the definition of "the ability to lead a productive social and economic life" was also included in the definition. The term well-being, by definition, has contributed to the conceptual confusion about what health is and what QoL is.

Most health and social sciences methodologies have 3 dimensions in mind, for measuring QoL or health status: physical function, mental state, and the ability to encompass social interactions (post 2014).

The first estimate of QoL is known as the Qitz-Spitzer Index, based on the measurement of socio-professional variables: physical, social and emotional function, attitude towards disease, personal characteristics of patients' daily lives and the cost of the disease (Spitzer et al., 1981).

In the mid-1980s, a new term related to QoL appeared, the health-related quality of life (HRQOL), defined by Torrance (1987) as the QoL aspects of existing health.

Gradually, the terms “perceived health”, “health”, “HRQoL” and “QoL” are considered synonymous by researchers and doctors.

Currently, the term quality of life is considered ambiguous, with multiple meanings, which refers to both the individual’s experience of his life and living conditions, which gives the term subjective character. At the same time, QoL needs to be approached multidimensional, in terms of health:

- physical health: somatic sensations, symptoms of the disease, side effects of the treatment;
- mental health: positive feelings of well-being, up to non-pathological psychological forms of suffering and up to psychiatric disorders;
- social health: social contacts and interactions, in terms of quantity and quality, in the family and at work;
- functional health: self-care, daily and professional physical activity.

Methods

We conducted a systematic review of scientific literature using the PubMed database. The search strategy included original articles, reviews or systematic reviews with “colorectal cancer” and “quality of life” as search terms in the title or abstract. We restricted the search to papers written in English or Romanian and published in the last twenty five years; 215 matching articles were identified. We filtered the results by publication years because witnessed rapid development in the recent years. We selected the articles relevant to review using the PRISMA 2020 checklist (Page, 2021).

We included all the papers relevant to the following research questions: 1) how is the quality of life defined and measured / evaluated? 2) What symptoms do patients report that their quality of life impacts? 3) What are the socio-demographic and clinical factors that prove to be statistically significant correlations with the average score of quality of life in each study. We included observational studies, both quantitative and qualitative, population-based studies, as well as previous review, systematic review and/or meta-analysis papers. We excluded reports from randomized controlled trials as these can be biased by the controlled environment.

Results

In total, 44 articles were identified for reviewing. Twenty seven quantitative studies met the inclusion criteria and were included in the review process. Seventeen studies were retrospective observational studies of which one was a case-case study, twelve were cross-sectional studies and four were longitudinal studies. Five studies were population-based retrospective studies. Five studies had a prospective design. Another four qualitative studies also met the inclusion criteria. We also reviewed previous four review papers and eight systematic review papers of which two also included meta-analysis.

Colorectal cancer and quality of life

Colorectal cancer is manifested by impaired quality of life, caused by the direct consequences of the disease on the one hand: abdominal pain, changes in bowel motility,

bleeding and anemia, fatigue and weight loss and the effects of surgical treatment, chemotherapy and radiation associated with diet and physical activity on the other hand (Smith & Weisner, 2014). Weight loss and reduced physical activity are especially common in elderly patients with comorbidities.

Each type of treatment is associated with specific side effects and complications.

a) Surgical treatment consists of rectal amputation and colorectal or colostomy anastomosis. One of the most serious complications is a fissure in the anastomosis, which requires new surgery or radiology associated with significant morbidity, prolonged hospitalization and mortality.

Another common complication is dehiscence (rupture along the surgical suture) and herniation of the abdominal scar.

The impact on the quality of life does not differ between classical open surgery and laparoscopic surgery (Imperiale 2014, quoted by Kuipers et al., 2015). However, benefit of oncologic surgery is diminished by declines in physical and mental health (Blakely, 2019). QoL improves up to 8 months after colostomy but later chemo/radio therapy can have a negative influence (Silva, 2020). Also, patient-reported comorbidities were found as important predictors of QoL after surgery, in a prospective cohort study (Cummings, 2018).

Recent studies showed that social action to support health promotion behavior had a significant impact on the quality of life after colorectal cancer surgery (Yeom & Suh, 2022; Kraemer et al., 2022).

