



Evaluating the impact on quality of life of chemoradiation in gastric cancer

Z. Kassam MBBS MSc, *† H. MacKay MBChB MD, †‡
 C.A. Buckley RN BScN, * S. Fung, †§
 M. Pintile MSc, †§ J. Kim MD, *† and
 J. Ringash MD MSc *†

ABSTRACT

Objective

Our phase I study prospectively evaluated quality of life (QOL) in patients undergoing adjuvant chemoradiation for gastric adenocarcinoma.

Methods

Thirty-three patients receiving radiotherapy (45 Gy in 25 fractions), together with 12 weeks of infusional 5-fluorouracil and escalating doses of cisplatin every 2 weeks, completed the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 at five time points: baseline, completion of radiation, 4 weeks after completion of radiation, 6–12 months after completion of chemoradiation, and 2–3 years after completion of chemoradiation.

Results

Mean age of the patients was 56 years (range: 31–77 years); 55% of the patients were male. Median follow-up was 2.7 years (range: 0.3–5 years). The 3-year overall survival was 83%. Five patients experienced dose-limiting toxicity (DLT). Median scores on global QOL and on the social, role, emotional, nausea and vomiting, and fatigue scales showed clinically and statistically significant worsening at completion of radiation. Statistical but not clinical worsening was found for the physical and appetite scales. By 6–12 months, no subscale showed a difference, on average, from the baseline score. However, up to 45% of the patients remained below baseline on at least 1 subscale. Patients with DLT had worse scores on the emotional and the nausea and vomiting scales. Scores for global QOL and for nausea and vomiting were significantly associated with chemotherapy dose.

Conclusions

During chemoradiation, QOL is impaired. Although most scores return to baseline, recovery may take 6–12 months, and subscale scores remain below baseline in a significant proportion of patients.

KEY WORDS

Chemoradiation, gastric cancer, quality of life

1. INTRODUCTION

Quality of life (QOL) is increasingly recognized as an important endpoint in clinical trials of cancer therapies. However few data are available on QOL in patients who have received abdominal radiation therapy^{1,2}.

In 2001, Macdonald *et al.* published a landmark study, the Intergroup 0116 trial³. This randomized controlled trial showed a significant survival advantage for adjuvant chemoradiation (CRT), as compared with surgery alone, in patients with completely resected high-risk gastric and gastroesophageal adenocarcinoma³. Adjuvant CRT treatment using the regimen of the Intergroup 0116 trial is now the standard of care in North America and in certain centres in Europe. This prolonged treatment course (taking 5 months) is associated with a 40% or worse rate of acute toxicity. Alternative chemotherapy regimens are being explored in this setting to improve survival outcomes and toxicity⁴.

Few data are available on the QOL of patients undergoing adjuvant therapy for gastric adenocarcinoma². Here, we present a prospective evaluation of QOL for patients with completely resected gastric or gastroesophageal adenocarcinoma undergoing adjuvant abdominal radiation therapy with chemotherapy using infusional 5-fluorouracil (5FU) and escalating doses of cisplatin in a single-institution phase I study.

Based on the results of that study, a phase II study is currently underway⁵.

We hypothesised that QOL would be reduced during treatment, but that it would return to baseline levels at 6–12 months after completion of treatment. We also hypothesised that the experience of greater toxicity and the higher doses of chemotherapy would both be associated with poorer QOL.

2. METHODS

Approval to conduct this study was granted by the institutional research ethics board. All study patients provided informed consent.

2.1 Patient Population

This phase I study enrolled 34 patients with histologically confirmed Union Internationale Contre le Cancer stage IB to IV (M0) completely resected gastric or gastroesophageal junction adenocarcinoma. Patients had an Eastern Cooperative Oncology Group performance status of 2 or less. An upper age limit was not initially defined for the study, but because of significant therapy-related adverse events, the protocol was later amended to exclude patients over the age of 70. Participants were required to have a pre-treatment nutritional intake of at least 1500 calories daily. Patients were excluded if they had previously received radiation therapy or if they had a contraindication to radiation therapy. Tests for complete blood count, electrolytes (sodium, potassium), creatinine, bilirubin, aspartate transaminase, alanine transaminase, and alkaline phosphatase were obtained, as was a computed tomography scan of the chest, abdomen, and pelvis (to exclude patients with progressive disease or comorbidity that would preclude adjuvant therapy).

