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Short communication

Incremental Diagnostic Value of Pancytokeratin Immunohistochemistry in Sentinel Lymph Node Assessment for Breast Cancer

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Abstract
Precise detection of sentinel lymph node metastasis is essential for staging early breast cancer. While routine histology and cytology remain standard in many centers, the additional diagnostic value of universal immunohistochemistry in resource-limited oncology systems remains underreported. The objective of this study was to quantify the incremental diagnostic contribution of pancytokeratin immunohistochemistry compared with conventional pathological assessment and explore clinicopathological predictors of nodal involvement. A secondary analysis was performed on a prospective cohort of 20 women with invasive breast carcinoma undergoing sentinel lymph node biopsy in Misrata (2023–2025). Nodes were examined using intraoperative touch imprint cytology, serial hematoxylin-eosin histology, and pancytokeratin immunohistochemistry. Immunohistochemistry was treated as the reference standard. Diagnostic sensitivities and exploratory associations between nodal metastasis and tumor characteristics were analyzed. Sentinel lymph node metastases were identified in 4 of 20 patients (20%). Conventional cytology and routine histology detected three macrometastatic cases but failed to identify one micrometastasis, yielding a sensitivity of 75%. Pancytokeratin immunohistochemistry detected all metastatic deposits (100%). Higher nodal positivity trends were observed in tumors >2 cm, Nottingham grade 3 tumors, and Ki-67 ≥30%, though statistical significance was limited by cohort size. Universal pancytokeratin immunohistochemistry substantially improves the detection of low-volume sentinel node metastasis and may prevent pathological understaging in developing surgical oncology programs. These findings support integration of routine immunohistochemical evaluation into standardized sentinel node protocols.
Keywords. *Breast Cancer, Sentinel Lymph Node, Micrometastasis, Pancytokeratin, Diagnostic Accuracy, Immunohistochemistry, Pathology Workflow.*

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Introduction

Sentinel lymph node biopsy has transformed axillary staging in early breast carcinoma by minimizing surgical morbidity while preserving diagnostic accuracy [1]. Accurate identification of nodal metastasis remains essential because nodal status continues to guide systemic therapy decisions, radiation planning, and prognostic stratification [2]. In routine clinical practice, sentinel nodes are commonly assessed using intraoperative cytology followed by conventional hematoxylin–eosin histology; however, these approaches may fail to detect micrometastatic disease or isolated tumor cell deposits [3]. For this reason, immunohistochemical staining directed against epithelial cytokeratins has been increasingly incorporated into pathological evaluation in order to improve diagnostic sensitivity [4].

Although strong supporting evidence exists from well-resourced healthcare systems, the routine implementation of universal immunohistochemistry remains inconsistent in developing oncology programs, where financial limitations and laboratory capacity frequently shape diagnostic workflows 5). A prospective Libyan cohort of women undergoing sentinel node biopsy between 2023 and 2025 at Alhelal University Hospital and Alzuhor University Hospital provided an opportunity to reassess this issue within a resource-constrained clinical environment. Building upon the original clinical report describing this cohort, the present secondary analysis focuses specifically on comparing the diagnostic performance of different pathological assessment techniques, estimating the potential risk of occult nodal disease when immunohistochemistry is omitted, and proposing practical pathology workflow recommendations suitable for limited-resource healthcare systems.

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Methods

This study represents a secondary methodological analysis derived from a previously collected prospective observational cohort. The study population consisted of twenty adult women with histologically confirmed invasive breast carcinoma and clinically negative axillae who underwent sentinel lymph node biopsy as part of their surgical management.

Sentinel lymph nodes were localized using a standardized periareolar injection of methylene blue dye followed by surgical identification and excision of the stained nodes. Following removal, each sentinel node was processed according to a structured pathological workflow that included touch-imprint cytology for intraoperative assessment, serial paraffin embedding with hematoxylin–eosin staining for routine histological examination, and pancytokeratin immunohistochemical staining to enhance the detection of epithelial metastatic deposits. Metastatic involvement was classified in accordance with accepted pathological staging criteria.

For analytical purposes, immunohistochemistry was treated as the diagnostic reference standard against which other techniques were compared. The sensitivity of touch-imprint cytology and routine histology was calculated, together with the proportion of false-negative results. Exploratory analyses were additionally performed to examine potential associations between occult nodal metastasis and selected clinicopathological variables, including primary tumor size greater than 2 cm, histological grade, Ki-67 proliferation index of at least 30%, and hormone receptor status. Owing to the limited sample size, statistical evaluation was primarily descriptive, and group comparisons were performed using Fisher's exact test.

