

Early Diagnosis, Overdiagnosis, Prevention and Patient (Mis)Perceptions

Avram M Cooperman*

Emeritus Surgeon, The Pancreas and Biliary Center, NY, USA

***Corresponding Author:** Avram M Cooperman, Emeritus Surgeon, The Pancreas and Biliary Center, NY, USA.

Received: October 06, 2021; **Published:** December 31, 2021

Abstract

Screening to detect occult lesions is an integral part of health care and annual exams. The goal is to detect the common malignancies at a curable stage. Absent symptoms, a number of imaging and laboratory tests including chest x-rays, mammography, colonoscopy, ultrasound are routinely done. The yield is small and the downside risks are false positive, false negative and overdiagnosis- the detection of cancers in name only. These are discussed for breast, prostate and thyroid lesions. Prevention through lifestyle could do much to limit or prevent these diseases and issues.

Keywords: *Diagnosis; Overdiagnosis; Prevention*

Introduction

The widespread use of surgery, medicine, radiology, and laboratory procedures, facilitate the diagnosis and treatment of occult lesions. This is important for families at genetic risk (5 - 10%) as well as the 90% of the population who develop sporadic or non familial cancers. The hopes of screening are earlier diagnosis. For most tumors there is a long latent period, years to decades, between tumor onset and detection, an asymptomatic period during which microscopic metastases may occur. This review will examine the benefits and flaws of early diagnosis/screening and contrast them with prevention.

Patient understandings and (mis)perceptions

The most common cancers are screened. They include breast, lung, prostate, and colon which combined lag behind heart disease in incidence. They have been joined by renal and thyroid cancer and melanoma. Screening seeks to find and cure occult lesions. Autopsy studies show 40 - 50% of men and women, age 40 - 50 have foci of microscopic pancreatic and breast cancer and 96% have foci of thyroid cancer. These are microscopic and most will never progress to clinical cancers. Early detection is a relative term. The evolution from induction to diagnosed breast cancer is lengthy, 24 years with screening and 25 years without screening. Early detection is primarily by imaging, supported by serum markers. Screens are lauded by the public because they are safe, relatively painless, quick and most often negative for tumors! Less understood and appreciated are the down sides of screening; false negatives, false positives, and over-diagnosis detected indolent lesions that are harmless, do not kill, spread or need treatment. An estimated 4 billion dollars are spent annually because of these three mammogram risks.

Behavior of cancer is tumor and host specific. An intact immune system combats cancer. Some cancers i.e. lung, brain, and pancreas inherently have a poor survival. Additionally, patient expectations and misconceptions of screening far exceed reality. Responders to screening surveys greatly overestimate its benefits; 90% overestimate the benefits of breast cancer screening, 94% overestimate the benefits of

bowel screening, 82% overestimate the benefits of medication to prevent hip fractures; and 69% overestimate preventive medicine for heart disease. A review of 32 studies and 27,323 patients, indicated at least 2/3 overestimate benefit, and underestimate the harms of screening. The number of incidents prevented per 5000 patients screened annually for 10 years (50,000 screens) are few; 2 - 15 breast cancers, 5 - 10 colon cancers, 75 - 85 cardiovascular events and 50 hip fractures. Overestimation of the benefits of antihypertensive and lipid lowering medicines are also ingrained.

Mammography

Mammography was heralded as a breakthrough to diagnose and cure non palpable early stage breast cancers and lower mortality from breast cancer. After mammography was introduced in the 1970's the proportion of small breast tumors (< 2 cm) increased from 36 - 68% and invasive tumors (> 2 cm) decreased from 64% to 32%. The change was almost all from an increase in small tumors. The mortality rate for breast cancer decreased 50%, but the decline was due to better therapy, both anti estrogen and chemotherapy, not earlier diagnosis. Time has taught that most mammographic detected cancers have more favorable features and a better prognosis than newly palpated or "interval tumors", aggressive lesions that present between exams. Another questioned long standing tradition, is teaching breast self-examination. This is no longer advocated as women who self discover breast lesions naturally note fewer lesions and less anxiety. The theoretical benefit of mammography, finding "early" asymptomatic cancers is the main reason women adhere to annual or "recommended" mammography guidelines which are continually questioned and changing. The traditional annual exam in the US is a custom with diminishing support as evidence supports biennial, triennial or "not at all" mammography, the standards in much of the world. The benefits of mammography are emphasized while three pitfalls: false positive, false negative and overdiagnosis are less appreciated. Overdiagnosis is the detection and treatment of lesions that will not spread, kill or need treatment. These lesions are found by screening and create confusion about treatment and intervals between mammograms. There are disagreements amongst the 4 agencies that make screening recommendations that are hopefully based on the "best" available data and not organizational, lobby and economic interests. The most independent of the 4 is The US Preventive Services Task Force (USPTF) who in 2009 to the chagrin of others advised mammography beginning at age 50 and be done every 2 years. This was based on evidence alone. It has not changed the annual custom that starts at age 40 for many. False positive and negative findings range from 10 - 20+%, and increases with length of follow up and number of screens. The harms of screening have been assessed and in multimodal cancer screening programs as the Prostate, Lung, Colorectal and Ovarian Cancer randomized control trial. 68,436 received screens for 5 cancers using prostate specific antigen (PSA), digital rectal exam, transvaginal sonogram, Ca 125, chest x ray, and flexible sigmoidoscopy. The tests were done within 24 hours, and the cumulative probability of a false positive test was 37% for men and 26% for women. After 3 years (14 tests) the probability rose to 60% for men and 49% for women. Because of a false positive finding 29% of men and 22% of women underwent an invasive procedure.

