



*INDICACIONES DE LINFADENECTOMIA
AXIL.LAR EN GANGLI SENTINELLA
AXIL.LAR POSITIU.*

Dra. Amparo García Tejedor

Cirugía del cáncer de Mama

Evolución Histórica. Reducir Morbilidad



Quemar lesiones
Antiguo egipto
1.600 a.C



Mastectomia radical
Halsted
(S XVII-XIX)



Q. Conservadora +
RDT
S XX



Linfadenectomia
axilar radical
(nivel III)



Técnica del ganglio
centinela
(LA solo si GC positivo)
1990-2000



LA GC positivo?
Controversia actual

MAMA

AXILA

Morbilidad de la linfadenectomía vs Ganglio Centinela

6-24 meses postcirugía

Morbilidad	Linfadenectomía	Ganglio Centinela
Dolor axilar postoperatorio	91-39 %	16-8 %
Parestesia brazo operado	85-68 %	2-1 %
Movilidad brazo operado (80-100%)	73-79%	100-100 %
Diferencia circunferencia > 1cm brazo operado/brazo sano	25-37 %	0-1%

*E. Prospektivo Veronesi, IEO Milan,
The New England Journal of Medicine, 2003*



Morbilidad de la linfadenectomía

Riesgo de Linfedema

Técnica Tratamiento	Riesgo linfedema
Ganglio centinela	0-7%
Radioterapia axilar	8.3%
Ganglio centinela + RDT	9.1%
Linfadenectomía	6-30% (hasta 50%)
Linfa axilar + RDT	38%

Diseases of the Breast. Fourth edition. Harris 2009



Factores ↑ Riesgo linfedema

- Edad
- Masa corporal
- Periodo de seguimiento
- Disección nivel III
 - sólo si >afección
 - NCCN no en est. I/II

