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Original Paper

Quality of Life in Oncology Practice: Prognostic Value of EORTC QLQ-C30 Scores in Patients with Advanced Malignancy

A. Coates,[1,2] F. Porzsolt[3] and D. Osoba[4]

[1]Department of Cancer Medicine, University of Sydney, NSW; [2]Australian–New Zealand Breast Cancer Trials Group, Sydney, NSW, Australia; [3]Tumour Centre, University of Ulm, Germany; and [4]British Colombia Cancer Agency, Vancouver, British Columbia, Canada

Quality of life (QL) scores may be used to assess the impact of disease and treatment, and to predict survival of cancer patients in prospective clinical trials. The aim of this study was to evaluate the prognostic association of QL scores among patients with advanced malignancies in routine practice. Adult patients with advanced malignancy from 12 institutions in 10 countries completed the EORTC QLQ-C30 questionnaire, in their native language, once at study entry. Baseline patient and disease characteristics were recorded. We used a proportional hazards model stratified on diagnostic category to test whether QL scores from the QLQ-C30 were significantly and independently predictive of overall survival duration from the time of QL measurement. In all, 735 eligible patients were entered between November 1989 and September 1995. On 1 October 1995, follow-up information was obtained on 656 patients, of whom 411 had died. Patient and disease factors predictive of worse survival were age and performance status. The global scale and the scales of physical, role, emotional, cognitive and social function were each significantly predictive of subsequent survival duration in univariate analyses. Single-item QL scores for overall physical condition (question 29), overall quality of life (question 30), and the global and social functioning scales remained independently prognostic after allowing for performance status and age, and, among solid tumour patients, metastatic site. QL can be measured in an international setting based on routine oncology practice. QL scores carry prognostic information independent of other recorded factors. © **1997 Elsevier Science Ltd.**

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INTRODUCTION

QUALITY OF life (QL) is an important consideration during management of patients with incurable cancer. Methods now available allow reliable and valid measurement of aspects of health-related QL which are affected by advanced malignancy and its treatment [1–7]. QL measurements are used as outcome measures by which to compare different treatments [2, 6, 8–10]. Additionally, prognostic associations between QL scores and survival duration have been reported among patients with breast cancer [6, 10–12], melanoma [13] and lung cancer [14]. In this study our aim was to ascertain the prognostic significance of a standard modern QL instrument, the EORTC QLQ-C30 [1], in typical general oncology practice among adult patients.

PATIENTS AND METHODS

Patients with advanced malignant disease were eligible for this study provided they were able and willing to complete the QLQ-C30 in their own language. All patients gave informed consent to the submission of baseline and follow-up data to the study co-ordinating centre. Patient information recorded included primary site of tumour, age, gender, marital status, performance status (ECOG scale) and loss of body weight, while disease information included primary site and sites of known metastases. For leukaemic patients, anaemia, granulocytopenia, leucocytosis, thrombocytopenia, splenomegaly, lymphadenopathy, hepatomegaly

Correspondence to A. Coates.
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Table 1. Patient characteristics

(a) All patients

		Total	*Follow-up*	*Deaths*
All patients		735	656	411
Age	<median (57.7 years)	366	321	187
	>median	369	335	224
Sex	Male	298	296	175
	Female	437	360	236
Marital status	Not Married	127	126	77
	Currently married	346	344	214
	Unknown	262	186	120
Diagnostic group	Breast	305	229	153
	Small cell	45	45	40
	Non-small cell	85	85	71
	Acute leukaemia	42	41	22
	Other haematological	65	65	35
	Head and neck	82	81	36
	Gastrointestinal	47	47	23
	Other	64	63	31
ECOG PS	0	233	199	96
	1	304	272	171
	2	141	129	97
	3	45	45	40
	4	10	10	7
	Unknown	2	1	0
Weight Loss	None	235	235	129
	<5%	89	87	65
	5–10%	72	72	50
	>10%	61	60	37
	Unknown	278	202	130