Reportedly, higher levels of low to medium intensity physical activity have been associated longitudinally with better health-related quality of life and less fatigue in colorectal cancer patients up to two years after treatment (van Roekel et al., 2020).

b) Long-term complications

They occur frequently and include: fecal incontinence and increased bowel movements, reduced toxicity after chemotherapy, erectile dysfunction in men, dysphoremia in women (Kuipers et al., 2015).

A number of preparations such as oxaliplatin or irinotecan may cause neutropenia and diarrhea. Antiangiogenic agents can cause bleeding, thromboembolism, hypertension, and proteinuria (Hurwitz et al., 2004 quoted by Kuipers et al., 2015).

A prospective multi-center study found that age, stoma formation, adjuvant treatment, and rectal cancer reduce long-term QoL (Valeikaite-Tauginiene et al., 2022).

c) Metastases

CRC metastases cause impairments such as loss of appetite, cachexia, anemia, liver disease, biliary obstruction and impaired lung function (Dionf et al., 2014 quoted by Kuipers et al., 2015). Fatigue and pain have a negative impact on QoL of patients with advanced or metastatic CRC (Borchert et al., 2020).

The consequences of surgical treatment are aimed at the quality of life from a medical point of view, but also at a psychological and social level. Because most colorectal cancer patients have a survival of more than 5 years, assessing the quality of life of long-term survivors

is essential for a comprehensive approach to these patients (Siassi et al., 2008; Grimmert et al., 2011; Sharma et al., 2013). There is a growing interest for moving the focus from detection of disease progression or recurrence to community interventions with the aim to improve quality of life of CRC patients (Gray et al., 2013) at a more complex scale that would take into account psychological and social issues (Aminisani et al., 2017; Son et al., 2018; Blum-Barnett et al., 2019; Dun et al., 2022). The influence of modifiable factors such as nutritional status and lifestyle before and after diagnosis is increasingly being investigated in recent years (Winkels et al., 2014; Eyl et al., 2018; Balhareth et al., 2019; Balderas-Peña et al., 2020). A prospective cohort study investigating the associations between eating habits and longitudinal changes in quality of life in colorectal cancer patients found that specific dietary habits are associated with changes in quality of life after surgery. Namely, patients who adopted the “Western” diet were less likely to improve their overall health / QoL and physical function, while a diet rich in fruits and vegetables appeared to be beneficial for patients’ QoL changes in time (Gigic et al., 2018).

Early identification of patients with CRC who are at risk of a low quality of life in the future allows preventive measures to be taken (Reyes et al., 2017). In a systematic review study, Bours et al. in 2016, found that one or more comorbidities are the strongest predictors for a lower health-related quality of life up to ten years after diagnosis. Additionally, higher BMI, fatigue, psychological distress, anxiety, and depression are strongly associated with lower quality of life up to five years postdiagnosis (Vissers et al., 2016). Evidence for the influence of sex and age is inconsistent (Rodriguez et al., 2015; Trinquinato et al., 2017; Miller et al., 2021). Also, no significant difference was found between patients with sporadic CRC and those with hereditary cancer in terms of self-reported quality of life (Burton-Chase et al., 2017).

In 2011, a study of QoL in colorectal cancer patients performed in London evaluated QoL in the last 5 years after the diagnosis of colorectal cancer in 495 patients using EORTC OLO-C30. The conclusion of the study was that the quality of life of these patients was very good (Pachler & Wille-Jorgensen, 2004).

Another study conducted by the US Cancer Center (CTCA) between 2001 and 2008 focused on improving the quality of life of colorectal cancer patients. Using the EORTC QLQ-C30 questionnaire, the results showed that while the overall physical health score was 87-100 for the general population, in the study population this score was 77. Moreover, the average mental health score was 67-100 in the general population and approximately 71 in the study group. Low QoL in these patients has been found in other studies (Camilleri-Brennan & Steele, 2002b).

