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Editorial

Approaches for Early Detection and Intervention of Cancer

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Metastatic cancer remains incurable in almost all cases, despite of advancements in treatment modalities and technologies. Mortality and morbidity increases as the disease become incurable and patients receive palliative treatment. Here is the importance of early detection of cancers for improving survival outcome and quality of life. In addition to clinical evaluation; radiological imaging, cytopathological tests, biochemical and molecular analyses have expanded the scope of early detection of cancer. As early stage cancers are often symptomless or have vague symptoms, it is imperative to increase awareness amongst general population as well as health care providers working at different levels.

Primary prevention for cancers intends to reduce the incidence of cancer. It relies on improving awareness and educating the general population. The habits like smoking, tobacco chewing, alcohol, HPV (human papilloma virus) infection, which are established causes for cancer, can only be reduced, if people become aware about it. Early detection is the method of secondary prevention, where we intend to detect the disease before it causes any symptoms. This can only be achieved by screening asymptomatic population, who may or may not be at risk. Many factors (sensitivity, specificity, positive predictive value, negative predictive value, acceptability of the tests in the intended population, prevalence of particular cancer in that population, cost effectiveness, etc) are taken into consideration when a screening tool is designed for a particular cancer. At the same time a robust process to further investigate and provide timely treatment for those detected with abnormality during screening, must be in place. Follow up of those at high risk and frequency of follow up is equally important while designing the screening tool.

A major assumption about the natural history of carcinogenesis is based on the models of carcinogenesis of colorectal cancer proposed by Vogelstein., *et al* [1]. The model predicted a slow-growing, linear progression from a pre-cancer to a localized cancer that would occur at a rate of time that was amendable to cancer screening, similar to the pattern of carcinogenesis observed in cervical cancer. Cervical cancer screening represents an example of the use of an accurate screening test (PAP smear, colposcopy, HPV testing) with adequate sensitivity, specificity and positive and negative predictive value leading to the identification of a high risk population, a pre-cancer or a cancer. Similarly, colorectal cancer screening using colonoscopy has improved identification of precursor lesions and early cancers.

Breast cancer is the most common cancer in women worldwide [2]. Mammography screening has been shown to be associated with a reduction in breast cancer mortality across a range of study designs, with most studies demonstrating a significant benefit. American cancer society recommends that women with an average risk of breast cancer should undergo regular screening mammography starting at age 45 years [3]. Lung cancer is a leading cause of death amongst cancer patients with average 5 year survival of 16.8%. Large majority of patients are diagnosed with regional and distant metastsis [4]. Numerous studies have demonstrated that smoking cessation measurably reduces the risk of developing and dying from lung cancer compared with continuing smoking. Combination of chest x-ray and sputum cytology as screening tool has not proved to reduce mortality in lung cancer. In contrast use of low dose computed tomography as lung cancer screening has demonstrated considerably greater sensitivity in the detection of small pulmonary nodules. American cancer society recommends that clinicians with access to high-volume, high-quality lung cancer screening and treatment centers should initiate a discussion about screening with apparently healthy patients aged 55 years to 74 years who have at least a 30-pack-year smoking history and who currently smoke or have quit within the past 15 years [5]. Oral cancer and precancerous lesions (leukoplakia, erythroplakia), common among tobacco chewers, are screened with simple clinical examination with torch

light. This is quite inexpensive and acceptable to population in general. Brush cytology or biopsy can be employed to have confirmatory diagnosis, in those detected with abnormality.

Prostate specific antigen (PSA), a serum biomarker, is in routine use for screening of prostate cancer. Carcinoembryonic antigen (CEA) and cancer antigen 125 (CA-125) are other familiar molecular biomarkers that were found to be ineffective for screening, but are currently used for follow-up in patients with colorectal and ovarian cancer, respectively. CEA & CA- 125 lacks sensitivity and specificity for early detections of tumors as there levels are affected by many other neoplastic and non-neoplastic conditions [6,7]. New technologies for detecting circulating tumor cells, circulating cell free tumor DNA (CtDNA), microRNAs and long non-coding RNAs, tumor-derived exosomes, and tumor-educated platelets are expanding horizons for early detection [8].

However, there is risk to individuals when introducing screening interventions in otherwise healthy populations, which include over-diagnosis and overtreatment, anxiety associated with abnormal testing results, additional imaging tests and biopsy procedures associated with false-positive results. Over-diagnosis of indolent cancer, which would not have affected the survival, and morbidity and mortality associated with treatment of the same, is one the issues related to screening.

So, early detection through a well designed and implemented screening programme, with a robust process of follow up of at risk population and timely intervention for those detected with abnormality, would improve the survival outcome for cancer patients.

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