2.2 Chemotherapy

All patients were prescribed 12 weeks of infusional 5FU 200 mg/m² daily. Patients were recruited in 5 consecutive cohorts. Three patients without dose-limiting toxicity (DLT) were treated per cohort, in a standard 3+3 dose-escalation design: If 1 of 3 patients experienced a DLT, 3 further patients were treated at the same dose level. Cisplatin every 2 weeks was added to the treatment plan in escalating dose intensity⁵. In cohorts 1–4, the cisplatin dose was 0 mg/m², 20 mg/m², 30 mg/m², and 40 mg/m² respectively, given 4 times starting at week 1 (that is, weeks 1, 3, 5, and 7). In cohort 5 (the final cohort), an additional dose of 40 mg/m² was given in week 9 (see Table 1)⁵. “Dose-limiting toxicity” was defined as grade 3 or greater toxicity requiring treatment or hospitalization. “Maximal tolerated dose” was the highest dose cohort in which no more than 1 of 6 patients experienced a DLT.

TABLE 1 Cisplatin administration by cohort

Cisplatin administration	Cohort				
	1	2	3	4	5
Dose (mg/m ²)	0	20	30	40	40
2-Week cycles (n)	0	4	4	4	5

2.3 Radiation Therapy

Participants were treated according to institutional protocol with three-dimensional conformal planning and delivery^{6,7}. Radiation dose was 45 Gy in 25 fractions starting on day 16 after commencement of the chemotherapy.

2.4 Toxicity

Acute toxicity was scored according to the *Common Toxicity Criteria*, version 2.0 (CTC v2.0). Late toxicity was scored using the Radiation Therapy Oncology Group late toxicity score^{8,9}. All toxicities occurring 90 days or more after completion of CRT were considered late toxicities.

2.5 QOL Assessment

The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C-30 (EORTC QLQ-C30) was used to assess QOL. The QLQ-C30 was completed at 5 time points: enrolment (before CRT, but after definitive surgery), at completion of radiation therapy, and then at 4 weeks, 6–12 months, and 2–3 years after completion of chemotherapy. The EORTC QLQ-C30 is a self-administered, cancer-specific questionnaire¹⁰. It has 5 functional scales (each scale consisting of questions reflecting the physical, role, social, emotional, and cognitive functioning of the patient), 3 symptom scales (fatigue, pain, and nausea and vomiting), and global health status and overall QOL scales. A number of single items assess additional symptoms of dyspnea, sleep disturbance, constipation, diarrhea, and perceived financial impact. This measure has been rigorously developed and has demonstrated reliability, validity, and responsiveness in a variety of cancer populations, both for discriminative and for evaluative purposes^{1,10–15}.

2.6 Analyses

Survival and follow-up were determined from the date of diagnosis. Overall and relapse-free survival were estimated using the Kaplan–Meier method.

Each QOL domain was scored and reported separately using previously described standard methods¹⁰. Raw scores were linearly transformed to give values between 1 and 100. Higher scores in the functional domains and in global QOL indicate better functioning;

higher symptom scores indicate worse symptoms. For this study, a 10-point difference in QOL score was determined *a priori* to be a clinically significant difference. This difference was determined to be clinically meaningful in the “moderate” category (10–20 points) by a previous prospective study that correlated changes in QOL score with a patient’s perceived difference in QOL. In that study, a 5- to 10-point change in QOL score corresponded to a “little” change in QOL as perceived by the patient; a 10- to 20-point change, to a “moderate” change; and a greater than 20-point change, to a “very much” change¹⁶.

For analysis of compliance with questionnaires, patients that on follow-up had not reached the analysis time point and those that had died or relapsed before that time point were excluded from the numerator and the denominator¹⁷. In other words, compliance is reported as the proportion of expected questionnaires actually able to be scored.

Mean and median scores were calculated for each QOL domain at each time point. Nonparametric testing (signed rank test) was used to determine the significance of changes in QOL during follow-up as compared with baseline. For each domain at each time point, the percentages of patients with QOL scores that had improved (10-point or more improvement), remained unchanged (less than a 10-point

change), or worsened (10-point or more deterioration) were calculated.

In an exploratory analysis, the QOL scores at completion of therapy were individually examined for patients who experienced a DLT and were compared with the mean scores for the rest of the cohort. Also, the potential associations of QOL domains with dose cohort were assessed using the linear mixed-model across all time points.

