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REVIEW ARTICLE

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Quality of life in patients with ovarian cancer: current state of research

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Abstract Ovarian cancer is the most malignant cancer in women, where it is the fifth leading cause of cancer-related death. The disease and its treatment have considerable effects on the quality of life of patients with this cancer. This study reviews existing literature on quality of life in patients with ovarian cancer to demonstrate the importance of the topic, to comment on improvements achieved and to consider their implications for the implementation of optimal treatment. A literature search was carried out through MEDLINE and of published papers on quality of life in patients with ovarian cancer from 1976 to 1994. Twenty papers have been reviewed, of which, 10 were treatment-related assessments of quality of life and the remaining 10 dealt with different topics including psychometric issues in measuring health-related quality of life. Twenty-four instruments were employed to measure quality of life. Of these, the Rotterdam Symptom Checklist (RSCL) and The European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30) were found to be the most appropriate. Although meta-analysis of results is impossible, it appears that debulking surgery followed by platinum-based chemotherapy could improve both quality of life and survival. In addition to effective and efficient treatment, psychological counselling, palliative and home care, nutritional support and pain relief are the most important areas for improving quality of life of patients with ovarian cancer. Knowledge and insight into the quality of life of patients with ovarian cancer are still limited, and a large carefully planned international study is required. Use of existing standard measures is preferable and agreement should be reached on a selected single instrument.

Key words Quality of life · Ovarian cancer · Optimal treatment · Quality of life measures

Introduction

Cancer of the ovary is the most malignant tumour of the female genital tract [20, 60]. It accounts for 6% of all deaths from cancer in women and its prognosis is poor [4].Epidemiological studies have provided evidence of a significant improvement in survival of patients with ovarian cancer over the past decade [5, 32], but until now the factors responsible for this improvement in ovarian cancer outcome have not been fully demonstrated.

The West of Scotland Cancer Surveillance Unit originated and carried out a series of investigations on variations in the care of ovarian cancer in the West of

Scotland and demonstrated significant differences in outcome of therapy between hospitals inside and outside Glasgow [18, 26]. Their recent study shows that the improvement in survival is significantly associated with multi-disciplinary therapy and optimal treatment [30]. A fundamental question remains: does optimal treatment result in better quality of life [38]?

Assessment of quality of life is one of the most important issues in cancer. There is a growing concern to include quality of life measurements in clinical trials, since, although prolongation of survival is critical to patients with cancer, the quality of that time should also be seen as crucial. Quality of life or more correctly health-related quality of life can be seen not only as perceived health rated by patients themselves, but also as an outcome measure of the health-care system. There is considerable debate over the concept of quality of life (many researchers preferring more limited terms such as "perceived health status"), techniques of measurement, reliability, validity and the contribution of these measures to health-care policy, outcomes and resource allocation [16]. It is argued that measurements provided by quality of life studies, although not available from routinely collected data, may add valuable information to clinical practice, especially in clinical decision making.

Quality of life in patients with cancer has been reviewed extensively [1, 22, 40, 54]. This paper reviews the existing literature on quality of life in patients with ovarian cancer to assist with the implementation of optimal treatment.

Methods

Two methods of investigation were carried out: a MEDLINE search, and a search through published papers from 1976 to 1994 for citations of other useful works. For the MEDLINE search the key words "quality of life" and "ovarian cancer" were used. These provided the initial database for the review. The year 1976 was chosen since from 1977 quality of life has been a key word in the MEDLINE computer search system [29]. However, if there were papers published, for example, in 1994 but which appearing in the 1995 search, they were listed under the 1994 papers. The initial search was carried out in 1993 and it was up-dated twice in 1994 and once at the end of March 1995.

In the second step, using the initial database, the papers cited in the literature were examined for possible additional existing papers. The criteria for inclusion of papers in the review were based on the use of standard instruments or an identified set of questions documented in the paper. Papers, for example, on psychological aspects of gynaecological cancer were excluded, since this was beyond the scope of this review (see, for example, [8, 37, 51]).

