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Economic Evaluation

Core Needle Biopsy Versus Fine-Needle Aspiration for Lymph Node Evaluation in Breast Cancer: Diagnostic Accuracy and Cost Analysis in a Public Health System

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ABSTRACT

Objectives: Accurate lymph node evaluation is essential for breast cancer staging, treatment planning, and the diagnosis of recurrent disease. Fine-needle aspiration (FNA) and core needle biopsy (CNB) are the 2 main percutaneous techniques used, but they differ in diagnostic yield, complication rates, and associated healthcare costs. To compare the diagnostic performance and economic impact of FNA vs CNB for lymph node evaluation in breast cancer patients within the Brazilian public healthcare system, emphasizing the relevance of cost-effective strategies in low- and middle-income countries.

Methods: A retrospective cohort study was conducted, including women with clinically suspicious lymph nodes who underwent FNA or CNB between 2015 and 2023. Diagnostic outcomes and rates of inconclusive results were compared. An economic analysis based on a decision-tree model assessed the cost-effectiveness of each strategy from the public payer's perspective.

Results: Among 300 biopsies analyzed, CNB demonstrated significantly lower rates of inconclusive results compared with FNA (2.7% vs 50.7%, $P < .05$). Although the initial cost of FNA was lower, the need for additional procedures after inconclusive results made CNB more cost-effective overall. A CNB-led diagnostic strategy reduced total costs by nearly 50% compared with an FNA-led pathway.

Conclusions: CNB offers superior diagnostic performance and greater economic efficiency compared with FNA for lymph node evaluation in breast cancer. Prioritizing CNB as the first-line diagnostic approach could improve resource allocation in public healthcare systems, particularly in low- and middle-income countries where cost-effectiveness is crucial to expanding access to high-quality cancer care.

Keywords: breast cancer, core needle biopsy, cost-effectiveness, fine-needle aspiration, low- and middle-income countries, lymph node biopsy, real-world data.

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Introduction

Breast cancer (BC) remains the most prevalent malignancy among women worldwide, with approximately 2.3 million new cases and 670 000 deaths in 2022 alone.[1] Although BC incidence continues to rise—by 1% to 5% annually—mortality rates have declined by up to 2.5% per year in 29 countries with a very high Human Development Index, reflecting the success of organized screening programs and access to effective treatment.[1] Countries such as Belgium and Denmark, for example, have met the Global Breast Cancer Initiative mortality reduction target of 2.5% annually.[2] However, this progress has not been uniformly observed in low- and middle-income countries (LMICs), where health-system disparities persist.[1]

Brazil, as the largest economy and most populous nation in Latin America, plays a pivotal role in regional cancer control strategies. The age-standardized incidence rate for BC in Brazil is 62.9 per 100 000 women—comparable to Argentina (61.1) and higher than Mexico (49.6)—highlighting the relevance of Brazilian epidemiological patterns to neighboring countries.[3] Given its public health infrastructure and regional influence, Brazil's experience can serve as a model for scalable, cost-effective cancer care interventions.[4]

A critical determinant of treatment strategy and prognosis in BC is axillary lymph node (ALN) status. ALN involvement is the principal route of regional dissemination, typically preceding distant metastases.[5] Consequently, accurate assessment of axillary disease remains a cornerstone of staging, guiding decisions regarding systemic therapy, regional radiation, and surgical management. The current standard of care involves selective axillary surgery, with sentinel lymph node biopsy (SLNB) replacing full axillary dissection in many early-stage cases[6] even when a limited number of lymph nodes are positive.[7] This shift reflects a growing body of evidence supporting deescalation of axillary intervention without compromising oncologic safety.[7,8]

Despite the growing role of SLNB, preoperative axillary imaging and minimally invasive sampling remain fundamental, particularly in patients with suspicious lymphadenopathy on physical exam or ultrasound. Ultrasound is widely adopted as the first-line imaging modality for axillary assessment because of its accessibility, cost-effectiveness, and real-time guidance capabilities. Suspicious lymph nodes—typically characterized by cortical thickening (>3 mm), absence of fatty hilum, round shape, or eccentric cortical bulge[9]—often require histopathological confirmation before neoadjuvant chemotherapy or upfront surgery.

In addition to its role in initial staging, lymph node evaluation is also critical in the diagnosis and management of recurrent BC.[9] Isolated nodal recurrence—particularly in the axillary, supraclavicular, or cervical chains—can be the first sign of disease relapse and often occurs in the absence of detectable distant metastasis.[10] Timely and accurate histopathological confirmation in these cases is essential to distinguish true recurrence from benign reactive changes, guide systemic therapy, and determine the need for locoregional interventions. Moreover, immunohistochemical (IHC) discordance between primary and recurrent tumors is not uncommon, and reassessment of hormone receptor and HER2 status through lymph node biopsy may significantly alter treatment decisions.[11] Therefore, robust biopsy techniques capable of providing sufficient tissue for molecular profiling are crucial in the recurrent setting.

