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Routine use of standard breast MRI compared to axillary ultrasound for differentiating between no, limited and advanced axillary nodal disease in newly diagnosed breast cancer patients

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ABSTRACT

Objectives: To compare standard breast MRI to dedicated axillary ultrasound (with or without tissue sampling) for differentiating between no, limited and advanced axillary nodal disease in breast cancer patients.
Methods: All patients who underwent breast MRI and dedicated axillary ultrasound between 2009 and 2014 were eligible. Exclusion criteria were recurrent disease, neoadjuvant systemic therapy and not receiving completion axillary lymph node dissection after positive sentinel lymph node biopsy (SLNB). Two radiologists independently reassessed all MRI exams. Axillary ultrasound findings were retrospectively collected. Probability of advanced axillary nodal disease (pN2-3) given clinically node negative (cN0) or limited (cN1) findings was calculated, with corresponding negative predictive value (NPV) to exclude pN2-3 and positive predictive value (PPV) to identify axillary nodal disease. Histopathology served as gold standard.
Results: A total of 377 cases resulted in 81.4% no, 14.4% limited and 4.2% advanced axillary nodal disease at final histopathology. Probability of pN2-3 given cN0 for breast MRI and axillary ultrasound was 0.7–0.9% versus 1.5% and probability of pN2-3 given cN1 was 11.6–15.4% versus 29.0%. When cN1 on breast MRI was observed, PPV to identify positive axillary nodal disease was 50.7% and 59.0%.
Conclusions: Evaluation of axillary nodal status on standard breast MRI is comparable to dedicated axillary ultrasound in breast cancer patients. In patients who underwent preoperative standard breast MRI, axillary ultrasound is only required in case of suspicious nodal findings on MRI.

1. Introduction

Nowadays, preoperative axillary nodal staging in breast cancer patients consists of axillary ultrasound with concomitant tissue sampling if indicated [1]. Although, detection of every positive node was important in the past [2], recent studies such as the ACOSOG Z0011, IBCSG 23-01 and AATRM 048/13/2000 trials have shown that completion axillary lymph node dissection (ALND) after the detection of limited axillary nodal disease (i.e. 1–3 positive nodes) does not improve prognosis [3–5]. As a consequence, excluding advanced axillary nodal disease (i.e. more than 3 positive nodes)

Abbreviations: ALND, axillary lymph node dissection; cN0, no suspicious lymph nodes; cN1, 1-3 suspicious lymph nodes; MRI, magnetic resonance imaging; NPV, negative predictive value; pN2-3, ≥3, axillary lymph node metastases; PPV, positive predictive value; SLNB, sentinel lymph node biopsy.

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rather than detecting clinically node positive disease is becoming increasingly important.

Previous studies addressing the diagnostic performance of axillary ultrasound reported a negative predictive value (NPV) of 96% to exclude advanced nodal disease in case of node negative findings [6,7]. However, axillary ultrasound appears unable to differentiate between limited and advanced axillary nodal disease in case of positive axillary ultrasound findings, with a reported NPV of 50% [8].

According to a recent systematic review, MRI might be a promising non-invasive nodal staging tool for preoperative evaluation of the axilla to determine node negative and node positive disease in breast cancer patients [9]. However, the publications studied in this review did not investigate the ability of MRI to determine the number of positive nodes for differentiating between no, limited and advanced axillary nodal disease. Only a few studies compared MRI to ultrasonography, the most frequently used imaging modality for this purpose in daily practice [10]. If preoperative MRI, which is often part of the diagnostic work-up of newly diagnosed breast cancer patients, could improve nodal staging, axillary treatment could be even more patient-tailored.

Thus, the aim of this study was to investigate the diagnostic performance of standard breast MRI compared to dedicated axillary ultrasound to differentiate between no, limited and advanced axillary nodal disease, with pathology serving as the gold standard.

2. Material and methods

2.1. Patient selection

All patients diagnosed between 2009 and 2014 with invasive breast cancer who underwent both standard breast MRI and axillary ultrasound prior to surgery were eligible for this study. Exclusion criteria were recurrent breast cancer, patients primarily treated with neoadjuvant systemic therapy or patients with a positive sentinel lymph node biopsy (SLNB) who did not receive a completion ALND. Due to the retrospective design of this study, the necessity to acquire informed consent from the study subjects was waived by the local medical ethics committee.

