

Update on Health-related Quality of Life in Colorectal Cancer Patients

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Along with the recent trend of improved survival in patients with colorectal cancer (CRC), health-related quality of life (HRQoL) has become a significant outcome measure and its improvement is an important goal. The most widely adopted CRC specific HRQoL questionnaires are the European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire (EORTC QLQ-CR38) and the Functional Assessment of Cancer Therapy (FACT-C). CRC survivors without serious comorbidity or recurrence experience only minor deficits of overall HRQoL when compared to the general population. However, disease recurrence, progression, and more specific limitations, including weight loss, reduction in energy, and psychosocial problems like psychological distress and depression, could result in lower HRQoL. To improve HRQoL, further research is required to develop appropriate health education regarding lifestyle changes and personalized intervention strategies for CRC survivors.

Key Words: Colorectal cancer, Quality of life, Survivors

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer in men and the second in women, with an estimated 1.4 million cases and 693,900 deaths occurring in 2012.¹ In Korea, CRC is the second most common cancer in male and the third most common cancer in female in 2012, and its incidence has continued to increase by 5.3% per year (5.7% in males, 4.3% in females) from 1999 to 2012.² Although mortality rates due to CRC have increased continuously in Korea,² decreasing CRC mortality rates have been observed throughout the last decades in a number of countries.¹ These findings are mainly attributed to CRC screening, improved diagnostic tests, reduced prevalence of risk factors, introduction of adjuvant therapy, and advances in the treatment for metastatic disease.^{1,3} Eighty percent of patients now survive the first year

after diagnosis of CRC, and 62% survive 5 years and more worldwide.⁴ Along with the recent trend of improved survival, health-related quality of life (HRQoL) has become a significant outcome measure and its improvement is an important goal for cancer patients. HRQoL assessment, especially in CRC, may improve our knowledge of how disease and treatment influence the patients' lives and how to adapt therapeutic modalities.⁵ In the present article, we review studies, which measured HRQoL in patients with CRC, and discuss intervention to improve HRQoL.

QUALITY OF LIFE ASSESSMENT IN CRC

1. Methods to measure HRQoL in CRC

The term quality of life (QoL) and, more specifically, HRQoL, is generally recognized as a subjective, dynamic, and multi-dimensional concept which includes physical and functional, emotional, social, and occupational well-being.⁶ Most used generic QoL instruments, such as short form 36 (SF-36), its short version (SF-12), and EQ-5D, are useful for making comparisons between different diseases. However, they might lack the specificity which is required to determine the real impact of treatment strategies.⁶ The most widely adopted cancer specific questionnaires are the European Organization for Research

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and Treatment of Cancer Quality-of-Life Questionnaire (EORTC QLQ-C30)⁷ and the Functional Assessment of Cancer Therapy General (FACT-G).⁸ In addition, the EORTC (EORTC QLQ-CR38)⁹ and FACT (FACT-C)¹⁰ have developed CRC specific modules. Both instruments have been extensively validated and translated and field tested in different languages. In 2005, Yoo et al.¹¹ validated FACT-C in Korean and patients' overall QoL was lower at one month after colectomy and recovered to the pre-surgery level at six months after colectomy. Recent systematic review reported that EORTC QLQ-CR38 is recommended to measure HRQoL in CRC patients, regardless of tumor stage and primary tumor site, because it had the most positive ratings on measurement property.¹² EORTC QLQ-CR38 consists of 38 items covering symptoms and side-effects related to different treatment modalities, body image, sexuality and future perspective.⁹ Meanwhile, the FACT-C is a self-report instrument which combines the FACT-G with the 9-item Colorectal Cancer Subscale.

2. Impact of treatment for CRC on HRQoL

Although the majority of studies for QoL in CRC patients have some methodological limitations, the use of valid QoL questionnaires after surgery for CRC has improved multidimensional health assessment.^{13,14} Surgical procedures may have a negative impact on various aspects of patients' QoL, including sexual dysfunction (impotence, ejaculation and dyspareunia), urinary dysfunction (incontinence, retention and dysuria), bowel dysfunction (stoma or gastrointestinal problems), and psychosocial problems.¹³ Abdominoperineal resection (APR), which is the preferred surgery when the tumor is close to the anus, results in permanent colostomy with its major shortcomings. Recent meta-analysis including cross-sectional studies or studies having longitudinal design demonstrated that a colostomy influences the overall QoL negatively.¹⁵ The colostomy-related problems include sexual problems, gas, constipation, depressive feelings, dissatisfaction with appearance, change in clothing, travel difficulties, feeling tired and worry about noises.¹⁵ A Korean study including 155 patients with rectal cancers who underwent an anterior resection (AR), a low anterior resection (LAR), or an APR showed that the presence of stoma influenced negatively QoL when compared to patients undergoing AR or LAR.¹⁶ In addition, the scores for stoma problems were worse than those for pain and for male sexual problems. However, some studies reported favorable QoL scores in patients undergoing APR or no significant difference in QoL scores between patients with colostomy and those undergoing sphincter saving surgery.^{17,18}

Taken together, patients with colostomy generally have worse QoL than patients with intact sphincter, however, sphincter saving surgery may still have a negative impact on gastrointestinal symptoms, sexual function, and subsequent psychological distress.