Results

Trends

The MEDLINE search from 1976 to 1994 provided 48 citations. A review of abstracts of these papers showed that 36 made only a passing reference to quality of life of patients with ovarian cancer. For example, from these 36 papers one of the articles was examined fully. Petru et al. [47] in a study on long-term survival in advanced (stage III and IV) ovarian cancer reported that out of 104 who were operated between 1977 and 1984, only 13 patients survived 5 years or longer. At 5 years, 9 were free of disease and had a high quality of life. Out of the 9 patients, 6 were able to perform daily activities without restriction, the other 3 were physically limited to light work. The other 4 patients were either capable of limited self-care or totally confined to bed. There was no systematic measurement of quality of life, and the authors did not indicate how they assessed this. The remaining 12 papers dealt explicitly with measurement of quality of life. Of those 10 were in English, one was in Dutch, and one was in German. The abstract of the German paper was not available and was excluded. Of those in English, one was a paper on outcome assessment of home parenteral nutrition in patients with gynaecological malignancies including an assessment of quality of life. Since in this paper the characteristics of patients, that is disease site and corresponding numbers, were not demonstrated, it was excluded too [31]. Therefore, in total 2 papers out of 12 were excluded. The trend of appearance of these papers in biomedical journals as indicated in a MEDLINE search is presented in Table 1.

From the second approach to the literature search it appeared that there were 12 additional publications with the above criteria cited in published papers. Of those, 1 was a commentary [3], and 1 made only a passing reference to quality of life [35], while the remaining 10 provided data. These papers usually dealt with quality of life not only for ovarian cancer patients, but also for patients with other cancers.

A total of 20 papers (10 from the MEDLINE search and 10 from the literature search) are reviewed.

Features

Table 2 summarises the studies. In this table the objective(s), treatment types, sample size, and disease stage are identified. Five studies were concerned with methodological issues in quality of life [10, 24, 41, 48, 56], and 10 papers were either part of a clinical trial or attempted to compare therapies on the basis of a systematic measurement of quality of life [7, 11, 15, 21, 23, 28, 46, 55, 58, 59]. The remaining 5 papers used quality

Table 1 The number of papers with key words "quality of life" and "ovarian cancer" by MEDLINE search 1976–1994. Quality of life became a key word in MEDLINE search after 1977. Systematic assessment means those papers which used standard instrument(s) to measure the quality of life

Year	Quality of life	Ovarian cancer	Quality of life and ovarian cancer	Systematic assessment
1976–1977	379	102	0	0
1978–1979	524	168	0	0
1980–1981	566	211	0	0
1982	350	130	0	0
1983	371	189	1	1
1984	406	214	0	0
1985	471	308	2	0
1986	569	261	2	0
1987	705	321	1	0
1988	741	348	1	0
1989	1206	469	6	1
1990	1384	467	3	2
1991	1394	442	6	1
1992	1638	585	9	3
1993	1899	682	7	3
1994	2046	662	10	1
Total	14649	5559	48	12[a]

[a] Of these, 10 papers have been reviewed

of life as an outcome measure for different objectives, mainly supportive care, such as assessment of relationship between dietary intake and quality of life [34, 42, 43, 49, 50].

Instruments

In total among many available measures, 24 different instruments (or parts of an instrument) were used to measure quality of life in patients with ovarian cancer. Of these, 3 were ad hoc tools using a set of questions on areas such as normal activities and continued employment [10], and questions related to side-effects of cancer chemotherapy [11]. The instrument covering side-effects of cancer chemotherapy consisted of two sets of white cards (group A and group B) on each of which was the name of one potential side-effect of chemotherapy: group A (45 cards) listed physical side-effects, and group B (28 cards) non-physical side-effects. The patients were asked to select any cards that described a side-effect they attributed to their current chemotherapy. One study employed the visual-analogue scale technique including psychological items and questions about nausea and vomiting [15]. The remaining instruments are listed in Table 3 and the main feature of each quality of life measure has been shown. Some of these instruments, such as the World Health Organisation (WHO) performance status, the Eastern Co-operative Oncology Group scale (ECOG) and the Karnofsky performance status (KPS), although widely used, are not full quality of life measures, since they measure only performance status. In addition, three papers used study-specific questionnaires: one using a questionnaire on pain, general well-being, social and family life, diet etc. [15], one measuring 18 symptoms commonly associated with cytotoxic chemotherapy [46], and one using 2 items on sexual activity and side-effects of chemotherapy [21]. None of these measures was specific to ovarian disease. Such instruments do not appear in recent publications. Since the timing of assessment of quality of life is considered to be important, Table 4 demonstrates the time of administration of these measures, the name and the number of instruments employed in each individual study.

