

RESEARCH ARTICLE

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# Health related quality of life in colorectal cancer patients: state of the art

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## Abstract

**Background:** Colorectal cancer (CRC) is the third most commonly diagnosed cancer in males and the second in females with a progressive increase in prevalence in industrialized countries. The loss of health due to the cancer and/or the consequence of the treatment may result in psychophysical, functional and social impairment; all of these affect health-related quality of life (QoL).

**Description:** The most frequently CRC-specific QoL questionnaires is the FACT-C. QoL is not only important for the well-being of cancer patient but it also influences survival and response to therapy. Many studies investigated various determinants involved in the assessment of QoL in CRC, suggesting that symptoms, surgical procedures and the number of comorbidity significantly affected QoL.

**Conclusion:** Despite that CRC patients have a relatively good QoL compared with the general population, a wide range of intervention could be undertaken to improve their QoL. The finding of this review may be useful for cancer clinicians in taking therapy and surveillance-related decisions. However, future research should be directed to large-scale prospective studies using well validated QoL instruments to facilitate comparison of results.

## Background

Colorectal cancer (CRC) is the third most commonly diagnosed cancer in males and the second in females, with over 1.2 million new cancer cases [1]. In the past two decades incidence rates for CRC have remained largely unchanged, instead mortality rates have fallen due to improvements in early detection and cancer treatment [2,3]. Survival at 5 years is 56% in Europe and 66% in the United States of America [4]. Moreover, Baade et al. concluded that survival expectations increase the longer they survive, reaching 93.2 % at 5 years after diagnosis [5]. This leads to a rising prevalence of patient living with CRC with an estimated worldwide prevalence of more than 3 million persons within 5 years of diagnosis in 2008 [6]. The rise of patients living with the consequence of CRC and its treatment has increased greatly the interest of their

impact on health-related quality of life (QoL) [7]. The loss of health due to the cancer and/or the consequence of the treatment may result in psychophysical or functional impairment or disruption of social and family interactions, all of these affect QoL [8]. Several studies assess prospectively the impact of CRC in the patient's QoL, both in short-term [9,10] and long-term periods [11].

In the present article, we review the studies in colorectal cancer that have incorporated previously validated instruments.

## Quality of life: definition and assessment

QoL is a multidimensional, dynamic, subjective and centered on patient construct, comprising physical, functional, emotional, and social/family well-being [12]. Therefore, QoL is an important outcome for evaluating the full impact of the disease on the individuals, their family and their community [13].

Quality of life, being a subjective, patient-rated concept, is difficult to quantify. To assess QoL the use of

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patient-reported questionnaires has become a standard practice. However the lack of a “gold standard” instrument is reflected in the wide range of available instruments, generic or disease-specific. The most used questionnaires are presented in table 1. Short Form 36 (SF-36) [14], its short version (SF-12) [15] and the EQ-5D [16] are the some of the most frequent generic questionnaire used to assess QoL. The use of generic QoL instruments allows comparison with the general population, or with people with no cancer. Instead, some cancer-specific questionnaires are the Functional Assessment of Cancer Therapy-General (FACT-G) [17] and the European Organization for the Research and Treatment of Cancer QLQ-C30 (EORTC QLQ-C30) [18]. The FACT-C [17] is the most used CRC specific questionnaire, although the EORTC also has a CRC-specific module, the QLQ-CR29 [19]. The FACT-C, used together with the FACT-G, has been extensively validated in English [20], Spanish [21] Korean [22], French [23] and Chinese patients [24]. It is formed by 37 items, grouped in five dimensions with a time frame of seven days. The first four dimensions are subscales of the FACT-G [20] (physical, social/family, emotional and functional well-being) and the last is an additional one focused on CRC. All the items are based on a five-point Likert scale except for the one investigating the presence of stoma (yes/no). This questionnaire was principally designed for self-administration, but it can also be administered by interviewers [25]. Both total and single dimensions scores could be calculated to assess QoL in CRC patient.

### Determinant of quality of life

QoL in colorectal cancer patients is associated with a several number of factors. To simplify the discussion, we divided these factors into five broad categories: socio-demographic characteristics; health-related factors;

cancer-related and surgical procedures factors; lifestyle factors; and other factors.

### Socio-demographic characteristics

Gender has not been reported as significant determinant in patients' QoL [26]. However, this is not true for specific problems like sexual functioning in man [27] or physical problems and pains in woman [28].

Results on age and CRC QoL are controversial. Forsberg et al. reported that age did not play a significant role in patients' QoL [29]. Nevertheless, in some studies QoL increase with age [30,31], whereas others reported a lower QoL with increasing age [32,33]. This controversy is present for both physical and psychological aspect of QoL [34].

Education level is not a determinant for QoL, because its role is subordinated to income [35]. With regards to income, there is evidence that low income correlates with worse physical, social and emotional well-being dimensions of QoL[11,31,35]. Also, home ownership was an independent predictor of QoL score [36].

The presence of a wide social network is positively related to patient's QoL [32]. Patients living alone reported a lower perceived well-being than those who live with family [29], but marital status was not associated with a higher QoL [11].