(b) Solid tumour patients—sites of metastases

Site	*Total*	*Deaths*
Any distant metastases	598	348
No distant metastases	69	27
Individual sites		
Bone	212	129
Nodular lung	175	92
Lymphangitis carcinomatosa	48	29
Liver	197	109
Brain	24	21

Table 2. Quality of life scores

(a) Distribution of scale scores

Scale	*N*	*Possible scores*	*Median score*	*Interquartile range*
Physical	711	0–100	60	40–100
Role	717	0–100	50	50–100
Emotional	701	0–100	50	31–63
Cognitive	716	0–100	63	50–75
Social	717	0–100	50	25–75
Global QL scale	718	0–100	57	43–71
Single item scores				
Q29	719	1–7	4	3–5
Q30	719	1–7	4	3–5

(b) Correlations between scale scores: Spearman's rho [17]

Scale	*Physical*	*Role*	*Emotional*	*Cognitive*	*Social*	*Global*	*Q29*
Role	0.64						
Emotional	0.37	0.31					
Cognitive	0.30	0.24	0.42				
Social	0.47	0.51	0.49	0.34			
Global QL	0.60	0.45	0.53	0.36	0.53		
Q29	0.59	0.45	0.49	0.37	0.48	0.94	
Q30	0.56	0.41	0.53	0.33	0.52	0.95	0.81

Table 3. Factors predictive of QL scores—odds ratio

(a) All patients: general characteristics[1]

Scale	*N*[2]	*Age*[3]		*ECOG PS*	
		Odds ratio	*P* value	Odds ratio	*P* value
Physical	708	0.22	<0.001		
Role	714	1.02	0.004	0.31	<0.001
Emotional	698	1.01	0.06	0.62	<0.001
Cognitive	713	0.69	<0.001		
Social	714	1.02	0.009	0.44	<0.001
Global	715	0.38	<0.001		
Q29	716	0.39	<0.001		
Q30	716	0.40	<0.001		

(b) All patients: diagnostic categories[4]

Scale	*NSL*		*AL*		*HN*		*GI*	
	OR	*P*	OR	*P*	OR	*P*	OR	*P*
Physical			2.5	0.06	5.6	0.002		
Role								
Emotional	2.0	0.04					3.1	0.004
Cognitive								
Social	2.4	0.01			2.4	0.02		
Global	1.9	0.07	2.5	0.03			2.5	0.03
Q29	2.3	0.02	7.3	<0.001				
Q30								

(c) Solid tumour patients—impact of metastatic site[5]

Scale	*N*	*Bone*		*Brain*	
		OR	*P*	OR	*P*
Physical	585	0.46	0.001		
Role	589	0.58	0.03		
Emotional	576	0.61	0.01		
Cognitive	589			0.43	0.07
Social	590	0.53	0.001		
Global	588	10.52	0.002		
Q29	589	0.58	0.008		
Q30	589	0.57	0.008		

[1]Logistic regression using QL scores dichotomised at the median, allowing for diagnosis.
[2]Number contributing to final regression equation.
[3]Older patients reported better role, emotional and social scale scores.
[4]Compared with breast cancer allowing for age, sex and ECOG PS. Numbers are as in (a) above. Odds ratios >1 indicate better QL scores associated with that diagnostic group.
[5]Controlling for sex and ECOG PS. In each case, the presence of the relevant metastatic site yielded an OR <1, indicating an association with worse QL.
NSL: non-small cell lung cancer; AL: acute leukaemia; HN: head and neck cancer; GI: gastrointestinal cancer; OR: odds ratio.

and fever were recorded instead of metastatic site. Primary tumour sites were grouped as shown in Table 1.

