PERGAMON

European Journal of Cancer 38 (2002) 1427–1428

European Journal of Cancer

www.ejconline.com

Editorial Comment

Comment on "The frequency of breast cancer screening: results from the UKCCCR Randomised Trial"

I. Andersson*

Screening Unit, Malmo University Hospital, 2140 Malmo, Sweden

Received 31 January 2002; accepted 14 February 2002

Although breast cancer screening with mammography can be considered more evidence-based than most medical procedures, there are several questions that remain unresolved. One such question is the optimal screening interval. Partly based on inferences from knowledge about sojourn time and interval cancer incidence and partly based on common sense, an interval between 1 and 2 years has generally been considered reasonable. By the same token, a 3-year interval as recommended in the UK National Breast Screening Programme (NHSBSP) has been considered too long. In addition, a too long screening interval (usually approximately 2 years) has been blamed for the relatively lower effect seen among woman under the age of 50 years in some programmes and a 1-year interval has been suggested [1]. However, a statistically significant reduction of the breast cancer mortality has been demonstrated in this particular age group in two programmes with an interval between 1.5 and 2 years [2,3].

Furthermore, the screening interval is one of the major determinants of the cost of screening. With todays scarce healthcare resources in terms of money, as well as manpower, solid data on the optimal screening interval would certainly be welcome. It is therefore highly commendable that a study comparing a 1-year interval screening with a 3-year interval is being conducted within the UKNHSBSP as reported in this issue. Women in five screening units within the NHSBSP were randomly allocated either to invitation to a regular incidence screening after a 3-year interval (control group) or to three annual screenings (study group). Only those who had attended the prevalence screen and in whom no breast cancer was found at the prevalence screening were actually included in the study (38 492 in the control group and 37 530 in the study group). The attendance among those included was 85% and approximately 80%, respectively. Cancers detected at screening and in the intervals were identified and tumour size, axillary node status and histological grade for invasive cancers were recorded and entered into two predictive indices, the Nottingham Prognostic Index (NPI) and the Swedish two-county index (STC).

The proportion predicted to die within 10 years was 38 and 36%, respectively. The relative risk was 0.95 and 0.89 for the study group using the NPI and STC indices, respectively; neither was statistically significant.

The main conclusion of the study was that shortening the interval from 3 years to 1 year does not influence the mortality rate from breast cancer.

The results are somewhat unexpected. With the shorter screening interval, one would expect a substantial advancement in the time of the diagnoses which should be reflected in the parameters that make up the prognostic indices. The tumour size was smaller in the study group, and this was marginally statistically significant. However, there was no reduction in the rate of axillary metastasis or shift in histological grade. Accordingly, the median lead time (the advancement in time of the detection) was only 7 months. In this situation, two issues have to be considered: the study design and the radiographical quality.

The randomisation seems to have been appropriate, although data to support a successful randomisation are not presented.

The assumption of a 25% difference between study and control groups seems a bit optimistic when the total breast cancer mortality reduction in a screening programme can be expected to be of approximately that magnitude. This implies a risk of a beta error.

The fact that non-attenders in the prevalence screening, as well as in the incidence screenings, have been

* Fax: +46-4033-7062.
E-mail address: eva.prahl@rontgen.mas.lu.se

PII: S0959-8049(02)00121-1

excluded means that a large group of the screening eligible population was not included. The attendance in the study group was lower compared with the control group. Does more frequent invitations reduce attendance? Were the non-attenders the same in all screening rounds? How many women got all three screening examinations?

Experience from controlled trials shows that there is a self-selection bias in that non-participants have a greater risk of dying from breast cancer than participants and also greater than the control group women with breast cancer [4]. This can at least partly be explained by the stage of the disease at diagnosis, but other factors may also be important. Is there any indication that such self-selection occurred in the current study? In other words: what were the tumour characteristics of the non-participants in the study and control groups?

In addition to the breast cancer detection rate, the interval cancer rate provides some information on the radiographical quality. The interval cancer rate was clearly lower in the study group. The interval cancers represented a substantial proportion of all cancers detected: the interval cancers comprised 30% (69/235) of the study group and 50% (104/208) of the control group. The corresponding figure in the Malmö trial was 20%.

Several studies have shown an increased risk of dying from breast cancer among interval cancers. In the Malmö trial, the interval cancer group had a relative risk of 2.3 of dying from breast cancer compared with the control group. In addition, in the first follow-up of the Malmö trial (follow-up time 8.8 years), 63% of the breast cancer deaths among the screened woman occurred in interval cancer patients. Therefore, more data on the interval cancers would be of great interest. What was the distribution of tumour attributes between screen-detected and interval cases and between the study and control groups?

Furthermore, the current trial should help to provide further insight into the natural history of interval carcinomas.

Another question concerns the use of prognostic indices to predict mortality. The NPI was based on a clinical series of patients, while the current material consists of screening-detected cancers plus interval cancers. The STC index is based on a screening population including non-attenders and controls. It can be questioned whether the NPI can be applied to a population of screening-detected and interval cancers. In the NHSBSP trial, a surprisingly high proportion of breast cancer patients are predicted to die within 10 years (38 and 36%, respectively). In the first follow-up of the Malmö mammographical screening trial (mean follow-up 8.8 years), only 8% (31/390) of patients with invasive breast cancer detected at screening (including the prevalence screening) and in the intervals had died from their breast cancer. This might suggest that the tumour population on which the NPI is based is not equivalent to a sample of tumours detected at screening and in the intervals between screenings. The STC index predicted a more favourable outcome.

In summary, this paper addresses a significant problem. The answer is not yet clear. More baseline data would have been welcome and mortality data are eagerly awaited. ''Prediction is difficult, especially of the future'' (Niels Bohr).

References

1. Andersson I, Aspegren K, Janzon L, *et al*. Mammographic screening and mortality from breast cancer: the Malmö mammographic screening trial. *Br Med J* 1988, **297**, 943–948.
2. Andersson I, Janzon L. Reduced breast cancer mortality in women under age 50: updated results from the Malmö Mammographic Screening Program. *JNCI Monographs* 1997, **22**, 63–67.
3. Bjurstam N, Björneld L, Duffy SW, *et al*. The Gothenburg Breast Screening Trial: first results on mortality, incidence, and mode of detection for women ages 39–49 years at randomization. *Cancer* 1997, **80**, 2091–2099.
4. Tabar L, Fagerberg G, Hsiu-His C, *et al*. Efficacy of breast cancer screening by age. *Cancer* 1995, **75**, 2507–2517.