3. RESULTS

3.1 Baseline Characteristics and Compliance

Our phase I study included 34 patients treated between September 2002 and March 2007. One patient was not eligible for the QOL assessment because of a language barrier. Of the remaining 33 eligible patients, 1 did not complete treatment because of social issues and therefore only had a baseline QOL assessment; another patient completed follow-up QOL assessments, but lacked a baseline assessment. Those 2 patients were included in the analysis. Table II shows patient and tumour characteristics. At the 5 time points, the number of QOL forms that could be scored were 33 (baseline), 32 (completion of radiation), 32 (4 weeks after CRT), 28 (6–12 months after CRT), and 19 (2–3

TABLE II Baseline characteristics for all patients and for patients by dose cohort

Variable	All patients (N=33)	Cohort				
		1 (N=6)	2 (N=9)	3 (N=7)	4 (N=6)	5 (N=5)
Age (years)						
Mean	56	59	54	51	57	53
Range	31–77	52–64	40–75	31–77	32–67	37–70
Sex (n)						
Females	15	4	3	3	4	1
Males	18	2	6	4	2	4
Stage (n)						
IIB	8	2	0	4	1	1
II	10	0	6	3	0	1
IIIA	8	3	0	0	4	1
IIIB	3	0	3	0	0	0
IV (M0)	4	1	0	0	1	2
Gastrectomy (n)						
Partial	27	5	6	6	5	5
Total	5	1	2	1	1	0
Subtotal	1	0	1	0	0	0
Lymph node resection (n)						
D0	2	1	0	0	0	0
D1	19	4	8	1	2	4
D2	12	1	1	5	4	1
Unknown	0	0	0	1	0	0

years after CRT), for completion rates of 97%, 91%, 84%, 75%, and 74% respectively.

3.2 Relapse and Survival

Median follow-up for the 28 patients alive at the time of analysis was 2.7 years (range: 0.3–5 years). Relapse had occurred in 9 patients (26%), and 6 patients (18%) had died of their disease. At 3 years, overall survival and relapse-free survival were 83% and 71% respectively, with median survival not yet reached⁵.

3.3 Toxicity

Acute toxicity was measured using the CTC v2.0. Toxicities experienced by the patients included skin toxicity (rashes, dryness, erythema), weight loss, fatigue, anorexia, nausea, dehydration, gastritis, hand–foot syndrome, sepsis, hyponatremia, and hematologic events⁵. Five patients experienced DLTs, all grade 3 in severity: 1 sepsis (cohort 1), 1 fatigue (cohort 2), and 3 upper gastrointestinal toxicities (1 in cohort 2, 2 in cohort 5). Only 1 patient experienced a grade 4 toxicity, an uncomplicated neutropenia (cohort 5). No grade 5 events occurred. The MTD occurred in cohort 4, with no patients in cohort 4 experiencing DLT.

3.4 QOL Over Time

Figure 1 shows the mean scores for global QOL and for the functional and symptom scales at each time point. Table III shows median differences from baseline in the scores for each domain at completion of radiation and at 4 weeks, 6–12 months, and 2–3 years after CRT completion. Median scores for several domains—global QOL and the social, role, emotional, nausea and vomiting, and fatigue scales—showed clinically and statistically significant worsening at the completion of radiation. In addition, statistically significant worsening of scores was seen for the physical and appetite scales. At 4 weeks after completion of CRT, global QOL and fatigue remained significantly worse than at baseline. By 6–12 months, no subscale showed a difference from baseline on average. However, at that time point, a proportion of patients did show worse scores as compared with baseline. Figure 2 shows the proportion of patients with improved, unchanged, and worsened QOL scores for each domain at completion of radiation therapy and at 6–12 months after CRT.

3.5 QOL and Dose Cohort

Global QOL ($p = 0.0007$) and the nausea and vomiting scale ($p = 0.04$) were both significantly worse with higher chemotherapy doses. Figure 3 shows the mean scores for these domains across all time points and dose levels.

