INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

FACTORS AFFECTING IDENTIFICATION OF SENTINEL LYMPH NODES IN BREAST CANCER PATIENTS USING METHYLENE BLUE DYE: A COMPARATIVE ANALYSIS

Original Research

Muhammad Faizan Saleem[1]*, Usra Parvez[2], Warda Haroon[1], Bushra Shirazi[3], Muhammad Arsalan Khan[4]
[1]Resident General Surgeon, Sindh Institute of Urology and Transplantation, Pakistan.
[2]Assistant Professor, General Surgery, Sindh Institute of Urology and Transplantation, Pakistan.
[3]Professor of Surgery, Pakistan.
[4]Professor of Surgery, Consultant HPB Surgeon, Pakistan.
Corresponding Author: Muhammad Faizan Saleem, Resident General Surgeon, Sindh Institute of Urology and Transplantation, Pakistan, fks123.fk@gmail.com
Acknowledgement: We sincerely thank the patients, healthcare professionals, and all contributors who supported this study.

Conflict of Interest: None | Grant Support & Financial Support: None

ABSTRACT

Background: Sentinel lymph node biopsy (SLNB) is an integral procedure for staging axillary lymph nodes in breast cancer patients, traditionally performed using a combination of radioactive tracers and blue dye. However, in low- and middle-income countries (LMICs), the exclusive use of methylene blue (MB) dye is more common due to limited resources. This study aimed to evaluate the factors contributing to failure in identifying an adequate number of sentinel lymph nodes (SLNs) during SLNB with MB dye in breast cancer patients.

Objective: To identify patient, tumor, and procedural factors associated with inadequate SLN identification (<3 nodes) using MB dye exclusively in SLNB for breast cancer patients.

Methods: A prospective observational study was conducted from 2022 to 2024 at the Sindh Institute of Urology and Transplantation, Karachi. A total of 108 breast cancer patients undergoing SLNB were included and divided into cases (<3 SLNs identified) and controls (≥3 SLNs identified). Patient demographics, tumor characteristics, and procedural details were collected. Statistical analyses, including univariate and multivariate models, were performed using SPSS version 22.0. Key variables such as tumor size, breast cup size, tumor location, massage duration, and histopathological findings were analyzed.

Results: Among 108 patients, 57 (52.8%) were cases and 51 (47.2%) were controls. Larger breast size (cup size ≥C, p=0.005), retro-areolar tumor extension (p=0.01), and right-sided tumors (p=0.001) were significantly associated with SLN identification failure. Shorter massage duration (8.6 vs. 9.49 minutes, p=0.008) and H2N-negative status (p=0.032) were also linked to poor outcomes. Histopathological factors such as tumor grade and hormone receptor status were not significantly associated. Patients receiving neoadjuvant chemotherapy showed a non-significant trend toward reduced SLN identification (p=0.153).

Conclusion: This study highlights critical patient, tumor, and procedural factors influencing SLN identification with MB dye. These findings underline the need for tailored surgical techniques and alternative mapping strategies to optimize SLNB in resource-constrained settings.

Keywords: breast cancer, breast cancer staging, lymphatic mapping, methylene blue, sentinel lymph node biopsy, surgical oncology, tumor location.

INTRODUCTION

Sentinel lymph node biopsy (SLNB) has become the gold standard for staging clinically negative axilla in patients with breast cancer, offering a minimally invasive alternative to axillary lymph node dissection and reducing the risk of complications associated with more extensive surgical procedures (1). Among the various techniques available for SLNB, the combination of blue dye and radioactive sulfur colloid has demonstrated the highest sensitivity and specificity, making it the preferred approach in many clinical settings (2). However, low- and middle-income countries (LMICs) often face significant challenges in routinely implementing this combined technique due to the prohibitive cost of radioactive tracers. As a result, methylene blue (MB) dye has emerged as a viable and cost-effective alternative, especially in resource-constrained healthcare systems. Two blue dyes are commonly employed for SLNB: Patent Blue V and methylene blue. While both exhibit comparable efficacy in sentinel lymph node mapping, Patent Blue V has been associated with a higher incidence of adverse reactions, including anaphylaxis, which limits its widespread use. In contrast, methylene blue dye offers a safer profile and has demonstrated an accuracy rate of approximately 90% when used as a standalone agent (3, 4). These findings highlight the potential of methylene blue dye as a safer and more accessible alternative for SLNB, particularly in settings where access to radioactive tracers is restricted.

