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ORIGINAL ARTICLE

Sentinel Node Biopsy Positivity: Is Axillary Dissection Always Necessary? – A Retrospective Analysis

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Abstract: *Breast cancer remains a significant health concern, with predictions indicating a rise in global incidence. While the primary focus is on oncological radicality, the aesthetic and psychological impacts of surgical interventions, such as radical mastectomy, cannot be ignored. This study, conducted over 8 years, aimed to identify factors that can prevent unnecessary lymphadenectomy. The research analyzed various parameters, including age, BMI, tumor size, and immunohistochemistry, to determine their correlation with axillary lymph node invasion. The results highlighted the importance of tumor size and estrogen receptor status in predicting axillary lymph node metastasis. The study underscores the value of sentinel lymph node biopsy in early breast cancer treatment, emphasizing its benefits over complete axillary lymph node dissection.*

Keywords: *breast cancer, lymphadenectomy, sentinel node biopsy*

INTRODUCTION

According to the American Cancer Society, one out of eight women in the United States will develop breast cancer during their lifetime [1]. Predictions regarding the global incidence of breast cancer in women outline the idea that the incidence will reach approximately 3.2 million new cases per year by 2050.

These numbers reflect the magnitude of breast cancer incidence, its impact on women worldwide, and the ongoing and urgent need to take measures towards prevention and proper therapeutic management [2].

The goal of oncological radicality remains essential and obligatory, but breast neoplasm surgery must also consider the aesthetic component due to the psychological impact that a major surgical intervention, such as radical mastectomy, has on patients. In the early stages, breast cancer can be treated without such a procedure being necessary.

Therefore, in today's times, the gold standard of breast cancer surgery is represented by conservative treatment. It involves the resection of the primary tumor with oncological safe margins and sentinel lymph node biopsy, followed by adjuvant radiotherapy [2,3].

The surgical management of the axilla has always been a controversial topic. For a very long time, it was believed that achieving good loco-regional control involves a complete axillary lymph node dissection, with this method being the gold standard of that era.

In recent years, due to the observed increase in morbidity and decrease in the quality of life for these patients, the method has been abandoned and replaced by sentinel lymph node biopsy.

The technique of identifying the sentinel lymph node (SLN) is based on the theory of the lymphatic spread of cancers, with the neoplastic invasion occurring in a lymph node that drains lymph from the site of the tumor [4,5] .

The prime objective of this study is the identification of factors that can prevent unnecessary lymphadenectomy.

MATERIALS AND METHODS

Based on the purpose and objectives of the research, the research design and methodology have been defined, with its main characteristics being: retrospective - spanning over an 8-year interval - January 1, 2014 - December 31, 2021, single-center, descriptive and correlational, non-interventional.

The eligibility criteria were as follows:

- Diagnosis of breast cancer
- The presence of axillary management after a positive sentinel node biopsy
- Female sex
- Stage IIA-IIIB:
  - o IIA (T2N0M0, T1N1M0)
  - o IIB (T2N1M0, T3N0M0)
  - o IIIA (T3N1M0)
  - o IIIB (T4N1M0)
- Single tumor, excluding multifocal and bilateral cases
- The presence of all required data
- Age > 18 years
- M0
- Any Histopathological type

RESULTS

The working hypothesis considers patients who underwent the sentinel lymph node technique, and the result was positive. In this situation, studies have shown that up to 1/3 of cases present a negative result of the axillary lymphadenectomy. To assess the risk factors for a positive axillar biopsy, we made a comparison between group E – a positive result of axillary lymphadenectomy (34 cases), and group D – a negative result of axillary lymphadenectomy (15 cases) (Table 1).

Table 1: Comparative data of groups (E vs. D)

Study lot	D	E
SNB	✓	✓
SNB results	+	+
ALND	✓	✓
ALND results	-	+
Case numbers	15	34

Age

There was no statistical correlation between the age of the patients and the presence of axillary invasion in patients with a positive sentinel lymph node, even though there was a mean difference of 5.85 years - p=0.175 (Table 2 and Figure 1).

