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Certain Death in Uncertain Time: Informing Hope by Quantifying a Best Case Scenario

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INTRODUCTION

Research informs us that the majority of patients with metastatic cancer desire information about their likely survival duration.[1] The literature also recommends that prognostic information be communicated to those who request it in a manner that is meaningful and realistic, but maintains hope.[2] Knowing these general principles is different than applying them in practice, and when confronted by versions of "how long have I got?" we struggle to find suitable answers. Although patients, caregivers, and health care professionals have identified hope as an integral part of prognostic discussions, the key practical questions of how to define, quantify, and convey realistic hope remain unanswered. The following edited extract from Edward Kennedy's memoir conveys the importance of trying to answer these questions.

"A biopsy the following Monday confirmed that I had a brain tumor—malignant glioma in my left parietal lobe. My wife Vicki and I privately were told that the prognosis was bleak—a few months at most. I respect the seriousness of death—I've had many occasions to meditate on its intrusions. But I wasn't willing to accept the doctor's prognosis for two reasons. The first was my own obstinate will to carry on in the face of adversity, one of the many habits of discipline that my father instilled in me…. The second was the way the message was delivered. Frankly, it made me furious. I am a realist, and I have heard bad news in my life. I don't expect or need to be treated with kid gloves. But I do believe in hope. And I believe that approaching adversity with a positive attitude at least gives you a chance for success. Approaching it with a defeatist attitude predestines the outcome: defeat. And a defeatist's attitude is just not in my DNA."[3]

Kennedy did not receive the hope he desired from his doctors and was left feeling defeated. It may have been that knowing the median survival time, his doctors did indeed feel hopeless. We need to believe hope exists before we can convey it. But how do oncologists find hope? A potential source of hope stems from our experiences with patients who manage to defy the odds and become long-term survivors. Such experiences can help us envision, and therefore convey, hope. A recent example is instructive.

WHEN PATIENTS OUTLIVE OUR ESTIMATES

Mr S, a 59-year-old warehouse manager presented in October 2002 with generalized bone pain, multiple hot spots on a bone scan, and a prostate-specific antigen (PSA) of 26 ng/mL. Biopsies confirmed adenocarcinoma of the prostate with a Gleason score of 8. He commenced goserelin and bicalutamide and the tumor responded for longer than 12 months, but by December 2003 his PSA had begun to rise. Bone pain recurred despite further hormone manipulations. He was referred for consideration of palliative chemotherapy in April 2004, 18 months after his initial diagnosis, with a PSA of 57 ng/mL.

Mr S attended his first medical oncologist consultation with his wife and two daughters (6 and 8 years old). He asked for all the details about his disease. He was informed that with chemotherapy the most likely scenario would be a survival time of 1 to 2 years. If his cancer failed to respond to any treatment, it could progress rapidly, and he could die within 6 months. Alternatively, if the cancer responded well to treatments, he could live 2 to 3 years or longer. Mr S decided to have chemotherapy and he completed 10 cycles of mitoxantrone over the next 6 months. Pain and quality of life scores improved over the first few weeks, and although his PSA was no lower after 3 cycles, it was undetectable (< 0.1 ng/mL) after 6 cycles. Since ceasing chemotherapy in November 2004, Mr S's treatment has included goserelin every 3 months and zoledronic acid every 6 months.

Mr S's last medical oncology clinic visit was in August 2009, more than 5 years after discussing the uncertainties of prognosis with his oncologist. He was well, symptom free, had a serum PSA lower than 0.1 ng/mL, and his daughters were now 11 and 13.

