The Stage IV Shuffle: Elusiveness of Straight Talk About Advanced Cancer

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During the initial consultation with a patient to communicate a diagnosis of late-stage cancer, the oncologist may refrain from giving survival statistics, redirecting the conversation from the bad news (incurability) to the practical aspects of the patient's care (treatments, timetables, appointments, and testing to monitor response to treatment). Whether conscious or unconscious, this diversion helps cushion the impact of the disturbing news. This paper shows that clinicians' gingerly handling of harsh facts when they talk with patients also applies to health educators and researchers when they write about late-stage cancer. As a result, these cancer patients typically lack an understanding of their poor prognosis and the limited effectiveness of most available treatments, possibly compromising their ability to make informed choices. To remedy this problem, I describe an approach to straight talk about late-stage cancer that can give a patient realistic hopes instead of false hopes that are apt to betray later on. I also propose an enhanced method of displaying and interpreting comparative efficacy data that can facilitate understanding and serve as a basis for shared decision making.

KEY WORDS: cancer; communication; patient engagement; ethics.

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This paper will show that clinicians' gingerly handling of harsh facts when they talk with patients also applies to health educators when they prepare materials about advanced cancer for the general public and to researchers when they report cancer research findings in the medical literature. While the intentions may be benevolent, the combined effect is to distort perceptions about what medical science has to offer patients with late-stage cancer, possibly compromising the ability of patients and families to make informed choices.[3]

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CLINICIANS AND HEALTH EDUCATORS

On receiving a diagnosis of advanced cancer, most patients especially want to know the answer to a single question, typically phrased as "What are my chances" or "How long have I got?"[1, 4] These formulations of the question mirror the two standard formats for presenting statistical data on prognosis: five-year survival (or survival using a different interval) and median survival time. Although pertinent data are available,[5] the patient does not always receive a straight answer. Instead, the oncologist may offer, "it is extremely difficult to give any indication of the general prognosis because each patient is unique."[1] Such a response may represent a well-meaning effort to mitigate the shock of the bad news, but the patient may sense that critical information is being withheld—that the clinician is ignoring the elephant in the room.

If the patient fails to elicit a meaningful response from the clinician and turns to a cancer research or advocacy organization, obtaining the data from that source will be no easier (Box 1). Discussions about treatment efficacy are even less common.[6–8, 10] The conversation focuses on what will be done, not how well it will work. What could explain this communication blackout?

First, most treatments for late-stage cancer offer such modest benefits that clinicians and health educators may prefer to gloss over the facts of efficacy. It is difficult to inform a patient not only that the prognosis is poor, but that treatment is likely to offer only marginal survival gains.[10–12] Instead, the clinician may state, "Your cancer is incurable, but it is treatable"[13] and "We never know how an individual patient will respond to this therapy."[1] The UK's National Institute for Health and Care Excellence systematically omits efficacy data from lay educational materials about advanced cancer.[10] Since patients are not likely to appreciate the distinction between "treatable" and "effectively treatable," they mentally substitute the latter for the former.[1] This substitution may explain why so many patients believe their metastatic cancer can be cured[3] and why so few patients with advanced cancer decline chemotherapy.[14]

Second, the usual way of presenting efficacy data in the medical literature can be difficult for clinicians to interpret. Randomized controlled trials and meta-analyses typically

Box 1 Hiding survival data in educational materials

On its website, the American Cancer Society devotes a large amount of space and thousands of words to incidence, diagnosis, staging, and treatment options, while nearly ignoring survival.[6] Just one brief sentence buried several layers deep gives a single survival statistic for patients with stage IV breast cancer. One must also work to track down survival information on the National Cancer Institute or Susan G. Koman website.[7, 8] If a patient does manage to find survival data, it comes with caveats clearly intended to soften the impact:

> Cancer survival rates don't tell the whole story…they can't predict what will happen in any particular person's case…As treatments are improving over time, women who are now being diagnosed with breast cancer may have a better outlook than these statistics show.[9]