The only follow-up information required was the date and cause of death, or the fact that a patient was alive at the defined closing date of the study. Analysis was designed to test associations between QL scores obtained from the various scales of the QLQ-C30 and subsequent survival, with and without allowance for other significant prognostic factors. Regressions used a proportional hazards model [15] stratified by diagnostic group to examine survival and logistic regression [16] on QL scores dichotomised at the median to examine associations between QL scores and clinical characteristics. Correlations between QL scores were examined using the non-parametric Spearman's rank correlation (rho) coefficient [17, 18]. All calculations were performed using the SPIDA statistical software package [19].

RESULTS

Patients

From November 1989 to September 1995, 735 patients from 12 institutions in 10 countries completed the EORTC QLQ-C30 questionnaire in their own language (German: 513 patients, English: 131, French: 66, others: 25). Patient and disease characteristics are summarised in Table 1(a). Sites of metastases are recorded in Table 1(b). Because it was expected that the type of disease might have an impact on prognosis, a decision was made before analysis began that the main analysis would be stratified by diagnostic category. For this purpose, patients were grouped as those with breast cancer (305), non-small cell lung cancer (85), small cell lung cancer (45), head and neck cancer (82), gastrointestinal cancers (47), acute leukaemias (42), other haematological malignancies (65) or other sites (64). Follow-up was

Table 4. Prognostic significance of QL scores: all patients

(a) Univariate analyses (N = 629–644)

Variable	Coefficient[6]	Hazard ratio	95% CI	P value
Physical	−0.012	0.988	0.984, 0.991	<0.001
Role	−0.007	0.993	0.990, 0.996	<0.001
Emotional	−0.008	0.992	0.988, 0.997	0.003
cognitive	−0.006	0.994	0.989, 1.000	0.045
Social	−0.012	0.988	0.984, 0.992	<0.001
Global	−0.018	0.982	0.977, 0.987	<0.001
Q29	−0.227	0.80	0.75, 0.85	<0.001
Q30	−0.235	0.79	0.74, 0.85	<0.001

(b) Independent QL scores added together

Variable	Coefficient	Hazard ratio	95% CI	P value
Physical	−0.006	0.994	0.989, 0.998	0.006
Social	−0.005	0.995	0.990, 0.999	0.025
Global	−0.010	0.990	0.983, 0.996	0.002

(c) Independent non-QL variables (N = 655)

Variable	Coefficient	Hazard ratio	95% CI	P value
Age[7]	0.09	1.009	1.000, 1.018	0.055
ECOG PS[8]	0.49	1.633	1.469, 1.816	<0.001

(d) Multivariate analysis: QL variables added singly to models with age and ECOG PS (N = 628–643)

Variable	Coefficient	Hazard ratio	95% CI	P value
Physical	−0.004	0.996	0.992, 1.000	0.08
Role	−0.002	0.998	0.995, 1.001	0.17
Emotional	−0.004	0.996	0.991, 1.001	0.12
Cognitive	−0.002	0.998	0.993, 1.004	0.6
Social	−0.007	0.993	0.988, 0.997	0.001
Global	−0.011	0.989	0.984, 0.995	<0.001
Q29	−0.126	0.881	0.819, 0.948	0.001
Q30	−0.139	0.871	0.809, 0.937	<0.001

Notes 1–5 as for Table 3.

[6]Scores for Q29 and 30 are 1–7, and for other QL scales 0–100, so that coefficients for Q29 and Q30 appear larger. Negative coefficients indicate that a higher score (better QL) is associated with a lower hazard (better survival).

[7]Age was modelled as a continuous variable. Coefficient for age is expressed per decade.

[8]In other models, ECOG PS was dichotomised at 0,1 v 2,3,4, or included as an indicator variable for each score, with similar results.

never intended for one group of 73 patients, whose QL data were contributed on that basis for descriptive purposes. Among the remaining 662 patients, follow-up data were available for 656 (99%), and, by the analysis date, 411 of these patients (63%) were known to have died. The last contact was more than 90 days before the analysis date for 68 patients (10%) not known to have died. Such patients were treated in survival regressions as censored at the date on which they were last known to be alive.

