Is Quality of Life Data Predictive of the Survival in Cancer Patients? A Rapid and Systematic Review of the Literature

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Abstract

Objective: To review literature on relationship between quality of life data and the length of survival in cancer patients.

Methods: A literature search was carried out using MEDLINE to assess existing knowledge on relationship between quality of life data as a prognostic factor and survival in cancer patients. The intention was to review all full publications in English language biomedical journals. The search strategy included the combination of keywords 'cancer', 'prognostic', 'predictor', 'predictive', 'quality of life' and 'survival' in titles of publications. The literature was also examined to ensure that the study used multivariate analyses. Pure psychological studies were excluded. The initial search was carried out twice in December 2008 and twice for a final check in early and late January 2009. A manual search also was performed for including possible additional papers.

Results: In all 146 citations were identified and reviewed. Of these, 88 citations on relationship between quality of life and survival were found relevant and examined in this rapid and systematic review of the literature. The findings are summarized under different headings including studies on heterogeneous sample of cancer patients, lung cancer, breast cancer, gastro-oesophageal cancers, colorectal cancer and other cancers. Except a few exceptions most studies found that quality of life data or some aspects of quality of life measures were significant independent predictors of survival duration. Global quality of life, functioning domains and symptom scores such as appetite loss, fatigue and pain individually or in combined were the most important factors that predicted the length of survival in cancer patients after adjusting for one or more demographic and known clinical prognostic factors.

Conclusion: Studies reported in this review provide evidence for a positive relationship between quality of life data or some aspects of quality of life measures and the length of survival in cancer patients. Pre-treatment quality of life data are appeared to be most reliable information that could help clinicians to establish prognostic criteria for treatment of their cancer patients. Indeed, conducting studies using valid instruments, applying sound methodological approaches and adequate but not sophisticated multivariate statistical analyses adjusted for demographic characteristics and known clinical prognostic factors are recommended in order to yield more specific quality of life related prognostic variables for specific cancers.

Keywords: quality of life, prognostic factor, predicting factor, survival, cancer, patient-reported outcomes

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Introduction

Health-related quality of life is now considered an important endpoint in studies of outcomes in oncology. Studies of quality of life can indicate the directions needed for more efficient treatment of cancer patients. In addition it has been shown that assessing quality of life in cancer patients could contribute to improved treatment and could even be as prognostic as medical factors [1-6].

The aim of this review was to examine literature published since the topic first appeared in English language biomedical journals. It was hoped that this review may contribute to existing knowledge, help

both researchers and clinicians to have a better profile on the topic, and consequently aid in improving quality of life in cancer patients.

Methods

A literature search was carried out using MEDLINE to assess existing knowledge on relationship between quality of life data as a prognostic factor and survival in cancer patients. The intention was to review all full publications that have been appeared in English language biomedical journals between 1982 and 2008. The year 1982 was chosen because the first study on the topic was published then. The search strategy included the combination of keywords 'cancer', 'prognostic', 'predictor', 'predictive', 'quality of life' and 'survival' in titles of publications. The literature was also examined to ensure that the study used multivariate analyses. Pure psychological studies were excluded. It was though that this might help to focus the investigation. It provided the initial database for the review. The initial search was carried out twice in December 2008 and twice for a final check in early and late January 2009. A manual search also was performed for including possible additional papers.

Results

Statistics

A total of 146 citations were identified and after exclusion of duplicates, the abstracts of 135 citations were reviewed. Of these, 88 citations on relationship between quality of life and survival were identified and examined in this rapid and systematic review of the literature. Here, the major findings are summarized and presented under the following headings.

Early studies

It was in 1980s that a few papers reported on positive relationships between some psychosocial and quality of life parameters and the length of survival in cancer patients. The first paper on relationship between quality of life data and survival in cancer patients was published in 1982. In this paper existing records of 651 patients with bronchogenci carcinoma were assessed in order to determine the relationship between survival and four 'non-anatomic' prognostic factors including symptomatic history, performance status, weight loss and age. Adjusting for stage, histologic factors and treatment, the analysis showed that weight loss and performance status were significantly associated with survival [7]. In 1985 Cassileth et al. reported that studying 359 cancer patients they did not find any association between

