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REVIEW ARTICLE

Quality of life after surgery for colorectal cancer: clinical implications of results from randomised trials

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Abstract
Goals of work Health-related quality of life (HRQL) is an important outcome after surgery for colorectal cancer (CRC), and accurate assessment is required to fully inform clinical decision making. The purpose of this review is to summarise randomised surgical trials in CRC with robust HRQL to consider the role of HRQL in surgical decision making.
Materials and methods A systematic review in Medline and the Cochrane Controlled Trials Register identified randomised surgical trials with HRQL. HRQL assessment was categorised as robust according to predefined criteria, and the clinical implications of HRQL were considered.
Main results One hundred seventy-seven articles were identified, and a detailed review reduced this to eight trials. Four compared laparoscopic with open surgery, and four evaluated coloanal anastomotic techniques. The most commonly used HRQL instrument was the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30, and HRQL was usually a secondary outcome measure. In four (50%) trials, HRQL assessment was categorised as methodologically robust, although only two trials had sample size calculations based upon a HRQL endpoint. Six trials based the final treatment recommendation in the context of the HRQL outcomes.
Conclusion In randomised surgical trials in CRC, HRQL assessment informs clinical decision making, and future trials require robust assessment of relevant patient-reported outcomes.

Keywords Health-related quality of life · Colorectal cancer · Surgery · Clinical decision making

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Introduction

Colorectal cancer (CRC) is one of the most common malignancies in the Western part of the world. Surgery is the mainstay of treatment, and it may be combined with preoperative radiotherapy or adjuvant chemotherapy. Although surgery offers a good chance of cure, it also has short- and long-term detrimental impacts on patients' health-related quality of life (HRQL). For several post-operative months, patients experience fatigue, pain and reduced activity levels. Many struggle with an altered bowel habit, and the patient may need to adapt to life with a permanent or temporary stoma [1, 2]. After rectal surgery, sexual and urinary dysfunction frequently occurs, and these problems may persist. The

diagnosis and treatment of CRC also has a psychosocial impact; patients worry about disease recurrence, and the combination of physical and emotional difficulties inevitably impact on social well-being. Assessment of self-reported HRQL in surgical trials is therefore important.

There are now several valid measures of HRQL suitable to use in patients with CRC [3–7]. Although these instruments are widely available, careful application of the tools in clinical studies is needed to produce reliable and clinically useful results [8, 9]. The criteria recommended for HRQL in randomised trials includes reporting of HRQL hypotheses, reasons for choice of instrument, baseline compliance and follow-up, reporting of HRQL results and analyses, as well as clinical interpretation of the data. Methods for assessing whether HRQL influences clinical decision making are also emerging. A recent review of randomised surgical trials in oncology suggested that HRQL may influence decision making in three ways: if HRQL outcomes are reported by the investigators of the trial to have influenced final treatment recommendations, if investigators reported that HRQL information was useful for informed consent and if HRQL was assessed robustly [10]. The purpose of this review is to summarise the surgical randomised trials in CRC with HRQL and to assess HRQL methodology and its role of HRQL in surgical decision making.

Materials and methods

Review methodology

Electronic searches were undertaken in June 2007 in the following databases: MedLine (March 1980–December 2006) and the Cochrane Controlled Trials Register (March 1980–December 2006) to identify the relevant trials.

Unrestricted search strategies were combined: "colorectal neoplasms or CRC or colorectal neoplasm$ or colorectal neoplasm," "rectal neoplasms or rectal cancer or rectal neoplasm$ or rectal neoplasm," "colon neoplasms or colon cancer or colon neoplasm$ or colon neoplasm" using the operator "OR." This search was then restricted to surgical trials by incorporating the following: "surgery or surg$ or operation or operable or resect$" using the operator "AND." Additionally, keywords that related to HRQL were added to the search: "quality of life," "QoL," "HRQL," "outcome assessment," "health status" and "patient reported outcome." The search was further restricted to randomised controlled trials by use of the following terms/keywords: "randomized controlled trial," "controlled clinical trial," "randomized controlled trials," "random allocation," "double blind method," "single blind method," "clinical trial," "placebo," "random," "comparative study," "follow up study" and "prospective study." The search incorporated a wild card (* or $) to identify those abstracts containing words with the stem "random." There were no restrictions in the search-field description for any of the keywords used. Studies were selected based on the criteria listed below. All candidate studies were checked for possible inclusion in the review and in addition, significant articles listed as references were included for possible inclusion.