Quality of life scores

Scales for physical, role, emotional, cognitive and social functioning and for global quality of life were calculated from the relevant questions in the QLQ-C30 as previously described [1]. These scales range from 0 (worst) to 100 (best). The single-item scores for questions 29 (overall physical condition) and 30 (overall quality of life), seven-point scales which combine to form the global QL scale, were tested separately, because of their similarity to the single-item scales found to be prognostically significant in earlier studies. Other individual symptom scales and individual question scores from the QLQ-C30 were recorded, but have not yet been analysed.

Median QL scores and their distributions are shown in Table 2(a). The various QL scores were significantly correlated with each other (Table 2(b)).

Disease and patient characteristics

Multivariate analysis allowing for diagnosis and patient characteristics showed that, among all patients, the performance status (ECOG scale) had a major independent association with each QL scale, while an effect of age may also have been present (Table 3(a)). The *p*-values shown are not corrected for multiple comparisons, and are presented as illustrative only.

The association of the various diagnostic categories with QL scores (allowing for age, sex and performance status) was only marginal (Table 3(b)). Among patients with solid tumours, for whom metastatic sites were recorded, bone metastases appeared to have a major impact on many aspects of QL, while brain metastases were weakly associated with worse cognitive function (Table 3(c)).

Prognostic associations of QL scores

The association between QL scores and subsequent survival duration was defined in the protocol as the major end-

Table 5. Prognostic significance of QL scores: solid tumours

(a) Independent non-QL variables (N = 569) Variable	Coefficient	Hazard ratio	95%CI	*P* value
ECOG PS	0.569	1.77	1.57, 1.99	<0.001
Liver metastasis	0.249	1.28	1.00, 1.65	0.052
Brain metastasis	0.678	1.97	1.25, 3.14	0.004

(b) QL variables added singly to models with ECOG PS, liver and brain metastases (N = 547–557) Variable	Coefficient	Hazard ratio	95% CI	*P* value
Physical	−0.004	0.996	0.991, 1.001	0.1
Role	−0.002	0.998	0.995, 1.002	0.35
Emotional	−0.002	0.998	0.992, 1.003	0.47
Cognitive	0.00	1.00	0.994, 1.007	0.9
Social	−0.007	0.993	0.988, 0.998	0.003
Global	−0.011	0.989	0.984, 0.995	0.001
Q29	−0.121	0.89	0.82, 0.96	0.003
Q30	−0.139	0.87	0.80, 0.94	0.001

point of the study. The first analysis used information from all patients for whom follow-up information was available. All of the QL scales, and the single-item scores for questions 29 and 30, were significantly predictive of subsequent survival duration in univariate analyses (Table 4(a)). Independent prognostic data were provided by the physical, social and global scales in multivariate analysis, not including non-QL variables (Table 4(b)). The patient factors significantly related to survival duration were age and PS (Table 4(c)). Allowing for these non-QL variables, the social functioning and global QL scales and the single-item QL scores for overall physical condition and overall QL were independently significant prognostic factors for survival duration. Models including significant non-QL variables were not improved by adding more than one QL scale at a time.

Impact of metastatic site

Among patients with solid tumours, the best set of non-QL variables predictive of survival was PS, liver and brain metastases (Table 5(a)). Allowing for these variables, the social functioning and global QL scales and the questions on overall physical condition and overall QL remained independently significant prognostic factors for survival (Table 5(b)).

Emotional functioning scale

In a previous Canadian study, an association between superior survival and lower emotional functioning scale score was found, limited to patients with lower than average global quality of life [20]. We therefore examined our corresponding subgroup of 211 patients with global QL scores below the mean. In this subgroup, the median survival of patients with lower than average emotional functioning scale scores was 257 days, slightly but not significantly greater than the 234 day median survival for patients with low global QL and higher emotional functioning scale scores ($p = 0.96$).