Historically, early research on SLNB emphasized the identification of at least four sentinel lymph nodes to minimize the risk of false-negative results (5, 6). Subsequent studies, however, demonstrated that identifying three nodes provides comparable sensitivity, with rates as high as 96.3% (7). This paradigm shift has been reflected in current guidelines, such as those from the National Comprehensive Cancer Network (NCCN), which recommend the identification of at least three sentinel lymph nodes for accurate axillary staging. Despite these advancements, there remain instances where the identification of three nodes is challenging, particularly when methylene blue is used exclusively, and there is limited evidence regarding the factors contributing to such failures. While earlier investigations, such as those by Haigh et al., explored potential factors influencing sentinel lymph node mapping using 99mTc-sulfur colloid, no significant associations with identification failure were identified (8). The scarcity of data is even more pronounced for methylene blue dye, leaving a critical gap in understanding the variables that may impede successful sentinel lymph node identification. Hypothetically, factors such as patient obesity, larger breast size, tumor location, or variations in lymphatic drainage patterns could obscure dye uptake, complicating the identification process. This study aims to address these gaps by systematically analyzing the factors associated with the failure to identify a minimum of three sentinel lymph nodes using methylene blue dye exclusively.

The findings of this investigation are anticipated to provide valuable insights for surgeons, enabling them to anticipate potential challenges and consider alternative approaches in cases where the use of methylene blue dye may be insufficient for successful sentinel lymph node mapping. By identifying and addressing these limitations, the study seeks to enhance the overall accuracy and reliability of sentinel lymph node biopsy procedures, particularly in resource-limited settings, ultimately contributing to improved clinical outcomes for patients with breast cancer.

METHODS

The study was conducted at the Breast Surgery Unit of the Sindh Institute of Urology and Transplantation in Karachi, Pakistan, and included all patients undergoing sentinel lymph node biopsy (SLNB) for breast cancer within a two-year period. Patients with a prior history of breast surgery on the same side were excluded to ensure the integrity of the lymphatic mapping process. Patient data were recorded in a customized database specifically designed for this study. In all cases, 4 ml of 1% methylene blue dye was injected circumferentially at four predefined locations—12, 3, 6, and 9 o'clock positions around the periareolar region. This was followed by a standardized massage protocol lasting approximately 10 minutes to facilitate dye uptake and lymphatic drainage. While documentation of massage duration varied in some instances, all recorded durations exceeded a minimum of seven minutes, ensuring adequate dye distribution. Blue-stained lymph nodes were excised either before or after breast tissue removal, depending on the surgical procedure employed. Patients were then categorized into two groups: cases, comprising those with fewer than three blue-stained sentinel lymph nodes, and controls, consisting of those in whom three or more lymph nodes were identified.

Histopathological evaluation of sentinel lymph nodes was conducted using both intraoperative frozen sections and postoperative permanent histopathology. Additionally, subgroup analysis was performed for patients who had undergone neoadjuvant therapy to account for potential confounding factors related to treatment-induced changes in lymphatic drainage. Data analysis was conducted using SPSS version 22.0. Continuous variables were assessed for normality and expressed either as means with standard deviations for normally distributed data or as medians with interquartile ranges for non-normally distributed data. Categorical variables were presented as frequencies and percentages. Associations between categorical variables were evaluated using chi-square tests or Fisher's exact tests, as appropriate, and odds ratios with 95% confidence intervals were calculated to assess the strength of associations. Multivariate analysis was performed using Cox regression models to identify independent predictors of inadequate sentinel lymph node identification, with statistical significance determined at a p-value of less than 0.05.

This methodology was designed to maintain rigor and reproducibility, although it should be noted that variations in massage duration, while documented, may introduce an element of procedural inconsistency. Such variations, albeit minor, could potentially influence the uptake and identification of sentinel lymph nodes and may warrant further investigation in future studies.

RESULTS

Among the 2791 patients seen at the Breast Diseases Clinic over a two-year period, 18.6% were diagnosed with breast cancer. After excluding 59 patients due to metastatic or unresectable locally advanced disease, the remaining patients underwent operative resection. Of these, 24.7% (n=114) underwent sentinel lymph node biopsy (SLNB). Among these patients, 47.2% (n=51) were classified as controls, achieving adequate sentinel lymph node identification (≥3 nodes), while 52.8% (n=57) were categorized as cases due to failure in identifying the minimum required number of nodes.

