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Current Perspective

Quality of life in elderly cancer patients

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ABSTRACT

The incidence of most types of cancer is age-dependent and progressive ageing is rapidly increasing the number of elderly people who need treatment for cancer. Elderly patients (older than 70 years) present particular characteristics that make the choice of the correct treatment more difficult; for this reason, these patients are often undertreated and largely underrepresented in cancer trials making the experimental evidence on this topic even weaker. Only relatively recently has Health-Related Quality of Life (HRQoL) begun to be considered as one of the hard end-points for clinical cancer research in the elderly. Treatment of elderly cancer patients represents a typical situation where its assessment is particularly useful because of the expected toxicity of treatment and several unresolved methodological problems (higher frequency of illiteracy, worse compliance with the questionnaires, concomitant diseases, use of instruments not validated in the aged population). The aim of this review is to underline the importance detected by the too small number of studies on elderly QoL evaluation and the need in future trials either to improve QoL assessment in this subcategory of patients undergoing treatment for cancer or not, or find specific assessment tools to do it.

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1. Introduction

Ageing is rapidly affecting the median age of all Western populations, mostly due to the reduction in birth-rates, coupled with the increased life expectancy. This demographic phenomenon is rapidly increasing the number of people who are diagnosed and treated for cancer, because the incidence of most types of cancer is age-dependent and the risk of developing a tumour is progressively higher with increasing age.¹

Elderly patients present particular characteristics^{2,3} that make the choice of the appropriate treatment more difficult, often exposing these patients to the risk of being undertreated.⁴ Although chronological age is not necessarily equiv-

alent to biological age, ageing determines physiological changes in organ functions and pharmacokinetics. Furthermore, in addition to tumour symptoms, concomitant diseases are very frequent, significantly affecting the functional, psychological status and general performance. In the attempt to get a more reliable prognosis of these patients and the risks associated with specific treatments, a correct approach to elderly people with cancer should not leave out a comprehensive geriatric assessment (CGA).⁵ Many aspects of physical limitations that are usually not fully recognised by performance status (PS), in particular those aspects of daily life that require instrumental activities and that may affect adherence to diagnostic or therapeutic protocols, might need an accurate CGA

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and quality of life (QoL) evaluation. In fact, up to now, how elderly persons live their life as newly diagnosed cancer patients has been insufficiently investigated. Only relatively recently has QoL, as a main objective in the management of elderly cancer patients, been recognised by clinicians.⁵

The aim of this review is to underline the lack in the published literature of trials about QoL evaluation in elderly cancer patients and the need in future trials either to improve QoL assessment in this subcategory of patients undergoing treatment for cancer or not, or find specific assessment tools to do it. Through the paper the Authors visit physiology of the aged, tools available to assess QoL in oncogeriatric patients and a small number of clinical trials present in literature on some cancers. A PubMed search for cancer, QoL, elderly (≥ 70 years), trials, has been carried out.

2. What does QoL mean in the elderly population?

Since survival benefits may decline and the risks of treatment progressively increase with age, preservation and improvement of QoL should be one of the major goals of geriatric oncology. In clinical practice, QoL means maintenance of function and symptom control. For this reason, CGA and QoL evaluation should be more useful for decision-making in elderly cancer patients than those criteria that for a long time have been the major barriers excluding their participation in common treatments or in clinical trials (i.e. aggressive therapies with substantial toxicity, coexisting illnesses, small number of trials designed for them, patients' limited expectations of long-term benefits and lack of financial, logistic and social support).^{6–8} Despite the universal recognition of the importance of clinical trials to inform clinical practice and to guide therapeutic decisions, it has been repeatedly reported that elderly patients are largely underrepresented in cancer treatment trials or excluded from them and when included they represent the minority of very 'fit' elderly.^{9–19} Clinical trials specifically dedicated to elderly patients are more and more needed because common results are probably more generalised to clinical practice than subgroup analysis of retrospective studies without upper age limit. Systemic therapy in advanced disease, i.e. may prolong survival, decrease tumour-related symptoms, improve general well being or maintain it at a high level for a longer period of time if compared to best supportive care (BSC); nevertheless, QoL improvements and subjective responses have to be the most important objectives for this category of patients.^{20–22}

