International Journal of Radiation Oncology biology • physics

www.redjournal.org

Clinical Investigation

Role of Ultrasonography of Regional Nodal Basins in Staging Triple-Negative Breast Cancer and Implications For Local-Regional Treatment

Simona F. Shaitelman, MD, EdM,* Welela Tereffe, MD, MPH,* Basak E. Dogan, MD,† Kenneth R. Hess, PhD,‡ Abigail S. Caudle, MD, MS,§ Vicente Valero, MD,‖ Michael C. Stauder, MD,* Savitri Krishnamurthy, MD,¶ Rosalind P. Candelaria, MD,† Eric A. Strom, MD,* Wendy A. Woodward, MD, PhD,* Kelly K. Hunt, MD,§ Thomas A. Buchholz, MD,* and Gary J. Whitman, MD†

**Division of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas; †Department of Diagnostic Radiology, The University of Texas MD Anderson Cancer Center, Houston, Texas; ‡Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, Texas; §Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas; ‖Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas; and ¶Department of Pathology, The University of Texas MD Anderson Cancer Center, Houston, Texas*

Received Mar 4, 2015, and in revised form May 1, 2015. Accepted for publication May 12, 2015.

Summary

Ultrasonographic staging of nodes is now recommended prior to neoadjuvant systemic therapy for breast cancer. How this impacts clinical stage and treatment decisions among women with triple-negative breast cancer is uncertain. In this

Purpose: We sought to determine the rate at which regional nodal ultrasonography would increase the nodal disease stage in patients with triple-negative breast cancer (TNBC) beyond the clinical stage determined by physical examination and mammography alone, and significantly affect the treatments delivered to these patients.

Methods and Materials: We retrospectively reviewed the charts of women with stages I to III TNBC who underwent physical examination, mammography, breast and regional nodal ultrasonography with needle biopsy of abnormal nodes, and definitive local-regional treatment at our institution between 2004 and 2011. The stages of these patients' disease with and without ultrasonography of the regional nodal basins were compared using the Pearson χ^2 test. Definitive treatments of patients whose nodal

Reprint requests to: Simona F. Shaitelman, MD, EdM, Division of Radiation Oncology, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Unit 1202, Houston, TX 77030. Tel: (713) 563-8491; E-mail: sfshaitelman@mdanderson.org

Part of the findings herein were presented at the 56th Annual Meeting of the American Society of Radiation Oncology, San Francisco, CA, Sep 2014.

Conflict of interest: S.F.S. has received a grant from Elekta for work unrelated to that described in this article and is a consultant for the MD Anderson Physicians Network. M.C.S. is a consultant for the MD Anderson Physicians Network.

Int J Radiation Oncol Biol Phys, Vol. 93, No. 1, pp. 102–110, 2015
0360-3016/$ - see front matter
http://dx.doi.org/10.1016/j.ijrobp.2015.05.015

retrospective chart review, 19.4% of patients had an increase in clinical disease stage with the incorporation of ultrasonography. Ultrasonographic upstaging significantly increased the use of axillary lymph node dissection and radiation to the regional nodal basins.

disease was upstaged on the basis of ultrasonographic findings were compared to those of patients whose disease stage remained the same.

Results: A total of 572 women met the study requirements. In 111 (19.4%) of these patients, regional nodal ultrasonography with needle biopsy resulted in an increase in disease stage from the original stage by physical examination and mammography alone. Significantly higher percentages of patients whose nodal disease was upstaged by ultrasonographic findings compared to that in patients whose disease was not upstaged underwent neoadjuvant systemic therapy (91.9% and 51.2%, respectively; $P<.0001$), axillary lymph node dissection (99.1% and 34.5%, respectively; $P<.0001$), and radiation to the regional nodal basins (88.2% and 29.1%, respectively; $P<.0001$).

Conclusions: Regional nodal ultrasonography in TNBC frequently changes the initial clinical stage and plays an important role in treatment planning.

Introduction

The 2014 National Comprehensive Cancer Network guidelines recommend that patients who have breast cancer and clinically negative axillary lymph nodes on physical examination and who are being considered for neoadjuvant systemic therapy undergo axillary ultrasonography (1). When axillary ultrasonography reveals suspicious lymph nodes, the suspicious nodes should be sampled via fine-needle aspiration biopsy (FNAB) or core biopsy, and an image-detectable marker clip should be placed in the biopsied lymph node to ensure its removal at the time of definitive surgery (1).

How definitive local-regional treatment is altered on the basis of initial staging using ultrasonography and lymph node biopsy remains uncertain. Accurate initial staging of the lymph nodes before the start of systemic therapy may allow for appropriate local-regional treatment decisions to be made. For example, patients who are staged with node-negative disease by physical examination and do not undergo ultrasonography could have involved lymph nodes that resolve with neoadjuvant systemic therapy. These lymph nodes would not be detected by sentinel lymph node biopsy, and such patients might not receive adequate surgery or radiation therapy to ensure the eradication of microscopic residual nodal disease.

Because patients with triple-negative breast cancer (TNBC) typically undergo neoadjuvant systemic therapy as the standard of care, ultrasonography during initial staging can help ensure that diseased lymph nodes do not go undetected. TNBC has been found to be more responsive to neoadjuvant systemic therapy than other forms of breast cancer (2); as such, accurate initial clinical staging is important to ensure thoughtful targeting of local-regional treatment, particularly for radiation that targets areas at risk of harboring microscopic residual disease. Conversely, identifying those patients whose TNBC is refractory to systemic therapy, which portends worse outcomes, may allow for intensified systemic and local-regional treatments.

The goal of our study was to characterize the rate of nodal disease upstaging as a result of regional nodal ultrasonography and ultrasonography-guided biopsy in TNBC patients. We also sought to determine how changes in nodal staging affected local-regional treatment.

Methods and Materials

Using a prospectively maintained database, we conducted a retrospective review of all patients with TNBC evaluated at our institution between 2004 and 2011. This retrospective study was approved by the institutional review board at our institution. Electronic medical records were also reviewed to obtain detailed information about staging evaluation and local-regional treatment delivered. Patients were excluded from analysis for the following reasons: they had stage 0 or IV breast cancer at presentation, had inflammatory breast cancer at presentation, were male, had a history of breast cancer, had synchronous or metachronous contralateral breast cancer, a lack of definitive local-regional surgery, or had had treatment with breast-conserving surgery without adjuvant radiation therapy. Patients were also excluded if all definitive local-regional treatment (including surgery and radiation therapy, if delivered) was not performed at our institution; if the estrogen receptor, progesterone receptor, and *HER2/neu* amplification status were not confirmed at our institution; or if the initial staging did not include physical examination, diagnostic mammography, and ultrasonography of the breast and regional nodal basins with needle biopsy as clinically indicated.

Physical examination of each patient's breasts and regional lymph nodes had been conducted by a breast oncologist (medical, surgical, or radiation). Bilateral diagnostic mammography was performed and interpreted by one of our institution's breast radiation specialists. All patients underwent breast and regional nodal basin ultrasonography, which was performed by 1 of 12 dedicated radiologists in our institution, using Antares ultrasonography units (Siemens