The first randomized study including 449 patients undergoing laparoscopic-assisted colectomy (LAC) or open colectomy for colon cancer evaluated Scores on the Symptoms Scale, QoL index, and a single-item global rating scale at 2 days, 2 weeks, and 2 months after surgery. The study results showed the only significant difference in the global rating scale score for 2 weeks after surgery, suggesting only minimal short-term QoL benefits with LAC.¹⁹ In the subsequent long-term follow up study, clinically moderate improvement from baseline for LAC in total QoL index was observed at 18 months. In addition, independent predictor of poor QoL at 2 months after surgery was poor preoperative QoL.²⁰ Another study reported that global QoL was significantly impaired in elderly patients undergoing LAC compared with younger patients undergoing same operation, even if elderly patients undergoing LAC had less postoperative local complications than elderly patients undergoing open colectomy.²¹

Although improvement in local control after preoperative radiotherapy (PRT) was achieved for the treatment of resectable rectal cancers, there was no difference in overall survival between transmesorectal excision (TME) and PRT followed by TME. In addition, PRT may increase treatment-related morbidity.²² A large randomized study by a Dutch group reported that there were few differences in QoL between patients treated with or without PRT, but PRT leads to more sexual dysfunction, slower recovery of bowel function, and impaired daily activity after surgery. In addition, patients undergoing APR had fewer physical and psychological problems but more voiding problems compared with patients undergoing LAR, suggesting that sphincter saving procedures do not always improve QoL.²³ A recent multicenter randomized study with follow-up of 14 years confirmed the results of previous study and PRT increased bowel dysfunction in patients without stoma.²⁴

A number of studies have investigated HRQoL in patients with CRC undergoing 5-fluorouracil (FU)-based chemotherapy. Adjuvant chemotherapy had no negative impact on QoL as compared with surgery alone.^{25,26} A recent study from Netherlands showed no differences in HRQoL and disease specific symptoms between surgery alone and surgery followed by adjuvant chemotherapy in both younger and elderly colon cancer patients.²⁷ Taken together, withholding colon cancer patients adjuvant chemotherapy, based on concerns for long-

term HRQoL or disease specific symptoms, does not seem recommendable. Chau et al.²⁸ reported that 12 weeks of protracted venous infusion 5-FU was associated with significantly better QoL during treatment and faster time to recovery compared to 6 months of adjuvant bolus 5-FU/leucovorin. In addition, QoL significantly improved in both groups during follow-up with a plateau by 1 year and without incremental improvement between years 2 and 5. There are limited studies for HRQoL in CRC patients undergoing adjuvant chemotherapy in Korea. Recent study including 144 Korean CRC patients reported that QoL scores during chemotherapy was lower as compared to baseline QoL or QoL after chemotherapy and lower QoL was associated with depression, symptoms, anxiety, treatment place, and occupational status. Among several factors, depression was the strongest predictive factor, suggesting that physicians need to pay attention to relieving depression in addition to physical symptoms.²⁹ In recent years, the use of molecularly targeted therapy, such as bevacizumab, cetuximab, and panitumumab, has increased in combination with 5-FU-based chemotherapy for patients with metastatic disease. Combined molecularly targeted therapy may improve QoL due to efficacy in prolonging wellness rather than negative impact on QoL.³⁰

3. QoL in long term CRC survivors

A US survey study of QoL for a representative community-based sample of individuals who have survived at least 5 year from diagnosis of CRC demonstrated that long term survivors reported a relatively uniform and high QoL, regardless of stage at diagnosis and time from diagnosis. Although physical symptoms such as diarrhea and depression remained a problem, survivors reported higher overall QoL compared to age-matched populations.³¹ The first population-based study comparing QoL among CRC survivors 1 year after diagnosis with controls from the general population showed that overall QoL and physical functioning was comparable to the controls. However, deficits in emotional and social functioning and specific limitations such as fatigue, dyspnea, insomnia, constipation, diarrhea, and financial difficulties were major factors hampering QoL in CRC patients at 1 year after diagnosis and predominantly affected younger patients.³² These deficits persisted at three years after diagnosis in patients with CRC. Improvements in QoL from the first to the third years were very modest and limited to less financial difficulties, a better future perspective and fewer stoma-related problems.³³ A recent study to evaluate the longitudinal development of QoL in CRC survivors over a 10-year period reported overall

QoL of survivors comparable to the general population irrespective of patient age or duration of follow-up. In this study, younger survivors continuously reported restrictions in several QoL dimensions throughout the entire 10-year follow-up. Meanwhile, older survivors showed comparable or even better QoL compared to the general population within the first 3 to 5 years and comparable to worse QoL 5 to 10 years after diagnosis of CRC.³⁴

HOW TO IMPROVE QOL IN CRC ?

