Original article

Prospective analysis of quality of life and survival following mesorectal excision for rectal cancer

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Background: Little is known of how the quality of life of patients with rectal cancer changes after surgery, and whether or not quality of life is associated with and predictive of survival. The aims of this study were to address these issues.
Methods: The Medical Outcomes Study Short Form 36 (SF-36), and the European Organization for the Research and Treatment of Cancer QLQ-C30 and QLQ-CR38 quality of life questionnaires were administered to patients before surgery for rectal cancer, on discharge home and at 3-month intervals after operation for up to 1 year. Survival was measured in days from the time of surgery to death.
Results: Sixty-five patients with a median age of 67 years participated. Most quality of life scores dropped significantly below baseline in the early postoperative period. From the third month onwards some scores, such as the global quality of life score and emotional function score on the QLQ-C30, improved. Other scores, including role function, fatigue and pain on the QLQ-C30, were similar to baseline values after 3–6 months and remained unchanged. However, scores such as sexual enjoyment and male sexual problems on the QLQ-CR38 were worse than baseline in the early postoperative period and remained poor thereafter. Stepwise regression analyses showed that preoperative quality of life dimension scores for physical function, nausea/vomiting and sexual enjoyment, together with age, predicted postoperative 1-year survival with an accuracy of 76·8 per cent.
Conclusion: The findings of this study confirm that quality of life after rectal cancer surgery changes with time. It is generally worst in the early postoperative period. Preoperative quality of life is a good predictor of survival at 1 year.

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Introduction

Rectal cancer and the consequences of rectal surgery and adjuvant treatment have an important bearing on a patient's quality of life[1]. Quality of life assessment is regarded an important outcome measure in addition to traditional endpoints such as tumour recurrence and survival[2]. However, although quality of life is dynamic, little is known about how the quality of life of patients with rectal cancer changes with time after surgery.

Some studies have shown that quality of life scores may predict survival[3–9]. These studies involved patients who were having chemotherapy or best supportive care for advanced malignant disease. No studies have been done to determine the prognostic significance of preoperative quality of life scores for survival in primary rectal cancer.

This paper describes a prospective analysis of the quality of life of patients with rectal cancer undergoing resection of the primary tumour. The main aim was to determine how the quality of life of patients having surgery for rectal cancer changes with time. A subsidiary aim was to determine to what extent preoperative sociodemographic and clinical variables and quality of life scores predict survival at 1 year after surgery.

Patients and methods

From September 1997 to April 1999, 82 patients with cancer of the rectum or rectosigmoid junction were scheduled for elective rectal resection at Ninewells Hospital, Dundee. The patients were considered to be eligible for the study if they had primary adenocarcinoma of the rectum or rectosigmoid junction that was locally resectable. Patients with locally recurrent cancer, with multifocal colorectal cancer or who suffered from another malignancy were excluded. Three patients were considered

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Table 1 Demographic and clinical details of participating patients who had surgery for rectal cancer

Median (range) age (years)	67 (44–84)
Men	45
Women	20
ASA grade	
I	17
II	40
III	8
Deprivation categories	
1 and 2 (affluent)	30
3, 4 and 5	27
6 and 7 (deprived)	8
Dukes' stage of rectal cancer	
A	16
B	14
C	28
'D' (liver metastases)	7
Type of operation	
Anterior resection	21
Anterior resection + ileostomy	26
Abdominoperineal resection	18
Mesorectal excision	
Partial	19
Total	46
Adjuvant treatment	
Preoperative radiotherapy	8
Postoperative radiotherapy	9
Postoperative chemotherapy	26
Cryotherapy of liver metastases	3

ASA, American Society of Anesthesiologists

to be ineligible at this stage. The remaining 79 patients were then contacted and invited to participate in the study. Seventy-two patients agreed to participate, giving their full informed consent. The study was approved by the Tayside Committee on Medical Research Ethics.

Those who accepted were given three quality of life questionnaires in the week before surgery: the European Organization for Research and Treatment of Cancer QLQ-C30[10] and QLQ-CR38[11] and the Medical Outcomes Study Short Form 36 (SF-36)[12]. Seventy patients filled in a baseline questionnaire. Quality of life was also assessed on discharge home (early postoperative assessment), and at 3, 6, 9 and 12 months after operation.