Criteria for selecting studies

For the purposes of this review, articles meeting the following criteria were included: randomised clinical trials involving adults aged 18 years and over with colon or rectal cancer as a primary site of disease regardless of stage or grade of the tumour. Studies of patients with benign colorectal disease were not eligible. All trials evaluating surgical procedures comparing different types of surgery were eligible. Studies dealing with psychosocial interventions or interventions with chemotherapy or radiotherapy were excluded as were trials of screening and preventative studies.

Studies including assessment of HRQL as either primary or secondary endpoints were considered. HRQL was defined as the self-report of key aspects of function (e.g. physical, emotional or social health). Studies were only included if they used multi-dimensional HRQL measures with published robust psychometric properties with a minimum of two HRQL domains. A baseline assessment of HRQL was also considered essential for inclusion.

Types of studies

Randomised controlled trials (RCTs) published in English, from 1980 to 2006, were included. Publications meeting the above criteria but involving a heterogeneous sample were excluded because of difficulties in interpreting the HRQL results specifically in relation to CRC patients. Papers only reporting feasibility analyses, without giving details of results were excluded, as were abstracts from conference proceedings. Unpublished studies were not taken into account.

When more than one paper reported HRQL data from the same trial data, the initial paper that reported HRQL findings or if available the paper specifically reporting HRQL outcomes was selected. Trials that did not report both clinical and HRQL outcomes (either in the same article or in a separate analysis) were excluded.

Methods of evaluation of the studies

Two reviewers (Gujral and Blazeby) analysed all identified RCTs, unblinded for the authorship of the articles. Any discrepancy about the analysis of a study was discussed until agreement was reached. The selected trials were

evaluated on the level of HRQL reporting and HRQL methodology.

There are currently no internationally agreed standards for assessing HRQL methodology in RCTs. Authors based the evaluation of good practice for reporting HRQL studies on recommendations from the current literature. Trials were classified as having a robust HRQL design if they used a validated multi-dimensional HRQL tool, had assessed baseline HRQL and reported compliance and reasons for missing data either at baseline or during follow-up. Trials were also required to satisfy two of the following criteria: an a priori HRQL hypothesis stated, the rationale for HRQL instrument-choice reported, adequacy of domains covered, the mode of instrument administration reported, and timing of HRQL assessments documented. It was also noted whether HRQL results were presented with a discussion of their clinical significance.

Assessment of whether HRQL-influenced clinical decision making was reported in a similar fashion to an earlier systematic review [10]: Articles were categorised as having influenced clinical decisions if HRQL outcomes were reported by the investigators of the trial to have influenced final treatment recommendations, and articles were graded as to whether HRQL was assessed robustly according to pre-defined criteria described.

Results

The search on Medline and the Cochrane Controlled Trials register for surgical RCTs reporting HRQL for patients with CRC yielded 148 and 29 candidate studies, respectively. After duplicate citations and publications not fitting the inclusion criteria were eliminated, a total of eight trials were

Table 1 Methodological details of randomised trials with validated HRQL in colorectal cancer

Authors [reference]	Method of randomization stated	Informed consent reported	Inclusion criteria reported	Number of patients	Disease stage	Site	Type of intervention	HRQL primary endpoint	HRQL an inclusion criteria	Sample size calculation
Schwenk et al. [21]	No	Yes	Yes	60	Uncertain	Colon and rectum	Laparoscopic vs open surgery	Uncertain	No	No
Furst et al. [11]	Yes	Yes	Yes	74	Metastatic and local	Rectum	J-Pouch vs straight colo-anal anastomosis	Uncertain	No	No
Ho et al. [16]	Yes	Yes	Yes	88	Local, loco-regional or metastatic	Rectum	J-Pouch vs coloplasty after anterior resection	Secondary	No	No
Sailer et al. [12]	Yes	Yes	Yes	64	Local, loco-regional or metastatic	Rectum	J-pouch vs straight colo-anal anastomosis	Primary	Yes	Yes
Weeks et al. [15]	Yes	Yes	Yes	449	Metastatic and local	Colon	Laparoscopic vs open surgery	Secondary	No	Yes
Guillou et al. [13]	Yes	Yes	Yes	794	Local, loco-regional or metastatic	Colon and rectum	Laparoscopic vs open surgery	Secondary	No	Yes
Park et al. [22]	Yes	Yes	Yes	50	Local or loco-regional	Rectum	J-Pouch vs straight colo-anal anastomosis	Secondary	No	No
King et al. [14]	Yes	Yes	Yes	62	Local or loco-regional	Colon and rectum	Laparoscopic vs open surgery	Secondary	No	Yes

