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Journal of Oncology and Cancer Screening

Open Access Mini Review

Diagnostic Images in Screening for Cancer (Citi Screen Experience)

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Article Info

Received: September 24, 2022
Accepted: October 25, 2022
Published: November 07, 2022

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Citation: B. Petrikovsky and M. Terrani. (2022) "Diagnostic Images in Screening for Cancer (Citi Screen Experience)", J Oncology and Cancer Screening, 4(3); DOI: http;//doi.org/010.2022/1.1061.

Abstract:

Introduction:

The ultimate goal of screening for cancer is its detection either as a precursor lesion or at an early stage when the disease is curable thus decreasing cancer mortality. The latter has decreased by 25% from 1990 to 2015 mostly for colorectal and breast cancers (47% and 39%, respectively), partially due to successful screening programs. [1-3]

The most successful cancer screening programs were based on the identification of precursor lesions (e.g., cervical intraepithelial neoplasia (CIN), with cervical cancer screening and colonic polyps with colorectal malignancy. This is based on the Vogelstein theory of carcinogenesis, based on the model of linear progression from pre cancer to a localized earlystage cancer, which allows ample time for early detection and management. [4]

In designing successful screening programs, the researchers rely on modified Wilson and Jungner principles which are: the natural history of each type of cancer, is known. [2]

The disease's natural history and slow progression allows time for screening and detection on a treatable stage. [5]

Human papillomavirus is the etiologic agent for cervical cancer. HPV infection leads to a precancerous lesion (cervical intraepithelial neoplasia) which can be detected by a positive cytology (Pap testing). The removal of the precancerous lesion led to a decrease in the cervical cancer rate. Cervical cancer screening represents an ideal example of the use of an accuratescreening test. [1, 3]

Screening for colon cancer also conforms to Wilson and Jungner principles and led to improvements in overall cancer survival. A main feature of cervical and colon cancers is the ability to directly access the tissue of interest which allows to apply an adequate screening modality. [1] However, screening, detection, and removal of precancer or early cancer in other cancer types has not always been as successful. [1-3] Thus, not all cancers are uniform in their biology and correspond to Vogelstein hypothesis. For example, not all breast ductal carcinomas and indolent prostate cancers progress to an invasive disease. Screening in such cases may cause overtreatment.

Thus, slow tumor progression allows for detection at an early stage or even at precursor stages, which allows for timely management with good outcomes. Cancer screening is less effective for some rapidly growing and aggressive forms of disease. Pre-screening counseling should address these issues to avoid overtreatment and unreasonable expectations.

Diagnostic Imaging in Cancer Screening:

All diagnostic modalities have the potential of cancer screening. Pelvic ultrasounds are used for endometrial and ovarian cancer screenings, thyroid ultrasounds for thyroid cancer, abdominal ultrasounds for lesions in the liver, spleen, and other abdominal organs. [6]

Total Body MRI (TB MRI):

There is increasing interest in using TB MRI to detect cancers in the general population, given the high sensitivity of the method that is free from ionizing radiation. [2] Peer review articles on the topic are very few and contain a limited number of patients. [7] Tarnoki et al [8] conducted a retrospective analysis of healthy adults (mainly managers, lawyers, accountants, chief executive officers, and company directors) with extreme health consciousness who underwent whole-body MRIs at the Institute of Diagnostic and Interventional Radiology, St. Theresia, Germany. These authors reported one malignancy out of 22 body scans. Accidental findings were multiple and required diagnostic workup by a urologist (17cases), rheumatologist (15 cases), internist (13 cases), otorhinolaryngologist (6 cases), pulmonologist (6 cases), surgeon (5 cases), gynecologist (4 cases), and dermatologist (1 case). Zugni et al (9) reported results of a meta-analysis on TB MRI for cancer screening in asymptomatic populations. TB MRI scanning protocols for cancer screening are similar to protocols for metastasis detection. Both T1 and T2 weighted images without fat suppression are required for the optimal examination. T1 weighted imaging can be performed using a GRE Dixon sequence, with fat-only and water-only images.