Main outcome results

Surgery

The initial approach to treatment of patients with ovarian cancer remains surgery, but controversy still exists regarding the impact of the surgery upon overall survival [44]. Therefore, if the prolongation of survival is debatable, studying quality of survival and considering patients' views seem crucial. It has been shown that debulking surgery (to remove masses greater than 2 cm) could improve the quality of life as well as the length of survival. Blythe and Wahl [7] reported that the average length of survival in a group of patients who received debulking surgery was 14.3 months, with more enjoyment of life, while in patients who did not receive such treatment survival was 12.2 months with a lower quality of life.

The effect of second debulking surgery (surgery to remove all tumour tissue after diagnosed recurrence and proper and complete response to primary surgery) on survival and quality of life was studied by Janicke et al. [28]. They found that survival time correlated inversely with the residual tumour after the second operation. Patients with complete resection of the tumour had a significantly longer survival time (median, 29 months) than those patients with residual tumour, even when the residual tumour was less than 2 cm (median, 9 months). They estimated the quality of life in patients according to the ECOG scale and observed that during the first 6 months 48% of the patients were able to take care of themselves. At 6–12 months after surgical procedure the same proportion of patients were able to take care of themselves. After 1 year, the proportion surviving patients who were able to take care of themselves was reduced to 38%. However, they concluded that "radical surgical procedure can prolong survival time in patients with recurrent ovarian cancer. Patients who had a complete resection of cancer tissue in the

Table 2 Summary information of studies on quality of life in patients with ovarian cancer by treatment, objective, number of patients and stage of disease (*Hexa-CAF* hexamethylmelanine, cyclophosphamide, 5-FU, methotrexate, *CHAP-5* cisplatin, adriamycin, hexamethylmelanine, cyclophosphamide, *CAP-5* cyclophosphamide, adriamycin, cisplatin, *CP-5* cyclophosphamide, cisplatin. Other abbreviations as in Table 3)

Author(s)	Treatment	Objective	*n*	Stage of disease
		1. Psychometric		
Coates et al. (1983) [10]	Oral chlorambucil (OC) or intravenous cisplatin with or without OC	To seek correlation between subjective and clinical measures	39[a]	Not available[b]
Warde et al. (1984) [56]	Palliative treatment	To assess psychometric properties of an instrument based on LASA technique	60	Advanced
Haes et al. (1990) [24]	Chemotherapy	Description of principal component analysis of RSCL	56[a]	Advanced
Portenoy et al. (1994) [48]	Not available	To assess reliability and validity of the MSAS	50[a]	Not available[b]
Osoba et al. (1994) [41]	Chemotherapy	To assess psychometric properties and responsiveness of the EORTC QLQ-C30	111[a]	Advanced
		2. Treatment-related		
Blythe and Wahl (1982) [7]	Debulking surgery	Comparing those undergoing debulking surgery with those who did not	36	III or IV
Coates et al. (1983) [11]	Chemotherapy	To identify and rank side-effects of chemotherapy	18[a]	Advanced
Haes et al. (1987) [23]	Chemotherapy	Comparing two combination chemotherapies: Hexa-CAF and CHAP-5	56	III or IV
Willemse et al. (1990) [58]	Initial optimal surgery and chemotherapy	Efficacy and toxicity of short intensive CAP-5 therapy	68	III and IV
Willemse et al. (1991) [59]	Chemotherapy	Efficacy and toxicity of carboplatin-based therapy	76	Advanced
Walczak et al. (1991) [55]	Chemotherapy	Comparing intensive and non-intensive CP-5 therapy	200	Advanced
Furst et al. (1992) [15]	Postoperative chemotherapy	Comparing two anti-emetic treatments	80	I–IV
Payen (1992) [46]	Palliative chemotherapy (PC)	Comparing hospital-based PC and home low-dose intermittent PC	17[a]	Advanced
Janike et al. (1992) [28]	Second radical surgery and chemotherapy	To assess the effect of second debulking surgery on survival and quality of life	30	I–III
Guidozzi (1993) [21]	Cytoreductive surgery and chemotherapy	To assess overall effect of cytoreductive surgery followed by CP-5 therapy	28	II, III, IV
		3. Weight loss and nutrition		
Ovesen et al. (1993) [43]	Chemotherapy	To assess relationship between dietary intake and quality of life	47[a]	Not available[b]
Ovesen et al. (1993) [42]	Chemotherapy	To examine the effect of nutritional counselling on quality of life	45[a]	Not available[b]
		4. General		
Malone et al. (1994) [34]	Chemotherapy	Measurement of health-related quality of life	13[a]	Not available[b]
		5. Experience of symptoms and pain		
Portenoy et al. (1994) [49]	Not available	To assess relationship among patient characteristic, symptom distress and quality of life	50[a]	Not available[b]
Portenoy et al. (1994) [50]	Surgery or chemotherapy	To study the influence of pain and other symptoms on quality of life	151	I–V