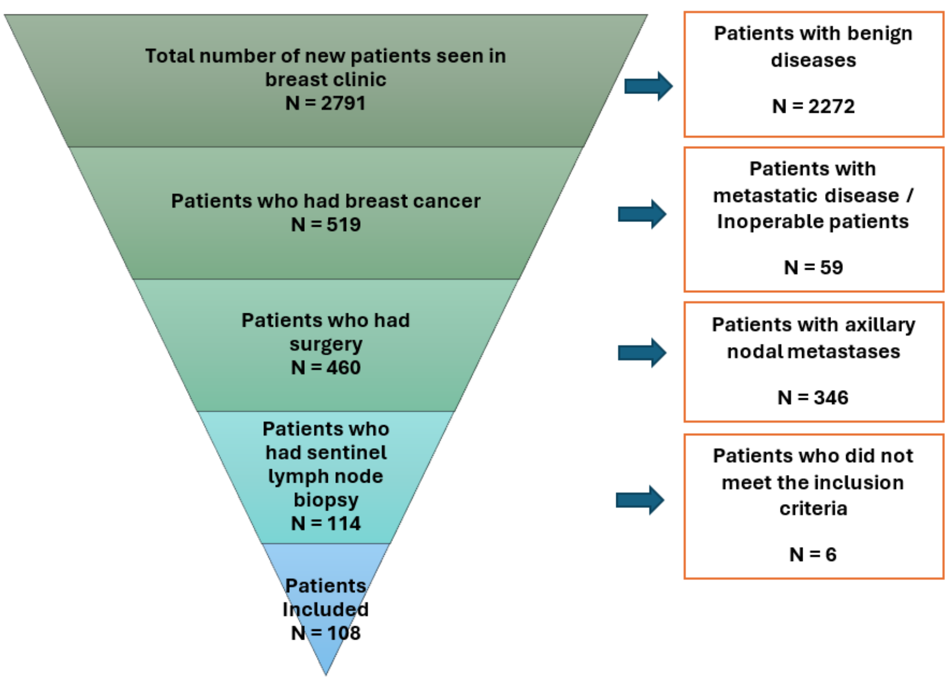

Figure 1 Patient distribution and case selection.

Patient demographics revealed significant differences between cases and controls. Cases were found to have a higher mean weight (67.66 kg vs. 62.94 kg, p=0.02) and a higher prevalence of larger breast sizes (cup size C or D: 44.8% vs. 33.3%, p=0.005). Although the mean BMI was higher among cases (27.64 vs. 26.12), this did not reach statistical significance (p=0.07). No significant differences were observed for age (47.05 years vs. 47.15 years, p=0.94) or height (156.78 cm vs. 156.19 cm, p=0.71). The distribution of comorbidities, such as hypertension (58.3% in cases vs. 41.7% in controls, p=0.41) and diabetes (46.7% vs. 53.3%, p=0.6), did not differ significantly between groups. Patients who underwent neoadjuvant chemotherapy were more frequently observed among cases (75.4%) compared to controls (62.7%), though this trend was not statistically significant (p=0.153).

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

Table 1 Comparison of Patient Characteristics.

Patient's characteristics		Group				p Value
		Case		Control		
Age		47.05 (SD 11.05)		47.15 (SD 11.10)		0.94
Weight		67.66 (SD 11.96)		62.94 (SD 9.81)		0.02
Height		156.78 (SD 5.92)		156.19 (SD 6.12)		0.71
BMI		27.64 (SD 4.77)		26.12 (SD 4.03)		0.07
Comorbidities	Yes	30	55.6%	24	44.4%	0.56
	No	27	50.0%	27	50.0%	
Hypertension	Yes	21	58.3%	15	41.7%	0.41
	No	36	50.0%	36	50.0%	
Diabetes	Yes	7	46.7%	8	53.3%	0.6
	No	50	53.8%	43	46.2%	
Neoadjuvant chemo	Yes	43	57.3%	32	42.7%	0.153
	No	14	42.4%	19	57.6%	
Beast cup size	A	1	33.3%	2	66.7%	0.005
	B	18	36.0%	32	64.0%	
	C	29	65.9%	15	34.1%	
	D	9	81.8%	2	18.2%	
Large Breast b	Yes	38	69.1%	17	30.9%	0.001
	No	19	35.8%	34	64.2%	