The QLQ-C30[10] is a cancer-specific questionnaire covering a wide range of dimensions that are relevant to any patient with cancer. Levels of functioning in various areas, such as physical and emotional, and symptoms such as pain and fatigue, are assessed. In addition there is a global quality of life scale which is used as the overall summary measure of quality of life. The colorectal cancer module, the QLQ-CR38[11], addresses areas of particular relevance to patients with colorectal cancer, such as gastrointestinal, defaecation and stoma-related problems, sexuality and image. The SF-36[12] is a generic, multidimensional questionnaire that was designed to measure health-related quality of life in various clinical settings and to be applicable across social and demographic groups.

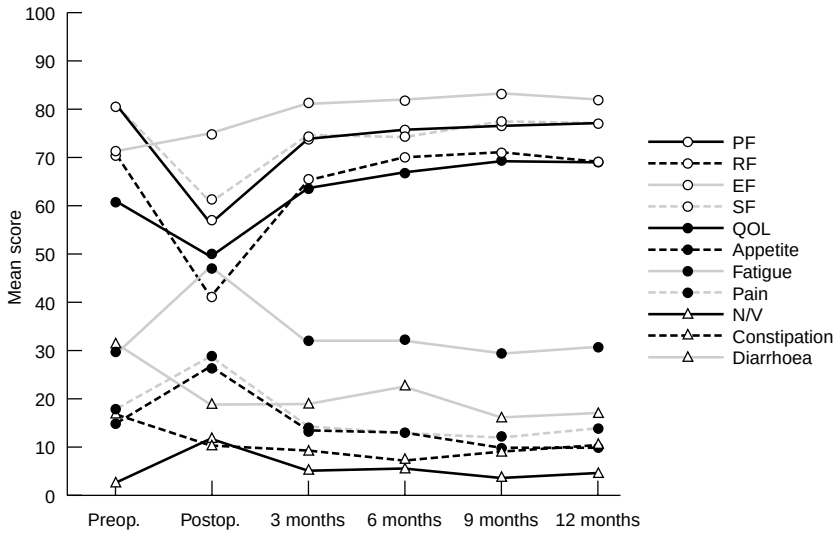

Fig. 1 Quality of life profiles of all patients treated for rectal cancer, QLQ-C30 questionnaire. Values are mean scores. Higher scores for functional scales (physical function (PF), role function (RF), emotional function (EF) and social function (SF)) and global quality of life scale (QOL) represent a higher level of functioning and quality of life, while higher scores for symptom scales (fatigue, nausea and vomiting (N/V), appetite, pain, constipation and diarrhoea) represent a higher level of symptoms. Preop., preoperative; postop., postoperative

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Details regarding age, gender, deprivation category (a measure of socioeconomic status based on the postcode)[13], American Society of Anesthesiologists (ASA) score, Dukes' stage of tumour, operation type, and neoadjuvant and adjuvant treatment were collected. The patients were followed up for 1 year. Survival was measured in days from the time of surgery to death.

Statistical analysis

The non-parametric Friedman's two-way analysis of variance test was used to identify any overall significant differences between the scores at different time points for each dimension. When the overall *P* value was significant, a Wilcoxon signed rank test for paired data was used to compare pairs of quality of life scores. Survival curves were estimated by the Kaplan–Meier method, using the log rank test to assess the significance of differences. Kendall's correlation was used to assess correlations between variables. A stepwise regression analysis was used to establish which variables best predicted survival. A 2 per cent level of significance was chosen ($P < 0{\cdot}02$) to reduce the risk of type I errors arising from multiple testing. Statistical analyses were carried out using SPSS version 9.0 (SPSS, Chicago, Illinois, USA).

Results

Of the 70 patients who answered the questionnaires, five were excluded from the study. The total number of eligible participants was thus 65 (*Table 1*). Forty-six patients had rectal excision using the technique of total mesorectal excision[14]. In the other 19 patients partial mesorectal excision with a lower excision margin of at least 5 cm was performed. Eight participants (all men) died during the first year after operation.

