



The effect of internal mammary lymph node biopsy on the therapeutic decision and survival of patients with breast cancer

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Abstract

Background: The role of internal mammary lymph node biopsy (IMLNB) is still being discussed in breast cancer treatment. The aim of this study was to investigate the role of IMLNB on adjuvant therapy and survival of patients with breast cancer.

Patients and methods: The data of 72 patients with clinically negative axilla and IMLNB were evaluated. IMLNB was performed either through a small separate intercostal incision or from the same incision for tumor resection or mastectomy by using both blue dye and radioisotope. Pathological analysis was performed on formalin-fixed paraffin-embedded tissues.

Results: Ten of the patients (14%) were IMLNB-positive. The axillary sentinel lymph node and IMLN were negative in most of the patients (52.8%). In one patient (1.4%), the axilla was negative but the IMLNB was positive. IMLNB changed the pathologic stage in eight patients (11%). Adjuvant internal mammary radiotherapy was added to the treatment protocol for 10 patients due to IMLNB positivity and adjuvant chemotherapy was added in for only one patient with negative axilla. The factors found to be related with IMLN positivity were SLN positivity ($p = 0.033$), mastectomy ($p = 0.022$), and the number of resected IMLN ≥ 2 ($p = 0.040$).

The median follow-up time was 115.5 months (range, 30–162 months). The ten-year overall survival (OS) rate was 86%. Systemic metastasis ($p = 0.007$), SLNB positivity ($p < 0.001$), and IMLNB positivity ($p = 0.005$) were statistically related to overall survival.

Conclusion: IMLNB positivity in patients with breast cancer changed the pathologic stage and adjuvant treatment modalities of patients and also adversely affected the overall survival.

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Keywords: Internal mammary lymph node biopsy; Early stage breast cancer; Sentinel lymph node biopsy; Stage migration; Survival

Introduction

Sentinel lymph node biopsy has replaced axillary dissection in patients with node negative breast cancer in recent years and become the standard procedure to stage the axilla. Despite the progress in breast cancer management, the role of internal mammary lymph node biopsy in breast

cancer treatment is controversial.^{1–3} In contrast to the high success rate of IMLNB, the lymphatic flow by lymphoscintigraphy to the extra-axillary lymph nodes were low in different series, ranging from 0% to 37%.^{4–9} Over the last two decades, visualization of internal mammary lymph nodes by preoperative lymphoscintigraphy has attracted attention again, most recently to the internal mammary chain.^{1–3}

The increase in evaluation of IMLNs required change in the American Joint Committee on Cancer (AJCC) staging system.¹⁰ The staging system of AJCC has included the

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internal mammary chain lymph nodes and IMLNB positivity raises the stage, thus indicating worse prognosis and requiring adjuvant internal mammary chain radiotherapy.¹⁰ The adjuvant treatment protocol should be changed, especially in patients with negative axilla and positive IMLNs.^{11–13} Radiation therapy to the internal mammary chain may be omitted in patients with negative IMLN, thus sparing patients from its cardiac and pulmonary toxicities.^{14–16}

IMLN positivity has been accepted as an important prognostic and predictive factor in many studies.^{17,18} Its positivity rate has increased in patients with positive axilla, and 5–17% of patients with breast cancer are IMLN positive only, but negative in the axilla.^{19–21} In patients with IMLN involvement only, prognosis is similar to patients with negative axilla regarding both locoregional recurrence and survival.^{18,21} Adjuvant radiation and systemic treatments are necessary in these patients. The prognosis of patients with axillary and IMLN involvement have been found to be worse than for those who are positive in either lymphatic region alone.^{17,22} Many studies showed that IMLN positivity is an independent predictor of poorer outcome in patients with breast cancer.²³

In this study, we reviewed our experience at a single institution where IMLN biopsies are performed. The aim of the study was to analyze 72 patients who underwent IMLN biopsy to investigate the rate of nodal positivity, evaluate the association with axillary nodal status, and determine how identification of IMLN metastasis affected staging, management, and survival of patients with breast cancer.

