Annals of Nuclear Medicine Vol. 18, No. 4, 309–313, 2004

Value of axillary lymphoscintigraphy in patients with operated breast carcinoma

Gülin VURAL,* Elçin ÖZALP,* Tamer ÇALIKOGLU,** Ali Rıza ÜÇER,**
Sema DURMUŞ,** Bülent TURGUT* and Nur ERÇAKMAK*

*Department of Nuclear Medicine, **Department of Radiation Oncology,
Ankara Oncology Hospital, Ankara, Turkey

Purpose: To evaluate axillary dissection with axillary lymphoscintigraphy (ALS) in postoperative patients with breast carcinoma and its role in adjuvant radiotherapy (RT). Additionally, to define axillary dissection as complete and incomplete with ALS and to correlate it with the number of removed lymph nodes. ***Material and Methods:*** In the last two years, 121 women were studied four weeks after operation. Bilateral second interdigital subcutaneous injections were performed for ALS. Complete and incomplete axillary dissection were interpreted according to the number of surgically removed lymph nodes. ALS was interpreted as complete if no accumulation was shown. ***Results:*** There was a good correlation between the number of surgically removed lymph nodes and complete and incomplete interpretation on ALS ($p < 0.004$). The number of removed lymph nodes was equal to or greater than 15 in 72% patients with complete dissection according to ALS. Of 48 patients with surgically incomplete axillary dissection, 18 (38%) showed no accumulation in the axillary region, while 25 of 68 (37%) patients with surgically complete dissection showed accumulation in the axillary region and were interpreted as incomplete according to ALS. Indication of RT was changed after ALS in patients with 1 to 3 involved lymph nodes. While RT was not considered in 12 of these patients before ALS, they were included in RT planning. On the other hand, 17 patients, considered for RT previously, were excluded from RT planning after ALS. ***Conclusion:*** Evaluation of axillary dissection with ALS especially in suspicious patients with 1 to 3 lymph node metastases might prevent unnecessary morbidity and can be useful in selecting patients who truly need axillary irradiation.

Key words: breast cancer, axillary lymphoscintigraphy, radiation therapy

INTRODUCTION

ADJUVANT THERAPY (Radiotherapy-RT, Chemotherapy-CT) is performed for local and regional control and to prolong survival in patients with operated breast carcinoma.[1,2] Axillary nodal status and tumor size are the most important factors in deciding on the need for adjuvant therapy.[3,4] Axillary nodal status is defined according to the number of removed lymph nodes and those involved by tumor cells. The benefits of axillary dissection, apart from prognostic information obtained by pathologic staging, are not clear.[5] It has been generally accepted that axillary dissection in a patient with clinically negative axilla does not impact on disease free or overall survival.[6] However, the omission of lymph node dissection also raises concern about local recurrence.[5] This concern is perhaps less relevant to patients who are receiving conservative surgery and radiation therapy, because radiation to the axilla has been shown to provide excellent local control in clinically negative axilla cases.[7]

Since there was no standardization in radiation therapy techniques or indications for patients with breast carcinoma, our radiation oncology department improved their criteria in addition to classical points and requested our help in defining axillary dissection status before adjuvant

Received April 21, 2003, revision accepted February 25, 2004.

For reprint contact: Gülin Vural, M.D., Associate Professor, Bülbülderesi Caddesi, 124/3, 06660, Küçükesat/Ankara, TURKEY.

E-mail: drgulin@yahoo.com

RT planning. Axillary lymphoscintigraphy (ALS) has been used to demonstrate normal and pathologic lymph nodes and lymphatic drainage patterns in preoperative evaluation and to establish the presence of residual lymph nodes in the postoperative stage.[8,9] In this study, our aim was to evaluate axillary dissection with ALS in postoperative patients with breast carcinoma and its role in adjuvant RT planning and to correlate the number of removed lymph nodes with ALS results.

MATERIAL AND METHODS

Patients

During the last two years 121 women (mean age 49 yr, range 24–76 years) who had undergone modified radical mastectomy were studied four weeks after operation and before radiation therapy. According to the TNM classification, there were 3 stage I, 79 stage II and 39 stage III patients. Sixty-nine patients of 121 (57%) were operated on our hospital. Axillary lymph nodes showed histopathologically metastases in 93 patients (76%). Of them 53 had 1 to 3, 40 had 4 or more metastatic lymph nodes. Five patients with massive metastases were excluded from the study.

