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Perspectives and Commentaries

Quality of Life in Patients with Non-Small Cell Lung Cancer Treated with Chemotherapy

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(A COMMENT ON: Bakker W, Van Oosterom AT, Aaronson NK, van Brenkelin FJM, Bins MC, Hermans J. Vindesine, cisplatin and bleomycin combination chemotherapy in non-small cell lung cancer: survival and quality of life. *Eur J Cancer Clin Oncol* 1986, **22**, 963–970.)

ALTHOUGH some improvements have occurred in the staging and treatment of lung cancer in recent years, we are still faced with the fact that less than 10% of patients with this disease survive 5 years or longer after diagnosis [1]. Most long-term survivors undergo resection and usually have early stage disease and they more commonly have squamous histology [2]. Patients with more advanced disease (that is, unresectable or metastatic) survive for much shorter periods with median survivals ranging from 3 to 4 months, up to just over a year, depending on whether they have gross metastatic disease or are just beyond the point of being resectable.

Various forms of adjuvant therapy have been used in resectable patients primarily consisting of postoperative radiotherapy and combination chemotherapy or combined modality therapy attempting to use both modalities in the best possible way [2]. For more advanced disease the same modalities are used in an attempt to palliate but, at least at present, long-term survival benefits are not obtainable. If we are unable to improve survival with potentially toxic therapy then we must ask the question, is the treatment benefitting the patient by improving his "quality of life" even if survival benefits are not obtained, or are we seeing responses but the toxicity is so overwhelming that in fact, treatment is not beneficial or is actually detrimental? This pressing question has led investigators in the 1970's and 1980's to try to better investigate "quality of life" in the patient with malignancy.

It is extremely difficult to define "quality of life" but it certainly includes the individual's physical, psychological and social functions, whether they be feelings of well-being, or negative feelings. The main approach that has been used in the past is performance status [ex. Karnofsky or Eastern Cooperative Oncology Group (ECOG) scales]. Unfortunately this method relies on an observer's assessment of the patient's performance and is specific to physical performance but does not consider the psychological or social issues. Also, the validity of the Karnofsky performance status scale has been questioned by some [3] although it has been recently validated [4]. In recent years considerable work has been done in an effort to develop a comprehensive but workable instrument to assess the "quality of life" in cancer patients [6]. This has been carefully reviewed by Fayers and Jones [3, 5] and by Till *et al.* [7]. A detailed discussion of this subject is beyond the scope of this article but a brief description of some of the methodology and terminology will follow.

Schipper *et al.* [8] have pointed out that it is important for the investigator to achieve a consensus on the factors compromising "quality of life" among physicians, nurses, patients, family and others who are concerned with the patient. Also of course, the questionnaire must be compact enough to enable repeated use but complete enough to adequately evaluate components of "quality of life". Each component of the questionnaire must be interpretable by all patients in the study group and the instrument must be sensitive enough to detect changes in the overall "quality of life" and its component factors. It is, of course, difficult to

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compare "quality of life" between different patients with different life-styles. Once an index is available, a method of weighing the relative importance of the contribution made by each of the items to the "quality of life" of individual patients is extremely important but difficult to carry out. Fayers *et al.* point out that the questions, the timing and the methods of asking the questions are all important factors [5]. The choice of questions to ask depends on the nature of the disease and the treatment, that is, one cannot use an all encompassing method for all types of cancer. For example, in the case of lung cancer, one must design a specific set of questions that are appropriate for the symptomatology and effects of treatment for that disease. These may be totally different than, for example, breast cancer where mastectomy may produce totally different psycho-social problems than thoracotomy. They also point out that the wording of the questions in different questionnaires has a substantial influence on the results, even if the intent of the questions in two different questionaires is similar.