Table 2: Comparative statistical data regarding age (E vs. D)

	Age	
	E	D
Valid	34	15
Missing	0	0
Mean	63.324	57.467
Std. Deviation	14.367	12.118
Minimum	28.000	29.000
Maximum	89.000	78.000

	t	df	p	Mean difference	SE difference
Age	1.376	47	0.175	5.857	4.258

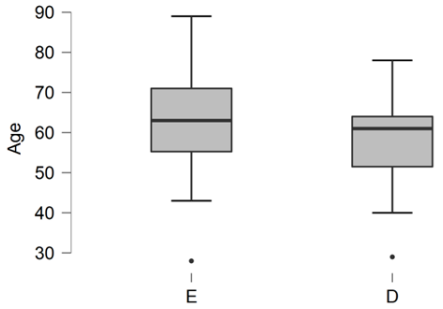

Figure 1: Comparative statistical data regarding age (E vs. D)

BMI

The Body Mass Index (BMI) value calculated for the two groups showed a higher average in the case of patients with axillary invasion, with a difference of 3.58 and moderate statistical significance - p=0.05 (Table 3 and Figure 2).

Table 3: Comparative statistical data regarding BMI (E vs. D)

	BMI	
	E	D
Valid	34	15
Missing	0	0
Mean	28.696	25.107
Median	28.100	24.900
Std. Deviation	6.187	4.608
Minimum	18.970	19.760
Maximum	45.650	33.650

	t	df	p	Mean difference	SE difference
BMI	2.009	47	0.050	3.589	1.786

Bio-clinical analysis

Comparative assessment of routine laboratory test values collected upon admission highlights relatively small differences between the groups discussed in this hypothesis.

The only parameter that demonstrated moderate statistical significance was the white blood cell count - with a mean difference of 1.44 and p=0.065 (Table 4 and Figure 3). Tumor markers did not show statistically significant differences.

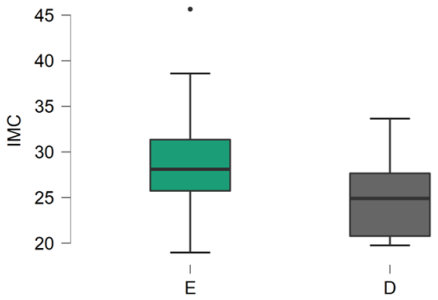

Figure 2: Comparative statistical data regarding BMI (E vs. D)

Table 4: Comparative statistical data regarding bio-clinical analysis (E vs. D)

	Hb		Ht		WBC		ESR		INR		Fibrinogen	
	E	D	E	D	E	D	E	D	E	D	E	D
Valid	34	15	34	15	34	15	34	15	34	15	34	15
Mean	12.515	12.647	40.529	40.067	8.726	7.280	31.971	29.800	1.189	1.130	434.029	378.600
Std. Deviation	1.259	1.148	3.518	4.559	2.550	2.253	18.909	16.618	0.313	0.215	186.974	174.482
Minimum	8.50	9.90	35.00	31.00	5.00	3.90	8.00	3.00	0.830	0.840	201.00	205.00
Maximum	15.30	13.80	48.00	47.00	14.70	10.90	101.00	57.00	1.940	1.60	835.00	823.00

Quadrant

The location of the tumor did not correlate with the extent of the axillary invasion, even though there were differences in the distribution of cases concerning this parameter, the statistical significance was not relevant (Tables 5 and 6).

Table 4: Comparative statistical data regarding bio-clinical analysis (E vs. D) – cont.

	t	df	p	Mean difference	SE difference
Hb	-0.347	47	0.730	-0.132	0.380
Ht	0.387	47	0.701	0.463	1.196
WBC	1.893	47	0.065	1.446	0.764
ESR	0.384	47	0.703	2.171	5.659
INR	0.657	47	0.514	0.059	0.089
Fibrinogen	0.975	47	0.334	55.429	56.830

