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Review

Do Oncologists Have an Increasing Interest in the Quality of Life of Their Patients? A Literature Review of the Last 15 Years

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The aim of this review is to evaluate the extent to which Quality of Life (QoL) assessment has been incorporated into clinical oncological trials in the last 15 years. All phase II and III trials published in the *Journal of Clinical Oncology, Cancer, The British Journal of Cancer* and the *European Journal of Cancer* during the years 1980, 1985, 1990 and 1995 were reviewed ($n = 827$). During this period, while the number of studies assessing performance status (PS) increased from 15% in 1980 to 56% in 1995, the number of trials noting a QoL assessment increased only slightly, from 0% in 1980 to 3% in 1995. Moreover, only four of the 13 studies with a QoL evaluation met our criteria for adequate QoL assessment. Thus, despite an increasing interest in QoL, it is still rarely included as an objective in clinical trials, or adequately assessed. © **1997 Published by Elsevier Science Ltd. All rights reserved.**

Key words: quality of life, performance status, cancer, clinical trials

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INTRODUCTION

IN ONCOLOGY, parameters usually taken into consideration in determining the efficacy of new treatments include survival, disease-free survival and response rate. However, whether a treatment should be considered effective if it only gives an objective tumour response, with no improvement of symptoms, and produces side-effects, is debatable. When curing a patient is no longer possible, most physicians prefer to relieve symptoms and find a treatment that can help them live as comfortably as possible.

In the last 10 years, a new entity called Quality of Life (QoL) has been developed [1, 2]. This term has a broad meaning which includes not only health-related factors, such as physical, functional and mental well-being, but also non-health-related elements, such as social, work or relationship issues. Before this period, the primary measure of functional status approach was performance status (PS) (Karnofsky Index or ECOG scale [3, 4]). PS has been demonstrated to be one of the most important prognostic factors in nearly all cancers [5].

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The purpose of this literature review was to evaluate the extent to which QoL has been incorporated into phase II and III clinical oncological trials over the last 15 years.

MATERIALS AND METHODS

Four of the major oncological journals were selected which report results of clinical trials: *Journal of Clinical Oncology* (*JCO*), *Cancer*, *British Journal of Cancer* (*BJC*) and the *European Journal of Cancer* (*EJC*). All the issues in these journals were reviewed for the years 1980, 1985, 1990 and 1995. For *JCO*, the review began in 1985, because this journal was not published in 1980. The publications that were reviewed were original studies, editorials and reviews. Short communications or letters were not included for the purposes of this review.

All phase II and phase III therapeutic trials in cancer patients were examined for their assessment of QoL, including surgical, radiotherapeutic, chemotherapeutic or other trials involving supportive care medications, such as antiemetics or growth factors. Pilot studies or phase I trials were excluded from consideration because the objectives of these studies are limited to dosage and toxicities.

The adequacy of the QoL assessments were evaluated according to the following criteria: (1) Instruments were

described precisely, with references given concerning validity; (2) Each domain was assessed by more than one item; (3) Assessment covered several domains (physical, psychological, social, etc.); (4) Instruments included patients' self-report and not only health workers' assessment; (5) Results were presented; (6) When appropriate, instruments were validated in the language of the patients.

The use of PS scales (Karnofsky (KPS) or ECOG [3, 4]) were also examined. When PS was reported at baseline only, PS was considered more as a prognostic factor than as a 'well-being index'.

The following descriptive parameters of the articles were obtained for the last year (1995): (1) Intention of treatment (curative or palliative); (2) Type of therapy (chemotherapy, surgery, etc.); (3) Type of trial (phase II or III, multicentric or not); (4) Nationality of the first author; (5) Number of patients included in the study; (6) Site of tumour.

This review was conducted manually and double-checked by computer searches using MEDLINE and CURRENT CONTENTS to insure that no important study was missed.

RESULTS

Of 5197 publications that were reviewed in these journals for the selected years, 84% ($n = 4370$) were excluded from this review, because they were not related to a clinical trial or because they did not meet the inclusion criteria.

Of the 4370 excluded studies, 58 (1.3%) had Quality of Life or psychosocial adaptation to cancer as their main topic. Of these 58, fifteen were general review articles, 17 were a descriptive evaluation in certain cancer sites, nine described the development of a new scale, and the last 17 had diverse topics (e.g. health worker's issues, prognostic factors, sequel upon survivals). The number of publications with QoL or psychosocial adaptation to cancer as a main topic increased greatly from 1980 (Figure 1).