The timing of the questionnaire may influence the usefulness of the data collected. During the therapeutic period it may be important to have multiple questionnaires at frequent intervals while, when treatments are more spread apart and less intensive, it may be quite appropriate just to assess patients during their clinic visits. This is complicated by the fact that although ideally one might assess "quality of life" very frequently, patients may find this tedious and even depressing with resulting non-compliance. It has even been suggested that the enquiry itself may have some therapeutic value and therefore affect the "quality of life" measurement. Linear analog scales are frequently used to assess "quality of life". Although this is thought by some to be better than the more standard categoric method with discreet categories, when compared by Remington *et al.* in the assessment of psychiatric symptomatology, the two methods were not found to be significantly different [9]. Another relatively new approach that Fayers *et al.* describe [5] is a daily diary card which is used by the MRC Cancer Group in the United Kingdom. This uses a 5-point scale and is filled in each day with various important categories evaluated and spaces left for the patient to add extra information or comments. This is a categorical type of questionnaire. A new card is provided each clinic visit. Whether good compliance is achievable with this method is not really known.

With all the various methods available and new ones constantly being developed around the world, it is important that each scale used be evaluated for its reliability and validity, and, as well, that it be sensitive enough to detect meaningful changes in "quality of life". The assessment of *reliability* involves the measurement of internal consistency and test–retest reliability with the individual patient at different times, and perhaps even with different assessors such as the patients themselves, a nurse, physician, etc. The *validity* is the degree to which an instrument measures what it is supposed to measure. One can use indirect methods or one can compare it to a "gold standard" such as the Sickness Impact Profile [10]. If the questionnaire is *feasible* and passes reliability and validity testing, then it can be safely used in the clinic.

Various approaches have been applied to "quality of life" assessment in lung cancer. Carlen's Vitagram Index [11] has been used in Sweden. The EORTC, the NCI of Canada and a number of groups in the United States, Australia, etc. have all developed scales or are using one recently described by Schipper *et al.* from Winnipeg, Canada [12]. This instrument has been used in cross-Canada trials in advanced non-small cell lung cancer and is also being used by the Lung Cancer Study Group and the Eastern Cooperative Oncology Group in their lung cancer studies. Which will be the best instruments will only be determined by comparison of the various approaches available worldwide.

In a recent issue of the Journal [13], Bakker *et al.* described a study in 28 patients with non-small cell lung cancer, with good performance status who received tri-weekly treatment with vindesine, cisplatin and bleomycin. A 48% response rate was observed with a median survival of 33 weeks. A scale was developed in which patients were asked to rate their anticipated difficulties with chemotherapy 24 hr before each treatment course. They also evaluated performance status using the Karnofsky Index. They showed that the performance status fell during chemotherapy and that 7 patients (25%) found their treatment "dreadful" although only 1 discontinued therapy. They also noted many patients lost weight. They concluded that the toxicity of treatment had the greatest effect on performance status and weight loss and that it was not due to the tumor itself.

Although in this paper they unfortunately do not describe in detail their method of assessment which will be published elsewhere, Bakker *et al.* should be commended for assessing this most important measure of the negative value of the toxicity of treatment in this disease. Osoba *et al.* recently published a paper showing a 44% response rate in patients with advanced, non-small cell lung cancer treated with VP-16, cisplatin and bleomycin [14]. Although they did not use a formal system of evaluating "quality of life" they were able to correlate response and control of symptoms suggesting a benefit to patients who responded, even though it is inappropriate to look for possible survival benefit within that subgroup [15]. Therefore, both positive and negative effects of treatment can be ascertained using some type of "quality of life" assessment in these patients. There certainly is a need for assessment of "quality of life" in lung cancer trials, especially with the relatively poor outcome of treatment seen to date, especially in advanced disease. I would emphasize that one may pick up either the benefits of treatment as Osoba *et al.* observed [14] or one may pick up evidence of significant toxicity as was noted by Bakker *et al* [13]. Both types of observations are equally important to patients with advanced non-small cell lung cancer treated with present day chemotherapy especially those involved in clinical trials. Further work on this subject is to be encouraged.

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