In other words, look at these statistics, then please ignore them.

report results using the statistical measure, hazard ratio, often accompanied by survival curves comparing treatments.[15] The hazard ratio summarizes in a single number the magnitude of the difference between alternative treatments over a study's entire period of follow-up. While this mathematical construct does incorporate the essential information, it does not effectively communicate the meaning of the information in a way that can help clinicians and patients compare alternatives and make informed choices. A non-statistician gains little insight from knowing that, for colorectal cancer, the hazard ratio for chemotherapy vs. no chemotherapy is 0.65 (95% confidence interval, 0.56 to 0.76).[16]

CANCER RESEARCHERS

When reporting hazard ratios, researchers also frequently report a related statistical measure containing the same information: reduction in the risk of death. This measure is easily misinterpreted in a way that exaggerates the benefit of a treatment (Box 2). The widespread use of the measure in the medical literature may contribute to a blurring of the truth—an academic version of the stage IV shuffle.

Another practice, commonplace for decades, involves a shift in focus from survival to a different endpoint, such as "tumor response" or "progression-free survival." In a clinical trial, these surrogate outcomes have a practical advantage over survival: they require a shorter period of follow-up for data collection. In everyday practice, the rationale for measuring these outcomes is that they indicate if and how well a treatment is working. If a tumor shrinks or fails to grow for 6 months, that must be a good thing. It shows that the treatment has suppressed the cancer and gained the patient some time.

The problem with this narrative is that indicators of disease progression have not shown a consistent correlation with patient survival—the uncontested scientific gold standard for measuring efficacy.[18] When chemotherapy does suppress tumor growth, this does not necessarily mean that the patient will live longer. Nevertheless, researchers often report tumor response or progression-free survival in cancer trials, sometimes designating one or the other as the primary outcome in place of survival. In fact, in recent years, more than half of all clinical trials leading to approval of a drug by the U.S. Food and Drug Administration for oncologic indications have used surrogate outcomes.[19] Since chemotherapy almost always has a greater effect on these outcomes than on survival, the shift in focus tends to make results look more favorable.

GETTING TO STRAIGHT TALK

The first obstacle to straight talk about advanced cancer—uncertainty about how to balance candor with tact when communicating with a profoundly distraught patient—presents a greater challenge than the second obstacle—confusion caused by opaque methods of presenting data. Solving the first problem will require a divergence from entrenched professional and social norms. Patients, themselves, exacerbate this problem by colluding with physicians to keep the focus on the treatment calendar and steer the conversation away from the illness trajectory.[1] Solving the second problem requires a better data display.