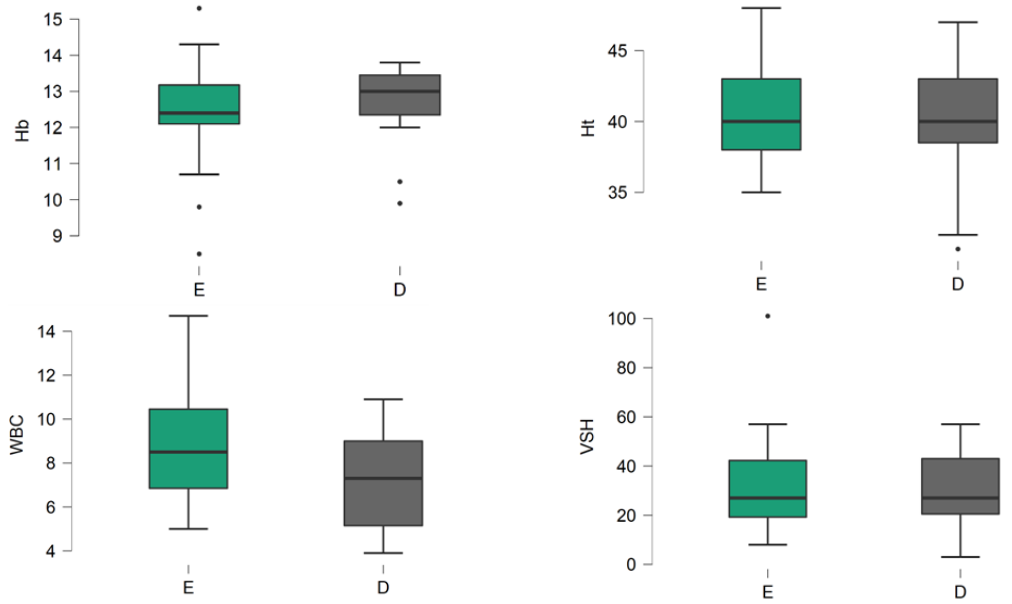

Figure 3: Comparative statistical data regarding bio-clinical analysis (E vs. D)

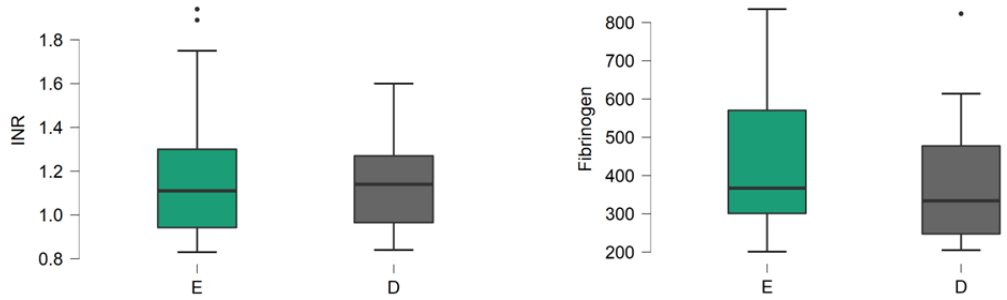

Figure 3: Comparative statistical data regarding bio-clinical analysis (E vs. D) – cont.

Table 5: Comparative statistical data regarding the tumor location (E vs. D)

Frequencies for Quadrant					
Hypothesis 2	**Quadrant**	**Frequency**	**Percent**	**Valid Percent**	**Cumulative Percent**
E	C	3	8.824	8.824	8.824
	SE	20	58.824	58.824	67.647
	SI	3	8.824	8.824	76.471
	IE	7	20.588	20.588	97.059
	II	1	2.941	2.941	100.000
	Missing	0	0.000		
	Total	34	100.000		
D	C	2	13.333	13.333	13.333
	SE	12	80.000	80.000	93.333
	SI	0	0.000	0.000	93.333
	IE	1	6.667	6.667	100.000
	II	0	0.000	0.000	100.000
	Missing	0	0.000		
	Total	15	100.000		

Chi-Squared Tests			
	Value	**df**	**p**
X^2	3.922	4	0.417
N	49		

Tumor size

The distribution of tumor sizes highlights higher values within group E - with axillary lymph node invasion, with a mean difference of 8.7 mm and a statistical significance of p=0.04 (Table 7 and Figures 4 and 5).

Immunohistochemistry

From the perspective of evaluating the presence of hormone receptors in the immunohistochemical assessment of breast resection specimens, only estrogen receptors have been identified as a risk factor for axillary invasion beyond the sentinel lymph node. The calculated risk is 7.33 times with a statistical significance of p=0.005 (Tables 8 - 10).

Subtype

From the perspective of molecular subtypes, the division into Luminal A, Luminal B, and Triple Negative did not show a statistically significant correlation with the presence of axillary lymph node invasion in patients with a positive sentinel lymph node. In the case of the HER2 sub-type, the risk of axillary lymph node invasion was nearly 10 times higher - p=0.084 (Tables 11-14).

Table 6: Distribution of cases concerning the localization in the interior of the exterior quadrant of the tumor (E vs D)

Ext 1 vs Int 0 quadrant		**Hypothesis 2**		
		0	**1**	**Total**
0	Count	7.000	2.000	9.000
	% within row	77.778 %	22.222 %	100.000 %
	% within column	20.588 %	13.333 %	18.367 %
1	Count	27.000	13.000	40.000
	% within row	67.500 %	32.500 %	100.000 %
	% within column	79.412 %	86.667 %	81.633 %
Total	Count	34.000	15.000	49.000
	% within row	69.388 %	30.612 %	100.000 %
	% within column	100.000 %	100.000 %	100.000 %

Table 6: Distribution of cases concerning the localization in the interior of the exterior quadrant of the tumor (E vs D) – cont.

