Trends in diagnostic confirmation and treatment of pre-malignant abnormalities at screening mammography

Valorization

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The national breast cancer screening program is a free of charge biennial screening mammography for women aged 50-75 years.[1,2] Yearly, approximately 1.3 million women are invited to the nationwide breast cancer screening program in the Netherlands, of whom almost 1 million women participate. Ever since the introduction of the screening program there has been a broad support among Dutch women, which is expressed by an attendance rate of approximately 80%.[3]
After its introduction many scientific papers have reported about the favorable results of the screening program. Detection of the disease in a less advanced stage will improve the prognosis and allows a less extensive and aggressive treatment with less side-effects.[4-6] In an effort to detect breast cancer in its earliest phase any breast abnormality found at screening mammography is examined in close detail, which has resulted in a sharp increase in the detection rates of DCIS and other pre-malignant diseases. A substantial part of these pre-malignant abnormalities may not proceed into invasive breast cancer during a woman's lifetime,[7,8] and part of them may even regress spontaneously.[9] From the aforementioned we can conclude that the diagnosis and subsequent treatment of pre-malignant lesions may not be necessary in some women and could be seen as overtreatment, thereby creating avoidable morbidity.[10-12] Another downside of screening mammography which must not be overlooked are the false positives recalls, which not only cause extra medical costs and psychological stress, but also a potential burden of subsequent unnecessary invasive biopsies.[13] A careful consideration of the harm-benefit balance associated with breast cancer screening continues to be a matter of debate.
This thesis provides a substantiated contribution to the discussion about overtreatment, because it creates more awareness of the magnitude of the problem. Moreover, this thesis helps clinicians to safely refrain from interventions and form the basis for further research in order to combat overdiagnosis and subsequent overtreatment.

Social and economic relevance

This thesis provides additional evidence for the beneficial effect of screening mammography programs. Our study shows that screen-detected DCIS was mainly high grade in contrast to invasive carcinomas which were mainly found to be low or intermediate grade. This observation suggests that treatment of poorly differentiated DCIS detected through mammographic screening could play a role in the relative reduction of the incidence of poorly differentiated invasive carcinoma, assuming that high-grade DCIS was removed before it could develop into high-

grade invasive cancer.[14,15]. Furthermore, our study justifies repeated screening, as in every subsequent screening round new and clinically relevant abnormalities are detected.

This thesis also addresses the risk of overdiagnosis and subsequent overtreatment associated with screening, by creating awareness of the trends in invasive diagnostics procedures and their outcome in women with a breast abnormality found at screening mammography. Our data suggest that it is safe omit invasive diagnostic interventions, such as secondary excision biopsies, which should only be considered if radiologic surveillance and repeated percutaneous biopsy continue to yield indeterminate results. Furthermore, there are growing concerns about the increasing trend of recall for suspicious microcalcifications, which is accompanied with a growing number of recalled women with benign pathology. Therefore, invasive diagnostic intervention for microcalcifications should be considered carefully and preference should be given to radiologic surveillance if possible.

In the treatment of DCIS, this thesis shows that the trend of additional radiotherapy following breast conserving surgery (BCS) is decreasing. A more restrictive use of invasive diagnostic procedures and therapeutic interventions such as radiotherapy will not only reduce the physical and psychological burden for the patients, but it will also reduce healthcare costs.

Target audience

This thesis targets a broad audience as it contains valuable information for all members of the multidisciplinary tumor board, namely surgeons, radiologists, medical oncologists, pathologists, radiotherapists and other specialists such as general practitioners (who will eventually perform follow-up of these patients). This thesis attempts to contribute to the discussion in the multidisciplinary tumor board to more often refrain from invasive interventions instead of following the motto 'better be safe than sorry'. Omitting invasive unnecessary diagnostic or therapeutic interventions prevents avoidable morbidity. Furthermore, patients undergoing BCS for non-palpable disease will benefit from new localization methods, such as iodine-125 guided localization, which proved to be as accurate as wire-guided localization, but is reported as more patient friendly, less painful and has logistic advantages [16-19].

The future

As for this moment, predicting which pre-malignant lesions will regress and which will proceed to invasive breast cancer is almost impossible. For that reason, most

patients will undergo surgical treatment. This thesis contributes to the shift of 'one size fits all'-treatment to a more personalized treatment of pre-malignant lesions detected at mammographic screening. Less invasive treatment options for these pre-malignant lesions are currently subject of ongoing studies consisting of close follow up versus surgical excision.[20,21] Tailoring treatment of these lesions to the likelihood of progression to invasive disease is the next step in preventing overtreatment. The main goal for future research should be improving our ability to refrain from invasive diagnostics and treatment whenever possible.

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