social and psychological factors and the length of survival or the time to relapse. Their They did not collected data on health related quality of life but they concluded that although these factors may contribute to the initiation of morbidity, the biology of the disease appears to predominate and to override the potential influence of life-style and psychosocial variables once the disease process is established [8]. The third paper on the topic was appeared in 1987. This paper compared quality of life during chemotherapy for advanced breast cancer receiving intermittent and continuous treatment strategies. The study findings indicated that changes in the quality of life scores, as measured by a series of Linear Analog Self Assessment (LASA) scales for physical well-being, mood, pain, and appetite (as quality of life index), were independent prognostic factors in proportional hazards models of subsequent survival [9]. Kaasa et al. also published a paper on the topic in 1989. They in their study of inoperable non-small-cell lung cancer showed that general symptoms and psychological well-being were the best predictive value for survival duration [10].

Heterogeneous sample of cancer patients

There were studies that included a heterogeneous sample of cancer populations [11-16]. Global quality of life, physical, social, emotional and cognitive functioning were found to be independent prognostic factors for survival. The results are shown in Table 1.

Lung cancer

There were relatively considerable studies that examined the relationship between quality of life data and survival in lung cancer patients [7,10,17-38]. The studies included a sample of either lung cancer patients (both small-cell and non-small-cell) or mostly advanced non-small-cell lung cancer patients. Except one study that reported overall quality of life score was not predictor of survival [22], in most instances baseline overall or global quality of life scores were found to be independent prognostic factor of survival duration. In addition, in many studies pain, and appetite loss were found to be independent determinants of overall survival. Table 2 summarizes the results.

Breast cancer

Studies that examined the relationship between quality of life data and survival in breast cancer patients are presented in Table 3 [9,39-56]. Studies have shown that baseline quality of life predicts

Table 1: *Studies on relationship between quality of life data and survival in heterogeneous sample of cancer patients*

Author(s)	Year	Cancer	HRQOL measure(s)	Results*
Degner and Sloan [11]	1995	Ambulatory heterogeneous sample of cancer patients	SDS	The single measure of symptom distress was a significant predictor of survival.
Ringdal et al. [12]	1996	Heterogeneous sample of cancer patients	Psychosocial variables	Physical functioning was prognostic factor of survival but psychosocial covariates were not.
Tamburini et al. [13]	1996	Terminal cancer patients	TIQ	Confusion, cognitive status and global health status were independent prognostic of survival.
Coates et al. [14]	1997	Advanced malignancies	EORTC QLQ-C30	Global QOL and social functioning were significantly predictive of survival.
Dancey et al. [15]	1997	Heterogeneous population of cancer patients	EORTC QLQ-C30	Global QOL and emotional functioning were significantly associated with survival.
Chang et al. [16]	1998	Heterogeneous sample of cancers patients (colon, breast, ovary or prostate)	MSAS	Physical symptom subscale score significantly predicted survival.

Abbreviations: EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire; MSAS: Memorial Symptom Assessment Scale; QOL: quality of life; SDS: Symptom Distress Scale; TIQ: Therapy Impact Questionnaire.

* All results obtained from multivariate analyses after controlling for one or more demographic and known biomedical prognostic factors.

survival in advanced breast cancer but not in early stage of disease [44]. Two recently published papers also confirmed that baseline quality of life was not a prognostic factor in non-metastatic breast cancer patients. One of these two studies, using Cox survival analysis, indicated that neither health-related quality of life nor psychological status at diagnosis or 1 year later was associated with medical outcome in women with early-stage breast cancer [52]. The other study, on a sample of 448 locally advanced breast cancer patients, reported that baseline health-related quality of life parameters had no prognostic value in a non-metastatic breast cancer population [50]. However, A study using the Daily Diary Card to measure quality of life in advanced breast cancer showed that the instrument offered accurate prognostic data regarding subsequent response to treatment and survival duration [40]. Similarly, Seidman et al. [41] evaluated quality of life in two phase II clinical trials of metastatic breast cancer and found that baseline scores of two validated quality of life instruments independently predicted the overall survival. In addition, studies have demonstrated that some aspects of quality of life data including physical health [39], pain [45,48], and loss of appetite [51] are significant prognostic factors for survival in women with advanced breast cancer. In addition, one study demonstrated that baseline physical aspects of quality of life and its changes were related to survival, but psychological and social aspects were not [46].