Imaging

Bilateral second interdigital subcutaneous injections were performed by using 18.5 GBq (500 μCi) Tc-99m nanocolloid in 0.3 m*l*. Anterior images of chest and axilla were obtained 1–2 hr later using LFOV gamma camera. Late images (4–24 hr) were also obtained to differentiate lymphatic pooling from lymph nodes. Body contour was drawn with point source for better anatomic visualization (internal mammary lymphoscintigraphy was also performed in some patients but is not mentioned here).

Interpretation

In our radiation oncology department, the indications of chest wall and axillary RT are T3–T4 tumors, incomplete axillary dissection, complete dissection with 4 or more positive lymph nodes, N2, N3 metastatic lymph nodes, axillar and supraclavicular fossa relapse.

Complete or incomplete axillary dissection was interpreted according to the number of surgically removed lymph nodes. Generally, complete axillary dissection was accepted in patients with at least 10 removed lymph nodes without metastases or 16 with metastases.

ALS was interpreted as complete if no accumulation was shown, and incomplete if accumulation was observed in the axillary region. The patients with massive metastases had been excluded from evaluation, because the chance of false negative ALS would be too high.

Statistical Analysis

The number of removed lymph nodes was correlated with complete and incomplete axillary dissection according to ALS using the Mann-Whitney U test. A statistically significant difference was considered present when p value < 0.05.

RESULTS

ALS was negative (no accumulation in the affected site) in 66 of 121 patients (52%) and interpreted as complete dissection. Five of these patients with metastases in all their removed lymph nodes showed no uptake on ALS, and were excluded from the evaluation. Only 61 patients with negative ALS were included in the study as complete dissection according to ALS.

There was a good correlation between the number of removed lymph nodes and complete and incomplete interpretation on ALS ($p < 0.004$). In patients with negative ALS (61 patients), 72% (44 patients) had 15 and more lymph nodes removed. On the other hand, 78% of patients with incomplete interpretation with ALS had equal to or fewer than 19 removed lymph nodes. Additionally, according to ALS, complete and incomplete groups

Table 1 Number of surgically removed lymph nodes and ALS results

Number of removed lymph nodes	Complete ALS		Incomplete ALS	
	pts (n)	%	pts (n)	%
<10	3	5	20	36
10–14	14	23	15	27
15–19	17	28	8	15
20–24	11	18	7	13
25–29	12	20	4	7
>30	4	6	1	2
	61	100	55	100

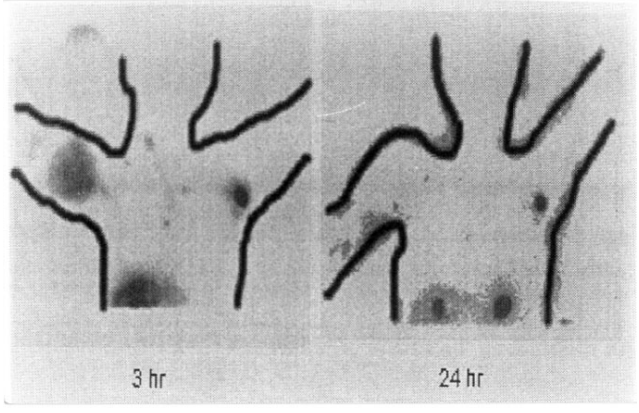

Fig. 1 Right axillary region shows lymphatic pooling on 3 hr image. Twenty-three lymph nodes were resected with 3 metastases. On the other hand, late image (24 hr) shows complete dissection. According to ALS, axillary RT was not considered for this patient. One right and one left (cross drainage) internal mammary node were observed on 3 hr image.

