VIEWPOINT

Overdiagnosis and Overtreatment in Cancer
An Opportunity for Improvement

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Over the past 30 years, awareness and screening have led to an emphasis on early diagnosis of cancer. Although the goals of these efforts were to reduce the rate of late-stage disease and decrease cancer mortality, secular trends and clinical trials suggest that these goals have not been met; national data demonstrate significant increases in early-stage disease, without a proportional decline in later-stage disease. What has emerged has been an appreciation of the complexity of the pathologic condition called cancer. The word "cancer" often invokes the specter of an inexorably lethal process; however, cancers are heterogeneous and can follow multiple paths, not all of which progress to metastases and death, and include indolent disease that causes no harm during the patient's lifetime. Better biology alone can explain better outcomes. Although this complexity complicates the goal of early diagnosis, its recognition provides an opportunity to adapt cancer screening with a focus on identifying and treating those conditions most likely associated with morbidity and mortality.

Changes in cancer incidence and mortality[1] reveal 3 patterns that emerged after inception of screening (Table). Screening for breast cancer and prostate cancer appears to detect more cancers that are potentially clinically insignificant.[4] Lung cancer may follow this pattern if high-risk screening is adopted.[5] Barrett esophagus and ductal carcinoma of the breast are examples for which the detection and removal of lesions considered precancerous have not led to lower incidence of invasive cancer. In contrast, colon and cervical cancer are examples of effective screening programs in which early detection and removal of precancerous lesions have reduced incidence as well as late-stage disease. Thyroid cancers and melanoma are examples for which screening has expanded and, along with it, the detection of indolent disease.

Optimal screening frequency depends on the cancer's growth rate. If a cancer is fast growing, screening is rarely effective. If a cancer is slow growing but progressive, with a long latency and a precancerous lesion (eg, colonic polyps or cervical intraepithelial neoplasia), screening is ideal and less frequent screening (eg, 10 years for colonoscopy) may be effective. In the case of an indolent tumor, detection is potentially harmful because it can result in overtreatment. These observations provide an opportunity to refocus screening on reducing disease morbidity and mortality and lower the burden of cancer screening and treatments.

In March 2012, the National Cancer Institute convened a meeting to evaluate the problem of "overdiagnosis," which occurs when tumors are detected that, if left unattended, would not become clinically apparent or cause death. Overdiagnosis, if not recognized, generally leads to overtreatment. This Viewpoint summarizes the recommendations from a working group formed to develop a strategy to improve the current approach to cancer screening and prevention.

Periodic screening programs have the potential to identify a reservoir of indolent tumors.[4] However, cancer is still perceived as a diagnosis with lethal consequences if left untreated.

An ideal screening intervention focuses on detection of disease that will ultimately cause harm, that is more likely to be cured if detected early, and for which curative treatments are more effective in early-stage disease. Going forward, the ability to design better screening programs will depend on the ability to better characterize the biology of the disease detected and to use disease dynamics (behavior over time) and molecular diagnostics that determine whether cancer will be aggressive or indolent to avoid overtreatment. Understanding the biology of individual cancers is necessary to optimize early detection programs and tailor treatments accordingly. The following recommendations were made to the National Cancer Institute for consideration and dissemination.

Physicians, patients, and the general public must recognize that overdiagnosis is common and occurs more frequently with cancer screening. Overdiagnosis, or identification of indolent cancer, is common in breast, lung, prostate, and thyroid cancer. Whenever screening is used, the fraction of tumors in this category increases. By acknowledging this consequence of screening, approaches that mitigate the problem can be tested.