Two percutaneous techniques are most commonly used for tissue sampling in this context: fine-needle aspiration (FNA) and core needle biopsy (CNB). FNA utilizes a thin needle to aspirate cellular material for cytologic evaluation, whereas CNB obtains a histologic core sample using a larger-gauge needle. Although FNA is less invasive, faster, and associated with minimal complications, CNB provides more tissue for histological and IHC analysis, which is increasingly important in the era of molecular subtyping and personalized therapy.[12,13]

Recent meta-analyses report that CNB offers higher sensitivity (87%-88%) than FNA (73%-74%) for detecting axillary metastasis.[14,15] The specificity of both techniques is comparable (>95%), but the diagnostic inadequacy rate—defined as insufficient or inconclusive samples—has consistently been higher for FNA. In practice, this often necessitates repeat biopsies or surgical excision, increasing costs, delays, and patient anxiety. Furthermore, CNB enables assessment of hormone receptor and HER2 status, which can be discordant in recurrent or metastatic settings. Accurate receptor status is essential for tailoring systemic therapy and avoiding under- or overtreatment.

International guidelines increasingly recommend CNB for axillary staging when tissue is needed to confirm nodal involvement before initiating neoadjuvant therapy or omitting SLNB in selected cases. Despite this, FNA remains widely used in LMICs due to its lower upfront cost and operational simplicity. This raise concerns in health systems such as Brazil's Unified Health System (SUS), in which cost-effectiveness and diagnostic precision must be carefully balanced.

In this context, inconclusive results from FNA can lead to a cascade of negative consequences: diagnostic delays, unnecessary surgeries, inappropriate staging, and increased psychological burden for patients. Although the clinical superiority of CNB is well supported, real-world studies evaluating its economic impact, especially in public healthcare systems within LMICs, are still lacking. Generating local evidence to guide policy and optimize resource allocation is essential for improving BC care equity.

Objectives

The primary objective of this study was to compare the diagnostic adequacy FNA and CNB for lymph node evaluation in BC patients treated within SUS. Specifically, we aimed to assess and contrast the rates of inconclusive results between the 2 biopsy methods.

The secondary objective was to conduct a cost-effectiveness analysis of both diagnostic strategies, using a decision-tree model informed by real-world data. By integrating clinical and economic perspectives, this study sought to determine whether CNB, despite its higher upfront cost, offers greater diagnostic value and resource efficiency in a publicly funded, resource-constrained setting.

Ultimately, our goal was to generate context-specific evidence that may guide national protocols and inform best practices for axillary staging in BC, particularly in LMIC where diagnostic accuracy and cost containment are critical to expanding equitable access to cancer care.

Methods

Study Design

This was a mixed-methods study combining a retrospective observational cohort with a budget impact analysis. The clinical component aimed to evaluate the diagnostic adequacy of FNA and CNB in women with axillary, cervical, or supraclavicular lymph nodes suspicious for breast cancer metastasis. Diagnostic adequacy was defined as the proportion of conclusive vs inconclusive biopsy results, according to histopathological classification.

The primary clinical endpoint was the rate of inconclusive biopsy results, defined as samples deemed insufficient for diagnosis or lacking definitive benign/malignant classification. Secondary analyses compared the frequency of inconclusive results by biopsy technique and clinical scenario (primary tumor, recurrence, or occult carcinoma).

The study was not designed to assess diagnostic performance parameters, such as sensitivity or specificity, as a uniform reference standard (surgical pathology confirmation for all cases) was not available. Instead, the focus was on the adequacy of material obtained through each method and the subsequent economic impact of inconclusive results on healthcare resource utilization.

The economic component utilized a decision-tree model to estimate the short-term budgetary impact of each biopsy strategy from the perspective of the SUS. The model incorporated real-world data from the observational cohort to simulate clinical pathways and resource utilization.

The cohort component followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational research reporting.[16] The budget impact model was developed in accordance with ISPOR Task Force recommendations for BIA,[17] and economic results were reported according to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.[18,19]

Retrospective Cohort Study

The observational cohort was derived from RWD collected at the Hospital da Mulher-São Paulo (formerly Hospital Pérola Byington), a tertiary public referral center for women's health. Clinical, radiological, and pathological data were extracted retrospectively from electronic medical records using a standardized abstraction tool. Data collection spanned from January 1, 2015, to December 31, 2023.

Each patient record was reviewed by trained abstractors and independently verified by a second reviewer. Discrepancies were resolved by consensus.

Inclusion criteria

We included female patients aged 18 years or older with clinically and/or radiologically suspicious axillary, cervical, or supraclavicular lymph nodes—defined according to World Health Organization criteria[20] or classified as BI-RADS 4-5 on ultrasound[21]—who underwent FNA or CNB as the initial diagnostic procedure between January 1, 2015, and December 31, 2023. All included patients had a minimum follow-up of 6 months to allow for final pathological confirmation of lymph node status (benign or malignant).

Exclusion criteria

We have excluded patients with incomplete medical records or loss to follow-up before pathological confirmation and lymph node biopsies performed outside the institution.

Economic Analysis

The economic evaluation was based on a budget impact model structured as a decision tree, comparing FNA and CNB as initial diagnostic approaches (Fig. 1). The model simulated 3 potential outcomes per diagnostic test: benign, malignant, or inconclusive. Inconclusive cases triggered a second diagnostic intervention—either repeat CNB or surgical biopsy—leading to a final diagnosis.

The cost analysis was conducted from the SUS payer perspective, using standardized procedure costs sourced from the Brazilian government's SIGTAP database. Costs were converted to US dollars (USD) using the average exchange rate from the Brazilian Central Bank (1 USD = R$5.67, 6 months information, Brazilian Central Bank).