Table 2 Complete and incomplete evaluation

ALS	Axillary dissection surgically	
	Complete	Incomplete
Complete	43	18
Incomplete	25	30
Total	68	48

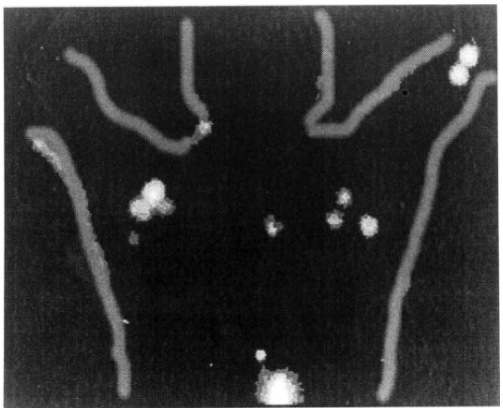

Fig. 2 Left axillary region shows radiocolloid uptake as three groups in this patient with 20 lymph nodes resected with 3 metastases. After ALS, axillary RT was planned. Additionally, two internal mammary lymph nodes were visualized on the left side.

showed similar percent values in patients removed between 10 and 14 lymph nodes (23% and 27% respectively) (Table 1).

Of 48 patients with surgically incomplete axillary dissection, 18 (38%) showed no accumulation in the axillary region and were interpreted as complete dissection according to ALS (Fig. 1). On the other hand, 25 of 68 (37%) patients with surgically complete dissection showed radiocolloid accumulation in the axillary region and were interpreted as incomplete dissection scintigraphically (Table 2, Fig. 2).

ALS results were not taken into account, and RT planning did not change in patients with T3, N2, 4 or more involved lymph nodes, N0 with at least 10 removed lymph nodes. However, indication of RT was changed after ALS in patients with 1 to 3 involved lymph nodes. While axillary and/or chest wall RT was not considered in 12 patients previously, they were included in RT planning, because ALS showed incomplete axillary dissection. On the other hand, 17 patients considered for axillary RT were excluded from RT planning, since their ALS showed no accumulation.

DISCUSSION

Local regional failure occurs as the first site of failure in approximately 15–20% of node negative[10,12] and 25–40% of node positive patients[11,13,14] with early stage cancer who do not receive systemic therapy. On the other hand, long term local-regional failure rates in patients with locally advanced tumors may be 40 % or higher.[15] Axillary lymph node status is the single most important prognostic variable in patients with early breast cancer and is an important determinant of which patients should receive adjuvant systemic therapy.[3] However, management of the axilla is currently far from being uniform and includes axillary node biopsy or sampling,[16,17] partial or lower axillary dissection,[18,19] total axillary dissection[20,21] and radiotherapy to the regional lymph nodes alone or in combination with a surgical staging procedure.[22,23]

Total axillary dissection is routinely performed for breast cancer at our oncology hospital. It has been reported that the risk of axillary relapse was inversly related to the number of axillary nodes resected,[18] and routine total axillary lymphadenectomy in patients with breast cancer is highly effective in preventing axillary recurrence while morbidity is low.[3] Moreover, recently, Touboul et al.[24] suggested that the risk of distant metastases increased with increased incidence of isolated local recurrences. There is no doubt that the use of postmastectomy radiotherapy will reduce local-regional failure rates.[25] The risk of nodal recurrence is low in patients with 1–3 positive nodes following level I, II or complete axillary dissection. Patients with 4 or more involved nodes have been irradiated in most series, but the results have not usually been subdivided by treatment techniques.[26] On the other hand, the risk of arm edema is substantially increased by giving full axillary irradiation to patients who have had a complete axillary dissection, but not when patients undergo a more limited dissection.[27,28]

Therefore, we should be able to make more certain decisions whether axillary dissection is complete or incomplete. With this goal in mind, we correlated ALS results with the number of removed lymph nodes. We evaluated 121 patients who had undergone modified radical mastectomy with ALS. In our study, it was found that of 48 patients whose axillary dissection was accepted as incomplete before ALS, 18 patients (38%) showed no accumulation in the axillary region and were interpreted as complete, 25 of 68 patients (37%) interpreted as complete dissection before ALS, showed radiocolloid accumulation in the axillary region and were interpreted as incomplete.

