



Editorial Comment

The art and science of prognosis in patients with advanced cancer

D.P. Steensma, C.L. Loprinzi *

Mayo Clinic, Department of Oncology, 200 First Street SW, Rochester, MN 55905, USA

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Prognosis has always held a fascination for humanity. Many of the earliest medical writings on Mesopotamian cuneiform tablets and Egyptian papyri are treatises about prognostication [1]. From the Hippocratic corpus through the modern era of complex multivariate analyses, the art and science of forecasting and foretelling the course of illnesses have been steadily refined [2,3].

In patients with advanced cancer, the ultimate outcome of disease is not often in doubt. But the art and science of prognostication still remains important in this group, as terminally ill patients and their families want and need to know what to expect from the disease and whether palliative services such as hospice care need to be considered.

The article by Llobera and colleagues in this issue of the *European Journal of Cancer* (p 2036–2043) adds to the body of knowledge regarding the prediction of survival time in patients with advanced cancer. The investigators prospectively studied 200 Mallorcan patients with advanced cancer for whom no further antitumour therapy was planned. Oncologists, oncology nurses and family physicians were all asked to provide an estimate of each patient's life expectancy at the time of study enrolment. Periodic assessments were made of Karnofsky performance scores, quality of life indices, and the presence or absence of 21 specific symptoms. In a multivariate analysis, low quality of life scores, the presence of asthenia, and a poor prognosis as determined by oncologists were all independent predictors of a short survival time.

The authors reported that the predictions of oncologists and oncology nurses correlated with actual survival times. These data are in concert with recent experiences from a North Central Cancer Treatment Group (NCCTG) trial of cancer-related anorexia and

cachexia [4]. In the NCCTG study, physicians were asked to place patients into three groups: those with predicted survival times of less than 4 months, 4–6 months or greater than 6 months. In both the NCCTG trial and the Llobera and colleagues study, there was a strong correlation between oncologists' predictions and actual patient survival times, but also a clear trend toward overly optimistic survival estimates. The latter finding is corroborated by data from numerous other investigators [3,5–8].

Why does this tendency towards excessive optimism exist? One potential reason is that patients with advanced cancer often appear relatively stable when they come to visit their doctors. A rapid demise may seem implausible, despite an intellectual awareness of the stage of disease and probable outcome. But catastrophic complications such as thromboembolic disease, haemorrhage and infection can intervene at any time, often precipitously accelerating the final phase of an otherwise slowly progressive, chronic illness. It is important to keep such possibilities in mind when formulating a prognosis for a patient with advanced cancer. Even in cases where physicians are able to accurately forecast a dismal prognosis, they may be reluctant to disclose the full truth in order to avoid taking away a patient's hope [2,3]. But hope is a dynamic entity, and it is important for patients to know when hope for a cure or a lengthy survival is a misplaced hope, in order for more appropriate goals to be substituted.

The overly optimistic predictions of oncologists are probably responsible, at least in part, for the relatively short time that patients spend in palliative care programmes such as hospice care. The median survival of patients enrolled in the hospice programme at our own institution is 59 days [9], exactly the same survival time as that seen in the population studied by Llobera and colleagues. A significant number of patients are actually in the programme for less than a week.

* Corresponding author. Tel.: +1-507-284-2511; fax: +1-507-284-1803.

E-mail address: cloprinzi@mayo.edu (C.L. Loprinzi).

A concern that is repeatedly voiced is that it is inappropriate to enrol a patient in a hospice programme if that patient might possibly survive for more than 6 months. This may be related to the fact that a life expectancy of 180 days or less is a requirement for admission to Medicare-funded hospice care in the USA. Although a hospice programme would indeed stand out if the average survival of its enrollees were greater than 6 months, this has not been a realistic concern. Only 9% of patients enrolled in the Mayo Clinic Hospice Program survive longer than 180 days, and hospice benefits are renewable at the end of each 180-day period if the prognosis remains grim.

The Llobera and colleagues study identified the presence of asthenia as a major predictor of short survival. Asthenia (from the Greek *ασθενος* “without strength”) is a devastating symptom for which few effective treatments exist. It has been defined as “profound tiredness occurring after usual or minimal effort, accompanied by an unpleasant anticipatory sensation of generalised weakness.” [10]. Unfortunately, approximately 90% of patients admitted to many palliative care settings have asthenia, limiting its value as a prognostic sign due to its ubiquitous nature [10,11]. The study by Llobera and colleagues was somewhat unusual in that only 34% of the patients included in their study had asthenia at the outset of what they called the (terminal period). This may be due to the authors’ fairly liberal definition of the terminal period, which did not include a specific life expectancy such as 6 months, but instead was based on therapeutic modalities available to the afflicted patients. The Mallorcan study may also have been underpowered to demonstrate the independent prognostic ability of specific symptoms in terminally ill cancer patients. Other investigators have shown that symptoms besides asthenia, such as weight loss [12] and dyspnoea [13], remain significant prognostic factors in multivariate analyses of terminally ill patients.

Many different attempts have been made to quantify an answer to the more general question, “How well is the patient doing?” These have included indices of overall patient performance (Karnofsky performance status, Eastern Cooperative Oncology Group performance scale, etc.), as well as numerous specific symptom and ‘well-being’ inventories (Spitzer Quality of Life Index, Functional Life Index, European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire, the McMaster and McGill Quality of Life Scales, Palliative Prognostic Index, etc.) [14–17]. Llobera and colleagues demonstrated that a poor quality of life (as measured by a modified version of the Spitzer Quality of Life Index) was a strong, independent predictor of short survival. The authors also noted that the Karnofsky performance status predicted survival, although not independently of the prognostic assessment by physicians and nurses. These findings are not

surprising. Over the past several decades it has become clear that for almost every stage and site of cancer, the general overall condition of the afflicted patient is a major predictor of the ultimate outcome of their disease.

The ultimate goal of prognostication might be considered to be the prediction of the precise day and hour of death and the route that the patient will take to that endpoint. One might envision inputting an enormous array of information about symptoms, signs, disease data, and demographic and biological parameters into a supercomputer and asking the machine to generate an exquisitely accurate prediction for the time and style of demise. Such an analysis would not have to be limited to terminal cancer patients. Because of the unpredictable nature of the multitude of factors that determine the trajectory of a final illness, however, medical science will likely never get to that point. Even if such a clinical tool could be developed, it probably would not be clinically, psychologically or socially beneficial.

What, then, is the value of being able to predict survival in general terms? Primarily, the recognition of short survival times in patients for whom no effective antitumour therapy exists allows the appropriate institution of palliative care programmes such as hospice care. This may allow patients and their families to attend to symptom control and to the important psychosocial and spiritual issues of the final phase of life. Shifting the focus of therapy from curative to palliative goals at the appropriate time can permit patients and their families and friends to partake of what has been termed “the gifts of last days” [18,19]. The study by Llobera and colleagues contributes to the refining of the art and science of prognosis that is necessary to allow this to happen.

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