Cancer Screening

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Cancer is a fast growing health problem in India with an estimated 11.5 million new cases each year. Screening is an effective method of early detection of some premalignant conditions and cancers; leading to prompt treatment and improved survival.

Concept of cancer screening

Screening involves testing of normal asymptomatic individuals for hidden medical conditions. So the concept of screening is for the early diagnosis and treatment of diseases (secondary prevention) as opposed to their prevention (primary prevention). Screening for medical conditions is a common practice; some examples being screening of blood donors for HIV or Hepatitis B and screening of pregnant women for gestational diabetes mellitus. Cancer screening differs from the above example is that usually the results of a cancer screening test are not definitive for the presence or absence of cancer, but often require further testing like a biopsy to conclusively diagnose cancer. So as an example a mammogram might reveal a suspicious breast abnormality but to prove that it is a breast cancer, a tissue sampling, usually a biopsy is required. The individuals undergoing cancer screening need to be counselled regarding the need for further testing in case of a positive test.

Only a minority of cancers like breast, cervix, colon, prostate and lung have approved screening modalities. There is no universal screening test for cancer and the techniques differ for each particular cancer; from imaging in breast (mammogram) to a blood test (PSA in prostate). The yield of cancer screening also depends on the general prevalence of that cancer; unplanned screening for rare cancers is seldom useful. Breast, cervix and oral cancers constitute a significant proportion of cancer cases in the country and are amenable to screening. Last but not the least, two important considerations in cancer screening are an individual's risk and financial resources. Screening guidelines usually are formulated for populations at average risk but individuals having higher risk of cancers may require a personalised approach. For instance, young women having genetic abnormalities like BRCA mutations might benefit from MRI breast screening.

Breast cancer screening

Breast cancer is the most common cancer in Indian women and it has been on the rise in both the urban and rural cancer registries in India since 1990.

Mammography is the cornerstone of breast cancer screening. It uses low dose X-rays to study the breast anatomy. In its most basic form it involves the compression of each breast in between two X-ray plates and two views - mediolateral

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oblique and craniocaudal view are taken. It can reveal various pathologies of the breast including cancer. Breast cancer may be visualised as a mass with irregular margin distorting the normal architecture of the breast. It may be associated with small calcifications called microcalcifications. The mammograms are interpreted by a trained radiologist and the mammogram is reported in the form of a BIRADS category.[1] BIRADS refers to breast imaging reporting and data system and classifies the mammogram into categories from 0 to 6 ; the more the score the more is the probability of the lesion being cancerous. Score 6 refers to pathologically proven malignancy. The patients having lesions with BIRADS 4 or BIRADS 5 are recommended to undergo a biopsy for definitively proving the presence or absence of malignancy.

Mammograms have been shown to decrease the mortality associated with breast cancer by 20%.[2] They have the ability to detect breast cancer around 2 to 3 years before a lump becomes palpable. Screening mammograms have a reported sensitivity of 64% to 90% and specificity of 82% to 93 %. They can miss up to 10-20 % of cancers and it cannot be emphasised more that any post-menopausal female with a breast lump needs a biopsy irrespective of a mammogram report. Other than minor breast discomfort mammograms are well tolerated. The advent of modern mammography machines has ensured good quality images with very limited radiation exposure; the hazard associated with radiation during periodic screening mammograms is small.[3]

The age at which to start screening has been subject to controversy. The earliest age when routine screening mammography can be offered is 40 years. The sensitivity of mammograms also improves with age as the fat content of the breast increases and the glandular tissue involutes. Earlier the western guidelines almost universally recommended annual screening mammograms in all females starting from the age of 40 years. But due to the increasing recognition of unnecessary breast biopsies in a significant proportion of patients, the age at which to start screening has been pushed forward to 50 years in many guidelines like the United States Preventive Task Force and the UK guidelines.[4,5] The World Health organisation also recommends starting screening at age 50 with an interval of 2 years till the age of 69 years which may be extended to 75 years with shared decision making between the doctor and the patient. In India, there is a suggestion in some studies that the median age of breast cancer diagnosis is a decade earlier than that of the west and the breast cancer incidence peaks below the age of 50 years. So it may be prudent to discuss screening from the age of 40 years for affording patients which includes shared decision making about the benefits as well as harms of screening like false positive results. Ultrasound as an adjunct to

screening especially in younger women where dense glandular structures may obscure the cancer in mammography is still an experimental technique and is not recommended routinely.

Clinical breast examination by doctors or trained health care professionals is being recommended in the National Health progammes but the scientific data to suggest their routine use over mammography is lacking. Its sensitivity is much lower as compared to mammography; but it remains a valid option in resource limited settings and should be offered in patients not affording mammography.[6]

Self breast examination has not been shown to reduce breast cancer mortality but still should be encouraged not as a means of screening but as a means to foster breast awareness among females. Females beyond the age of 40 years may be encouraged to watch online educational videos demonstrating the procedure.

Patients who have a very high risk of breast cancer like those with deleterious BRCA mutations and past history of irradiation to the chest may be offered annual MRI from age 25 years as a means of screening.