Although most authors currently agree that it is not necessary to irradiate the regional lymhpatics if an adequate axillary dissection was performed, considerable controversy exists regarding this subject.[29] Postmastectomy radiotherapy should not routinely be given to patients with negative axillary nodes or 1 to 3 positive nodes with tumors smaller than 5 cm in diameter. However, especially for patients with 1 to 3 positive nodes other factors (such as tumor size and the precense of lymphatic or vascular invasion) may be important in modifying this

recommendation. All patients with 4 or more positive nodes, primary tumors larger than 5 cm with involved axillary nodes or locally advanced (T4, N2) tumors should be irradiated.[30] We did not change RT planning in this group of patients. But, 12 patients who had 1 to 3 involved lymph nodes and were considered complete axillary dissection surgically, were included in RT planning since ALS showed activity accumulation in residual lymph nodes. On the other hand, 17 patients considered for radiotherapy were excluded from radiotherapy planning, because their ALS showed no accumulation. In our study, it was found that the number of removed lymph nodes was 15 or greater in 72% patients with complete dissection on ALS. Interestingly, patients with 10–14 dissected lymph nodes showed very close percent values in groups of complete and incomplete dissection, according to ALS (23% and 27% respectively). Our radiation oncology department also accepts complete dissection in patients with at least 10 lymph nodes removed without metastasis or 16 lymph nodes with metastasis. Although our radiation therapy indications have very large ranges, the radiation therapy planning was changed in a total of 29 patients after ALS.

In conclusion, risks of local and regional recurrences are decreased by adjuvant radiotherapy and chemotherapy. However after surgery, axillary radiotherapy increases the frequency of arm edema. Consequently, evaluation of axillary dissection with ALS, known as a noninvasive and physiologic method, especially in suspicious (indeterminate) patients with 1 to 3 lymph node metastases and/or dissection of fewer than 15 lymph nodes, might prevent unnecessary morbidity and can be useful in selecting patients who truly need axillary irradiation.

REFERENCES

1. Bonadonna G, Valagussa P. Adjuvant chemoendocrine therapy in breast cancer. *J Clin Oncol* 1986; 4: 451–454.
2. Early Breast Cancer Trials' Collaborative Group. Effect of adjuvant tamoxifen and cytotoxic therapy on mortality in early breast cancer: an overview of 61 randomized trials among 28896 women. *N Engl J Med* 1988; 319:1681–1692.
3. Gregory MS, Frederick LM, Kevin D, Mohammed MM, Kimberley CC, David SR, et al. Total axillary lymphadenectomy in the management of breast cancer. *Arch Surg* 1991; 126: 1336–1342.
4. Osborne CK, Clark GM, Ravdin PM. Adjuvant systemic therapy of primary breast cancer. In: Harris Lippmann ME, Morrow M, Helman S, eds. *Disease of the breast*. Philadelphia; J.B. Lippincott, 1996: 548–578.
5. Warmuth MA, Bowen G, Prosnitz LR, Chu L, Broadwater G, Peterson B, et al. Complications of axillary lymph node dissection for carcinoma of the breast : A report based on a patient survey. *American Cancer Society* 1998; 38 (7): 1362–1368.
6. Fisher B, Redmond C, Fisher ER, Brauer M, Wolmark N, Wicherham DL, et al. Ten year results of randomized clinical trial comparing radical mastectomy and total mastectomy with or without radiation. *N Engl J Med* 1985; 321: 674–681.
7. Haffy BG, McKhann C, Beinfield M, Fischer D, Fischer JJ. Breast conservation therapy without axillary dissection: a rational treatment strategy in selected patients. *Arch Surg* 1993; 128: 1315–1319.
8. Mattheiem W, Bourgeois P, Delcorde A, et al. Axillary dissection in breast cancer revisited. *Eur J Surg Oncol* 1989; 15: 490–495.
9. Mc-Lean RG, Ege GN. Prognostic value of axillary lymphoscintigraphy in breast cancer patients. *J Nucl Med* 1986; 27: 1116–1124.
10. Axelsson CK, Blichert-Toff M. Low risk breast cancer patients treated by mastectomy and lower axillary dissection: the present status of the Danish Breast Cancer Cooperative Group Trial 77-A. *Acta Oncol* 1988; 27: 605–609.
11. Arriagada R, Rutqvist CE, Mattsson A, Kramar A, Rotstein S. Adequate locoregional treatment for early breast cancer may prevent secondary dissemination. *J Clin Oncol* 1995; 13: 2869–2878.
12. Fisher B, Dignam J, Mamounas EP, et al. Sequential methotrexate and fluorouracil for the treatment of node negative breast cancer patients with estrogen receptor negative tumors: eight year results from the National Surgical Adjuvant Breast and Bowel project (NSABP) B-13 and first report of findings from (NSABP) B-19 comparing methotrexate, and fluorouracil with conventional cyclophosphamide, methotrexate and fluorouracil. *J Clin Oncol* 1996; 14: 1982–1992.
13. Rubens RD, Hayward JL, Knight RK, et al. Controlled trial of adjuvant chemotherapy with melphalan for breast cancer. *Lancet* 1983; 1: 839–843.
14. Castiglione-Gertsch M, Johnsen C, Goldhirsch A, et al. The International (Ludwig) Breast Cancer Study Group Trials I–IV: 15 years follow-up. *Ann Oncol* 1994; 5: 717–724.
15. Haagensen CD. *Diseases of the breast, 3rd ed*. Philadelphia; W.B. Saunders, 1986.
16. Kissin MW, Thompson EM, Price AB, Slavin G, Kark AE. The inadequacy of axillary sampling in breast cancer. *Lancet* 1982; 2: 1210–1212.
17. Steele RJC, Forrest APM, Gibson T, Stewart HJ, Chetty U. The efficacy of lower axillary sampling in obtaining lymph node status in breast cancer: a controlled randomized trial. *Br J Surg* 1985; 72: 368–369.
18. Graversen HP, Blichert-Toft M, Andersen JA, et al. Breast Cancer: risk of axillary recurrence in node negative patients following partial dissection of the axilla. *Eur J Surg Oncol* 1988; 14: 407–412.
19. Siegel BM, Mayzel KA, Love SM. Level I and II axillary dissection in the treatment of early-stage breast cancer: an analysis of 259 consecutive patients. *Arch Surg* 1990; 125: 1144–1147.
20. Rosen PP, Lesser ML Kinne DW, Beattie EJ. Discontinuous or "skip" metastases in breast carcinoma: analysis of 1228 axillary dissection. *Ann Surg* 1983; 197: 276–283.
21. Veronesi U, Rilke F, Luini A, et al. Distribution of axillary node metastases by level of invasion: an analysis of 539 cases. *Cancer* 1987; 313: 683–687.
22. Delouche G, Bachelot F, Premont M, Kurtz JM. Conservation treatment of early breast cancer: long term results and

