Cancer Screening : What, When and How?

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INTRODUCTION

Prevention is better than cure was repeatedly hammered into our heads during our medical school days and its importance cannot be overemphasized. However, not every disease is preventable. Screening provides us with the second best option of catching them early. Although there are various definitions for screening it can be summed up simply as detecting disease early in asymptomatic individuals.

PRE-REQUISITES

1. The disease in question must be a fairly common health problem in the given population.
2. Cost effective investigations having high accuracy (sensitivity and specificity) to detect the disease in asymptomatic stage should be available.
3. Evidence must be available that treatment initiated earlier as a consequence of screening results in an improved outcome.

Even if above pre-requisites are met, it may not necessarily prove the efficacy of screening, which is provided by reduction in cause-specific mortality.

BENEFITS, HARMS AND BIASES IN SCREENING

Screening also has its share of pros and cons. It is estimated to reduce mortality by 3-35% depending on various assumptions, cervical cancer being an excellent example (1). As a result of early diagnosis, treatment is usually less mutilating thereby decreasing the morbidity and improving quality of life.

However, potentially harmful effects must be kept in mind while recommending screening tools for an individual (2). Some of the screening tests are either invasive themselves (e.g. colonoscopy) or may result in invasive procedures if found to be abnormal (e.g. abnormal mammogram leading to biopsy which may finally reveal a benign lesion). A false positive result may cause undue anxiety and unnecessary invasive investigations. On the contrary, a false negative result may reassure the person who may ignore future symptoms thus losing precious time in getting timely diagnosis and effective treatment. As the sensitivity of screening tools increases, it leads to discovery of very small lesions of doubtful clinical significance that might never become clinically apparent in lifetime of the individual as has been shown by several autopsy studies.

Sources of bias (3) are of particular importance while evaluating a screening programme. Lead-time bias is the interval between diagnosis of disease at screening and when it would have been detected due to development of symptoms. If this is not taken into consideration, screening would show increase in survival erroneously. Length-time bias is overrepresentation among screen-detected cases of those with a long preclinical period (thus less rapidly fatal), leading to the incorrect conslusion that screening was beneficial. Volunteer bias is introduced because those who choose to participate in screening programmes (volunteers) are likely to be more health conscious as compared to general population.

Other problems include the strength of data available to recommend screening for a particular cancer, whether the mortality reduction reported is disease specific or all-cause mortality and the development of interval cancers (i.e. cancers detected due to development of symptoms in between two screenings).

WHICH CANCERS TO SCREEN FOR?

Screening proven to be beneficial

- ❑ Breast cancer
- ❑ Cervical cancer
- ❑ Colorectal cancer

Screening not proven to be beneficial

- ❑ Lung cancer
- ❑ Ovarian cancer
- ❑ Testicular cancer
- ❑ Prostate cancer

Screening beneficial is high risk region or population

- ❑ Hepatocellular cancer
- ❑ Oral cancer
- ❑ Esophageal and Gastric cancers
- ❑ Endometrial cancer

BREAST CANCER

Breast cancer incidence is on the rise and has taken over cervical cancer as the most common cancer affecting women in metropolitan areas of India. Mammography has been shown in several randomized trials (4,5) and a meta-analysis (6) to reduce mortality from breast cancer in women between 40 and 65-70 years of age. Figure 1 shows mammographic appearance of a breast cancer. Clinical breast examination also reduces mortality. Although breast self examination was not found to be beneficial in a very large study from Shanghai, China (7), it's the cheapest and easiest method of screening for breast cancer and women should be taught and encouraged to practice this periodically.

Following are the recommendations according to the risk of breast cancer development.

