



## Outcomes and bioethical implications of lymphadenectomy in mastectomized patients: Importance and indication of ultrasound-guided fine-needle aspiration biopsy

Resultados e implicaciones bioéticas de la linfadenectomía en pacientes mastectomizadas: Importancia y recomendación de biopsia por aspiración con aguja fina guiada por ecografía

Resultados e implicações bioéticas da linfadenectomia em pacientes mastectomizadas: Importância e recomendação da biópsia aspirativa com agulha fina guiada por ultrassom

Marta Huertas-Moreno<sup>1</sup> [orcid.org/0000-0002-9202-7758](https://orcid.org/0000-0002-9202-7758)

Margarita Gonzalvo-Cirac<sup>2\*</sup> [orcid.org/0000-0002-7851-703X](https://orcid.org/0000-0002-7851-703X)

1. Radiology Department, Hospital General Universitario Morales Meseguer. Murcia, España.
2. Facultad Odontología, Universitat Internacional de Catalunya (UIC). Barcelona, España.

Received: Feb 28 - 2022

Revised: Sep 05 - 2022

Accepted: Jan 27- 2023

Published: Jan 31- 2023

**Citation:** Huertas-Moreno M, Gonzalvo-Cirac M. Outcomes and bioethical implications of lymphadenectomy in mastectomized patients: Importance and indication of ultrasound-guided fine-needle aspiration biopsy. *Univ. Salud.* 2023; 25(1):D6-D14. DOI: <https://doi.org/10.22267/rus.232501.296>

### Abstract

**Introduction:** Lymph node involvement is the main prognostic factor in breast cancer. Mastectomized patients usually undergo lymphadenectomy (LA) of micrometastatic sentinel lymph nodes (SLNs) despite the evidence of AMAROS trial to replace this therapy with radiotherapy in select cases. **Objective:** Demonstrate the ability of ultrasonography to detect non-metastatic or micrometastatic SLNs. **Materials and methods:** 132 patients who underwent mastectomy were evaluated. Ultrasound-guided fine-needle aspiration biopsy (FNAB) was indicated for suspicious lymph nodes. LA and SNL biopsy (SLNB) were performed in patients with positive and negative FNAB, respectively. LA was performed in FNAB positive or SLNB positive cases, except in the presence of isolated tumor cells and micrometastatic SLNs. The tumor burden after LA in patients with negative FNAB and positive SLNB was measured; the presence of two or fewer positive SLNs was considered a low burden. **Results:** Sensitivity of FNAB for detecting positive lymph nodes in patients with a high tumor burden was 93% and specificity was 84%. Positive (PPV) and negative predictive value (NPV) were 60% and 79%, respectively. **Conclusions:** LA could have been avoided in 90% of mastectomized patients with negative FNAB and a low tumor burden who met the AMAROS criteria with a high NPV (79%).

**Keywords:** Bioethics; breast cancer; sentinel lymph node; public health; lymphedema (Source: DeCS, Bireme).

### Resumen

**Introducción:** La afectación ganglionar es el principal factor pronóstico en cáncer de seno. Generalmente, pacientes mastectomizadas se someten a linfadenectomía (LA) de ganglios linfáticos centinela micrometastásicos (GLCs), a pesar de la evidencia del ensayo AMAROS en ciertos casos para reemplazarla con radioterapia. **Objetivo:** Demostrar la importancia de la ecografía para detectar GLCs no metastásicos o micrometastásicos. **Materiales y métodos:** Se evaluaron 132 pacientes sometidas a mastectomía. Se recomendó biopsia aspirativa con aguja fina (BAAF) por ultrasonido para ganglios linfáticos sospechosos. Se realizó Biopsia LA y biopsia de GLCs (BGLC) en pacientes con BAAF positiva y negativa, respectivamente. En casos positivos de BAAF o BGLC se ejecutó LA, excepto en presencia de células tumorales aisladas y GLCs. Se evaluó la carga tumoral posterior a LA en pacientes con BAAF negativa y BGLC positiva. La presencia de dos o menos GLC positivos se consideró carga baja. **Resultados:** La sensibilidad de BAAF para detectar nódulos linfáticos positivos en pacientes con alta carga tumoral fue del 93%; la especificidad fue del 79%. Valores predictivos positivo (60%) y negativo (79%). **Conclusiones:** Se podría haber evitado LA en 90% de pacientes mastectomizadas con BAAF negativa y baja carga tumoral que cumplieran criterios AMAROS con alto VPN (79%).