Another prospective study found that patients who underwent surgery and chemotherapy had deficiencies in mental and social activities. Clinical symptoms and signs such as fatigue, dyspnea, insomnia, constipation, and diarrhea, as well as financial difficulties have been reported. With the exception of constipation, all other problems worsened with age ($p < 0.001$) (Camilleri-Brennan & Steele, 2002a).

In 2004, Sultan et al. monitored the effect of social support on improving QoL in 636 patients diagnosed with colorectal adenocarcinoma between 1997 and 2001. The investigators assessed two targets called mental health status (MHS) and psychic health status (PHS) with a variability between 0-100, 0 being the most altered status, and 100 the best status using the SNJ (Raw Scale Score) questionnaire. The results showed a score of 52.6 ± 11 for MHS and 37.3 ± 11.4 for PHS. In general, these scores were with altered values. Patients with strong social support had a higher MHS and PHS score ($p < 0.01$).

Mohler et al., in 2008, evaluated QoL in colorectal cancer survivors. They compared patients with stoma after surgery with a control group that did not have stoma after surgery using a modified version of the City of Hope Quality of Life (mCOH-QOL) and SF-36V2 questionnaires. The results of this study showed that patients with colectomy and stoma had a better quality of life than patients who did not have a stoma. One factor may be that patients with stoma have received more careful care from medical staff. Careful follow-up and multidisciplinary pre- and postoperative care have ensured patient satisfaction and a higher QoL. Other studies have shown that despite very good clinical care, QoL in colorectal cancer patients is still very poor physically, socially, clinically, and financially (Flyum et al., 2021).

Another study included 120 patients diagnosed with colorectal cancer for 5 consecutive years. The EORTC QLQ-C30 quality of life questionnaire was applied to several aspects of patients’ lives, and the results were reported as an average compared to the maximum score of 100. The mean age of the patients was 60.31 ± 15 , 71 years (14-88 years). 63 patients were men and 57 women. The results showed that the following aspects were negatively affected by cancer: financial status of patients (score = 5.3 ± 11.0), social function (32.5 ± 15.4), pain (32.4 ± 19.8), and physical functional status (40 ± 19.7). A significant relationship was found between these variables and the age of the patients ($p < 0.001$) (Arndt et al., 2004).

Previous studies have shown that QoL is assessed soon after the diagnosis of colorectal cancer or independently correlated with survival (Lee et al., 1997; Michelson et al., 2000). Thus, a strong correlation was observed between QoL, in particular the score of physical QoL, and the risk of mortality. Interestingly, the correlation between a very low QoL score and mortality in colorectal cancer survivors was similar to the results that assessed the correlation between QoL and mortality in the general population (Lee et al., 1997) and between individuals comparable in age with colorectal cancer survivors. (Jess et al., 2002; Michelson et al., 2000).

Thus, these results suggest that, similarly to the general population, a very low QoL score identifies colorectal cancer survivors at high risk of death. However, the absolute mortality rate for long-term colorectal cancer survivors averaged 44.6 deaths per 1,000 person-years, a higher rate than the general population of the U.S. of comparable age (e.g., approximately 23 and 36 per 1,000 person-years for the ages 70-74 years and 75-79 years, respectively, even though most causes of death in the colorectal cancer population were due to causes other than

colorectal cancer (Adams et al., 2016; Montazeri, 1999).

A lower quality of life score was associated with older age, female gender, obesity, smoking and diabetes or other comorbidities; a lower mental score was associated with younger age and female gender. A very low physical quality of life score was associated with old age, obesity, poor education, smoking, comorbidities, and late diagnosis; smoking was associated with a very low mental score. A very low physical score of quality of life was associated with high mortality (hazard ratio (95% confidence interval): 3.97 (2.95-5.34)).

Conclusions

1. Studies show that approximately 5 years after diagnosis, on average, the quality of life of colorectal cancer survivors is close to the QoL of the general population.

2. Patients with colorectal cancer, especially those with comorbidities, obesity, smoking, old age, poor education, have a very low physical QoL score and long-term support may be needed given the correlation between low QoL and increased risk of death.

Conflict of interests

There is no potential conflict of interests to declare.

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