	Log Odds Ratio	95% Confidence Intervals		p
		Lower	Upper	
Odds ratio	0.522	-1.183	2.227	
Fisher's exact test	0.512	-1.331	2.926	0.702

Table 7: Comparative statistical data regarding the tumor size (E vs. D)

	Size	
	E	D
Valid	34	15
Mean	21.235	12.533
Std. Deviation	14.078	11.154
Minimum	4.000	1.000
Maximum	58.000	47.000

	t	df	p	Mean Difference	SE Difference
Size	2.115	47	0.040	8.702	4.115

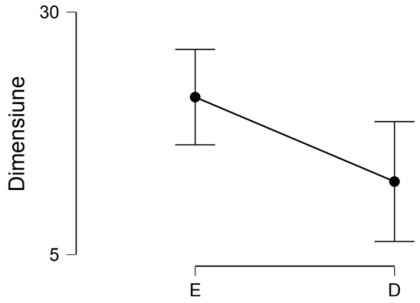

Figure 4: Comparative statistical data regarding tumor size (E vs. D)

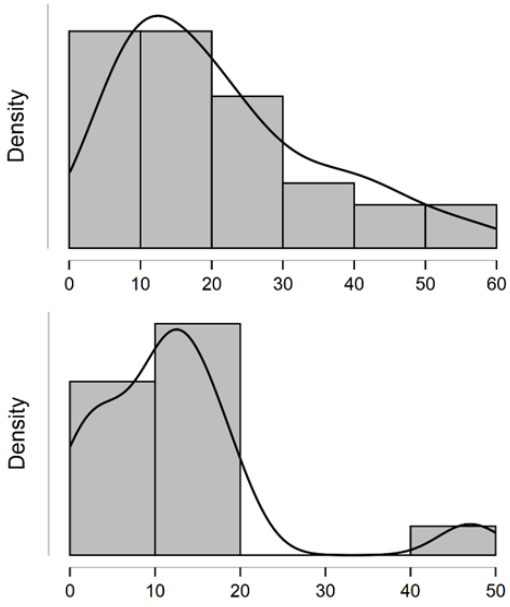

Figure 5: Distribution of cases concerning the tumor size (E left vs. D right)

Table 8: Distribution of cases concerning the presence of ER receptors (E vs D)

ER+		Hypothesis 2		Total
		0	1	
0	Count	22.000	3.000	25.000
	% within row	88.000 %	12.000 %	100.000 %
	% within column	64.706 %	20.000 %	51.020 %
1	Count	12.000	12.000	24.000
	% within row	50.000 %	50.000 %	100.000 %
	% within column	35.294 %	80.000 %	48.980 %
Total	Count	34.000	15.000	49.000
	% within row	69.388 %	30.612 %	100.000 %
	% within column	100.000 %	100.000 %	100.000 %

	Odds Ratio	95% Confidence Intervals		p
		Lower	Upper	
Odds ratio	7.333	1.724	31.186	
Fisher's exact test	7.019	1.498	46.390	0.005

Table 9: Distribution of cases with the presence of PR receptors (E vs D)

PR+		Hypothesis 2		Total
		0	1	
0	% within row	72.000 %	28.000 %	100.000 %
	% within column	52.941 %	46.667 %	51.020 %
1	Count	16.000	8.000	24.000
	% within row	66.667 %	33.333 %	100.000 %
	% within column	47.059 %	53.333 %	48.980 %
Total	Count	34.000	15.000	49.000
	% within row	69.388 %	30.612 %	100.000 %
	% within column	100.000 %	100.000 %	100.000 %

	Odds Ratio	95% Confidence Intervals		p
		Lower	Upper	
Odds ratio	1.286	0.381	4.344	
Fisher's exact test	1.279	0.321	5.206	0.762

Table 10: Distribution of cases with the presence of PR receptors (E vs D)

HER2+		Hypothesis 2		Total
		0	1	
0	Count	22.000	10.000	32.000
	% within row	68.750 %	31.250 %	100.000 %
	% within column	64.706 %	66.667 %	65.306 %
1	Count	12.000	5.000	17.000
	% within row	70.588 %	29.412 %	100.000 %
	% within column	35.294 %	33.333 %	34.694 %
Total	Count	34.000	15.000	49.000
	% within row	69.388 %	30.612 %	100.000 %
	% within column	100.000 %	100.000 %	100.000 %

	Odds Ratio	95% Confidence Intervals		p
		Lower	Upper	
Odds ratio	0.917	0.254	3.308	
Fisher's exact test	0.918	0.198	3.851	1.000

