Original article

Quality-of-life outcomes following pelvic exenteration for primary rectal cancer

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Background: **For patients with locally advanced tumours and contiguous organ involvement, pelvic exenteration (PE) can offer cure with relatively low mortality. The literature surrounding quality of life (QoL) in patients undergoing PE is limited. Furthermore, there are no matched comparisons of QoL between abdominoperineal resection (APR) and PE. The aim of this study was to compare differences in long-term QoL for patients with primary rectal cancer undergoing APR *versus* PE.**

Methods: **All patients who underwent either APR or PE between January 2011 and December 2012 were identified. Patients were asked to complete the European Organization for Research and Treatment of Cancer QLQ-C30 questionnaire before surgery and 2 weeks afterwards. Subsequent questionnaires were requested at 3, 6, 12 and 24 months after operation.**

Results: **A total of 110 patients were included in the study (54 APR, 56 PE). Median length of stay following operation was 11 (range 3–70) days for APR and 15 (7–84) days for PE. Patients undergoing PE experienced lower physical (mean score 42 *versus* 56; $P = 0{\cdot}010$), role (20 *versus* 33; $P = 0{\cdot}047$), emotional (57 *versus* 73; $P = 0{\cdot}010$) and social (34 *versus* 52; $P = 0{\cdot}005$) functional levels 2 weeks after surgery. Long-term dyspnoea and financial worries were experienced only after PE. Patients undergoing PE had a lower overall global health status at 2 weeks after operation (40 *versus* 53; $P = 0{\cdot}012$). Levels were comparable between groups from 3 months after surgery.**

Conclusion: **QoL recovery following PE was equivalent to that after APR alone. Patients should not be denied exenterative surgery based on perceived poor QoL.**

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Introduction

The management of locally advanced rectal cancer is challenging. The goals of surgery are to improve overall survival while maintaining a patient's quality of life (QoL)[1]. Abdominoperineal resection (APR) provides a means of curative resection for distal rectal tumours where sphincter preservation is not possible. Pelvic exenteration (PE) can offer cure with relatively low morbidity and mortality for patients with locally advanced tumours and contiguous organ involvement[2,3].

Differences in postoperative QoL between patients undergoing anterior resection *versus* APR have been studied previously[4,5]. Anterior resection can be considered the less aggressive of the two procedures, and it is therefore not surprising that patients experience a higher QoL after this operation[4,5]. The literature surrounding QoL in patients undergoing PE is limited by heterogeneous data, small samples sizes and short follow-up[6,7]. Furthermore, there remain no similar matched comparisons of QoL between APR and PE.

QLQ-C30 is a validated cancer-specific questionnaire designed by the European Organization for Research and Treatment of Cancer (EORTC)[8]. The questionnaire comprises 30 questions assessing 15 different QoL categories. The aim of this study was to evaluate and compare differences in long-term QoL after APR *versus* PE for primary rectal cancer.

Methods

All consecutive patients undergoing APR or PE between January 2011 and December 2012 were included in the

study. Patient demographics, tumour characteristics, intraoperative details and postoperative outcomes were collected from a pelvic oncology unit database, and verified alongside theatre records and hospital patient management systems.

Patients were staged with CT at presentation. MRI was used for assessment of contiguous organ involvement, with further endorectal ultrasonography and examination under anaesthesia as necessary. All patients were discussed at multidisciplinary team meetings for consideration of operability and requirement for neoadjuvant therapy. Indications for neoadjuvant chemoradiotherapy (CRT) were a threatened circumferential resection margin (CRM) or extensive nodal disease[9].

Posterior pelvic exenteration (PPE) was defined as *en bloc* resection of the rectum with or without the reproductive organs (prostate, seminal vesicles, uterus, vagina, cervix) and regional lymph nodes. Total pelvic exenteration (TPE) was defined as complete resection of the rectum (with or without sphincter preservation), genitourinary viscera, reproductive organs and regional lymph nodes[10–12].