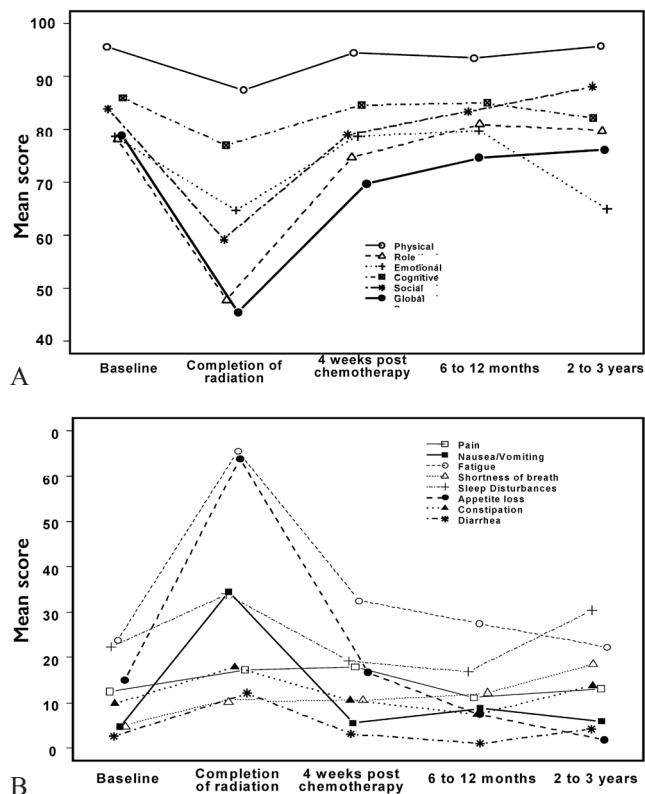


FIGURE 1 Mean scores of (A) global and functional scales across all time points and (B) symptom scales across all time points.

3.6 QOL and Toxicity

Compared with the other patients, the 5 patients who experienced DLTs scored worse at completion of radiation on the emotional ($p = 0.05$) and the nausea and vomiting ($p = 0.02$) scales. Figure 4 shows the scores in those domains across all time points for each patient with a DLT and the mean scores for the remaining cohort.

4. DISCUSSION

Very few data are available on the QOL of patients undergoing adjuvant therapy for gastric and gastroesophageal adenocarcinoma, and no long-term data are available². Our sample size is small, but the results show that QOL is impaired during adjuvant CRT treatment. Our results suggest that higher chemotherapy doses are associated with poorer scores for the nausea and vomiting scale and for global QOL. Moreover, the small number of patients experiencing a DLT had poorer scores on the emotional and the nausea and vomiting scales at completion of radiation. In most patients, QOL scores return to baseline, but recovery may take 6–12 months. Importantly, subscale scores at 6–12 months remain below baseline in a significant proportion of patients.

This study was primarily a dose-finding study for an alternative chemotherapy regimen in the

TABLE III Score difference^a between baseline and follow-up

Domain	At completion of radiation		After completion of chemoradiation					
	MD	p Value	4 weeks		6–12 months		2–3 years	
			MD	p Value	MD	p Value	MD	p Value
Physical	-6.7	0.0002	0	0.31	0	0.33	0	1
Role	-33	<0.0001	0	0.23	0	0.50	0	0.81
Emotion	-13	0.06	0	0.53	0	0.78	-4.17	0.02
Cognitive	0	0.29	0	0.31	0	0.86	0	0.06
Social	-17	0.002	0	0.14	0	0.70	0	0.69
Global	-29	<0.0001	-8.3	0.0002	-4.2	0.11	0	0.43
Pain	0	0.32	0	0.28	0	0.97	0	0.34
Nausea and vomiting	17	<0.0001	0	0.5	0	0.11	0	1
Fatigue	44	<0.0001	13.9	0.001	0	0.21	0	0.13
Shortness of breath	0	0.30	0	0.29	0	0.06	0	0.19
Sleep	0	0.46	0	0.56	0	0.8	0	0.11
Appetite loss	3.3	<0.0001	0	0.75	0	0.61	0	1
Constipation	0	0.34	0	0.67	0	1	0	0.75
Diarrhea	0	0.07	0	1	0	1	0	1

^a Boldface type indicates median difference values (MD) and p values associated with pre determined clinical or statistical significance.