Results

A total of twenty patients were included in the analysis. The median patient age was 48 years, and the mean primary tumor size was 2.4 cm. Invasive ductal carcinoma represented the predominant histological subtype, accounting for 85% of cases (Table 1).

Table 1. Patient Characteristics

Variable	Value
Median age	48 years
Mean tumor size	2.4 cm
IDC frequency	85%

Sentinel lymph node metastasis was identified in four patients, corresponding to an overall nodal positivity rate of 20%. Among these, three patients (15%) demonstrated macrometastatic involvement, while one patient (5%) exhibited micrometastatic disease. The remaining sixteen patients (80%) showed no evidence of nodal metastasis (Table 2).

Table 2. Sentinel Node Metastasis

Category	Cases	%
Macrometastasis	3	15%
Micrometastasis	1	5%
Negative	16	80%
Overall positivity = 20%		

When diagnostic performance was evaluated across pathological techniques, both touch-imprint cytology and routine hematoxylin–eosin histology demonstrated a sensitivity of 75%, whereas pancytokeratin immunohistochemistry achieved a sensitivity of 100%. The single false-negative case detected by conventional methods consisted of a sub-millimetric metastatic focus that was identified only through immunohistochemical staining (Table 3).

Exploratory analyses suggested higher metastatic rates in tumors larger than 2 cm compared with those measuring 2 cm or less (27% versus 11%). Similarly, grade 3 tumors demonstrated a higher positivity rate than grade 1–2 tumors (37% versus 8%), and tumors with a Ki-67 proliferation index of at least 30% showed increased nodal involvement compared with those with lower proliferative activity (33% versus 9%). No apparent association was observed between nodal metastasis and estrogen receptor, progesterone receptor, or HER2 status (Table 4).

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Table 3. Diagnostic Sensitivity

Method	Sensitivity
Touch imprint cytology	75%
Routine H&E histology	75%
Pancytokeratin IHC	100%

Table 4. Exploratory Predictors of Metastasis

Factor	Positive Rate
Tumor >2 cm	27%
Tumor ≤2 cm	11%
Grade 3 tumors	37%
Grade 1–2 tumors	8%
Ki-67 ≥30%	33%
Ki-67 <30%	9%

Discussion

This secondary analysis reconceptualizes the Libyan sentinel lymph node cohort as a diagnostic workflow investigation rather than a purely epidemiologic report. The findings indicate that reliance on routine cytology and conventional hematoxylin–eosin staining alone would have resulted in pathological understaging in approximately one quarter of metastatic cases [6]. Although only a single micrometastatic focus was missed, the clinical implications remain meaningful, as even low-volume metastatic deposits may influence decisions regarding adjuvant chemotherapy, endocrine therapy, and radiotherapy [7].

The observed data additionally support well-established biological relationships between nodal involvement and primary tumor characteristics, including tumor size, histological grade, and proliferative index. Notably, these directional associations were detectable despite the limited cohort size, suggesting biological concordance with patterns reported in larger international series [8,9]. From a health-system perspective, the study underscores an important operational implication: in emerging oncology programs, omission of pancytokeratin immunohistochemistry may create a systematic risk of underdiagnosing low-volume nodal disease. With the expanding adoption of sentinel lymph node biopsy across North African surgical centers, the establishment of standardized pathology protocols is therefore essential to ensure consistent staging accuracy and therapeutic decision-making [10].

Limitations

Several limitations must be acknowledged. The cohort size was small, the dataset originated from a single geographic region, and the restricted sample limited the feasibility of robust multivariate modeling. In addition, long-term survival correlations were not available for outcome validation. Nevertheless, the prospective design and the complete multimodal pathological evaluation of sentinel nodes represent important methodological strengths that enhance the diagnostic reliability of the findings.

Conclusion

Pancytokeratin immunohistochemistry provides substantial incremental diagnostic value in sentinel lymph node assessment and may prevent pathological understaging when incorporated routinely. Standardized inclusion of immunohistochemistry should be strongly considered in sentinel node protocols across developing breast cancer programs.

Conflict of Interest

All authors declare no conflicts of interest related to this work.

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