3. Evolution of instruments to measure QoL assessment

During the last decades, instruments to measure QoL have been developed and included in clinical trials to document this therapeutic endpoint.²³ The assessment of QoL in general oncology has provided new and important information related to the value of breast preservation in the management of breast cancer, to the value of sexual function in the management of prostate cancer and to the effects of limb amputation on QoL.²³

A QoL evaluation at the beginning of treatment seems to have, in fact, independent prognostic implications. In geriatric oncology, assessment of QoL may allow trade-off between QoL and survival (OS), and may determine the choice among alternative forms of life-prolonging and palliative treatments.²⁴

In one of the few studies on QoL evaluation in 131 elderly cancer patients by Rustoen et al.²⁵ elderly population (age range 60–78 years, 33% of the total sample) showed a higher QoL than the younger group (19–39 years), especially if living alone. The aim of this study was to examine which domains of QoL were most strongly affected in patients with newly diagnosed cancer and to examine if QoL was related to gender, age, educational level, cohabitation, time since diagnosis, treatment or type of cancer in these patients. Time since diagnosis was not associated with QoL, while treatment was associated with QoL as measured by Ferrans and Powers Quality of Life Index. The bias of the study was that it did not specifically focus on people recently diagnosed with cancer and the median time since diagnosis was 5 months.

In a Swedish study,²⁶ cancer patients aged more than 75 years ($n = 150$) were compared to a group without cancer ($n = 138$). Those with cancer had a lower QoL compared to those without cancer and patients in the study group reported more health complaints than those without cancer. These patients, however, were diagnosed with cancer over a 5-year period and were thus not necessarily newly diagnosed. The result indicated that the combination of being elderly and having cancer influenced QoL.

These types of studies are actually few, but may be important for developing directions for optimal care and identifying factors related to QoL, especially in elderly persons newly diagnosed with cancer.

Nowadays, despite the increasing focus of patients QoL assessment,⁷ there is no consensus about the definition of QoL and how it should be measured, although plenty of tools are available. Several instruments for the assessment of QoL have in fact been validated, but none has been calibrated to the distinctive problems of older people. Some consensus has been achieved concerning domains of importance in relation to QoL, such as functional ability, role functioning, social and community interaction, well-being, somatic sensation and life satisfaction.²⁷ Actually, the problems involve diverse evolution of health and disease around variable models, potential age-related shifts in values and focus, and barriers to the use of questionnaires (such as poor visual and auditory function, easy fatigability, slower reactions and dementia). Individualised questionnaires may represent the ultimate goal in the assessment of QoL in the elderly.^{24,28,29} HRQoL, i.e. refers to health as well-being physically, psychologically and socially functioning. It is the assessment of characteristics at a point of time in a person's life when health, illness and treatment conditions are relevant.³⁰ Up to now, chronological age has generally been taken as an expression of declined physical abilities, and the interaction between cancer and the general ageing process has not been given due attention. Knowledge based on HRQoL contributes to bridging this gap of understanding and can potentially make nursing care more targeted to the specific needs of the individual patient. The concept of HRQoL holds that the preservation of health

and physical function is necessary to the maintenance and improvement of QoL, and encompasses several constructs, including physical, functional, emotional, social and spiritual domains. Although seeking meaning and hope is fundamental for human beings,³¹ it is seldom included in the definitions of QoL or in instruments that measure QoL.³² This is the case even though having a cancer diagnosis often threatens the individual's future.³² Loss of hope may well be threatening to an elderly person with cancer because of a strong reminder that life is limited.²⁶