[a] These represent the number of patients with ovarian cancer only

[b] In these studies the stage of disease was not identified for each site

Table 3 Summary information of studies on quality of life in patients with ovarian cancer by feature of instruments used. In alphabetical order: *BPI* the Brief Pain Inventory, *ECOG* the Eastern Co-operative Oncology Group scale, *EORTC QLQ-C30* the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire, *EPQ* the Eysenck Personality Questionnaire, *FLI-C* the Functional Living Index-Cancer, *GHO* the General Health Questionnaire, *HADS* the Hospital Anxiety and Depression Scale, *KPS* the Karnofsky Performance Status, *LASA* the Linear Analogous Self Assessment, *MHI* the Rand Mental Health Inventory, *MHLC* the Multidimensional Health Locus of Control Scale, *MPAC* the Memorial Pain Assessment Card, *MSAS* the Memorial Symptom Assessment Scale, *QL-I* the Quality of Life Index, *RSCL* the Rotterdam Symptom Checklist, *RSES* the Rosenberg Self Esteem Scale, *SDS* the Symptom Distress Scale, *SIP* the Sickness Impact Profile, *TWiST* the Time Without Symptoms and Toxicity, *UKSIP* the United Kingdom Sickness Impact Profile, *WHO performance status* the World Health Organisation performance status

Instrument	Items	Feature	Dimensions and areas of assessment
ECOG scale	5	Generic	Performance status
KPS	11		Performance status
UKSIP	136		Physical and psychological dimension, sleep and rest, eating, home duties, recreation, pastimes and work
WHO performance status	5		Performance status
LASA	1	LASA scales	Global quality of life
LASA	4		Well-being, pain, breathlessness, and physical activity
LASA (+SIP)	31		Functional status (16 items derived from SIP), 14 items on disease- or treatment-related, and one overall quality of life
EOTRC QLQ-C30	30	Cancer specific	Five functional domains, disease- and treatment-related symptoms and global quality of life
FLI-C	22		Physical symptoms, mood, physical activity, work and social interaction
QL-I	5		Activity, daily living, health, support, outlook
QL-I (modified)	5		Activity, daily living, health, appetite, outlook
RSCL (+daily activity +overall well-being)	34 (+8+1)		Physical and psychological symptoms, daily activity, overall well-being
TWiST	—		Quality-adjusted survival analysis
EPQ	?	Psychological	Personality assessment
GHQ	30		Social functioning, depression/anxiety, outlook/happiness, insomnia
HADS	14		Anxiety, depression
MHI	24 (38)		Anxiety, depression, behavioural/emotional control (in addition main instrument covers positive well-being and emotional ties and in total has 38 items)
MHLC	81		Internal locus, chance and external locus, powerful others
RSES	10		Overall sense of being capable, worthwhile, and competent
MSAS	32	Symptoms	Psychological and physical symptoms (severity, frequency, distress)
SDS	13		Symptom distress (nausea, mood, appetite, insomnia, pain, mobility, fatigue, bowel pattern, concentration, appearance)
BPI	7	Pain	Pain interference with general activity, mood, social relation, walking, work, sleep and life enjoyment
MPAC	11		Pain intensity, pain relief, mood

primary operation or those who experienced a disease-free interval of more than 12 months after primary operation are most likely to benefit from a second operation in recurrent ovarian cancer". Yet the question remains: does second radical surgery improve quality of life?