Gastro-oesophageal cancers

The findings are summarized Table 4 [57-63]. Studies have shown that physical functioning was an important prognostic factors of survival in this group of cancer patients. Symptoms such as fatigue, reflux and appetite loss also were found to be independent prognostic factors of survival duration in patients with either gastric or oesophageal cancers.

Colorectal cancer

Social functioning as measured by the EORTC QLQ-C30 or health and physical subscales as measured by the Ferrans and Powers Quality of Life Index were shown to be prognostic factors of survival in colorectal cancer patients. The results are shown in Table 5 [19,64-68].

Other Cancers

Other studies of relationship between quality of life data and survival reported findings on different cancer populations including brain, ovarian, liver and bladder cancers. The findings of such studies are presented in Table 6. Except two studies in live and ovarian cancer patients [Fielding and Wong, Gupta et al], other studies found a significant relationship between quality of life scores and survival duration in these patients. The results are summarized in Table 6 [8, 37, 69-94].

Table 2: *Studies on relationship between quality of life data and survival in patients with lung cancer*

Author(s)	Year	Cancer	HRQOL measure(s)	Results*
Pater and Loeb [7]	1982	Bronchogenic carcinoma	Symptomatic history, performance status, weight loss and age	Weight loss and performance status were significantly affected survival.
Kaasa et al. [10]	1989	Inoperable non-small-cell	Psychological well-being + disease-related symptoms + personal functioning + everyday activity	General symptoms and psychological well-being were the best predictive value for survival.
Ganz et al. [17]	1991	Advanced metastatic lung cancer	FLI-C	A statistically significant relationship was observed between initial patient-rated QOL and subsequent survival.
Ruckdeschel et al. [18]	1994	Lung cancer	FLI-C	Total FLI-C score was significant predictor of survival.
Loprinzi et al. [19]	1994	Advanced colorectal or lung	A designed questionnaire	Patients' assessment of their own performance status and nutritional factors such as appetite, caloric intake, or overall food intake were prognostic of survival.
Buccheri et al. [20]	1995	Lung	TIQ	The self-estimated difficulty at work and doing housework were significant independent prognostic determinants of survival.
Buccheri et al. [21]	1998	Lung	SDS	Depression was associated with survival.
Herndon et al. [22]	1999	Advanced non-small-cell	EORTC QLQ-C30 + Duke-UNC Social Support Scale	Pain was a significant predictor of survival but overall QOL was not.
Langendijk et al. [23]	2000	Inoperable non-small-cell lung	EORTC QLQ-C30	Global QOL was a strong prognostic factor of survival.
Montazeri et al. [24]	2001	Lung (small and non-small-cell)	NHP + EORTC QLQ-C30 + QLQ-LC13	Baseline global QOL was most significant predictor of the length of survival.
Auchter et al. [25]	2001	Non-small cell	FACT-L (TOI)	The change in TOI score was not associated with survival. A trend was noted for shorter survival with the largest negative change in TOI score.
Moinpour et al. [26]	2002	Advanced non-small-cell	FACT-L	Total FACT-L score was predictor of survival.
Nakahara et al. [27]	2002	Advanced lung cancer	Tokyo University Egogram	Mental state was prognostic of survival.
Naughton et al. [28]	2002	Small-cell	EORTC QLQ-C30 + CES-D + MOS Social Support Questionnaire + a sleep quality scale	Higher depressive symptoms were borderline significant in predicting decreased survival.
Eton et al. [29]	2003	Advanced non-small-cell	FACT-L + TOI	Baseline physical well-being and TOI scores predicted either survival duration or disease progression respectively.
Dharma-Wardene et al. [30]	2004	Advanced lung cancer	FACT-G	Baseline FACT-G total score was significantly associated with survival.
Nowak et al. [31]	2004	Pleural mesotheliomia	EORTC QLQ-C30 + QLQ-LC13	Functional domains and symptom scales (fatigue, pain) demonstrated predictive validity for survival.
Maione et al. [32]	2005	Advanced non-small-cell lung cancer	ADL + IADL + EORTC QOL-C30 (global QOL)	Baseline global QOL and IADL were significant prognostic factors for overall survival.

