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Does breast screening offer a survival benefit? A retrospective comparative study of oncological outcomes of screen-detected and symptomatic early stage breast cancer cases

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Summary

Introduction: Mammography screening reduces breast cancer mortality by up to 32%. However, some recent studies have questioned the impact of non-palpable breast cancer detection on mortality reduction. The aim of this study was to analyse the clinicopathological and long-term follow-up data of early stage screened and symptomatic breast cancer patients.

Patients and method: The institutional prospectively led database was systematically analysed for breast cancer cases diagnosed via the mammography screening program from 2002 to 2009. As a control group, symptomatic early stage breast cancer patients were collected randomly from the same database and matched for age and follow-up period. All medical records were reviewed retrospectively.

Results: Data from 298 breast cancer patients were collected from 47,718 mammography screenings. In addition, 331 symptomatic breast cancer patients were randomly selected. The screened group presented a significantly lower median tumour size ($P < 0.00001$). The incidence of negative regional lymph nodes was significantly higher in the screened group ($P < 0.0006$). The incidence of chemotherapy was 17% higher in the symptomatic group ($P = 4*10^{-5}$). At the median follow-up of 65 and 80 months, the screened group did not exhibit better overall ($P = 0.717$) or disease-free survival ($P = 0.081$) compared to the symptomatic group.

Conclusion: Our results do not suggest that mammography screening does not reduce breast cancer mortality but the mammography screening did not bring any significant improvement in patient overall or disease-free survival for the early stage breast cancer patients compared to the symptomatic group. The drawback of symptomatic early stage tumours compared to non-palpable tumours could be equalized by modern multimodality oncology treatments.

Keywords: Breast neoplasms; Mass screening; Mortality; Survival

Introduction

Oncological outcomes are generally more favourable during early stages of disease before symptoms appear in symptomatic (palpable) diseases. The goal of any screening program is to disclose breast tumours before they become palpable, optimally during stage 0. Mammography screening could bring about significant benefits in survival, which was the main reason for the implementation of breast screening programs in many countries.[1,2] Hungary

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organized a nationwide screening program for residents aged 45–65 years, with biannual screening commencing in January 2002.[3]

The efficacy of mammography screening in preventing breast cancer deaths was presented in some randomized controlled trials (RCTs), with reductions in mortality rate ranging from 17% to 32%.[4–7] On the contrary, some recent studies have questioned the efficacy of early stage tumour detection on mortality reduction.[8,9] Some authors believe that advanced breast cancer diagnosis and effective adjuvant therapy may play greater roles in reducing breast cancer mortality than screening.[10]

The aim of the present investigation was to compare the clinical outcomes of a group of patients that underwent mammography screening compared to a non-screened symptomatic group of early stage breast cancer patients.

Patients and method

This study was performed in accordance with the Research Ethics Committee of the National Institute of Oncology. Written informed consent was always obtained for data collection.

The inclusion period was from 1 January 2002 to 31 December 2009. Data were collected from the prospectively led database of the National Institute of Oncology, Budapest.

According to the Hungarian guideline on mammography screening the target population was invited for breast screening regionally by invitation letter.[11] Our investigated screened population represents the target population from the capital. Screened (SCR) breast cancer patients discovered by the mammography screening program of the National Institute of Oncology were collected prospectively. According to the international standards for breast screening, double-projection mammograms and double-read procedures were applied. A Siemens Mammomat 3000 mammography system was used for screening, diagnostics and stereotactic biopsy procedures. For suspicious and malignant cases, bimanual physical examination, breast and regional lymph node ultrasound and core biopsy or fine-needle aspiration cytology (FNAC) were used for further examination.[12]

The surely symptomatic (SYM) breast cancer patients with palpable tumours were collected randomly and prospectively from the institutional database by three researchers. The patients included to the SYM group were newly diagnosed breast cancer patients corresponding to a clinical stage from 0 to II/A with disease discovered by self-examination or via another physical breast examination by general practitioner or gynaecologists within the inclusion period. The main reason for breast examination of SYM patients were the changes in the breast shape, skin retraction, nipple inversion, breast pain, a palpable lump, nipple discharge, unexplained redness, swelling or a lump around the collarbone or under the arm. Patients whose disease was discovered by screening were excluded from the SYM group. Patients in SYM group were collected mainly from the capital. The database was led prospectively according to the standard methods of all disciplines involved in breast cancer diagnosis, treatment and follow-up, which included all relevant clinicopathological data of the SCR and SYM patients. Some of the patients were included in clinical trials from both groups but nobody has left undertreated.

According to the updated international European Society of Medical Oncology (ESMO) Clinical Practice Guidelines for diagnosis, treatment and follow-up, all patients received multimodality oncology treatments and a follow-up at the National Institute of Oncology.[13–17]

The diagnosis of breast cancer was based on clinical examination in combination with imaging and was confirmed via pathological assessment. MRI was used in cases of breast implants, ILC, the suspicion of multifocality/multicentricity, or large discrepancies between conventional imaging and the clinical examination.

For surgical procedures, breast conserving surgery (BCS), mastectomy, sentinel lymph node (SLN) biopsy with dual radio-colloid/blue dye technique were used. In SLN-positive cases or for clinically positive axillary lymph nodes, axillary node clearance was used. In case of BCS, palpable tumours were resected via a wide excision and non-palpable tumours were resected via a wide excision using radio-guided occult lesion localization (ROLL) technique, with a minimum microscopically surgical margin of 1 mm.

Postoperative pathological examination and assessments had not been significantly changed during the investigated period.[18] The assessments included the number, the location and the size of the tumours removed, the total number of removed and positive lymph nodes, and the extent of metastases in the lymph nodes, such as isolated tumour cells, micrometastasis (0.2–2 mm) and macrometastasis. The report included the histological type and grade of the tumour, evaluation of the resection margins, vascular invasion, and a biomarker analysis, such as an immunohistochemical (IHC) evaluation of oestrogen receptors (ERs), progesterone receptors (PRs) and human epidermal growth factor 2 receptor (HER2) gene expression. HER2 gene amplification for tumours with an ambiguous (2+) IHC score was evaluated using a fluorescent in situ hybridization (FISH) technique. The minimum distance of the free margin was determined as 1 mm for invasive cancers and in situ carcinoma cases. Breast cancer classification into surrogate intrinsic subtypes was based on the IHC assessment of ER, HER2 and Ki67 with a 20% cut-off.

During the investigated period, the chemotherapy regimen was based on FAC (5-fluorouracil, doxorubicin, and cyclophosphamide), FEC (5-fluorouracil, epirubicin, and cyclophosphamide) and taxanes. Chemotherapy was indicated in triple-negative, HER2-positive breast cancers and in high-risk luminal HER2-negative tumours.

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