DISCUSSION

QL scores have been applied clinically in two distinct ways. Firstly, they have been used as outcome measures to compare treatments in clinical trials [6, 10]. Secondly, an association has been noted between QL and subsequent survival [6, 10, 14]. This association stimulated the present study.

We have shown a significant independent association between aspects of QL recorded by patient self-report using the EORTC QLQ-C30 and subsequent survival duration. In contrast to earlier reports, based on opportunistic re-analysis of QL data initially recorded as outcome variables in the course of a clinical trial, this study was primarily designed to test the prognostic associations of QL. We chose the QLQ-C30 as a well-defined, psychometrically characterised instrument, available in the various languages appropriate to our participating centres.

The association between quality of life and subsequent prognosis has been noted in studies of patients with several different types of cancer [6, 10, 12, 14, 21, 22].The approach previously used was to analyse existing clinical trial data sets [12, 13]. This had the advantage that mature outcome data were readily available but the limitation that the only aspects of QL available for analysis were those included in the design of the original clinical trials to measure the effects of treatment. Prospective studies, such as that described here, have the advantage that they can choose the aspects of QL to be measured. The association observed in this and previous studies does not, of course, establish a causative relationship between QL and survival, since QL may merely act as a marker for an otherwise undetected prognostic factor.

Among the QL scales previously described as predictive of survival were single-item linear analogue self-assessment (LASA) scales for physical wellbeing and overall QL [12, 13]. The items in the present study, most closely similar to these LASA scales, were the single-item questions on overall physical condition (question 29) and overall QL (question 30), each of which was rated on a seven-point Likert scale. The significant independent prognostic information carried by such single-item questions was again shown in the present study.

Understanding the nature of these associations may be important in deciding whether QL can be manipulated in order to prolong survival. Preliminary studies have demonstrated an association between psychological response to cancer and survival [23, 24], and noted prolonged survival in patients receiving psychological support [25, 26]. Rational design of psychological interventions aimed at

prolonging survival would be aided by definition of the detailed psychosocial factors most closely associated with survival. Ultimately, the usefulness of the association between QL scores and survival will only be demonstrated if deliberate interventions aimed at improving QL are shown to enhance survival.

The patient population for the present study was drawn from routine oncology practice. Eligibility was deliberately inclusive, and follow-up demands were kept to a minimum. The results may therefore be more closely relevant to everyday patient care than data derived from highly selected clinical trial participants. Successful completion of the study demonstrates the feasibility of collecting QL information in a very broad range of oncology patients. The clear demonstration that the QL results convey otherwise unobtainable information about prognosis may encourage more widespread measurement of QL in the course of routine patient care.

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APPENDIX

International Gruppe Lebensqualität in der Onkologie (IGLOO)

Coordinating centre, Tumorzentrum Ulm, University of Ulm, Ulm, Germany. F. Porzsolt, C. Welke.

Participating Groups

Australian–New Zealand Breast Cancer Trials Groups, Sydney, Australia: A. Coates, E. McNeil.

Breast Cancer Study Group of the Tumorzentrum Ulm, Ulm, Germany. F. Prozwsolt.

Cancer Agency of British Colombia, Vancouver, BC, Canada: D. Osoba, L. Young, L. Unger.

Epidemiology Project of the Cancer Registry Weser-EMs, Oldenburg, Germany: J. Illiger, S. Mencke.

Friedrich Schiller University Jena, Department of Urology, Jena, Germany: J. Schubert, S. Kümmerling, G. Eschholz.

Institute of Medical Oncology and Haematology, Klinikum Nord, Nuremberg, Germany: W. Gallmeier, H. Kappauf, K. Bench.

University of Freiburg, Department of Thoracic Surgery, Freiburg, Germany: R., Grahmann.

University of Paris, Service d'Hématologie, Hôtel-Dieu, Paris, France: R. Zittoun, J.-M. Lassaunière.

Department of ENT, University of Ulm, Ulm, Germany: S. Brosch.

Department of Medicine, University of Ulm, Ulm, Germany: F. Porzsolt.