PROceeding With the Patient-Reported Outcomes (PROs) Version of the Common Terminology Criteria for Adverse Events.

Benjamin Movsas
Henry Ford Health System, BMOVAS1@hfhs.org

Follow this and additional works at: https://scholarlycommons.henryford.com/radiationoncology_articles

Recommended Citation
Movsas B. PROceeding with the patient-reported outcomes (PROs) version of the common terminology criteria for adverse events. JAMA Oncol 2015; 1(8):1059-1060.

This Article is brought to you for free and open access by the Radiation Oncology at Henry Ford Health System Scholarly Commons. It has been accepted for inclusion in Radiation Oncology Articles by an authorized administrator of Henry Ford Health System Scholarly Commons.
PROceeding With the Patient-Reported Outcomes (PROs) Version of the Common Terminology Criteria for Adverse Events

Benjamin Movsas, MD

For more than 30 years, the standard process for reporting toxicities in clinical oncology trials has been via the National Cancer Institute’s (NCI’s) Common Terminology Criteria for Adverse Events (CTCAE). Overall, this system, which includes approximately 800 items, has served our field well, such that toxicities can be compared across clinical trials using a consistent language. Approximately 10% of the items represent symptoms (eg, fatigue, nausea) that are currently reported by clinicians. Prior studies, however, have shown that there is often a disconnect, with substantial discrepancies between patient and clinician reports of symptoms. This begs the question: When it comes to reporting symptomatic adverse events, should the perspective of the patient or the clinician be primarily considered?

Some would argue that the clinician is most qualified to report symptomatic adverse events. After all, they have the professional training and background to place the patient’s symptoms into the overall context of the disease process. However, prior studies have demonstrated that, compared with patients, clinicians tend to underreport the incidence and severity of patients’ symptoms. Quinten et al provide evidence that the accuracy of clinician-based CTCAE reporting was enhanced by adding patient-reported outcomes (PROs) gleaned directly from patients. At a fundamental level, how can anyone know the patient’s subjective experience better than the patient?

Others may contend that PROs are not scientifically rigorous because they are based on subjective reporting. However, many PRO instruments (such as the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLC-C30) and the Functional Assessment of Cancer Therapy) have been rigorously tested for scientific validity and reliability. The fact is that much PRO research is currently hypothesis driven and based on clinically meaningful changes using validated instruments. On the other hand, the CTCAE itself was developed empirically by expert consensus but not evaluated for validity or reliability. Indeed, limitations of the CTCAE as a psychometric instrument to measure cancer symptom burden have previously been described. In addition, PROs have often been shown to be more powerful than standard prognosticators for predicting survival in clinical oncology trials. Both the Food and Drug Administration and NCI have adopted PROs in trials as the benchmark for measuring subjective experiences.

In light of these considerations, the NCI decided to develop a PRO measurement system as a companion to the CTCAE, called the PRO-CTCAE. In the article by Dueck and colleagues in this issue of JAMA Oncology, the authors took on the daunting task of analyzing the construct validity, reliability, and responsiveness of the PRO-CTCAE system, which includes a library of 124 patient self-reporting items. This study included almost 1000 adult English-speaking patients with cancer undergoing chemotherapy and/or radiation therapy from 9 US cancer centers and community oncology practices. Patients completed the PRO-CTCAE items on tablet computers or by telephone at 2 clinic visits, 1 to 6 weeks apart, with a subset 1 day apart. The key comparators for validation were the Eastern Cooperative Oncology Group performance status and a validated quality-of-life (QOL) instrument (EORTC-QLQ-C30). Overall, they demonstrated favorable validity, reliability, and responsiveness of the PRO-CTCAE even in a rather diverse sample of patients with cancer, including some with impaired performance status. They also found significant correlations between the PRO-CTCAE item changes and the corresponding QOL scale changes.

Dueck and colleagues\(^2\) deserve credit for validating such a large number of individual symptomatic toxicity items in such a diverse group of patients with cancer. Although this is an important first step, more work is needed. For example, less than 4\% of the patients in this study underwent cancer surgery, so this group requires further study. As the authors point out, this study included only English-speaking, US-residing patients with cancer. Future studies will need to focus on linguistic and cultural adaptations of PRO-CTCAE both inside and outside the United States. The reliability data were limited to a subset of items, such that further analysis of the test reliability will be required. Practical issues will also need to be addressed regarding how PRO-CTCAE may affect administrative time, cost, and patient burden over time. Beyond logistic issues, the ultimate success of the PRO-CTCAE will depend on imparting its importance and relevance to patients, clinicians, and other stakeholders.

The PRO-CTCAE is exciting because it is a novel patient-centered approach to adverse event (AE) reporting. By incorporating PROs into the AE reporting system, it provides a direct and unbiased account of the patient experience that can guide future treatment recommendations. This can provide a more accurate summary of the patient’s treatment experience, which will be relevant for labeling decisions and informing stakeholders and future users about the effects of treatment. As Basch and colleagues\(^4\) have pointed out, a fundamental premise of the PRO-CTCAE project is that whereas clinicians have the ultimate responsibility for AE reporting regarding patient safety, patients are best able to describe their own experiences. Thus, both patients and clinicians should play key roles in the reporting of symptomatic AEs.

In summary, the perspectives of the patients and the clinicians are indeed both essential in that they each provide valuable and complementary input, which, when integrated, provides a more robust appreciation of patients’ symptoms. Clinicians contribute their professional experience to this evaluation, while patients directly communicate their subjective experiences.\(^3\) The power of the PRO-CTCAE is that it intertwines the patient perspective directly into the AE reporting using a validated methodology that can facilitate informed decision making. In the future, the PRO-CTCAE may be used as a strategy to provide real-time information about patients’ symptoms so that clinicians can enhance their communication with patients regarding symptom management. Importantly, randomized data have demonstrated that when inquiries are made regarding PROs in the clinic, not only did physician-patient communication significantly improve, but almost all patients also expressed interest in continuing this approach.\(^5\) One thing is reasonably clear: when it comes to optimally understanding and appreciating the patient experience, our patients want us to "PROceed with PROs."