

Incremental Cancer Detection of Locoregional Restaging with Diagnostic Mammography Combined with Whole-Breast and Regional Nodal Ultrasound in Women with Newly Diagnosed Breast Cancer

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Rationale and Objectives: This study aims to determine if locoregional restaging with diagnostic mammography and ultrasound (US) of the whole breast and regional nodes performed for quality assurance in women with newly diagnosed breast cancer who were referred to a tertiary care center yields incremental cancer detection.

Materials and Methods: An institutional review board-approved retrospective, single-institution database review was performed on the first 1000 women referred to our center in 2010 with a provisional breast cancer diagnosis. Locoregional restaging consisted of diagnostic full-field digital mammography combined with US of the whole breast and regional nodal basins. Bilateral whole-breast US was performed in women with contralateral mammographic abnormality or had heterogeneously or extremely dense parenchyma. Demographic, clinical, and pathologic factors were analyzed.

Results: Final analyses included 401 women. Of the 401 women, 138 (34%) did not have their outside images available for review upon referral. The median age was 54 years (range 21–92); the median tumor size was 2.9 cm (range 0.6–18.0) for women whose disease was upstaged and 2.2 cm (range 0.4–15.0) for women whose disease was not upstaged. Incremental cancer detection rates were 15.5% (62 of 401) in the ipsilateral breast and 3.9% (6 of 154) in the contralateral breast ($P < 0.0001$). The total upstage rate was 25% (100 of 401). Surgical management changed from segmentectomy to mastectomy in 12% (50 of 401). The re-excision rate after segmentectomy was 19% (35 of 189).

Conclusions: Locoregional restaging with diagnostic mammography combined with whole-breast and regional nodal US that is performed for standardization of the imaging workup for newly diagnosed breast cancer patients can reduce underestimation of disease burden and impact therapeutic planning.

Key Words: Breast cancer; staging; nodes; mammography; ultrasound.

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INTRODUCTION

Locoregional staging of breast cancer is performed not only to determine the primary tumor size (T stage) and the regional nodal status (N stage), but also to identify additional foci of malignancy and to delineate the extent of disease to facilitate optimal treatment. The primary tumor size and the regional nodal status are important prognostic indicators. Neoadjuvant chemotherapy (NAC) is offered to women with node-positive or aggressive disease (ie, triple-negative or human epidermal growth factor receptor 2-positive [HER2+] subtypes) or large tumors. Defining the extent of the disease aids surgical planning and helps determine the appropriateness of breast-conserving surgery (BCS) vs mastectomy. The clinical N stage, which is based in part on imaging data, guides adjuvant radiation planning.

The standard of care for initial staging of breast cancer is imaging with mammography. The most common adjunct modalities to mammography are ultrasound (US) and magnetic resonance imaging (MRI). The use of breast US varies from whole breast to mammographic- or MRI-directed, targeted breast US. Additionally, the use of US to examine nodal basins has not been universally adopted. When regional nodes are examined using US, some centers evaluate only the axilla and other centers evaluate all regional nodal basins of the breast, including the axillary, infraclavicular, internal mammary, and supraclavicular regions. Despite reports in literature showing that MRI can identify additional disease in both the ipsilateral and contralateral breasts, the use of breast MRI for staging remains practice dependent (1,2). Controversy remains regarding benefits of preoperative breast MRI as measured by rates of re-excision, recurrence, and survival (3–6).

For women with newly diagnosed breast cancer who are referred to tertiary care centers, the pre-referral diagnostic breast imaging workup varies widely in the approach and the extent of the staging evaluation. Because of this variability, breast imaging for these women may have to be repeated for quality assurance. The primary aim of the present study was to determine if locoregional restaging using diagnostic mammography and whole-breast and regional nodal US in women with newly diagnosed breast cancer impacts the incremental cancer detection rate (ICDR) relative to initial interpretations based on outside imaging (OSF). The secondary aim was to determine how locoregional restaging impacts the clinical stage.

MATERIALS AND METHODS

Patient Selection

This single-institution, Health Insurance Portability and Accountability Act-compliant, retrospective study was approved by the institutional review board with a waiver of informed consent. We reviewed the records of the first 1000 women who were referred to our imaging center with a provisional diagnosis of breast cancer in 2010. Women with the following characteristics were excluded: (1) prior excisional biopsy,

which provided the diagnosis of breast cancer ($n = 131$); (2) missing OSF reports ($n = 119$); (3) prior OSF staging breast MRI ($n = 117$); (4) consultation at our institution before 2010 ($n = 83$); (5) stage IV disease ($n = 39$); (6) receipt of NAC ($n = 35$); (7) suspected rather than biopsy-proven breast cancer ($n = 19$); (8) prior OSF positron emission tomography-computed tomography or breast-specific gamma imaging for staging ($n = 16$); (9) recurrent breast cancer ($n = 16$); (10) ductal carcinoma in situ with no residual calcifications after biopsy ($n = 12$); (11) restricted charts that required patient permission for review ($n = 7$); or (12) lymphoma or metastatic disease to the breast ($n = 5$). Thus, a total of 401 of the first 1000 women referred to our imaging center in 2010 were included in our data analysis.

Clinicopathologic Assessment

The following data were extracted directly from the OSF reports and on-site imaging reports and compared: largest index tumor dimension; chest wall, skin, or nipple involvement; nodal disease; focality or centricity (unifocal, multifocal, or multicentric disease); laterality (ipsilateral \pm contralateral disease); clinical stage; and the type of definitive surgery performed (segmentectomy or mastectomy). Multifocal disease was defined as a disease with two or more foci separated by ≥ 0.5 and < 4.0 cm within the same quadrant of the breast (7). Multicentric disease was defined as disease extending over two or more quadrants of the breast or disease with foci separated by ≥ 4.0 cm (7).

All outside breast and nodal histopathology data were routinely reviewed by dedicated breast pathologists. Diagnosis of invasive lobular carcinoma (ILC) was confirmed with E-cadherin staining. Diagnosis of HER2+ tumors was determined by immunohistochemistry or by fluorescence in situ hybridization.

On-Site Mammography Performed During Locoregional Restaging

Bilateral full-field digital mammography (FFDM) was performed by obtaining three standard views (craniocaudal, mediolateral oblique, and lateromedial) with a mammography unit (Selenia; Hologic, Bedford, MA). Additional views were performed as necessary. Each mammogram was originally interpreted by 1 of 14 dedicated breast radiologists with ≥ 5 years of experience; these radiologists had access to the diagnostic findings from the OSF if the patients had the images and reports with them at the time of referral to our center.

On-Site US Performed During Locoregional Restaging

Grayscale and color Doppler US were performed using a Sonoline Antares system with a 5- to 13-MHz broadband linear transducer (Siemens Ultrasound, Mountain View, CA) by one of nine dedicated breast sonographers. Unilateral whole-breast ultrasound (UWBUS) of the affected breast including

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