Guidozzi [21] found that cytoreductive surgery that eliminated all tumour deposit having a diameter of more than 1.5 cm followed by eight cycles of chemotherapy containing cisplatin and cyclophosphanide reduced the quality of the period of survival. In other words, the overall effect of surgery and chemotherapy on the quality of life of patients with ovarian cancer indicated that significant behavioural disruption and emotional distress occurred during the first year of the study and were similar both in patients who had persistent disease (12 out of 28) and in those who had a complete response (16 out of 28). After 1 year, continued deterioration in quality of life was reported by patients with persistent disease while 72% of the patients with no evidence of disease reported improvement of quality of life compared with their response at the first year. This, however, indicates that quality of life deteriorates even in patients with a complete response to therapy. For example, 19 patients out of 28 reported on their sexual activity. There was no difference between the two groups of patients, with a significant decline in frequency of intercourse being reported: 80% at 3 months, 71% at 12 months and 66% at 24 months. Only about 40% of the patients had returned to their usual frequency within two years.

Chemotherapy

During the past two decades there has been substantial progress in developing more effective and less toxic chemotherapy regimes, yet there has been only a modest improvement in long-term survival and this is also associated with a significant number of unpleasant side-effects [45]. Coates et al. [11] conducted a survey to identify and rank side-effects perceived by a group of patients (including patients with ovarian cancer) receiving cancer chemotherapy. They found that the major physical side-effects were vomiting, nausea and hair loss. Non-physical side-effects were the thought of coming for treatment, the length of time taken by treatment and having an injection. Patients with ovarian cancer ranked abdominal pain higher compared to other cancer patients. Comparing standard treatment Hexa-CAF (hexamethylmelamine, cyclophosphamide, 5-fluorouracil, and methotrexate) and CHAP-5 (cisplatin, adriamycin, hexamethylmelamine, and cyclophosphamide), Haes et al. [23] studied differences between these treatment regimes with respect to the quality of life and in terms of overall differences, differences related to treatment and rest periods, and differences related to the number of chemotherapy cycles received. They found that there was no clear-cut overall difference between these two regimes but, if distinction is made for treatment weeks, rest periods and for successive cycles in the course of the treatment, the Hexa-CAF regime appeared superior to CHAP-5. The most important symptoms reported by the patients who received Hexa-CAF were tiredness, lack of energy and heartburn, while those who received CHAP-5 reported more tiredness, nervousness, feeling tense and alopecia.

The quality-adjusted survival analysis of the efficacy and toxicity of a short intensive cisplatin-based chemotherapy (a combination of cyclophosphamide, adriamycin and cisplatin; CAP-5) indicated that the period of progression-free survival reduced from 18 months to 10 months. This was mainly due to treatment and its side-effects such as general malaise, loss of appetite, nausea and fatigue. The median overall survival was 22 months [58]. In the same analysis (quality-adjusted survival) of the effect of a combination of carboplatin and cyclophosphamide, the median overall survival was found to be 25 months and the median period of progression-free survival reported to be 22 months (compared to 10 months after CAP-5). The findings suggested that treatment with carboplatin and cyclophosphamide provides better quality of life and it was concluded that carboplatin should replace cisplatin [59].

In a large randomised trial, as part of a study of the effect of intensive and non-intensive chemotherapy on quality of life, 200 patients with ovarian cancer were assessed [55]. The chemotherapy consisted of cyclophosphamide and cisplatin. The results showed that, although overall 64% of patients reported improved quality of life after one course for both dosing schedules, patients in the intensive regimen reported more frequent and severe nausea. After completion of treatment, the study concluded that the intensive regimen has a greater negative impact on the perceived quality of life than the non-intensive regimen.

Studies have shown that the most common side-effects of cyclophosphamide plus cisplatin therapy reported by ovarian cancer patients are nausea and vomiting, and alopecia. Thus, to control cisplatin-induced emesis, Furst et al. [15] investigated the effect of two anti-emetic treatments: experimental and standard regimes. They found significant differences in favour of the experimental anti-emetic protocol, although there was no correlation between emesis and any of the parameters of quality of life measured. In a recent trial of anti-emetics tested for their efficacy in a group of cancer patients including patients with breast, ovarian and lung cancer, Osoba et al. [41] found that patients with ovarian cancer had the lowest scores for role functioning (limited or unable to do either their work or to do household jobs) compared with all other patients.