Histopathology for all patients was reviewed. A negative CRM was defined by a clear margin of 1 mm or more, and a positive CRM by tumour less than 1 mm from the margin. Data on pathological node status for all patients were collected.

QLQ-C30 (version 3.0)

Patients were asked to complete the QLQ-C30 questionnaire at baseline (preadmission appointment) and 2 weeks after surgery. Subsequent questionnaires were requested at 3, 6, 12 and 24 months following surgery. Data were initially collected on all pelvic tumour types before a subset analysis of patients with primary rectal cancer. For these purposes, the generalizability of the QLQ-C30 was chosen at the start of the study without the colorectal-specific module (QLQ-CR38) being used.

The QLQ-C30 comprises 30 individual questions that can be categorized into five functional scales (physical, role, emotional, cognitive, social), three symptom scales (pain, fatigue, nausea and vomiting), six individual symptom items (insomnia, dyspnoea, appetite, constipation, diarrhoea, financial worries) and an overall global health status scale. For scales that comprised two or more items, a raw score was calculated by taking the mean of all scores within that scale. The six individual items did not require an average and so the numerical value for each was carried forward as the raw score. Linear transformation was then applied as described in the EORTC protocol, to standardize all raw scores into a value ranging between 0 and 100[13]. A higher score reflected a higher level of functioning, or a higher frequency of symptoms. Missing data were handled using the EORTC imputation model[13].

Statistical analysis

All questionnaire results are presented as mean(s.d.). Baseline characteristics were compared using χ^2 test for nominal data and independent-samples *t* test for continuous variables. Comparison of patient scores between baseline and subsequent time intervals was performed using the Wilcoxon signed-rank test. Comparison of patient groups within time intervals was carried out using the Mann–Whitney *U* test. Survival rates were calculated by the Kaplan–Meier method and compared by means of the log rank test. All statistical analysis was done using SPSS® version 20 (IBM, Armonk, New York, USA).

Results

A total of 123 patients were identified over 2 years. Three patients declined the invitation before surgery and ten patients with recurrent tumours were excluded. The

Table 1 Baseline characteristics of patients

	Abdominoperineal resection ($n = 54$)	Pelvic exenteration ($n = 56$)	P†
Median age (years)*	70 (50–89)	64 (31–88)	0·014‡
Sex ratio (M : F)	37 : 17	19 : 37	0·001
Neoadjuvant therapy			0·554
No	31	29	
Yes	23	27	
Myocutaneous flap perineal reconstruction			0·001
No	36	14	
Yes	18	42	
Postoperative histology			0·002
yp/pT4	4	21	
yp/pT3	23	20	
yp/pT2	19	11	
yp/pT1	8	4	
Node status			0·304
Negative	36	32	
Positive	18	24	
Circumferential resection margin			0·537
Negative	52	55	
Positive	2	1	
Adjuvant chemotherapy			0·114
No	34	43	
Yes	20	13	
Postoperative complication			0·136
No	45	40	
Yes	9	16	
Length of hospital stay (days)*	11 (3–70)	15 (7–84)	0·080‡

*Values are median (range). †χ^2 test, except ‡independent-samples *t* test.

remaining 110 patients were included in the study. The cohort consisted of 56 men and 54 women with a median age of 68 (range 31–89) years (*Table 1*).

Operative details

A total of 54 patients had APR and 56 underwent PE (38 PPE, 18 TPE). Perineal reconstruction with a myocutaneous flap was carried out in 60 patients.

Morbidity and mortality

Median length of stay following operation was 11 (range 3–70) days for APR and 15 (7–84) days for PE. A total of 25 patients (22·7 per cent) developed postoperative complications, nine following APR and 16 after PE (*Table 2*). The overall rate of return to theatre was 2·7 per cent. No deaths occurred within 30 days of surgery. Disease-free

Table 2 Postoperative complications

Grade of complication*	Abdominoperineal resection	Pelvic exenteration
I	2	4
II	2	6
III	4	6
IV	1	0
V	0	0

*Dindo–Demartines–Clavien classification[14].

