

Staging Investigations in Early-Stage Breast Cancer Patients: Are Clinically Significant and Rational?

S ALAM^a, MMA SAYED^b, MA RAHMAN^c, K RAHMAN^d

Abstract:

Introduction: Multiple studies have demonstrated that the yield of imaging for distant metastatic disease is low in patients with early-stage breast cancer without signs and symptoms of metastatic disease. So, a study was carried out to assess the clinical significance and usefulness of staging investigations in newly diagnosed early-stage breast cancer patients.

Materials and method: A retrospective review of medical records of 171 patients with early-stage (stage I & II) breast cancer referred to the Tumor Board & Radiation Oncology department of NICRH and one private hospital after having surgery & adjuvant chemotherapy during the two-year period (January 2019-December 2020), were performed. The staging investigations the patients underwent perioperatively and the value of those in detecting metastasis were evaluated.

Result: All patients had chest radiography and routine blood tests performed preoperatively. Postoperative chest radiography evaluation in various frequencies were done in 156 (91.22%) patients. CT scans of the chest were performed in 13 patients

(7.6%). One patient (0.64%), who had complained of cough was diagnosed with pulmonary metastasis after evaluation. An ultrasonogram (USG) of the whole abdomen was done preoperatively in 135 patients (78.9%) & postoperatively and subsequently in 162 patients (94.7%) in various frequencies and CT scans of the abdomen were done in 7 patients (4.1%). No metastasis was detected by USG or CT scan of the abdomen. Bone scan was done in 53 patients (31%). Four patients (4/53) were diagnosed with bony metastases out of which 2 had symptoms of bone pain. Routine bone scan can pick up 2(3.7%) bone metastases in asymptomatic patients.

Conclusion: Staging investigations for distant metastases in newly diagnosed early-stage breast cancer patients in the absence of signs and symptoms of metastatic disease have low yield, not evidence-based, not cost-effective and thus not recommended.

Keywords: staging investigations, early-stage breast cancer, Clinically significant

(J Bangladesh Coll Phys Surg 2024; 42: 38-42)
DOI: <https://doi.org/10.3329/jbcps.v42i1.70640>

Introduction:

Breast cancer is the most frequently diagnosed cancer in females globally and is the leading cause of cancer-related death, accounting for 25% of cancer cases and 15% of cancer Death.¹ Breast cancer is also the top malignancy in females in Bangladesh. Hospital Cancer

Registry Report 2015-2017, published by the National Institute of Cancer Research & Hospital, Bangladesh, shows that Breast cancer is the top most cancer in females accounting for 30.4%, and the second most common malignancy when both sexes combined (14.1%) among 35370 cancer patients attended at NICRH during that period.²

Treatment and prognosis of breast cancers are navigated by the stage of the disease, which primarily reflects the anatomical extent of the disease. Staging aims to convey a consistent method for understanding the extent and hence the risk of cancer and guiding the therapeutic decision. The widely used AJCC system is a clinical and pathological staging system based on the TNM system. TNM stages I and II (T1-3, N0-1) are the early stages of breast cancer and are traditionally operable. Together they constitute 75% to 80% of all breast cancer cases in developed countries where screening mammograms have been adopted.³

- Dr. Shahida Alam, Associate Professor, Department of Radiation Oncology, National Institute of Cancer Research & Hospital (NICRH), Mohakhali, Dhaka.
- Dr. Mollah Md. Abu Sayed, Associate Professor of Surgery. Project Director, Modernization and Expansion of Bangladesh College of Physicians and Surgeons.
- Dr. Md. Ashiqur Rahman, Assistant Professor, Department of Surgical Oncology, NICRH, Mohakhali, Dhaka.
- Dr. Khadija Rahman, Assistant Professor, Department of Surgical Oncology, NICRH, Mohakhali, Dhaka.

Address of Correspondence: Dr. Shahida Alam, Associate Professor, Department of Radiation Oncology, National Institute of Cancer Research & Hospital (NICRH), Mohakhali, Dhaka. Mobile : 01711785326, E-mail : dr.shahida.alam@gmail.com

Received: 4 Oct., 2022

Accepted: 19 June, 2023

Besides a complete history and physical examinations for clinical staging, consensus guidelines concerned have made recommendations regarding further work up. For the assessment of general health status full blood count, liver, renal and cardiac functions are recommended. The extent of the disease evaluation usually consists of the chest and abdominal CT scan with contrast, radionuclide whole body bone scan, and /or PET Ct scan.⁴ Multiple studies have demonstrated that the yield of imaging for distant metastatic disease is low, particularly in patients with early stages of breast cancer without signs and symptoms of metastatic disease.^{5,6} Cough, respiratory distress, abdominal pain, jaundice or skeletal pain, or neurological signs and symptoms are suggestive of metastatic disease.

