

Mammography Screening in Denmark

Clinical guidelines

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BACKGROUND

Mammography screening is offered asymptomatic women and consists of a standardized breast x-ray examination at predetermined intervals. At this examination, there is no patient/doctor contact.

Screening by mammography does not reduce the risk of developing cancer, but has the potential to identify breast cancer at an earlier stage, thereby increasing the likelihood for survival.

An overview of the Swedish Randomized studies showed a 29% reduction in breast cancer mortality among women invited to screening after a follow-up period of 5-13 years (1). Strongly influenced by these results population based organized screening by mammography started in Copenhagen in 1991, in the county of Funen in 1993 and in 1994 in the municipality of Fredriksberg. Together these three programs cover approximately 20% of the Danish female population in the age group 50 – 69 years. In 2001 mammography screening was introduced on Bornholm and in 2004 in the county of West Zealand.

In 1999 a law was passed that demanded mammography screening to be offered to all Danish women in age group 50 – 69 years but no date was set for the implementation. In a later amend

ment the implementation was set to occur no later than the end of 2007.

Preceding this nationwide implementation was a revival of the debate about the value of mammography screening, heavily influenced by the report by Gøtzsche and Olsen (2,3). International meetings were held and papers produced focusing on this subject. The concurrent conclusion was, that screening by mammography does reduce breast cancer specific mortality (4,5,6,7,8,9)

It has been documented, that the results from the Swedish randomized studies can be reproduced in a Danish service-screening program. Thus breast cancer specific mortality in Copenhagen fell by 25% after 10 years of screening among those invited and by 37% among those who attended one or more times (10).

PURPOSE

The endpoint of success for a screening program is to achieve a substantial reduction in disease specific morbidity and mortality with as few negative side effects as possible. To reach this goal it is necessary to build up and maintain a high standard on the professional and organizational level not only in the screening-program as such but even concerning the ensuing diagnostic work-up and treatment.

In order to reduce negative side effects the screening program must be well organized and the staff well educated. A continuous monitoring of the quality of all aspects of the screening program as well as derived interventions is essential to obtain and maintain a high standard.

The purpose of these guidelines is to support organizing and monitoring of the regional screening programs.

INDICATORS

It is not possible to monitor the effect on breast cancer morbidity and mortality in a population until several years after the implementation of a screening program. Therefore it is necessary to use process indicators to monitor the screening program (11). Appendix 1 lists quality indicators selected and defined by the steering committee of the Danish Quality Database of Mammog-

raphy Screening to monitor the Danish mammography screening programs. These indicators were part of those used to monitor two of the earliest Danish screening programs i.e. those in Copenhagen and Funen (12,13,14).

Tumor size and axillary status are two very important prognostic factors for breast cancer survival, and characterizing a screening-program of high quality is a high detection-rate of invasive cancers < 1cm and lymph node negative cancers, with as few negative side effects as possible.

To achieve the objective of screening on a population basis a high level of attendance is essential.

To minimize worry on behalf of the screened women and to ensure cost-effectiveness recall for further diagnostic work-up of benign lesions not demanding any treatment per se should be kept as low as possible.

The number of recalled women without cancer (false positives) and the number of women with benign lesions referred to surgery should be kept as low as possible with due respect to the detection rate. Ratio between surgery for benign versus malignant lesions is an indicator of the quality of the integrated diagnostic team consisting of specialized radiologists, surgeons and pathologists. This has to be monitored at a local as well as at a central level.

The number of recalls is greater among younger women and at first screening (15).

No screening program will identify all malignant tumors at any given time. The possibility of identifying a tumor at the time of screening depends on several factors. Some of those factors are: density of the breast tissue, type of cancer, growth rate of the tumor, technical quality, skills/experience of the radiographers and the radiologists and recall level. As an indicator of the number of over-looked, fast growing or radiologically undetectable tumors, the number of interval cancers is used (number of invasive malignant tumors diagnosed in the 2-year interval after the women are tested negative) compared to the occurrence of breast cancer in the background population in the absence of screening

Screening by mammography leads to a decrease in breast cancer mortality and also has the potential to lead to less aggressive treatment. The number of women with invasive breast cancer treated with breast conserving therapy increases, and the number of women needing systemic adjuvant therapy should decrease.