The time horizon for the analysis was restricted to the diagnostic phase, defined as the period from initial biopsy to final pathological diagnosis. Market share and long-term projections (eg, over 5 years) were not included because the objective was to analyze short-term budget impact based on actual clinical practice. Also, projecting future market shares would include considerable uncertainties in the results and low clinical reasoning. Sensitivity analyses were conducted to explore uncertainties and scenarios (described in the next session). Model parameters were validated through direct expert elicitation, using structured interviews with a multidisciplinary group of specialists in breast imaging, interventional procedures, and health-system management within the SUS context. Experts were identified based on recognized clinical and managerial expertise. Each expert independently reviewed model assumptions (diagnostic pathways, procedure frequencies, cost inputs) and provided feedback through iterative discussion until consensus was achieved.

The cost data for the economic analysis were based on SIGTAP information,[22] including the following procedure costs: FNA: $22.22; CNB: $37.04; ALN biopsy: $341.76; Supraclavicular lymph node biopsy: $319.12.

The costing approach was conducted from the perspective of the Brazilian public healthcare system (payer's perspective).

All costs were based on official SUS reimbursement values (nominal), not inflation-adjusted, and were converted to US dollars using the average exchange rate (Central Bank of Brazil, 2023), to maintain consistency with the public-payer perspective.

Node costs in the decision-tree figure represent unit per-procedure SUS tariffs (USD, price year 2023), whereas tabled results present probability-weighted cohort totals.

In addition to the base-case analysis, an extended scenario-based economic analysis was performed following the framework proposed by the reviewer. Five diagnostic strategies were explicitly modeled: (1) FNAC followed by repeat FNAC; (2) FNAC followed by CNB; (3) FNAC followed by excision biopsy; (4) CNB followed by repeat CNB; and (5) CNB followed by excision biopsy. For each strategy, costs were recalculated assuming FNAC inadequacy rates of 40%, 30%, 20%, and 10%, in addition to the observed real-world rate. All analyses used identical unit costs to the base case and a fixed CNB inadequacy rate derived from cohort data.

Statistical Analyses

The retrospective cohort analysis compared the diagnostic performance of FNA and CNB. Data were stratified by biopsy technique and summarized using descriptive statistics. When appropriate, statistical comparisons were performed using the t test or Mann-Whitney U test for continuous variables, and the chi-square or Fisher's exact test for categorical variables.

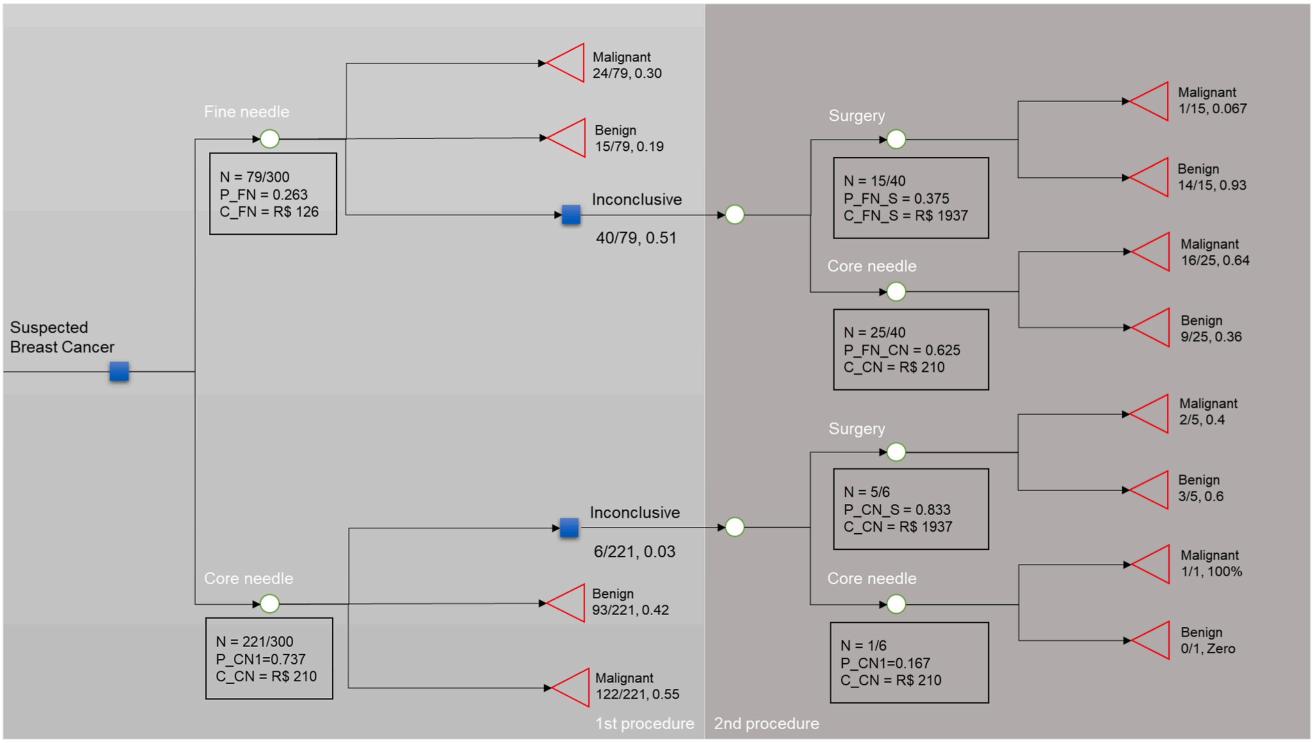
The economic analysis evaluated the short-term budget impact of each diagnostic strategy by reporting total and procedure-specific costs (first- and second-line biopsies). The decision-tree model was used to identify which approach—FNA or CNB—provided more efficient resource allocation. Three deterministic sensitivity analyses were performed: (1) assuming all patients underwent CNB as the initial diagnostic procedure, (2) assuming that all patients underwent FNA first, and (3) assuming that the number of inconclusive results would be 50% more or less of what was found in the cohort (FNA: 25% and 75%). This analysis was not done with inconclusive cases from CNB, due to the low rates of inconclusive cases.

