

review

Do we need axillary dissection in early breast cancer?

Tanja Cufer

Institute of Oncology, Ljubljana, Slovenia

Background. In the existing paradigm of the invasive breast cancer, the treatment with the axillary lymph-node dissection (ALND) and histologic staging of the axilla, which is associated with a substantial morbidity, is considered necessary for the treatment decision and local control of disease.

However paradigms are changing and, since primary tumor characteristics are increasingly used for treatment decision and since there is a trend towards the broad application of preoperative chemotherapy, ALND is less and less important for the treatment planning. In a small subgroup of patients in whom the information on nodal status is still important it can be obtained accurately by the sentinel lymph node biopsy. For good local control of the disease, ALND can be replaced with irradiation of the axilla with substantially lesser morbidity.

Conclusions. Abandoning ALND together with breast conserving surgery is one of the major steps towards less mutilating surgery leading to a better quality of life of breast cancer patients at the end of this millennium.

Key words: breast neoplasms-therapy; lymph node excision; axilla; sentinel node mapping

Introduction

In the existing paradigm of the invasive breast cancer, the treatment with the axillary lymph-node dissection (ALND) and histologic staging of the axilla, which is associated with a substantial morbidity, is considered necessary for the treatment decision and local control of disease. However, paradigms are

changing, and today, it is questionable if ALND is still needed for either treatment planning or local control of disease.

Do we really need the information on nodal involvement for treatment planning in early breast cancer?

According to the information obtained from the meta-analyses of all randomized trials of adjuvant systemic therapy performed by Early Breast Cancer Trialists' Collaborative Group,¹⁻³ the benefits of adjuvant systemic therapy are equally shared among node posi-

Received 6 February 2000

Accepted 27 March 2000

Correspondence to: Assist. Prof. Tanja Cufer, Ph.D., M.D., Institute of Oncology, Zaloška 2, 1000 Ljubljana, Slovenia. Phone: +386 61 1314 225; Fax: +386 61 1314 180; E-mail: TCufer@onko-i.si

tive and node negative patients. The relative benefits of the risk of recurrence and death were similar for all patients regardless of the node status. Today, the treatment decision depends much more on the primary tumor characteristics (e.g. size, hormone receptors) than on the nodal involvement. The effectiveness of the particular systemic therapy does not seem to be influenced by the number of the axillary lymph nodes involved but on the biological characteristics of the primary tumor, such as hormonal receptors, growth factor receptors and inherited resistance to chemotherapy. Innovative, intensive, dose-dense and sequential anthracycline-based chemotherapy regimens were equally found to be more effective than standard chemotherapeutic regimens in both, node positive and node negative disease⁴ and it is realistic to expect that the taxane-including regimens will also turn out to be equally effective.

Presently, there is only a small subset of patients in which the indications for systemic therapy are at borderline. These are patients with small tumors, less than 1 cm in diameter. In these patients, we still need the information on axillary lymph node involvement for the treatment decision. However, by sentinel lymph node mapping, accurate information on lymph node status can be obtained in these patients without ALND. During the last few years, sentinel lymph node biopsy was found to be a highly accurate method in predicting occult lymph node metastasis. In skilled hands, it is nearly hundred percent accurate.⁵⁻⁷ With the use of preoperative

chemotherapy for the treatment of operable breast cancer, the information on lymph node status for the treatment planning has become obsolete. In this setting, the treatment strategy depends on much more reliable criteria, such as measurable response of primary tumor to systemic therapy. If the tumor does not respond to primary chemotherapy, a crossover to a different chemotherapeutic agent is recommended, no matter what the axillary nodal status is.

Do we still need axillary lymph-node dissection for the local control of disease?

