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The Value of Quality of Life Scores in Clinical Cancer Research

INTRODUCTION

THE 1980s saw a rapid growth in the field of quality of life measurement [1, 2]. From the occasional inclusion of rather incomplete assessments of quality of life in clinical research [3] we are at a point where a series of quality of life (QL) measures have been developed, detailed work has been done on many aspects of their psychometric properties, and the emphasis of the research is shifting towards exploring their most appropriate use in clinical practice and clinical research. The place of QL measures in cancer clinical trials has been recognised by many national and international trial groups including the European Organisation for Research and Treatment of Cancer [4], the United Kingdom Medical Research Council [5], the U.S. National Cancer Institute [6] and the National Cancer Institute of Canada [7]. Perhaps the Canadians have come furthest in integrating quality of life assessment into their clinical trials programmes with the recommendation that investigators should include quality of life scores unless they have a special reason for not doing so. They provide detailed assistance to investigators in developing the appropriate methodologies for their trials [7]. However, no single quality of life measure is perfect and research on the methods will continue. The U.K. MRC surveyed available measurement instruments in 1989 and concluded that the 'best buys' were the Rotterdam Symptom Checklist [8, 9] and the Hospital Anxiety and Depression Scale [10]. Since that time detailed work has been completed on the EORTC questionnaire and particularly wide application of the Functional Living Index Cancer [11] has been carried out.

In this issue Alan Coates and his colleagues from a number of Australian centres report the use of linear analogue self-assessment (LASA) scales and the Spitzer's QL Index in their prospective randomised trials comparing two different treatment approaches in advanced malignant melanoma. In their report they concentrate on the value of individual QL scores in predicting survival for their patients. They convincingly show that the variables of quality of life measured by linear analogue scores such as physical well-being, mood, pain, appetite, nausea and vomiting and an eight item questionnaire known as the GLQ8 were all highly significant in univariate analysis in predicting survival of patients. The Spitzer's QL Index was also an independent predictor. On a multivariate analysis the overall QL scores generated from the LASA scales and from Spitzer's Index together with the individual LASA scales for mood and appetite independently predicted survival when the commoner clinical variables were included.

Their study is a clear and well performed confirmation of the prognostic significance of QL variables. The authors outline the previous reports of such significance in breast cancer and lung cancer and in patients receiving palliative care. The observation is now a robust one and appears to be repeated with a range of different QL instruments. Importantly, QL measures have independent prognostic significance for survival in a multivariate analysis which includes performance status. There is therefore additional information in the QL scores over and above that about physical well-being which is contained in performance status scores. It is not surprising that the significance of the physical well-being items within quality of life disappears on multivariate analysis which includes performance status. The persisting significance of mood and overall quality of life would be expected. Factor analyses of items used in a range of quality of life scores suggest that physical well-being and emotional well-being are independent factors [8, 12, 13] and the current study suggests that these and other factors independently contribute to prognostic information about survival.

These findings are valuable in their own right as a tool to be used by clinical investigators. These are quite powerful prognostic variables and may be useful under some circumstances to separate patients for different studies, different treatments, or to stratify within trials. They should be considered in studies which match patients for known prognostic variables in an attempt to compare non-randomised series. The conclusion from Alan Coates and colleagues that it is necessary to pay attention to the quantitation of quality of life in clinical cancer research is well supported by their data and is now established in the 'received wisdom' of clinical trials. Their data also help to support the often held clinical impression that an assessment of the patient's overall well-being can be more informative than detailed investigation with blood and imaging tests. The patient's quality of life, perhaps recognised during the clinical appraisal by many experienced health care professionals, is a powerful piece of information and the approach by Coates and others which seeks to quantify this will be supported by many such experienced health care professionals.

In discussion, the investigators touch on a broader question about the significance of quality of life and outcome. The case for an *association* between quality of life at the outset of treatment and the subsequent outcome is confirmed by their study and the others quoted in the paper. They speculate about the nature of this association. Most investigators and practising oncologists would accept that the association reflects the severity of the disease process when treatment is started. Hence a patient with aggressive, widespread, bulky disease or deposits of the tumour which are strategically placed to cause most disability are likely to be symptomatic, ill and are likely to die sooner than those who do not. In addition, we know that performance status predicts for response both to chemotherapy and biological therapy and it seems likely that quality of life will do likewise. It is, however, possible that the patient's well-being will be reflected in their attitudes and that these attitudes may in themselves have a direct causative influence on the outcome. The work of Spiegel *et al.* [14, 15], although controversial, has suggested this possibility. The importance of identifying a causative link lies in its potential for generating interventions. If

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interventions designed to improve quality of life by, for instance, improving emotional well-being, are capable of improving survival, then they take on even greater urgency and importance. This question remains unresolved but justifies further serious attention.

Quality of life is therefore established as an outcome measure, a prognostic variable, an aid to patient's management and a target for therapy. Where will the field of quality of life research go from here? Further refinements of measurement instruments are appropriate. The portfolio of available questionnaires is now quite broad and suitable for many purposes. However, there is room for further work on brief but informative questionnaires for use in routine clinical practice. Some will seek a scale which generates a single figure estimate for QL. However, a single number reflecting overall quality of life may be an illusion for such a complex and multi-factorial concept. The routine use of QL measures in clinical research is likely to increase and integration of QL, survival and economic appraisal will become common practice.

Enquiry and measurement of QL has increased the awareness among practising oncologists of the issues which surround quality of life of patients receiving cancer treatments particularly when they are toxic and when the purpose of treatment is palliation. These ideas need to be more firmly integrated into the curriculum for undergraduate and postgraduate training of oncologists of all kinds and the clinical oncology community may have much to offer to other medical specialties in this respect.

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