identified (Table 1). Of these eight trials, four evaluated laparoscopic vs open surgery, and four compared different anastomotic techniques after rectal resection. HRQL was the secondary outcome in seven trials, although not an inclusion criteria. Only two trials included more than 100 patients, and four reported a sample size calculation based on the primary clinical endpoint (Table 1).

Table 2 summarises the HRQL methodology in the trials. Four used the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 and Quality of Life Questionnaire Colorectal Module 38 [11–14]. All but one trial reported a rationale for the choice of instrument. Five of the eight studies made a statement about hypothesised HRQL outcomes. Only two trials performed sample-size calculations for HRQL outcomes [12, 15], and just two reported how the questionnaire was completed (e.g. self-report vs interview administered). Four trials were considered to be robust with respect to HRQL methodology [12–15].

The impact of clinical and HRQL outcomes in decision making in CRC is summarised in Table 3. Six of the trials addressed the clinical significance of the HRQL findings and six based final treatment recommendations in the context of HRQL outcomes, these included the four trials with robust HRQL methodology. In three of the papers, the actual HRQL data were not published, although there were descriptive statements in the text [11, 14, 16]. Of the trials comparing laparoscopic and open surgery, three trials had robust HRQL methodology [13–15]. Weeks et al. reported that laparoscopic surgery resulted in slightly better overall HRQL 2 weeks post-procedure and less pain. The small trial by King et al. reported no HRQL differences between treatment groups as did the larger UK multi-centre trial [13]. Of the trials comparing different anastomotic techniques after resection for rectal cancer, one of the four trials fulfilled criteria to be considered robust in its HRQL design [12]. This study demonstrated better short-term HRQL with J-pouch reconstruction.

Discussion

In this review, eight surgical randomised trials in CRC with HRQL were identified. In six of them (75%), the investigators reported that HRQL influenced clinical decision making. There were four trials (50%) with robust HRQL design, and although none were powered for HRQL

Table 2 Health-related quality of life methodology in RCTs in colorectal cancer

Authors [reference]	HRQL instruments	Rationale for instrument(s)	Instrument administration reported	Baseline compliance (%) reported	Missing data reported	Timing of assessments documented	HRQL sample size calculation reported	HRQL hypothesis stated	Robust HRQL design
Schwenk et al. [21]	VAS	Yes	No	No	No	Yes	No	Yes	No
Furst et al. [11]	EORTC QLQ-C30	Yes	No	66 (89%)	No	Yes	No	No	No
Ho et al. [16]	FIQL	Yes	No	No	No	Yes	No	No	No
Sailer et al. [12]	EORTC QLQ-C30, QLQ-CR38 and GIQLI	Yes	No	39 (61%)	Yes	Yes	Yes	Yes	Yes
Weeks et al. [15]	Symptom Distress Scale and QLI	No	Yes	428 (95%)	Yes	Yes	Yes	Yes	Yes
Guillou et al. [13]	EORTC QLQ-C30 and QLQ-CR38	Yes	No	562 (81%)	Yes	Yes	No	No	Yes
Park et al. [22]	FISI, FIQL scales	Yes	Yes	No	No	Yes	No	No	No
King et al. [14]	EORTC QLQ-C30 and QLQ-CR38	Yes	No	60 (97%)	Yes	Yes	No	Yes	Yes

VAS Visual analogue scale, *EORTC QLQ-C30* European Organisation For Research And Treatment Of Cancer Quality Of Life Questionnaire, *FIQL* Fecal Incontinence Quality of Life Scale, *QLQ-CR38* Quality of Life Questionnaire Colorectal Module, *GIQLI* Gastro-intestinal Quality of Life Index, *FISI* fecal incontinence severity index, *RSCL* Rotterdam Symptom Checklist

Table 3 The impact of clinical and HRQL outcomes in decision making in colorectal cancer