As part of the Choosing Wisely Campaign, the American Society of Clinical Oncology (ASCO) recommended against the use of routine PET, CT and radionuclide bone scans for evaluation of asymptomatic patients with stage I-II breast cancer, since in that setting there is a low risk of having identifiable metastatic disease.⁷ According to NCCN guidelines, a chest diagnostic CT is indicated only if pulmonary symptoms are present. Abdominal imaging using diagnostic CT on MRI is indicated only if the patient has elevated Alkaline phosphatase, abnormal liver function tests, abdominal symptoms, or abnormal physical examination. A bone scan is only indicated in patients with localized bone pain or elevated alkaline phosphatase.⁴

Many patients have extensive staging investigations to complete their metastatic work-up following a diagnosis of breast cancer.^{5,8} Chest radiography, Ultrasonography of the whole abdomen along with whole body bone scan are still commonly used to detect subclinical metastatic disease though the usefulness of these tests is debatable considering their sensitivities and specificities.^{6,9,10}

Despite guidelines recommending against its routine use, perioperative imaging for distant metastasis is frequently performed in newly diagnosed breast cancer patients uncovering incidental findings of uncertain significance. So, a study was carried out to assess the clinical significance and usefulness of staging investigations in newly diagnosed early-stage breast cancer patients.

Materials and method:

A retrospective review of medical records of 171 patients with early-stage (stage I & II) breast cancer referred to the Tumor Board & Radiation Oncology department of NICRH and one private hospital after having surgery & adjuvant chemotherapy during a two-year period (January 2019-December 2020), were performed. The staging investigations the patients underwent perioperatively that is chest radiography, ultrasonography of whole abdomen and whole-body bone scan were evaluated and the value of those investigations in detecting metastasis were looked at. Data were analyzed using SPSS for Windows (version 25.0, Armonk, NY: IBM Corp.) software.

Results:

Among the 171 early-stage breast cancer cases available for review, the median age at diagnosis was 45.0 (SD ± 10.33) years. On the basis of pathological staging, five patients (2.9%) were in stage 0, thirty-one patients (18.1%) were in stage IA, fifty-seven patients (33.3%) were in stage IIA & seventy-eight patients (45.6%) were in stage IIB. Eight patients had complained of bone pain, five patients had complained of cough and two patients complained of abdominal pain.

All patients (100%) had chest radiography and routine blood tests performed preoperatively as part of staging and anesthetic workup. The subsequent investigations were done either by the surgeon post-operatively or by the oncologist before starting chemotherapy, during chemotherapy, and before starting radiotherapy. Postoperative chest radiography evaluations in various frequencies were done in 156 (91.2%) patients. CT scans of the chest were performed in 13 patients (7.6%). Four patients had a suspicious lesion in chest radiography which was evaluated by a CT scan of the chest with contrast. CT scan was nonsignificant for three patients. One patient (0.64%), who had complained of cough was diagnosed with pulmonary metastasis after abnormal CT scan finding and CT-guided FNAC of lung lesion.

An Ultrasonogram (USG) of the whole abdomen was done preoperatively in 135 patients (78.9%) & postoperatively and subsequently in 162 patients (94.73%) in various frequencies. It was done once in 81 (47.0%) patients, twice in 68 (40.0%) patients, thrice in

10 (6.0%) patients and quadruple in 4 (2.0%) patients. CT scans of the abdomen were done in 7 patients (4.1%). Two patients had suspicious hepatic SOL, which was proved nonsignificant by USG-guided FNAC from the lesions.

A bone scan was done in 53 patients (31%), and increased tracer uptake was identified in six patients (6/53). Out of which two patients who were asymptomatic underwent MRI evaluation and proved as no metastatic bony lesion. Four patients (4/53) were diagnosed with bony metastases out of which two (3.7%) had symptoms of bone pain. Routine bone scan could pick up 2 (3.7%) bone metastasis in asymptomatic patients.