In addition, we conducted extended deterministic sensitivity analyses to evaluate the impact of varying the FNA inadequacy rate across a wide range of hypothetical scenarios (10%, 20%, 30%, 40%, and 50%), while maintaining all other model parameters constant. This aimed to assess the robustness and generalizability of the economic findings under different potential performance levels for FNA. Importantly, the budget impact model focused solely on the diagnostic phase and did not project long-term costs or market share trends. Such projections were considered of limited practical relevance to clinical and policy decision-making. Instead, the analysis was grounded in real-world clinical data, with the sensitivity scenarios designed to explore potential shifts in diagnostic pathways.

Sample Size

In the cohort study, the primary objective was to estimate the rate of inconclusive biopsy results. The sample size was calculated based on quantitative and clinical reasoning.[15] The sample size calculation was based on the following assumptions: an expected inadequacy rate of 6% for the sampling technique,[15] a 95% confidence level, and a margin of error of 6% within a target population of 216 patients who had undergone FNA.[15]

Figure 1. Decision-tree model based on the retrospective cohort. Decision-tree structure comparing diagnostic pathways for FNA and core needle biopsy (CNB). Each node displays unit (per-procedure) costs in USD from SIGTAP (SUS reimbursement schedule; price year 2023), converted using the Central Bank of Brazil average exchange rate (R$5.67 = US$1). Branch labels represent the observed probabilities of malignant, benign, or inconclusive outcomes, as well as second-procedure pathways (repeat CNB or surgical biopsy). Note: Costs shown in the figure are per-procedure values; probability-weighted cohort totals are presented in Table 3.



Additionally, a previously study reported inconclusive rates of 12% (8 out of 66 cases).[14] Based on these parameters, a minimum of 45 inconclusive cases was required to ensure 95% statistical confidence and 6% margin of error in a defined population.

Although the study was conducted in a single tertiary center, the sample size calculation is statistically generalizable to broader settings (local, state, or national), because it is based on the probability of inconclusive results—defined by confidence level, expected rate, and margin of error—rather than on geographic population parameters.

Ethical Considerations

This study was approved by the Research Ethics Committee of Pérola Byington Hospital, under protocol number 67582923.9.0000.5463. Informed consent was waived because of the retrospective nature of the study and the use of anonymized data, in accordance with national regulations.

Results

Cohort Characteristics

A total of 300 women underwent axillary, supraclavicular or cervical lymph node biopsy between 2015 and 2023 at a tertiary public cancer center. Among them, 79 (26.3%) underwent FNA and 221 (73.7%) underwent CNB. The groups were comparable in age (mean: FNA 53.0 vs CNB 54.4 years, $P = .35$) and tumor size distribution, with T2 tumors being the most common presentation in both arms (FNA 50.0% vs CNB 43.8%, $P = .36$).

Axillary lymph nodes were the most frequently sampled site, significantly more so in the CNB group (86.0% vs 67.1%, $P < .05$), whereas FNA was more commonly used for supraclavicular lymph nodes (22.8% vs 7.7%, $P < .05$). Nodal staging was similar across groups, with N1 disease being the most frequent status (CNB 46.0% vs FNA 37.8%, $P = .21$). The majority of patients had nonmetastatic disease at the time of biopsy (M0 in >95% in both groups).

The key finding was the markedly higher rate of inconclusive results with FNA: 50.7% compared with only 2.7% with CNB ($P < .001$). In contrast, CNB yielded a significantly higher proportion of definitive malignant (55.2% vs 30.3%, $P < .05$) and benign (42.1% vs 19.0%, $P < .05$) diagnoses. Only 1.1% of patients in the CNB group required a second biopsy, compared with 12.2% in the FNA group ($P < .001$), reinforcing the superior diagnostic adequacy of CNB. These findings are shown in table 1.

Pathological Results by Tumor Type

When stratified by clinical context—primary tumor, recurrence, or suspected occult carcinoma—CNB consistently outperformed FNA (Fig. 2). Among patients with suspected occult BC, FNA yielded an 80% inconclusive rate, compared with 0% for CNB ($P < .001$). For recurrent disease, FNA produced inconclusive results in 62.5% of cases, whereas CNB maintained a low rate of 3.7% ($P < .001$). Even in primary tumor cases, CNB demonstrated superiority (inconclusive: 1.9% vs 32.4% for FNA, $P < .001$). These findings underscore CNB's diagnostic reliability across diverse clinical scenarios.