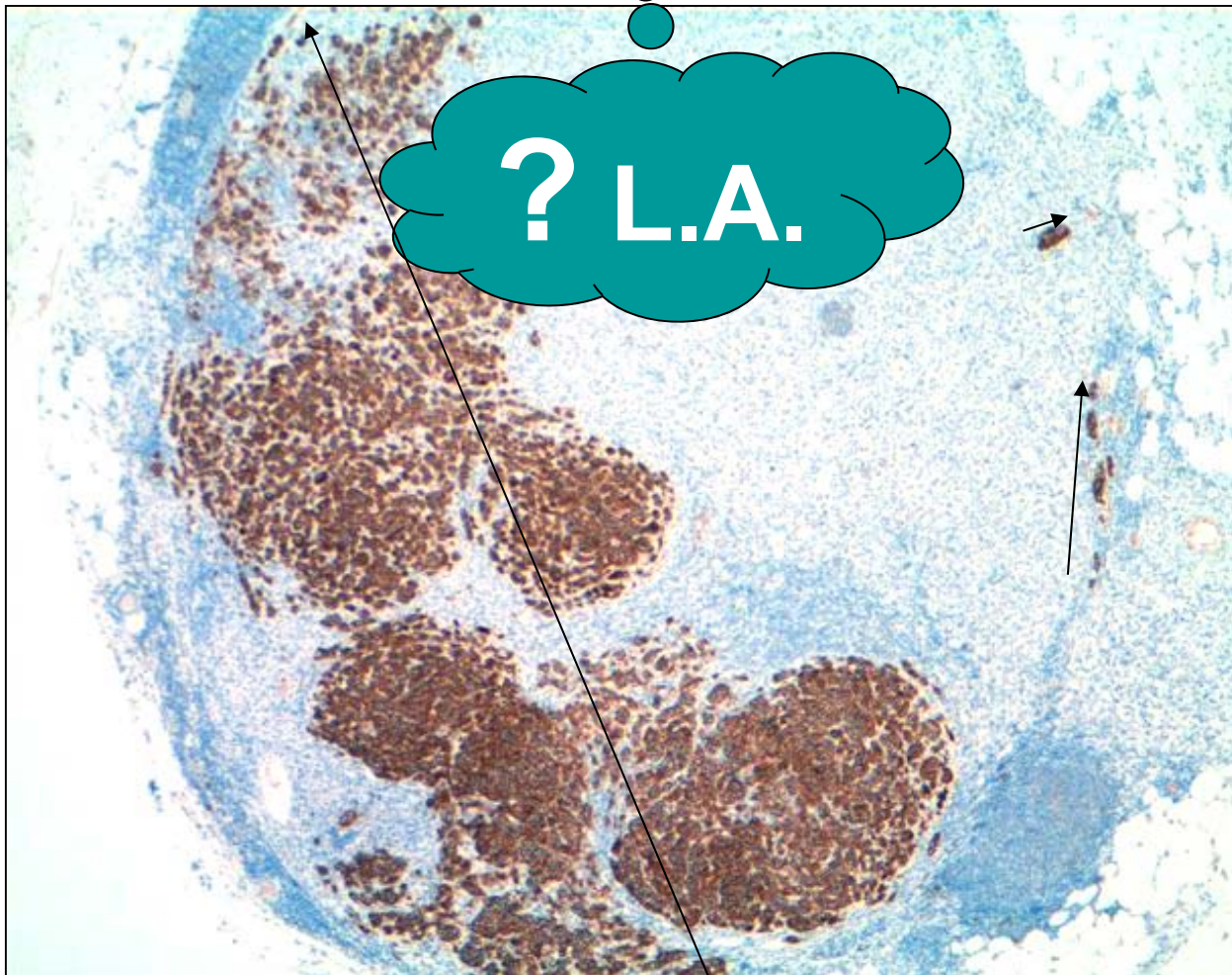


GANGLIO CENTINELA POSITIVO

Paradigmas en controversia

MACROMETÁSTASIS

MICROMETÁSTASIS



Importancia LA en GC positivo

Cuestiones a Valorar

 ¿Cuál es el porcentaje de ganglios adicionales afectados en la L.A. tras GC positivo?

 ¿Cambia el estadiaje?

 ¿Perder información sobre el número total de ganglios afectados cambia el tratamiento adyuvante?

 Tratamiento sistémico

 Radioterapia

 ¿Dejar ganglios afectados en la axila empeora el pronóstico?

 ¿Cuáles son las recomendaciones de las guías clínicas internacionales?

I.- Ganglios adicionales afectados si GC positivo

IEO Milan 1228 GC positivos

- ★ **54% sólo GC metastásico**
- ★ **46% otros ganglios metastásicos**

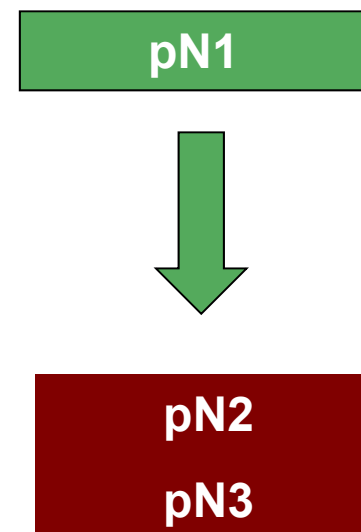
GANGLIO CENTINELA	OTROS GANGLIOS AXILARES AFECTOS
MACROMETÁSTASIS	50.3 %
MICROMETÁSTASIS	21.4 %
ITC	14.7 %
NEGATIVO	4-6 %

I.- Ganglios adicionales afectados si GC positivo

¿Cambio de estadiaje?