Change cancer terminology based on companion diagnostics. Use of the term "cancer" should be reserved for describing lesions with a reasonable likelihood of lethal progression if left untreated. There are 2 opportunities for change. First, premalignant conditions (eg, ductal carcinoma in situ or high-grade prostatic intraepithelial neoplasia) should not be labeled as cancers or neoplasia, nor should the word "cancer" be in the name. Second, molecular diagnostic tools that identify indolent or low-risk lesions need to be adopted and validated. Another step is to reclassify such cancers as IDLE (indolent lesions of epithelial origin) conditions.[4] An example is the reclassification of grade 1 papilloma to urothelial neoplasia of low malignant potential.[6] Presciently, the rationale for reclassifying papilloma and grade 1 carcinoma as "papillary urothelial neoplasia of low malignant potential" was "to take the lowest grades of tumor, the most benign-appearing lesions, and remove the word carcinoma."[6] A multidisciplinary effort across the pathology, imaging, surgical, advocate, and medical communities could be convened by an independent group (eg, the Institute of Medicine) to revise the

Table. Change in Incidence and Mortality of Cancers Over Time From 1975 to 2010 as Reported in Surveillance, Epidemiology and End Results[1]

	Incidence			Mortality		
	Per 100 000		%	Per 100 000		%
Change[a]	1975	2010[b]	Change	1975	2010[b]	Change
Example 1						
Breast[c]	105.07	126.02	20	31.45	21.92	−30
Prostate	94	145.12	54	30.97	21.81	−30
Lung and bronchus[d]	52.26	56.68	8	42.56	47.42	11
Example 2						
Colon	41.35	28.72	−31	28.09	15.51	−45
Cervical	14.79	6.71	−55	5.55	2.26	−59
Example 3						
Thyroid	4.85	13.83	185	0.55	0.51	−7
Melanoma	7.89	23.57	199	2.07	2.74	32

[a] Example 1: Indolent and consequential tumors are identified with screening, leading to an overall increase in incidence rates. Example 2: Prescreened tumor population is more homogeneous, slower-growing but consequential. Screening substantially decreases incidence (through detection and removal of precursor lesions) and mortality. Example 3: Screening expands the population of indolent tumors, with little or no effect on the small population of more aggressive tumors.

[b] Represents period in which screening (except for lung cancer) is prevalent.

[c] At least two-thirds of the mortality reduction is believed attributable to adjuvant therapy.[2,3]

[d] The National Lung Screening Trial conducted among individuals at risk for lung cancers shows that the proportion of stage I detected tumors is more than 2-fold higher than the decrease in the higher-stage tumors, accounting for its inclusion in example 1.[5]

taxonomy of lesions now called cancer and to create reclassification criteria for IDLE conditions.[7]

Create observational registries for low malignant potential lesions. Providing patients and clinicians with pathologic diagnosis and information related to disease prognosis is crucial to informed decision making, including comfort with alternate treatment strategies such as active surveillance. Prognosis for precancerous lesions includes the risk of development of invasive cancer, the period over which such a tumor would develop, and the prognosis of that type of tumor should it occur. Prognosis for invasive cancer includes risk and timing of development of metastatic disease and death. Large registries for potentially indolent conditions would provide data linking disease dynamics[8] (eg, tumor growth rate over time) and diagnostics needed to provide patients and physicians with confidence to select less invasive interventions.

Mitigate overdiagnosis. Strategies to reduce detection of indolent disease include reducing low-yield diagnostic evaluations appropriately, reducing frequency of screening examinations, focusing screening on high-risk populations, raising thresholds for recall and biopsy, and testing the safety and efficacy of risk-based screening approaches to improve selection of patients for cancer screening. The ultimate goal is to preferentially detect consequential cancer while avoiding detection of inconsequential disease.

Expand the concept of how to approach cancer progression. Future research should include controlling the environment in which precancerous and cancerous conditions arise, as an alternative to surgical excision.

Conclusion

The original intent of screening was to detect cancer at the earliest stages to improve outcomes; however, detection of cancers with better biology contributes to better outcomes. Screening always results in identifying more indolent disease. Although no physician has the intention to overtreat or overdiagnose cancer, screening and patient awareness have increased the chance of identifying a spectrum of cancers, some of which are not life threatening. Policies that prevent or reduce the chance of overdiagnosis and avoid overtreatment are needed, while maintaining those gains by which early detection is a major contributor to decreasing mortality and locally advanced disease. The recommendations of the task force are intended as initial approaches. Physicians and patients should engage in open discussion about these complex issues. The media should better understand and communicate the message so that as a community the approach to screening can be improved.

ARTICLE INFORMATION

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