The review of the studies that looked at the rate of axillary failure in patients with clinically node negative invasive breast cancer who received no axillary treatment⁸ shows that there is a high rate of local recurrence in the axilla (from 15 to 37%) in patients who received neither dissection nor irradiation of the axilla (Table 1). There is a very small subset of patients for whom the risk of nodal involvement is so low that ALND can be omitted. These are the patients with small microinvasive disease and patients with small, with less than 1 cm in diameter, pure tubular carcinomas.⁸ In all other subset of patients with invasive breast cancer, the risk of local recurrence is too high to allow for no routine axillary treatment. Although delayed axillary node dissection is surgically possible and radical in all but about 2% of these patients⁹ and the survival of these patients does not seem to be compromised,¹⁰ the psy-

Table 1. Axillary failure rates in clinically node-negative patients receiving no axillary treatment

Reference	No. of pts in trial	Mean follow-up (months)	Axillary failure (%)
Ribeiro et al, 1993	708	65	23
Cerotta et al, 1997	408	84	15
Lythgoe & Palmer, 1982	714	60	37
Gravesone et al, 1988	3128	60	19
Fisher et al, 1985	1079	126	19
Gatly et al, 1991	450	72	18

Table 2. Axillary failure rates in clinically node negative patients treated with axillary radiotherapy

Reference	No. of pts in trial	Mean follow-up (months)	Axillary failure (%)
Baeza et al, 1988	171	62	1
Cabanes et al, 1992	332	54	2
Dolouche et al, 1987	281	60	1
Fisher et al, 1985	352	126	3
Leung et al, 1986	446	120	0
Osborne et al, 1984	211	120	1
Peirquin et al, 1986	1040	60	2
Recht et al, 1991	335	73	1
Wazer et al, 1994	73	54	1

chologic burden of the disease recurrence for the patient is too high to be acceptable. Therefore, some kind of axilla treatment for a good local control of the disease is necessary.

In clinically node positive disease, surgical removal of the axillary nodes i.e. ALND, despite its high rate of morbidity, is still recommended. However, in clinically lymph node negative disease, nodal irradiation with a lesser degree of morbidity was found to be as effective as ALND in terms of local control of disease without compromising the patients survival. In nine published studies with follow-up times that ranged from 54 to 126 months, the percentage of axillary failure in node negative patients who received axillary nodal irradiation without ALND was only about 1%¹⁰⁻¹⁸ (Table 2). Also the results of a meta-analysis performed by Early Breast Cancer Trialists' Collaborative Group¹⁹ showed no difference in mortality in eight trials comparing axillary surgical clearance to irradiation. Morbidity from axillary nodal irradiation seems to be minimal when compared with the extensive side effects of ALND.^{20,21} The risk of arm edema is approximately half that seen in axillary nodal dissection;²² likewise, brachial plexus injury and shoulder pain morbidity are extremely rare with radiotherapy alone.²³ Another possibility of axilla sparing treatment in clinically negative lymph-node patients is sentinel lymph-node biopsy, which allows for axillary lymph-node dissection sparing procedure in all patients

with negative sentinel lymph node. This is approximately half of patients with clinically negative disease in axilla. Morbidity from sentinel lymph-node mapping does not seem to be worth mentioning.

Conclusions

In conclusion, since primary tumor characteristics are increasingly used for the treatment decision and since there is a trend towards the broad application of preoperative chemotherapy, ALND is becoming less and less important for the treatment planning. In small subgroup of patients in whom the information on nodal status is still important, it can be obtained accurately by the sentinel lymph node biopsy. For a good local control of the invasive disease ALND can be replaced with the irradiation of axilla with substantially lesser morbidity. Abandoning ALND together with a breast conserving surgery is one of the major steps towards the less mutilating surgery leading to a better quality of life of breast cancer patients at the end of this millennium.

References

1. Early Breast Cancer Trialists' Collaborative group. Systemic treatment of early breast cancer by hormonal, cytotoxic, or immune therapy: 133 randomised trials involving 31000 recurrences and 24000 deaths among 75000 women. *Lancet* 1992; 339: 1-5, 71-85.