LONG-TERM SURVIVORS

Long-term survivors, like Mr S, are neither typical nor common, but neither are they rare—most oncologists have similar stories. Such patients are memorable, and not only because they make us feel good. They have more clinic visits than patients with cancers that do poorly. In a study of 102 patients with recently diagnosed advanced cancer, about one in 20 lived three to four times longer than their oncologist's prediction.[4]

Long-term survivors provide oncologists with hope, and telling stories of long-term survivors with similar cancers is an obvious way of conveying hope when discussing life expectancy. However, this hope needs to be tempered by the realization that few achieve such long survival times. Long-term survivors are outliers, and the more extreme their experience, the greater the doubt that they represent a realistic example. Quantifying and explaining the best case scenario representing the best 10% of patients is preferable to describing an individual long-term survivor, and is more realistic. Because survival distributions are skewed to the right (toward longer times), the longest survival times in a distribution are generally several times longer than the median. Best case scenarios should therefore be substantially longer than the median survival and can form the basis of realistic hope.

HOW TO EXPLAIN LIFE EXPECTANCY AND CONVEY REALISTIC HOPE

One of the reasons we struggle to communicate information on life expectancy is a lack of obvious data on which to base our estimates. Current literature and communication courses provide excellent guidance on how to broach discussions about prognosis, but little guidance on how to estimate and explain the likely survival time. How long does a typical patient starting chemotherapy for metastatic prostate cancer live? What would we have told Mr S when he asked about his prognosis? Sources of information to answer such frequent and important questions are remarkably limited.

MEDIAN IS NOT THE MESSAGE

Pertinent clinical trials are an obvious starting point to inform our survival predictions; however, the survival data in trials are usually summarized with a median, a term commonly misinterpreted by patients.[5,6] As Stephen Gould published 3 years after reading that his median survival with abdominal mesothelioma was 8 months, "the median isn't the message."[7] He argued that median survival can be both misleading and discouraging and believed few people have sufficient understanding of statistics to evaluate what the term median really means. He noted that most people would read such a statement as "I will probably be dead in 8 months." Explaining that a median survival of 8 months means that 50% of patients will live longer than 8 months, and encouraging patients to review aspects of their personal situation that move them into the better 50% is a way of using the median to convey hope.

- Check patient expectations and information desired
- Explain median survival of 12 months means 50% will live longer than 12 months
- Use simple multiples of the median to estimate and explain the typical, best-case and worst-case scenarios
  - Typical - about half of similar patients would live for somewhere between 6 months and 2 years (half to double the predicted median)
  - Best case – about 10% of patients could expect an excellent response to treatment with prolonged control and survival beyond 3 years (three to four times the predicted median).
  - Worst case - about 10% of patients will experience rapid progression and death within 2-3 months (1/6 of the predicted median).

Fig 1. Suggested approach for a patient with predicted survival of 12 months. Predicted survival based on median survival of a group of patients with similar characteristics and adjusted to account for any differences between the individual and the reference group.

CONSTRUCTING REALISTIC SCENARIOS USING MULTIPLES OF THE MEDIAN

The interquartile range of a survival distribution (25th to 75th percentiles) represents the middle 50% of observations, and can be thought of as reflecting a range of typical survival times. Survival curves from clinical trials include this information, but are typically summarized by the median survival and its CI (reflecting how precisely the median has been estimated).

Using survival data from trials to estimate the best case (best 10%), worst case (worst 10%), and typical (middle 50%) survival times could be helpful for informing patients. Simple multiples of predicted life expectancy provided good estimates of these scenarios in a study comparing predicted and actual survival times in 102 patients with advanced cancer.[4] The suggested steps for predicting the life expectancy of a patient with advanced cancer are summarized in Figure 1 and provide a useful framework to base discussions about prognosis. The first step requires the clinician to estimate the median survival of a group of similar patients (eg, from a pertinent clinical trial). This median can then be adjusted to account for any important differences between the individual and the reference group. Simple multiples of the adjusted median can then be used to estimate and explain the best case (three to four times the median), typical range (half to double the median), and worst case (one sixth of the median) scenarios.

Presenting patients with ranges for different scenarios provides meaningful information, accurately conveys the inherent uncertainty, and avoids the unwarranted precision implied by a single-point estimate of median survival. The uncertainty of survival predictions in itself can form the basis of hope for the best outcomes.

