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Breast cancer screening

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The present state of mass-screening for early breast cancer is reviewed. Some early reservations like radiation hazard of mammographies and overreferral to unnecessary breast biopsies are shown as unsubstantiated and a clear benefit of such screening is demonstrated particularly in post-menopausal women. Modern radiological equipment and highly skilled examiners are prerequisites. High costs of this screening and lack of trained professionals remains the main difficulty in many countries including Slovenia.

Key words: screening, mass screening; breast neoplasms, breast cancer; review, update; objections and arguments; in Slovenia

Introduction

In Slovenia, breast cancer is expected to soon afflict about one woman in 20 whereas in some other countries the rate has already doubled and is still rising.[1-3] The etiology of this tumor is unclear and the method of prevention unknown. In spite of many therapeutic improvements its 5-year survival is hardly above 50 %,[1, 4] and has remained so for decades. The individual prognosis depends much on the tumor size at the time of first therapy, and in (UICC) stage I. tumors the 5-year survival is around 90 %.[2, 4, 5] Early detection by mass-screening of apparently healthy women at risk is thus a medical challenge and a matter of great public health interest. Screening and screening procedures, however, have been subjected to criticisms which will be briefly discussed in this article.

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To screen or not to screen?

This basic question seems to have been answered by the single most important screening trial initiated in 1961 by the Health Insurance Plan of Greater New York and commonly known as HIP. By 1971, the follow-up of about 60.000 trial and control women demonstrated that physical examinations (PX) and mammographies (MG) reduced mortality by 30 % in the 50–64 year age group.[6, 7, 8] After 18 years the study showed that also women aged 40-49 benefited a 21 % death reduction.[2, 6] Contrary to that, a similar nation-wide program conducted in Canada 20 years later did not seem to reduce the mortality in either group at its 7-year evaluation.[4] Nevertheless, HIP and many other studies have led to the firm belief that mass-scree-

ning of women at risk is currently the only method capable of reducing breast cancer mortality by 16–25 % and according to some reports even by more.[4, 6, 9] In spite of the generally recognised advantage of mass-screening a number of reservations have been voiced.

An early and then relevant objection was the radiation risk induced by mammography which is best suited for detecting unpalpably small, curable tumors.[10, 11] In the early 60's the dose absorbed in the midbreast during two-view mammography was anywhere between 0.3 and 7 cGy allegedly rendering the radiation hazard comparable to the benefit of repeated examinations.[2, 5, 12] Later technical advances in MG reduced the exposure substantially, down to 0.05 cGy and simultaneously increased its sensitivity by a factor of 2-4.[2, 5] One very conservative risk-to-risk assessment assuming a 0.8 cGy glandular dose and 18 yearly examinations concluded that the risk of radiation-induced cancer-deaths is less than 1/10th of the risk of early death caused by omission of this examination.[13] The radiation hazard involved in MG with a modern equipment is, indeed, much lower and now considered negligible.[2]

Another serious objection was that there would be an increase in unnecessary breast biopsies owing to an overinterpretation of mammograms and resulting in a referral-to-surgery rate as high as 10 % of all screenees.[14, 15]

It was shown, however, that well trained and highly skilled radiologists can cut the rate of negative biopsies down to an acceptable level of 1/4[6] or even 1/7.[16]

An obvious problem of mass-screenenig is the sheer size of the task. It was estimated that in the USA every radiologist would have to interpret 10 MG daily if screening were conducted according to current recommendations.[15]

Nevertheless, a number of developed countries including the United Kingdom, Canada, the Netherlands and the Scandinavian countries embarked on large-scale screening programs, mostly to evaluate their feasibility, benefits and cost.

The last and the most important common objection to mass-screening is that it should not be considered unless it proves to be a valuable health service in terms of the cost-benefit ratio. In a free-market environment the direct cost of a single screening is easy to assess and reportedly amounts to between 25–250 $ per case, with the mean around 100 $.[1-3, 15, 17] It seems that both the costs and benefits increase with the length of the follow-up[4, 19] but according to some estimations the expenses of including women aged under 50 years are not acceptable when compared with the number of tumors detected.[19] Indirect costs including downstream diagnostic procedures, lost working days and other are more difficult to determine.

The benefit of a medical procedure may be measured in a number of ways ranging from life-years saved to social and personal benefits expressed in some arbitrary units. In the Netherlands one such study showed that one year of life saved by mass-screening (5 invitations in 20 years) costs 3800 $ directly plus the same amount of marginal expenses.[4] It is true, of course, that in the long run expenses of health services cannot be expected to drop before the number of advanced cancers decreases. The immediate costs of screening clearly outweigh the savings[6] and, thus, remain prohibitive for most countries.

