Is sentinel lymph node biopsy more accurate than axillary dissection on staging the nodal involvement in breast cancer patients?

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Riassunto

Attualmente la valutazione del coinvolgimento neoplastico dell'ascella nel carcinoma mammario può essere effettuato di routine mediante la tecnica della biopsia del linfonodo sentinella (SLNB). Uno dei maggiori vantaggi di tale metodica è la quasi totale assenza di complicanze. È tuttavia fondamentale comprendere se l'SLNB è superiore alla dissezione ascellare tradizionale nella stadiazione dei linfonodi.

Valutare l'accuratezza diagnostica nella stadiazione dell'ascella confrontando tre differenti metodiche: lo svuotamento ascellare, la biopsia del linfonodo sentinella effettuando le tradizionali 4-6 sezioni e la biopsia del linfonodo sentinella con l'analisi completa del linfonodo asportato.

527 pazienti consecutivi (525 donne e 2 uomini) con carcinoma infiltrante della mammella ≤ 3 e linfonodi ascellari clinicamente negativi suddivisi in 3 gruppi differenti: gruppo A, pazienti trattati con dissezione ascellare; gruppo B, pazienti sottoposti a biopsia del linfonodo sentinella che veniva analizzato con le 4-6 sezioni classiche; gruppo C, pazienti trattati con biopsia del linfonodo sentinella in cui il linfonodo asportato veniva interamente analizzato. Tutti i pazienti sono stati sottoposti a quadrantectomia. Le differenze fra i gruppi sono state valutate con il test di Anova.

La percentuale di N+ nei gruppi A e B è stata rispettivamente del 25.8% e del 28%, mentre nel gruppo C essa sale sino al 45%, quasi la metà dei pazienti esaminati; tale differenza è risultata statisticamente significativa ($p = 0.02$). Dai nostri dati è emerso che l'analisi delle 4-6 sezioni del linfonodo sentinella e la dissezione ascellare hanno praticamente la stessa accuratezza diagnostica, mentre l'analisi dell'intero linfonodo ha una maggiore capacità di stadiare l'ascella.

La biopsia del linfonodo sentinella con l'analisi completa del linfonodo asportato può essere considerata la migliore metodica per la stadiazione dell'ascella in pazienti con carcinoma mammario. Nel nostro studio, la percentuale di metastasi dopo analisi completa del linfonodo è stata del 45%, confrontata con il 25.8% dopo svuotamento ascellare. Inoltre, tale approccio evita un'inutile pulizia dell'ascel-

Introduction

Until a few years ago the management of early stage breast cancer required the examination of the whole axillary node, so axillary lymph node dissection (ALND) has been a mandatory component of surgical treatment of breast cancer for almost a century[1]. The justification for the continued performance of this surgical procedure is twofold. For one thing, the presence or not of positive axillary node at histology and the total number of such involved nodes remain the most powerful predictors of the risk of recurrence and death from breast cancer, with lymph node-negative patients enjoying a 10-year survival in excess of 70%, while patients with 10 or more positive nodes dying of breast cancer within 10 years more than 80% of the time[2]. The

second purpose is therapeutic: if an ALND is performed in a breast cancer patient with a clinically normal axilla, the incidence of positive nodes at histology is roughly 30%. This would imply that the failure to perform an ALND in a clinically negative patient would place that patient at risk of axillary recurrence of the same 30%, which might compromise patient disease-free survival and overall survival.

To date, an evaluation of axillary involvement can be routinely performed with the technique of sentinel node biopsy (SLNB). One of the greatest advantages of SLNB is the nearly total absence of local post-operative complications[3]. By contrast, total axillary dissection is associated with significant post-operative pain, and limitations in arm motion are common. Chronic arm lymphoedema, the most debilitating sequelae of total axillary dissection, has never been observed after SLNB[1,4,5]. Apart from improved quality of life, another advantage of SLNB is its lower cost because the operation can be performed on an outpatient basis under local anaesthesia without axillary drainage[6].

But is the SLNB better than ALND on staging the axillary nodal involvement?