Table 11: The distribution of cases concerning the Luminal A subtype (E vs D)

Luminal A		Hypothesis 2		Total
		0	1	
0	Count	21.000	7.000	28.000
	% within row	75.000 %	25.000 %	100.000 %
	% within column	61.765 %	46.667 %	57.143 %
1	Count	13.000	8.000	21.000
	% within row	61.905 %	38.095 %	100.000 %
	% within column	38.235 %	53.333 %	42.857 %
Total	Count	34.000	15.000	49.000
	% within row	69.388 %	30.612 %	100.000 %
	% within column	100.000 %	100.000 %	100.000 %

	Odds Ratio	95% Confidence Intervals		p
		Lower	Upper	
Odds ratio	1.846	0.541	6.302	
Fisher's exact test	1.823	0.455	7.538	0.363

DISCUSSION

The literature describes four parameters as independent factors of lymph node metastasis, namely lymphovascular invasion, primary tumor size, multiple foci, and tumor localization.

An independent prognostic factor for disease-free survival (DFS) that has been recently analyzed in literature for patients with breast carcinoma is the degree of lymphovascular invasion [6].

Additionally, lymphovascular invasion is associated with a higher frequency of axillary lymph node metastases [7]. To use this data as a tool in determining the indication for sentinel lymph node biopsy (SLNB) or axillary lymphadenectomy, more extensive studies are needed to specifically determine the degree of invasion and the cutoff value that necessitates radical intervention.

Table 12: The distribution of cases concerning the Luminal B subtype (E vs D)

Luminal B		Hypothesis 2		Total
		0	1	
0	Count	26.000	10.000	36.000
	% within row	72.222 %	27.778 %	100.000 %
	% within column	76.471 %	66.667 %	73.469 %
1	Count	8.000	5.000	13.000
	% within row	61.538 %	38.462 %	100.000 %
	% within column	23.529 %	33.333 %	26.531 %
Total	Count	34.000	15.000	49.000
	% within row	69.388 %	30.612 %	100.000 %
	% within column	100.000 %	100.000 %	100.000 %

	Odds Ratio	95% Confidence Intervals		p
		Lower	Upper	
Odds ratio	1.625	0.428	6.171	
Fisher's exact test	1.608	0.331	7.329	0.500

Table 13: The distribution of cases concerning the Luminal B subtype (E vs D)

Her2		Hypothesis 2		Total
		0	1	
0	Count	27.000	15.000	42.000
	% within row	64.286 %	35.714 %	100.000 %
	% within column	79.412 %	100.000 %	85.714 %
1	Count	7.000	0.000	7.000
	% within row	100.000 %	0.000 %	100.000 %
	% within column	20.588 %	0.000 %	14.286 %
Total	Count	34.000	15.000	49.000
	% within row	69.388 %	30.612 %	100.000 %
	% within column	100.000 %	100.000 %	100.000 %

	Odds Ratio	95% Confidence Intervals		p
		Lower	Upper	
Odds ratio	0.118	0.006	2.214	
Fisher's exact test	0.000	0.000	1.466	0.084

A series of studies have demonstrated that younger age is a risk factor for positive axillary lymph nodes (ALN) [8–11]. This has been attributed to more biologically aggressive tumors in this younger age group. The average age of menopause is around 50 years, so most literature establishes 50 years as a cutoff point in exploring the relationship between age and clinicopathological factors in invasive breast cancer [8,12]. The current study did not show correlations between the risk of axillary lymph node spread and age, BMI, and the biological status of breast cancer patients, with results similar to those described in the studies.

Table 14: The distribution of cases concerning the Triple-negative subtype (E vs D)

Triple negative		Hypothesis 2		Total
		0	1	
0	Count	28.000	13.000	41.000
	% within row	68.293 %	31.707 %	100.000 %
	% within column	82.353 %	86.667 %	83.673 %
1	Count	6.000	2.000	8.000
	% within row	75.000 %	25.000 %	100.000 %
	% within column	17.647 %	13.333 %	16.327 %
Total	Count	34.000	15.000	49.000
	% within row	69.388 %	30.612 %	100.000 %
	% within column	100.000 %	100.000 %	100.000 %

	Odds Ratio	95% Confidence Intervals		p
		Lower	Upper	
Odds ratio	0.718	0.127	4.051	
Fisher's exact test	0.723	0.063	4.803	1.000

Histologic grade and tumor size (often over 5 centimeters in size) are also important predictors of lymph node metastasis. The probability is high if a patient has a large tumor and a high histologic grade. Our presented data show that patients with larger tumor sizes and a high histologic grade are more likely to have axillary invasion, a finding that aligns with those from previous studies [1,6,13–15]. Patients with small invasive breast cancer might benefit from SLNB.

