COMMENTARY

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Personalizing guideline-driven cancer screening

Reports of cancer date back thousands of years to Egyptian texts. Its existence baffled scientists until the 1950s, when Watson, Crick, and Franklin discovered the structure of DNA, laying the groundwork for identifying the genetic pathways leading to cancer. Currently, cancer is a leading global cause of death and the second leading cause of death in the United States.[1,2]

In an effort to curtail cancer and its related morbidity and mortality, population-based screening programs have been implemented with tests that identify precancerous lesions and, preferably, early-stage rather than late-stage cancer.

Screening for cancer can lead to early diagnosis and prevent death from cancer, but the topic continues to provoke controversy.

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VALUE OF SCREENING QUESTIONED

In a commentary in the March 2019 *Cleveland Clinic Journal of Medicine*, Kim et al[3] argued that cancer screening is not very effective and that we need to find the balance between the potential benefit and harm.

Using data from the US Preventive Services Task Force (USPSTF) and various studies, the authors showed that although screening can prevent some deaths from breast, colon, prostate, and lung cancer, at least 3 times as many people who are screened still die of those diseases. Given that screening does not eliminate all cancer deaths, has not been definitely shown to decrease the all-cause mortality rate, and has the potential to harm through false-positive results, overdiagnosis, and overtreatment, the authors questioned the utility of screening and encouraged us to discuss the benefits and harms with our patients.

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In view of the apparently meager benefit, the USPSTF has relaxed its recommendations for screening for breast and prostate cancer in average-risk populations in recent years, a move that has evoked strong reactions from some clinicians. Proponents of screening argue that preventing late-stage cancers can save money, as the direct and indirect costs of morbidity associated with late-stage cancers are substantial, and that patients prefer screening when a test is available. Current models of screening efficacy do not take these factors into account.[4]

Kim et al, in defending the USPSTF's position, suggested that the motivation for aggressive testing may be a belief that no harm is greater than the benefit of saving a life. They illustrated this through a Swiftian "modest proposal," ie, universal prophylactic organectomy to prevent cancer. This hypothetical extreme measure would nearly eliminate the risk of cancer in the removed organs and prevent overdiagnosis and overtreatment of malignancies, but at substantial harm and cost.

In response to this proposal, we would like to point out the alternative extreme: stop all cancer screening programs. The pendulum would swing from what was previously considered a benefit—cancer prevention—to a harm, ie, cancer.

IN DEFENSE OF CANCER SCREENING

Observational studies, systematic reviews, meta-analyses, and modeling studies show that screening for cervical, colorectal, breast, and prostate cancer decreases disease-specific mortality.[5–11]

For example, in lung cancer, the National

Lung Screening Trial demonstrated reductions in disease-specific and overall mortality in patients at high risk who underwent low-dose screening computed tomography.[12]

In breast cancer, a systematic review demonstrated decreased disease-specific mortality for women ages 50 through 79 who underwent screening mammography.[13]

In cervical cancer, lower rates of cancer-related death and invasive cancer have also been shown with screening.[14]

In colorectal cancer, great strides have been made in reducing both the incidence of and mortality from this disease over the past 30 years through fecal occult blood testing. Early detection shifts the 5-year survival rate—14% for late-stage cancer—to over 90%.[15] Colorectal cancer screening has also been shown to be cost-effective, with savings in excess of $30,000 per life-year gained from screening.[16]

Moreover, recent data from the Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) screening trial[17] demonstrated a 2-fold higher overall non-cancer-related mortality rate in participants who did not adhere to screening compared with those who were fully adherent to all sex-specific PLCO screening tests when adjusted for age, sex, and ethnicity. Although a possible explanation is that people who adhere to screening recommendations are also likely to have a healthier lifestyle overall, the association persisted (although it was slightly attenuated) even after adjusting for medical risk and behavioral factors.

ON THIS WE CAN AGREE

Like Kim et al, we also believe an informed discussion of screening should occur with each patient—and challenge Kim et al to design an efficient and practical approach to allow providers to do so in a busy office visit aimed to address and manage other competing diseases.

In addition, medical science needs to improve. Methods to increase the efficacy of screening and decrease risks should be explored; these include improving test and operator performance, reducing nonadherence to screening, investigating novel biomarkers or precursors of cancer and pathways that escape current detection, and devising better risk-stratification tools.

Bodies such as the USPSTF should use models that account for factors not considered previously but important when informing patients of potential benefits and harm. Examples include varying sensitivities and specificities at different rounds of testing and accounting for the variability in risk or efficacy affected by race, ethnicity, sex, and patient preferences.

We practice in the era of evidence-based medicine. Guidelines and recommendations are based on the available evidence. As more studies are published, disease mechanisms are better understood, and the effects of previous recommendations are evaluated, cancer screening programs will be further refined or replaced. The balance between benefit and harm will be further delineated.

Kim et al knocked on the door of personalized medicine, where individual screening will be based on individual risk. Until that door is opened, screening should be personalized through the risk-benefit discussions we have with our patients. Ultimately, the choice to undergo screening is the patient's. ■

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