Table 1. Cohort Characteristics and biopsies of lymph nodes suspected breast cancer according to needle type, biopsy site, and pathological results from 2015 to 2023.

	Total *n* = 300		FNA *n* = 79		CNB *n* = 221		
	N, mean	%, SD	*N*, mean	%, SD	*N*, mean	%, SD	*P* value
Age (years)	54.1	11.6	53.0	10.9	54.4	11.8	.35
Tumor size (T)							
T0	6	2.3	0	0	6	3.2	.12
T1	40	15.3	14	18.9	26	13.9	.30
T2	119	45.6	37	50.0	82	43.8	.36
T3	55	21.1	15	20.3	40	21.4	.84
T4	41	15.7	8	10.8	33	17.6	.16
Lymph node (N)							
N0	87	33.3	29	39.2	58	31.0	.20
N1	114	43.7	28	37.8	86	46.0	.21
N2	54	20.7	15	20.3	39	20.9	.92
N3	6	2.3	2	2.7	4	2.1	.79
Metastasis (M)							
M0	249	95.4	71	95.9	178	95.2	.79
M1	12	4.6	3	4.1	9	4.8	.79
Biopsy site							
Axillary	243	81.0	53	67.1	190	86.0	<.05
Cervical	22	7.3	8	10.1	14	6.3	.26
Supraclavicular	35	11.7	18	22.8	17	7.7	<.05
Pathological results							
Malignant	146	48.7	24	30.3	122	55.2	<.05
Benign	108	36.0	15	19.0	93	42.1	<.05
Inconclusive	46	15.3	40	50.7	6	2.7	<.05

Note. The sum of observations in staging and treatment does not equal the total number of included women, as these were only performed in malignant cases and inconclusive results in which cancer was confirmed.
SD indicates standard deviation.

Immunohistochemistry Results

Among patients with confirmed malignancy, discordance in IHC profiles between the lymph node and the primary breast tumor was observed in 23.1% of recurrent cases and in 2.5% of primary tumors ($P = .004$). IHC evaluation was performed only in samples obtained through CNB (Appendix Tables 1 and 2).

Management After Inconclusive Results

The choice of second procedure differed according to the initial biopsy type. After an inconclusive FNA (n = 40), 62.5% of patients underwent CNB as a second-line test, whereas 37.5% proceeded directly to surgery. In contrast, after an inconclusive CNB (n = 6), most patients (83.3%) underwent surgical biopsy, and only 1 had a repeat CNB. Though not statistically significant (P = .072), this pattern suggests clinicians may be more inclined to repeat CNB after FNA failure but proceed to definitive surgery after CNB—reflecting higher confidence in CNB's initial accuracy (Appendix Table 3).

Predictors of Inconclusive Biopsy Results

In univariate and multivariate logistic regression analyses, the only factor independently associated with inconclusive biopsy results was the type of needle used. CNB was strongly protective against inconclusive results (OR = 0.027; 95% CI: 0.011-0.070; $P <$ .001). No significant associations were found with patient age, lymph node location, tumor stage, or nodal status. The multivariate model demonstrated excellent discriminative ability (AUC = 0.82) and good fit (Hosmer-Lemeshow P = .62), confirming needle type as the dominant determinant of diagnostic adequacy (Table 2).

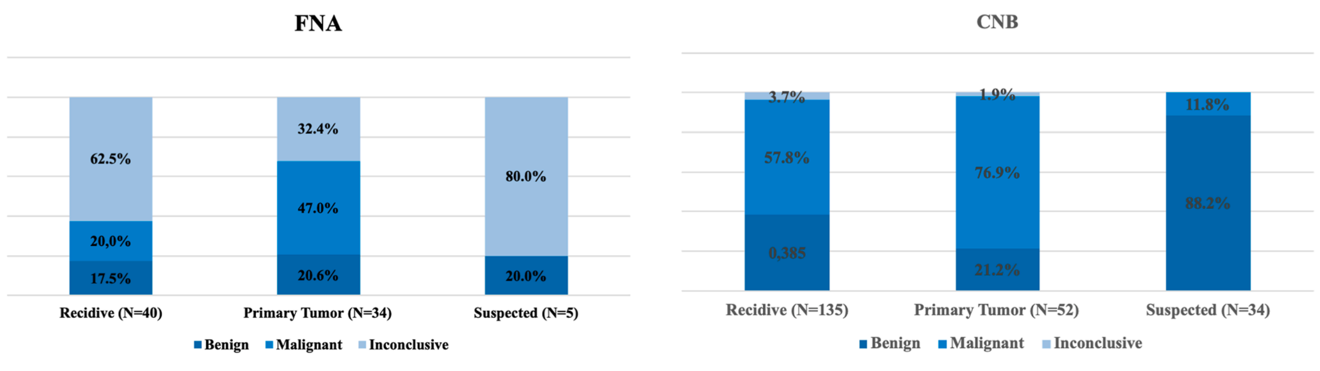
Economic Analyses

Base case

Base-case results are reported in Table 3. Despite a lower initial cost, the FNA strategy incurred substantially higher downstream costs because of the need for additional procedures. Total costs for the FNA-first approach reached $7805, whereas the CNB-first strategy totaled only $9930. In the base-case analysis reflecting actual clinical practice, the cumulative cost across all 300 patients was $17 736 (Table 3).