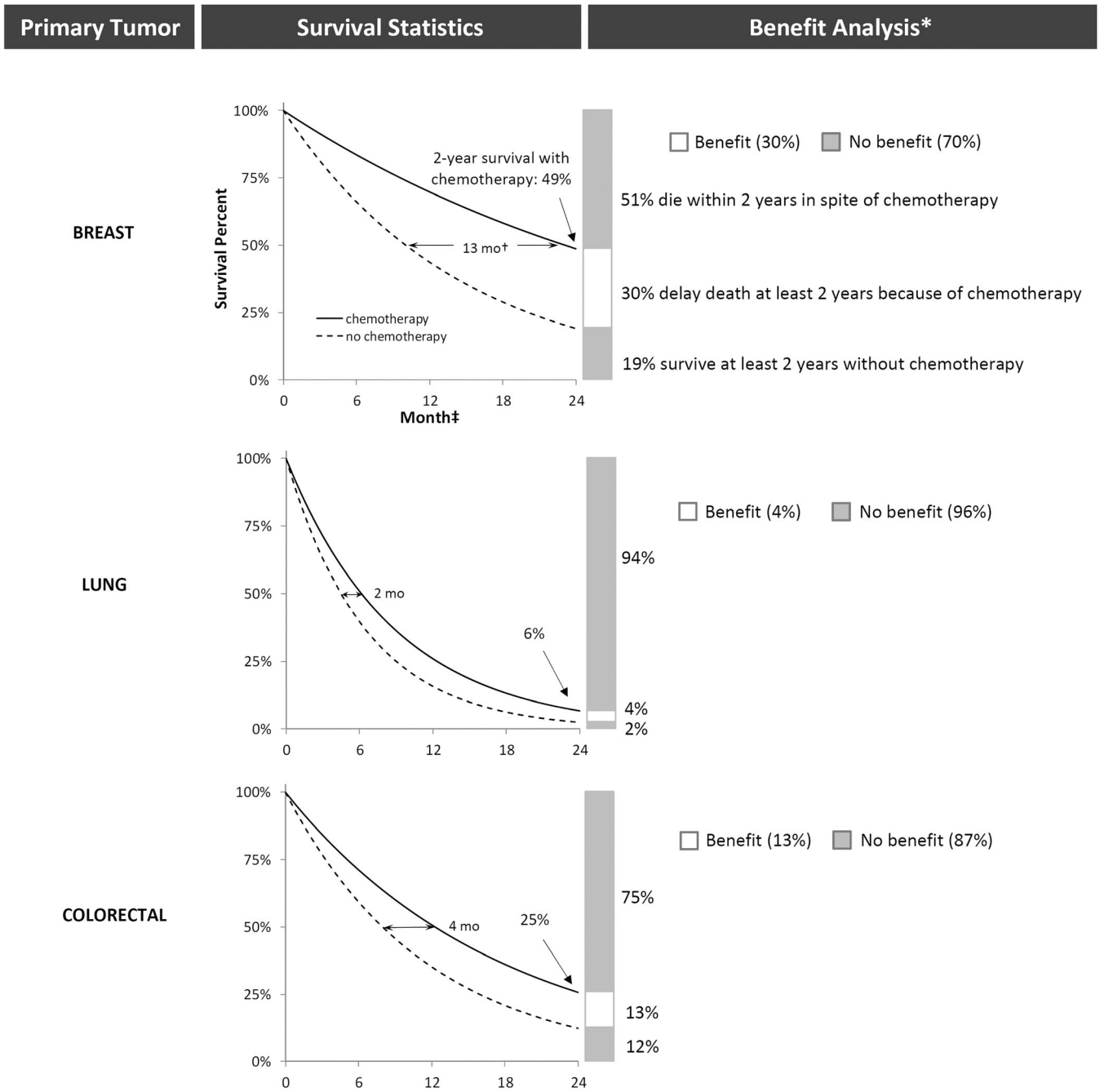
A Better Data Display

Survival curves are easier to interpret than hazard ratios. A survival curve offers visually compelling answers to questions about prognosis. A pair of survival curves representing the two arms of a clinical trial (e.g., chemotherapy vs. best supportive care) conveys information about efficacy in a straightforward manner. Adding one more component to this graphic—a stacked bar that interprets the displayed curves—converts a set of survival statistics to a "benefit analysis," a proposed framework for straight talk and informed decision making (Fig. 1).

Figure 1 illustrates benefit analyses for selected neoplasms typically treated with chemotherapy in advanced stages of disease: breast, lung, and colorectal. These 3 malignancies account for about 35% of all new cases of cancer.[20] The graph for breast cancer was constructed using data from an observational cohort study that compared survival in patients diagnosed before and after the introduction of fluorouracil

Box 2 Confusion associated with "reduction in the risk of death"

Citing a meta-analysis that evaluated platinum-based chemotherapy for advanced lung cancer, the authors of a review article stated that "…there was a 27% reduction in the risk of death (hazard ratio, 0.73; 95% CI, 0.63 to 0.85; p<0.0001)."[17] While this statement is technically true, it is bound to be misinterpreted by many readers who are not statisticians. They will probably envisage a 27% reduction in cumulative *mortality*. The death rates in this lung cancer example do differ by 27%, but mortality in the two groups does not differ by that amount: the reduction in 2-year mortality is only 4%. It can therefore be very misleading to report reduction in risk of death without clarification.



