Edmonton symptom assessment system global distress score and overall survival among patients with advanced cancer receiving early palliative care

To the Editor

The Edmonton Symptom Assessment System (ESAS) is a patient-reported outcome (PRO) measure assessing 10 key symptoms and has been widely adopted in several studies mainly including patients with palliative care cancer.[1] The Global Distress Score (GDS) is a validated subscale including the first 9 items of this measure and it has been recently shown to provide prognostic information for overall survival (OS) in a large cohort of 333 patients with metastatic cancer.[1]

While PRO data have traditionally been used as outcome measures in comparative efficacy trials, convincing evidence-based information has been accumulated over the most recent years on their independent prognostic value for survival outcomes.[2] A number of other studies have found an independent association between PRO measures (including the ESAS) and survival in cancer patients.[3] Notably, in a recent large matched case cohort study, Barbera *et al*[4] found that patients with cancer exposed to ESAS had longer survival than those who were not.

We investigated the association between the ESAS and OS in a cohort of patients with advanced cancers, receiving an early palliative care (PC) intervention, recently reported.[5]

Continuous variables were described as mean±SD or median and IQR, and categorical variables as absolute and percentage numbers. Patients were divided in two groups, based on the observed median GDS score (high GDS score: ≥44; low GDS score: <44). OS after PC start was defined as the time from the PC start and death or last available visit. The median OS time after PC start was assessed with the Kaplan-Meier method. OS curves were compared using log-rank test, and the difference between the two groups was reported as the HR from a Cox regression model with 95% CI. We also performed two secondary analyses; in the first one, patients were divided in two groups based on a previously reported cut-off (high GDS score: ≥35; low GDS score: <35).[1] In the second one, the association between the overall GDS score as a numeric variable and OS was assessed by using a Cox model with one regression slope. Results of this latter analysis were reported as the HR for a one-unit increase in GDS score. All analyses were carried out considering the whole sample and in subgroups based on patient's age (<65 years or ≥65 years). Statistical significance was set at p<0.05. Analyses were carried out with R V.3.6.3 statistical software (The R Foundation for Statistical Computing, Wien).

One hundred seventy-eight patients were included in the analysis : 87 (49%), and 91 (51%) had high and low GDS score, respectively. The median and average GDS scores were 43 (37 to 47) and 41.5±9, respectively. Average age was 66±10 years and 50% of patients were men. Within the study period, 151 (84.8%) patients died, 77 (84.6%) in the low GDS group and 74 (85.1%) in the high GDS group. As shown in figure 1, there was no significant difference in OS between the two groups (p=0.237). The HR was 1.21 (95% CI 0.88 to 1.68) and the median OS times were 15.6 months (95% CI 12.5 to 21.3) in the low GDS score group and 15.5 months (95% CI 13.0 to 17.9) in the high GDS score group. According to the secondary analysis, no difference was observed between patients with GDS score ≥35 (n=144) and patients with GDS score <35 (n=34) (p=0.957, HR=1.01, 95% CI 0.68 to 1.50). There was also no association between the overall GDS score and OS (HR=1.00, 95% CI 0.99 to 1.02, p=0.727). Analysis by age groups confirmed no association between GDS and OS. In the subgroup of patients aged less than 65 years, no difference was observed between high and low GDS groups using both 44-point and 35-point cut-offs (p=0.957 and p=0.357, respectively) and no linear association was found between GDS and OS (HR=0.99, 95% CI 0.97 to 1.02). Similar results were found in the subgroup of patients aged 65 years or more (p=0.102 and p=0.380 and HR=1.01, 95% CI 0.99 to 1.03, respectively).

Our findings suggest that a higher GDS score was not associated with a statistically significant decrease in OS. While median age was similar between the two compared cohorts, the GDS more and equal to 35 was detected in more than 80% of the patients from our and about the 55% of the patients from the cohort from Subbiah *et al*.[1] These results suggest that our cohort had a higher overall level of distress. In our cohort, the early PC intervention was associated with a significant and rapid symptom improvement, as early as in the first week.[5] Of note, all analysed subjects from our cohort were early PC patients, 26% and 35% of whom taken in charge

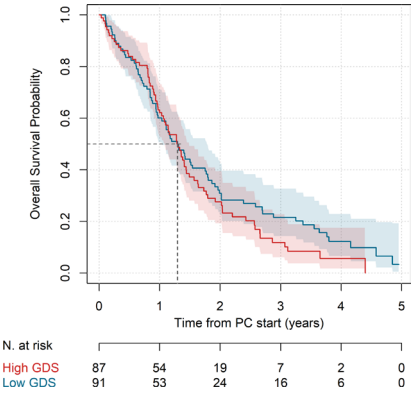

Figure 1 Overall survival after palliative care start by GDS high versus low. GDS, Global Dystress Score; blue line represents patients with low GDS score (<44) and red line represents patients with high GDS score (≥44); areas represent 95% CIs; dotted lines indicate median survival times. PC, palliative care.

within 60 and 90 days, respectively, from advanced/metastatic cancer diagnosis. On the contrary, all the patients from the cohort of Subbiah *et al*[1] were not receiving early PC. The characteristics of our patient population is consistent with its median OS of about 15 months, namely more than double that of the cohort from Subbiah *et al* showing about a median OS of 6 months.[1] Recognition and monitoring of patient-reported outcomes might have contributed to improve survival after early PC start in our series, as already found in previous studies.[2–4]

ESAS subscales is associated with OS among patients with advanced cancers receiving PC late, in their disease trajectory.[1] We could speculate that our early PC approach in our cohort of patients with metastatic cancer[5] may have contributed to this finding, thereby indirectly reinforcing the overall value of an early PC intervention. Our findings also emphasise the usefulness of ESAS when employed for clinical research studies.

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