General trends in quality of life changes with time

The results are shown in *Fig. 1* (QLQ-C30), *Fig. 2* (QLQ-CR38) and *Fig. 3* (SF-36). In the early postoperative assessment (on discharge home) the scores of most quality of life dimensions were significantly worse than baseline values. By 3–6 months after operation most scores had returned to baseline levels. Some scores, such as global quality of life score and emotional function (QLQ-C30) were significantly better than baseline values. Some areas of quality of life, however, such as sexual enjoyment, male sexual problems and perception of body image (QLQ-CR38) were significantly worse at each postoperative assessment compared with baseline.

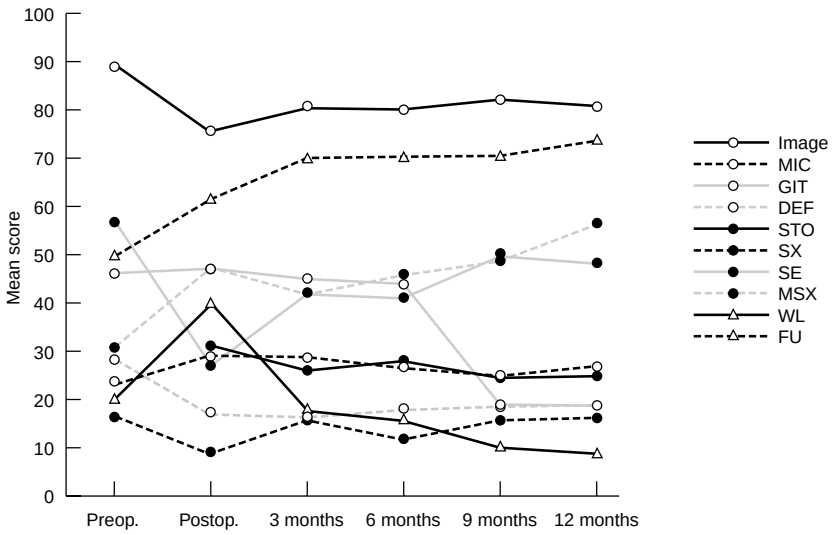

Fig. 2 Quality of life profiles of all patients treated for rectal cancer, QLQ-CR38 questionnaire. Values are mean scores. Higher scores for functional scales (body image perception (image), sexual function (SX), sexual enjoyment (SE) and future perspective (FU)) represent a higher level of functioning, while higher scores for symptom scales (micturition problems (MIC), gastrointestinal tract problems (GIT), defaecation-related problems in patients who had anterior resection without an ileostomy (DEF), stoma-related problems in patients who had an abdominoperineal resection (STO), male sexual problems (MSX) and weight loss (WL)) represent a higher level of symptomatology. Preop., preoperative; postop., postoperative

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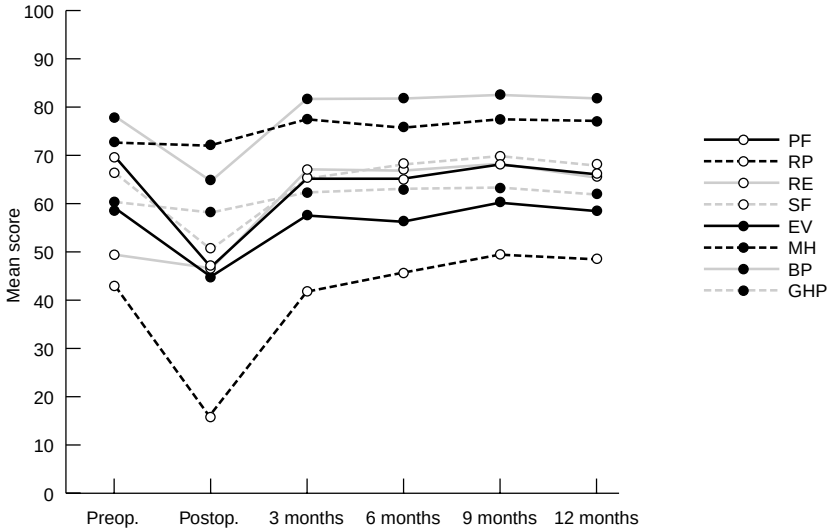