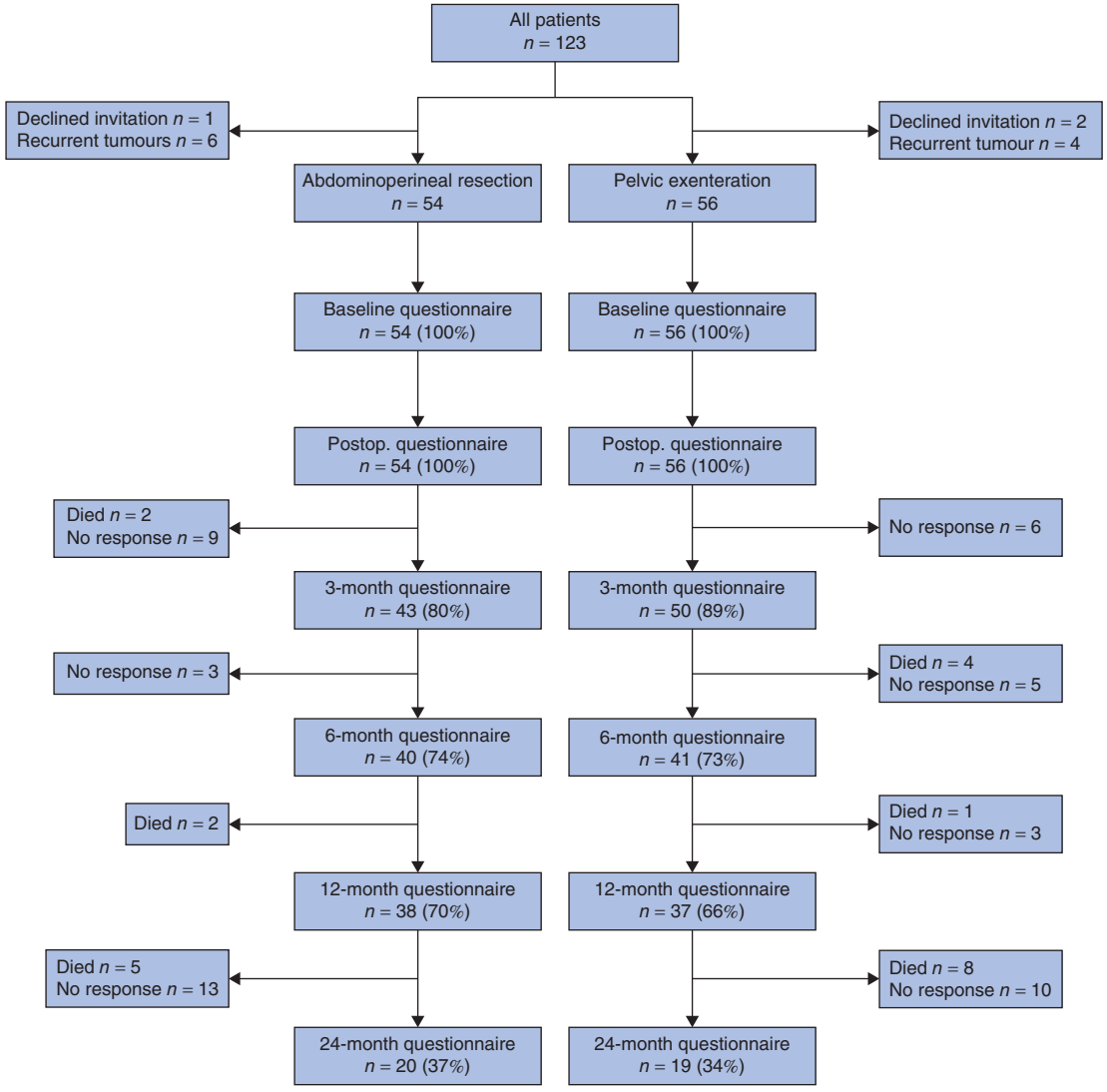

Fig. 1 Patient questionnaire completion rates

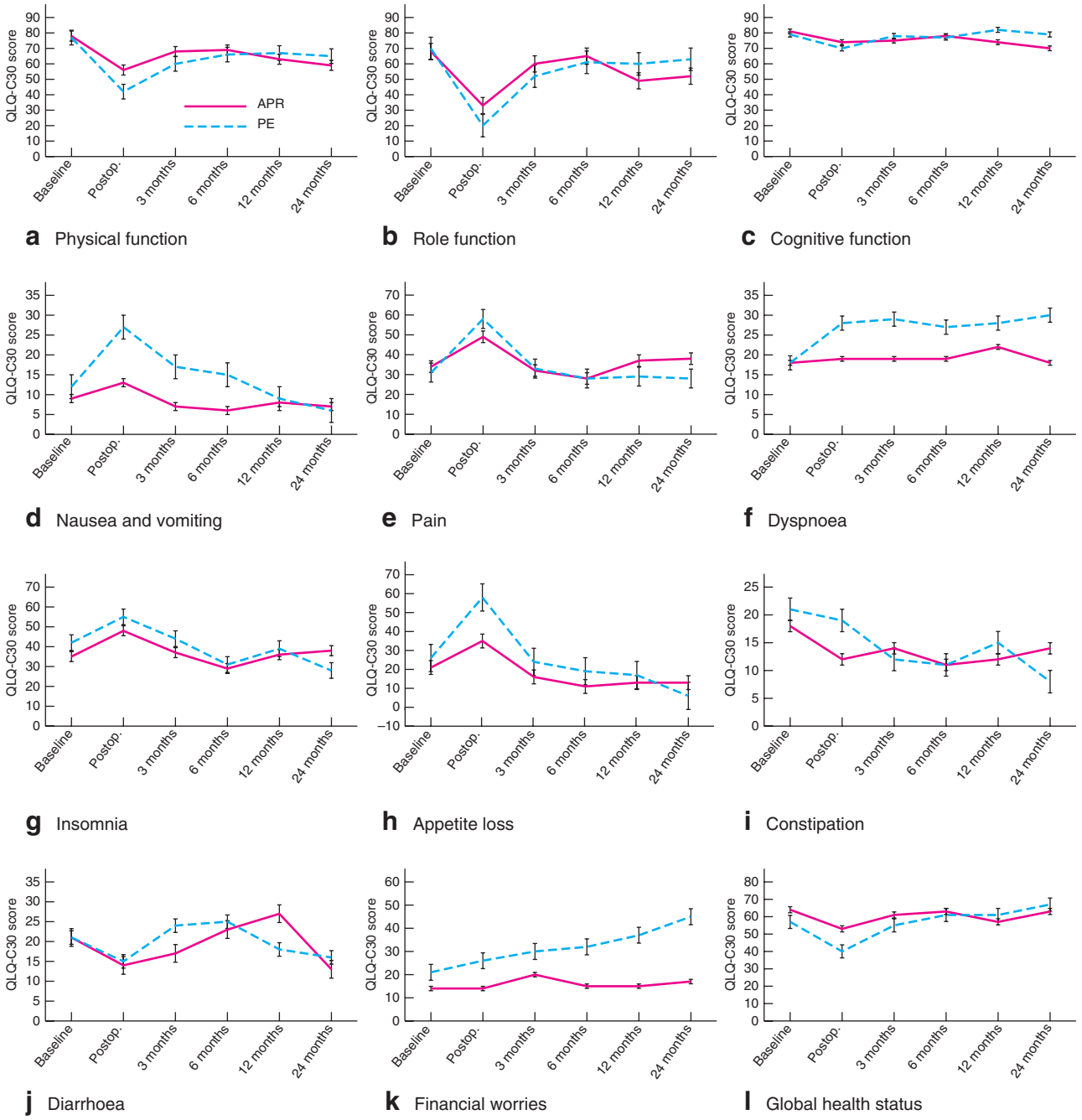

Fig. 2 European Organization for Research and Treatment of Cancer QLQ-C30 patient scores before and after abdominoperineal resection (APR) and pelvic exenteration (PE) on **a** physical function, **b** role function, **c** cognitive function, **d** nausea and vomiting, **e** pain, **f** dyspnoea, **g** insomnia, **h** appetite loss, **i** constipation, **j** diarrhoea, **k** financial worries and **l** global health status scales. Values are mean(s.d.). A higher score on function scales indicates a higher level of functioning, a higher score on symptom scales indicates an increased frequency of symptoms, and a higher score for financial worries indicates increased difficulties[8,13]. A fuller version of this figure can be found in the Supporting Information (*Fig. S1*)

survival rates at 24 months were 82 per cent for APR and 73 per cent for PE. Overall survival rates at 24 months were 83 and 77 per cent respectively ($P = 0{\cdot}333$).

Quality of life

At baseline and 2 weeks after surgery, a 100 per cent questionnaire response rate was achieved in both groups. At 12 months, response rates were 70 per cent (APR) and 66 per cent (PE). Full completion of all six questionnaires was achieved in 20 of 45 (APR) and 19 of 43 (PE) of patients alive after 2 years (*Fig. 1*). Non-responders were contacted by telephone, but declined further participation.