Table 2 (continued)*: Studies on relationship between quality of life data and survival in patients with lung cancer*

Author(s)	Year	Cancer	HRQOL measure(s)	Results*
Brown et al. [33]	2005	Non-small-cell lung cancer	EORTC QLQ-C30 + QLQ-LC17 + DDC	Global QOL, role functioning, fatigue, appetite loss and constipation were prognostic indicators of survival.
Efficace et al. [34]	2006	Advanced non-small-cell lung cancer	EORTC QLQ-C30 + QLQ-LC13	Pain, and dysphagia were significant prognostic factors for survival.
Sundstrom et al. [35]	2006	Stag III non-small-cell lung cancer	EORTC QLQ-C30	Appetite loss was the most significant prognostic factor of survival.
Bottomley et al. [36]	2007	Malignant pleural mesothelioma	EORTC QLQ-C30 + QLQ-LC13	Pain, and appetite loss were independent prognostic indicators of survival.
Fielding and Wong [37]	2007	Liver and lung cancer	FACT-G	Global QOL scores did not predict survival in liver cancer. Physical well-being predicted survival in lung cancer.
Jacot et al. [38]	2008	Non-small-cell lung cancer	LCSS	Global symptoms score was independent determinants of overall survival.

Abbreviations: CES-D: Centre for Epidemiologic Studies-Depression Scale; DDC: Daily Diary Card; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire; FACT-G: Functional Assessment of Cancer Therapy-General module; FACT-L: Functional Assessment of Cancer Therapy-Lung module; FLI-C: Functional Living Index-Cancer; IADL: Instrumental Activities of Daily Living; LCSS: Lung Cancer Symptoms Scale; MOS: Medical Outcomes Study; ADL: Activities of Daily Living; NHP: Nottingham Health Profile; QLQ-LC13 (or QLQ LC17): EORTC Lung Cancer specific Quality of Life Questionnaire (previously containing 17items); QOL: quality of life; SDS: Self-rating Depression Scale; TIQ: Therapy Impact Questionnaire; TOI: Trial Outcome Index.
* All results obtained from multivariate analyses after controlling for one or more demographic and known biomedical prognostic factors.

Table 3*: Studies on relationship between quality of life data and survival in patients with breast cancer*

Author(s)	Year	Cancer	HRQOL measure(s)*	Results**
Coates et al. [9]	1987	Advanced breast cancer	LASA scores for physical well-being + mood, pain, and appetite (as QOL index)	Changes in QOL scores were independent prognostic of survival.
Coates et al. [39]	1992	Advanced breast cancer	LASA scores for physical well-being + mood, nausea, vomiting, and appetite (as QOL index)	Both QOL index and physical well-being were independent prognostic factors of survival.
Fraser et al. [40]	1993	Advanced breast cancer	DDC + LASA + NHP	The DDC provided accurate prognostic data regarding subsequent response and survival.
Seidman et al. [41]	1995	Advanced breast cancer	MSAS + MSAS-GDI + FLI-C + RMHI + BPI + MPAC	Baseline global QOL and distress index scores independently predicted the overall survival.
Tross et al. [42]	1996	Early stage breast cancer	SCL-90-R	No significant predictive effect of the level of depression on length of disease-free and overall survival observed.
Watson et al. [43]	1999	Early stage breast cancer	MAC + CECS + HADS	Depression score of the HADS and helplessness and hopelessness category of the MAC had determinant effect on survival.
Coats et al. [44]	2000	Metastatic and early stage breast cancer	Physical well-being + mood, appetite, and coping (as QOL index)	Disease-free survival was not significantly predicted by QOL scores at baseline or by changes in QOL scores. After relapse QOL scores were predictive for subsequent survival.
Kramer et al. [45]	2000	Advanced breast cancer	EORTC QLQ-C30	Pain was prognostic for survival. However, fatigue and emotional functioning were significant in backward selection model.

Table 3 (continued): *Studies on relationship between quality of life data and survival in patients with breast cancer*