Of the 5197 publications, 827 met the criteria for this review (66 in 1980, 209 in 1985, 252 in 1990 and 300 in 1995). Table 1 shows the characteristics of the 300 therapeutic trials published in 1995. One third of the studies were phase III, and two thirds phase II.

The majority of the studies had a European first author (58%), and 80% involved palliative care. Breast, lung or haematological sites were the most common tumours studied.

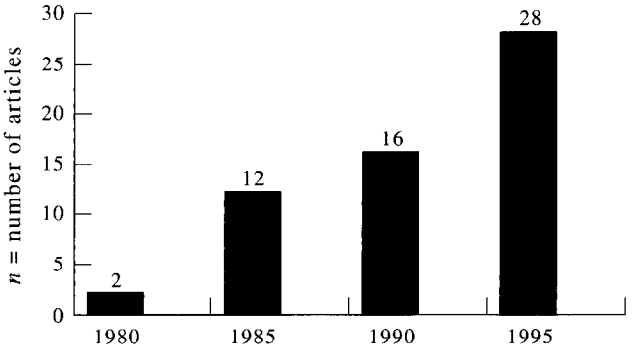

Figure 1. Articles with QoL or psychosocial adaptation as the topic ($n = 58$).

Table 1. Characteristics of the trials

Therapeutic trials published in 1995 ($n = 300$)		
Phase II or III trial	II	199 (66%)
	III	101 (34%)
Intention of treatment	Curative	60 (20%)
	Palliative	240 (80%)
Number of patients in the trial	≥100	107 (36%)
	<100	193 (64%)
Institutional involvement	Multicentred	119 (40%)
	Single institution	181 (60%)
Nationality of first author	U.S.A.	88 (29%)
	European	174 (59%)
	Other	38 (13%)
Cancer site	Haematological	61 (20%)
	Breast	52 (17%)
	Lung	44 (15%)
	Paediatric	28 (9%)
	Other	115 (38%)

ASSESSMENT OF THE STUDYING VARIABLES

Performance status

As shown in Figure 2, most of the studies included assessment of PS (more than 50% since 1990), but there were very few studies that assessed PS over the course of the trial. Further, when there was a description of the change in PS over time, it was usually calculated in terms of decreasing PS—listed in the toxic effects—so there was no possibility of observing an improvement for some patients.

There were some malignancies for which the patients' PS was assessed infrequently. In haematological tumours, less than one third of the studies reported a PS in 1995 and in paediatric tumours, only 4%.

The scale used to determine PS has changed over the last 15 years. In 1980, the KPS was used twice as often as ECOG, but since 1990, the ECOG scale has been used more than twice as often as KPS.

Quality of life

The numbers of therapeutic trials in oncology noting a QoL assessment increased slightly, from 0 in 1980, to 1 in 1985, 3 in 1990 and 9 in 1995 (Figure 2), but the proportion of trials with a QoL component was still very low: 1.6% in 1990 and 3% in 1995. Five of 13 studies were multicentred (5/13), with 7 of 13 involving more than 100 patients (Table 2). Only four of these 13 studies completely met our criteria for adequate QoL assessment [6–9], but

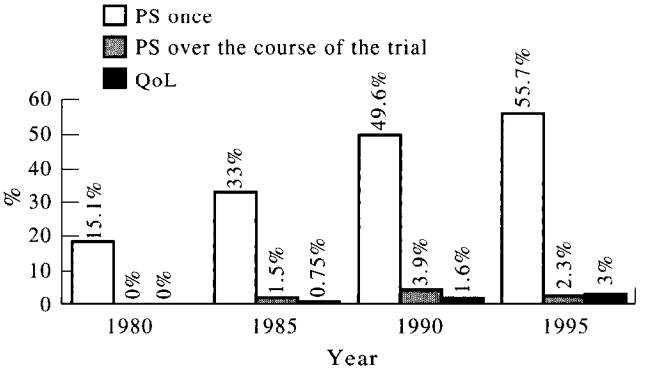

Figure 2. Studies including performance status and QoL ($n = 827$).