European Organization of Research and Treatment of Cancer (EORTC) 10981-22023 AMAROS trial, Ann Surg Oncol, 2010
n=2.000 pacientes

GANGLIO CENTINELA	OTROS GANGLIOS AXILARES AFECTOS
MACROMETÁSTASIS (n=200) 0 ganglios 1-3 ganglios 4-9 ganglios >9 ganglios	117 (59%) 65 (32%) 10 (5%) 8 (4%)
MICROMETÁSTASIS (n=84) 0 ganglios 1-3 ganglios 4-9 ganglios >9 ganglios	69 (82%) 10 (12%) 3 (4%) 2 (2%)
ITC (n=33) 0 ganglios 1-3 ganglios 4-9 ganglios >9 ganglios	27 (82%) 5 (15%) 1 (3%) 0 (0%)



I.- Ganglios adicionales afectados si GC positivo

[McGhan LJ](#), et al., [J Surg Oncol.](#) 2011,
Mayo Clinic
**The changing landscape of axillary surgery:
Which breast cancer patients may still benefit
from complete axillary lymph node dissection?**

[van la Parra RF](#), et al. [Eur J Surg Oncol.](#) 2011
Gelderse Vallei Hospital The Netherlands
**Meta-analysis of predictive factors for non-sentinel
lymph node metastases in breast cancer patients
with a positive SLN.**

Factores de riesgo predictores de ganglios adicionales afectos

- Tamaño tumor
- RH
- Invasión angiolinfática
- Metástasis ganglionar >2mm

- Extensión extracapsular en GC
- >1GC metastasico
- ≤1 GC negativo
- Ratio GC positivos >50%

Online nomograms for predicting nonsentinel lymph node status in sentinel lymph node-positive breast cancer.

- Stanford (3 variables)
- MD Anderson (7 variables)
- Memorial Sloan Kettering Cancer Center (9 variables)



Breast Cancer Nomogram: Breast Additional Non SLN Metastasis

This nomogram can be used to help newly diagnosed breast cancer patients assess the likelihood of additional lymph nodes.

Enter Your Information [Clear](#) [Calculate](#)

Frozen Section Performed? YES
Was a frozen section analysis performed during pathological examination? This does not have to be the method that detected the cancer in the sentinel lymph nodes, but it is necessary to know as a variable for this calculator.

Pathological Size (0.1 to 9.0 cm)
Size of the primary tumor, in centimeters.

Tumor Type and Grade
Indicate if tumor type is ductal or lobular, as noted in the pathology report. If ductal, indicate the nuclear grade – I: slight or no variation in the size and shape of the nucleus; II: moderate variation in the size and shape of the nucleus; III: marked variation in the size and shape of the nucleus.

Number of Positive Sentinel Lymph Nodes nodes (1 to 7)
Indicate the number of sentinel lymph nodes found to have cancer when biopsied.

SLN Method of Detection
Select the method used to detect cancer spread to the sentinel lymph nodes.

Number of Negative Sentinel Lymph Nodes nodes (0 to 14)
Indicate the number of sentinel lymph nodes that were found not to have cancer when biopsied.

Lymphatic or Vascular Structure Involvement (Lymphovascular Invasion) YES
Check box if one or more tumor cells were found in blood or lymphatic vessels.

Multifocality? YES
Check box if patient has cancer cells that have separated from the main tumor mass.

Patient and Cancer Information
 Education and Research
 Keyword
 Search

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- > Scientific Resources
- > Professional Educational Resources

Breast Cancer Nomogram to Predict Additional Positive Non-SLN, with Neoadjuvant Chemotherapy

Probability of positive non-sentinel lymph nodes: 18%

This software calculates the probability of finding additional positive non-sentinel lymph nodes in breast cancer patients found to have disease on sentinel lymph node biopsy without completion of neoadjuvant chemotherapy. This nomogram was developed at the University of Texas M. D. Anderson Cancer Center and has been externally validated.

[Enter SLN metastasis size as a categorical variable \(ITC, micrometastasis or macrometastasis\).](#)

Histology: Choose the histologic type of the tumor. The "Other" category includes mucinous, tubular, papillary and medullary tumors.