To try to answer this question we performed the present study. We report here the findings from the observation of 527 patients treated for breast carcinoma and divided into 3 groups (patients that received ALND, patients who underwent SLNB with traditional 4-6 sections and patients who underwent SLNB with complete analysis of the removed sentinel node). The three different groups were evaluated to assess the accuracy of the employed methods.

la in circa il 55-60% dei casi, riducendo la percentuale di complicanze postoperatorie in termini di morbilità e mortalità.

Parole chiave: carcinoma della mammella, biopsia del linfonodo sentinella, dissezione linfonodale ascellare, stadiazione dell'ascella

Summary

Is sentinel lymph node biopsy more accurate than axillary dissection for staging nodal involvement in breast cancer patients? *A. Marrazzo, P. Taormina, V. Gebbia, M. David, I. Riili, D. Lo Gerfo, L. Casà, A. Noto*

Today evaluation of axillary involvement can be routinely performed with the technique of sentinel lymph node biopsy (SLNB). One of the greatest advantages of SLNB is the nearly total absence of local postoperative complications. It is important to understand whether SLNB is better than axillary lymph-node dissection (ALND) for staging axillary nodal involvement.

The aim of the study was to evaluate the axillary staging accuracy comparing three different methods: axillary dissection, sentinel node biopsy with the traditional 4-6 sections and sentinel node biopsy with complete analysis of the lymph node.

527 consecutive patients (525 females and 2 males) with invasive breast cancer ≤3 cm and clinically negative axillary nodes were divided into 3 different groups: group A treated with axillary dissection, group B treated with sentinel nodal biopsy analysed with 4-6 sections, and group C treated with sentinel node biopsy with analysis of the entire node. All patients underwent a quadrantectomy to treat the tumor. Group differences and statistical significance were assessed by ANOVA.

The percentages of N+ in group A and group B were 25.80% and 28% respectively, while in the third group it rose to 45%, or almost half the patients. The differences among the three groups were statistically significant ($p = 0.02$). From our analysis of the data it emerges that axillary dissection and sentinel node biopsy with analysis of 4-6 sections have the same accuracy in staging the nodal status of the axilla; analysis of the entire sentinel lymph node revealed an increased number of patients with axillary nodal involvement, proving more powerful in predicting nodal stage.

SLNB with complete examination of the SLN removed can be considered the best method for axillary staging in breast cancer patients with clinical negative nodes. In our study, the percentage of metastases encountered after complete examination of SLN was 45% compared to the accuracy of axillary dissection that was only 25.8%. Moreover, this approach avoids the useless axillary cleaning in about 55-60% of cases, decreasing postoperative morbidity and mortality.

Key words: breast carcinoma, sentinel lymph node biopsy, axillary staging

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Patients and methods

1. Characteristics of the patients

Up to February 2005, 527 consecutive patients with invasive breast cancer ≤ 3 cm and clinically negative axillary nodes referred to our Breast Unit and underwent surgical treatment of cancer. Patients who had previous excision of the primary tumor and patients with multicentric cancer were excluded.

We considered three different periods of our activity: the first one, from 1995 to 1998, consisting of 186 patients who underwent an axillary dissection (group A), the

second (169 patients), from 1999 to February 2003, when we performed sentinel node biopsy and the node was examined with the traditional technique of 4-6 sections (group B), and the third period (from March 2003) when the sentinel nodes underwent careful complete examination to better detect micrometastases (group C, including 172 patients).
The mean age was 57.01 years (range 24-83) for group A, 54.1 years (range 29-83) for group B and 56.95 years (range 31-78) for group C. The average size of the primary carcinoma was 1.73 for Group A, 1.57 for group B and 1.66 for group C. All patients characteristics are summarized in Table I.

2. Treatment of the primary carcinoma

96 patients of group A were treated with breast conservative surgery, consisting of a quadrantectomy, while the other 90 patients received a more aggressive approach with a mastectomy. All patients of group B underwent quadrantectomy with the only exception being 2 males who underwent mastectomy. Quadrantectomy was the only intervention performed on all the patients in group C.