Fig. 3 Quality of life profiles of all patients treated for rectal cancer, Short Form 36 questionnaire. Values are mean scores; the higher the score, the better the quality of life. PF, physical functioning; RP and RE, role limitations because of physical and emotional problems respectively; SF, social functioning; EV, energy and vitality; MH, mental health; BP, body pain; GHP, general health perception; preop., preoperative; postop., postoperative

Correlation with survival

A positive correlation was present between survival and preoperative physical function (PF) (QLQ-C30) (Kendall's coefficient t = 0·37), PF (SF-36) (t = 0·30), social function (SF-36) (t = 0·22), mental health (SF-36) (t = 0·23) and energy/vitality (SF-36) (t = 0·23). There was a negative correlation between survival and age (t = – 0·27), preoperative ASA status (t = – 0·30), preoperative fatigue (QLQ-C30) (t = – 0·22) and dyspnoea (QLQ-C30) (t = – 0·42). There was no correlation between Dukes' stage and survival at 1 year.

Prediction of survival

The overall probability of survival at 1 year after elective surgery for primary rectal cancer was 0·88 (95 per cent confidence interval 0·80–0·96). Stepwise multiple regression analysis showed that preoperative ASA score and gender could explain 15·4 per cent of the variation in survival (adjusted R^2 = 0·154). There was a difference in survival (log rank 3·87, P = 0·049) between male and female patients. Dukes' stage of tumour was not predictive of survival at 1 year.

Stepwise multiple regression analysis was also done using quality of life scores alone as independent variables. The domains of preoperative PF, pain and appetite (all QLQ-C30), and pain (SF-36) could explain 39·4 per cent of the variation in survival (adjusted R^2 = 0·394). Other quality of life domains did not give a significant contribution. There was a significant difference in survival (log rank 15·5, P < 0·001) between patients with a preoperative PF (QLQ-C30) score of 60 or less and patients with a score of more than 60 (*Fig. 4*). A patient with a PF score of 60 or less is either housebound or is limited to short walks outside the

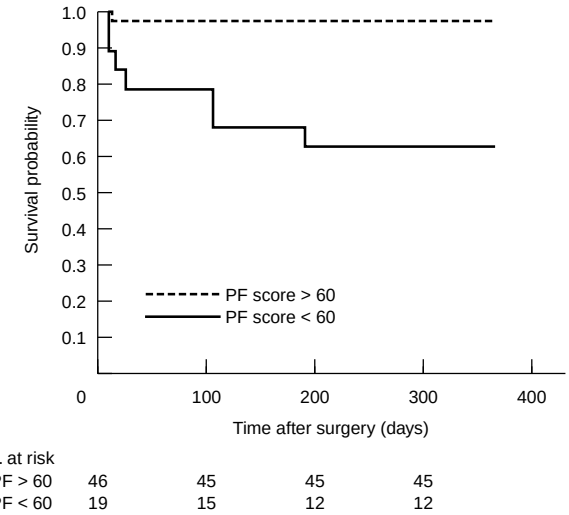

Fig. 4 Kaplan–Meier curves comparing the probability of surviving 1 year after surgery for rectal cancer between patients with a physical function (PF) score of more than 60 and patients with a PF score of 60 or less (log rank 15·5, P < 0·001)

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Table 2 Model that best predicts 1-year survival after surgery for rectal cancer

Step	Variable	R	R^2	Adjusted R^2
1	Physical function (QLQ-C30)	0·628	0·394	0·361
2	Nausea/vomiting (QLQ-C30)	0·801	0·642	0·599
3	Age	0·857	0·734	0·685
4	Sexual enjoyment (QLQ-CR38)	0·904	0·817	0·768

house. On the other hand, a score of more than 60 represents a good PF, with the patient able to carry out at least moderately strenuous activities such as walking for long distances.

Stepwise multiple regression analysis was repeated using survival as the outcome variable and sociodemographic, clinical and preoperative quality of life variables as independent variables. The results showed that preoperative PF and nausea and vomiting (both QLQ-C30), sexual enjoyment (QLQ-CR38) and age could explain 76·8 per cent of the variation in survival (adjusted R^2 = 0·768) (*Table 2*) .