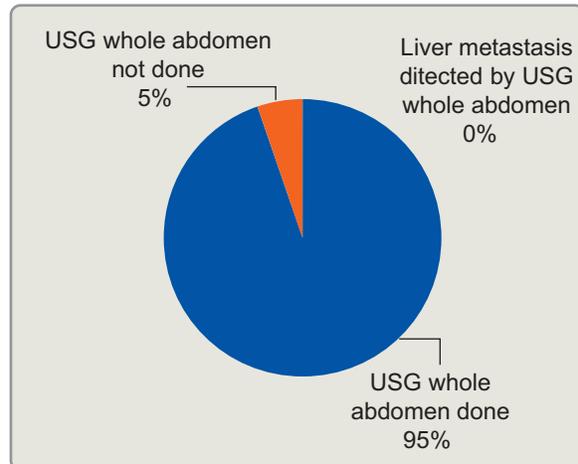


Fig.-3: Evaluation of abdomen by USG of whole abdomen.

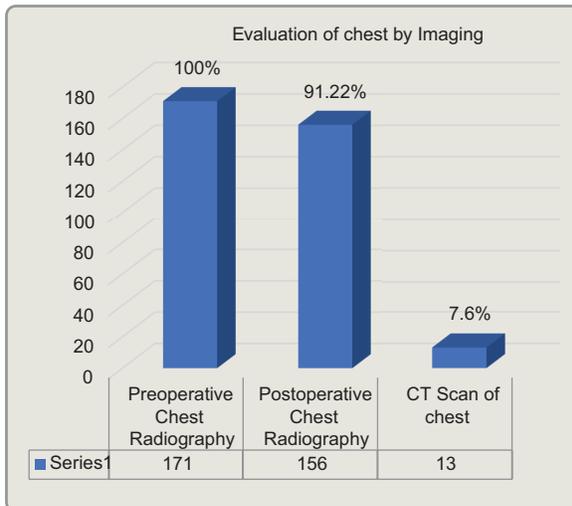


Fig.-1: Evaluation of chest by imaging.

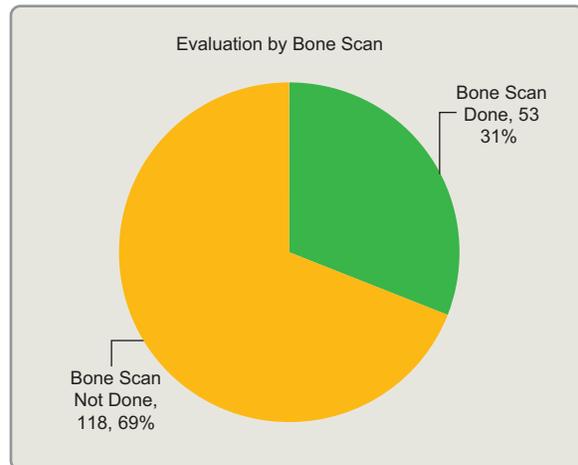


Fig.-4: Evaluation by whole body bone scan.

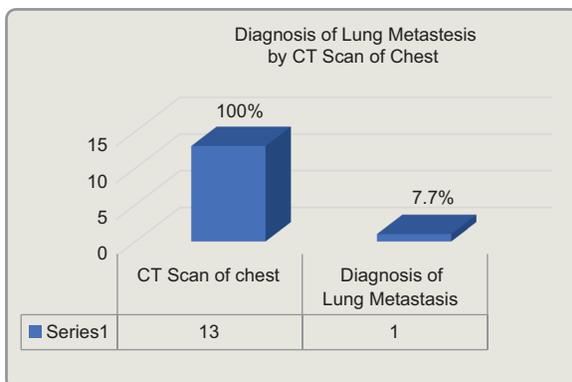


Fig.-2: Diagnosis of lung metastases by CT scan of chest.