**Palabras clave:** Bioética; cáncer de mama; ganglio linfático centinela; salud pública; linfedema. (Fuente: DeCS, Bireme).

### Resumo

**Introdução:** O comprometimento dos gânglios é o principal fator prognóstico no câncer de mama. Geralmente, pacientes mastectomizadas são submetidas a linfadenectomia (LA) de gânglios linfáticos sentinelas de micrometástases (GLSs), apesar da evidência do estudo AMAROS em certos casos para substituí-la por radioterapia. **Objetivo:** Demonstrar a importância da ultrasonografia na detecção de GLSs não metastáticos ou micrometástase. **Materiais e métodos:** Foram avaliadas 132 pacientes submetidas à mastectomia. A biópsia aspirativa com agulha fina (BAAF) ultrassônica foi recomendada para gânglios linfáticos suspeitos. A biópsia LA e a biópsia do GLSs (BGLS) foram realizadas em pacientes com BAAF positivo e negativo, respectivamente. Nos casos positivos de BAAF ou BGLS, a LA foi realizada, exceto na presença de células tumorais isoladas e GLSs. A carga tumoral após a LA foi avaliada em pacientes com BAAF negativa e BGLS positiva. A presença de dois ou menos GLS positivos foi considerada carga baixa. **Resultados:** A sensibilidade do BAAF para detectar linfonodos positivos em pacientes com alta carga tumoral foi de 93%; a especificidade foi de 79%. Valores preditivos positivos (60%) e negativos (79%). **Conclusões:** a LA poderia ter sido evitada em 90% das pacientes mastectomizadas com BAAF negativa e baixa carga tumoral que preencheram os critérios AMAROS com alto VPN (79%).

**Palavras chave:** Bioética; neoplasias da mama; linfonodo sentinela; saúde pública; linfedema. (Fonte: DeCS, Bireme).

#### \* Corresponding Autor

Margarita Gonzalvo-Cirac  
e-mail: [mgonzalvocirac@gmail.com](mailto:mgonzalvocirac@gmail.com)

the clinical stage N0, indicating the importance of this examination for identifying patients with non-metastatic and micrometastatic SLNs.

However, despite this evidence, there is no consensus regarding axillary surgical management. For instance, a group evaluated<sup>(23)</sup> compliance with the clinical guidelines of the ACOSOG Z0011 trial using a survey of 488 surgeons who treated 5,080 early-stage breast cancers between 2013 and 2015. Their study concluded that there were considerable variations in compliance with significant overtreatment (49% and 63% of surgeons would recommend LA in the presence of one and two micrometastatic SLNs, respectively). This study is a clear example of the adoption of paternalism. Most surgeons prefer overtreatment over performing a lower-morbidity technique such as ART<sup>(24,25)</sup>.

## Conclusions

Lymph node involvement is the main prognostic factor and primary cause of morbidity in breast cancer.

LA has been the standard treatment for axillary involvement in patients who undergo mastectomy. However, patients with cT1-T2cN0 breast cancer with an indication for mastectomy who do not meet the criteria for NC and with clinically negative axillary lymph nodes on FNAB can substitute LA with RT according to the AMAROS trial evidence with a high NPV (79%) to exclude patients with a high tumor burden.

From the ethical point of view, 13 LA procedures could have been avoided in the total mastectomized population (nine of these patients met the AMAROS trial criteria) in our series because of their low tumor burden, which represents a 90% reduction in the number of LA surgeries in this group of patients. This approach decreases morbidity and causes fewer physical and psychological sequelae (principle of beneficence) without reducing the overall survival and disease-free period (principle of non-maleficence) according to AMAROS trial evidence.

The sensitivity of FNAB for diagnosing positive SLNs in breast cancer patients with a high tumor burden was 93% in our series, which demonstrates the high relevance of this minimally invasive technique.