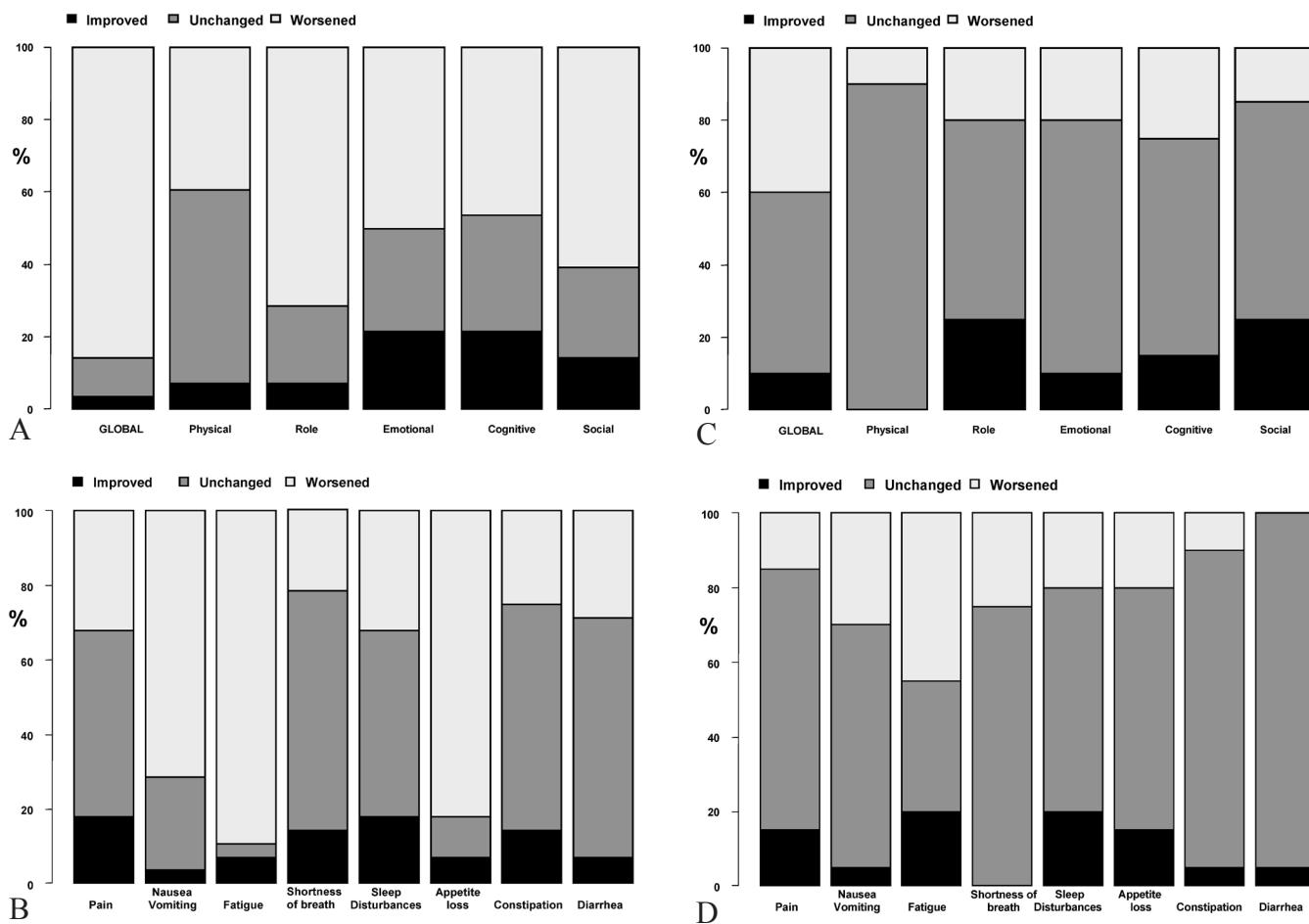


FIGURE 2 Percentage change in scores for global quality of life (GLOBAL) and for functional scales (A) from baseline to completion of radiation and (B) from baseline to 6–12 months. Percentage change in the scores for symptom scales (C) from baseline to completion of radiation and (D) from baseline to 6–12 months.

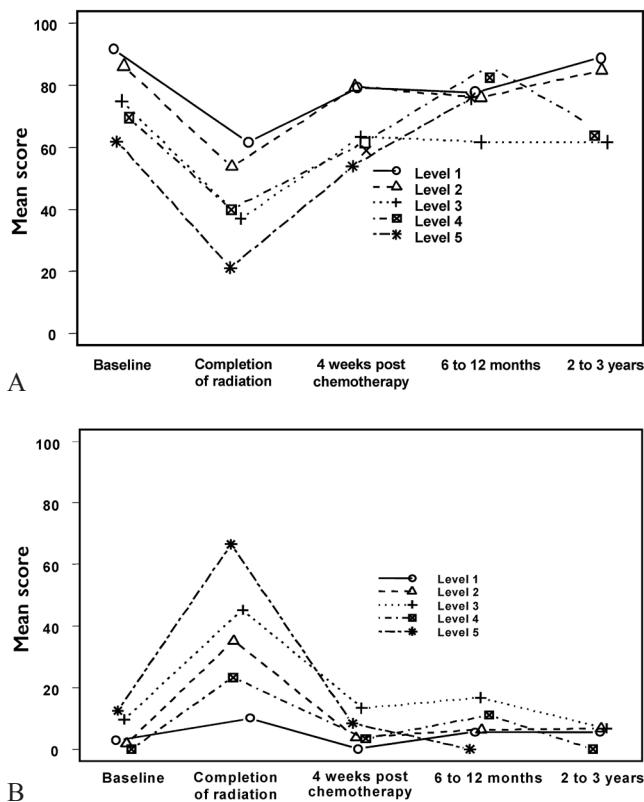


FIGURE 3 Mean scores (A) for global quality of life by time point and dose level and (B) for the nausea and vomiting scale by time point and dose level.