2.2. Standard breast MRI exam and image analysis

All included patients underwent a standard breast MRI protocol to evaluate breast cancer extent and the presence of contralateral breast cancer. Breast MRI was performed in prone position on two different 1.5 T MRI scanners (Ingenia and Intera, Philips Healthcare, Best, the Netherlands). Both MRI scanners used a body coil, which was in 2011 replaced by a dedicated 16-channel breast coil. Evaluation of the axillary lymph nodes was performed on a non-enhanced 3D T2W Turbo Spin Echo sequence. This sequence is part of the standard breast MRI protocol, which further consisted of dynamic, contrast-enhanced T1W sequence protocols using fat saturation and diffusion weighted imaging (DWI). Over the years, the MR sequence protocols were only slightly changed (Appendix A).

A resident in radiology (M.S.) with two years of experience in breast radiology, pre-screened all breast MRI exams on technical quality criteria. Eligibility criteria were inclusion of the full axillary region including for example the sternoclavicular joint, axillary vein and the latissimus dorsi muscle. In addition, the axillary region had to be free of motion artefacts or inadequate signal-to-noise-ratio.

All axillary lymph nodes (i.e. axillary level 1–3, without assessment of the periclavicular and/or internal mammary lymph nodes) within one patient were separately counted and qualitatively assessed by two expert breast radiologists with 7 years (M.B.I.L.) and 5 years (S.V.) of breast imaging experience, respectively. Both radiologists were blinded for each other's results and to the histopathological outcome of the tumour and lymph nodes. However, radiologists were aware of the clinical tumour size, as assessed on mammography, ultrasound and/or breast MRI, similar to clinical practice.

Each individual lymph node was scored according to the criteria previously defined by Baltzer et al., using a confidence scale from 0 (no lymph nodes) to 4 (definitely malignant) [11]. Suspicious characteristics included irregular margins, inhomogeneous cortex, perifocal edema, absent fatty hilum, asymmetry, and absence of chemical shift artefacts [11–13] (Fig. 1).

Clinical axillary nodal staging was based on the number of suspicious axillary lymph nodes: none (cN0), limited (cN1, 1–3 suspicious lymph nodes) and advanced (cN2-3, >3 suspicious lymph nodes) axillary nodal disease. In patients diagnosed with bilateral invasive breast cancer, lymph nodes were assessed in both axillae separately.

2.3. Axillary ultrasound

Axillary ultrasound exams were performed by dedicated breast radiologists, using an ATL-HDI5000 system in combination with a linear 5 to 12-MHz array transducer, which in 2011 was replaced by an iU22-xMATRIX ultrasound system with a linear 2 to 17-MHz array transducer (both systems: Philips Healthcare, Best, the Netherlands). Criteria for a suspicious axillary lymph node on axillary ultrasound consisted of diffuse cortical thickening, focal cortical mass and/or thickening and loss of the fatty hilum [6]. The result of these exams, including the number of suspicious axillary lymph nodes, was extracted from the radiology report for each individual patient. Tissue sampling was performed in case of suspicious axillary lymph nodes using 16–18 gauge core needle biopsy. When core needle biopsy was challenging, fine needle aspiration cytology was used. In cases of multiple suspicious nodes, only the most suspicious node was sampled and the number of suspicious nodes was reported [8,14]. In this study, dedicated axillary ultrasound was defined as axillary ultrasound with or without tissue sampling if deemed necessary by the radiologist on call.

In contrast to MRI, clinically node positive disease with ultrasound was always histopathologically confirmed. Diagnostic performance of axillary ultrasound was described earlier by Schipper et al., by using the same study subjects between 2009 and 2012 ($n = 243$) [8]. In our current study, axillary ultrasound results were used for per-patient comparison with results of breast MRI.

2.4. Surgical nodal staging

In clinically node negative patients, based on negative axillary ultrasound findings or sampled tissue without evidence of tumour cells, SLNB was performed. The sentinel lymph node was identified by using a triple technique consisting of lymphoscintigraphy (using 80 MBq Technetium–99 m nanocolloid injected peri-areolar), blue dye to detect lymphatic vessels (Bleu Patente V®; Guerbet, Aulnay-sous-Bois, France), and a gamma probe to detect radioactivity. In case of one or more histopathologically confirmed metastases, a completion level I–II ALND was performed. In clinically node positive patients, based on tissue sampling with evidence of tumour cells after suspicious axillary ultrasound findings, ALND was performed.

2.5. Histopathological evaluation

Sentinel lymph nodes were sliced with a maximum thickness of 3 mm and paraffin embedded for histological evaluation. Step-sectioning at 500 micrometer intervals was done at three levels and