The inclusion of extranodal extension in the evaluation protocol is necessary to achieve precise oncologic staging. Although attempts have been made to establish cut-off values for the circumferential and perpendicular diameters of invasion extension, these have not yielded significant predictive values. Therefore, more extensive studies are needed to specifically determine the dimensions of invasion from which axillary lymph node metastatic burden can be predicted, subsequently guiding the appropriate therapeutic approach [16,17].

Estrogen receptor status was another factor that showed a significant correlation with axillary lymph node involvement, with a calculated risk of axillary invasion beyond the sentinel lymph node being 7.33 times higher in HER+ patients. Various studies have evaluated the role of hormonal receptor status in predicting axillary lymph node metastasis (ALNM) with contradictory results. Capdet et al. [18,19], in their study of 1416 patients with early breast cancer, found no association between hormonal status and lymph node involvement. In contrast, Lee et al. [20] reported a high incidence of ALNM regardless of tumor size in the Korean population with T1-2 breast carcinoma. Finally, in a recent study conducted by Holm-Rasmussen et al. [21], patients with ER-negative tumors had a reduced risk of ALN involvement at the time of diagnosis compared to other patients.

Large integrative analyses are necessary to explain why ER-negative tumors have a low rate of axillary metastases and a high rate of distant metastases. Conversely, HER2-positive tumors have an axillary metastasis rate closely linked to tumor size and a high rate of distant metastases [22,23].

Among the limitations of the study, the retrospective nature of its design, the small number of tracked patients, and the lack of information regarding the use of chemotherapy, radiotherapy, or hormone therapy are identified.

Systemic therapies, including hormonal therapy, cytotoxic chemotherapy, and/or radiation therapy, remain critically important, especially in the treatment of breast cancer with positive lymph nodes [24–28]. Therefore, the results of this study will contribute to decision-making regarding the addition of axillary lymph node dissection (ALND), systemic therapy, and/or radiotherapy in the case of SLN metastases efforts to determine the cost of QALY in Romania [26,27,28].

CONCLUSIONS

Regional lymph node staging is necessary for tumor staging and surgical planning. Previous studies have identified several important factors in predicting axillary lymph node metastasis (ALNM), but the predictive power has not been satisfactory.

With advancements in surgical techniques, sentinel lymph node biopsy (SLNB) is now widely used in early breast cancer and has become a standard procedure in clinically node-negative patients. The benefits of SLNB include fewer surgical complications than complete axillary lymph node dissection (ALND) and effectiveness and accuracy in long-term follow-up.

Conflicts of interest and sources of funding

The authors declare no conflict of interest. This research received no external funding.

Authors' contribution

Conceptualization, R.A-M. and D.N.P.; methodology, O.A.; software, S.N.; validation, A.B., F.S. and M.C.D.; formal analysis, D.I.; investigation, R.A-M.; resources, D.N.P.; data curation, O.A.; writing—original draft preparation, S.N.; writing—review and editing, A.B.; visualization, F.S.; supervision, M.C.D.; project administration, D.I.; funding acquisition, R.A-M. All authors have read and agreed to the published version of the manuscript.

Ethics approval and consent to participate

The study was conducted following the Declaration of Helsinki, and approved by the Institutional Review of University Emergency Hospital of Bucharest.

Patient consent for publication

Informed consent was obtained from all subjects involved in the study.

References:

1. Hammond MEH, Hayes DF, Dowsett M, Allred DC, Hagerty KL, Badve S, et al. American Society of Clinical Oncology/College of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. Arch Pathol Lab Med [Internet]. 2010 Jun [cited 2023 Oct 31];134(6):907–22. Available from: https://pubmed.ncbi.nlm.nih.gov/20586616/

2. Ferrarazzo G, Nieri A, Firpo E, Rattaro A, Mignone A, Guasone F, et al. The Role of Sentinel Lymph Node Biopsy in Breast Cancer Patients Who Become Clinically Node-Negative Following Neo-Adjuvant Chemotherapy: A Literature Review. Current Oncology 2023, Vol 30, Pages 8703-8719 [Internet]. 2023 Sep 25 [cited 2023 Oct 31];30(10):8703–19. Available from: https://www.mdpi.com/1718-7729/30/10/630/htm

3. Franceschini G, Sanchez AM, Di Leone A, Magno S, Moschella F, Accetta C, et al. New trends in breast cancer surgery: a therapeutic approach increasingly efficacy and respectful of the patient. G Chir [Internet]. 2015 Jul 1 [cited 2023 Oct 31];36(4):145. Available from: /pmc/articles/PMC4732583/