Patients and methods

Between October 1998, and December 2008, 890 patients with stage I and II breast cancer underwent SLNB in the Breast Unit of Istanbul University, Istanbul Medical Faculty, Department of General Surgery. Patients who had bilateral breast cancer, without internal mammary lymph flow at lymphoscintigraphy, and did not have regular follow-up were excluded from the study. SLN procedure was performed with the combination of lymphoscintigraphy, blue dye and intraoperative gamma probe (Europrobe, Eurorad, France). Preoperatively, lymphoscintigraphy was performed with both peritumoral and subareolar injection of Tc-99m sulfur radiocolloid (Nanocis, Cis-Bio International, Schering, France). The criteria to perform IMLNB was clinically node-negative breast cancer in patients who had undergone SLN dissection and drainage to the internal mammary chain. Drainage to the internal mammary chain (IMC) was detected in 72 of the 890 patients (8.1%) and IMLN biopsy was performed either through a small separate intercostal incision or from the same lumpectomy or mastectomy incisions. After the pectoral muscle fibers were split, the intercostal muscles were cut to expose the fatty tissue along the internal mammary vessels on the

surface of the parietal pleura. An intercostal retractor was used to widen the intercostal space. SLNs resected from IMC were sent to pathology and routine pathologic analysis was performed in formalin-fixed paraffin-embedded tissues. SLNs were analysed using hematoxylin and eosin and immunohistochemical techniques.

The patients' age, surgical techniques, surgical morbidity, tumor localisation, tumor size, histopathologic types, local and systemic recurrences, and mortality were recorded from the files. The TNM AJCC 6th edition was used in the staging of patients.²⁴ This study was approved by the University Ethics Committee and all participating patients gave informed consent. We analyzed the visualization of the IMLNs, and the presence of IMLN metastasis using SPSS 22.0 (IBM SPSS software). Chi-square tests were used to compare the patient groups with respect to age, tumor localisation, tumor type, tumor size, axillary nodal status, and IMLN status.

The ability to find factors that predict IMLN positivity before surgery in patients with positive drainage to the internal mammary chain on lymphoscintigraphy and gamma probe may help to identify patients who can avoid IMLN biopsy because lymphatic drainage to the internal mammary lymphatic region does not mean metastasis to these specific lymph nodes. Furthermore, if factors related with IMLN positivity are known before surgery in patients who do not have lymphoscintigraphy, this will enable physicians to make better informed decisions as to whether an IMLN biopsy is required. A multivariable logistic regression analysis was performed to determine the independent predictive effect of these co-variables on IMLN positivity. Kaplan–Meier survival analysis was used to show the 10-year overall survival rate and a Cox regression analysis was used to detect the factors related to survival.

Results

Among the 890 patients, 72 patients (8.1%) underwent IMLN biopsy. The median age of 72 patients was 50.0 years (range, 24–74 years). The patients' characteristics are given in [Table 1](#). IMLN biopsy was performed by using the combination of lymphoscintigraphy, blue dye and gamma probe in all patients. The tumors were localized in the upper inner quadrant in 40 patients (55.6%), lower inner quadrant in 12 patients (16.7%), central in 9 patients (12.5%), upper outer quadrant in 8 patients (11.1%), and lower outer quadrant in 3 patients (4.1%). Regarding tumor stages, 37 patients had T1 (≤ 2 cm) and 35 patients had T2 or T3 tumors. The histopathology report showed invasive ductal carcinoma in 52 patients, invasive lobular carcinoma in 4, mixed type in 8 patients, and other pathologies in 8 patients. Most of the patients (62.5%) underwent breast conserving surgery. The median number of dissected IMLNs was 1 (range, 1–6).

The intra-operative morbidity rate for IMLNB was 5/72 (7%). The pleural cavity was breached and repaired without

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