Kennedy recalls being told his life expectancy was "a few months at most," a time likely based on the adjusted median survival. Perhaps if the possible best case scenario had also been explained he would have felt less defeated. As it turned out, he lived 15 months from diagnosis, significantly longer than his clinician predicted.

OPTIMISM AND POSITIVE FRAMING

Patients understandably want hope and optimism from their doctors. A previous Art of Oncology article described a patient who requested

that her oncologist "be more optimistic" about her prognosis.[8] The oncologist's optimism was necessary for the patient to maintain hope. Achieving the correct balance between conveying hope and being realistic is where the difficulty arises. We need to be honest without being blunt. We need to foster realistic hope without creating false expectations of longevity that might lead to wasted time and futile treatments that impair quality of life. Discussing the best case, worst case, and typical scenarios is a simple method that appropriately balances hope with realism.

Positively framed prognostic information, such as the chance of surviving 2 years, is preferred by many patients to the negatively framed chance of dying in 2 years,[1,5] and is another way of conveying hope. Positive framing can be difficult when discussing life expectancy with a patient who has incurable cancer, but it is still possible. Some patients prefer to infer the negative (chance of dying) from hearing the positive (chance of surviving), rather than to hear the negative directly from their oncologist.[5] Explaining that there is a 20% chance of surviving 2 years may be sufficient information for the many patients who will understand without further explanation that 80% will not survive 2 years. Explaining the best case scenario, such as the time the best 10% of patients will live, before explaining the worst case scenario, is another way of framing positively.

Setting optimistic and achievable goals is also an important means of conveying and sustaining hope for patients with incurable cancer. There is more to life than its length, and we sometimes forget this as we focus our attention on survival times.

Providing a range of prognostic estimates, including outcomes that are more likely, and outcomes that are less likely, but still possible, allows patients to both maintain hope for the best and plan for the worst. We hypothesize that efforts to convey hope, suitably balanced by realism, will leave fewer patients feeling defeated after discussion of their prognosis. A patient's expectations of their survival must also be considered. It is when these expectations exceed reality that an estimate of survival becomes bad news.

CONCLUSION

Using multiples of the median to estimate and provide typical, best, and worst case scenarios offers a way of conveying more meaning, hope, and realism than a single point-estimate of median survival. Remembering long-term survivors can help oncologists envision hope, and explaining that 5% to 10% of patients might live beyond 3 to 4 times their predicted median can help oncologists quantify and convey realistic hope.

Life is inherently uncertain and unpredictable, with or without cancer. We cannot tell patients how long they will live, but we can do much better than giving them a single number. Improving the accuracy of our predictions is important, but conveying the limitations and uncertainty of these predictions is even more important, not in the least because it offers a means of quantifying and conveying realistic hope and understanding.

REFERENCES

1. Hagerty RG, Butow PN, Ellis PA, et al: Cancer patient preferences for communication of prognosis in the metastatic setting. J Clin Oncol 22:1721-1730, 2004

2. Hagerty RG, Butow PN, Ellis PM, et al: Communicating with realism and hope: Incurable cancer patients' views on the disclosure of prognosis. J Clin Oncol 23:1278-1288, 2005

3. Kennedy E: True Compass: A Memoir. London, United Kingdom, Little Brown, 2009

4. Stockler MR, Tattersall MH, Boyer MJ, et al: Disarming the guarded prognosis: Predicting survival in newly referred patients with incurable cancer. Br J Cancer 94:208-212, 2006

5. Davey HM, Butow PN, Armstrong BK: Cancer patients' preferences for written prognostic information provided outside the clinical context. Br J Cancer 89:1450-1456, 2003

6. Lobb EA, Butow PN, Kenny DT, et al: Communicating prognosis in early breast cancer: Do women understand the language used? Med J Aust 171:290-294, 1999

7. Gould SJ: The median is not the message. Discover 6:40-42, 1985

8. Francis PA: Surprised by hope. J Clin Oncol 26:6001-6002, 2008

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