complications. *Int J Radiat Oncol Biol Phys* 1987; 13: 29–34.
23. Langlands AO, Prescott RJ, Hamilton TA. Clinical trial in the management of operable breast cancer. *Br J Surg* 1980; 67: 170–174.
24. Touboul E, Buffat L, Belkacemi Y, Leranc JP, Uzan S, Lhuillier P, et al. Local recurrences and distant metastases after breast conserving surgery and radiation therapy for early breast cancer. *Int J Radiat Oncol Biol Phys* 1999; 43: 25–38.
25. Kuske RR, Hayden D, Bischoff R, Farr GH, Fineberg BB. The impact of extracapsular axillary nodal extension (ECE) with and without irradiation on patterns of failure and survival from breast cancer (Abstr). *Int J Radiat Oncol Biol Phys* 1996; 36 (suppl 1): 277.
26. Marks LB, Helperin EC, Prosnitz LR, et al. Post mastectomy radiotherapy following adjuvant chemotherapy and autologous bone marrow transplantation for breast cancer patients with ≥10 positive axillary lymph nodes. *Int J Radiat Oncol* 1992; 23: 1021–1026.
27. Calitchi E, Otmezquine Y, Feuilhade F, et al. External irradiation prior to conservative surgery for breast cancer treatment. *Int J Radiat Oncol Biol Phys* 1991; 21: 325–329.
28. Pierquin B, Huart J, Raynal M, et al. Conservative treatment for breast cancer: long term results (15 years). *Radiother Oncol* 1991; 20: 16–23.
29. Yarnold JR. Selective avoidance of lymphatic irradiation in the conservative management of breast cancer. *Radiother Oncol* 1984; 2: 79–92.
30. Taylor ME, Perez CA, Levitt SH. Breast: Locally advanced (T3 and T4), inflammatory and recurrent tumors. *Principles and practice of radiation oncology. Third ed.* Perez CA, Brady LW, eds. Philadelphia; Lippincott-Raven Publishers, 1997: 1415–1443.