a Overweight: BMI ≥ 25kg/m2. b Large Breast: Breast cup size ≥ C

Tumor characteristics demonstrated significant findings. Right-sided tumors were more prevalent in cases (72.1%) than in controls (27.9%), showing a statistically significant association (p=0.001). While the average tumor size was slightly smaller in cases (2.98 cm) than in controls (3.39 cm), this difference did not reach statistical significance (p=0.06). Retro-areolar extension was less common in cases (44.4%) compared to controls (55.6%, p=0.01). There were no significant differences in tumor location in the upper outer quadrant (54.2% in cases vs. 45.8% in controls, p=0.73) or in histopathological subtypes, with invasive ductal carcinoma remaining the most common type in both groups (54.8% in cases vs. 45.2% in controls, p=0.14). Hormone receptor status (ER and PR positivity) was higher in cases, but these differences did not reach statistical significance. However, HER2-positive tumors were significantly more frequent in controls (74.2%) compared to cases (25.8%, p<0.001).

Table 2 Comparison of Tumor Characteristics.

Tumor characteristics						
		Group				p Value
		Case		Control		
Tumor side	Right	31	72.1%	12	27.9%	0.001
	Left	26	40.0%	39	60.0%	
Tumor size		2.98 (SD 1.01)		3.39 (SD 1.20)		0.06
Tumor Histopathology	Invasive ductal carcinoma	51	54.8%	42	45.2%	0.14
	DCIS	3	27.3%	8	72.7%	
	Invasive lobular carcinoma	3	75.0%	1	25.0%	
Tumor grade	Well differentiated	4	40.0%	6	60.0%	0.45
	Moderately differentiated	42	56.8%	32	43.2%	
	Poorly differentiated	11	45.8%	13	54.2%	
ER	Yes	35	58.3%	25	41.7%	0.19
	No	22	45.8%	26	54.2%	
PR	Yes	32	60.4%	21	39.6%	0.12
	No	25	45.5%	30	54.5%	
H2N	Yes	8	25.8%	23	74.2%	0.000
	No	49	63.6%	28	36.4%	
Retro-areolar extension	Yes	32	44.4%	40	55.6%	0.01
	No	25	69.4%	11	30.6%	
Upper outer quadrant	Yes	32	54.2%	27	45.8%	0.73
	No	25	51.0%	24	49.0%	

Procedure-related factors revealed that breast-conserving surgery (BCS) with SLNB was more commonly performed in cases (69.4%) compared to controls (30.6%, p=0.01), while mastectomy with SLNB was more frequent in controls (55.6%) compared to cases (44.4%, p=0.01). Massage duration was significantly shorter in cases (8.6 minutes) than in controls (9.49 minutes, p=0.008). Although adequate massage was documented more frequently in controls (54.1%) than in cases (45.9%, p=0.03), the time to node retrieval was comparable between the groups.

Table 3 Comparison of Procedure-related Factors

Procedure factors		Group				p Value
		Case		Control		
Procedure	Mastectomy + SLNB	32	44.4%	40	55.6%	0.01
	BCS + SLNB	25	69.4%	11	30.6%	
Adequate massage a	Yes	34	45.9%	40	54.1%	0.03
	No	23	67.6%	11	32.4%	
Massage time		8.6 (SD 1.85)		9.49 (SD 1.2)		.008
Time of node retrieval b		31.67 (SD 4.75)		31.67 (SD 4.76)		1.000

a Adequate Massage: The procedure of massaging the breast for at least 10 minutes after the methylene blue dye has been injected. b Time of Node Retrieval: The duration between the injection of methylene blue dye and the identification of blue-stained nodes.

Multivariate analysis identified retro-areolar extension as a significant protective factor against inadequate sentinel lymph node identification (OR 0.293, p=0.020). Tumor laterality was associated with increased odds of inadequate node identification, with right-sided tumors demonstrating a higher likelihood (OR 2.716, p=0.041). HER2 positivity also emerged as a significant protective factor (OR 0.284, p=0.032). Although trends were observed for variables such as larger breast size (OR 2.631, p=0.064) and shorter massage duration (OR 0.414, p=0.061), these did not reach statistical significance.