### Health-related factors

Patient with CRC reported significantly more comorbidity conditions and poorer physical and mental QoL compared with patients without cancer and a worse effect was found in patient with two or more comorbidities or those who had recent diagnosis [37]. Some specific diseases, such as heart disease [38], anxiety/depression [36] or urinary disorder [30] had a significant role on overall QoL. In particular, the higher prevalence of depression, compared to the general population of similar age [11] could be partially explained by the worries of a recurrence or of a second cancer, even after 5 or more years after diagnosis of cancer [39].

Concerning the association between body mass index and QoL, healthy-weight and overweight cancer survivors reported better scores in physical functioning, general health and vitality than obese cancer survivors [40].

### Cancer-related and surgical procedures factors

The stage and site of colorectal cancer at diagnosis are important in determining QoL, as they determine symptoms, treatment modalities and therapy duration [41,42]. Patient with stage I experienced a progressive positive trend in QoL; on the contrary patient with stage IV experienced a negative one. Instead, an initial QoL decrease, followed by better QoL scores, was experienced by those with stage II and stage III [43]. A possible explanation

**Table 1 List of QoL tools frequently used in oncology**

Name of instruments	Type
SF-36 [14] and SF-12 [15]	Generic
EQ-5D [16]	Generic
FACT-G [17]	Cancer specific
EORTC QLQ-C30 [18]	Cancer specific
QoL-CS [84]	Cancer specific
EORTC QLQ-CR29 [19]	CRC specific
mCOH-QOL and abridged version for non-stoma patients [85]	CRC specific
FACT-C [17]	CRC specific

EORTC= European Organization for the Research and Treatment of Cancer; FACT= Functional Assessment of Cancer Therapy; mCOH= Modified City of Hope Quality of Life-Ostomy

could be the perception (or re-conceptualization) of QoL after CRC diagnosis [44]. Nevertheless other studies reported no association between tumor stage and QoL [11,30].

Surgical procedures can affect various aspects of QoL due to physical and psychological consequences. Patients undergoing surgical procedures experienced a rapid QoL decline after surgery with a gradually restore about 3 month after [45]. Moreover, older patients are slower to restore their QoL [46].

Lower QoL both in laparoscopic and open surgery was found in older patient compared to the younger one [46], but only short-term QoL differences were found between open and laparoscopic surgery [47]. A possible reason may be the different occurrence of complications between the two surgical techniques [48]. Furthermore, baseline QOL was an important predictor of postoperative overall QOL and all QOL subdomains with a higher risk for difficult postoperative courses and auxiliary services associated with poor baseline QoL [49].

An important consequence of colorectal surgery is stoma. The presence of stoma influenced negatively the QOL if compared with patients undergoing a sphincter-saving resection [50], but not all authors found a significant difference [9,51]. The most important aspect influenced by the presence of stoma was the social component of QoL as assessed by a recent systematic review conducted on 10 studies [52].

The physical and psychological disorders resulting from stoma vary by gender. In female patients, a worse psychological [28] and physical [32] QoL score was reported. On the contrary, a reduction in mental health [28] and sexual functioning [53] was found in man. These and other problems related to stoma, such as worse fatigue, dyspnea, loss of appetite and changing in body image perception, gradually reduce a person's confidence and his social relations [54]. However, the impact of stoma could be influenced negatively by low income and problems in paying for stoma supplies [55], and positively by receiving therapy support with stoma-education programs and counseling [56,57].

Symptoms induced by cancer or its treatment are also very important. Many prospective studies investigated the role of bowel symptoms such as diarrhea, fecal control and constipation [58,59], but also fatigue and loss of appetite are very common and affected significantly QoL in CRC [36].

#### **Other factors**

Some lifestyle factors such as physical activities, diet, alcohol intake and smoke were associated to QoL. A moderate or intense physical activity is correlated to a higher physical QoL due to lower levels of fatigue and distress [60]. A quality diet (rich in fruit and vegetables, and low in fat) and the administration of probiotics

reduced bowel dysfunction, which can markedly decrease QoL [61-64]. Smoking was associated with a lower QoL [65], and controversy to alcohol intake [30]. Multiple behaviors changes have a better cumulative effect on QoL than single lifestyle modifications [63,66].

#### **Intervention to improve QoL in CRC**

In order to improve QoL in CRC patients it is important to, first identify the patient with a higher risk to have a low QoL and then intervene to the modifiable factors.

Fixed factors such as age or sex have only a marginal role in QoL and others are potentially modifiable. Therefore, a wide range of interventions have been developed to improve QoL in CRC survivors. We can improve QoL by reducing psychological morbidity and facilitating crisis adaptation with educational programs, self-help groups, psychosocial interventions, cognitive behavioral therapy, coping, and certainly drugs. For example, a randomized trial on 200 with cancer found an improvement in depression and anxiety by physical exercise, intervention group therapy and antidepressants [67]. A moderate physical activities should be suggested, when possible, to reduce some symptoms such as fatigue, pain and insomnia [64]. Bowel symptoms could be reduced with modification of diet and the use of probiotics [62-64].