Normal Risk women

- ❑ Mammogram every 1-2 years after the age of 40
- ❑ Clinical Breast Examination – 1-3 yearly between 20 – 40 years and annually for those above forty years of age.
- ❑ Breast self examination periodically after the age of 20 years

High Risk Women

- ❑ Thoracic radiation
- ❑ Strong family history or genetic predisposition
- ❑ Personal history of breast cancer

- LCIS (lobular carcinoma in situ) / DCIS (ductal carcinoma in situ) / Atypical hyperplasia

Five year risk of having breast cancer more than 1.7% according to modified Gail model in women aged 35 years or more (for Gail model see www.nci.nih.gov).

This group of higher risk women would require more frequent and intense screening measures. Breast MRI is recommended as an adjunct to mammogram in selected high risk women. Certain group of high risk women would also benefit from risk reduction strategies in form of prophylactic use of Tamoxifen, Raloxifene or even bilateral mastectomy with or without immediate reconstruction.

CERVICAL CANCER

It is the commonest cancer affecting Indian women, particularly in rural India and can be detected at a precancerous stage with available screening methods, a stage at which the cure rate is 100 percent.

How to screen?

- Pelvic examination every 3 years
- Pap smear every 3 years (8) (reported in accordance with Bethesda guidelines)
- In March 2003, FDA has approved incorporation of HPV DNA testing in conjunction with pap test for screening women 30 years or older.

An abnormal pap test must be followed by a specialist referral for further investigation and therapy.

When to start screening?

It should begin approximately 3 years after the onset of vaginal intercourse and no later than 21 years of age. Adolescents who do not need screening must be counselled regarding preventive aspects and about sexually transmitted diseases.

When to discontinue Screening ?

1. Women at age 70 years and older with an intact cervix who have had three or more documented, consecutive, technically satisfactory normal / negative cervical cytology test and no abnormal / positive test, within the 10 year period prior to age 70 may choose to cease cervical cancer screening.

2. Those who have had a total hysterectomy

There are certain exceptions to above two categories. Women who are HIV or HPV positive, who had hysterectomy for cervical cancer or Cervical intraepithelial neoplasia (CIN) I / II, and those with a history of in-utero exposure of diethylstilbesterol (DES)

3. Women with co-morbid, life threatening medical conditions.

Alternative Screening and Treatment Strategies in Low-Resource Settings

Choice in methods of screening for cervical cancer in resource-limited countries or underserved populations has prompted the evaluation of one-time "screen and treat" approaches for cervical cancer screening. A clustered randomized controlled trial evaluating a one-time screening with either visual inspection with acetic acid (VIA), cytology, or human papillomavirus (HPV) screening versus a control education arm is under way in a rural region of India (9).

COLORECTAL CANCER

The screening recommendations for individuals vary according to the risk category (10).

Average / Normal risk individuals

Fifty years or older with no history of adenoma, inflammatory bowel disease and no family or personal history of colorectal or HNPCC (hereditary non-polyposis colorectal cancer) related cancers belong to this category. Such population is adviced to undergo one of the following as screening

1. Colonoscopy every 10 years.
2. Annual Faecal occult blood test (FOBT) and 5 yearly sigmoidoscopy.
3. Double contrast barium enema every 5 years.

Increased risk

1. Personal history of adenoma, colorectal carcinoma, endometrial or ovarian carcinoma at age less than 60 years, inflammatory bowel disease.
2. Family history of first degree relative with colorectal carcinoma or two first degree relatives (related to each other) with colorectal carcinoma

Hereditary high risk

1. Colorectal cancer in a first degree relative less than 50 years of age
2. Clustering of colorectal or HNPCC related cancers in the family
3. Personal or family history of polyposis,
4. HNPCC

Those with increased risk need more frequent and intensive screening. Individuals with history of early onset colorectal cancers in family or history suggestive of hereditary risk should be interviewed to obtain detailed family history, their medical history, subjected to appropriate examination to rule out related cancers and adviced genetic counselling.