Table 2. Data on the thirteen articles that describe the evaluation of QoL

Author (year) [Ref.]	Country	Disease site	Treatment	Phase	Multicentred	*n*	QoL instrument	QoL criteria: comments
Lazlo (1985) [12]	U.S.A.	Mixed	Pal	II	No	32	MAS-CGI	No (no ref for instrument; unidimensional)
Willemse (1990) [6]	Holland	Ovary	Chemo	II	No	68	TWiST	Yes
North (1990) [15]	U.S.A.	Brain	RT	II	No	77	Order scale	No (no patient self report; single item)
Bruera (1990) [16]	Canada	Mixed	Pal	II	No	40	VAS	No (single item; unidimensional)
Clavel (1995) [11]	France	Mixed	Pal	III		259	FLIC	Yes but no reference for instrument in French
Hill (1995) [7]	U.K.	Colon	Immuno	III	No	160	EORTC	Yes
Cunningham (1995) [8]	U.K.	Colon	Chemo	III		439	EORTC	Yes
Jones (1995) [14]	U.S.A.	Breast	Chemo	III		183	Personal	No (personally developed instrument; no validation, no results)
Ludwig (1995) [10]	Austria	Mixed	Pal	II		102	Priestman	Yes but no reference for instrument in German
Sundaresan (1995) [9]	U.S.A.	Mixed	Surgery	II	No	110	FACTG	Yes
Hayes (1995) [18]	U.S.A.	Breast	Hormonal	III		648	VAS	No (only one item for mood and enjoyment)
Robertson (1995) [17]	U.K.	Mixed	Clodronate	III	No	55	VAS	No (unidimensional; single item)
Bjermer (1995) [13]	Norway	Mixed	Chemo versus Pal	III	No	30	Personal	No (personally developed instrument; no validation)

Pal, palliative; Chemo, chemotherapy; RT, radiotherapy; VAS, visual analogue scale.

two others nearly met them, with the authors only failing to give the validation of the instrument in their language [10, 11]. The other seven studies did not have valid quality of life assessment for the following reasons: (i) Reference for the source of the instrument was not given (1) [12]; (ii) Author developed personal instrument without description of validation (2) [13, 14]; (iii) Unidimensional (3) [12, 16, 17]; (iv) Single item (4) [14, 16–18]; (v) No self report QoL measure (1) [15].

The following scales were used for studies that had an adequate quality of life assessment: EORTC [7, 8], TWIST [6], FLIC [11], FACT/G [9] and The Priestman Scale [10].

DISCUSSION

Among the 827 trials that were reviewed, only three included an adequate assessment of the different domains that are components of a multidimensional QoL evaluation. Such a low rate was surprising because all the review articles recently published reported an increased interest in this field [19, 20]. In fact, an increasing number of publications with QoL as the main topic were found (Figure 1), but the aim of our study was not to measure the interest of the oncologists in QoL, but its assessment in their therapeutic trials.

Our review shows that there was a very low number of clinical trials in which QoL was considered as an endpoint, and even when QoL was studied, most of the evaluations were not adequate, usually because the assessment was unidimensional or because a non-validated instrument was used.

Wilson and Cleary [23] described a model of QoL where measures of health can be thought of as existing on a continuum of increasing biological, social and psychological complexity. The biological and physiological level is not affected by any characteristic of the individual or the environment. The next four levels, symptom status, functional status, general health perception and overall quality of life, are strongly affected by individual characteristics (e.g. motivations, personality or preferences) and environmental characteristics (e.g. social and economical supports). When QoL is impaired, it is important to be able to study these different domains and, therefore, to use an instrument with subscales for each dimension of the 'overall quality of life'. In multidimensional instruments, such as the EORTC QLQ 30 [1] or the FLIC [2], the correlation between the different scores or subscales has been found to be low [20], which indicates that these subscales are really measuring different dimensions of QoL. A single visual analogue scale of well being—even if it represents a global evaluation—will not be able to provide detailed information about the impact of treatment in the different areas of a patient's functioning.

While clinicians frequently incorporated performance status in their therapeutic trials, it was generally not assessed over the course of the trial. PS was not usually used as an index of well-being, but as a prognostic or stratification factor. In fact, PS is moderately correlated to results of multidimensional instruments [20–22].

CONCLUSION

Despite an increasing interest by oncologists in QoL, it is still rarely included as an objective in their clinical trials.

Therefore, our recommendations concerning the design of clinical trials are the following: (1) QoL assessment should be considered for every phase III palliative care trial, and included in those in which significant treatment side-effects are expected. Our review showed that only 30% of the trials published in 1995 included that aspect; (2) Adequate QoL assessment requires measurement of physical symptoms, physical functioning, psychological state and social functioning. Therefore, a single visual analogue scale should not be considered as sufficient; (3) While it is important to measure PS over the course of a clinical trial, it is not adequate by itself as a measurement of overall QoL.

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