3. Sentinel lymph node biopsy technique

The procedure applied to the patients at our Institute is the following. Three hours before surgery or sometimes the afternoon of the day before surgery, 5-10 MBq of technetium-99-labelled human colloid particles in 0.2 ml saline were injected in the subdermis above the tumor or in the tissue immediately surrounding it when located deep in the breast. Mammary and axillary planar scintigrafic scans, anterior and anterior-oblique, were taken 30 minutes after the injection of the radiotracer. If no nodes were visualized, a further scan was taken three hours later. A second injection of tracer was not needed in all patients. The skin above the first radioactive node was marked to assist the surgeon.
In the operative theater the surgeon performed the quadrantectomy and the removal of marked sentinel node through the same incision or, in case of localization of cancer in the internal regions of the breast, through a small incision of 1.5-2 cm in the axilla.
Following removal of each node, the gamma probe was placed back into the wound to identify additional sentinel nodes. Suspicious palpable nodes detected during the procedure were also excised. A detailed discussion of the technique is described in a previous work published by the Authors[7].

4. Pathology

In all patients in group B, the sentinel nodes were examined with the traditional 4-6 sections of formalin fixed tissue, stained with Haematoxylin-Eosin (H&E), a technique similar to that one employed for the analysis of nodes after axillary lymphadenectomy (group A).
The technique employed for the complete analysis of sentinel lymph node in group C patients was the following: first of all the SLN was sliced at 0.2 mm intervals perpendicular to long axis. One routine Haematoxylin-Eosin (H&E) stained section was examined; if negative, serial level slices were performed through each block (two sections for each level, with a spacing of 50 μ between the following levels). One segment for each level was stained with H&E and one for an eventual additional immunohistochemical analysis with keratins to compare cluster of histologically suspected cells, if there was a suspicion of metastasis.
The histological findings of the three groups are shown in Table II.

Table I. Characteristics of study patients (n = 527).

	N.	Mean age	Tc T1	Tc T2	T size (cm)
Group A	186	57.01 (SD 13.47 range 24-83)	134	52	1.73 (range 0.5-3)
Group B	169	54.1 (SD 11.3 range 29-83)	148	21	1.57 (range 0.5-3)
Group C	172	56.95 (SD 12.85 range 31-78)	130	42	1.66 (range 0.5-3)

N. = number of patients; Tc = clinical T stage; SD = standard deviation.

Table II. Histological findings in 527 study patients.

	pT		
	1a + 1b	1a + 1b + 1c	2
Group A	42 (22.5%)	128 (68.7%)	58 (31.3%)
Group B	47 (27.7%)	143 (84.5%)	26 (15.5%)
Group C	40 (23%)	131 (76%)	41 (24%)

	pN			
	0	+	mic	ITC
Group A	138 (74.2%)	48 (25.8%)	0	0
Group B	122 (72.2%)	47 (27.8%)	0	0
Group C	95 (55%)	77 (45%)	24 (31.1%)	8 (13.7%)

is = *in situ*; mic = micrometastases; ITC = isolated tumoral cells.

5. Statistics

The results for the groups of patients were expressed as mean +/– standard deviation or as numbers. Group differences and statistical significance were assessed by Anova test. *P* values of 0.05 or lower were considered statistically significant.

6. Purposes

The primary goal of the study was the evaluation of accuracy on detecting nodal status of axilla comparing the three different methods: axillary dissection, sentinel node biopsy with traditional 4-6 sections and sentinel node biopsy with complete analysis of the lymph node.

Results

The patients of the three different groups were homogeneous with regard to age; the average being 57 years for group A, 54.1 for group B and 56.9 for group C. See Table I for further details about patient's age.
In contrast, when considering the clinical status of the neoplasm, there was a significant difference between the groups (p value = 0.006). To be precise, the Anova test showed a significant difference only among the first two groups (Table III).
The same result was also found considering the pT, whereas the significance was assessed by a p value of 0.007. In fact in group A the pT1 was 68.8%, in group B 84.7% and in group C 76%, once more showing that the first two groups were not homogeneous. This event can be better understood considering that in the first period when we performed the technique of sentinel node biopsy, probably, there was a higher trend

Table III. Clinical T, pT status and nodal involvement in the three different groups.

	Group A	Group B	Group C	p value
T1	134 (71.70%)	148 (87.60%)	130 (76.00%)	
T2	52 (28.30%)	21 (12.40%)	42 (24.00%)	$p = 0.006$
pT1	128 (68.70%)	143 (84.50%)	131 (76.00%)	
pT2	58 (31.30%)	26 (15.50%)	41 (24.00%)	$p = 0.007$
N+	48 (25.80%)	47 (28.00%)	80 (45.00%)	
N–	138 (74.20%)	122 (72.00%)	92 (55.00%)	$p = 0.02$

to enroll smaller tumors for this approach (Table III).