When focusing solely on second procedures (Table 3), surgical biopsies after inconclusive FNA accounted for $5124 in expenditures, most of which were ultimately benign. In contrast, second-line CNB procedures incurred significantly lower costs ($1745.15) and often avoided the need for surgery. These findings

Figure 2. Comparison of Fine-Needle Aspiration (FNA) vs Core Needle Biopsy (CNB) Results in Recidive, Primary Tumor, and Suspected Breast Cancer Cases. Stacked bar charts illustrating the distribution of benign, malignant, and inconclusive findings across 3 clinical contexts (recidive, primary tumor, and suspected) for both biopsy methods. CNB consistently demonstrates markedly lower rates of inconclusive outcomes and higher diagnostic adequacy compared with FNA in all evaluated scenarios.



underscore the dual advantage of CNB: it not only delivers superior diagnostic accuracy but also leads to meaningful cost savings within public health systems.

Sensitivity analysis

In sensitivity analyses, a strategy using FNA as the initial diagnostic method (100% of patients undergoing fine-needle aspiration) resulted in a total diagnostic cost of US$29 808, largely driven by the high proportion of inconclusive results and the subsequent need for additional procedures, including surgery. Conversely, adopting CNB as the first-line diagnostic approach (100% of patients undergoing core needle biopsy) reduced overall diagnostic costs to US$13 718, representing an almost 50% reduction compared with the FNA-first pathway (Fig. 3).

Additional deterministic sensitivity analyses varying the rate of inconclusive results did not change the overall direction of the base-case findings. When simulating 50% fewer inconclusive cases in the FNA arm, the number of patients requiring additional procedures decreased from 40 to 8, resulting in a reduction of total FNA-related costs from US$7805 to US$4780 (−63%). Conversely, assuming a 50% increase in inconclusive cases, the number of patients undergoing additional CNB or surgical biopsy increased to 38, raising total FNA-related costs to US$13 856 (+77%).

Probabilistic sensitivity analyses further confirmed the robustness of the base-case results. After simultaneous variation of all parameters, more than 80% of simulations maintained the same direction of the economic comparison, with median overall costs of US$7503 (IQR: US$5678-9980) for the FNA-first strategy and US$9007 (IQR: US$7401-11 444) for the CNB-first strategy, indicating minimal uncertainty around the primary findings (Table 3).

To address variability in FNAC performance across clinical settings, an extended scenario-based analysis was conducted. Table 4 presents a direct comparison of 5 predefined diagnostic strategies, recalculated using identical unit costs from the base-case analysis and assuming FNAC inadequacy rates of 50.7%, 40%, 30%, 20%, and 10%. Under optimized FNAC performance (inadequacy ≤ 20%), an FNAC-first strategy followed by CNB for inconclusive cases resulted in lower total diagnostic costs

Table 2. Univariate and multivariate logistic regression analysis of factors associated with inconclusive lymph node biopsy results.

Variable	Comparison	OR (Univariate)	95% CI (Univariate)	*P* (Univariate)	OR (Multivariate)	95% CI (Multivariate)	*P* (Multivariate)
Needle type	Core vs Fine	0.031	0.012-0.077	<.001	0.027	0.011-0.070	<.001
Biopsy site	Cervical vs Axillary	1.859	0.189-18.274	.595	0.555	0.122-2.518	.445
Biopsy site	Supraclavicular vs Axillary	0.784	0.094-6.528	.822	1.353	0.493-3.712	.557
T staging	T1 vs T0	0.971	0.383-2.462	.950	0.577	0.095-3.493	.549
T staging	T2 vs T0	1.326	0.291-6.035	.715	1.326	0.291-6.035	.715
T staging	T3 vs T0	0.670	0.121-3.720	.647	0.670	0.121-3.720	.647
T staging	T4 vs T0	0.825	0.128-5.332	.840	0.825	0.128-5.332	.840
N staging	N1 vs N0	0.776	0.413-1.458	.431	0.993	0.401-2.457	.988
N staging	N2 vs N0	0.543	0.153-1.928	.345	0.543	0.153-1.928	.345
N staging	N3 vs N0	0.990	0.065-15.002	.994	0.990	0.065-15.002	.994
Age (years)	—	0.994	0.967-1.021	.666	1.001	0.966-1.037	.974

Multivariate model performance: Hosmer-Lemeshow test *P* = .62; AUC = 0.82.
CI indicates confidence interval; OR, odds ratio.

Table 3. Base-case overall modeling results.

Overall	Cost	Malign cases	Benign cases	Inconclusive
PAAF initiated biopsy	$7805.82	52%	48%	
CNB initiated biopsy	$9930.33	57%	43%	
Total	$17 736.15			
Data breakdown				
1st Procedure Only	Cost	Malign cases	Benign Cases	Inconclusive
PAAF	$1755.55	30%	19%	51%
CNB	$8185.18	42%	55%	3%
Total	$9940.74			
2nd Procedure Only (Inconclusive Cases)	Cost	Malign cases	Benign Cases	Inconclusive
Surgery (after PAAF)	$5124.34	6.7%	93.3%	
CNB (after PAAF)	$925.93	64%	36%	
Surgery (after CNB)	$1708.11	40%	60%	
CNB (after CNB)	$37.04	100%	0	

Footnote: Costs are expected cohort totals obtained by multiplying unit SUS tariffs (USD, price year 2023) by the probabilities of each pathway and by the cohort size. Figure 1 displays unit (per-procedure) costs only.

compared with a CNB-only strategy. However, as FNAC inadequacy increased to 30% or higher, FNAC-based pathways rapidly lost economic efficiency because of repeated procedures and higher downstream diagnostic costs. In contrast, CNB-based strategies demonstrated greater cost stability across all scenarios, reflecting their consistently low inconclusive rate.