In a qualitative study, Benzein et al.³³ identified the 'hope' of healthy persons as a process that was linked to meaning. Hope was also identified as the fundamental will to engage in living life and was linked to a positive attitude to life. Therefore, hope is a notion that not only contains the number of years to live, but also the meaning of life. Few studies describe hope in relation to cancer patients and to elderly people.^{34–37}

Interpretation of results in QoL studies still remains problematic^{38–40} (a difference of more than 10 units on the 0–100 scale could be interpreted as clinically significant). When analysing results from a Swedish study³⁸ with two earlier population based studies (using EORTC QLQ-C30) performed, respectively, in Denmark⁴¹ and Sweden,⁴² differences of more than 10 units could be identified in similar age groups. Hence, elderly persons newly diagnosed with cancer from the Swedish study, had a clinically important lower QoL in physical and role functioning. They reported more fatigue and dyspnoea compared with reported data from the other two trials. In addition, elderly persons with cancer in the current study had a 10-unit lower score in global HRQoL compared with elderly people not having cancer from a population study.^{38,41} Despite no significant differences in EORTC QLQ-C30 being found when comparing different age groups and that advanced age was not associated with low QoL, the results indicated that age in combination with cancer disease could influence life in other ways. It is crucial that health-care providers assess the individual patients' QoL and focus on age as a complex process rather than a chronological fact. Limited financial resources available for the elderly person with cancer led, in fact, to decreased ability to conduct or participate in social activities, low health status, poor emotional well-being and loneliness⁴³ and thus probably led to low QoL. In interpreting the results of this study it must be taken into account that QoL was measured by a cancer disease specific HRQoL instrument. Moreover, EORTC QLQ-C30 (as FACT-G and SF-36) was primarily developed for clinical trials to measure symptoms and the degree of side-effects following chemotherapy treatment in young patients. Perhaps it might be the reason why such instruments as EORTC QLQ-C30 focus on negative aspects and limitations in a person's life⁴⁴ and that an existential dimension, such as hope, was not integrated in the instruments. Also from the current study, a low level of hope was associated with low QoL in elderly persons newly diagnosed with cancer. However, based on the literature, the relationship between the two different concepts, hope and QoL, continues to remain unclear.^{45,46} Based on this study it was not possible to explain the causality between low level of hope and decreased QoL, only that hope interacted with QoL. In conclusion, the oldest age group (older than 80

years) had a poorer social network and needed more support from home-help services than the younger participants. Dependency, getting help from grown-up children and receiving help in daily living were also related to low QoL for the total sample. The results also showed that the type of cancer diagnosis and perceived seriousness of it were of importance to QoL. Additionally, limited financial resources and low level of hope for an elderly person newly diagnosed with cancer were associated with a higher risk for low QoL. The results could be relevant for nursing care for elderly persons newly diagnosed with cancer (older than 65 years) and indicate areas with a need for further investigations and research. Because of the continuous increase of cancer in the elderly, research and educational initiatives targeted to this population should also be a priority probably with a majority of these studies providing a QoL assessment. As described, this assessment in the elderly is still complicated by several unresolved methodological problems. Therefore, planning of new trials should be made with caution. QoL assessment could also be useful to allow for the discussion with the patient of the answers given to specific items of the questionnaire. This discussion could help the clinician to better assess the overall burden of symptoms suffered by the patient and the relative importance given to each of them, in order to plan better and modify the best treatment strategy.

4. QoL in specific conditions

4.1. QoL in lung cancer

Lung cancer is significantly associated with low QoL.^{35,47,48} Lung cancer holds a unique position among solid tumours, because at the time of diagnosis the disease is more advanced and the median survival is relatively short.⁴⁹ Lung cancer diagnosis and treatment often produce stress resulting from the actual symptoms of the disease. The results emphasise that elderly persons newly diagnosed with lung cancer are especially vulnerable and need special attention in clinical conditions to compensate for their grave situation in relation to QoL.