The primary goal of the study was, as above mentioned, the evaluation of accuracy on detecting nodal status of axilla comparing the three methods. Table IV shows the results in term of percentage of nodal status for the groups. The percentage of N+ in group A and group B was 25.80% and 28% respectively, while in the third one the whole of positive nodes increases to 45%, almost half of the patients. The *p* value among the three groups shows a significant difference and it settles on 0.02. By the analysis of this data, it is clear that group A and group B are similar, while the statistical difference is related to group C. In other terms, this data means that axillary dissection and sentinel node biopsy with analysis of 4-6 section have the same accuracy in staging the nodal status of the axilla; the analysis of the entire sentinel lymph node increase the number of patients with axillary nodal involvement, proving more powerful in predicting the nodal stage. Table II shows that 68.7% of group A had a pT1 cancer and this percentage of patients rises to 76% in group C. So we thought we would discover a decreasing incidence of nodal metastases because of the early discovery of the tumor.

After that we analyzed the nodal involvement in relationship to pT, in particular considering the subcategories of pT1, i.e. 1a, 1b and 1c, and the pT2 patients as showed in Table IV. In detail, the complete analysis of removed sentinel node was more powerful than the other methods on detecting metastases: in particular, considering that in pT1a+pT1b tumors the *p* value was 0.01, equal to the *p* value found in pT1 patients; the Anova test showed that this difference is between group A and group C. In patients with a breast tumor larger than 2 cm (pT2) we also observed statistical signficance with a *p* value of 0.002.

Discussion

Since the introduction of widespread mammographic screening, there has been a decrease in the percentage of involved nodes because the diagnosis of breast cancer is made earlier and the median size of tumoral lesions is smaller[8,9]. In our series of 2004, axillary metastases were found in 49% of patients, while in other series this percentage was about 40%[10]. Kingsmore *et al.* described a relationship between tumor size and nodal involvement in a group of women with breast cancer and ten or more sampled nodes; in particular, tumor size is directly related to nodal metastases, ranging from 25% for neoplasms less than 10 mm to 76% for tumors greater than 40mm. For T1 tumors, i.e. smaller or equal to 2 cm, the incidence of nodal involvement varies from 0 to 8.4% in T1a to 6.9-22.2% in T1b, to 13.1-62.5% in T1c[11]. Reviewing different series in which the size of the invasive component was related to the incidence of axillary lymph node involvement we found an incidence ranging from 6.9% to 22.2% for T1a+b tumors and an incidence of 13.1-62.5% for T2. In particular the lower incidence is reported by Ciatto *et al.*[12], while the higher incidence is reported in Seidman series[13]. In a Memorial Sloan-Kettering Cancer Center study by Mann *et al.* of 291 patients with T1a+b neoplasms 21.7% were found to have pN+[14]. In his review of 2003, Kingsmore reported an incidence of pN+ equal to 25% for pT1a+b. It seems possible that the difference of incidence of pN+ might be explained by the fact that different authors include palpable or not palpable mammographically detected tumors and the number of lymph nodes removed and examined is < or >10[11].

Table IV. Evaluation of nodal status regarding the pT stage of the tumor.

		Group A	Group B	Group C	*p* value
*p*T1a + pT1b	N+	8 (19%)	7 (14.9%)	11 (27.5%)	
	N–	32 (25%)	40 (85.1%)	29 (72.5%)	0.01
*p*T1	N+	34 (81%)	35 (24.5%)	56 (42.7%)	
	N–	96 (75%)	108 (75.5%)	75 (57.3%)	0.01
*p*T2	N+	16 (27.5%)	12 (46.1%)	24 (57.4%)	
	N–	42 (72.5%)	14 (53.9%)	17 (42.6%)	0.002

The nodal involvement in our series in the ALND group was 19% in pT1a+b women, 25 % in pT1 and 27.5% in pT2 breast tumors showing that our data are similar to those reported in the literature. It is interesting to note that when considering the SLNB group (C), these percentages increase with statistical significance. In fact the axillary nodal involvement rises to 27.5% in pT1a+b patients, 42.7% in pT1 and to 49.4% in pT2. The rate of micrometastases in the SLN varies in different series from 7 to 22% of all detected SLN.