2. Early Breast Cancer Trialists' Collaborative group. Ovarian ablation in early breast cancer: overview of the randomized trials. *Lancet* 1996; **348**: 1189-96.
3. Early Breast Cancer Trialists' Collaborative group. Tamoxifen for early breast cancer: an overview of the randomized trials. *Lancet* 1998; **351**: 1451-67.
4. Hutchins L, Green S, Ravdin P, Lew D, Martino S, Aleloff M, et al. CMF versus CAF with and without tamoxifen in high-risk node-negative breast cancer patients and a natural history follow-up study in low-risk node-negative patients: first results of inter-group trial Int 0102. *Proc Annu Meet Am Soc Clin Oncol* 1998; **17**: 2.
5. Veronesi U, Paganelli G, Galimberti V, Viale G, Zurrida S, Bedoni M, et al. Sentinel-node biopsy to avoid axillary dissection in breast cancer with clinically negative lymph nodes. *Lancet* 1997; **349**: 1864-7.
6. Albertini JJ, Lyman GH, Cox C, Yeatman T, Balducci L, Ku N, et al. Lymphatic mapping and sentinel node biopsy in the patient with breast cancer. *JAMA* 1996; **276**: 1818-22.
7. Giuliano AE, Jones RC, Brennan M, Statman R. Sentinel lymphadenectomy in breast cancer. *J Clin Oncol* 1997; **15**: 2345-50.
8. Singletary SE. Management of the axilla in early-stage breast cancer. In: Perry MC, editor. American Society of Clinical Oncology, Educational Book, 34th annual meeting. Alexandria, VA: American Society of Clinical Oncology, 1998, p. 132-42.
9. Fisher ER, Sass R, Fisher B. Pathologic findings from National Surgical Adjuvant Project for Breast Cancers (protocol no. 4). X. Discriminants for tenth year treatment failure. *Cancer* 1984; **53**: 712-23.
10. Fisher B, Redmond C, Fisher ER, Bauer M, Wolmark N, Wickerham DL, et al. Ten-year results of a randomized clinical trial comparing radical mastectomy and total mastectomy with or without radiation. *N Engl J Med* 1985; **312**: 674-81.
11. Baeze MR, Sole J, Leon A, Arraztoa J, Rodriguez R, Claire R, et al. Conservative treatment of breast cancer. *Int J Radiat Oncol Biol Physiol* 1988; **14**: 669-76.
12. Cabanes PA, Salmon RJ, Vilcoq JR, Durand JC, Fourquet A, Gautier C, et al. Value of axillary dissection in addition to lumpectomy and radiotherapy in early breast cancer. *Lancet* 1992; **339**: 1245-8.
13. Delouche G, Bachelot F, Premont M, Kurtz JM. Conservation treatment of early breast cancer: long term results and complications. *Int J Radiat Oncol Biol Physiol* 1987; **13**: 29-34.
14. Leung S, Otmegguine Y, Calitchi E, Mazon JJ, Le Bourgeois JP, Pierquin B. Locoregional recurrences following radical external beam irradiation and interstitial implantation for operable breast cancer: A twenty three year experience. *Radiother Oncol* 1986; **5**: 1-10.
15. Osborne MP, Ormiston N, Harmer CL, McKinna JA, Baker J, Greening WP. Breast conservation in the treatment of early breast cancer: A 20-year follow-up. *Cancer* 1984; **53**: 349-55.
16. Pierquin B, Mazon JJ, Glaubiger D. Conservative treatment of breast cancer in Europe: Report of the Groupe Europeen de Curietherapie. *Radiother Oncol* 1986; **6**: 187-98.
17. Recht A, Pierce SM, Abner A, Vicini F, Osteen RT, Love SM, et al. Regional nodal failure after conservative surgery and radiotherapy for early stage breast carcinoma. *J Clin Oncol* 1991; **9**: 988-96.
18. Wazer DE, Erban JK, Robert NJ, Smith TJ, Marchant DJ, Schmid C, et al. Breast conservation in elderly women for clinically negative axillary lymph nodes without axillary dissection. *Cancer* 1994; **74**: 878-83.
19. Early Breast Cancer Trialists Collaborative Group. Effects of radiotherapy and surgery in early breast cancer. *N Engl J Med* 1995; **333**: 1444-55.
20. Maunsell E, Brisson J, Deshenes L. Arm problems and psychological distress after surgery for breast cancer. *Can J Surg* 1993; **36**: 315-20.
21. Hladiuk M, Huchcroft S, Temple W, Schnurr BE. Arm function after axillary dissection for breast cancer: A pilot study to provide parameter estimates. *J Surg Oncol* 1992; **50**: 47-52.
22. Bruce J. Operable cancer of the breast: A controlled clinical trial. *Cancer* 1971; **18**: 1443-53.
23. Pierce SM, Recht A, Lingos TI, Abner A, Vicini F, Silver B, et al. Long-term radiation complications following conservative surgery and radiation therapy in patients with early stage breast disease. *Int J Radiat Oncol Biol Physiol* 1992; **23**: 915-23.