Overdiagnosis is estimated by clinical studies or by modeling, and mathematical probability. An estimated 11,000 Australian women and 18,000 men are over diagnosed annually. The harms of over diagnosis are a major concern since by definition no benefit is derived from an intervention. An important 25 year study of nearly 90,000 women age 40 - 59 years included randomization to annual exam and mammography or annual exam alone. The all cause mortality, incidence, survival and follow-up of breast cancers, were similar in both groups. Screening detected many small non palpable lesions half of which were over diagnosed. One in five mammogram cancers were over diagnosed. This very important study gives pause to several issues. Those who have strong beliefs in the value, timing, necessity and benefits of annual mammography, now have less firm ground to stand upon. The European mammography guidelines vary with each country but are more often every 2-3 years or longer depending on age. With the Covid pandemic, screening has been on hold in several countries. As the adage goes "Those who have enthusiasm have no controls and those who have controls have no enthusiasm." The guidelines for mammography in the US need further refinement.

Prostate cancer

Prostate cancer is widely present and over diagnosed. The lifetime risk of clinical prostate cancer is 17% and the mortality 3%. The incidence to mortality ratio of 6:1 affirms that most die with and not from prostate cancer. More than 2 million asymptomatic men live with prostate cancer in the US. Autopsy studies of 60 - 79 year old U.S. men reveal a prevalence of 68 - 77%. In Europe the autopsy incidence is less (14 - 30%) and in Asian countries, pre western lifestyle, it was even less common. The long latent period is supported by incidental autopsy findings of foci of cancer in young men. The diagnosis is suggested by an elevated Prostate Specific Antigen (PSA) and confirmed by biopsy. To prevent 1 death from prostate cancer 1400 men, need be screened and 48 treated. Welch and Black estimated that 60% of screen detected prostate cancers were over diagnosed. Mortality is dependent on tumor aggressiveness, frequency of surveillance and length of followup. In clinically detected disease the 10 year mortality was 9.1% for moderately differentiated cancer and 25.6% for poorly differentiated disease. Trials have compared watchful waiting, radical prostatectomy and radiation therapy. Outcomes are more dependent on tumor pathology than treatment, the percent of over diagnosed and early stage cancers, the frequency of followup, and patients age at diagnosis. The 10 - 23 year survival difference between watchful waiting, radiation or radical prostatectomy ranged from zero to 2.9 years. Patients with extra capsular invasion and high Gleason score do the poorest. When observed patients fare as well as treated patients at 10 or more years most lesions were likely over diagnosed.

The treatment modalities for prostate cancer are, surgery, radiation (including proton beam) and recently high intensity frequency ultrasound (HIFU). The direct side effects affect the bladder, rectum and sexual function and cause physical and emotional issues. Many indolent prostate tumors are treated because of an uncertainty of future behavior. This is more so in the US than Europe where watchful waiting is common. It is important to limit the many who are over treated by differentiating over diagnosed from aggressive lesions. Additionally, a healthy lifestyle emphasizing a whole food plant based diet can arrest and reverse early prostate cancer. In a controlled trial by Ornish., *et al.* 93 volunteers were randomized to a control or healthy lifestyle (plant based diet, 30" walk 6 days a week and meditation.) At one year the PSA level increased 6% in the controls and 10% had a radical prostatectomy, while in treated patients the PSA fell 4% and none required treatment.

Thyroid cancer

Thyroid cancer has increased annually since the 1970s. It accounts for 2% of all cancers, and more than 50,000 new cases/yr. The incidence is greater in women (20.0 cases/100,000) than men (6.3 cases/100,000). The 25 year survival for < 2m localized papillary cancer is 98%. The increased incidence of small papillary cancer reflects over diagnosis due to the increase use of sonography, CT, and MRI of the chest and neck. Most detected lesions are < 1 cm. Lim., *et al.* have suggested that mortality for thyroid cancer between 1994 - 2013 has increased. Obesity, and environmental pollutants are raised, unsubstantiated factors. Genetic markers BRAF, RAS, and TERT alone may not influence outcome but in combination may indicate a more aggressive tumor with higher mortality. The most likely and obvious cause of over diagnosis is over screening. The US Preventive Services Task Force holds there is insufficient data to support thyroid screening. They cite 3 reasons: rarity of thyroid cancer, no change in mortality over time and similar outcomes in treated and untreated patients.