Table 4 Multivariate analysis

Multivariate analysis of statistically significant variables	OR	95% C.I.for OR		Sig.
		Lower	Upper	
Weight	1.007	.959	1.058	.781
Massage time	.414	.165	1.041	.061
Adequate massage	5.628	.291	109.041	.253
Retro-areolar extension	.293	.104	.823	.020
Tumor side	2.716	1.039	7.099	.041
Large Breast	2.631	.946	7.319	.064
H2N	.284	.090	.895	.032
Constant	878.734			.066

Subgroup analysis of patients receiving neoadjuvant therapy showed comparable proportions of invasive ductal carcinoma and no residual tumor between groups (p=0.89). However, the control group demonstrated a higher rate of complete response (19 cases vs. 17 cases, p=0.03), while the case group exhibited a greater frequency of no response (17 cases vs. 4 cases). No significant differences were observed in tumor stage (pT or pN), lympho-vascular invasion, or the presence of positive sentinel lymph nodes between groups.

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

Table 5 Sub-group analysis of final histopatholgy of patients who had neoadjuvant chemotherapy

Subgroup analysis of Neoadjuvant recepients				
		Group		p Value
		Case	Control	
Final histopathology	Invasive ductal carcinoma	26	13	0.89
	No residual tumor	17	19	
Response	Complete response	17	19	0.03
	Partial response	9	9	
	No response	17	4	
pT	.0	16	17	0.145
	1.0	9	9	
	2.0	15	6	
	3.0	3	0	
pN	.0	37	29	0.67
	1.0	4	3	
	2.0	1	0	
	3.0	1	0	
Lympho-vascular invasion	Yes	7	5	0.93
	No	36	27	
Positive sentinel lymph nodes	Yes	11	5	0.29
	No	32	27	