4. Tonellotto F, Bergmann A, de Souza Abrahão K, de Aguiar SS, Bello MA, Thuler LCS. Impact of Number of Positive Lymph Nodes and Lymph Node Ratio on Survival of Women with Node-Positive Breast Cancer. Eur J Breast Health [Internet]. 2019 Apr 1 [cited 2023 Oct 31];15(2):76. Available from: /pmc/articles/PMC6456272/

5. Wu JL, Tseng HS, Yang LH, Wu HK, Kuo SJ, Chen ST, et al. Prediction of axillary lymph node metastases in breast cancer patients based on pathologic information of the primary tumor. Med Sci Monit [Internet]. 2014 Apr 8 [cited 2023 Oct 31];20:577–81. Available from: https://pubmed.ncbi.nlm.nih.gov/24714517/

6. Mittendorf EA, Sahin AA, Tucker SL, Meric-Bernstam F, Yi M, Nayeemuddin KM, et al. Lymphovascular Invasion and Lobular Histology are Associated with Increased Incidence of Isolated Tumor Cells in Sentinel Lymph Nodes from Early-Stage Breast Cancer Patients. Ann Surg Oncol [Internet]. 2008 Dec [cited 2023 Oct 31];15(12):3369. Available from: /pmc/articles/PMC4331098/

7. Gurleyik G, Gurleyik E, Aker F, Aktekin A, Emir S, Gungor O, et al. Lymphovascular invasion, as a prognostic marker in patients with invasive breast cancer. Acta Chir Belg [Internet]. 2007 [cited 2023 Oct 31];107(3):284–7. Available from: https://pubmed.ncbi.nlm.nih.gov/17685254/

8. Hwang RF, Krishnamurthy S, Hunt KK, Mirza N, Ames FC, Feig B, et al. Clinicopathologic factors predicting involvement of nonsentinel axillary nodes in women with breast cancer. Ann Surg Oncol [Internet]. 2003 [cited 2023 Oct 31];10(3):248–54. Available from: https://pubmed.ncbi.nlm.nih.gov/12679309/

9. Łukasiewicz S, Czeczelewski M, Forma A, Baj J, Sitarz R, Stanisławek A. Breast Cancer-Epidemiology, Risk Factors, Classification, Prognostic Markers, and Current Treatment Strategies-An Updated Review. Cancers (Basel) [Internet]. 2021 Sep 1 [cited 2023 Oct 31];13(17). Available from: https://pubmed.ncbi.nlm.nih.gov/34503097/

10. Momenimovahed Z, Salehiniya H. Epidemiological characteristics of and risk factors for breast cancer in the world. Breast Cancer (Dove Med Press) [Internet]. 2019 [cited 2023 Oct 31];11:151–64. Available from: https://pubmed.ncbi.nlm.nih.gov/31040712/

11. Petca A, Miron BC, Pacu I, Dumitrașcu MC, Mehedințu C, Șandru F, et al. HELLP Syndrome—Holistic Insight into Pathophysiology. Medicina (B Aires) [Internet]. 2022 Feb 1 [cited 2023 Oct 24];58(2). Available from: /pmc/articles/PMC8875732/

12. Nicolau CD, Cormos B, Enache L, Tarta A, Sipos R, Saftoiu A. First Romanian Tele-Echography Network – Preliminary Results. Romanian Journal of Military Medicine. 2023 Aug 1;126(4):411–7.

13. Cristian Dumitrascu M, Maria Alexandra Stanescu A, Bejan C, Sandru F, Oana Toader D, George Radavoi D, et al. Obesity and its Implications on Stress Urinary Incontinence. [cited 2023 Oct 24]; Available from: https://www.cdc.gov/

14. Wong JS, O'Neill A, Recht A, Schnitt SJ, Connolly JL, Silver B, et al. The relationship between lymphatic vessell invasion, tumor size, and pathologic nodal status: can we predict who can avoid a third field in the absence of axillary dissection? Int J Radiat Oncol Biol Phys [Internet]. 2000 Aug 1 [cited 2023 Oct 31];48(1):133–7. Available from: https://pubmed.ncbi.nlm.nih.gov/10924982/

15. Chiu CW, Chang LC, Su CM, Shih SL, Tam KW. Precise application of sentinel lymph node biopsy in patients with ductal carcinoma in situ: A systematic review and meta-analysis of real-world data. Surg Oncol [Internet]. 2022 Dec 1 [cited 2023 Oct 31];45. Available from: https://pubmed.ncbi.nlm.nih.gov/36332555/

