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Level III lymph node involvement in breast carcinoma

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ABSTRACT

As the trend is towards conservative surgery for the breast carcinoma, the necessity of the complete axillary dissection is being questioned much more today. In this study, we aimed to analyze the frequency of level III lymph node metastases and the contributing risk factors. Eighty-seven female, histopathologically proven breast carcinoma patients underwent modified radical mastectomy and complete axillary dissection in the Department of First General Surgery, Ankara Oncology Hospital. The level III specimen was sent separately to the pathological examination. Age, menopausal status, tumor location, histopathological type, grade, pathological T and N stage, estrogen (ER) and progesterone (PR) receptor status, multicentricity, total metastatic lymph nodes in level I+II, lymph node capsule invasion (N1b3, N2) were analyzed as the risk factors. Mean age of the 87 patients was 49±11.6 (median: 48, min.: 24, max.: 75). Most of the patients were premenopausal (52.9%, 46/87) and had their tumors located in the upper outer quadrant (64.4%, 56/87) with the histopathological type of invasive ductal carcinoma (88.5 %, 77/87). Forty-four of the cases (50.6%) were in T2 stage. Fifty-one patients (58.6%) had grade 2 tumors. The pathological workup revealed ER positivity in 52.9% patients (46/87), PR positivity in 31% patients (27/87), lymph node capsular invasion (N1b3 and N2) in 37.9% (33/87) and multicentricity in 16.1% patients (14/87). There were 7 patients (8%) in Stage I, 18 (20.4%) in Stage IIA, 30 (34.5%) in Stage IIB and 32 (36.8%) in Stage IIIA. Sixty-two out of 87 (71.2%) had axillary lymph node metastases. Lymph node metastases in level I+II were detected in 61 patients (70.1%), where level III involvement were detected in 27 patients (31%). Forty-two percent of the patients that had involved level I+II lymph nodes also had metastases in level III. Level III skip metastasis was detected in one patient (1.14%). The stage, lymph node capsular invasion and the presence of more than 2 metastatic nodes in level I+II were found to be statistically significant for level III metastases. According to our results for appropriate staging and adequate local control we recommend complete axillary dissection including level III lymph nodes except for a selected group of patients. [Turk J Cancer 2007;37(3):109-113]

KEY WORDS:

Breast carcinoma, level III lymph node, metastases

INTRODUCTION

Today treatment of the axilla with surgery remains an integral part of the management of patients with invasive cancer. In general the minimum standard treatment of the axilla involves surgical clearance of axillary nodes from Level I and II. There is yet little evidence that axillary treatment improves survival but the issue remains controversial (1).

The axillary lymphatics are the major regional drainage area of the breast and are frequently involved with metastatic disease from the breast cancer (2). The pathological status of the axillary lymph nodes is regarded as the most important prognostic factor in breast cancer (3,4). However management of the axilla is currently far from being uniform and includes axillary node biopsy or sampling, sentinel lymph node biopsy, partial or lower axillary node

dissection, complete axillary lymphadenectomy (CAL) and radiotherapy to the regional lymph nodes alone or in combination with a surgical procedure (5).

The extent to which the axilla should be dissected to provide accurate pathologic information remains unclear. Some authors believe in that a complete axillary dissection is necessary to provide accurate information for staging and prognostic purposes. Opponents, however, feel that a partial axillary dissection reliably assesses the axillary contents and at the same time is associated with less morbidity (6-8). To clarify this issue we assessed the frequency and pattern of Level III lymph node involvement in a series of patients undergoing modified radical mastectomy with complete axillary dissection as primary treatment for operable breast cancer.

MATERIALS AND METHODS

Eighty-seven female, histopathologically proven breast carcinoma patients who underwent modified radical mastectomy and complete axillary dissection in the Department of First General Surgery, Ankara Oncology Hospital between the years of 1999-2001 were analyzed in this prospectively designed study. The level III specimen was sent separately to the pathological examination. The independent parameters used were; age, menopausal status, tumor location, histopathological type, grade, pathological T stage, pathological N stage, Estrogen and Progesterone receptor status, multicentricity, number of metastatic lymph nodes in the axilla level I+II, lymph node capsular invasion and TNM stage (1997, fifth edition). Because of the time the study was conducted staging was analysed according to the fifth TNM edition. The involvement of Level III LN was accepted to be the dependent parameter. The locally advanced breast cancer patients who were operated after receiving neoadjuvant chemotherapy weren't included in this study.