Author(s)	Year	Cancer	HRQOL measure(s)*	Results**
Shimozuma et al. [46]	2000	Advanced or end stage breast cancer	QOL-ACD	Physical aspects of QOL were significantly related to survival. The change in scores of both overall QOL and the physical aspects of QOL were also significant predictors of survival.
Butow et al. [47]	2000	Metastatic breast cancer	Cognitive appraisal of threat + coping + psychological adjustment + perceived aim of treatment + social support + QOL	Minimization was associated with longer survival while a better appetite predicted shorter duration of survival.
Luoma et al. [48]	2003	Advanced breast cancer	EORTC QLQ-C30	Baseline severe pain was predictive for a shorter overall survival. QOL scores had no great importance in predicting primary clinical endpoints such as time to progression or overall survival.
Winer et al. [49]	2004	Metastatic breast cancer	FLI-C + SDS	Global QOL and symptom distress scores were prognostic for survival.
Efficace et al. [50]	2004	Nonmetastatic breast cancer	EORTC QLQ-C30	Baseline QOL had no prognostic value.
Efficace et al. [51]	2004	Matastatic breast cancer	EORTC QLQ-C30 + QLQ-BR23	Loss of appetite was a significant prognostic factor for survival.
Goodwin et al. [52]	2004	Early stage breast cancer	EORTC QLQ-C30 + PMS + PAIS + IES + MACS +ACS + CECS	QOL and psychological status at diagnosis and 1 year later were not associated with medical outcome.
Watson 2005 et al. [53]	2005	Early stage breast cancer	MAC + HADS	Helplessness/hopelessness was a significant predictor of disease-free survival but depression was not.
Lehto et al. [54]	2006	Localized breast cancer	Coping + emotional expression + perceived support + life stresses + QOL	Longer survival was predicted by a minimizing-related coping while shorter survival was predicted by anti-emotionality, escape coping, and high level of perceived support.
Gupta et al. [55]	2007	Breast carcinoma	Ferrans and Powers QLI	Baseline patient satisfaction with health and physical functioning and overall HRQOL were significant prognostic of survival.
Groenvold et al. [56]	2007	Breast cancer	EORTC QLQ-C30 + HADS	Emotional functioning and fatigue were independent predictors of survival.

Abbreviations: ACS: Adjustment to Cancer Scale; BPI: Brief Pain Inventory; CECS: Courtauld Emotional Control Scale; DDC: Daily Dairy Card; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire; FLIC: Functional Living Index-Cancer; HADS: Hospital Anxiety and Depression Scale; IES: Impact of Events Scale; LASA: Linear Analog Self Assessment; MAC: Mental Adjustment to Cancer Scale; MPAC: Memorial Pain Assessment Card; MSAS: Memorial Symptom Assessment Scale; MSAS-GDI: Memorial Symptom Assessment Scale-Global Distress Index; NHP: Nottingham Health Profile; PAIS: Psychological Adjustment to Illness Scale; PMS: Profile of Mood States; QLI: Quality of Life Index; QOL: quality of life; QOL-ACD: Quality of Life Questionnaire for Cancer Patients Treated with Anticancer Drugs; RMHI: Rand Mental Health Inventory; SCL-90-R: Symptom Check List-90 items-Revised; SDS: Symptom Distress Scale.
* All results obtained from multivariate analyses after controlling for one or more demographic and known biomedical prognostic factors.

Table 4: *Studies on relationship between quality of life data and survival in patients with gastro-oesophageal cancers*

Author(s)	Year	Cancer	HRQOL measure(s)	Results*
Blazeby et al. [57]	2000	Oesophageal	EORTC QLQ-C30 + Dysphagia scale of QLQ-OES24	Physical functioning at baseline was significantly associated with survival.
Blazeby et al. [58]	2001	Oesophaageal	EORTC QLQ-C30 + Dysphagia scale of QLQ-OES24	Physical functioning at baseline was significantly associated with survival. After treatment, improved emotional functioning was significantly related to longer survival.
Fang et al. [59]	2004	Oesophageal squamous cell	EORTC QLQ-C30	Pretreatment physical functioning was the most significant survival predictor while QOL scores during treatment were not. After treatment dysphagia was the most significant predictor.
Chau et al. [60]	2004	Locally advanced or metastatic esophago-gastric	EORTC QLQ-C30	Pretreatment physical and role functioning and global QOL predicted survival.
Park et al. [61]	2008	Advanced gastric	EORTC QLQ-C30	Social functioning was significant prognostic factor for survival.
Bergquist et al. [62]	2008	Advanced oesophageal	EORTC QLQ-C30 + QLQ-OES18	Physical functioning, fatigue and reflux were significant prognostic of survival.
McKernan et al. [63]	2008	Gastric or oesophageal	EORTC QLQ-C30	Appetite loss was significantly independent predictor of survival.

Abbreviations: EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire; QLQ-OES18 (previously QLQ-OES24): EORTC Oesophageal Cancer specific Quality of Life Questionnaire; QOL: quality of life.