In Denmark the interval between screens for women age 50 – 69 years has been set to 24 months (+/- 3 months), which is in accordance with the majority of other population based screening programs. It is important for the trustworthiness of the program to adhere firmly to this scheme. Monitoring the screening interval is an important factor in the quality assurance of the screening program.

Overdiagnosis defined as the identification of cancers that would not have been found in the lifetime of the woman in the absence of screening is a potential negative effect of a screening-program. In order to minimize the risk of overdiagnosis and overtreatment the relative number of DCIS cases identified in a screening pro-

gram should not exceed 20%, neither should it make up less than 10%, since it is estimated that around 30-50% of DCIS – lesions progress to invasive cancer. Or reversely: the relative number of invasive cancers among all screening detected malignancies should be between 80 and 90 %. Especially the identification and treatment of poorly differentiated DCIS lesions has a potential to decrease mortality from breast cancer (11). To monitor overdiagnosis it is necessary, that the entire target-group is offered screening within defined intervals.

A successful screening program depends on optimal diagnostic information, which again depends on knowledgeable radiographers and technical equipment of high quality. Technical quality control must ensure that the radiologist gets best possible diagnostic information with as low a radiation dose as possible. The radiation dose should only be lowered below generally recommended levels if diagnostic acuity can be maintained (11).

Most women participating in a screening program are symptomless. Those recalled for assessment from the screening program therefore differ considerably from women referred due to breast related symptoms. Recall after initial screening will in many women cause anxiety. Therefore women with a normal or benign test after recall must be reassured as fast as possible whereas those with malignancy must be diagnosed and treated without unnecessary delay. The monitoring of a screening program therefore must include time from screening test to information of the result.

ORGANIZATIONAL DEMANDS

To achieve the purpose of reduction in breast cancer mortality without significant adverse effects a screening program must maintain high professional and organizational standards.

EUREF (The European Network of Reference Centre's for Breast Cancer Screening) has established a series of standards for breast cancer screening, some valid for regional programs and some for centers of reference (11). The following list of organizational requirements for a Danish screening program is based partly on these and partly on Danish Breast Cancer Cooperative Group's (DBCG) guidelines concerning diagnosis (16).

ORGANIZATIONAL REQUIREMENTS FOR A SCREENING PROGRAM

- Personal invitations to screening by mammography are based on updated population data (CPR)
- Information on screening is posted with the invitation
- A questionnaire is posted with the invitation or presented at the time of the screening. The questions must at least concern previous or actual treatment with estrogen hormones, previous operations in the breast, and whether the woman herself has felt any lumps in the breast. The answers to these questions are important for the evaluation of the mammographic images.
- All women in the target group 50 – 69 years are invited biannually
- The women can at any time decline participation and even at any time rejoin the screening program
- Each screening unit performs at least 5000 screening examinations each year in a target group of 20.000 women

- Mammography screening is performed within an organizational framework complying with these demands and with facilities for complete diagnostic work-up of abnormal findings at the screening examination
- A steering-group is established with members from relevant specialties and headed by a leader, which is responsible for the program. The leader refers to the steering group
- At each screening session 2 views are taken on each breast (cranio-caudal and mediolateral oblique)
- All participants are by letter informed of the result of the examination
- All screening organizations have a centralized quality assurance following the physical-technical recommendations included in the European Guidelines for Quality assurance (11)
- Data are collected and used for monitoring of the program
- The leader of the program is responsible for organizing a structure to assure that the entire target group receives invitations and that a decision to recall is acted upon
- Screening images are read independently by two persons, of which at least one is an experienced screening radiologist, who as a minimum reads 5000 screening examinations a year.
- All images are archived to allow comparing with consecutive examinations and for research purposes

ORGANIZATIONAL REQUIREMENTS FOR A REFERENCE CENTER BEYOND THE ABOVE MENTIONED

- Performs at least 10.000 screening pr year
- Provides educational programs for evaluation of performance and educational material including handling of interval cancers
- Has a physicist as a member of the team
- Is part of an integrated team containing specially trained radiologists, pathologists, surgeons and oncologists
- Evaluates and reports results on a regular basis
- Has epidemiological/statistical support for monitoring and reporting

INFORMATION

Information on the screening program must be balanced, honest, evidence-based and targeted to the different phases of the program.