Tumor Size: Size of the primary tumor, in centimeters, on surgical pathology.
 (cm)

of lymph nodes removed: Total number of lymph nodes removed, either SLN or non-SLN, during SLN dissection. Enter a number from 1-13.

of Positive SLNs Total number of SLNs found to contain cancer. Enter a number from 1-6.

SLN max. size of metastasis Indicate the size of the largest focus of metastasis found in the SLN by

II.- ¿Ganglios adicionales afectados modifica el tto?

TRATAMIENTO SISTEMICO

★ QMT = pN1-pN3

FEC x 4 → Paclitaxel

Esquema de GEIC

Martin M, Rodriguez

Cyclophosphamide

100:805

, epirubicin, and
Cancer Inst 2008,

depende de los RH
no del número de ganglios

II.- ¿Ganglios adicionales afectados modifica el tto?

RADIOTERAPIA CADENAS

★ Nivel I-II

- ✍ Afectación extensa de la grasa axilar
- ✍ Disección axilar incompleta (<10 ganglios)
- ✍ cN2

9% Macrometástasis

5% Micrometástasis

★ Nivel III y supraclavicular

- ✍ Afectación > 4 ganglios axilares
- ✍ Disección axilar incompleta (<10 ganglios)
- ✍ 1-3 ganglios si factores de riesgo
 - ▶ <50 años
 - ▶ >20% ganglios afectados

3% ITC

Irradiar en GC+

ASCO 2011 (Whelan) MA.20

Irradiación N III y supraclavicular en pN1 mejora SLE 5 à (local y M) y tendencia SG.

Pte. publicar

EORTC 10981 (AMAROS)

*After mapping of the axilla:
Radiotherapy or Surgery*

Fin reclutamiento Mayo 2010

III.- ¿Dejar ganglios afectados en la axila empeora el pronóstico?

MICROMETÁSTASIS

S. Pernas, et al. Ann Surg Oncol, 2009

ICO-Bellvitge

Avoiding Axillary Treatment in Sentinel Lymph Node Micrometastases of Breast Cancer: A Prospective Analysis of Axillary or Distant Recurrence

n= 59 GC con micrometástasis (76% no LA) →5à. no recurrencia axilar ni metastasis

Toussaint A, et al. Breast J. 2011.

Université Libre de Bruxelles, Brussels

Axillary recurrence rate in breast cancer patients with negative sentinel lymph node biopsy or containing micrometastases and without further lymphadenectomy: a monocentric review of 8 years and 481 cases.

n= 45 GC con micrometástasis sin LA →2à. no recurrencia axilar

Viehl CT, et al. J Surg Oncol. 2011

University Hospital Basel, Switzerland

Prognostic impact and therapeutic implications of sentinel lymph node micro-metastases in early-stage breast cancer patients.

Salhab M, et al. Surg Oncol. 2011.

The Princess Grace Hospital, London

Sentinel lymph node micrometastasis in human breast cancer: An update.

In selected cases of SLN **MM**, complete **ALND** may be safely **omitted** provided that **adjuvant systemic** therapy recommendations are equal to patients with **node-positive** disease.

III.- ¿Dejar ganglios afectados en la axila empeora el pronóstico?

MACROMETÁSTASIS

JAMA 2011

Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis A Randomized Clinical Trial

Armando E. Giuliano, MD

Kelly K. Hunt, MD

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Peter D. Beitsch, MD

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Linda M. McCall, MS

Monica Morrow, MD

AXILLARY LYMPH NODE DISSECTION (ALND) has been part of breast cancer surgery since the description of the radical mastectomy.¹ ALND reliably identifies nodal metastases and maintains regional control,^{2,3} but the contribution of local therapy to breast cancer survival is con-

Context Sentinel lymph node dissection (SLND) accurately identifies nodal metastasis of early breast cancer, but it is not clear whether further nodal dissection affects survival.

Objective To determine the effects of complete axillary lymph node dissection (ALND) on survival of patients with sentinel lymph node (SLN) metastasis of breast cancer.