* All results obtained from multivariate analyses after controlling for one or more demographic and known biomedical prognostic factors.

Table 5: *Studies on relationship between quality of life data and survival in patients with colorectal cancer*

Author(s)	Year	Cancer	HRQOL measure(s)	Results*
Loprinzi et al. [19]	1994	Advanced colorectal or lung	A designed questionnaire	Patients' assessment of their own performance status and nutritional factors such as appetite, caloric intake, or overall food intake were prognostic of survival.
Earlam et al. [64]	1996	Colorectal with liver metastases	RSCL + HADS + SIP	Diarrhea, eating, restlessness, and ability to work and sleep were predictors of survival.
Maisey et al. [65]	2002	Locally advanced and metastatic colorectal	EORTC QLQ-C30	Baseline physical, role, social, emotional functioning, global QOL and pain, nausea, dyspnea, and sleep difficulties were strong independent predictors of survival.
Lis et al. [66]	2006	Colorectal	Ferrans and Powers QLI	Health and physical subscale was predictive of survival.
Efficace et al. [67]	2006	Metastatic colorectal	EORTC QLQ-C30	Social functioning was a prognostic measure of survival beyond a number of previously known biomedical parameters.
Efficace et al. [68]	2008	Metastatic colorectal	EORTC QLQ-C30	Social functioning was prognostic factor for survival.

Abbreviations: EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire; HADS: Hospital and Anxiety Depression Scale; QLI: Quality of Life Index; QOL: quality of life; RSCL: Rotterdam Symptom Checklist; SIP: Sickness Impact Profile.

* All results obtained from multivariate analyses after controlling for one or more demographic and known biomedical prognostic factors.

Table 6: *Studies on relationship between quality of life data and survival in patients with different cancers*

Author(s)	Year	Cancer	HRQOL measure(s)	Results*
Cassileth et al. [8,69]	1985 and 1988	Unresectable cancers + early stage melanoma or breast	Social and psychological factors	Social and psychological factors individually or in combined did not influence the length of survival.
Coates et al. [70]	1993	Metastatic melanoma	LASA scales + Spitzer QLI	QLI and LASA scores for mood, appetite, and overall QOL were significant predictors of survival.
Tannock et al. [71]	1996	Symptomatic hormone-resistant prostate	EORTC QLQ-C30 + QLQ-PR25 + PROSQOLI	Appetite loss, pain, and physical functioning were associated with survival.
Wisloff and Hjorth [72]	1997	Multiple myeloma	EORTC QLQ-C30	Physical functioning was independent prognostic factor of survival.
De Bore [73]	1998	Head and neck	Self-reported psychosocial and physical functioning	Patients with higher perceived physical abilities were likely to survive more.
Butow et al. [74]	1999	Metastatic melanoma	Cognitive appraisal of threat+ coping + psychological adjustment + perceived aim of treatment + social support + QOL	Perceived aim of treatment, minimization, anger and better QOL were independently predictive of longer survival.
Brown et al. [75]	2000	Early stage melanoma		Shorter survival duration was associated with a positive mood.
Meyers et al. [76]	2000	Brain (recurrent glioblastoma multiforme or anaplastic astrocytoma)	FACT-Br + ADL	Measures of QOL and ADL were not independently related to survival.
de Graeff et al. [77]	2001	Head and neck	EORTC QLQ-C30 + QLQ-H&N35 + CES-D	Cognitive functioning was prognostic factor of survival while physical functioning, mood and global QOL were not.
Jerkeman et al. [78]	2001	Lymphoma	EORTC QLQ-C30	Pretreatment global QOL was an independent prognostic marker of survival.
Roychowdury et al. [79]	2003	Locally advanced and metastatic bladder	EORTC QLQ-C30	Longer survival was associated with high physical functioning, low role functioning and no anorexia.
Chiarion-Sileni et al. [80]	2003	Advanced melanoma	RSCL	Baseline overall QOL and the physical symptom distress scores were significant independent prognostic factors for survival.
Fang et al [81].	2004	Advanced head and neck	EORTC QLQ-C30 + QLQ-H&N35	Baseline fatigue was predictive of survival while changes in QOL scores during treatment were not.
Collette et al. [82]	2004	Symptomatic metastatic hormone-resistant Prostate	EORTC QLQ-C30	Insomnia and appetite loss were significant independent predictors of survival.
Monk et al. [83]	2005	Advanced cervix	FACT-G + Cervix subscale + FACT/GOG-Ntx+ BPI	Baseline FACT-Cx (FACT-G + Cervix subscale) scores was associated with survival.
Brown et al. [84]	2006	Brain (high grade glioma)	LASA scales (to measure overall QOL)+ FACT-Br + Fatigue (SDS) + excessive daytime somnolence (ESS) + depression (POMS-SF)	Fatigue was significant independent predictor of survival.