*"Benefit" refers to prolongation of life.

†Gain in median survival time.

‡Since patient was diagnosed with stage IV cancer.

Sources: Survival statistics used to construct the graphs are based on JAMA 1966 for breast,[21] BMJ 1995 for lung,[15] and BMJ 2000 for colorectal.[16]

Fig. 1 Survival benefit of conventional chemotherapy for stage IV cancer. These smooth exponential survival curves were constructed using median survival times reported in the pertinent literature, relying on the fact that survival curves for most stage IV cancers closely approximate negative exponential functions

Box 3 Straight talk about chemotherapy for metastatic cancer

If 100 patients with stage IV colorectal cancer undergo conventional chemotherapy, 13 of them will benefit from the treatment and 87 of them will not. It is impossible to know which group you will fall into, but these are the statistical facts. Given these facts, it's up to you to decide if you want to undergo chemotherapy. There is no "correct" decision. The right decision for you depends on how you weigh the potential benefit against the demands and expected side effects of treatment.

Box 4 Using the "benefit" concept to engage patients in shared decision-making

A patient could be asked to specify a personal benefit threshold—probability or time—below which the benefit of chemotherapy would be too small to justify its use. A patient deciding on a 10% probability threshold, for example, would choose to undergo chemotherapy for stage IV breast or colorectal cancer, but would decline treatment for lung cancer (Fig. 1). This hypothetical exchange between a patient and a clinician illustrates how the concept of "benefit" could help engage cancer patients in shared decision-making

chemotherapy in the mid-1950s.[21] The graphs for lung and colorectal cancers are based on survival data derived from meta-analyses of chemotherapy trials from the 1970s and 1980s involving each type of malignancy.[15, 16] The reason for relying on older studies is that recent chemotherapy trials rarely include an untreated control arm, which is needed to compare the benefit of chemotherapy vs. no chemotherapy. A suggested method for updating results from earlier studies is discussed later in this section.

A benefit analysis can answer these questions: (1) What is the probability that I will benefit from treatment? and (2) How much time will I gain? From Fig. 1, a patient with stage IV colorectal cancer has a 13% chance of benefitting from conventional chemotherapy, assuming a 2-year time horizon. This information yields a straight answer to the first benefit question (Box 3). The figure also shows the gain in median survival time—4 months in the case of colorectal cancer—providing an answer to the second question. The two ways of expressing benefit (probability and time gained) correspond to the vertical and horizontal distances between the survival curves measured at the 2-year and 50% survival milestones, respectively. These ideas can help engage patients in shared decision-making (Box 4) and facilitate clear thinking about the observed effects of treatment (Box 5).

The "benefit" in benefit analysis is identical to the "absolute risk reduction" sometimes used to report results of clinical trials. Scientific reporting guidelines[22] and leading medical journals encourage authors to use this measure rather than the alternative "relative risk reduction," which can make modest gains seem to be more substantial than they are.

Prolongation of life may not be the only goal of chemotherapy. If other goals such as symptom relief influence decision-making, then the efficacy of chemotherapy in achieving those goals should be quantified and incorporated into a benefit analysis. The patient needs an evidence-based answer to the question, "What am I going to gain from this treatment?"

To the extent that contemporary chemotherapy—and newer approaches such as immunotherapy—outperforms or enhances the effects of conventional chemotherapy, the survival benefit based on earlier placebo-controlled trials must be adjusted accordingly. Since present-day cancer trials usually lack a placebo or null control group, it is difficult to determine the survival benefit of the new treatment compared with supportive care alone. One possible approach is illustrated in Box 6. Developing rigorous methods for estimating treatment-vs.-supportive care differences in the absence of an appropriate control group deserves high-priority attention as a topic for cancer research methodology. Such methods would make it possible to determine if improvements in treatment over the past 4 decades have increased survival enough to alter the essential message of Fig. 1—that only a minor fraction of patients with stage IV cancer derive any survival benefit from treatment.