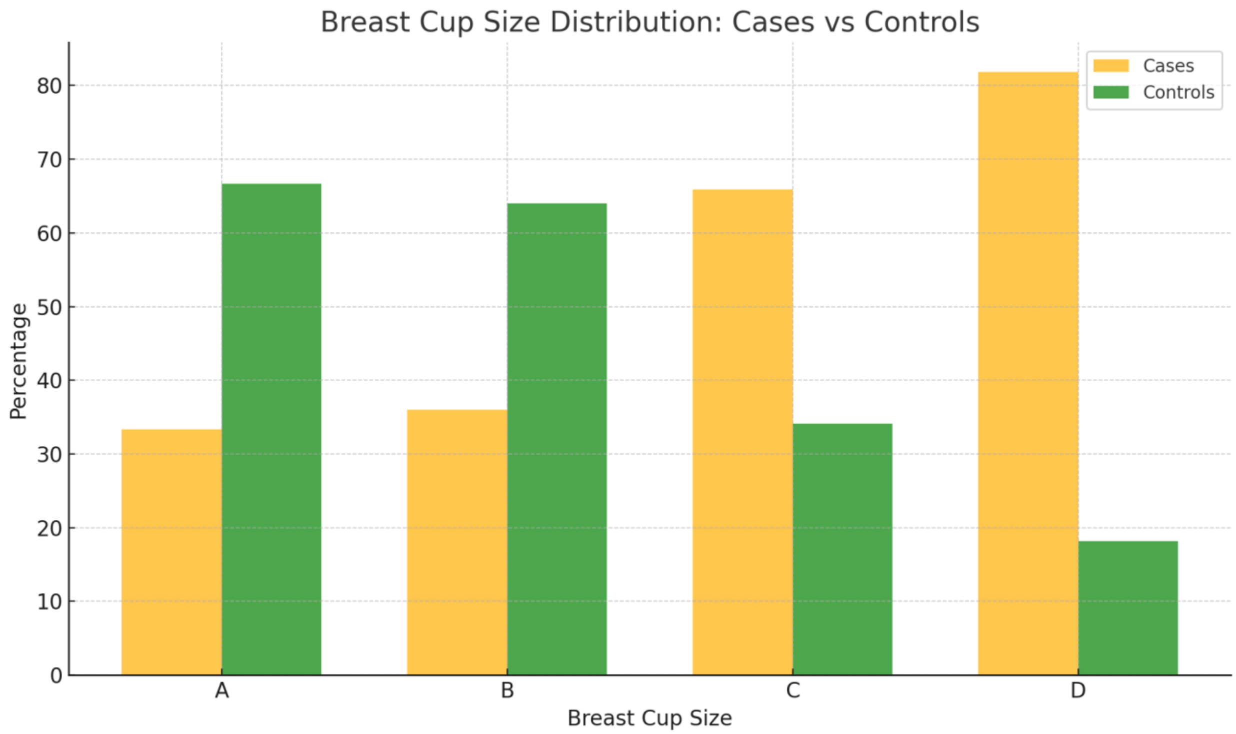

Figure 2 Breast cup size Distribution: Cases vs Controls

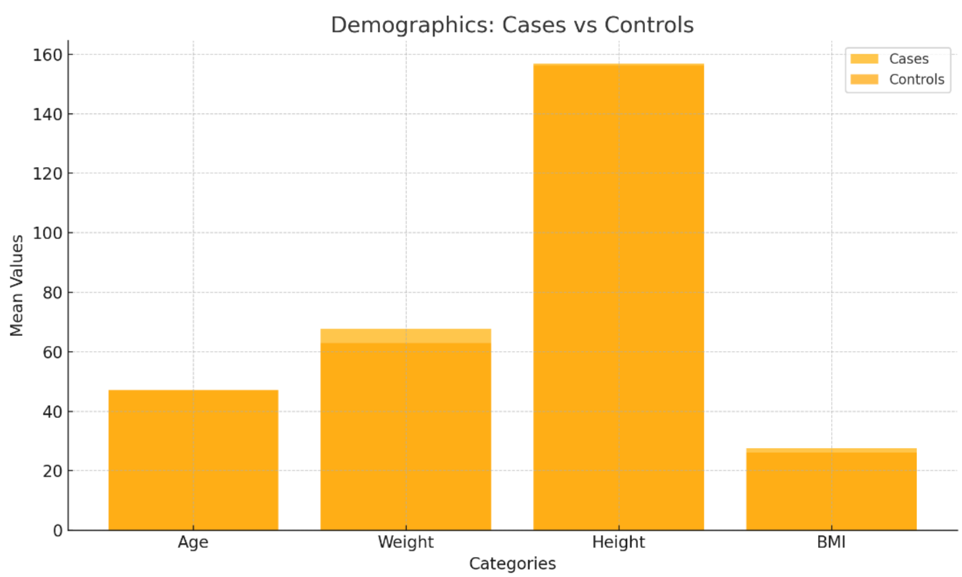

Figure 3 Demographics: Cases vs Controls

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

DISCUSSION

The study aimed to identify factors contributing to the failure of sentinel lymph node identification when methylene blue dye is used exclusively for sentinel lymph node biopsy (SLNB) in breast cancer patients. Several patient-related, tumor-related, and procedural factors were found to influence outcomes, providing valuable insights into optimizing this cost-effective alternative in resource-limited settings. Larger breast size and higher patient weight emerged as significant contributors to failure in lymph node identification. These findings are consistent with the hypothesis that increased adiposity and breast volume impair the distribution and uptake of methylene blue dye by lymphatic channels. Larger breasts may require modifications in technique, such as injecting additional dye volume or optimizing massage protocols, to enhance lymphatic visualization and improve outcomes (9, 10, 11). Anatomical variations in lymphatic drainage patterns appear to play a role in sentinel lymph node identification failure, particularly in right-sided tumors, which were more commonly associated with unsuccessful outcomes. This observation underscores the complexity of lymphatic mapping in certain tumor locations, suggesting that variations in lymphatic anatomy could pose technical challenges during dye uptake and node identification. Retro-areolar tumor extension further compounded the failure rates, likely due to disruptions in normal lymphatic drainage pathways. This finding aligns with earlier studies that emphasized the impact of tumor location and extension on sentinel lymphatic mapping success (12, 13).

The study observed that shorter massage duration and inadequate massage were associated with lower identification rates, albeit without statistical significance. Massage facilitates dye dispersion by enhancing lymphatic flow, a principle supported by prior research demonstrating its positive impact on sentinel node identification rates (9). However, in this study, the influence of massage duration may have been moderated by other more dominant factors, such as tumor biology and patient anatomy. Differences in procedural techniques between breast-conserving surgery (BCS) and mastectomy were also evident, with mastectomy yielding higher success rates for sentinel node identification. The broader surgical exposure during mastectomy allows for more precise visualization of lymphatic channels, whereas the limited incisions in BCS can obscure landmarks critical for locating sentinel nodes (14). Tumor biology significantly influenced outcomes, with H2N-negative status independently associated with sentinel node identification failure. This observation reflects the potential impact of tumor-related alterations in lymphatic architecture, particularly in cases of axillary metastasis where lymphatic channels may be obstructed, reducing methylene blue dye uptake (15, 16). Hormone receptor status, tumor grade, and histological subtype did not demonstrate significant associations with sentinel lymph node identification, indicating that these factors may not directly affect the efficacy of methylene blue dye.