Statistical analysis

The statistical methods used included Pearson χ^2, Fisher's exact, Student t, Kruskal Wallis and Mann Whitney U test.

Technique of dissection

All axillary dissections were performed with the transaction of the insertion of pectoralis minor muscle and removal of all lymph node bearing fibroadipose tissue inferior to the axillary vein from Halsted's ligament me-

Table 1
Patient characteristics of the study group

	n	%
Premenopausal	46	52.9
Postmenopausal	41	47.1
Upper Outer	56	64.4
Upper Inner	13	14.9
Lower Outer	12	13,8
Lower Inner	5	5.7
Central	1	1.1
Invasive Ductal Ca	77	88.5
Invasive Lobular Ca	4	4.6
Tubular Ca	6	6.9
T1	14	16.1
T2	44	50.6
T3	29	33.3
Stage I	7	8.0
Stage IIA	18	20.7
Stage IIB	30	34.5
Stage IIIA	32	36.8
N0	25	28.7
N1	29	33.3
N1b3	17	19.5
N2	16	18.4
MC (+)	14	16.1
MC (-)	73	83.9
G I	10	11.5
G II	51	58.6
G III	26	29.9
ER (-)	41	47.1
ER (+)	46	52.9
PR (-)	22	25.3
PR (+)	27	31.0
PR (?)*	38	43.7
CI (-)	54	62.1
CI (+)	33	37.9
Level I+II	61	70.1
Level I+II+III	62	71.2
Level III	27	31
Level III Skip	1	1.14

Ca: Carcinoma; MC: Multicentricity; CI: Capsular invasion of lymph nodes
*PR was not available due to technical inadequacy

Table 2
Level III metastases according to "p" N status

"p" N Status	Level III Metastases (n)		Total
	(-)	(+)	
"p" N0	25	0	25
"p" N1	30	16	46
"p" N2	5	11	16
Total	60	27	87

Table 3
The relation between the no. of metastatic lymph nodes in Level I+II and Level III metastases

Level III Metastases	Level I+II Metastases (n)		Total
	0-2	>2	
(-) %	41 (68.3%)	19 (31.7%)	60 (100%)
(+) %	3 (11.1%)	24 (88.9%)	27 (100%)
Total %	44 (50.6%)	43 (49.4%)	87 (100%)

dially, to the latissimus dorsi laterally and inferiorly to the junction of the thoracodorsal vessels with the latissimus dorsi and long thoracic nerve with the serratus anterior muscle. As the defined lateral margin of Level III (infraclavicular region) is the medial border of pectoralis minor muscle; before cutting the insertion of pectoralis minor for the complete axillary dissection the fibrofatty tissue was drawn align near the medial border of pectoralis minor by using electrocautery in order to define the margins clearly for not to include lymph nodes from Level I and II and where level I and II were signed together by silk suture. The borders of Level III dissection was accepted as follows: The medial border is costoclavicular ligament (Halsted's Ligament), lateral border is the drawn line with electrocautery, superior border is the axillary vein and the inferior border is the intersection between the thoracic wall and pectoralis minor.

RESULTS

The mean age of 87 patients was 49.8 ± 11.6 (median: 48, min.: 24, max.: 75). As seen on the table 1, 62 out of 87 (71.2%) had axillary lymph node metastases. Lymph node metastases in level I+II were detected in 61 patients (70.1%), where level III involvement was detected in 27 patients (31%). Forty-two percent of the patients that had involved level I+II lymph node also had metastases in level III. Level III skip metastasis was detected in one patient (1.14%). The mean numbers of dissected total lymph nodes in the Level I+II and Level III were 14.5±5.7 and 5.7±4.8, respectively whereas the mean numbers of dissected metastatic lymph nodes in the Level I+II and Level III were 4.0±5.0 and 1.1±2.2, respectively.

Sixteen out of 46 "p" N1 patients and 11 out of 16 "p" N2 patients had Level III metastases. This finding was found to be statistically significant (p=0.001) (Table 2).

As seen on table 3, 88.9% of cases who had more than 2 metastatic LN in Level I+II also had Level III metastases. This correlation was also found to be statistically significant (p=0.0001).

According to table 4, LN capsular invasion was detected in 19 out of 27 Level III metastatic patients which was found to be statistically significant (p=0.0001).

As seen on the table 5, 9 of 30 Stage IIb patients and 15 of 32 Stage IIIa patients also had metastases in Level III. A statistically significant result was found between TNM Stage and Level III metastases (p=0.034).