Cervical Cancer screening

Cervical cancer is the second most common cancer in Indian women and even though the incidence is showing a declining trend ; it constitutes a significant cancer burden in females. Cervical cancer is caused by chronic infection by the Human Papilloma Virus (HPV) which is transmitted by sexual contact. The infection in some cases results in dysplastic changes in the cervical epithelial cells which transform into cervical intra epithelial neoplasia (CIN) which may transform into invasive cervical cancer. This evolution is slow and may take from 10 to 20 years. So, cervical cancer is amenable to screening and treatment of CIN may result in prevention of invasive cervical cancer. The techniques for cervical cancer screening included the cytology based tests like Papanicolau or Pap smear, HPV testing and visual inspection with acetic acid (VIA).

The most commonly performed test is the Pap smear wherein the cervical epithelial cells on a glass slide and examined by a trained pathologist to look for dysplastic changes. Modern techniques like liquid based cytology have improved the detection of cellular changes. HPV detection is usually performed by detecting the nucleic acid - either the DNA or RNA in samples collected from the cervix. Visual inspection with acetic acid involves applying 3-5% of acetic acid to the cervix and demarcating areas that turn white (the so- called acetowhite areas) as those harbouring HPV infected cells. This test is based on coagulation of abnormal proteins in the virus infected cells due to acetic acid and has the advantages of being easily applied at a community level in resource limited settings as well as facilitating treatment of lesions in the same sitting.

The age of starting screening is usually

25 to 30 years as below this age there is a rapid immunological clearance of HPV infection in case of infection. The screening is usually continued till age 65 years. Pap smear testing is usually performed every 3 years and HPV testing is done every 5 years. These tests may be combined and are referred to as Co testing. HPV detection has been shown to perform better in reducing cervical cancer mortality as compared to Pap testing and has the advantage of self-collection of specimens, but is more expensive. VIA is relevant in Indian setting and multiple large studies have demonstrated the efficacy in reducing cervical cancer mortality.[7] At least 1 to 3 tests in a women's lifetime should be the aim. Testing is not recommended for women undergoing hysterectomy for benign conditions. An important point to be noted is that screening is also advocated in females who have had HPV vaccination.

Oral cancer

Oral cancer is one of the most common cancers in both genders in India especially due to the use of smokeless tobacco and chewing of tobacco quid. Studies in India and Cuba have demonstrated that early detection of oral cancer is feasible by performing periodic clinical examinations. In India screening may be performed annually in age beyond 30 years in patients with well defined risk factors like smoking, tobacco chewing and alcohol use. Precancerous lesions like leucoplakia may be detected and treated. Various chemicals like toluidine blue have been used to detect precancerous lesions but none is recommended for routine use. Screening should also be accompanied by guidance on smoking cessation and tobacco and alcohol de addiction.

Other cancers

Colon cancer screening may be considered beyond the age of 50 years. The techniques used are high sensitivity faecal occult blood testing and sigmoidoscopy or colonoscopy. The frequency of repeating an occult blood testing is every year where as the frequency of repeating a colonoscopy if the initial result was normal is every ten years.

Prostate specific antigen (PSA) blood test may be offered beyond age 50 to men as a screening modality for prostate cancer. Routine PSA testing is highly controversial and involves a significant risk of over diagnosis and over treatment. An approach of shared decision making between the doctor and patient is recommended. Infections like prostatitis may cause transient elevations of PSA level.

Lung cancer screening with annual low radiation dose helical chest CT scans in high risk individuals are recommended in USA. In India due to high prevalence of tuberculosis such an approach is expected to reveal many incidental abnormalities on the chest CT leading to significant negative biopsies.

Pitfalls in cancer screening

Cancer screening is associated with risk of over diagnosis which means that it may diagnose small tumours which may

never lead to clinically relevant health consequences in the patient's life time. This is especially the case in certain cancers like prostate cancer. This in turn may lead to unnecessary diagnostic procedures - for example trans rectal USG guided biopsies and prostatectomies. This in turn leads to significant morbidity as well as expenditure. A meta-analysis has estimated that for every 1000 men screened, approximately 1, 3, and 25 more men would be hospitalised for sepsis, require pads for urinary incontinence, and report erectile dysfunction, respectively.[8] Also, no cancer test is 100 per cent sensitive and specific, so prior to the screening test the probability of false positives and false negatives needs to be discussed.

But in spite of these pit falls, cancer screening is definitely associated with reduced mortality in certain malignancies and should form a part of health related discussion between the primary health provider and the patient.

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Neoadjuvant Cancer Immunotherapy

Immunotherapies that are based on blocking the axis of the programmed death 1 (PD-1) pathway are having a transformational effect in cancer medicine.

Although this pilot study revealed important pharmacodynamic information, the sample size was small, and the rate of clinical benefit needs to be confirmed in a larger cohort. It is not yet known whether cancer recurrence will be prevented, whether recurrent tumours will retain responsiveness to PD-1 blockade, whether challenging recurrent tumours, and whether overall patient survival will be improved. Nonetheless, the observation that two doses of nivolumab could be administered without logistical delay of planned surgical resection will undoubtedly encourage additional studies of neoadjuvant immunotherapy in a range of tumour types. Planned phase 3 trials involving patients with non-small cell lung cancer (NSCLC) will ultimately determine whether recurrence-free and overall survival are improved, thus placing immunotherapy on the front line of cancer treatment.

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