Functional scales

Patients undergoing PE experienced a significant drop in physical and role function up to 24 months after operation. Long-term role function was not affected significantly following APR, and physical function returned to normal levels by 24 months. Social function failed to return to normal in both groups by 24 months. In comparison with APR, patients undergoing PE experienced a significantly lower physical ($P = 0{\cdot}010$), role ($P = 0{\cdot}047$), emotional ($P = 0{\cdot}010$) and social ($P = 0{\cdot}005$) functional level 2 weeks after operation. This difference between groups disappeared as early as 3 months after surgery. No differences in cognitive function were identified between groups (*Fig. 2*; *Table S1*, supporting information).

Symptom and single-item scales

Pain, insomnia, appetite, and nausea and vomiting returned to normal levels for both procedures following the initial postoperative period. No differences in symptoms of diarrhoea were identified. Symptoms of constipation decreased up to 3 months (APR) and 6 months (PE) after operation, whereas increased fatigue persisted until 12 months in both groups. Long-term dyspnoea and financial worries were experienced only after PE.

Scores for loss of appetite ($P = 0{\cdot}002$), fatigue ($P = 0{\cdot}002$), pain ($P = 0{\cdot}034$) and nausea and vomiting ($P = 0{\cdot}001$) were higher for PE than APR 2 weeks after surgery. Levels were comparable from 3 months for appetite, pain and fatigue, but nausea and vomiting remained significantly worse until 6 months after PE. Financial worries were significantly greater in patients undergoing PE at 6 months ($P = 0{\cdot}016$), 12 months ($P = 0{\cdot}041$) and 24 months ($P = 0{\cdot}049$). There were no differences between groups for symptoms of constipation, diarrhoea, dyspnoea or insomnia.

Global health status

Patients undergoing APR experienced a significant drop in global health status after surgery ($P = 0{\cdot}004$), but by 3 months there was no significant difference compared with baseline ($P = 0{\cdot}316$) and this was maintained up to 2 years ($P = 0{\cdot}959$). A similar pattern was noted following PE, with a significant drop only at 2 weeks after surgery ($P = 0{\cdot}002$). In comparison of procedures, there was a significant difference only at 2 weeks ($P = 0{\cdot}012$), with patients undergoing PE experiencing lower global health status.

No significant differences in global health status were identified up to 24 months after in patients receiving either neoadjuvant ($P = 0{\cdot}422$) or adjuvant ($P = 0{\cdot}758$) therapy compared with surgery alone. Patients undergoing either PPE or TPE within the exenteration group showed no differences in global health status up to 24 months ($P = 0{\cdot}703$).

