Numbers Have Life: A Commentary on "Predictors of Survival in Patients with Advanced Gastrointestinal Malignancies Admitted to the Intensive Care Unit"

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"Numbers have life; they're not just symbols on paper" [1]. In this issue of *The Oncologist*, Ko et al. [2] report on a provocative study that examined predictors—including a numerically based predictor—of poor outcomes in cancer patients. As their primary goal, Ko et al. [2] sought to determine predictors of hospital mortality in intensive care unit (ICU) patients who had been diagnosed with a metastatic gastrointestinal malignancy. In doing so, they built a prognostic model with the Sequential Organ Failure Assessment (SOFA) score in conjunction with other clinical parameters [3].

By way of background, the SOFA score has generated hundreds of publications, mostly in patients with sepsis and systemic inflammatory response syndrome, less so in cancer patients whose aggressive malignancy was the root cause of their ICU admission [3]. In general, the SOFA score requires clinicians to input the worst organ-based values of the PaO2, FiO2, platelet count, Glasgow Coma Scale, serum bilirubin, mean arterial pressure (or the use of vasoactive agents), and serum creatinine (or urine output) over 24 hours. A summing of values generates a score from 0 to 24, with higher numbers indicative of greater concern for a poor clinical outcome. SOFA scores are a reliable gauge of the gravity and severity of illness; upward trends portend clinical decline. In sepsis, the generation and tracking of these scores help to "facilitate earlier recognition and more timely management of patients with sepsis or. . . risk of developing sepsis" [3].

Investigating SOFA scores in ICU patients with metastatic gastrointestinal malignancies, Ko et al. [2] from MD Anderson Cancer Center studied 200 such patients who had manifested a 41% in-hospital mortality rate. Ko et al. [2] found that a relatively high SOFA score (>5)—in conjunction with a poorly differentiated cancer and a short interval from diagnosis of metastatic cancer to ICU admission (≤7 months)—collectively appeared to predict that an ICU patient with cancer would eventually die in the hospital. Importantly, all three of these variables—SOFA scores, a poorly differentiated cancer, and a short interval from a diagnosis of metastatic disease to

ICU admission—appear to be plausible predictors of poor outcome, an observation that supports the potential clinical utility of these study findings.

Along these lines, Ko et al. [2] concluded, "Understanding the predictors of short- and long-term survival is important in treatment planning, especially terminal care management." But are we there yet? Are we at a point now where SOFA scores in conjunction with the other two clinical parameters, as noted above, should inform our decisions to transition a patient to "terminal care management"? We believe the answer is "no" and cite three reasons to support this opinion. First, this group of investigators has conducted other studies that have used SOFA scores in cancer patients for prognostication purposes, but it is important to note that a series of primarily single-institution studies runs the risk of unwittingly selecting patients unique to a specific cancer center and of creating a model irrelevant to other cancer centers. For a predictive model to be useful to a broad range of patients and health care providers, that model must demonstrate clinical validity beyond a single-institution setting. Testing a prognostic model chiefly within a single cancer center, as seems to have occurred for the most part with this specific cancer-relevant, SOFA score-based model, is a good starting point that hopefully will go on to generate widespread collaborative investigation. Second, all clinically applicable models must go beyond a single demonstration of statistical predictive significance. A model should re-demonstrate its ability to predict outcomes in a similar set of patients—in effect, show model validation—or, if an independent data set is unavailable, the model in question should be validated with multiple resampling procedures within a single data set to demonstrate its predictive ability. Because the predictive model from Ko et al. [2] was constructed from a heterogeneous retrospective data set of only 200 patients, we contend that both internal and external validation would be needed to drive its adoption into clinical practice.

Finally, what is the clinical benefit of this cancer model? Do we know that this model will help patients or their

families and, at the very least, that it will do no harm? In the absence of comparative data on outcomes with and without the model, it becomes challenging to answer these questions. Interestingly, a key difference between SOFA score-based models in sepsis and this SOFA score-based model in metastatic cancer is the envisioned clinical use of these respective models. The sepsis models are intended to prompt "earlier recognition and more timely management"—in effect, greater vigilance and monitoring of septic patients with the goal of keeping patients alive. In sharp contrast, the metastatic cancer model appears intended to prompt a transition to "terminal care management," or, in other words, de-escalation in the aggressiveness of cancer care. These dramatically different dispositions—particularly in view of the grave finality (death) of the withdrawal of cancer care—are such that a demonstration of the clinical merits of the model is an essential prerequisite for its incorporation into clinical practice.

So how does the study from Ko et al. [2] change our approach to patient care? In our opinion, the most important contribution of this study is that it summons attention to an unmet need. Health care providers need the invaluable prognostic information that can potentially be derived from relevant, valid, and usefully established models. Such models could conceivably enable clinicians to engage in thoughtful discussions with patients and family members about how and when to transition to palliative care exclusively. This transition to "terminal care management" is difficult for everyone but particularly for family members who often appear to drive the decision to maintain aggressive cancer therapy even when such care appears to be approaching the point of futility and appears to be creating undue suffering for the patient. One small study reported that close to 15% of cancer patients and their family members had "unrealistic expectations" of outcomes even when the end-of-life was very near [4]. Furthermore, a growing body of literature suggests that dying in an ICU yields a greater likelihood of complicated bereavement among family members and others left behind; thus, the work from Ko et al. [2] could also potentially lead to further research to help anticipate and mitigate complicated grief among loved ones [5].

In conclusion, "Numbers have life" and, of course, so do patients [1]. And even when the research focuses on the end-of-life, it behooves us to show the relevance of the research, demonstrate its validity, and prove its benefit to cancer patients and their families prior to incorporating research findings into routine clinical oncology practice.

References

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Editor's Note:

See the related article, "Predictors of Survival in Patients with Advanced Gastrointestinal Malignancies Admitted to the Intensive Care Unit," by Heidi Ko, Melissa Yan, Rohan Gupta et al., on page 483 of this issue.