It is important to identify CRC patients with a higher risk to have lower QoL and then correct the modifiable factors for the improvement of QoL.¹⁴ Emerging evidence suggests that lower physical activity and high body weight are associated with higher mortality and lower QoL among CRC survivors. Recent meta-analysis including seven studies reported that an increase in physical activity levels was associated with improved QoL, reduced disease-specific mortality risk, and reduced overall mortality. However, there were no positive or negative effects of weight gain on mortality, suggesting that weight gain might reflect the recovery of experienced weight loss associated with CRC, treatment, or both.³⁵ Further prospective studies with large sample size are required to clarify the effect of weight gain on QoL in CRC survivors. It has been known that exercise interventions may improve QoL, physical fitness and fatigue in mixed types of cancer patients.³⁶ However, meta-analysis of exercise interventions for CRC patients showed strong evidence for short-term improvements of physical fitness after aerobic exercise compared with controls but no evidence for short-term effects on QoL or fatigue.³⁷ Therefore, recommendation of exercise interventions as a routine intervention for CRC patients requires further well-designed prospective studies. A recent Korean study evaluated the effect of an increased level of exercise on QoL among 162 survivors of early-stage breast cancer and CRC. Exercise recommendation was to participate at least 150 minutes of moderate level physical activity per week and twice a week of strengthening exercise and exercise motivation package included exercise DVDs, a pedometer, an exercise diary, and a 15-minute exercise education session. While participants receiving only exercise recommendation did not increase their exercise participation level compared with control group, participants receiving exercise recommendation combined with an exercise motivation package significantly increased their level of exercise participation in terms of minutes and in Metabolic Equivalent of Task (MET)-hours per week.

Although there was no difference in QoL scores among the groups, participants receiving exercise recommendation combined with an exercise motivation package had significantly increased role functioning.³⁸

Increasing evidence suggests that healthy lifestyle changes including diet changes after diagnosis may affect outcomes in CRC survivors, but there are limited scientific data.³⁹ Prospective observational studies reported that Western dietary pattern characterized by high intakes of meat, fat, refined grains, and dessert,⁴⁰ high dietary glycemic load and total carbohydrate intake,⁴¹ and higher sugar-sweetened beverages intake⁴² following diagnosis have been associated with an increased risk of CRC recurrence and mortality, but these results are limited to single analyses from one of two US cohorts.⁴³ Recent meta-analysis of five prospective cohort studies including 2,330 CRC patients reported that higher serum 25-hydroxyvitamin D levels were associated with significantly reduced mortality in patients with CRC and breast cancer.⁴⁴ More recent study demonstrated that vitamin D supplementation with calcium following diagnosis in CRC survivors had a positive effect on QoL.⁴⁵ In addition, fish oil supplementation may increase symptom-related QoL (i.e. physical functioning) after diagnosis.⁴⁶ Probiotics also can improve bowel symptoms and CRC-related QoL.⁴⁷ However, future studies should evaluate what aspects of diet are most important, whether diet following diagnosis has an effect independent of diet before diagnosis, and whether the effect of dietary changes is dependent on stages of CRC or treatment.³⁹

After the diagnosis of cancer, patients and their families have considerable distress, which compounded by disruptions to normal life due to outpatient visits, examinations, hospital admission and surgery, possibly followed by adjuvant chemotherapy.⁴⁸ Lee et al.⁴⁹ reported a significant association between physical fitness and QoL and depression in 122 Korean stage II-III CRC survivors. Previous reviews reported the potential benefit of psychological intervention for cancer patients' survival, but no conclusions or recommendation regarding psychological intervention could be made.^{50,51} Two main approaches for psychological interventions are informative educational programs and psychotherapeutic interventions.¹⁴ In a randomized trial by Kuchler et al.,⁵² an individualized program of psychotherapeutic support, provided during the inpatient hospital period to patient with 271 gastrointestinal cancer patients (including 52 patients with CRC) and scheduled for surgery resulted in significant survival advantage when compared to patients not receiving program. Ten-year follow up study of the same cohort also reported better survival for the experimental group than the control group.⁵³

In addition, these interventions showed a significant improvement of adaptation and awareness in advanced CRC patients during chemotherapy, and patients appeared less anxious with a stable HRQoL.⁵⁴

CONCLUSIONS

CRC survivors usually experience only minor deficits regarding broad measure such as general health and overall QoL, at least as long as there is no serious comorbidity or recurrence when compared to the general population. However, disease recurrence, progression, and more specific limitations, including weight loss, reduction in energy, and psychosocial problems like psychological distress and depression, could result in lower QoL. To improve QoL in patients with CRC, the development of appropriate health education including lifestyle changes and personalized intervention strategies are important for CRC survivors.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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