DISCUSSION

The trend in breast cancer surgery is toward more conservative operative procedures, and many have questioned the value of complete axillary dissections in the

Table 4
LN capsule invasion and level III metastases

Capsule Invasion	Level III Metastases (n)		Total
	(-)	(+)	
(-)	46	8	54
(+)	14	19	33
Total	60	27	87

Table 5
TNM stage and level III metastases

TNM Stage	Level III Metastases (n)		Total
	(-)	(+)	
Stage I	7	0	7
Stage IIA	15	3	18
Stage IIB	21	9	30
Stage IIIA	17	15	32
Total	60	27	87

management of primary breast cancer (4,9). It is widely held that involvement of the lymph nodes occurs in a stepwise continuous fashion from the periphery of the axilla medially, and that the level of involvement at diagnosis has an important bearing on prognosis (8). This concept has been questioned by some who believe that prognosis is best predicted from the number of involved nodes and also because so-called discontinuous or skip metastases have been described in the literature (8,10).

Axillary lymph node status is the single most important prognostic variable in patients with breast cancer and is an important determinant of which patients should receive adjuvant systemic therapy (5). However, management of the axilla is far from being uniform. By the way, any of the lesser axillary surgical procedures would require the addition of therapy to the axilla for disease control (4,11). Fisher et al. (12) have noted a 21% axillary recurrence rate in patients with clinically negative axilla who received no additional treatment for that region. This recurrence rate can be reduced to 1% with complete axillary dissection (4,12). It has been shown that clinical examination of the axilla is notoriously inaccurate in staging with up to a 30% false (+) rate and up to a 45% false (-) rate.

As many as 40% or more of patients with positive level I axillary nodes will have involvement of higher levels in the axilla as well (4,9). In the analysis of five studies by Danforth et al. (2), metastatic lymph nodes would be left behind in 51.2% to 82% of patients after Level I dissection and 21.4% to 44.8% of patients after Level I+II dissection. In a study of Chevinsky et al. (4), 60% of patients with involved Level I lymph nodes had involvement of nodes in Levels II and III as well. If these nodes were left unattended, recurrence in local axillary nodes might take place, leaving the physician with a dilemma.

The studies in the literature revealed that approximately 35% to 50% of patients with clinically detected invasive cancer prove to be node positive following axillary lymph node dissection (ALND) (13). The skip level III metastases are ranging 0.1% to 12% in the literature. Furthermore, the highest level as well as number of LN metastases are significantly related to prognosis (8).

In our study, 62 out of 87 patients (71.2%) had axillary lymph node metastases (pN+). Lymph node metastases in level I+II were detected Forty-two percent of the patients that had involved level I+II lymph nodes also had metastases in level III. Level III skip metastasis was detected in one patient (1.14%). Our result of pN (+) patients (71.2%) is impressively higher than the reported studies.

Although the extent of the ALND seems to have no effect on breast cancer mortality, it does influence the risk of axillary relapse offering a more adequate local control. The greater the extent of ALND, the less the risk of axillary relapse is. In a retrospective review of 3128 clinically node negative patients, the 5 year risk of axillary recurrence ranged from 19% when no nodes were removed to 3% when more than five nodes were removed (1).

In some series of the literature it has been shown that apical metastases were more frequent (43.8% as compared with 6.1%) when gross disease was found in level I and II nodes (5). In our study, the Level III LN metastases were more frequent when there were more than 2 involved nodes in the Level I+II and when gross conglomerated LN -a sign of capsule invasion- was detected. Our study revealed that the Level III LN metastases were rare in the subgroup of patients who had 2 and lower metastatic nodes in the axilla; which may suggest performing Level I+II LN dissection would be appropriate in that group of patients.

Axillary recurrences are a marker of tumor biology, indicating an increased risk for distant metastases and death (1). Nonetheless, women are often emotionally devastated following a loco-regional relapse. Many regard such recurrences as a death sentence. Furthermore, recurrences often cause morbidity: major vessels and nerves of the axilla are sometimes invaded, causing pain or lymph edema. In such cases, the axilla is difficult to manage, and the risk of complications associated with axillary treatment is greatly increased. Thus, adequate treatment of the axilla at initial diagnosis of primary breast cancer is important. Failure to provide adequate treatment can adversely affect the quality of life and may cause significant morbidity in later years (1,13,14).

In conclusion, according to results of these series level III lymph node metastases are not rare cases and for today CAL offers a highly effective local control and appropriate staging except for a very selected group of patients who might have lower than two or less metastases in level I and II.

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