Letter to the Editor

Implementation of patient reported outcomes in definitive chemoradiation for non-small cell lung cancer

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We appreciate the critical review of our analysis of patient reported outcome measures (PROMs) in definitive chemoradiation for non-small cell lung cancer (NSCLC). In their editorial, Voong *et al.* thoughtfully discuss use of PROMs in locally advanced lung cancer. They highlight important limitations of our data, many of which are commonly encountered in studies of patient reported outcomes (PROs).

In our study we sought to assess the 3 broad categories of health status using PROMs as outlined by Voong *et al.* using Euroqol, the MD Anderson Symptom Inventory, and the functional assessment of cancer therapy-general. Given the complexity of analyzing multi-dimensional PROMs, risk of missing data, and use of multiple statistical testing, standardized methods for analyzing and reporting PROs in clinical trials have been recommended and are being developed (1). We acknowledge that our work is subject to statistical limitations and, given its exploratory nature, the findings should be considered hypothesis generating for validation on future studies.

We agree with their assessment that the cohort in our study is highly selected for patients receiving care at an academic, high volume medical center, and results may not be duplicated in a community setting. Despite being located in an urban setting, our center faces the well documented challenges of enrolling under-represented minorities on clinical trials (2). Disparities in access to treatment at high volume centers, enrollment on clinical studies, and survival have been frequently reported (3,4). Studies have suggested that underrepresented patients may be at higher risk for treatment-related toxicity (5). Including a diverse patient population is critical to studying health-related quality of life (HRQL) outcomes without bias and improving outcomes in these high-risk patients.

Difficulty with patient compliance has been noted in numerous studies of PROMs in both locally advanced and early stage NSCLC, including ours (6,7). High rates of missing data may lead to bias and erroneous conclusions and also limit publication of PROs. Many barriers to compliance, including length and format of assessments, methods of administration, patient and provider engagement, and deteriorating health status of participants, have been explored in the literature. Frequently cited methods to reduce missing data include use of baseline PRO completion as an eligibility criteria for study entry, development of guidance for site staff to standardize administration of PRO questionnaires, minimizing the length of questionnaires to reduce patient burden, aligning PRO assessment time points to clinic visits, and ensuring any recruitment site has sufficient resources to adequately manage a PRO study (8). At our center, techniques employed to minimize missing data included clinical research nursing to introduce the study and engage patients in initial participation and standardized assessment at the

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time of follow up appointments to minimize the burden for patients. Although not utilized on our study, electronic assessments, which provide notifications to patients, can be completed at home, and can be reviewed and acted upon by the clinician, may improve patient participation (9). Studies have also suggested that electronic PRO interventions may be particularly effective in patients who are older, less educated, and nonwhite race/ethnicity (10).

While our data provides an initial suggestion of patients who may be at risk of toxicity after chemoradiation for locally advanced NSCLC, further multi-institutional and prospective study is certainly indicated. Thoughtful implementation of PROMs in addition to other clinical measures in order to delineate patients at low, intermediate, and high risk of treatment-related toxicity as suggested by Voong *et al.* are needed to validate the findings from this and other single institution series. Ultimately, careful utilization of PROMs may help providers appropriately select patients for definitive chemoradiation, provide timely supportive care, and improve disease and HRQL outcomes.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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