Payen [46] studied whether the site and method of chemotherapy administration influenced the quality of life in patients with advanced breast and ovarian cancer. Patients received palliative chemotherapy either at home or hospital. There were no differences between the home- and hospital-treated groups. However, ovarian cancer patients had significantly more gastrointestinal pain and more rapid hair loss. The study concluded that there were no differences between treatment groups, although overall, home care was found to be more compatible with a better quality of life than hospital-based chemotherapy.

Weight loss and nutrition

This was the subject of two studies carried out by Ovesen et al. [42, 43]. Three groups of patients agreed to participate: patients with small-cell lung cancer, breast cancer and ovarian cancer. On the basis of weight, the patients were divided into two group, with and without weight loss. The study results showed that the quality of life, especially the dimension concerned with social interaction and outlook was affected in patients with weight loss. They also observed that dietary intake (protein and energy) in these groups of patients was low. Thus, although even a moderate weight loss was found to be associated with psychological distress and lower quality of life, it was not possible to conclude that insufficient food intake decreased quality of life or that weight loss decreased it. They also investigated the effect of nutritional counselling on food intake, weight, response rate to treatment, survival and quality of life. There was no significant difference in the overall survival time in patients who received nutritional counselling and control group. In general, weight-stable patients had significantly better quality of life as assessed by standard measures. Despite long-term and continuous improved food intake in cancer patients with solid tumours undergoing intensive chemotherapy, no clinical benefits were demonstrated.

Experience of symptoms and pain

Recent publications on quality of life in patients with ovarian cancer are concerned with two main issues: pain, and experience of symptoms. Portenoy et al. [49] reported a study on prevalence, characteristics and distress in a cancer population (colon, prostate, breast and ovary). They found that across tumour types, 40%–80% experienced lack of energy, pain, feeling sleepy, dry mouth, insomnia, or symptoms of psychological distress. Patients with ovarian cancer experienced more nausea, difficulty in sleeping and greater pain compared to the other patients. They observed a significant association between clinical measures and symptom prevalence. Thus, they concluded that the number of symptoms per patient could be seen as a useful indicator of quality of life. Portenoy et al. [50] in a population of 151 patients with ovarian cancer showed that pain, fatigue and psychological distress were the most prevalent symptoms among these patients. Most patients reported pain-related interference with various aspects of function: activity (68%), mood (62%), enjoyment of life (60%), walking (56%), sleep (52%) and social relations (33%). The findings of this study suggest that, for clinicians who are monitoring patients, pain potentially could be a useful indicator of disease remission after treatment.

Psychometric findings

Since some studies were carried out to investigate the psychometric property of the instruments, a summary of the main results is presented. These refer to reliability, validity and responsiveness of the instruments used to measure quality of life [25].

1. It was found that a significant association exists between the linear-analogue self-assessment (LASA) scores and clinical parameters such as performance status and response to treatment [10].

2. The component analysis of The Rotterdam Symptom Checklist (RSCL) showed first that psychological factors, experience of pain, gastrointestinal symptoms, and experience of fatigue and malaise all contribute to the quality of life of patients with ovarian cancer. Secondly, it was found that physical and psychological dimensions were independent factors in the experience of cancer [24].

3. The Memorial Symptom Assessment Scale (MSAS) was found to be valid. The total MSAS score, single dimensions of severity, frequency and distress, and major symptom groups were all correlated with valid measures such as the Rand Mental Health Inventory (MHI), the Functional Living Index–Cancer (FLI-C), and the KPS. Its component analysis distinguished three major symptom groups and several subgroups. The major groups comprised psychological symptoms, high-prevalence physical symptoms and low-prevalence physical symptoms [48].

4. The European Organisation for Research and Cancer Treatment Quality of Life Questionnaire (EORTC QLQ-C30) discriminates moderately well between varying severities of disease, the effects of chemotherapy and different levels of ECOG performance status [41].

