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Study of Principles of Cancer Screening and Early Detection

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Abstract

The current and potential biotechnological applications of cancer screening and early detections are reviewed. Image analysis systems have proven to be highly versatile and efficient tools for assisting academic biotechnological research.

It is expected that image analysis systems will allow more rapid and accurate quantification of numerous biotechnological analyses. There is, therefore, much scope for the implementation of image analysis/processing systems in a large variety of industrial and clinical applications.

Keywords: Cancer screening, sensitivity, specificity, screening recommendations, decision-making, early detection

INTRODUCTION

The goal of cancer screening and early detection is to cure cancer by detecting the malignancy, or its precursor lesion, at an early stage prior to the onset of symptoms, when treatment of cancer is most effective. Indeed, overall cancer mortality has decreased by 25% from 1990 to 2015 for the United States U.S.), with even greater declines in the mortality rates for colorectal cancer (47% among men and 44% among women) and, breast cancer (39% among women). A portion of this decrease can be attributed to the introduction of high-quality cancer screening for colorectal and breast cancer.1 The most successful cancer screening programs lead to the identification of precursor lesions (e.g., cervical intra-epithelial neoplasia (CIN) with cervical cancer screening and colonic polyps with colorectal cancer screening) where the treatment of the precursor lesion leads to a decrease in the incidence of invasive cancer over time. The guiding principles of screening for disease were proposed in 1968 by Wilson and Jungner2 of the World Health Organization (Table 1). Not all cancer screening recommendations meet each of these guiding principles; historically there has been a balance between the identification of early or precursor lesions and the avoidance of over diagnosis which may lead to overtreatment (Table 2).

Table 1

Wilson and Jungner Criteria for disease screening

1. The condition of screening should be an important health problem
2. There should be treatment for patients diagnosed with the disease
3. Facilities to diagnose and treat the disease should be available
4. There should be a recognizable latent or early symptomatic stage
5. A suitable test or examination should be available
6. The test should be acceptable to the population

7. The natural history of the condition should be adequately understood
8. There should be agreement in the policy of whom to treat as patients
9. The cost of screening, diagnosis and treatment should be economically balanced within the total cost of health-care spending
10. Screening should be a continuing endeavor to allow for refinement in screening methods, outcomes and process improvement

Table 2

Potential negative outcomes of cancer screening.

Over diagnosis: When tumors are detected that would never become symptomatic or lead to death
Overtreatment: When tumors are detected that would never become symptomatic or to death but are treated none-the-less

Application of Cancer Screening Principles

U.S. population screening for cervical cancer serves as an exemplar of a successfully designed and implemented screening program that has been modified as the biological mechanism of the carcinogenesis of cervical cancer is more clearly elucidated and methods for primary prevention (i.e., HPV vaccination) are developed. Cervical cancer screening programs in particular adhere to several of Wilson and Junger's principles, most importantly, that the natural history of the disease be understood and that it be an important health problem. Chronic human papilloma virus (HPV) infection is the underlying etiologic agent of the carcinogenesis of cervical cancer. Chronic HPV leads to a precancerous lesion (i.e., cervical intra-epithelial neoplasia) which can be visualized, after the detection of a positive cytology (through Pap testing), with colposcopy. The removal of the precancerous lesion using colposcopy successfully led to an overall decrease in the incidence of cervical cancers, even though there was over treatment of some early lesions. Cervical cancer screening represents an example of the use of an accurate screening test (i.e., PAP, colposcopy and now HPV testing) with adequate sensitive, specificity and positive and negative predictive value (PPV and PNV) leading to the identification of a high risk population, a pre-cancer or a cancer (Tables 3 and and4).4). Population screening for colon cancer also conformed to many of Wilson and Jungner's principles and led to improvements in overall survival of individuals who adopted screening recommendations.[1] A key feature of both cervical and colon cancer screening is the ability to directly access the tissue of interest and apply an adequate screening test. Population screening for cervical cancer reduced the incidence and mortality rates from cervical cancer and led to enthusiasm that screening programs for other cancers, or pre-cancers, would be equally successful. However, screening, detection and removal of pre-cancer or early cancer in other cancer types has not always been as successful.