Box 5 "We fought aggressively and the strategy paid off"

When a treated patient seems to "beat the odds" by surviving longer than expected, the good news is likely to prompt some version of, "We fought aggressively and the strategy paid off."[1] This narrative puts a positive spin on the path already taken, but the truth may lie elsewhere. For some cancers, such as breast and lung, it is true that the patient is more likely to have survived thanks to the middle portion of the corresponding bar graph in Fig. 1 (survived because of chemotherapy) rather than the bottom portion (would have survived without chemotherapy). For other cancers, such as colorectal, the two explanations would be about equally likely.

Box 6 Estimating the benefit of a contemporary treatment by combining recent and older data

A recent clinical trial evaluated nivolumab as second-line therapy for patients with advanced squamous non-small-cell lung cancer who had been pretreated with platinum-based chemotherapy.[23] These patients survived a median of 9.2 months after starting nivolumab. Adding this to the 6.2-month median survival with platinum-based chemotherapy alone derived from a 1995 meta-analysis[15] yields an estimated net median survival of 15.4 months when the two treatments are administered sequentially. A median survival of 15.4 months translates to a 2-year survival of 34%, or a 32% benefit relative to the 2% baseline survival (no chemotherapy) reported in the meta-analysis. Nivolumab after platinum-based chemotherapy therefore offers substantially greater benefit than platinum-based chemotherapy alone, but survival is still poor.

Box 7 The "preview, ask, tell, ask" approach to communicating with patients

The clinician previews the categories of available information (e.g., adverse events, tumor response, survival); asks what information the patient wants; communicates that information using the patient's preferred format; and, finally, asks patients to describe their understanding of the information they just received and their feelings about it.[26] The clinician can then correct any misunderstandings and address the patient's emotional response. If a patient does not want to hear statistics, the physician can offer qualitative descriptors or ranges ("a few months," "a year or two") to convey information truthfully, but in a manner that may feel less intrusive to the patient.[10]

A Candid Conversation

If a patient agrees to undergo chemotherapy without a basic understanding of treatment goals and efficacy, the minimum requirements for informed consent have not been satisfied.[10] Since patients receiving chemotherapy for advanced cancer typically lack this understanding,[2, 3, 10] they have most likely given uninformed consent. This may happen in spite of earnest efforts by the health care team to communicate risks and benefits of therapy to patients who cannot or do not want to hear the truth. While it is reasonable to draw attention to the ways in which clinicians, health educators, and researchers might contribute to a communication gap, it is also important to acknowledge the extraordinary complexity of the problem and fruitlessness of laying blame.

It might seem cruel to convey harsh facts about life expectancy and treatment benefit to patients with incurable cancer. While an insensitive presentation of the facts would, indeed, be cruel, clinicians who adhere to best practices for delivering bad news should be able to communicate compassionately and honestly.[24] Pointing out that treatment is unlikely to help does not "take away all hope," as some defenders of the stage IV shuffle might argue. A candid discussion can give the patient realistic hopes instead of false hopes that are apt to betray later on.[25] A patient with stage IV breast cancer can reasonably hope to live 2 years or longer. Hoping for 10 years is less realistic: the chances are currently about 8%—not impossible, but unlikely.[5] While it is not the oncologist's job to challenge a patient who hopes to beat the odds, it is the clinician's job to disclose the odds when a patient wants to know. A patient who has asked for a prognosis is entitled to the truth. A patient who has asked for a prognosis may prefer to see the statistics rather than to be left in the dark.

While cancer patients are entitled to the truth, they are also entitled not to have the truth forced upon them. Individuals vary in the information they want and the format that is most meaningful to them. A disarmingly straightforward and respectful approach to accommodating this variation[26] gives patients no more information than they want and no less (Box 7).

Much has been written about the need to improve doctor-patient communication about end-of-life issues. Given the legal and ethical implications of starting a course of treatment when the patient lacks an understanding of key facts, maintaining the status quo is not an option. It is time to put the stage IV shuffle to rest.

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