Authors [reference]	Clinical outcomes	Statistical significance of HRQL	HRQL outcomes	Clinical significance of HRQL considered	HRQL results presented	Clinical-decision influenced by HRQL
Schwenk et al. [21]	Significantly less analgesia required after laparoscopic surgery	Yes	Significantly less pain and fatigue after laparoscopic surgery	Yes	Yes	Yes
Furst et al. [11]	Significantly less incontinence after J-pouch at 6 months but more straining required for defecation	Yes	No significant differences	No	No	No
Ho et al. [16]	Significantly more morbidity after coloplasty	Yes	No significant differences	Yes	No	Yes
Sailer et al. [12]	No significant differences	Yes	Better HRQL with J pouch	Yes	Yes	Yes
Weeks et al. [15]	Duration of inpatient analgesia and hospital stay significantly shorter after laparoscopic surgery	Yes	Better global HRQL in laparoscopic group two weeks post-procedure	Yes	Yes	No
Guillou et al. [13]	No significant differences except that more complications after laparoscopic rectal surgery	Yes	No significant differences	No	Yes	Yes
Park et al. [22]	Significantly fewer defecations with J-pouch	Yes	HRQL significantly better after J pouch	Yes	Yes	Yes
King et al. [14]	Significantly lower analgesia and anti-emetic needs and shorter stay after laparoscopic surgery	Yes	No significant differences	Yes	No	Yes

outcomes, statistically significant differences in HRQL were reported in four of the trials. It is therefore concluded that for surgical randomised trials in CRC, HRQL outcomes are valuable to inform final decision making, and future trials require robust HRQL.

Although methods for incorporating HRQL into clinical trials are now well described, it is uncertain how to utilise HRQL outcomes alongside clinical data to reach final treatment recommendations. Where HRQL data support clinical outcomes or where there are equivalent HRQL findings between surgical treatments, then decisions will generally rest upon the clinical outcomes. Where there are better clinical outcomes (e.g. longer survival) but a detrimental impact on HRQL for some post-operative months, then the choice between surgical options will depend upon individual patient preferences and the magnitude of survival benefit vs the magnitude of HRQL impact. Although these choices can be made by patients, patients require this complex information in a format that they can understand. It is often difficult for clinicians to communicate HRQL trial outcomes to patients as they may be unfamiliar with the measures and the clinical interpretation of HRQL scores. Recently, different ways of communicating HRQL to patients with lung cancer have been tested. It was found that most patients understand simple graphical presentations of mean quality-of-life scores [17]. More work is needed to train surgeons to understand and communicate HRQL and clinical outcomes to patients.

In three of the eight trials in this review, the HRQL results were not formally presented, but the main results were described in the text. This may have occurred because of lack of journal space for each article, and some authors have overcome this difficulty by separately reporting clinical and HRQL trial outcomes [18, 19]. The disadvantage of splitting the HRQL data from the main trial paper is that surgeons are unlikely to read the HRQL paper once the main clinical message of a particularly trial has been published. If this occurs, then during the process of clinical decision making the HRQL impacts of treatment may be overlooked. It is therefore recommended that clinical and HRQL outcomes are published together so that clinical decision making is based upon relevant patient-centered endpoints.

Although this review identified surgical randomised trials in CRC, it did not include trials of neoadjuvant or adjuvant surgical therapies or trials of palliative treatment. A comprehensive review of randomised controlled clinical trials of palliative chemotherapy for CRC has recently been published [20]. This review identified 28 papers, and the importance of HRQL vs prolongation of life was evaluated.

In general, prolongation of life was a more important outcome than HQRL in patients with advanced CRC. It was also noted that the primary endpoints almost always considered prolongation of life outcomes rather than HRQL or toxicity endpoints.

In summary, this review of surgical randomised trials with HRQL found that 50% of trials had robust HRQL methodology and HRQL did influence final treatment decisions in most of the studies. For trials comparing laparoscopic with open surgery for CRC, recovery and HRQL seem particularly important endpoints, and careful assessment of patient reported outcomes at specific time points is needed to demonstrate advantages to patients of minimal access surgery. Future work training clinicians to understand the clinical interpretation of HRQL outcomes in randomised trials is required to ensure that treatment decision making is based upon HRQL outcomes as well as survival data.

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