Complexities of Cancer Screening: Considerations for Clinical Practice

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Improvements in cancer diagnosis, staging using sophisticated analytic techniques, predicting behavior with molecular probes, targeting therapies that are specific to an individual's cancer, and even understanding the genetic makeup of many common cancers provide a level of excitement for all. But the good news has its limits and caveats, which usually receive less attention.

Many people (patients and providers) may mistakenly believe that early detection is synonymous to cure. Media coverage of a national celebrity's screening colonoscopy,[1] male politicians urging blood testing for prostate cancer,[2] and front page coverage for new diagnostic techniques in breast cancer screening[3] all raise optimism among the lay public. And, while some cancer screening is beneficial *(see Pettiti, page 18)*, screening may be indiscriminately applied to cancers where an earlier detection does not result in better outcomes.[4]

Our increasing understanding of (some) cancers expands far into the biology of the cancer cell—its development, growth, behavior, and even genetic alterations that enable growth and metastases to occur. This research indicates that by the time a common cancer is diagnosed—by the most modern means—that cancer has been present in the patient's body for anywhere between five and eight years, in the commonly referred to "pre-clinical" phase.[5] So, while screening studies can detect cancers in their "earliest" clinical phases, in fact, nearly 70–80 percent of that cancer's natural history has already elapsed. During that long natural history—well before it is diagnosable—most of the cancer's spread has likely occurred, though still beneath the limits of current detection capabilities.

For example, consider two newsworthy cases: Elizabeth Edwards (breast cancer metastasized to bone[6]) and Tony Snow (colon cancer metastasized to liver[7]). Both cases involve patients who suffered relapses not long after the primary diagnosis. What received less media attention was the fact that these metastatic foci occurred well before the primary cancer was diagnosed, i.e., they did *not* occur in a relatively short window of time following their original diagnoses. This metastatic potential represents the genetic make up of the individual's cancer cells; it was *not* acquired during some arbitrary period of time that elapsed following their diagnosis. The more we learn, the more we understand that this scenario is, overwhelmingly, the norm. Obviously, that directly challenges the argument that an earlier diagnosis would have given the patient a better chance.

The legal implications of the "early is better" argument often promoted by medical professionals are significant. For example, studies that report more successful cancer survival rates as a result of screening are cited in malpractice allegations that a physician did not order a screening test. A patient whose cancer could have, hypothetically, been detected earlier places the physician in a precarious position when the patient presents "evidence" that cancers detected under these circumstances are reported to result in more favorable outcomes. Such evidence, however, may not be valid.

Rather than over emphasizing the relationship between early detection and life-extending treatments or cures, patients—and physicians—are better served by a two-way discussion about the more sobering realities of cancer screening and diagnosis, i.e.:

- a screening study may lead to a false positive test and its associated emotional distress,
- the need for diagnostic procedures performed on a cancer that may never have needed to be diagnosed, and
- harms resulting from treatments that result in unfavorable quality of life outcomes without providing any impact on overall survival.

A patient who has realistic expectations is a true partner in making decisions about screening (and the results) and perhaps less likely to pursue a "loss of chance" malpractice allegation. Of course, physicians still must take an accurate history (including a family history), elicit important factors that place an individual patient at higher risk of harboring a disease, and be knowledgeable about outcomes and biases of screening studies to enable patient counseling where shared decisions can be formulated. And, all of this—whether the decision is for or against screening—must be properly documented in the medical record.

Screening Biases

Understanding the biases of screening studies is as important to patients as it is to physicians. There are four important considerations in the interpretation of screening studies.

Selection bias

Of the potential screenees who could participate in a study, only a subset actually do present for screening.[8] Why did these patients come in for screening? What are their demographics? Were they more compulsive, or did they have concerns about their health? Patients who present for screening studies may have characteristics not representative of larger populations.

Lead time bias

A lead time bias challenges the assumption that diagnosing and treating a cancer early in its existence will result in a longer survival. In rare cases this may be true; more often it is not.[9] Assume, for example, that a cancer will kill a particular person eight years after it starts. If the cancer is diagnosed in the fifth year of its natural history, the patient will live three more years.

If the cancer is diagnosed in the third year (by screening), the patient will live five more years. One could assume that the earlier diagnosis provided the patient with a longer life span, but that is not true. Detection via screening just gave us more time to know the patient had the disease. The duration of survival after diagnosis is not sufficient to state that earlier diagnosis would have been associated with a longer survival.

Length bias

Multiple screening tests favor the diagnosis of slow growing tumors. Fast growing tumors may be missed during the first screening test, but show up during the subsequent one. Study results that state that earlier diagnosis finds more favorably staged cancers are only taking a snapshot of that cancer in a point of time and do not provide for when, in the course of that cancer, the process of metastases took place.

Over diagnosis

Imagine two similar patients: one has screening and is diagnosed with cancer; the other does not undergo screening. Both patients die of non-cancer causes. At autopsy, we learn that the non-screened patient had a similar cancer to the one detected in the screened patient. It is fair to say that that particular cancer never required a diagnosis, since it was biologically inactive during the patient's lifetime. Yet the patient whose cancer was detected via screening suffered potential morbidities as a result of treatment.

As screening tests detect ever smaller cancers, the problem of over diagnosis is likely to increase, as illustrated in the recent computed tomography screening and lung cancer outcomes study that demonstrated greater detection, but no meaningful reduction in the risk of advanced cancer or lung cancer mortality.[10] The American College of Physicians, too, just recently challenged the dogma that all women ages 40–49 undergo screening mammograms, given a better assessment of risk associated with the procedure. Similar recommendations have also been advocated by the Canadian Task Force of Preventive Health Care.[11]

A Question of Liability

The complexities surrounding cancer screening have profound implications related to medical malpractice claims alleging a failure or delay in diagnosis. If a physician chooses not to order a screening test, or fails to follow up on an abnormal test, only later to find a diagnosis of cancer, is there medical liability?

The question of liability is answered by the legal process triggered by a malpractice lawsuit. The likelihood of litigation increases when the patient's expectations do not align with the physician's—if the patient assumes that a different chronology would have led to a different outcome.[12] Certainly patients and physicians expect abnormal findings to be followed up, but it is also imperative that the physician provide the reasons and limitations for ordering the test in the first place. A discussion can then occur between the patient and physician regarding expectations and limitations of an abnormal test, if found, in a system referred to as "shared decision making."

In the case example on Page 5, the 62–year-old woman with a family history of colon cancer *should* have had a screening colonoscopy or other gastrointestinal evaluation. However, this may not have prevented the cancer that was eventually diagnosed or even altered this patient's subsequent fate. Moreover, a patient with a family history really does not fall within the true definition of routine screening,[13] but rather one with increased risk.

In the case example on Page 6, the 62-year-old man with the missed lung nodule should have had an earlier follow-up of the abnormality. But even the earliest detection of such nodules is unlikely to be associated with alterations in outcomes, regardless of when they are detected. Both the colon and lung cancer patients discussed have likely suffered adverse consequences as a result of their intrinsic biology of their respective cancers, rather than the specific timing of the cancer diagnosis.

Despite that harsh reality, we must strive to minimize the risk of these occurrences by putting into place foolproof processes to 1) ascertain that an appropriate medical history is taken and placed in the medical record to determine whether a reasonable excess risk of cancer exists, such as in the setting of a strong family history or occupational exposure; 2) perform (and document) an appropriate physical examination that assesses normal, equivocal, or abnormal findings, and 3) review abnormal laboratory or radiographic values. Of equal importance is the education of our patients about the limitations and consequences of this type of testing to minimize false expectations. ■

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