Who to screen and how often?

Most breast cancers occur after age 35 and their frequency increases steadily thereafter. Two thirds of patients are older than 50 years.[19] Does it make sense, then, to screen indiscriminately all women at risk? Since general screening is an expensive task aimed primarily at saving lives it should embrace only that part of a population in which a sufficient number of early cancers in a curable stage can be expected. Some workers argue that the life of a cancer patient after 75 can be neither saved nor prolonged by screening owing to the natural course of the disease and life expectancy at this age.[20] On the other hand, there are women at high personal and familiar risk which are an obvious target group, though not easy to identify. As to the age of screenees, the first results of the

HIP study already demonstrated its life-saving effect in women over 50 years of age which was amply documented thereafter.[6] Eventually, the HIP and other studies suggested but not unanimously confirmed a similar benefit between age of 40 to 49 years,[6, 21] so that some European researches have remained skeptic particularly if only MG is employed.[8, 22]

About 90 % of breast cancers are self-referred when the tumors reach palpable size.[5] Thanks to the sensitivity of MG, screening programs detect cancer usually at an early, non-palpable and still curable stage. The initial yield of such programs is, therefore, usually larger than expected. At subsequent screenings the detection rate decreases to the prescreening level.[6, 14, 23] This "lead-time" was suggested to be also an optimal interval for examinations because it minimalizes the occurrence of interval tumors and decreases expenses.[6, 9] The proposed intervals range from 1–3 years and tend to be shorter in the USA than in Europe.[8, 19, 22] Most programs have, thus, adopted a 12–18 months interval for women under 50 and 2–3 years for older ones.

How to screen?

HIP and many subsequent studies demonstrated that PX and MG are the cornerstones of early breast cancer detection which can save about 30 % of lives,[2, 5, 7] On the other hand, single oblique view MG used as the sole detection modality in the first ("two-county") Swedish study also decreased mortality in women over 40 years of age by 30 %.[2, 6] The idea to cut down expenses and to limit examinations to MG only, seemed inviting and prompted a number of studies for its evaluation.[2,5,7,14,21,23] It is now recognised that both modalities are needed. The group led by L. Tabar,[6, 21] however, is putting more weight on MG. Nevertheless, up to a quarter of tumors may remain undetected by MG and nearly half of them may escape PX.[5, 7, 14] PX is more likely to miss smaller tumors in women over 50 while false negatives in MG vary between 10–20 % regardless of the tumor size but are more likely to occur in younger populations.[14, 23, 24]

To cut down examination expenses, attempts have been made to recruit specially trained prescreeners, i.e. general practitioners and technologists to interpret MG and nurses to perform PX.[7, 17] It turned out that such personnel may be useful if properly trained but any prescreening, in fact, increases expenses because expert reviews are required.[17] In addition, it was found that non-radiologists are less accurate in interpreting MG than trained radiologists[9] whereas nurses miss slightly more tumors at PX than oncologists.[7] It is now generally accepted that screening programs ought to be performed by highly trained professionals and that quality-assurance, information feed-back, informal team-work and continuous training are essential prerequisites for inexpensive and efficient cancer detection.[3, 6, 17, 20, 21, 25] Comprehensive dedicated communal breast centers were suggested as the proper environment in which to perform this task.[3]

Screening in Slovenia

In Slovenia, there are some 180.000 women aged 50–64 and 120.000 aged 40–49 years. The present equipment consists of 8 modern mammographs but this number is expected soon to increase. There are only about 10 competent radiologists capable of interpreting MG because the professional training curriculum shows little understanding for and grossly neglects this field.[26] Similarly, only a few dozen oncologists, some surgeons and a few gynecologists are familiar with PX of the breast. A hypothetical, full employment of these resources would allow about 75.000 examinations per year, which does not warrant any nation-wide breast screening program.

The available means are, however, sufficient to run about 10 breast-diagnostic centers which take care of referred or self-referred women. In addition, three of these centers (Ljubljana, Maribor and Nova Gorica) initiated a screening feasibility trial which involves 12.400 randomly selected women aged 50–64. The screenees are

offered PX and a single-view MG. The first results are expected by the year 2000.[27]

At present, no nation-wide screening program can be considered. Its cost could not be realistically estimated because of the fluctuating prices of materials and services. It is precluded also by the lack of properly trained personnel. Before starting any comprehensive nation-wide program a radical change in the teaching of oncology should occur and special training of clinicians, radiologists and technologists for breast examinations should be made available and mandatory in order to achieve a workable professional level of such an undertaking.

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