Vinorelbine, a semisynthetic vinca alkaloid, represents a well-tolerated treatment for elderly patients with advanced non-small-cell lung cancer (NSCLC). Some authors⁵⁰ explored the QoL of 161 elderly patients in a multicentre randomised trial comparing vinorelbine treatment with BSC alone. QoL was evaluated with EORTC questionnaires QLQ-C30 and QLQ-LC13 and the QoL data were analysed by fitting a linear mixed model for each QoL scale. Vinorelbine-treated patients scored better than control patients on QoL functioning scales and they reported fewer lung cancer-related symptoms but worse toxicity-related symptoms. There was a statistically significant ($p = 0.03$) survival advantage for patients receiving vinorelbine; median survival increased from 21 to 28 weeks in the vinorelbine-treated group. Vinorelbine improved survival of elderly patients with advanced NSCLC and overall QoL.

In a more recent randomised phase III trial evaluating the efficacy and safety of docetaxel versus vinorelbine in NSCLC elderly patients, docetaxel improved progression-free survival, response rate and disease-related symptoms versus vinorelbine.⁵¹ Nowadays, docetaxel monotherapy is consid-

ered as the new option in the standard treatment of advanced NSCLC elderly patients.

In another phase III randomised Multicentre Italian Lung Cancer in the Elderly Study (MILES) trial on the OS prognostic value of baseline assessment of functional status, comorbidity and QoL, data of 566 elderly NSCLC patients treated with chemotherapy were analysed.⁵² Functional status was measured as activities of daily living (ADL) and instrumental ADL (IADL). The presence of comorbidity was assessed with a checklist of 33 items; items 29 and 30 of the EORTC QLQ-C30 questionnaire were used to estimate QoL. ADL was dichotomised as none versus one or more dependency. For IADL and QoL, three categories were defined using first and third quartiles as cut-off points. Comorbidity was summarised using the Charlson scale. Better values of baseline QoL ($p = 0.0003$) and IADL ($p = 0.04$) were significantly associated with better prognosis, whereas ADL ($p = 0.44$) and Charlson score ($p = 0.66$) had no prognostic value. Pretreatment global QoL and IADL scores, but not ADL and comorbidity, have significant prognostic value for survival of elderly patients with advanced NSCLC who were treated with chemotherapy. Using these scores in clinical practice could improve prognostic prediction for treatment planning.

Lung cancer, because of its history and short median tumour-related survival, is one of the few neoplasms in which QoL has been largely studied in elderly patients, demonstrating a good prognostic significance when improved.

4.2. QoL in breast cancer

There is a paucity of information in the literature that focuses on QoL issues after mastectomy with breast reconstruction in elderly women. The purpose of Girotto's study was to review the authors' experience with breast reconstruction after mastectomy in women older than 65 years of age.⁵³ Emphasis was placed on the types of reconstructions, outcomes and evaluation of issues related to QoL. Outcomes were assessed with the use of a self-reported questionnaire (SF-36) addressing HRQoL, body image and physical functioning. With respect to overall QoL issues after reconstruction, older patients with breast reconstruction had better outcomes than age-matched general population patients and previously reported mastectomy-only patients (older than 55 years) in all surveyed areas. Specifically, study patients reported better outcomes in the subscales that were strongly influenced by one's mental health but worse outcomes in the areas related to physical function. In conclusion, older patients maintained better outcomes over the younger patients when influenced by one's mental health. Declines in physical functioning among elderly cancer patients threaten in fact QoL and the ability to maintain independence. Adherence to healthy lifestyle behaviours may prevent functional decline.

Project Leading the Way in Exercise and Diet (LEAD), an intervention development study of the Pepper Older Americans Independence Centre, aimed to determine whether breast and prostate cancer survivors (older than 65 years) assigned to a 6-month home-based diet and exercise intervention experienced improvements in physical functioning when compared with an attention control arm receiving general health information.⁵⁴ Home-based diet and exercise

interventions held promise in improving lifestyle behaviours among older cancer survivors, changes that trended towards improved physical functioning. Future studies should incorporate larger sample sizes and interventions sustaining long-term effects and also take into account secular trends; these efforts will require adequate planning and resources to overcome the numerous barriers to intervening in this difficult to reach yet vulnerable population.