Psychosocial interventions can be classified in educational programs and psychotherapeutic interventions. Educational problems improve the cancer-related knowledge, its treatment and the emotional reactions to it. Psychotherapeutic interventions, individual or in groups, covers a wide range of approaches including assistance in expressing emotions, increasing patients' sense of coherence, enhancing personal resources, improving communication, gaining control and improving coping skills. These interventions help to decrease somatic symptoms and psychosocial sequelae of CRC and its treatment, and improving QoL as showed on a prospective study [68].

This is also true for surgery consequences. Specific training, like anal training after rectal resections by reducing stool frequency, improves both general and specific QoL [69]. A cross-sectional study and a recent systematic review found that education of patient living with stoma helped to deal with sexual difficulties, dietary and physical activity restriction and in general with their lifestyle [57,70]. Furthermore, in a prospective longitudinal study was showed that groups' activities by sharing personal experiences helps to reduce the isolation and the feelings of loneliness leading by stoma [71].

#### **Relationship to survival**

QoL is also known to be an independent predictor of survival and response to therapy in cancer patients

[72,73]. Broun et al. found that a 10-point increase in baseline global QoL scores (using EORTC QLQ-C30) was associated with a 7% decreased risk of death [74]. This result was also showed for other types of cancer [75,76]. Some authors proposed a theory according to which QoL could have a direct influence on tumor behavior and survival [77,78], others suggested that QoL had a direct influence on therapy adherence and consequently on survival [79]. Moreover, a recent 18-month trial suggested that baseline QoL influenced CRC patient's survival [49].

### Discussion and conclusion

Various determinants of QoL in CRC had been investigated and the results mainly shown that physical problems linked to symptoms and surgical procedures, such as bowel problems and stoma are the most common. On the socio-demographic characteristics, only the socioeconomic status seems to have a well determined role, probably due to the better access to medical care. The presence of a higher comorbidity number was the most important health-related factor, but it must be considered that some of them could be a consequence of CRC. Moreover, a significant higher prevalence of distress, depression and anxiety were reported in CRC patients than the general population.

Findings on CRC stage by determining symptoms, treatment procedure and consequently overall survival showed the importance of disease stage on QoL. Its role is essential both for the clinical aspect and the psychological consequences that affect QoL after diagnosis [43].

When comparing the effect of different surgical procedures on QoL, only short-term benefits were found for laparoscopy. This could be explained by less post-operative complications with laparoscopic procedure [2,46]. Similarly, higher QoL score for the younger patient was linked to the number and the severity of postoperative and late complications occurred after both open and laparoscopic surgery [46,48].

The importance of symptoms has been reported in many studies since they affect directly and indirectly QoL in CRC survival. In fact the presence of diarrhea, incontinence, fatigue and pain in addition to having direct effects on QoL influenced the daily activities and hobbies, and interfere with family and social life [36,59].

Despite specific physical and psychological problems, the overall QoL in CRC patient is good both in short [80] and long-term survivors [11,27]. Several theories can be called upon to explain these findings.

One could be the process of internal recalibration and the shift in personal values to new understanding, known as reframing/response shift. This changes the patient's internal standards leading to a different estimation of their QoL [81].

Other two constructs of positive consequences after cancer diagnosis/treatment describe the change following a so stressful experience, benefit finding (BF) and post-traumatic growth (PTG). These two concepts are slightly different, but sometimes have been used interchangeably [82]. BF is defined as an individual process in which the patient perceives that major positive changes have occurred as a result of challenging life events. In contrast, PTG refers to benefits associated with changes in appreciation of life, interpersonal relationship, and self-perception often manifested through personal strength, spiritual change and globally as life perspective. Moreover, these two concepts are temporally different. BF start immediately after diagnosis, instead PTG can be developed even years after the cancer diagnosis [83].

The limitations of a literature review of this nature are the lack of systematic research of articles and lack of a gold standard for measuring QoL. Very heterogeneous instruments and different statistical analyses were used, making difficult a comparison across studies. However, all studies used well-validated instruments. Other shortcomings of the examined studies which may introduce a bias when comparing QoL results are: data acquisition, low response rates, non-random drop-out, small sample size and the different correction for confounding factors. Furthermore role of chemotherapy and radiotherapy treatment was not investigated.

Despite some limitations, this review is useful for a better understanding of QoL and its determinants in CRC patients. Due to the burden of this disease and the higher survival rate, both for early diagnosis and new treatment, the QoL in survivors of CRC should be a priority for public health research. The knowledge about the determinants of QoL could help to identify survivors with special needs. Moreover these findings may be useful for cancer clinicians in taking therapy and surveillance-related decisions in order to enhance the QoL of people with CRC.

Finally, although patients have a good QoL compared with the general populations, a significant number of determinants are potentially modifiable variable. Future intervention studies are needed to improve certain aspects of quality of care to determine whether those changes lead to increased QoL. Moreover, research should be directed to large-scale prospective studies using well validated QoL instruments to facilitate the comparison of results.

#### Competing interests

The authors declare that they have no competing interests.

#### Authors' contributions

SM, MJF: conception and design, drafting the manuscript; GG, AM, GG, AP: drafting the manuscript; FB, SG, AB: critical revision, given final approval of the version to be published.

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