Discussion

This study offers real-world evidence on the diagnostic adequacy and economic impact of CNB vs FNA for lymph node evaluation in BC patients treated within the Brazilian public healthcare system. Among 300 women with suspicious lymph nodes, CNB yielded a significantly lower rate of inconclusive results (2.7%) compared with FNA (50.7%), regardless of tumor type, clinical stage, or disease setting.

It is important to note that the study did not assess diagnostic performance parameters (sensitivity or specificity) but rather the adequacy of the material obtained, represented by the rate of inconclusive biopsies.

It is important to emphasize that this study was designed to evaluate diagnostic adequacy rather than traditional diagnostic performance metrics, such as sensitivity or specificity. Because a uniform surgical reference standard was not available for all patients, these accuracy measures could not be reliably estimated. Therefore, the primary endpoint was the rate of inconclusive results, which directly reflects the adequacy of the diagnostic material obtained and has immediate practical implications because inconclusive findings invariably lead to additional diagnostic procedures, increased costs, and potential delays in treatment initiation.

These findings are consistent with international literature. A systematic review and meta-analysis demonstrated that CNB offers greater sensitivity than FNA (87%, 95% CI 84%-88% vs 74%, 95% CI 72%-77%) with similar specificity for both methods (CNB: 98%, 95% CI 96%-99% vs FNA: 96%, 95% CI 94%-98%).[13] A subsequent meta-analysis corroborated these results, while also reporting

Figure 3. Sensitivity Analyses Considering 100% of Cases Undergoing FNA or CNB as the First Procedure. Deterministic sensitivity analysis comparing total diagnostic costs under 2 hypothetical strategies: (1) all patients undergoing FNA as the initial biopsy and (2) all patients undergoing CNB as the initial biopsy. The CNB-first strategy results in substantially lower overall costs due to fewer inconclusive results and reduced need for surgical biopsies.

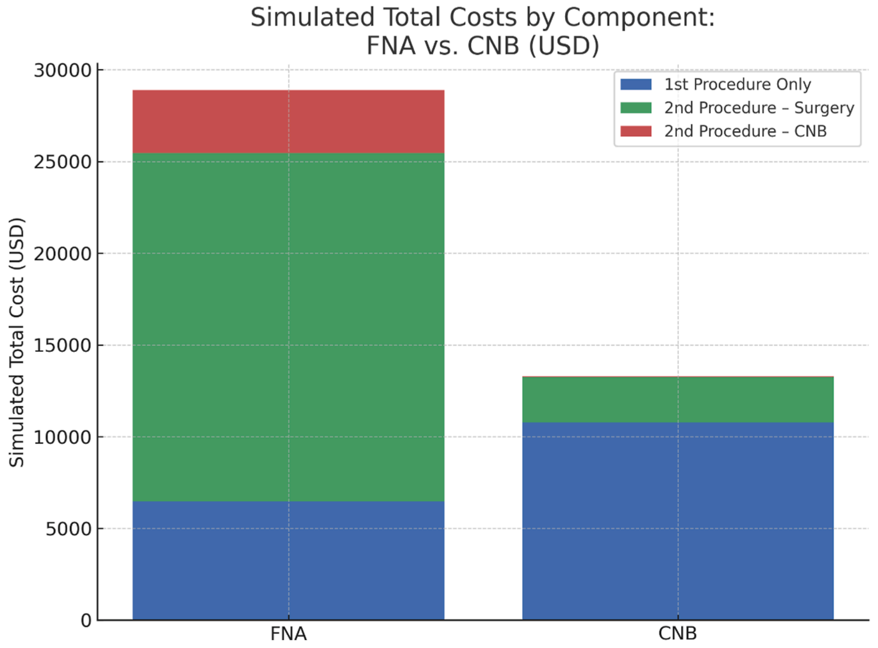


Table 4. Comparative cost analysis of diagnostic strategies.

Scenario	Diagnostic pathway	FNAC 50.7%	FNAC 40%	FNAC 30%	FNAC 20%	FNAC 10%
1	FNAC → repeat FNAC	44.25/4425	36.88/3688	31.72/3172	27.77/2777	24.69/2469
2	FNAC → CNB	41.48/4148	37.44/3744	33.63/3363	29.83/2983	26.02/2602
3	FNAC → excision	183.74/18374	149.82/14982	117.92/11792	86.02/8602	54.12/5412
4	CNB → repeat CNB	38.05/3805	38.05/3805	38.05/3805	38.05/3805	38.05/3805
5	CNB → excision	45.70/4570	45.70/4570	45.70/4570	45.70/4570	45.70/4570