5. The Time Without Symptoms and Toxicity (TWiST) could be used to measure quality of survival. It includes a survival-adjusted analysis and can be seen as months free of symptoms (the burden imposed on the patients due to treatment and its side-effects) [58, 59].

Discussion

Main issues

Importance of quality of life measures

These studies indicate that quality of life provides an additional measure of the end-product of health care as perceived by the patient. Quality of life studies provide useful information for improving care for the patients with ovarian cancer including need for psychological counselling [23, 24, 50], improving palliative and home care [46], nutritional support [42, 43] and initiatives for pain relief [49, 50]. A full insight into the issue of quality of life in patients with ovarian cancer has yet to be achieved.

Instruments

In general, all measures used were reliable and valid. The LASA technique, the Spitzer Quality of Life Index (QL-I), FLI-C and the RSCL are more widely used and the recent literature confirms such applications [6, 9, 52, 57]. However, the following points should be noted.

1. Four studies employed the LASA technique [10, 42, 43, 56]. Two used a single item on measuring global quality of life, one 31 items on functional status and disease- or treatment-related symptoms, and one 4 items on physical activity, well-being, pain and breathlessness. All these utilised different variables and were not comparable, although the technique was the same.

2. It is recommended that the Spitzer QL-I in research applications must be consistently completed by one type of respondent only (patients or physicians), because patients give themselves higher scores than do their physicians [36]. Furthermore, Spitzer himself suggested that the scale is not an adequate instrument for healthy people and therefore recommended the use of one of the broader scales such as Sickness Impact Profile [53].

3. Studies have shown that the FLI-C is difficult to administer. A study on quality of life in patients with lung cancer reported that difficulties resulting from administration of the FLI-C made it impossible to examine the difference between the effect of treatment arms on quality of life [17].

4. There are three studies that employed ad hoc instruments [7, 11, 15] and, since these studies did not demonstrate a robust methodological approach, they make a limited contribution to the development of instruments suitable for general use.

On the basis of methodological aspects both from the studies reported here and other cancer research on quality of life, the RSCL and the EORTC QLQ-C30 appear to be the best instruments used. The validity and reliability of these instruments are well documented [2, 33]. However, they have their own limitations. First, for example, the RSCL only covers physical and psychological dimensions. Second, it does not contain specific questions related to ovarian cancer, although it was developed in a study on quality of life in patients with ovarian cancer. Finally, none of the measures adequately addressed symptoms experienced by patients with ovarian cancer.

Problems

Meta-analysis

Because the studies under review employed different measures with different objectives, comparison is difficult if not impossible. For the same reason it was not possible to carry out meta-analysis of findings. This problem has also been highlighted by Fallowfield [13] in her comparative review of quality of life studies in patients with breast cancer. Providing a guideline may help to overcome the problem.

Complexity

Unfortunately most studies are presented in a complex way. This may especially discourage those who are not in favour of measuring quality of life from using proven instruments or seeking to develop new ones. Although considering a "gold standard" is far from reality, there is an urgent need for a simple language for quality of life studies if they are to be useful in practice.

It is argued that too much sophistication in analysing quality of life data would be misguided [14]. For example, some studies under review employed several instruments and compared every subscale or similar measures one by one, making it very difficult to follow (see list of instruments were used in each study, Table 4).

Study design

Most studies are rather poor in their design and methods. Overall, several limitations can be identified.

1. The time of assessments reported are variable and inconsistent (see Table 4).

2. There were uncertainties in the theoretical and operational concept of quality of life. Gotay and Moore [19] in their review of quality of life studies in patients with head and neck cancer observed similar problems. They pointed out that the absence of a definition of quality of life explains, in part, the widely varying instruments used across studies.

3. Since stage of disease and other prognostic factors have considerable effect on quality of life, it is essential to adjust outcomes against these factors, but in most studies such adjustment was lacking or was reported poorly. Therefore, in some papers it is not clear whether the deterioration in quality of life is due to these prognostic factors or due to the side-effects of the treatment. Different stages in the disease course require different assessment.

4. Some studies changed the original instruments or added extra questions. The validity and reliability of these converted instruments need to be examined.

Sample size

In all studies, except three [41, 50, 55], the number of patients is small (see Table 2). For example, a simple comparison of proportions to detect a true difference of 20% (at the 5% significance level, 90% power), requires more than 100 patients in each treatment group [27].

