Editor's Spotlight/Take 5

Editor's Spotlight/Take 5: Conditional Survival Greater Than Overall Survival at Diagnosis for Ewing's and Osteosarcoma

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Cancer patients need all the good news we can give them. In the absence of a guarantee

Note from the Editor-in-Chief:

In "Editor's Spotlight," one of our editors provides brief commentary on a paper we believe is especially important and worthy of general interest. Following the explanation of our choice, we present "Take Five," in which the editor goes behind the discovery with a one-on-one interview with an author of the article featured in "Editor's Spotlight."

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or cure (which often are absent), the next best thing is some hope that the disease will go away, and stay away, for a very long time.

"What are the odds?" is the first question many patients ask when diagnosed with cancer. Depending on how we look at things, this question is surprisingly complicated. The odds of survival may be different for a patient at the time of diagnosis than they are 2 and 5 years later. This is the principle of "conditional survival," and Dr. Benjamin J. Miller's (Fig. 1) group explored it for patients with osteosarcoma and Ewing's sarcoma. Happily, the news for our patients is good.

In short, for each year a patient survives after the diagnosis, the likelihood of surviving 5 more years goes up; for a patient with osteosarcoma who has no metastases at the time of diagnosis, the odds of surviving 5 years was 75%. If that patient survives 5 years, the odds of surviving another 5 years increase to more than 91%. The numbers were similar for patients with Ewing's sarcoma.

Of course, numbers do not tell the entire story. A cancer "survivor" with whom I am very close has said to me that until she dies of something else, she

will not know that she's "cured" of cancer. The work of Dr. Miller's group suggests that vigilance indeed is called for — the good news implied by these conditional survival data is, itself, conditional. Some patients will die of their disease 10 or even 20 years after they believed they beat the disease. Odds are not everything, and most cancer patients will take these kinds of reassurances with a large lump of salt anyway — 75% (or even 91%) may not be too reassuring for patients who find themselves on the short end of a 1:200,000 ratio (the approximate prevalence of osteosarcoma in patients younger than the age of 20).

Even so, conditional survival is a useful statistic when counseling patients who receive diagnoses that carry existential threat. Hope is precious.

Take 5 Interview with Benjamin J. Miller MD, MS, lead author of Conditional Survival Greater Than Overall Survival at Diagnosis for Ewing's and Osteosarcoma

Seth S. Leopold, MD: Thank you for a fascinating and thought-provoking study. What caused you to ask the

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Fig. 1 The study by Miller, shown here, and colleagues primarily focused on the risk of cancer mortality regardless of the details of treatment. The challenge was finding the best approach to enhance understanding of the reality and gravity of the situation without being overly severe.

question? What inspired or motivated the work?

Benjamin J. Miller MD, MS: When counseling patients with a new diagnosis of sarcoma, a subject of clear importance is the likelihood of cure. While approaches to answering this difficult question vary, the information used to gauge this is based upon our knowledge of survival rates at the time of diagnosis. Since we follow patients for years after their tumor removal, I

found myself wondering if that conversation could change in time. If there was no evidence of tumor recurrence or spread for years, that has to be good — but how good? We sought to put a number on this.

Dr. Leopold: *The conditional survival statistics for osteosarcoma and Ewing's sarcoma would appear to offer hope to patients with those conditions. How much do conditional survival statistics*

vary among the other malignancies that you treat?

Dr. Miller: Sarcomas are notoriously difficult to study due to their rarity and heterogeneity in histology, size, site, grade, treatment, and biologic activity. Generally, most sarcomas show similar trends in conditional survival. The estimates appear most dependent on stage (metastatic or not) and grade (high or low). Metastatic cancer has a much more dismal initial prognosis than nonmetastatic, but the slope of improvement is substantially greater, and the conditional survival rates approach each other if an individual survives more than a decade past diagnosis. Similarly, low-grade malignancies show a higher initial survival estimate and a flattened slope compared to high-grade tumors, as the prognosis is more favorable from the beginning. It also takes around 10 years for the conditional survivals of low- and high-grade tumors to equalize.

Dr. Leopold: *What, if anything, is known about how conditional survival should influence the way we counsel patients with nonmalignant orthopaedic conditions, such as the durability of common reconstructive procedures?*

Dr. Miller: This is an interesting question that has not been formally explored, to our knowledge. A major difference in using conditional survival in a reconstructive procedure like total

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joint replacement is that one would expect that an implant will eventually fail when given enough time. In cancer, the assumption is that, given enough time without an event, failure (mortality) is less likely. However, this approach may be able to select out anomalous short- and mid-term failure. For instance, if complications such as infection, material failure, and early aseptic loosening in the first 5 or 10 years are avoided, perhaps the revised estimates of long-term durability of an implant are improved from the estimates at the time of surgery. This could be a useful tool for patient counseling, and determining the appropriate frequency of clinical and radiographic monitoring of an implant.

Dr. Leopold: *The broad topic here is that of risk, which is a subject that not all surgeons understand very well, even though it plays into almost every important decision that we make. An important element of this is the difference between using relative and absolute risk when counseling patients. A patient may opt not to have an elective procedure if the surgeon says, “your risk of developing an infection is five times that of the average patient.” But the patient may be quite comfortable with a 2.5% risk of infection — yet those may be the exact same number. How do you use relative and absolute risk differently when you counsel your patients?*

Dr. Miller: There are two variations of risk assessment in oncology patients: the risk of mortality from the cancer itself, and the risks of the proposed treatment. Our study primarily focused on the risk of cancer mortality regardless of the details of treatment. The challenge is how best to enhance understanding of the reality and gravity of the situation without being overly severe. While broad discussions of relative risks given prognostic factors are helpful, investigators have shown that patients respond well to percentages and a clear indication of absolute risk, even if the numbers are not encouraging [1]. This approach can also be extrapolated into patient education regarding complications of a surgical procedure. Relative risk is important as it allows for direct comparisons, and can help a patient decide between two or more tangible options. However, it is also vital to include absolute numbers in order to place the risks of a complication in a more global context.

Dr. Leopold: *The subject of risk is important to patients and surgeons. What are the major unanswered questions in this area that you would like future studies — either yours or those of others — to take on?*

Dr. Miller: Two major areas within the broad topic of “risk” where investigators could focus more effort are in data

gathering and patient communication. For the former, adequate discussions of risk can only be had when there is enough information to speak of specific concerns intelligently and with actual numbers. This is a continuing challenge for interventions in rare conditions, where the data gathered by a single provider or institution are likely to be too small to draw generalizable conclusions. One potential solution is a population-based registry designed to gather longitudinal data, such as functional outcomes and complications. Not only would this allow for representative numbers to be available for risk assessment, but a registry could also become an integral source of information for many future research questions. Second, patient communication could be enhanced with projects focusing on informed consent and shared decision-making. It is difficult to ensure that patients truly understand the implications of any surgical procedure, and it would be of benefit to patient and provider alike if we could develop techniques to improve comprehension, and stimulate patient involvement in their own health care.

Reference

1. Mack JW, Wolfe J, Grier HE, Cleary PD, Weeks JC. Communication about prognosis between parents and physicians of children with cancer. *J Clin Oncol*. 2006;24:5265–5270.