SELF-EXAMINATION

Mammography is no perfect test in the sense that a normal screening test is no absolute guarantee that breast cancer is not present, or that breast cancer cannot occur even in the near future. It is therefore recommended that the letter to a participant in the screening program conveying a normal test result includes a caution to seek medical attention, should she be aware of anything abnormal or different in her breasts.

RADIOGRAPHER/IMAGING STAFF

The radiographers, x-ray nurses or other specially educated assistants performing the actual screening mammograms often are the only members of the team in contact with the attending woman. To assure continuous attendance it is mandatory that

these staff members are adequately educated and behaves in a professional way.

Complaints and praise, verbal as well as written, should be discussed at regular staff meetings.

Sensitivity as well as specificity depends on optimal positioning and high quality of the images. It is essential that the imaging staff is highly educated to achieve the defined standards of technical quality (11):

- More than 97% of the examinations should comply with internationally recognized radiographic standards
- Less than 3% of attendees will need repeated examinations for technical reasons (monitored for each imaging staff member on a regular basis for instance every 6 months)

All attending women can expect that the member of the staff, which they meet, is able to inform about the test itself and the timeframe within which they can expect a letter with the result of the test. Close to all women should be content with the screening examination as such.

At regular intervals audit should be made over a sample of the screening mammograms of each individual member of the screening staff. All technical recalls should be discussed at such an audit. The radiographers/ x-ray nurses should be fully aware of the importance of quality control in daily work

The radiographers/ x-ray nurses should if possible take part in consecutive diagnostic work-up, and be familiar with procedures included in this.

The radiographers/ x-ray nurses should participate in multidisciplinary meetings on a regular basis, and continuous feedback from the radiologist is essential.

THE RADIOLOGIST

The radiologist is responsible for maintaining a high image quality and for ensuring that quality control is performed physically/technically as well as professionally.

The radiologist working with screening must be a specialist in diagnostic radiology and must have undertaken specific education in symptomatic as well as screening breast imaging and in the diagnostic work-up of abnormalities detected by screening. Even a long experience with symptomatic cases cannot replace training in screening mammography and consecutive diagnostic work-up (11).

DIAGNOSTIC WORK-UP

The diagnostic work-up of abnormalities detected by screening should take place in departments fulfilling the requirements for a diagnostic breast center, as stated below. Furthermore the department should adhere to DBCG's guidelines for diagnosis of breast diseases (16).

Requirements for a diagnostic breast center

- Performs at least 2000 clinical mammography examinations per year
- Has at least one experienced radiologist evaluating at least 1000 mammography examinations pr year

- Has dedicated mammography equipment for diagnostic mammography with access to equipment for magnification exposures, with adequate conditions for reading of mammographies and with dedicated ultrasound equipment with high-frequency transducers
- Is able to perform clinical examination, ultrasound and the whole spectrum of relevant procedures
- Performs biopsy for cytology/histology, directed by ultrasound or stereotactically and by the same techniques perform preoperative marking of non-palpable lesions
- Work closely together with pathologists experienced in breast cytology and histopathology
- Partakes in multidisciplinary communication and review meetings with other team members responsible for diagnosis and treatment
- Partakes in monitoring of data and in analyzing feedback

The head of the screening unit is responsible for the establishment of a structure ascertaining that decisions on recall are executed. The organizations must also assure that a new letter of invitation is sent to women not responding to the recall-letter. Records should be kept matching those recalled to those actually showing up.

Recall should be by letter including a telephone number for contact. It is preferable not to recall by telephone as this can cause unnecessary anxiety. For many women a recall causes distress, and the time from receiving the recall letter to the actual examination should be as short as possible. Letters should be posted such that they are not received in weekend or public holidays, when contact to the screening unit is not possible (15).

Screen detected abnormalities must be clearly marked by the initial reader in order to clarify the reason for recall to the staff performing the diagnostic work-up.