T2 weighted sequences without fat suppression are more suitable for oncological studies and are recommended for TB MRI cancer screening. [9] Researchers have avoided the use of contrast agent in general cancer screenings. The gadolinium deposition in body tissues represent further disincentives for its use for cancer screening. [10,11]

A per-finding analysis of TB MRI reported a total of 17,961: 91% of findings were non-relevant and 9% were oncologically relevant, requiring further investigation. [9]. A meta-analysis by Blanks et al. [11] showed a TB MRI detection rate of 7.59 per 1000 subjects (0.08%). [11] A meta-analysis by Ballinger et al. [12] in subjects with Li-Fraumeni syndrome reported a higher cancer detection rate (7%). The presence of risk factors and family history for cancer allows personalized stratification of the individual cancer risk.

The Citiscreen program allows for rational use of TB MRI based on cancer screening algorithms. [3, 13, 14] Zugni et al. [10] suggested that a classification should be introduced to assess the likelihood of malignancy. Category 1 and 2 corresponds to normal and benign findings and categories 3, 4, and 5 for findings with increasing oncological significance. [15].

Classification System for Findings Detected by TB MRI:

Category	Interpretation
1	Normal
2	Benign
3	Equivocal
4	Suspicious
5	Very suspicious

Category level 2 requires no follow-up, while categories 3 to 5 require further investigation. None of the research papers addressed the frequency of TB MRI follow up studies. Citiscreen program is the only screening project which addresses the recommendation of the TB MRI follow up examinations based on family history, genetic and tumor markers studies [3].

Who does cancer screening:

Currently, screening for malignancies is a responsibility of primary care physicians: general practitioners, gynecologists, family physicians, and pediatricians. Most of the recommendations on preventative medicine including cancer screening are based on the research data collected by epidemiologists and medical statisticians [15]. They introduced the concepts of overdiagnosis and using mortality as the screening outcome rather than detection of early-stage cancers [17].

Breast Cancer Screening Using Imaging Modality:

In the USA, Clinical Preventive Services recommended screening women 50-69 every 1-2 years. Mammography screening for women age 40-49 was allocated a C grade, (insufficient evidence existed to make a recommendation for or against screening). In 2002, they revised their recommendation to screening every 1-2 years for women age 40 or older, a B grade (net benefit of screening was considered moderate) [18, 19].

Lung Cancer Screening:

Currently, no lung cancer screening is recommended by the US Preventive Task Force, even for high-risk populations. Low-dose CT demonstrated its usefulness in non-randomized and single-arm studies. These studies found increased survival and early-stage detection [20,21]. The Dutch-Belgian NELSON trial became the first randomized clinical trial of low-dose CT with sufficient statistical power to detect a reduction in lung cancer mortality. The study was halted in 2010 after investigators reported a reduction of lung cancer-related mortality of 20% in the low-dose CT group when compared to the chest X-ray [22].

Endometrial Cancer Screening:

Diagnostic pelvic ultrasound remains the main modality in screening for uterine (endometrial cancer), based on the appearance and thickness of the endometrial lining of the uterus. A recent met analysis included 18 studies with over 10,000 participants [23]. At an endometrial thickness of 3.0cm, the risk for cancer was increased three-fold relative to women below the cut-off (relative risk (RR) 3.77, 95% confidence interval (Cl) 2.26 to 6.32). Similar risk were reported for endometrial thickness between 3.0 and 5.9 mm (RR 5.08, 95% Cl 2.26 to 11.41, 6.0 and 9.9 mm (RR 4.34, 95% Cl 1.68 to 11.23), 10.0 and 13.9 mm (RR 4.11, 95% Cl 1.55 to 10.87, and over 14.0 mm (RR 2.53, 95% Cl 1.04 to 6.16. Therefore, using a 3.0 to 5.9 mm cut-off results in lower specificity, the overall improvement in sensitivity may justify using this cut-off in patients with suspected endometrial malignancy. [6,23]

Summary:

Cancer screening protocols appear as complex as the disease itself and should include a combination of modalities rather than a

single one. Lately, patients' selection for screening have been improved due to the development of genetic tests of predisposition to a particular malignancy.

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