adjuvant CRT therapy of gastric cancer; QOL was a secondary endpoint. Increasingly, QOL is being recognized as an important endpoint in clinical studies. In the setting of adjuvant treatment, the survival benefits of additional therapies are significantly smaller than they are in the definitive treatment setting. Consequently, the long-term adverse impact on QOL is an important issue in patient counselling and in the decision-making process. Quality of life is also an important endpoint in the overall evaluation of alternative therapies as compared with standard treatments.

All patients in our study had undergone radical surgery before they commenced adjuvant treatment. Several research groups, using a variety of instruments [Short Form (SF-36) Health Survey, D15, Spitzer Quality of Life Index, EORTC QLQ-C30 and -STO22], have reported a reduction in QOL in similar populations.^{18–21}

Tyrvainen *et al.*¹⁹ used the SF-36 and D15 to compare QOL in 25 long-term survivors after total gastrectomy for gastric cancer with QOL in a normal population. Those authors found that mental health, physical and social functioning, energy, and vitality were similar in both groups. However certain dimensions, such as sleeping, eating, and distress, scored worse in cancer survivors.

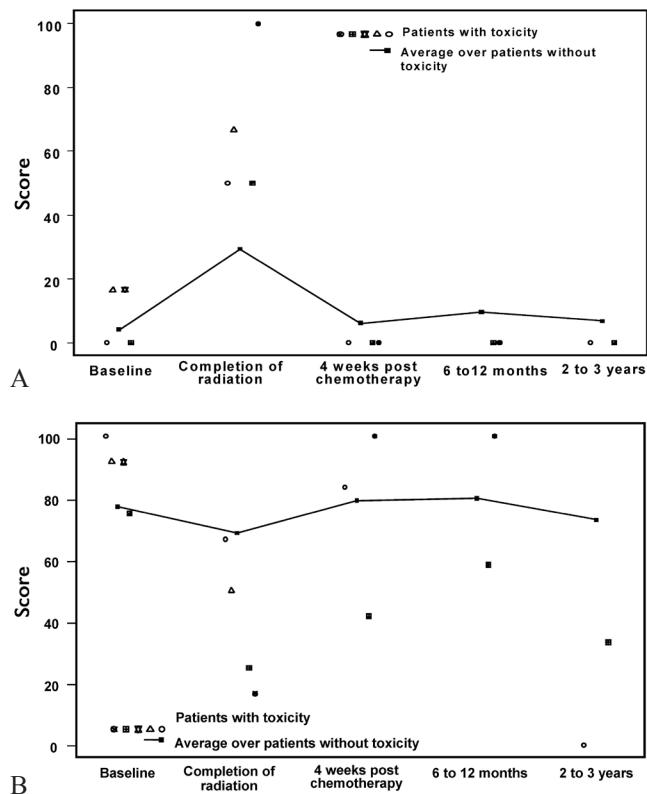


FIGURE 4 Scores for (A) the nausea and vomiting scale and (B) the emotional scale for each patient with dose-limiting toxicities compared with the mean scores for the remaining cohort.

Lee *et al.*²² assessed 408 gastric cancer survivors and found that they had more difficulties in performing housework and in maintaining employment than did a general population, with cancer survivors working fewer hours and having less work-related ability. A proportion of the patients in that study also received radiation therapy (12%) and chemotherapy (26%), but compared with patients treated by surgery alone, the patients receiving additional treatment did not show any additional effect with regard to ability to work.

The QLQ-C30 addresses general QOL issues. Blazeby *et al.*² reported favourable psychometric properties of the new gastric cancer QOL module, the QLQ-STO22, in 219 gastric cancer patients treated with palliative and radical intent. Thirty-three patients included in that study were treated radically with surgery and neoadjuvant or adjuvant chemotherapy with or without radiation therapy. The QLQ-STO22 assesses specific symptoms (reflux, eating, pain, hair loss, dry mouth), anxiety, and body image. This additional measure will be valuable for assessing QOL specific to gastric cancer patients in future studies of that population.