Even if breast cancer is the first neoplasm as incidence within women, QoL has been studied in only a small number of trials on elderly cancer patients. Considering the entity of surgery- (often physically and psychologically detrimental because of mastectomy), radiotherapy- (often related to local damage and small compliance because of the prolonged daily administration) and chemotherapy-related problems (often associated to alopecia and vomiting) a QoL evaluation could be very very useful in understanding these patients and their possible problems better.

4.3. QoL in rectal cancer

Temporary or final colostomy as colorectal sequel causes psychological problems felt especially by elderly oncology patients. Deep and fixed habits are usually modified, as far as evacuating and sexual behaviours are concerned. After demolitive surgery, most patients fear having to be dependent on others for situations which they feel are embarrassing (due to faecal smell, etc.).⁵⁵ Therefore, elderly patients and their QoL worsen, as a consequence. In these people, psychotherapy and psychological rehabilitation due to therapy stress are often difficult because old age itself reduces hope for the future. To prevent social withdrawal or anxiety, a psychological rehabilitation for patients and their families should be suggested from the diagnostic phase.

Also in this case, even if rectal cancer is a very diffused neoplasm, QoL has been studied in only a small number of trials on patients older than 70 years. Considering the entity of surgery- (often detriment with abdominal-perineal amputation, definitive colostomy and sexual impotency), radiotherapy- (also in this case, often related to local damage and small compliance because of the prolonged daily administration) and chemotherapy-related problems (with infusional pump device) a QoL evaluation could be useful in helping these patients improve both physically and psychologically.

4.4. QoL in lymphoma

In a randomised, multicentre trial, some authors studied the impact of cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) chemotherapy on the QoL of 132 aggressive non-Hodgkin's lymphoma (NHL) elderly patients.^{56,57} Patients aged 65 or older completed QoL questionnaires (EuroQol-5D, EORTC QLQ-C30 and MFI-20) on eight predefined time-points before, during and following treatment. At baseline, QoL was significantly better on almost all dimensions in patients with a lower age-adjusted International Prognostic Index (aaPI) compared to patients with a higher aaPI. During treatment, physical and role functioning and global QoL deteriorated and fatigue increased in the lower aaPI group, whereas QoL of the higher aaPI group remained stable. During

follow-up, the QoL was significantly better for patients in complete response (CR) or partial remission (PR) than for patients with progression/relapse. Soon after completion of therapy, the QoL of the lower aaPI group returned to pretreatment levels or better, while patients with higher aaPI showed a significant improvement in QoL compared to baseline levels. The effect of CHOP on the QoL of elderly patients could be used in counselling this group of patients.

5. Discussion

In the elderly, function preservation and maintenance of QoL represents a major goal in an increasing proportion of patients. Life expectancy is a function of age, comorbidity, disability, cancer type and stage. Decision-making involves a delicate balance among all these factors, evaluation of treatment related complications of the overall effects of cancer and cancer treatment on the patients' QoL. Despite several instruments for the assessment of QoL being validated, none have been calibrated to the special requirements of the older patients.

The structured interview administered by a trained clinician may represent a good approach for geriatric research and even for clinical practice because of the frailty of the older population. The combination of this approach with the self-administered questionnaire may be the most effective way to minimise missing data in collecting information for patients unable to complete the form.

6. Conclusion

Some steps have been made in the field of clinical cancer research dedicated to elderly patients, and the role of QoL assessment in this setting is promising. However, many methodological problems are still to be resolved, to allow the best use of these potentially useful instruments. A QoL assessment in clinical practice seems particularly useful for elderly patients, allowing better communication between patient and clinician. It might be useful to consider a wider application of properly selected instruments for future use.

Conflict of interest statement

None declared.

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