ELSEVIER

Critical Reviews in Oncology/Hematology 61 (2007) 97–103

Critical Reviews in Oncology Hematology

www.elsevier.com/locate/critrevonc

Early detection of cancer: Ideas for a debate

R. Gennari [a,*], U. Veronesi [a,b], C. Andreoli [c], J. Betka [d], A. Castelli [c], G. Gatti [b], J. Hugosson [e], J.M. Llovet [f], J. Melia [g], J.A. Nakhosteen [h], U. Pastorino [i], M. Sideri [b], C. Stephan [j], P. Veronesi [b], S. Zurrida [b]

[a] *European School of Oncology, Cordinator Task Force on Early Detection of Cancer, Via del Bollo, 4, 20123 Milan, Italy*
[b] *European Institute of Oncology, Milan, Italy*
[c] *The Maugeri Foundation, Pavia and Milan, Italy*
[d] *University Hospital Motol, Praha, Czech Republic*
[e] *Sahlgrenska University Hospital, Goteborg, Sweden*
[f] *Institut Català de Ricerca Avancada, Barcelona, Spain*
[g] *Cancer Screening Evaluation Unit, Sutton, Surrey, United Kingdom*
[h] *Augusta Teaching Hospital, Bochum, Germany*
[i] *Istituto Nazionale Tumori, Milan, Italy*
[j] *Universitaetsmedizin, Berlin, Germany*

Accepted 18 August 2006

Contents

Abstract

Even if the overall number of cancer is increasing, the mortality has started to decrease in the Western World. The role of early detection in this decrease is a matter of debate. To assess its impact on mortality it is important to distinguish between diagnosis of cancer in symptomatic patients, and early detection in asymptomatic individuals who may self-refer or who may be offered ad hoc or systematic screening. The policies for early detection and screening vary greatly between European countries, despite many similarities in their cancer burden, and this partly reflects the uncertainties surrounding asymptomatic testing for cancer.

A Task Force of European expert, held in Azzate (VA), Italy, established to address these issues, acknowledged the need for more research in the field of individual risk assessment since general statistics are more and more perceived as inadequate to design personal early detection plans. The group also recognised that combinations of early detection and screening will enforce the effectiveness of new treatments in curbing mortality curves, although policies will vary with different cancers.

Keywords: Early detection; Cancer; Health care services

* Corresponding author. Tel.: +39 392 2255766.
E-mail address: rgennari@fastwebnet.it (R. Gennari).

1040-8428/$ – see front matter © 2006 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.critrevonc.2006.08.002

1. Introduction

There is a growing demand – at least in the Western World – for dedicated services and procedures aimed at the prevention of cancer [1], or at the very least, at its early detection as to maximise the chances of cure [2].

As a consequence of awareness campaigns promoted through the media by cancer charities and associations on both sides of the Atlantic, people are increasingly ready to change their lifestyle and to adopt preventive measures to avoid cancer (or at least death from cancer). The concept of "individual cancer risk assessment" has gained favour mainly as a result of the seminal work conducted by Gail and coworkers in the field of breast cancer [3]. In addition, other mathematical models have been developed [4] and some are available on the Internet [5] to assess both risk cancer in general and specific cancer risk.

Based on literature, new data, data from ongoing studies, and recommendations from expert assembled at the workshop, the Task Force made the exercise of examining possible sound, feasible and significantly evidence based procedures, which could become useful recommendations to those who may consider setting up clinics dedicated to the early detection and prevention of cancer. The Task Force was selected searching through experts that published paper related on the topic.

An important and similar effort was already made in 2000 by the American Cancer Society [6] and the present paper aims at contributing to the debate on this topic, particularly in Europe.

2. Early diagnosis

2.1. Prostate cancer

Prostate cancer is now the sixth most common cancer in the world (in terms of number of new cases), and the third in importance in men [7].

Prostatic specific antigen (PSA) was the first FDA-approved tumor marker for the early detection of prostate cancer and has been in use since 1994. It is generally agreed that population screenings with PSA are not justified on a cost benefit ratio basis but also at individual level the use of PSA for early detection of prostate cancer remains controversial [8].

Within the PSA ranges 4–10 ng/mL (90 or 95% sensitivity) and also 2–4 ng/mL (90 or 95% specificity) the ratio of free to total PSA can increase the rate of detected cancers per biopsy [9], particularly when adjusted by age and prostate volume. Neural networks using PSA, free PSA and additional clinical data such as age and prostate size like in the programme "ProstataClass" can further increase the specificity at given sensitivities by about 20–30% [10].

Preliminary investigations on other members of the kallikrein family, especially human glandular kallikrein 2 (hK2) or human kallikrein 11 (hK11) could yield substantial additional information, which would prove valuable in detecting prostate cancer, especially at low PSA values [11]. Finally, studies are starting to provide preliminary data also on possible schedules of early detection programmes: according to the findings of the European Randomized Study of Prostate Cancer (ERSPC, Rotterdam) recently published, a 4 year screening interval seems to be reasonable for prostate cancer [12].

2.2. Colorectal cancer

Colorectal cancer comprises 13% of all cancers and is responsible for 10% of all cancer deaths. When stratified by local, regional, and distant disease, the overall 5-year survival rates are 90, 58, and 5%, respectively.

There is now solid evidence from randomised trials suggesting that it is possible to reduce mortality from colorectal cancer between 15 and 25% by screening with faecal occult blood tests (FOBTs) [13].

The major benefit results from the detection of early cancer in average-risk persons above 50 years of age who have a positive test followed by colonoscopy. The major possible alternative to FOBT is flexible sigmoidoscopy. The "flexiscope trial" is evaluating a one-off flexible sigmoidoscopy followed by colonoscopy for those in whom high-risk adenomas are detected. The aims of the trial are to test the efficacy, acceptability, and safety of the process [14].

The flexible sigmoidoscopy trial hopes to produce clear evidence of the efficacy and feasibility of this procedure which only needs an enema 30 minutes before the test, lasts a few minutes and requires no medication. Since 2/3 of cancers develop in the sigma its early detection effect is considerable and lasts 10 years. Flex sigmoidoscopy is safe (1 in 40,000 case of perforation) and relatively non-expensive (approximately €90) [15].

Moreover, a recent study showed that colorectal cancer screening is a high-impact, cost-effective service underused by persons aged 50 and older [16]. Finally, spiral CT with or without colography (virtual colonoscopy) has been proposed for early detection of colon polyps [17] and a DNA-based blood test called loss of IGF2 imprinting (LOI) has been studied as predictive marker of an individual's risk for colorectal cancer [18].

2.3. Melanoma

Although melanoma is a relatively uncommon malignancy worldwide, its incidence has shown a dramatic increase (150%) since 1971. However, the general population screening for melanoma is neither practical nor cost-effective. On the other hand, early detection of melanoma remains an interesting issue for three main reasons: (a) the incidence of melanoma starts to rise after the age of 25 years, and a higher proportion of deaths from melanoma occurs under the age of 60 than occur for most other cancers; (b) the greater