5. CONCLUSIONS

The factors associated with poorer QOL outcomes in the setting studied here are not yet clear. The complex

relationship between treatment-induced toxicity and QOL has been studied for various cancer sites. Cross-sectional and longitudinal studies have provided important information on the relationship between adverse events and QOL in prostate, head-and-neck, breast, and lung cancers^{23–32}. However, data are lacking on the relationship between long-term toxicity and QOL after radiation treatment for abdominal malignancies. Toxicity and other potential patient and therapy factors associated with poorer QOL outcomes in the short and long term are important areas for future study; these factors may contribute to the tailoring of therapy to the individual patient.

6. ACKNOWLEDGMENTS

Some of this information was presented at the Canadian Association of Radiation Oncology 2008 Annual Meeting, the American Society of Therapeutic Radiology and Oncology 2008 Annual Meeting, and the International Society for Quality of Life Research 2008 Annual Meeting.

7. CONFLICT OF INTEREST DISCLOSURES

All the authors declare that there are no financial conflicts of interest.

8. REFERENCES

- Kaasa S, Bjordal K, Aaronson N, et al. The EORTC core Quality of Life Questionnaire (QLQ-C30): validity and reliability when analysed with patients treated with palliative radiotherapy. *Eur J Cancer* 1995;31A:2260–3.
- Blazeby JM, Conroy T, Bottomley A, et al. Clinical and psychometric validation of a questionnaire module, the EORTC QLQ-STO22, to assess quality of life in patients with gastric cancer. *Eur J Cancer* 2004;40:2260–8.
- Macdonald JS, Smalley SR, Benedetti J, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. *N Engl J Med* 2001;345:725–30.
- Ajani JA, Fodor MB, Tjulandin SA, et al. Phase II multi-institutional randomized trial of docetaxel plus cisplatin with or without fluorouracil in patients with untreated, advanced gastric, or gastroesophageal adenocarcinoma. *J Clin Oncol* 2005;23:5660–7.
- Kassam Z, MacKay H, Buckley CA, et al. Adjuvant chemoradiation for gastric cancer with infusional 5-fluorouracil and cisplatin: a phase I study. *Curr Oncol* 2010;17:95–104.
- Kassam Z, Lockwood G, O'Brien C, et al. Conformal radiotherapy in the adjuvant treatment of gastric cancer: review of 82 cases. *Int J Radiat Oncol Biol Phys* 2006;65:713–19.
- Ringash J, Khaksar SJ, Oza A, et al. Post-operative radiochemotherapy for gastric cancer: adoption and adaptation. *Clin Oncol (R Coll Radiol)* 2005;17:91–5.
- Koller M, Lorenz W. Quality of life research in patients with rectal cancer: traditional approaches versus a problem-solving oriented perspective. *Langenbecks Arch Surg* 1998;383:427–36.
- United States, National Institutes of Health, National Cancer Institute, Cancer Therapy Evaluation Program (CTEP). *Common Toxicity Criteria (CTC)*. Version 2. Bethesda, MD: CTEP; 1999. [Available online at: ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/ctcv20_4-30-992.pdf; cited June 8, 2010]
- Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993;85:365–76.
- Osoba D, Aaronson N, Zee B, Sprangers M, te Velde A. Modification of the EORTC QLQ-C30 (version 2.0) based on content validity and reliability testing in large samples of patients with cancer. The Study Group on Quality of Life of the EORTC and the Symptom Control and Quality of Life committees of the NCI of Canada Clinical Trials Group. *Qual Life Res* 1997;6:103–8.
- Osoba D, Zee B, Pater J, Warr D, Kaizer L, Latreille J. Psychometric properties and responsiveness of the EORTC Quality of Life Questionnaire (QLQ-C30) in patients with breast, ovarian and lung cancer. *Qual Life Res* 1994;3:353–64.
- Bjordal K, Kaasa S. Psychometric validation of the EORTC core Quality of Life Questionnaire, 30-item version and a diagnosis-specific module for head and neck cancer patients. *Acta Oncol* 1992;31:311–21.
- Ringdal GI, Ringdal K. Testing the EORTC Quality of Life Questionnaire on cancer patients with heterogeneous diagnoses. *Qual Life Res* 1993;2:129–40.
- Niezgoda HE, Pater JL. A validation study of the domains of the core EORTC quality of life questionnaire. *Qual Life Res* 1993;2:319–25.
- Osoba D, Rodrigues G, Myles J, Zee B, Pater J. Interpreting the significance of changes in health-related quality-of-life scores. *J Clin Oncol* 1998;16:139–44.
- Neymark N, Kiebert W, Torfs K, et al. Methodological and statistical issues of quality of life (QOL) and economic evaluation in cancer clinical trials: report of a workshop. *Eur J Cancer* 1998;34:1317–33.
- Barbour AP, Lagergren P, Hughes R, Alderson D, Barham CP, Blazeby JM. Health-related quality of life among patients with adenocarcinoma of the gastro-oesophageal junction treated by gastrectomy or oesophagectomy. *Br J Surg* 2008;95:80–4.
- Tyrvainen T, Sand J, Sintonen H, Nordback I. Quality of life in the long-term survivors after total gastrectomy for gastric carcinoma. *J Surg Oncol* 2008;97:121–4.
- Wu CW, Chiou JM, Ko FS, et al. Quality of life after curative gastrectomy for gastric cancer in a randomised controlled trial. *Br J Cancer* 2008;98:54–9.
- Thybusch-Bernhardt A, Schmidt C, Kuchler T, Schmid A, Henne-Bruns D, Kremer B. Quality of life following radical surgical treatment of gastric carcinoma. *World J Surg* 1999;23:503–8.
- Lee MK, Lee KM, Bae JM, et al. Employment status and work-related difficulties in stomach cancer survivors compared with the general population. *Br J Cancer* 2008;98:708–15.
- Langendijk JA, Aaronson NK, de Jong JM, et al. Quality of life after curative radiotherapy in stage I non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2002;53:847–53.