Values shown as cost per patient (USD)/cost per 100 patients (USD). All unit costs used in Table 4 are identical to those applied in the base-case analysis and were derived from official SUS reimbursement values. The table presents an explicit scenario-based recalculation, as requested by the reviewer, using alternative FNAC inadequacy rates.

higher complication rates with CNB (7.1% vs 1.3%, $P < .001$) and a significantly greater need to repeat the procedure following FNA (4% vs 0.1%, $P < .001$).[12,14,15] The diagnostic yield of CNB was superior not only in detecting malignancy but also in confirming benign findings, minimizing the need for second procedures. Moreover, a systematic review estimated CNB sensitivity at 88% (95% CI 84%-91%) compared with 73% (95% CI 69%-76%) for FNA, suggesting a higher false-negative rate with FNA.[23]

Previous studies have emphasized the importance of preoperative axillary biopsy in guiding nodal staging and treatment decisions. Houssami et al (2011) demonstrated that ultrasound-guided biopsy of suspicious nodes is highly specific and that CNB provides superior sensitivity for axillary metastasis.[24] Similarly, van Roozendaal et al (2017) reported that axillary pathological status alters adjuvant systemic treatment recommendations in 15% to 34% of cases,[25] underscoring the clinical implications of accurate nodal assessment.

In this study, economic modeling based on RWD showed that the CNB-first strategy reduced total diagnostic costs by approximately 50% compared with an FNA-led approach. Although FNA was less expensive initially ($22.22 vs $37.04), its high rate of inconclusive results generated downstream expenditures, particularly due to surgical biopsies following nondiagnostic FNA results. In contrast, CNB minimized repeat procedures, leading to better resource utilization.

To improve the transparency and clinical relevance of the economic evaluation, we expanded the decision-tree model to explicitly represent alternative diagnostic pathways commonly encountered in routine practice. Rather than restricting the analysis to a single observed sequence of events, 5 predefined diagnostic strategies combining FNAC, CNB, and excision biopsy were modeled. This scenario-based approach allows isolation of the economic consequences associated with different clinical decisions and facilitates interpretation of cost drivers across alternative diagnostic algorithms.

An important nuance emerging from the scenario-based analyses is that the economic performance of FNAC-based strategies is highly dependent on local technical performance. In centers where ultrasound-guided FNAC achieves inadequacy rates of ≤10% to 20%, which are generally considered acceptable benchmarks for high-quality cytopathology services, an FNAC-first strategy followed by CNB for inconclusive cases may represent a cost-efficient diagnostic approach. In contrast, inadequacy rates exceeding these thresholds substantially erode the economic viability of FNAC-based pathways due to repeated procedures and downstream surgical interventions.

In our real-world public tertiary cohort, the FNAC inadequacy rate exceeded 50%, a level that would be considered unacceptable in high-performance settings but may occur in heterogeneous public healthcare systems with variable access to specialized cytopathology expertise. Under such conditions, FNAC-based strategies rapidly lose economic efficiency, whereas CNB-based approaches maintain stable cost profiles owing to their consistently low inconclusive rate. This finding supports CNB as a more robust and generalizable diagnostic strategy within public health systems, such as SUS, for which reproducibility and reliability across centers are critical.

Globally, the economic burden of cancer is projected to approach USD 25 trillion over the next 30 years, with LMICs bearing a disproportionate share of this cost burden.[26,27] In this context, diagnostic strategies that combine clinical accuracy with cost-effectiveness are essential. Our data support CNB as a high-value intervention that may reduce both direct healthcare costs and the indirect costs associated with diagnostic delays, surgical overtreatment, and repeat procedures.

In addition to clinical and economic outcomes, our findings showed a 23.1% rate of discordance in IHC profiles between lymph node and primary tumor in recurrent disease, compared with 2.5% in primary tumors ($P = .004$). As IHC characterization is only possible via CNB, this reinforces its relevance in tailoring systemic therapy, particularly in cases of tumor recurrence or suspected phenotypic shift.

Although psychological distress was not directly measured in this study, prior evidence suggests that inconclusive results and repeat procedures may increase patient anxiety, delay therapy, and negatively affect quality of life.[28,29] Thus, minimizing diagnostic uncertainty through initial CNB may also contribute to improved patient experience.

This study has some limitations. As a single-center retrospective analysis, generalizability may be constrained, and biopsy adequacy may vary across institutions depending on radiologist experience and local protocols. Furthermore, although the economic evaluation was robust, it focused exclusively on direct diagnostic costs and did not capture long-term financial implications or indirect societal costs.

Despite these limitations, to our knowledge, this is the first study to evaluate both clinical and economic outcomes of FNA vs CNB in lymph node evaluation within a real-world LMIC setting. The findings provide important data to support evidence-based guidelines and inform resource allocation in public health systems such as SUS.

Conclusions

In this real-world study, CNB proved significantly superior to FNA for ALN assessment in BC patients, with lower rates of inconclusive results and higher diagnostic adequacy. Although

FNA had a lower upfront cost, it led to more follow-up procedures and higher total expenditures. The economic analysis showed that a CNB-first approach reduced diagnostic costs by up to 50%.

These findings support the use of CNB as the preferred first-line biopsy method for suspicious lymph nodes in most centers, especially in public healthcare systems, particularly in LMICs.

Author Disclosures

Author disclosure forms can be accessed below in the Supplemental Material section.

Supplemental Material

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