Discussion

The patients in this study are representative of patients with rectal cancer attending a typical colorectal cancer unit in the UK. Trends for each dimension of quality of life in three questionnaires (QLQ-C30, QLQ-CR38 and SF-36) were studied. In general, the scores of many quality of life dimensions were lower than baseline in the early postoperative period. This was expected, especially in those dimensions that assessed physical performance such as physical function, role-physical and fatigue. Patients were in the convalescent period of major surgery, and they were also slowly adjusting themselves to a stoma (colostomy or ileostomy) or to a neorectum. Surgery also restricted the social life of these patients for the first few months. By 3–6 months most scores had returned to baseline (preoperative) values. The scores of most dimensions then remained similar to baseline, although some, such as the global quality of life score and emotional function, improved with time. On the other hand, other scores, including perception of body image, were worse than baseline for the whole year after operation. Poor perception of body image may have resulted from the difficulty in accepting a stoma or abdominal scars[15], although improved emotional function, mental health and future perspective reflect a positive and optimistic attitude despite disfiguring surgery.

There was a gradual return to normal bowel function over a period of 1 year, with diarrhoea being significantly improved at 9 and 12 months. Gastrointestinal problems, such as abdominal pain and bloatedness, improved from the third month onwards. Defaecation-related problems in patients who had a high anterior resection improved significantly with time, consistent with other results reported in the literature for this group of patients[1]. Patients with a permanent colostomy experienced a slight but non-significant improvement in stoma-related problems with time. Sexual function and sexual enjoyment deteriorated in the postoperative period and the latter remained poor over the year of assessment. Male sexual problems were likewise increased. Micturition problems also increased after operation, but improved to preoperative levels by 6 months. Sexual and urological problems usually occur because of damage sustained to the pelvic autonomic nerves and pelvic floor during dissection of the rectum[16], although attempts were made to minimize this by using the technique of total mesorectal excision and nerve preservation described by Heald and Ryall[14]. Pelvic radiotherapy may also have a detrimental effect[17,18]. However, part of the problem of postoperative sexual dysfunction may be psychological[15], and related to increasing age[19].

Quality of life scores have been shown to be predictors of survival in patients with advanced disease having palliative treatment[3–9]. However, the present study is the first to demonstrate the prognostic significance of preoperative quality of life scores for survival in primary rectal cancer. The combination of sociodemographic and clinical variables with quality of life scores gave a model that could predict 1-year survival with an accuracy of 76·8 per cent. Earlam and colleagues[7] similarly derived a model with an accuracy of 74 per cent for predicting survival, but in patients with advanced colorectal disease undergoing chemotherapy. Preoperative PF on the QLQ-C30 was a particularly important predictor of survival, and patients with a PF score of more than 60 had a significantly better survival than those with lower scores. Sexual enjoyment scores were also predictive of survival. High sexual enjoyment scores were associated with a younger age group and a good PF. On the other hand, preoperative nausea and vomiting and appetite loss conferred a survival disadvantage. These symptoms could indicate early bowel obstruction caused by the rectal cancer, which could have been a contributory factor in patients' deaths. It is of interest that, in the short term, these quality of life factors were more important than tumour staging in predicting survival. This observation is almost certainly related to duration of follow-up, but highlights the potential usefulness of quality of life assessments.

This study has demonstrated clearly that the quality of life of patients with rectal cancer is dynamic. Studies in other areas of surgical oncology, such as following resection of oesophageal carcinoma[20] and gastric cancer[21], support

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the importance of longitudinal assessment of quality of life. The measurement of the quality of life of individual patients is seldom done at present as part of routine surgical practice[22], but this should change. Quality of life measurement may help to identify those areas, before and after surgery, that may have been affected by the disease or by its treatment so that intervention may be directed towards improving specific areas of quality of life. In addition, assessment of quality of life gives valuable prognostic information, not only in patients with advanced disease but also in patients with mainly primary disease treated actively in a routine hospital setting. The availability of such information may help the surgeon when obtaining informed consent from patients before major surgery for rectal cancer.

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