Table 3

Characteristics of an accurate screening test.

The screening test (e.g., mammogram, coloscopy):
Is reliable → delivers same result each time, each instrument, each rater
Has validity → delivers the correct result each time:
Sensitive = correctly classify cases (pre=cancer or cancer)
Sensitivity=Cases found/all cases

Specificity = correctly classify non-cases (things that are not cancer)

Specificity= Non-cases identified/all non-cases

Table 4

Performance characteristics of a screening test

Positive Predictive Value: The chance that a person with a positive test (e.g., an abnormal pap test) has cancer or pre-cancer

Negative Predictive Value: The chance that a person with a negative test (e.g., a normal pap test) does not have cancer or pre-cancer

A major assumption about the natural history of carcinogenesis is based on the models of carcinogenesis of colorectal cancer proposed by Vogelstein et.al.[3] 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. It also assumed that there was similarity within cancer types, such that all prostate or breast cancers behaved similarly. Based on that assumption, population-based screening programs for other solid tumors were developed including breast and prostate cancer screening. However, outcomes from multiple screening programs between 1980–2010 demonstrated that breast and prostate cancers are a heterogeneous group of diseases that do not necessarily conform to the pattern of carcinogenesis as initially proposed in the Vogelstein model.[4] After population screening was introduced for breast and prostate cancer and outcomes documented overtime, lessons learned (Table 5) included that

Table 5

Lessons learned from population screening for breast, prostate and colon cancer

1. The success of cancer screening is more likely when the targeted cancer is slow growing and of uniform biology
2. Not all precancerous lesions lead to invasive cancers
3. Effective screening and removal of early stage cancer should cause a decrease in the incidence of late-stage cancers
4. Age matters: not all individuals will benefit equally from cancer screening

- Breast and prostate cancers were not uniform in their biology (they are heterogeneous)
- Not all early lesions (i.e., ductal carcinoma insitu or indolent prostate cancer) lead to invasive cancer
- Early detection does not always lead to improvements in overall survival, and
- There is risk to individuals when introducing screening interventions in otherwise healthy populations, including over diagnosis and overtreatment (Table 2)

In addition, other cancer screening techniques rely on indirect methods to screen for cancer such as radiographic imaging (e.g., mammography) or measuring a biomarker associated with cancer (e.g., CA-125 or PSA), rather than direct visualization and access to the target organ as in colorectal and cervical cancer screening. These indirect methods of cancer screening led to compromised screening efficacy due a decrease in performance characteristics of the screening technique [(including false positives and false negatives (Table 6)] and an increase in over diagnosis and overtreatment.[4] As more

evidence of screening efficacy accumulates, changes in cancer screening recommendations and practice continue to occur. Prostate cancer screening guidelines changed to include shared decision-making as it became evident that the risk-to-benefit ratio of routine prostate cancer screening in men over the age of 50 was unfavourable; routine prostate cancer screening led to over diagnosis of indolent cancer without a survival benefit while placing men at greater risk of injury related to the treatment of indolent prostate cancer.[5]

Table 6

Possible test outcomes of cancer screening

True Positive: Correctly indicates there is cancer *when cancer is present*
False Positive: Incorrectly indicates there is cancer *when no cancer is present*
True Negative: Correctly indicates that no cancer is present *when no cancer is present*
False Negative: Incorrectly indicates that *no cancer is present when cancer is present*

CONCLUSION

Cancer screening has contributed to decreasing the morbidity and mortality of cancer. Efforts to understand the biological basis of carcinogenesis and the development of new technologies for cancer screening will allow for improvements in the cancer screening over time.

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