Over diagnosis and over treatment of thyroid nodules are pandemic. A large increase in incidence (10%F 8%M) and operations (17%F, 15%M) for papillary thyroid cancer in Switzerland and the decline in mortality (3%F, 2%M) suggest over diagnosis and over treatment. This parallels the 31% increase in thyroidectomy between 2006-2011 in the United States, which is less than Korea. Finally, the increase in total thyroidectomy for microscopic papillary cancer is not justified. The large National Cancer Database (61,775 patients) and Surveillance Epidemiology, and End Results similar survival rates after total thyroidectomy and lobectomy and very low recurrence rates with each. The inherent complications of total thyroidectomy, voice and endocrine dysfunction from laryngeal nerve injuries and hypoparathyroidism are hopefully few. Increasing active surveillance and delaying screening and biopsy would do much to lower the rising incidence, over diagnosis and treatment of small papillary thyroid cancers.

Prevention of cause

Cancer is linked to genetic and cellular mutations. This happens over 10 - 20 or more years. While genetics is blamed for many illnesses, an unhealthy lifestyle is the more likely cause. The main cause is chronic inflammation, most often initiated by a poor diet. Four chronic diseases account for 80% of deaths in the Western world; cardiovascular (including stroke, hypertension,) cancer, obesity (and metabolic syndrome) and diabetes. Nearly all are lifestyle related. 30 - 70+% of cancer is caused or influenced by an unhealthy lifestyle. Asians who migrate to the United States and adapt a western lifestyle have a 25X higher incidence of prostate and 10X higher incidence of breast cancer. Monozygotic twins who share genes do not share the 85 - 90% of cancers that develop in one twin. As early as 1907 the NYTimes noted meat eating immigrants in Chicago developed an uncommon disease, cancer, which spared immigrant vegetarians. The evidence is unequivocal and worldwide that a plant based lifestyle can prevent, arrest, and reverse chronic diseases including cancer. To cite a few other benefits It lengthens life, reverses cardiac disease, autoimmune diseases, arthritis, obesity and inflammatory bowel disease, helps climate change and limits animal slaughter.

Prevention addresses the underlying cause and multicentricity of breast, prostate, thyroid and other cancers. Rather than trying to find the elusive needle in 1 or more haystacks and be concerned about over diagnosis it makes more sense to prevent the lesion. A 1 cm tumor, the smallest detected lesion has 100 million cells reflecting years or decades of growth. In the US the effective marketing of food and dairy, meat, fish, processed foods and sugar laden drinks encourage the initiation and progression of disease. Screening and early detection are useful and should support rather than surpass prevention and its lifestyle causes factor for many malignancies.

Conclusion

As imaging and laboratory tests become more advanced they detect smaller lesions many of which are benign, innocuous and preclinical cancers. The detection of lesions by screening is lauded because it detects earlier stage, more curable lesions. The downside risks are false positives, false negatives and over diagnosis. Periodic examinations to detect curable breast, prostate and thyroid lesions have been valuable, but overdiagnosed overtreated lesions cause harm, expense and emotional distress. Little attention is paid to prevent these issues and less about prevention. The cause of most illness is chronic inflammation negated primarily by lifestyle and a whole food plant based diet. Adopting a plant based lifestyle could do much to decrease chronic illness, including cancer by lowering the incidence of precursor and early lesions and perhaps limit the need and flaws of screening.

Bibliography

1. Wardle J., *et al.* "Screening for Prevention and Early Diagnosis of Cancer". *The American Psychological* (2015): 119-132.
2. Croswell JM., *et al.* "Cumulative incidence of false positive results in repeated multimodal cancer screening". *Annals of Family Medicine* 7.3 (2009) 2012- 2022.
3. Cooperman AM., *et al.* "Prevention and early detection of Pancreatic Cancer". *Sur. Clin No America* 98 (2018): 1-12.
4. Hruban R., *et al.* "Pathology of incipient cancer". *Annals of Oncology* 10 (1999): 9-11.
5. Greger M. "90% of women appear misinformed about mammograms Nutrition (2021).
6. Greger M. "Do mammograms save lives?" *Nutrition* (2018).
7. Sohn E. "Screening; Don't look now". *Nature* 527 (2015): 3118-3119.
8. Jergensen G. "Screening for Breast Cancer with Mammography". *Cochran Database Systemic Review* 5 (2015): CD001877.
9. Gigerenzer G. "Breast Cancer Pamphlets Mislead Women" *BMJ* 348.