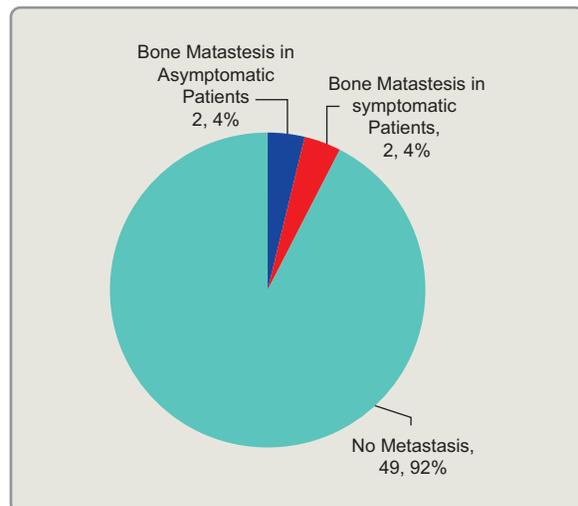


Fig.-5: Diagnosis of bone metastases by bone scan.

Discussion:

The evaluation of patients newly diagnosed with breast cancer begins with the determination of operability. The presence of distant metastases at diagnosis has traditionally been considered a contraindication of surgery. Extensive evaluation to look for metastatic disease is not warranted in asymptomatic patients with early stages because of the low likelihood of identifying metastatic disease.¹¹ Despite improvements in imaging modalities, clinical staging is still considered by many to be the most helpful and cost-effective.^{6,10}

Traditionally chest radiography, liver ultrasound, and isotope bone scan have been used to rule out chest, liver, and bone metastases in a patient newly diagnosed with breast cancer. However, the overall yield of these investigations is reportedly low^{5,6,8}, especially in early-stage diseases. Fewer than 5% of patients with early breast cancer have bone metastases at presentation¹¹, and the incidence of liver metastases is even lower.^{6,12} With locally advanced breast cancer (T3-4, N2), the incidence of metastases is much higher, and in those cases, more extensive investigations are justified.^{5,8}

According to NCCN guidelines, routine systemic imaging is not indicated for patients with early breast cancer without signs and/or symptoms of metastatic disease.¹⁴ These recommendations are based on studies showing no additional value of these tests in patients with early-stage disease.^{15,16,17} In one study evaluating patients with newly diagnosed breast cancer by bone scan, liver USG and chest radiography, metastases were identified by bone scan in 5.1%; 5.6%, and 14% of patients with stage I, II & III disease, respectively and no evidence of metastasis was detected by liver USG or chest radiography in patients with stage I or II diseases.¹⁴ Additional tests like contrast CT scan of the chest, CT scan of the abdomen with contrast, and bone scan may be considered only based on the signs and symptoms.⁴

A study by Rajiv Samant et al.¹⁸ confirmed the low yield of routine bone scans & liver imaging among patients with asymptomatic early-stage disease, overall, three percent (5/161) of patients with pathologic T1-2 N0-1 disease had metastases diagnosed compared with 30% (18/61) of a patient with pathological stage T3-4 or N2 disease. Only two patients with metastatic disease were diagnosed solely on bone scan results, none were diagnosed solely on liver USG.

A systemic review of the published literature combined with a consensus interpretation of the evidence in the context of conventional practice revealed, A total of 5407 women participated in 9 studies of bone scanning reported between 1985 and 1995; in these studies. Bone scans detected skeletal metastases in only 0.5% of women with stage I disease, 2.4% with stage II, and 8.3% with stage III. Among 1625 women in 4 studies of liver ultrasonography reported between 1988 and 1993, hepatic metastases were detected in 0% of patients with stage I disease. 0.4% with stage II and 2% with stage III. Among 3884 patients in 2 studies of chest radiography published in 1988 and 1991, lung metastases were detected in 0.1% of those with stage I, 0.2% with stage II and 1.7% with stage III. False positive rates ranged from 10% to 22% for bone scanning, 33% to 66% for liver ultrasonography, and 0% to 23% for chest radiography.¹⁹

In our study, it was observed that newly diagnosed patients with early-stage breast cancer frequently underwent staging investigations like chest radiography, ultrasonography of the whole abdomen, and whole-body bone scan. After evaluation of the staging investigations five patients (1 patient with lung metastasis and 4 patients with bone metastases -2.9%) were diagnosed as having a metastatic disease based on chest radiography, CT scan chest and bone scan out of which 3(1.75%) had symptoms at initial presentation. No metastasis was detected by USG or CT scan of the abdomen. These data are similar to other published data.