**Declaration of interest statement:** No conflict of interests

## References

- Sabadell-Mercadal MD, Izquierdo-Sanz M, Prats de Puig M, Modolell Roig A. Factores pronósticos y predictivos en cáncer de mama [Online]. Sociedad Española de Senología y Patología Mamaria. Madrid: Fundación Española de Senología y Patología Mamaria; 2017. Available from: <https://www.sespm.es/wp-content/uploads/2018/06/MONOGRAFIA-SESPM-2017-Ebook.pdf>
- Giuliano AE, Hunt KK, Ballman KV, Beitsch PD, Whitworth PW, Blumencranz PW, et al. Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis: A Randomized Clinical Trial. *JAMA* [Online]. 2001; 305(6):569-75. DOI: 10.1001/jama.2011.90.
- Giuliano AE, Ballman KV, McCall LM, Beitsch PD, Whitworth PW, Blumencranz PW. Locoregional Recurrence After Sentinel Lymph Node Dissection With or Without Axillary Dissection in Patients with Sentinel Lymph Node Metastases: Long-Term Follow-Up from the American College of Surgeons Oncology Group (Alliance) ACOSOG Z0011 Randomized Trial. *Ann Surg* [Online]. 2016; 264(3):413-20. DOI: 10.1097/SLA.0000000000001863.
- Straver ME, Meijnen P, van Tienhoven G, van de Velde CJH, Mansel RE, Bogaerts J. Sentinel Node Identification Rate and Nodal Involvement in the EORTC 10981-22023 AMAROS Trial. *Ann Surg Oncol* [Online]. 2010; 17(7):1854-61. DOI: 10.1245/s10434-010-0945-z.
- Donker M, van Tienhoven G, Straver ME, Meijnen P, van de Velde CJH, Mansel RE. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 201981-22023AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. *Lancet* [Online]. 2014; 15(12):1303-10. DOI: 10.1016/S1470-2045(14)70460-7.
- Amonkar SJ, Oates E, McLean L, Nicholson S. Pre-operative staging of the axilla in primary breast cancer. By redefining the abnormal appearing node can we reduce investigations without affecting overall treatment? *Breast* [Online]. 2013; 22(6): 1114-8. DOI: 10.1016/j.breast.2013.06.004.
- Houssami N, Turner RM. Staging the axilla in women with breast cancer: the utility of preoperative ultrasound-guided needle biopsy. *Cancer Bio Med* [Online]. 2014; 11(2):69-77. Available from: <https://www.cancerbiomed.org/content/11/2/69/tab-article-info>
- National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report [Online]. EEUU: Office for Human Resesarch Protections; 1979. Available from: <https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html>
- Goldhirsch A, Ingle JN, Gelber RD, Coates AS, Thürlimann B, Senn H-J. Thresholds for therapies: highlights on the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2009. *Ann Oncol* [Online]. 2009; 20(8):1319-29. DOI: 10.1093/annonc/mdp322.
- Gillespie TC, Sayegh HE, Brunelle CL, Daniell KM, Taghian AG. Breast cancer-related lymphedema: risk factors, precautionary measures, and treatments. *Gland Surgery* [Online]. 2018; 7(4):379-403. DOI: 10.21037/gs.2017.11.04.
- DiSipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphedema after breast cancer: A systematic review and meta-analysis. *Lancet Oncol* [Online]. 2013; 14(6):500-15. DOI: 10.1016/S1470-2045(13)70076-7.
- Verheuve NC, van den Hoven I, Ooms HWA, Voogd AC, Roumen RHM. The Role of Ultrasound-Guided Lymph Node Biopsy in Axillary Staging of Invasive Breast Cancer in the Post-ACOSOG Z0011 Trial Era. *Ann Surg Oncol* [Online]. 2015; 22(2):409-15. DOI: 10.1245/s10434-014-4071-1.
- Boone BA, Huynh C, Spangler ML, Sumkin J, Johnson R, McGuire KP, et al. Axillary Lymph Node Burden in Invasive Breast Cancer: A Comparison of the Predictive Value of Ultrasound-Guided Needle Biopsy and Sentinel Lymph Node Biopsy. *Clin Breast Cancer* [Online]. 2015; 15(5):243-8. DOI: 10.1016/j.clbc.2015.03.011.
- Ying Z, Wei Z, Jian-qiao Z, Xiao-chun F, Ting-Jun Y, Ou H, et al. Axillary Staging of Early-Stage Invasive Breast Cancer by Ultrasound-Guided Fine-Needle Aspiration Cytology: Which Ultrasound Criteria for Classifying Abnormal Lymph Nodes Should Be Adopted in the Post-ACOSOG Z0011 Trial Era? *J Ultrasound Med* [Online]. 2016; 35(5):885-93. DOI: 10.7863/ultra.15.06019.
- Moossdorff M, Nakhlis F, Hu J, Barry WT, Losk K, Haskertt C, et al. The Potential Impact of AMAROS on the Management of the Axilla in Patients with Clinical T1-2N0 Breast Cancer Undergoing Primary Total Mastectomy. *Ann Surg Oncol* [Online]. 2018; 9(25):2612-9. DOI: 10.1245/s10434-018-6519-1.
- Grossmith S, Nguyen A, Hu J, Plichta JK, Nakhlis F, Cutone L, et al. Multidisciplinary Management of the Axilla in Patients with cT1-T2 N0 Breast Cancer Undergoing Primary Mastectomy: Results from a Prospective Single-Institution Series. *Ann Surg Oncol* [Online]. 2018; 25(12):3527-34. DOI: 10.1245/s10434-018-6525-3.
- Gregorowitsch ML, Verkooijen HM, Houweiling A, Fuhler N, Koelemij R, Schoenmaeckers EJP. Impact of modern day axillary treatment on patient reported arm morbidity and physical functioning in breast cancer patients. *Radiother Oncol* [Online]. 2019; 131:221-8. DOI: 10.1016/j.radonc.2018.07.006.
- Recht A, Comen EA, Fine RE, Fleming GF, Hardenbergh PH, Ho AY, et al. Postmactectomy radiotherapy: an American Society of Clinical Oncology, American Society for Radiation