16. Jeruss JS, Newman LA, Ayers GD, Cristofanilli M, Broglio KR, Meric-Bernstam F, et al. Factors predicting additional disease in the axilla in patients with positive sentinel lymph nodes after neoadjuvant chemotherapy. Cancer [Internet]. 2008 Jun 15 [cited 2023 Oct 31];112(12):2646–54. Available from: https://pubmed.ncbi.nlm.nih.gov/18442039/

17. Zhang W, Xu J, Wang K, Tang XJ, Liang H, He JJ. Independent risk factors for axillary lymph node metastasis in breast cancer patients with one or two positive sentinel lymph nodes. BMC Womens Health [Internet]. 2020 Jul 9 [cited 2023 Oct 31];20(1). Available from: https://pubmed.ncbi.nlm.nih.gov/32646416/

18. Capdet J, Martel P, Charitansky H, Lim YKT, Ferron G, Battle L, et al. Factors predicting the sentinel node metastases in T1 breast cancer tumor: an analysis of 1416 cases. Eur J Surg Oncol [Internet]. 2009 Dec [cited 2023 Oct 31];35(12):1245–9. Available from: https://pubmed.ncbi.nlm.nih.gov/19574018/

19. Sopu A, Apel J. Leadership skills in surgeons: a review of the literature. Romanian Journal of Military Medicine. 2021;129(2).

20. Lee JH, Kim SH, Suh YJ, Shim BY, Kim HK. Predictors of axillary lymph node metastases (ALNM) in a Korean population with T1-2 breast carcinoma: triple negative breast cancer has a high incidence of ALNM irrespective of the tumor size. Cancer Res Treat [Internet]. 2010 [cited 2023 Oct 31];42(1):30. Available from: https://pubmed.ncbi.nlm.nih.gov/20369049/

21. Holm-Rasmussen EV, Jensen MB, Balslev E, Kroman N, Tvedskov TF. Reduced risk of axillary lymphatic spread in triple-negative breast

cancer. Breast Cancer Res Treat [Internet]. 2015 Jan 1 [cited 2023 Oct 31];149(1):229–36. Available from: https://research.regionh.dk/en/publications/reduced-risk-of-axillary-lymphatic-spread-in-triple-negative-brea

22. Reyal F, Rouzier R, Depont-Hazelzet B, Bollet MA, Pierga JY, Alran S, et al. The Molecular Subtype Classification Is a Determinant of Sentinel Node Positivity in Early Breast Carcinoma. [cited 2023 Oct 31]; Available from: www.plosone.org

23. Voinea OC, Sajin M, Dumitru A V, Pătrașcu OM, Georgescu TA, Cîrstoiu MM, et al. Emerging concepts regarding the molecular profile of breast carcinoma: one-year experience in a University Center. Romanian Journal of Military Medicine. 2018;17(1).

24. Gipponi M, Bassetti C, Canavese G, Catturich A, Di Somma C, Vecchio C, et al. Sentinel lymph node as a new marker for therapeutic planning in breast cancer patients. J Surg Oncol [Internet]. 2004 Mar 1 [cited 2023 Oct 31];85(3):102–11. Available from: https://pubmed.ncbi.nlm.nih.gov/14991881/

25. Sandru F, Petca RC, Costescu M, Dumitrașcu MC, Popa A, Petca A, et al. Cutaneous Mastocytosis in Childhood-Update from the Literature. J Clin Med [Internet]. 2021 Apr 1 [cited 2023 Oct 31];10(7). Available from: https://pubmed.ncbi.nlm.nih.gov/33918305/

26. Katz A, Niemierko A, Gage I, Evans S, Shaffer M, Fleury T, et al. Can axillary dissection be avoided in patients with sentinel lymph node metastasis? J Surg Oncol [Internet]. 2006 Jun 1 [cited 2023 Oct 31];93(7):550–8. Available from: https://pubmed.ncbi.nlm.nih.gov/16705723/

27. Lupușoru G, Ailincăi I, Frățilă G, Ungureanu O, Andronesi A, Lupușoru M, et al. Tumor Lysis Syndrome: An Endless Challenge in Onco-Nephrology. Biomedicines [Internet]. 2022 May 1 [cited 2023 Oct 31];10(5). Available from: /pmc/articles/PMC9138780/

28. 12. Vîrgolici HM, Ceban D, Răducu RC, Purcărea VL. Blockchain technology used in medicine. A brief survey. Romanian Journal of Military Medicine, 125(3): 506-514 2022, doi: 10.55453/rjmm.2022.125.3.23.