Patients who underwent neoadjuvant chemotherapy displayed a higher prevalence of sentinel lymph node identification failure, although this did not reach statistical significance. Neoadjuvant therapy is known to induce tumor regression and modify lymphatic drainage patterns, potentially diminishing the uptake of methylene blue dye. This finding supports the notion that neoadjuvant therapy may introduce unique challenges to SLNB accuracy, warranting further research to refine mapping techniques for this subgroup of patients (17, 18). The strengths of this study include its focused exploration of methylene blue dye as a standalone agent, providing context-specific insights relevant to resource-limited settings. The systematic analysis of patient, tumor, and procedural factors enhances its applicability to clinical practice. However, the study's single-center design and relatively small sample size limit its generalizability. Additionally, the exclusive use of methylene blue dye, while cost-effective, does not achieve the same sensitivity and specificity as combined techniques utilizing radioactive tracers. Future multi-center studies with larger cohorts and standardized protocols could provide more robust evidence. The integration of imaging modalities, such as lymphoscintigraphy, may further enhance the accuracy of sentinel lymph node identification, particularly in challenging cases (18).

This study contributes to the growing body of evidence supporting the use of methylene blue dye as an alternative for sentinel lymph node mapping in breast cancer patients. By identifying factors associated with its limitations, it underscores the need for tailored approaches to optimize outcomes and improve diagnostic accuracy in diverse clinical contexts.

CONCLUSION

The findings of this study emphasize the significance of patient, tumor, and procedural factors in determining the success of sentinel lymph node biopsy using methylene blue dye as a standalone agent. By identifying key challenges such as anatomical variations, tumor location, patient body habitus, and procedural nuances, the study highlights opportunities to refine surgical techniques and improve the accuracy of lymph node mapping. These insights provide a foundation for clinicians to anticipate potential limitations, adapt strategies accordingly, and enhance patient outcomes, particularly in settings where cost-effective alternatives to radioactive tracers are essential.

AUTHOR CONTRIBUTIONS

Author	Contribution
Muhammad Faizan Saleem	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Usra Parvez	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Warda Haroon	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Bushra Shirazi	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muhammad Arsalan Khan	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published

REFERENCES

1. Gradishar WJ, Moran MS, Abraham J, et al. NCCN Guidelines® Insights: Breast Cancer, Version 4.2023. J Natl Compr Canc Netw. 2023;21(6):594-608. doi:10.6004/jnccn.2023.0031

2. Li X, Wang L, Zheng R, Ding J, Gong Y, Yao H, et al. Omission of sentinel lymph node biopsy in patients with clinically axillary lymph node-negative early breast cancer (OMSLNB): A phase II clinical trial protocol. BMJ Open. 2024;14: e087700. doi: 10.1136/bmjopen-2024-087700.

3. Gupta V, Raju K, Rao TS, Naidu CK, Goel V, Hariharan N, et al. A Randomized Trial Comparing the Efficacy of Methylene Blue Dye Alone Versus Combination of Methylene Blue Dye and Radioactive Sulfur Colloid in Sentinel Lymph Node Biopsy for Early Stage Breast Cancer Patients. Indian J Surg Oncol. 2020;11(2):216-22.

4. Aydogan F, Celik V, Uras C, Salihoglu Z, Topuz U. A comparison of the adverse reactions associated with isosulfan blue versus methylene blue dye in sentinel lymph node biopsy for breast cancer. Am J Surg. 2008;195(2):277-8.

5. Chagpar AB, Scoggins CR, Martin RC, 2nd, Carlson DJ, Laidley AL, El-Eid SE, et al. Are 3 sentinel nodes sufficient? Arch Surg. 2007;142(5):456-9; discussion 9-60.

6. Ban EJ, Lee JS, Koo JS, Park S, Kim SI, Park BW. How many sentinel lymph nodes are enough for accurate axillary staging in t1-2 breast cancer? J Breast Cancer. 2011;14(4):296-300.