For educational purposes and to achieve experience it is essential the radiologists reading the screening mammograms also take part in the consecutive diagnostic work-up. Likewise imaging staff from the screening unit should at times be given opportunity to participate in the examination of recalled cases.

At the recall examination supplementary projections are made if warranted and ultrasound examination is performed on all abnormal radiological findings and all palpable lesions. Biopsy guided by ultrasound or x-ray is performed from all suspicious or obvious malignant lesions and from all palpable solid lesions. This also includes lesions that are considered benign based on the imaging studies (with few exceptions listed in the DBGG guidelines)

TRIPLE TEST

The triple test (clinical examination, imaging and needle biopsy) is the cornerstone of the diagnostic work-up. The diagnostic work-up takes place within an integrated diagnostic system staffed by doctors specialized in diagnosis and treatment of breast cancer, i.e. a team of doctors with expert knowledge in the fields of breast radiology, breast surgery and breast pathology. Such a team works in accordance with written local guidelines for the multidisciplinary cooperation. An essential part

of this system is that there is agreement within the team as to who is responsible for the patient at any given time in the diagnostic process. For radiologically benign lesions, this will often be the radiologist. If in such a case a needle biopsy is performed it is the examining radiologist who is responsible for assuring concordance between the radiological and pathological findings before the diagnostic process is brought to an end. In cases of suspected or proven malignant lesions the responsibility for the case is transferred to the breast surgeons.

The principles of the triple test (palpation, imaging and needle biopsy) shall be pursued:

- Consensus for benign lesion: case closed and the woman returns to the screening program
- Consensus for malignant lesion: referred to surgery
- Triple test not unequivocal: further imaging, repeated biopsy or eventually excisional biopsy should be performed

The diagnostic process should be as short as possible to assure that the woman can be calmed in case of benign lesions or in case of malignancy be referred to fast one step surgery as often as possible.

Surgery for non-symptomatic benign lesions should be avoided, but may be necessary to achieve a definite diagnosis. The ratio between benign and malignant lesions treated surgically is a good indicator of how well the integrated diagnostic team works and should be monitored locally.

MULTIDISCIPLINARY CONFERENCES

All cases where there is no consensus on the triple test and all cases referred to surgery should be discussed within the framework of the integrated diagnostic team in order to reach agreement on further examination or treatment. Such a conference should be held before the woman is informed of the results of the examinations.

FAMILY DOCTOR

The results of the screening test should— with her consent — be sent to the woman's family practitioner so that he or she can be informed on the progress of the diagnostic process and the final result.

SCREENING OF WOMEN WITH A GENETIC DISPOSITION TO BREAST CANCER

Women in the target population for the screening program aged 50 – 69 years with an increased risk of breast cancer determined by their family history can be followed within the routines of the general screening program whether they are considered to have a moderate or high risk of breast cancer. However women with a proven mutation in the BRCA 1/2 genes are offered more intensive surveillance outside the screening program (17).

SCREENING OF WOMEN PREVIOUSLY TREATED FOR BREAST CANCER

Women in the target population for the screening program aged 50 – 69 years, who have been treated for breast cancer more than 18 months ago, can be referred to the screening program according to the recommendations in the DBCG guidelines (18)

WOMEN WITH BREAST IMPLANTS

Women with implants placed behind the pectoral muscles can often but not always be sufficiently examined by mammography. It is important to notify the imaging staff in such cases, as the imaging technique may have to be changed to avoid the implants shadowing for the glandular tissue. Women with implants between muscle and glandular tissue are normally not suited for mammography screening.

There is no evidence for recommending screening by ultrasound.

SUMMARY

Mammography screening is offered healthy women, and a high standard on professional and organizational level is mandatory not only in the screening programme but even in the diagnostic work-up and treatment. The main goal is to achieve a substantial reduction in disease specific mortality, but it is not possible to evaluate the effect on mortality until several years later, and continuously monitoring of the quality of all aspects of a screening programme is necessary. Based on other European guidelines, 11 quality indicators have been defined, and guidelines concerning organizational requirements for a Danish screening programme as well as recommendations for the radiographic and radiological work have been drawn up.

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