Table 6 (continued): *Studies on relationship between quality of life data and survival in patients with different cancers*

Author(s)	Year	Cancer	HRQOL measure(s)	Results*
Yeo et al. [85]	2006	Unresectable hepatocellular	EORTC QLQ-C30	Appetite loss, physical and role functioning scores were significant predictor of survival.
Lis et al. [86]	2006	Pancreatic	Ferrans and Powers QLI	Health and physical subscale was marginally significant predictor of survival.
Dubois et al. [87]	2006	Refractory multiple myeloma	EORTC QLQ-C30 + QLQ-MY24 + FACIT-Fatigue + FACT/GOG-Ntx	Fatigue was significant predictor of survival.
Sullivan et al. [88]	2006	Metastatic hormon-refractory prostate	EORTC QLQ-C30 + FACT-P	Baseline QOL scores (global QOL, physical, role, and social functioning and pain, fatigue and appetite loss) were significant predictors of survival.
Mauer et al. [89]	2007	Brain (anaplastic oligodenroglimas)	EORTC QLQ-C30 + QLQ-BN20	Emotional functioning, communication deficit, future uncertainty, and weakness of legs were significant prognostic of survival. Baseline QOL scores added little to clinical factors to predict survival.
Mauer et al. [90]	2007	Brain (glioblastoma)	EORTC QLQ-C30 + QLQ-BN20	Cognitive functioning, global health status, and social functioning were significant prognostic factors of survival. Baseline QOL scores added little to clinical factors to predict survival.
Fielding and Wong [37]	2007	Liver and lung	FACT-G	Global QOL scores did not predict survival in liver cancer. Physical well-being predicted survival in lung cancer.
Lehto et al. [91]	2007	Localized melanoma	Coping with cancer + anger expression, perceived social support + life stresses + single item QOL	Anger non-expression, hopelessness, over-positive reporting of QOL reduced survival while denial/minimizing response to the diagnosis as such predicted longer survival.
Bonnetain et al. [92]	2008	Advanced hepatocellular carcinoma	Spitzer QLI	Baseline QOL was independent prognostic factor for survival.
Carey et al. [93]	2008	Advanced ovarian cancer	EORTC QLQ-C30	Performance status and global QOL scores at baseline were prognostic factors for both progression-free survival and overall survival.
Gupta et al. [94]	2008	Ovarian cancer	Ferrans and Powers QLI	No statistically significant prognostic association of patient satisfaction with QOL was observed with survival.

Abbreviations: ADL: Activities of Daily Living; BPI: Brief Pain Inventory; CES-D: Centre for Epidemiologic Studies-Depression Scale; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire; ESS: Epworth Sleepiness Scale; FACIT-Fatigue: Functional Assessment of Chronic Illness Therapy-Fatigue scale; FACT-Br: Functional Assessment of Cancer Therapy-Brain module; FACT-G: Functional Assessment of Cancer Therapy-General module; FACT-P: Functional Assessment of Chronic Illness Therapy- prostate module; LASA: Linear Analog Self Assessment; POMS-SF: Profile of Mood State-Short Form; PROSQOL: Prostate Cancer-Specific Quality-of-Life Instrument; QLI; Quality of Life Index; QLQ-BN20: EORTC Brain Cancer specific Quality of Life Questionnaire; QLQ-H&N35: EORTC Head and Neck Cancer specific Quality of Life Questionnaire; FACT/GOG-Ntx: FACT Gynecologic Oncology Group Neurotoxicity scale; QLQ-MY24: EORTC Myeloma specific Quality of Life Questionnaire; QLQ-PR25: EORTC Prostate Cancer specific Quality of Life Questionnaire; QOL: quality of life; RSCL: Rotterdam Symptom Checklist; SDS: Symptom Distress Scale.
* All results obtained from multivariate analyses after controlling for one or more demographic and known biomedical prognostic factors.