Our results confirmed that chest radiography, USG of the whole abdomen, whole body bone scan, and CT scan of the chest and abdomen in asymptomatic early-stage breast cancer patients are of low yield. Most patients (3/5) with metastatic diseases at presentation had clinical signs and symptoms suggestive of metastatic disease. One patient, who had complained of cough was diagnosed with pulmonary metastasis after abnormal CT scan finding and CT-guided FNAC of lung lesion. A Liver USG or CT scan of the abdomen did not detect any patient with subclinical metastatic disease.

Out of four patients diagnosed with bone metastases, two had localized bone pain. Routine bone scans only picked up two (3.7%) (N=51) bone metastasis in asymptomatic patients.

Conclusion:

Routine staging investigations in asymptomatic early-stage breast cancer patients are likely to be of low yield with minimum clinical significance. We can avoid psychological, financial burden and huge pressure on our overburdened infrastructure by simply not doing routine staging investigations in this setting. So, staging investigations for distant metastases in early-stage breast cancer patients who are asymptomatic have a low yield, not evidence-based, not cost-effective, and not recommended by the consensus guidelines.

References:

1. Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. *CA Cancer J Clin* 2015;65(2):87-108.
2. Hospital Cancer Registry Report 2015-2017. Dhaka: National Institute of Cancer Research & Hospital (NICRH); December 2020.
3. American Joint Committee on Cancer, AJCC Cancer Staging Manual. 8th Edition, 2018; Springer International Publishing.
4. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer Version 2.2022-December20,2021; MS-14. NCCN Guidelines for patients available at www.nccn.org/patients.
5. Nomura Y, Kondo H, Yamagata J, et al. Evaluation of liver and bone scanning in patients with early breast cancer, based on results obtained from more advanced cancer patients. *Eur J Cancer*. 1978; 14:1129-1136
6. Baker RR. Preoperative assessment of the patient with breast cancer. *Surg Clin North Am*. 1984; 64:1039-1050
7. Schnipper LE, Smith TJ, Raghavan D et al. American Society of Clinical Oncology identifies five key opportunities to improve care and reduce costs: the top five list of oncology. *J Clin Oncol*. 2012 May 10;30(14):1715-24.
8. Khansur TR, Haick A, Patel B, Balducci L, Vance R, Thigpen T. Evaluation of bone scan as a screening work-up in primary and loco-regional recurrence or breast cancer. *Am J Clin Oncol*. 1987; 10: 167-170.
9. Berman CG, Clark RA. Diagnostic imaging in cancer. *Prim Care*. 1992; 19:690-695
10. Kinne DW. Staging and follow-up of breast cancer patients. *Cancer*. 1991; 67:1196-1198
11. Tham YL, Kramer R, Osborne CK. Evaluation of patients for metastasis prior to primary therapy. In: Harris JR, Lippman ME, Morrow M et al. eds. *Disease of Breast*. 4th ed, Philadelphia: Lippincott Williams & Wilkins;2010-483.
12. Lee YN. Bone scanning in patients with early breast cancer: should it be a routine staging procedure? *Cancer*. 1982; 47:486-495
13. Sears HR, Gerber FH, Sturtz DC, et al. Liver scan and carcinoma of the breast. *Surg Gynecol Obstet*, 1975;140:409-411
14. Baseline staging tests in primary breast cancer: Practice guideline report# 1-14: Members of the Breast Cancer Disease Site Group.
15. Ravaoli A, Pasini G, Polselli A, et al. Staging of breast cancer: new recommended standard procedure. *Breast Cancer Res Treat* 2002;72:53-60.
16. Puglisi F, Follador A, Minisini AM, et al. Baseline staging tests after a new diagnosis of breast cancer: further evidence of their limited indications. *Ann Oncol* 2005; 16:263-266.
17. Brothers JM, Kidwell KM, Brown RK, Henry NL. Incidental radiologic findings at breast cancer diagnosis and likelihood of disease recurrence. *Breast Cancer Res Treat* 2016;155:395-403.
18. Rajiv Samant, MD; Pradip Ganguly MD. Staging Investigations in Patients with Breast Cancer- The Role of Bone Scans and Liver Imaging.
19. Robert E, Myers, Mary Johnston et al. and the Breast Cancer Disease Site Group of the Cancer Care Ontario Practice Guidelines Initiative. Baseline staging tests in primary breast cancer: a practice guideline. *Canadian Medical Association Journal*, May 2001;164(10): 1439-44