Design, Setting, and Patients The American College of Surgeons Oncology Group 20011 trial, a phase 3 noninferiority trial conducted at 115 sites and enrolling patients from May 1999 to December 2004. Patients were women with clinical T1-T2 invasive breast cancer, no palpable adenopathy, and 1 to 2 SLNs containing metastases identified by frozen section, touch preparation, or hematoxylin-eosin staining on permanent section. Targeted enrollment was 1900 women with final analysis after 500 deaths, but the trial closed early because mortality rate was lower than expected.

Interventions All patients underwent lumpectomy and tangential whole-breast irradiation. Those with SLN metastases identified by SLND were randomized to undergo ALND or no further axillary treatment. Those randomized to ALND underwent dissection of 10 or more nodes. Systemic therapy was at the discretion of the treating physician.

Main Outcome Measures Overall survival was the primary end point, with a noninferiority margin of a 1-sided hazard ratio of less than 1.3 indicating that SLND alone is noninferior to ALND. Disease-free survival was a secondary end point.

Results Clinical and tumor characteristics were similar between 445 patients randomized to ALND and 446 randomized to SLND alone. However, the median num-

Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis

A Randomized Clinical Trial

Giulano et al. JAMA 2011

MATERIAL Y METODOS

- ESTUDIO RANDOMIZADO MULTICENTRICO FASE III
- n=891 pacientes
- Criterios de inclusión
 - ✓ Cirugía conservadora de la mama (margenes libres)
 - ✓ T < 5 cm
 - ✓ No adenopatías palpables
 - ✓ 1-2 GC positivos
- Criterios de exclusión:
 - ✓ GC metastásico por IHC
 - ✓ ≥ 3 GC positivos o mucha enfermedad extraganglionar
 - ✓ Pacientes subsidiarias a tto neoadyuvante

Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis

A Randomized Clinical Trial

Resultados

Table 1. Baseline Patient and Tumor Characteristics by Study Group

Characteristic	No. (%)	
	ALND (n = 420)	SLND Alone (n = 436)
Age, median (range), y	56 (24-92)	54 (25-90)
Missing	7	10
Clinical T stage		
T1	284 (67.9)	303 (70.6)
T2	134 (32.1)	126 (29.4)
Missing	2	7
Tumor size, median (range), cm	1.7 (0.4-7.0)	1.6 (0.0-5.0)
Missing	6	14
Receptor status		
ER+/PR+	256 (66.8)	270 (68.9)
ER+/PR-	61 (15.9)	54 (13.8)
ER-/PR+	3 (0.8)	4 (1.0)
ER-/PR-	63 (16.5)	64 (16.3)
Missing	37	44
LVI		
Yes	129 (40.6)	113 (35.2)
No	189 (59.4)	208 (64.8)
Missing	102	115

Modified Bloom-Richardson score		
1	71 (22.0)	81 (25.6)
2	158 (48.9)	148 (46.8)
3	94 (29.1)	87 (27.5)
Missing	97	120
Tumor type		
Infiltrating ductal	344 (82.7)	356 (84.0)
Infiltrating lobular	27 (8.5)	36 (8.5)
Other	45 (10.8)	32 (7.5)
Missing	4	12
Lymph node metastases		
0	4 (1.2)	29 (7.0)
1	199 (58.0)	295 (71.1)
2	68 (19.8)	76 (18.3)
3	25 (7.3)	11 (2.7)
≥4	47 (13.7)	4 (1.0)
Missing	77	21

Abbreviations: ALND, axillary lymph node dissection; ER, estrogen receptor; LVI, lymphovascular invasion; PR, progesterone receptor; SLND, sentinel lymph node dissection.

Limitaciones

- 👁️ Posible sesgo selección
- 👁️ Her-2
- 👁️ RDT aplicada en axila?

Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis

A Randomized Clinical Trial

	Group A	Group B
Supervivencia 5a		
Supervivencia libre de enfermedad		
Recurrencia local		0.1 %
Recurrencia axilar		0.9 %

EL PRONOSTICO ES EL MISMO CON/SIN L.A. TRAS GC POSITIVO EN GRUPO SELECCIONADO DE PACIENTES



ALND indicates axillary lymph node dissection; SLND, sentinel lymph node dissection.

IV.- Recomendaciones de las guías clínicas internacionales

Consens St Gallen 2011

axillary surgery

The Panel was clearly of the view that the routine use of immunohistochemistry to look for low-volume metastatic disease in sentinel nodes was not indicated, since metastases shown only by immunohistochemistry would not alter

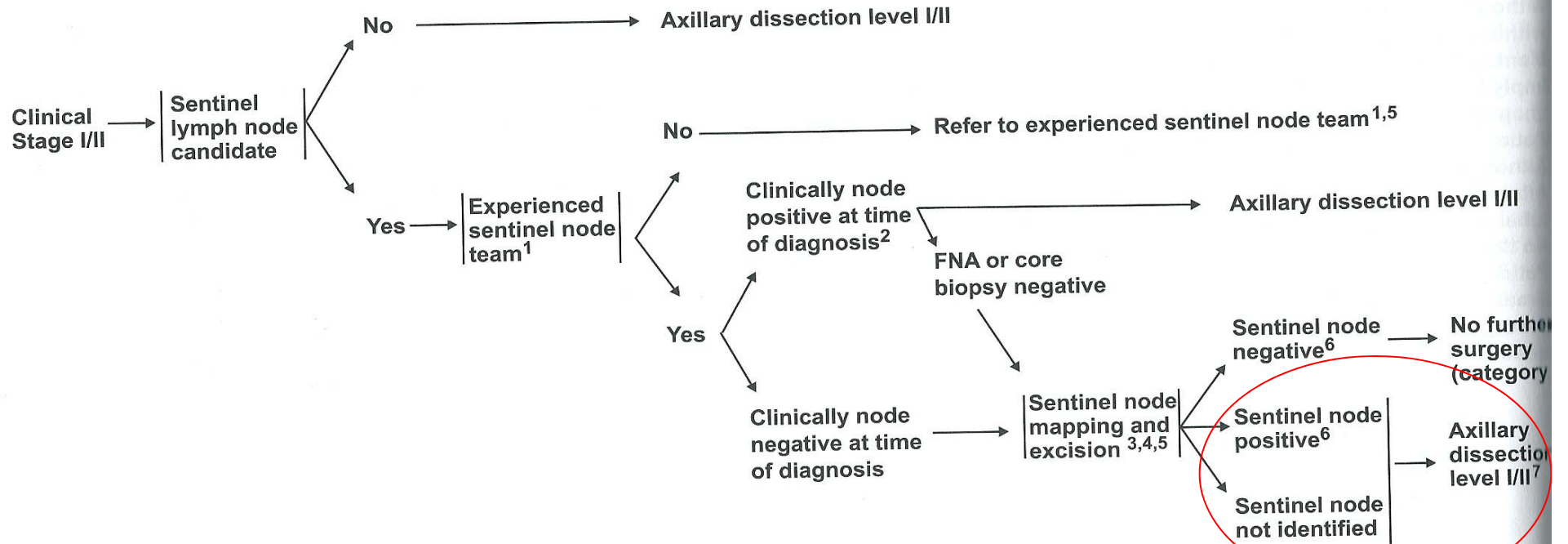
management. Furthermore, isolated tumor cells, and even metastases up to 2 mm (micrometastases) in a single sentinel node, were not considered to constitute an indication for axillary dissection regardless of the type of breast surgery

carried out. The Panel accepted the option of omitting axillary dissection for macrometastases in the context of lumpectomy and radiation therapy for patients with clinically node-negative disease and 1–2 positive sentinel lymph nodes as reported from ACOSOG trial Z0011 with a median follow-up of 6.3 years [20]. The Panel, however, was very clear that this

Excepciones

of 6.3 years [20]. The Panel, however, was very clear that this practice, based on a specific clinical trial setting, should not be extended more generally, such as to patients undergoing mastectomy, those who will not receive whole-breast tangential field radiation therapy, those with involvement of more than two sentinel nodes, and patients receiving neoadjuvant therapy.