ORAL CANCER

This is the commonest cancer affecting men of our country as a result of use of chewable tobacco in various forms. Although the studies done in India (11) and Sri Lanka (12) (involving over 250,000 subjects) have shown that it is possible for primary health care workers to detect pre-malignant lesions and early cancers in these populations at high risk due to habits of tobacco and betel nut chewing and reverse smoking, they were marred by a poor compliance. Contradictory oral cancer screening recommendations have been issued by the US Preventive Health Services Task Force (against) and the American Dental Association (for). In our country, it would be prudent to screen high risk individuals by periodic oral examination and specialist referral for abnormal findings. Such individuals must be encouraged to quit tobacco / alcohol and for regular self as well as clinical examination at each contact with medical personnel.

HEPATOCELLULAR CARCINOMA (HCC)

Screening, if at all, is useful only for the high-risk individuals (hepatitis B, C and cirrhotics). A randomised controlled trial involving more than 18000 hepatitis B positive

subjects from Shanghai (13) screened by 6 monthly alfa-feto protein (AFP) and ultrasound versus the usual care demonstrated decreased mortality from HCC.

OTHER CANCERS

The lifetime risk of endometrial cancer for women who meet the criteria for hereditary nonpolyposis colorectal cancer (HNPCC) or are at high risk for HNPCC is up to 60%. The recent American Cancer Society Cancer Detection Guidelines (updated January 2005) recommend annual screening with endometrial biopsy beginning at age 35 (14).

Screening for lung cancer has not been found to be effective. Nonetheless, based on a feasibility study (15), the National Cancer Institute (NCI) is conducting a randomized controlled trial designed to determine whether annual screening with low dose spiral CT versus chest x-rays can reduce lung cancer mortality among persons at increased risk.

There are ongoing trials by NCI (16) and in Europe (17) to study the role of screening in prostate cancer using digital rectal examination (DRE) and PSA estimation. Until the results are known, men who are keen to undergo screening must be informed about the possibility of false-positive or false-negative test results and that there is no consensus regarding the usefulness of such screening.

Long standing gastroesophageal reflux disease (GERD) leads to varying degree of dysplasia and frank malignancy. This has accounted for a rise in incidence of adenocarcinoma of the GE junction. However, the surveillance for such patients, though widely practiced, is based on uncontrolled studies or on recommendations of the experts in the field (18)

CONCLUSION

Screening is an effective tool to diagnose cancers at a pre-clinical stage thereby providing an opportunity to attain high cure rates by using less aggressive treatment options thus improving the quality of life as well. Notwithstanding the utility of screening, we must weigh the benefits and risks carefully before recommending it for an individual.

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Useful websites

www.nci.nih.gov, www.nccn.org

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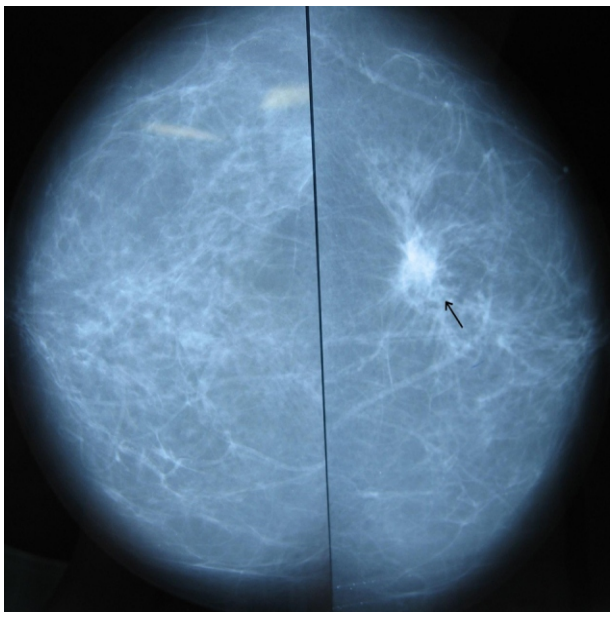

Figure 1. Mass lesion with spiculated margins typical of a cancer in the left breast (arrow) as seen on mammogram