Discussion

Although a helpful review on the topic was published recently [95], this is the first comprehensive study that reviewed the prognostic value of quality of life data for survival time in cancer patients. The review contained 88 studies and apart from a few exceptions in most instances the results indicated that health-related quality of life data or some aspects of quality of life measures were significant predictors of survival duration.

Early studies reported here were used ad hoc instruments while recent studies used well-validated cancer-specific quality of life questionnaires. Even

most recent studies supplemented site-specific questioner in their assessments. The EORTC QLQ-C30 was found to be the most utilized cancer-specific instrument and as one could observe in tables provided in this review in many occasions the questionnaire showed relatively consistent and reliable results. The EORTC QLQ-C30 and its supplementary modules such as QLQ-BR23, QLQ-LC13 and QLQ-BN20 are very useful instruments to be applied in prognostic factors analyses providing that other methodological requisites are ensured.

Many reported that global or overall quality of life was found to be independent significant predictor of survival. Global quality of life is usually a very straightforward question that in general asks people to evaluate their own health status or quality of life individually or in combined. It is argued measures such as global quality of life are patient-rated and thus are have potentials to reflect patients' well-being better than physicians observed indicators. However, it has been recommended that for instance since global quality of life scale of the EORTC QLQ-C30 is highly correlated with other scales, it should not be included in prognostic factor analyses when using other variables from the EORTC QLQ-C30 in order to achieve model stability [96].

There were several measures such as physical functioning that particularly showed significant association with the length of survival in cancer patients. It is argued that physical functioning might be a surrogate marker of an unrecognized biological prognostic factor and thus one should not conclude a causative association between physical functioning and survival time [58].

Among symptoms, appetite loss, pain and fatigue were found to be most important or strongest independent predictors of survival in many different studies among different cancer populations. One possible explanation is that these symptoms are very sensitive markers of the patients' well-beings. In addition as explained by Effcace et al. [51], such findings might be due to the fact that in multivariate analyses other quality of life measures mask each other in effect and therefore variables such as appetite loss or pain or fatigue appear as most important or strongest predictors of the length of survival.

As suggested by Gotay et al. [95] there are several explanations for association between health-related quality of life data and survival duration in cancer outcome studies. They summarized four possible explanations: (i) quality of life measures include different items and thus provide more sensitive information than traditional performance status and toxicity measures; (ii) quality of life data, especially those collected at baseline before disease progression, could pick up relevant information earlier that established clinical prognostic factors; (iii) quality of life data are markers of patients' behavior as it relates to the disease diagnosis, its treatment and subsequent outcomes; and that (iv) quality of life data are markers of individual characteristics such as personality style, and adapting coping strategies that affect the process and outcomes in cancer patients.

This review intended to include studies that examined the relationship between quality of life data and survival and thus excluding pure psychological studies that report on association between psychological data and survival. However, inevitably some papers that in principle belonged to psychological discipline were included in this review. Usually these papers reported that they incorporated a measure of quality of life in their studies, although for assessing the quality of life did not use well-known instruments. Contradictory to expectation, these papers found that in multivariate analyses better conditions such as over-positive reporting of quality of life [91] or having a better appetite were indicators of shorter survival [47].

This review was based on a single data bank that is MEDLIN and manual search only. In addition the search strategy was based on keywords in titles of the English language publications. Thus there is a risk for missing other possible papers, although manual search might be reduced the risk. Furthermore, the review was not examined the individual reports in details and thus the findings are not inclusive. However, as Bottomley and Efficace in their editorial stated studies on relationships between quality of life data and survival duration achieved considerable evidence, although it is still a relatively novel area of research in oncology and long way to go remain. As suggested more prospective studies that are hypothesis driven are needed to provide robust evidence to show that health-related quality of life data and patient-reported outcomes independently predict length of survival [97].

In conclusion, studies reported in this review provide evidence for a positive relationship between quality of life data or some aspects of quality of life measures and the length of survival in cancer patients. Pre-treatment quality of life data are appeared to be most reliable information that could help clinicians to establish prognostic criteria for treatment of their cancer patients. Indeed, conducting studies using valid instruments, applying sound methodological approaches and adequate but not

sophisticated multivariate statistical analyses adjusted for demographic characteristics and known clinical prognostic factors are recommended in order to yield more specific quality of life related prognostic variables for specific cancers.

Acknowledgment

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