SURGICAL AXILLARY STAGING - STAGE I, IIA, AND IIB



¹Sentinel node team must have documented experience with sentinel node biopsy in breast cancer. Team includes surgeon, radiologists, nuclear medicine physician, pathologist, and prior discussion with medical and radiation oncologists on use of sentinel node for treatment decisions.

²Consider pathologic confirmation of malignancy in clinically positive nodes using ultrasound guided FNA or core biopsy in determining if patient needs axillary lymph node dissection.

³Axillary sentinel node biopsy in all cases; internal mammary sentinel node biopsy optional if drainage maps to internal mammary nodes (category 3).

⁴Sentinel lymph node mapping injections may be peritumoral, subareolar or subdermal. However, only peritumoral injections map to the internal mammary lymph node.

⁵Results of randomized clinical trials indicate that there is a lower risk of morbidity associated with sentinel node mapping and excision than with level I/II axillary dissection.

⁶Sentinel node involvement is defined by multilevel node sectioning with hematoxylin and eosin (H&E) staining. Cytokeratin Immunohistochemistry (IHC) may be used for equivocal cases on H&E. Routine cytokeratin IHC to define node involvement is not recommended in clinical decision making.

⁷Data from a single, randomized trial suggests that complete axillary lymph node dissection in women with clinically node negative T1-T2 tumors, fewer than 3 involved sentinel lymph nodes, and undergoing breast-conserving surgery and whole breast radiation results in more morbidity, no improvement in locoregional recurrence rate and no difference in overall survival compared with sentinel lymph node procedure alone.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

IV.- Recomendaciones de las guías clínicas internacionales

Ann Surg Oncol
DOI 10.1245/s10434-011-1593-7

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

EDITORIAL

Multidisciplinary Considerations in the Implementation of the Findings from the American College of Surgeons Oncology Group (ACOSOG) Z0011 Study: A Practice-Changing Trial

Abigail S. Caudle, MD¹, Kelly K. Hunt, MD¹, Henry M. Kuerer, MD¹, Funda Meric-Bernstam, MD¹, Anthony Lucci, MD¹, Isabelle Bedrosian, MD¹, Gildy V. Babiera, MD¹, Rosa F. Hwang, MD¹, Merrick I. Ross, MD¹, Barry W. Feig, MD¹, Karen Hoffman, MD², Jennifer K. Litton, MD³, Aysegul A. Sahin, MD⁴, Wei Yang, MD⁵, Gabriel N. Hortobagyi, MD³, Thomas A. Buchholz, MD², and Elizabeth A. Mittendorf, MD¹

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MD Anderson Guidelines

ALND can be omitted in a subset of N+ patients with no impact on survival:

- ✓ T1 or T2N0 that undergo lumpectomy with limited disease in their SLN and will be treated with WBI and systemic therapy (nomogram)
- ✓ In the elderly, if T1-T3N0 HR-positive (even SLN can be omitted!)
- ✓ If SLN-micrometastasis and systemic therapy

GANGLIO CENTINELA POSITIVO

CONCLUSIONES

MICROMETÁSTASIS

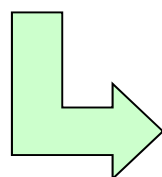


~~L.A.~~

MACROMETÁSTASIS



L.A.



✓ <2 Ganglios afectados

**GRUPO SELECCIONADO DE
PACIENTES → L.A. no BENEFICIO**

✓ RH-positivos/negativos?

✓ Nomogramas?

~~L.A.~~

**GRACIAS POR SU
ATENCIÓN**