Axillary staging is very important in breast cancer patients; axillary recurrence is about more than twice as likely after inadequate compared to adequate treatment of the axilla. The number of lymph nodes needed for accurate staging of the axilla is still controversial[15]. Many authors emphasize that the accuracy of staging is directly related to the number of resected lymph nodes[16-18]. In particular, it is observed that the mortality rate increases if sampling less than four axillary nodes irrespective of the number of involved axillary nodes. This poorer survival may be explained in two ways: either indirectly, having possibly influenced decisions regarding adjuvant therapy, or directly: untreated axillary disease itself may have led to poorer survival. On average 30% of nodal axillary recurrences will present as uncontrollable regional diseases, ranging from 29 to 53%[19-21].

The potentially beneficial effect of ALND on overall survival is still controversial. ALND in node-negative patients is purely a staging procedure; moreover, there are many suggestions that the removal of a high number of negative nodes from the axilla in node-negative patients decreases disease-free survival. Camp et al. have noted a disadvantage in survival for node-negative patients with more than 20 axillary nodes removed[22]. These data can be due to the role that lymph nodes may play in the antitumoral immune response. Recent advances in our understanding of the molecular events of antigen recognition by T-cells and T-cell activation have provided strong experimental evidence to demonstrate that these secondary lymphoid organs constitute the primary sites where the specific recognition of tumoral antigens and the proper activation of the immune system take place[23].

Patients treated without ALND because of sentinel node negativity show excellent results in terms of disease control and overall survival. The very low rate of distant metastases in different series might suggest that the maintenance of healthy immunological tissue may be beneficial[24].

From the data analysis, it is very interesting to observe that the percentage on SLN metastases increases in group C, where the sentinel node is thoroughly examined, showing better accuracy. This trend is observed despite an increase in the number of small tumors, where we would expect to find a lower incidence of metastatic lymph nodes.

SLNB with complete examination of removed SLN can be considered the better method of axillary staging in breast cancer patients with clinically negative nodes. In our study the percentage of metastasis encountered after complete examination of SLN was 45% compared to the accuracy of axillary dissection that was only 25.8%. Moreover this approach avoids unnecessary axillary cleaning in about 55-60%, decreasing postoperative complications in terms of morbidity and mortality as also recently documented by the Almanac Trialist Group monitorizing the quality of life in patients who underwent SLNB and ALND[25].

References

1. Schijven MP, Vingerhoets AJJM, Rutten HJT, Nieuwenhuijzen GA, Roumen RM, van Bussel ME, Voogd AC. Comparison of morbidity between axillary lymph node dissection and sentinel node biopsy. EJSO 2003; 29: 341-50.

2. Carter CL, Allen C, Hanson DE. Relation of tumor size, lymph node status and survival in 24740 breast cancer cases. Cancer 1989; 63: 181-7.

3. Veronesi U, Galimberti V, Mariani L, Gatti G, Paganelli G, Viale G, Zurrida S, Veronesi P, Intra M, Gennari R, Rita Vento A, Luini A, Tulli M, Bassani G, Rotmensz N. Sentinel node biopsy in breast cancer: early results in 953 patients with negative sentinel node biopsy and no axillary dissection. EJC 2005; 41: 231-7.

4. Dubernard G, Sideris L, Delaloge S, Marsiglia H, Rochard F, Travagli JP, Mathieu MC, Lumbroso J, Spielmann M, Garbay JR, Rouzier R. Quality of life after sentinel lymph node biopsy in early breast cancer. EJSO 2004; 30: 728-34.

5. Barthelmes L, Al-Awa A, Murali-Krishnan VP, Crawford DJ. The role of lymph node sampling and radiotherapy in the management of the axilla in early breast cancer. Breast 2002; 11: 236-40.

6. Ranieri E, Caprio G, Fobert MT, Civitelli L, Ceccarelli F, Barberi S, Virno F. One-day surgery in a series of 150 breast cancer patients: efficacy and cost: benefit analysis. Chirurgia Italiana 2004; 56: 415-8.