24. Langendijk JA, Aaronson NK, de Jong JM, *et al*. Prospective study on quality of life before and after radical radiotherapy in non-small-cell lung cancer. *J Clin Oncol* 2001;19:2123–33.
25. Curran D, van Dongen JP, Aaronson NK, *et al*. Quality of life of early-stage breast cancer patients treated with radical mastectomy or breast-conserving procedures: results of EORTC trial 10801. The European Organization for Research and Treatment of Cancer (EORTC), Breast Cancer Co-operative Group (BCCG). *Eur J Cancer* 1998;34:307–14.
26. Bjordal K, Kaasa S, Mastekaasa A. Quality of life in patients treated for head and neck cancer: a follow-up study 7 to 11 years after radiotherapy. *Int J Radiat Oncol Biol Phys* 1994;28:847–56.
27. Langendijk JA, ten Velde GP, Aaronson NK, de Jong JM, Muller MJ, Wouters EF. Quality of life after palliative radiotherapy in non-small cell lung cancer: a prospective study. *Int J Radiat Oncol Biol Phys* 2000;47:149–55.
28. Osoba D, Tannock IF, Ernst DS, Neville AJ. Health-related quality of life in men with metastatic prostate cancer treated with prednisone alone or mitoxantrone and prednisone. *J Clin Oncol* 1999;17:1654–63.
29. Ringash J, Warde P, Lockwood G, O'Sullivan B, Waldron J, Cummings B. Postradiotherapy quality of life for head-and-neck cancer patients is independent of xerostomia. *Int J Radiat Oncol Biol Phys* 2005;61:1403–7.
30. Litwin MS, Flanders SC, Pasta DJ, Stoddard ML, Lubeck DP, Henning JM. Sexual function and bother after radical prostatectomy or radiation for prostate cancer: multivariate quality-of-life analysis from CAPSURE. Cancer of the Prostate Strategic Urologic Research Endeavor. *Urology* 1999;54:503–8.
31. Madalinska JB, Essink-Bot ML, de Koning HJ, Kirkels WJ, van der Maas PJ, Schroder FH. Health-related quality of life in patients with screen-detected versus clinically diagnosed prostate cancer preceding primary treatment. *Prostate* 2001;46:87–97.
32. Fowler FJ Jr, Barry MJ, Lu-Yao G, Wasson J, Roman A, Wennberg J. Effect of radical prostatectomy for prostate cancer on patient quality of life: results from a Medicare survey. *Urology* 1995;45:1007–13.

Corresponding author: Zahra Kassam, Princess Margaret Hospital, Department of Radiation Medicine, 610 University Avenue, Toronto, Ontario M5G 2M9.

E-mail: zahrakassam13@yahoo.co.uk

* Department of Radiation Medicine, Princess Margaret Hospital, Toronto, ON.

† University of Toronto, Toronto, ON.

‡ Department of Medical Oncology and Hematology, Princess Margaret Hospital, Toronto, ON.

§ Department of Clinical Study Coordination and Biostatistics, Princess Margaret Hospital, Toronto, ON.