Predicting survival in advanced cancer patients: is it possible with patient-reported health status data?

How long will I live? That is one of the most fundamental questions humans have sought to answer over the ages. This question becomes far more important when patients develop a life threatening illness, such as cancer. Fundamentally, being able to predict how long the patient will survive can be essential in clinical decision making. Determining this key-issue assists clinicians to identify patients who will benefit from treatment; further, it could help avoid over-treatment of patients who will gain no benefit from, often, toxic and aggressive therapies.

There is now huge body of research being conducted to evaluate methods of prognostic analysis. In any mainstream oncology journal, it is increasingly difficult not to read an article trying to improve prognostic accuracy. While the bulk of this work has historically focused on tumor-related factors such as histology, clinical stage and laboratory parameters, recent evidence suggests that patient-reported health related quality of life (HRQOL) data provide additional prognostic information.

Recently, several studies provide relatively robust data, showing that pre-treatment HRQOL scores independently predict length of survival. This evidence has also been reproduced in a wide range of different cancer populations, for example, breast [1], colorectal [2], lung [3], melanoma [4] and oesophageal [5] as well as in a large cohort of patients with varied malignancies [6]. Overall, these studies, conducted on patients with advanced disease, show that patient judgment on their own underlying health conditions, as measured by multidimensional measures of HRQOL, provide prognostic information for survival duration in addition to previously known traditional biomedical data. It is also worthy of note that the studies in this area have used different HRQOL questionnaires and different statistical approaches. On the one hand, this has hindered clear outcome comparisons amongst studies, yet on the other, it provides complementary and robust evidence of the independent association between patient self reported HRQOL data and survival in advanced diseases. Gotay [7] recently presented a review of over 40 studies exploring the prognostic value of HRQOL, finding, generally, positive results, while still many studies were designed with some limitations. Our own work at the EORTC has also explored this field, knowing it represents an important study as it represents the first research investigating this issue in a population of hepatocellular carcinoma (HCC) patients.

Yeo and colleagues undertook a retrospective analysis on 233 patients with unresected HCC, drawn from two previously conducted randomized phase III trials. One of the two original studies was set up to compare two different palliative chemotherapeutic regimens (chemotherapy study) while the other one compared high dose tamoxifen versus placebo and was named by the authors, hormonal study. They used the robust and well validated EORTC QLQ-C30 to investigate the baseline prognostic value of a number of HRQOL parameters for overall survival. Survival was measured from the day of randomization to the date of death or last contact and the median survival of these 233 patients was 5.5 months.

One of the strengths of their study is the control of many previously known clinical prognostic variables including: age, gender, performance status, total bilirubin, albumin levels, alpha fetoprotein, Okuda stage and vascular involvement. The results note that role and physical functioning as well as appetite loss were independent prognostic factors for survival. In addition, Okuda stage, total bilirubin and treatment (chemotherapy versus hormonal), as independent prognostic factors for survival, were also identified.

While they used the appropriate approach of multivariate analysis, they included all 15 HRQOL parameters of the EORTC QLQ-C30 and we wonder if greater robustness would be evident if they had pre-selected endpoints expected to predict outcomes. As an example, it is not clear why, in a clinical study, a variable like financial difficulties is included.

Another challenge faced by Yeo and colleagues, indeed a problem with all prognostic factor analyses of this type of data, is the intercorrelation of the HRQOL scales, given that HRQOL scores are often highly intercorrelated. This might adversely affect the stability of the final model and the correct estimate of the parameters. Such phenomenon is previously described as a challenge when undertaking such prognostic factor analyses including a number of HRQOL parameters. One way to overcome this possible source of bias is to restrict the HRQOL parameters entering the analysis. Another way is to undertake internal validation of the final model by using, for example, bootstrap validation techniques [9]. It would be interesting to see Yeo and colleagues investigating this issue and providing further insights.

Interestingly these investigators found a 7% increase in the likelihood of death for an every 10 point increase (i.e. worse) in the appetite loss scale of the EORTC QLQ-C30. Using the
same HRQOL measures, the EORTC also found that appetitie loss was an independent prognostic factor for survival in a population of women with advanced breast cancer [10].

Yeo and colleagues also found that role and physical functioning independently predicted survival. These two EORTC QLQ-C30 scales were also previously shown to independently predict survival in other studies [5, 11].

Overall, it is pleasing to report that the Yeo and colleagues results mirror many others in advance cancer, often highlighting that some HRQOL parameters predict clinical outcomes. Yeo and colleagues also suggest that an additional module may add to the sensitivity of baseline scores. While such will certainly give more HRQOL information, there is no certainty this will help predict outcomes. Often additional modules evaluate treatment effects as well as more tumor-specific influences. Indeed, this could mean adding more endpoints in an already busy pot.

Overall, the Yeo and colleagues research is important. This topic is relevant to patients, clinicians and researchers. If we are able to provide new information to help predict survival then we have made a major impact on patient care. The question is: Are we there yet? We have to say that in the work of Yeo, and other research groups, we are getting there, but not quite. For example, we need more prospective studies that are hypothesis driven, as characterized in present EORTC studies. We also need to address the challenge of analysis inherent in complex data sets, whose variables are often highly inter-correlated.

The good news is that the results from this line of research seem to fill part of the same jigsaw whose picture is not yet entirely clear. After all, it is still a relatively novel area of research in oncology. The hope is that within the next few years, a clearer idea of which HRQOL parameters are predictive for a specific cancer population will be seen. A future challenge is using this information with individual patients in daily clinical practice to better help the clinician monitor disease progression and improve accuracy of prognosis.

references