Optimizing the axillary management in breast cancer

IMPACT PARAGRAPH

Breast cancer is the most common cancer amongst women worldwide and a major public health issue. Each year approximately 15.000 patients are diagnosed with invasive breast cancer in the Netherlands, accounting for 14.8% of the cancer health care costs. Over the past decades, the survival rates of breast cancer patients have increased substantially due to widespread screening, improved diagnosis, and treatment. The breast cancer treatment consists of breast and axillary surgery, complemented by radiation therapy and/or systemic therapy (chemotherapy, immunotherapy, hormone therapy) if indicated. Due to the improvement of survival rates, the treatment outcome has increasingly focused on optimizing the quality of life as well as the aesthetic outcome while preserving oncological safety.

At the time of breast cancer diagnosis, accurate assessment of the presence and extent of axillary lymph node metastasis plays a central role in disease prognosis, breast cancer staging, and treatment decision-making. Imaging techniques play an important role in the axillary lymph node staging to provide extensive preoperative information. Over the years, axillary staging for clinically node-negative patients (i.e, negative findings based on physical examination and axillary ultrasound) has evolved from axillary lymph node dissection (ALND; the surgical removal of all axillary lymph nodes) with its associated morbidity to the less invasive sentinel lymph node biopsy (SLNB; the surgical removal of the first lymph node(s) to which the breast tumor is likely to spread) procedure. For clinically node-positive patients (i.e., biopsy-proven axillary lymph node metastasis before any treatment), ALND or less invasive axillary staging procedures can be performed.

Relevance of the scientific results in this thesis

The first part of this thesis focused on optimizing the axillary lymph node staging with noninvasive imaging modalities. In the preoperative diagnostic workup, breast MRI is performed in around 30% of the breast cancer patients and enables the simultaneous assessment of the breast tumor and axillary lymph nodes in the same field of view. However, approximately 40% of the breast MRI examinations have an incomplete field of view of the axillary region. Therefore, dedicated axillary MRI (i.e., MRI of the complete axillary region) has been explored to improve axillary lymph node imaging. Within a single group of breast cancer patients, we compared breast MRI with a complete field of view of the axillary region to dedicated axillary MRI to investigate the axillary lymph node staging. Both MRI examinations showed no difference in diagnostic performance.

In clinical practice, a dedicated axillary MRI is therefore unnecessary if the standard breast MRI protocol is optimized with a complete field of view of the axillary region for the assessment of axillary lymph nodes.

Approximately 30% of breast cancer patients are treated with neoadjuvant systemic therapy (i.e., systemic therapy prior to definitive surgical treatment). Clinically node-positive patients treated with systemic therapy in the neoadjuvant setting can achieve a pathologic complete response (pCR; eradication of cancer cells) of the metastatic axillary lymph node(s), varying per breast cancer subtype. Currently, there is no noninvasive imaging modality that can accurately assess axillary pCR after neoadjuvant systemic therapy. Therefore, there is a trend towards less invasive axillary staging procedures to replace ALND. The second part of this thesis focused on the prediction of axillary pCR after neoadjuvant systemic therapy. We performed a systematic review and meta-analysis to provide an overview of axillary pCR rates for all breast cancer subtypes to implement these results in clinical practice. These data can help predict axillary treatment response in the neoadjuvant setting and thus select patients for more or less invasive axillary procedures.

After neoadjuvant systemic therapy, mastectomy (i.e., surgical removal of one or both breasts) is performed in about 30% of breast cancer patients. In patients receiving a mastectomy, breast reconstruction is increasingly chosen by women. The timing of breast reconstruction is one of the main considerations if reconstruction is considered: immediate reconstruction (i.e., at the time of mastectomy) or delayed reconstruction (i.e., at a later time). Immediate breast reconstruction is associated with a better aesthetic outcome, a major patient advantage for the psychological outcome, and lower overall costs. However, if postmastectomy radiation therapy (i.e., radiation therapy to the chest wall with or without the regional lymph nodes) is required after immediate breast reconstruction, this can lead to a higher risk of reconstruction complications. Residual axillary lymph node disease following neoadjuvant systemic therapy is one of the most important factors for the indication of postmastectomy radiation therapy, but the axillary lymph node status after neoadjuvant systemic therapy is unknown before the definitive surgery. In the third part of this thesis, we identified patient characteristics with a low and high risk of postmastectomy radiation therapy based on the axillary lymph node outcome after neoadjuvant systemic therapy to enable adequate shared decision-making regarding the timing of reconstruction.

Target population

The results of this thesis apply to newly diagnosed breast cancer patients who will undergo primary surgery or neoadjuvant systemic therapy. This thesis provides clinicians

in the multidisciplinary breast cancer team information about improving the imaging of the axillary lymph nodes. In addition, these results provide preoperative information about the axillary response to neoadjuvant systemic therapy to improve the selection of axillary surgery, and the sequence and outcome of breast reconstruction in the case of postmastectomy radiation therapy.

Implementation

In the first place, the results of this thesis were brought to attention by publications in renowned (inter)national journals with the breast cancer specialist as one of the target populations. In addition, these results were presented during both national and international meetings, creating a broad awareness among all clinicians involved in breast cancer care. By bringing these scientific results under the attention of clinicians, patients can be informed accordingly and contribute to adequate shared decision-making. Eventually, the ultimate goal is the implementation of these results in clinical guidelines to optimize breast cancer management. The third part of this thesis was brought to the attention of breast cancer clinicians by presenting the results multiple times during OncoZON, an oncology network meeting of nine hospitals and one radiation therapy institute of the Southeast Netherlands region. During these network meetings, based on the experience of the plastic surgeons, it was decided to perform the axillary surgery before the breast surgery in order to include the information of the axillary lymph node status after neoadjuvant systemic therapy in the decision-making process about the timing of breast reconstruction. However, in other hospitals, the decision to perform immediate or delayed reconstruction in the setting of postmastectomy radiation therapy can be individualized and take into account the experience of the (plastic) surgeon and the expectations of the patient.