Table 4 Summary information of studies on quality of life in patients with ovarian cancer by instruments used and time of assessment. (Abbreviations as in Table 3)

Reference	Instrument(s)	Time of assessment
[10]	LASA + WHO performance status + ECOG	Before treatment and at intervals (before each course of therapy)
[56]	LASA + SIP	Not available
[24]	RSCL	Before and after treatment
[48]	MSAS + MPAC + MHI + FLI-C + SDS + KPS	Once at out-patient or in-patient
[41]	EORTC QLQ-C30 + ECOG	Before treatment, 1 week and 3 weeks after treatment
[7]	Ad hoc (a set of questions)	After discharge from hospital or when first seen in referral
[11]	Ad hoc (two sets of white cards including the name of one side-effect of chemotherapy) + EPQ	During current chemotherapy
[23]	RSCL	Before and after treatment several times on various visits; mean no. completing questionnaire for Hexa group 5.3 and for CHAP group 7.3
[58]	TWiST	Follow-up for first year on a 6-weekly basis and 3-month intervals
[59]	TWiST	Median follow-up of 18 months
[55]	FLI-C	Before and after being treated
[15]	Ad hoc (visual-analogue scale techniques) + study specific	Before and after treatment and followed for three treatment cycles
[46]	HADS + RSES + MHLC + KPS + study specific	Follow-up for 6 months; assessments at monthly intervals
[28]	ECOG	Six-month intervals after operation
[21]	QL-I + study specific	Each patient was assessed at 3-month intervals for 2 years
[43]	GHQ + QL-I + LASA + ECOG	On the first day of diet registration
[42]	QL-I + LASA + ECOG	Before treatment, before the fourth and sixth cycles of chemotherapy
[34]	UKSIP	Patients attending an oncology unit completed the UKSIP
[49]	MSAS + MPAC + MHI + FLI-C + SDS + KPS	Not available
[50]	MSAS + MPAC + BPI + FLI-C + KPS	One week after operation or chemotherapy administration

Specificity

As indicated in Table 2, some of these studies were not specifically carried out for patients with ovarian cancer [10, 11, 24, 34, 41–43, 46, 48, 49]. This implies that the results of these particular studies should be interpreted with care. Patients with ovarian cancer in many aspects have different physical and psychological symptoms. Without understanding these concerns, measuring quality of life in this group of cancer patients would be useless. One might argue that, regardless of any assessment, it is obvious that quality of life will deteriorate in cancer patients as a result either of the disease itself or of the side-effects of the treatment. Thus, what is the point in measuring quality of life if these data do not provide further insight about what is actually happening to the patients?

Duplication

Two studies are the same, although the results in these two papers are presented differently [23, 24]. Two studies by Ovesen et al. [42, 43] are very similar in most aspects. This is even true for studies carried out by Portenoy et al. [48–50]. The problem of duplication in publication is evident and this may lead to confusion and misunderstanding.

Concluding remarks

Cancer of the ovary threatens female identity and psychological morbidity is one of the most important problems in women with gynaecological malignancies [12]. Thus, measuring quality of life in these patients is essential. On the other hand, quality of life is multidimensional, subjective and non-static [39] and these factors must be taken into account in such assessment. Such considerations may help to provide quality data so that scientific judgements can be made. Our review shows that measuring quality of life is not an easy task, but it can be accomplished. Several lessons from quality of life studies can be learned. For example, patients are the best source for identifying what is important to them for good quality of life. Psychological counselling, palliative and home care, nutritional support and pain relief alongside optimal treatment are the major areas related to improvement of quality of life of patients with ovarian cancer.

From this review it is clear that an agreed outcome assessment of health-related quality of life in patients with ovarian cancer is lacking. Such an approach is nearer for patients with breast cancer. It is often suggested that assessment should contain (a) a generic measure, (b) a cancer questionnaire, and (c) a disease-specific instrument, but this may prove an unacceptable burden to patients. It may be better to decide on a selected single instrument from the existing tested measures. A large carefully planned study is required to achieve this. The incidence of ovarian cancer is moderately low, and to solve the problem of recruitment of patients it is recommended that multi-centre or international studies are conducted.

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