10. Getzsche PC. "Mammography Screening is Harmful and Should be Abandoned". *Journal of the Royal Society of Medicine* 108.9 (2015): 34-35.
11. Hodis CA. "Biology before anatomy in early breast cancer- precisely the point". *The New England Journal of Medicine* 373 (2015): 2079-2080.
12. Bleyer A and Welch HG. "Effect of three Decades of Screening Mammography on Breast Cancer Incidence". *The New England Journal of Medicine* 367 (2012): 1998-2005.
13. Lannin DR. "Effect of Screening Mammography on breast cancer Incidence". *The New England Journal of Medicine* 368 (2013): 678.
14. Hoffman RM., et al. "Decision Making Process for Breast, Colorectal and Prostate Cancer1 screening. The Decisions survey". *Medical Decision Making* (2010): 534-545.
15. Ong MS and Mandl KD. "Natl Expenitures for False positive Mammograms and Breast Cancer". *Health Affairs* 34.4 (2015): 576-583.
16. Loberg M. "Lousdal Bretthauer egal Benefits and Harms of Mammography Screening". *Breast Cancer Research* 17 (2015): 63.
17. GotschePC and Jorggensen KJ. "Screening for Breast Cancer with Mammography". *Cochrane Database of Systematic Reviews* (2013): 6CDO.
18. Siu AL. "Screening for Breast Cancer USPTS Recommendations". *Annals of Internal Medicine* 164 (2016): 279-296.
19. Hersch J., et al. "Use of a decision aid including information on over detection yo support informed choice about breast cancer screening: a randomized control trial". *Lancet* 385 (9978): 1642-1652.
20. Hudson B., et al. "Patients Expectations of Screening and Preventive Treatments". *Annals of Family Medicine* 10.6 (2012): 495-502.
21. SEER Stat Database (1975-2012) Bethesda Md. National Cancer Institute Surveillance Research Program (2015).
22. Steineck G., et al. "Quality of Life after radical prostatectomy or watchful waiting". *The New England Journal of Medicine* 347 (2002): 790-796.
23. Bill-Axelson A., et al. "Radical Prostatectomy or Watchful Waiting in Prostate Cancer - 29 year Follow up". *The New England Journal of Medicine* 379.24 (2018): 2319-2327.
24. Welch HG and Albertson PC. "Reconsidering Prostate Cancertality- The Future of PSA Screening". *The New England Journal of Medicine* (2020): 1557-1563.
25. Schroder FH., et al. "Screening and prostate cancer; results of the European Randomized Study of Screening for Prostate Cancr(ER-SPC) at 13 years of follow up". *Lancet* 384 (2014): 2027-2035.
26. Pinsky PF., et al. "Extended mortality results for prostate cancer screening in the PLCO trial with median follow up of 15 years". *Cancer* 123 (2017): 592.
27. Wilt TJ., et al. "Radical prostatectomy versus observation for localized prostatic cancer". *The New England Journal of Medicine* (2012): 203-213.
28. Weich HG., et al. "Trends in metastatic breast and prostate cancer lessons in cancer dynamics". *The New England Journal of Medicine* 373 (2015): 1085-1087.
29. Hamdy FC., et al. "10 year outcomes after monitoring surgery, or radiotherapy for localized prostate cancer". *The New England Journal of Medicine* 375 (2016): 1415-1424.

30. Johansson E., *et al.* "Quality of life after radical prostatectomy or watchful waiting with or without androgen deprivation therapy: the SPCG=4 randomized trial". *Urology, Medical Oncology* 1 (2018): 134-142.
31. Welch HG and Doherty GM. "Saving Thyroids- Overtreatment of Small Papillary Cancers". *The New England Journal of Medicine* 379.4 (2018): 310-312.
32. Tuttle RM., *et al.* "Natural history and tumor volume kinetics of papillary thyroid cancers during active surveillance". *JAMA Otolaryngology – Head and Neck Surgery* 143 (2017): 1015-1020.
33. Adam MA., *et al.* "Extent of Surgery for Papillary Thyroid Cancer is not associated with Survival An Analysis of 61,775 Patients". *Annals of Surgery* 260.4 (2014): 601-607.
34. Davies L and Welch HG. "Thyroid cancer survival in the United States: observational data from 1973-2005". *JAMA Otolaryngology Head and Neck Surgery* 136 (2010): 440-444.
35. Woloshin S Schwartz. "Numbers Needed to Decide". *Journal of the National Cancer Institute* 101.17 (2009): 1163-1165.

Volume 9 Issue 1 January 2022

©All rights reserved by Avram M Cooperman.