7. Nikitenko R, Romak O, Kvasha A, Koichev E, Vorotyntseva K. Navigation surgery for intraoperative sentinel lymph node detection using ICG in breast cancer patients. Georgian Med News. 2022;333:57-60. Link.

8. Barrio A, Montagna G, Mamtani A, Sevilimedu V, Edelweiss M, Capko D, et al. Nodal recurrence in patients with node-positive breast cancer treated with sentinel node biopsy alone after neoadjuvant chemotherapy. JAMA Oncol. 2021;7(5): e213650. doi: 10.1001/jamaoncol.2021.4394.

9. James TA, Coffman AR, Chagpar AB, Boughey JC, Klimberg VS, Morrow M, Giuliano AE, Harlow SP. Troubleshooting Sentinel Lymph Node Biopsy in Breast Cancer Surgery. Ann Surg Oncol. 2016 Oct;23(11):3459-3466. doi: 10.1245/s10434-016-5432-8. Epub 2016 Jul 21. PMID: 27444110; PMCID: PMC5532881.

10. Posther KE, McCall LM, Blumencranz PW, Burak WE Jr, Beitsch PD, Hansen NM, Morrow M, Wilke LG, Herndon JE 2nd, Hunt KK, Giuliano AE. Sentinel node skills verification and surgeon performance: data from a multicenter clinical trial for early-stage breast cancer. Ann Surg. 2005 Oct;242(4):593-9; discussion 599-602. doi: 10.1097/01.sla.0000184210.68646.77. PMID: 16192820; PMCID: PMC1402354.

11. Ryu J, Lee H, Han W, et al. Selective avoidance of sentinel lymph node biopsy after neoadjuvant chemotherapy in HER2-positive/triple-negative breast cancer patients with excellent response. J Breast Cancer. 2024;27:130-140. doi: 10.4048/jbc.2023.0264.

12. Emi Yoshihara, Ann Smeets, Annouchka Laenen, Anneleen Reynders, Julie Soens, Chantal Van Ongeval, Philippe Moerman, Robert Paridaens, Hans Wildiers, Patrick Neven, Marie-Rose Christiaens, Predictors of axillary lymph node metastases in early breast cancer and their applicability in clinical practice,The Breast,Volume 22, Issue 3,2013,Pages 357-361,ISSN 0960-9776, https://doi.org/10.1016/j.breast.2012.09.003.

13. Collins CD. The sentinel node in breast cancer. Cancer Imaging. 2008 Oct 4;8 Spec No A(Spec Iss A):S10-8. doi: 10.1102/1470-7330.2008.9003. PMID: 18852076; PMCID: PMC2582497.

14. Brahma B, Putri RI, Sari L, et al. The Application of 1% Methylene Blue Dye As a Single Technique in Breast Cancer Sentinel Node Biopsy. J Vis Exp. 2019;(148):10.3791/57201. Published 2019 Jun 1. doi:10.3791/57201

15. Kędzierawski P, Bocian A, Radowicz-Chil A, Huruk-Kuchinka A, Mężyk R. Subtype of breast cancer influences sentinel lymph node positivity. Arch Med Sci. 2020 Sep 23;19(3):618-625. doi: 10.5114/aoms.2019.88595. PMID: 37313201; PMCID: PMC10259389.

16. Nowikiewicz T, Głowacka-Mrotek I, Tarkowska M, Nowikiewicz M, Zegarski W. Failure of sentinel lymph node mapping in breast cancer patients qualified for treatment sparing axillary lymph nodes-Clinical importance and management strategy-One-center analysis. Breast J. 2020;26(5):873-881. doi:10.1111/tbj.13769

17. Tinterri, C.; Sagona, A.; Barbieri, E.; Di Maria Grimaldi, S.; Caraceni, G.; Ambrogi, G.; Jacobs, F.; Biondi, E.; Scardina, L.; Gentile, D. Sentinel Lymph Node Biopsy in Breast Cancer Patients Undergoing Neo-Adjuvant Chemotherapy: Clinical Experience with Node-Negative and Node-Positive Disease Prior to Systemic Therapy. Cancers 2023, 15, 1719. https://doi.org/10.3390/cancers15061719.

18. Zhang B, Zhang G. Analysis of the feasibility of dual-tracer sentinel lymph node biopsy after neoadjuvant chemotherapy for breast cancer. Oncol Treat Discov. 2023;1(3). doi: 10.26689/otd.v1i3.5681.