- Oncology, and Society of Surgical Oncology Focused Guideline Update. *Ann Surg Oncol* [Online]. 2017; 24(1):38-51. DOI: 10.1245/s10434-016-5558-8.
19. Donker M, Straver ME, van Tienhoven G, van der Velde CJH, Mansel RE, Litiere S, et al. Comparison of the sentinel node procedure between patients with multifocal and unifocal breast cancer in the EORTC 10981-22023 AMAROS Trial: Identification rate and nodal outcome. *Eur J Cancer* [Online]. 2013; 49(9):2093-100. DOI: 10.1016/j.ejca.2013.02.017.
  20. Van Roozendaal LM, Smit LH, Duijsens GH, de Vries B, Siesling S, Lobbes MB, et al. Risk of regional recurrence in triple-negative breast cancer patients: a Dutch cohort study. *Breast Cancer Res Treat* [Online]. 2016; 156(3):465-72. DOI: 10.1007/s10549-016-3757-4.
  21. Farace P, Deidda MA, Amichetti M. Axillary irradiation omitting axillary dissection in breast cancer: is there a role for shoulder-sparing proton therapy? *BJR* [Online]. 2015; 88(1054):20150274. DOI: 10.1259/bjr.20150274.
  22. Boughhey JC. How do the AMAROS trial results change practice? *Lancet* [Online]. 2014; 15(12):1280-1. DOI: 10.1016/S1470-2045(14)71018-6.
  23. Morrow M, Jagsi R, McLeod MC, Shumway D, Katz SJ. Surgeon Attitudes Toward the Omission of Axillary Dissection in Early Breast Cancer. *JAMA* [Online]. 2018; 4(11):1511-6. DOI: 10.1001/jamaoncol.2018.1908.
  24. Magnoni F, Galimberti V, Corso G, Intra M, Sacchini V, Veronesi P. Axillary surgery in breast cancer: An updated historical perspective. *Semin Oncol* [Online]. 2020;47(6):341-352. DOI: 10.1053/j.seminoncol.2020.09.001.
  25. Chang DW, Bressel M, Hansen C, Blinman P, Schofield P, Chua BH. Axillary dissection in sentinel lymph node positive breast cancer: Is the staging information worthwhile for patients? *Asia Pac J Clin Oncol* [Online]. 2021; 17(2):e27-34. DOI: 10.1111/ajco.13238.