7. Marrazzo A, Taormina P, Noto A, Cardinale G, Casà L, Mercadante S, Lo Gerfo D, David M. Localization of the sentinel node in breast cancer: prospective comparison of vital staining and radioactive tracing methods. Chirurgia Italiana 2004; 56 (5): 621-7.

8. Chung MA, Steinhoff MM, Cady B. Clinical axillary recurrence in breast cancer patients after a negative sentinel node biopsy. Am J Surg 2002; 184: 310-4.

9. Chung MA, Fulton J, Cady B. Trends in breast cancer incidence and presentation in a population screened for breast cancer. Semin Breast Dis 1999; 2: 55-63.

10. Bourez RLJH, Rutgers EJTh, Van der Velde CJH. Will we need lymph node dissection at all in the future? Clin Breast Cancer 2002; 3(5): 315-22.

11. Kingsmore DB, Hole DJ, Gillis CR, George WD. Axillary recurrence in breast cancer. EJSO 2005; 31(3): 226-31.

12. Ciatto S, Del Turco MR, Bonardi L, Cataliotti L, Distante V, Cardona G, Bianchi S. Non-palpable lesions of the breast detected by mammography. Review of 1182 consecutive histologically confirmed cases. Eur J Cancer 1994; 30A: 40-4.

13. Seidman JD, Schapner LA, Aisner SC. Relationship of size of the invasive component of the primary breast carcinoma to the axillary lymph node metastasis. Cancer 1995; 75: 65-71.

14. Mann JB, Port E, Rizza C, Tan LK, Borgen PI, Van Zee KJ. Six-year follow-up of patients with microinvasive, T1a and T1b breast carcinoma. Ann Surg Oncol 1999; 6: 591-8.

15. Kingsmore DB, Ssemwogerere A, Hole DJ, Gillis CR, George WD. Increased mortality from breast cancer and inadequate axillary treatment. Breast 2003; 12: 36-41.

16. Graversen HP, Blichert-Toft M, Andersen JA, Zedler K and The Danish Breast Cancer Cooperative Group. Breast cancer: risk of axillary recurrence in node-negative patients following partial dissection of the axilla. EJSO 1988; 14: 407-12.

17. van der Wal BCH, Butzelaar RMJM, van der Meij S, Boermeester MA. Axillary lymph node ratio and total number of removed lymph nodes: predictors of survival in stage I and II breast cancer. EJSO 2002; 28: 481-9.

18. Axelsson CK, Mouridsen HT, Zedeler K. Axillary dissection of level I and II lymph nodes is important in breast cancer classification. The Danish Breast Cancer Cooperative Group (DBCG). EJC 1992; 28A(8-9): 1415-8.

19. Chua B, Ung O, Boyages J. Competing considerations in regional nodal treatment for early breast cancer. Breast J 2002; 8: 15-22.

20. Recht A, Pierce SM, Abner A, Vicini F, Osteen RT, Love SM, Silver B, Harris JR. Regional nodal failure after conservative surgery and radiotherapy for early-stage breast carcinoma. J Clin Oncol 1991; 9: 988-96.

21. Mckinna F, Gothard L, Ashley S, Ebbs SR, Yarnold JR. Lymphatic relapse in women with early breast cancer: a difficult management problem. Eur J Cancer 1999; 35: 1065-9.

22. Camp RL, Rimm EB, Rimm DL. A high number of tumor-free axillary lymph nodes from patients with lymph node negative breast carcinoma is associated with poor outcome. Cancer 2000; 88(1): 108-13.

23. Santin AD. Lymph nodes metastases. The importance of the microenvironment. Cancer 2000; 88: 175-9.

24. Zavagno G, Carcoforo P, Franchini Z, Renier M, Barutta L, de Salvo GL, Maravegias K, Capitanio G, Nitti D, Lise 25. M. Axillary recurrence after negative sentinel lymph node biopsy without axillary dissection: a study on 479 breast cancer patients. EJSO 2005; 31: 715-20.

25. Almanac Trialists Group. Sentinel lymph node biopsy for breast cancer: from investigational procedure to standard practice. Abstracts 9th Notingham International Breast Cancer Conference. 2005.