Patients aged 68 years (median age) or less experienced a significantly lower global health status 2 weeks after both APR ($P = 0{\cdot}006$) and PE ($P = 0{\cdot}004$) compared with baseline for the respective procedure; this change was not observed among older patients. In a comparison of operations, age was again significant only at 2 weeks after surgery, patients aged 68 years or less following PE faring worse than their counterparts after APR ($P = 0{\cdot}038$). Patients experiencing a postoperative complication had a significantly lower global health status at 2 weeks after surgery following both APR ($P = 0{\cdot}036$) and PE ($P = 0{\cdot}044$) compared with baseline for the respective procedure, but this did not persist beyond 3 months. In a comparison of APR and PE procedures following a complication, no differences were identified at this 2-week interval ($P = 0{\cdot}451$).

Discussion

This longitudinal observational study demonstrated that patients undergoing PE can expect a postoperative QoL similar to those undergoing APR.

The majority of differences in symptoms and functional outcomes fell within the 2-week postoperative time interval, which is not surprising given that PE is the more aggressive of the two procedures. As early as 3 months after surgery, the experiences of the two groups were almost identical. After this time, only nausea and vomiting (6 months) and financial worries (24 months) remained significantly different. Worse nausea and vomiting have been reported following anterior resection compared with APR[15]. It is therefore surprising to find that these symptoms were again less frequent after APR than PE. The increase in financial worries reported after PE is likely to be explained by difficulties experienced by these relatively young patients in returning to full-time employment, compounded by persistently high levels of fatigue.

The excellent results for PE in terms of early recovery for the majority of domains reflect the authors' careful selection policy for this aggressive procedure. The units considers not only the patient's physiological reserve but also their psychological status and motivation for recovery. The present findings reinforce the importance of this global assessment during the evaluation for surgery.

Preoperative CRT has been shown previously to have a negative impact on QoL and, more specifically, gastrointestinal symptoms[16–18]. In contrast, the present study found that patients undergoing CRT could expect a QoL similar to that of patients proceeding directly to surgery. Adjuvant chemotherapy has similarly been shown to have a negative impact on QoL, with younger patients affected more than the elderly population[19–21]. The median age in this study was 68 years, and interestingly chemotherapy did not have any influence on patient-reported QoL.

The present results are more encouraging than previous work[22] highlighting that patients can take up to 6 months to recover their preoperative QoL following exenteration. Other studies were limited by measuring QoL at only one time point following surgery, making any significant conclusions difficult[6]. The results of Young and colleagues[7] concurred with the present finding that patients experience a significant decline in QoL in the initial postoperative period after PE. In their cohort, QoL parameters returned to baseline by 9 months, considerably longer than demonstrated here.

This study assessed QoL prospectively at regular time intervals for up to 24 months following PE. Previous studies[7,22] have matched exenteration only with inoperable patients or palliative care, whereas the present study offers a balanced comparison with a second non-sphincter-preserving procedure. A recent Cochrane review[23] concluded that comparative studies following rectal cancer resection need to be larger and better executed in order to achieve firm assumptions[23]; the present study goes some way to addressing these concerns.

A limitation of the study is the lack of a disease-specific QoL measure[24]. The data were initially collected over 2 years for all patients undergoing APR and PE, to include gynaecological and urological malignancies. As this comprised a variety of pelvic tumour types, a generalized cancer questionnaire tool was chosen at the outset. The focus of the present study was the subset analysis of patients with primary rectal cancer.

This study has shown that QoL scores after PE are similar to those following APR. The use of CRT and adjuvant therapy did not influence postoperative QoL. These data will help counsel patients about recovery times.

Disclosure

The authors declare no conflict of interest.

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Supporting information

Additional supporting information may be found in the online version of this article:

Table S1 European Organization for Research and Treatment of Cancer QLQ-C30 questionnaire scores (Word document)

Fig. S1 European Organization for Research and Treatment of Cancer QLQ-C30 patient scores before and after abdominoperineal resection and pelvic extenteration (Word document)