

Diagnostic Accuracy of Bronchoalveolar Lavage and Bronchial Brushing Cytology, Alone and in Combination, in Patients with Histologically Confirmed Lung Adenocarcinoma and Squamous Cell Carcinoma

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Abstract

Introduction: Bronchoalveolar lavage (BAL) and bronchial brushing (BB) are minimally invasive cytology techniques used during the diagnostic work-up of lung cancer. They sample different anatomic compartments. Their performance for lung adenocarcinoma (ADC) and squamous cell carcinoma (SCC) may differ. This study evaluated their subtype-specific diagnostic performance, alone and in combination, using histopathology as the reference standard.

Method: This retrospective paired diagnostic-accuracy study included 38 patients at Prof. dr. Chairuddin Panusunan Lubis Teaching Hospital, Medan, from January 2023 to June 2024. All underwent BAL, BB, and lung biopsy. Cytology was evaluated on Giemsa-stained preparations and histopathology on hematoxylin and eosin-stained sections. Sensitivity and subtype-specific specificity, with exact 95% confidence intervals (CIs), were calculated for concordant cytologic subtype assignment.

Results: Histopathology showed ADC in 21 patients and SCC in 17. BAL sensitivity for ADC was 95.2% (95% CI: 76.2–99.9), compared with 76.2% (95% CI: 52.8–91.8) for BB. For SCC, BAL sensitivity was 47.1% (95% CI: 23.0–72.2) and BB sensitivity was 94.1% (95% CI: 71.3–99.9). The combined strategy matched the more sensitive individual test for each subtype. No cross-subtype cytologic assignments occurred; subtype-specific specificity was 100%, with wide CIs due to the small non-target groups.

Conclusion: BAL demonstrated higher sensitivity for ADC, whereas BB demonstrated higher sensitivity for SCC; together, the techniques can provide complementary preliminary cytologic information, although histopathological confirmation remains necessary.

Keywords: Bronchoalveolar lavage, Bronchial brushing, Adenocarcinoma, Squamous cell carcinoma, Diagnostic accuracy.

Akurasi Diagnostik Sitologi Bronchoalveolar Lavage dan Bronchial Brushing, Secara Tunggal dan Kombinasi, pada Pasien dengan Adenokarsinoma Paru dan Karsinoma Sel Skuamosa Paru yang Terkonfirmasi Secara Histopatologi

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Abstrak

Pendahuluan: Bronchoalveolar lavage (BAL) dan bronchial brushing (BB) merupakan teknik sitologi minimal invasif dalam pemeriksaan diagnostik kanker paru. Kedua prosedur mengambil material dari kompartemen anatomi yang berbeda. Kinerja keduanya pada adenokarsinoma paru (ADC) dan karsinoma sel skuamosa (SCC) dapat berbeda. Penelitian ini menilai kinerja diagnostik spesifik subtype BAL dan BB, secara tunggal maupun kombinasi, dengan histopatologi sebagai standar rujukan.

Metode: Studi akurasi diagnostik berpasangan retrospektif ini mencakup 38 pasien di Rumah Sakit Pendidikan Prof. dr. Chairuddin Panusunan Lubis Medan pada Januari 2023–Juni 2024. Semua pasien menjalani BAL, BB, dan biopsi paru. Sediaan sitologi diwarnai Giemsa dan histopatologi dengan hematoxylin-eosin. Sensitivitas dan spesifisitas spesifik subtype, beserta interval kepercayaan (IK) 95% eksak, dihitung berdasarkan kesesuaian subtype sitologi dengan histopatologi.

Hasil: Histopatologi menunjukkan ADC pada 21 pasien dan SCC pada 17 pasien. Sensitivitas BAL untuk ADC adalah 95,2% (95% CI: 76,2–99,9), sedangkan BB 76,2% (95% CI: 52,8–91,8). Untuk SCC, sensitivitas BAL adalah 47,1% (95% CI: 23,0–72,2) dan BB 94,1% (95% CI: 71,3–99,9). Pemeriksaan kombinasi setara dengan pemeriksaan tunggal yang paling sensitif pada masing-masing subtype. Tidak ditemukan penetapan sitologi silang antarsubtype; spesifisitas spesifik subtype 100% dengan CI lebar karena kelompok non-target kecil.

Kesimpulan: BAL berkinerja lebih baik untuk ADC, sedangkan BB berkinerja lebih baik untuk SCC. Kedua teknik dapat memberikan informasi sitologi awal yang saling melengkapi; namun, konfirmasi histopatologi tetap diperlukan.

Kata kunci: Bronchoalveolar lavage, Bronchial brushing, Adenokarsinoma, Karsinoma sel skuamosa, Akurasi diagnostik

Introduction

Lung cancer remains a major cause of cancer mortality worldwide. Lung adenocarcinoma (ADC) and squamous cell carcinoma (SCC) are major non-small-cell lung carcinoma subtypes. They have distinct morphologic and clinical features. Accurate subtype assignment informs diagnosis, treatment selection, and prognostication.^{1,2}

Current tumor classification and respiratory cytology reporting systems provide a framework for interpreting small specimens. Although histopathology remains the reference method for definitive tumor classification, particularly when immunohistochemical or molecular testing is required, clinicians

frequently first receive cytologic material obtained during bronchoscopy. In this setting, minimally invasive cytology can provide a preliminary assessment and guide further sampling; however, it does not substitute for histopathological confirmation.^{3–5}

Bronchoscopy provides several minimally invasive sampling options. BAL samples distal airway and alveolar material, whereas BB directly samples an accessible bronchial lesion. The procedures are not interchangeable, and their yields vary with lesion characteristics, sampling quality, and cytologic interpretation. Bronchial brushing has demonstrated useful diagnostic performance in lung cancer, although accuracy varies across clinical settings.^{6,7}

Both methods may be limited by scant cellularity and poor access to the target lesion. Tumor necrosis, inflammation, and the distribution of exfoliated malignant cells can also affect yield. Comparative studies of BAL and BB have reported variable sensitivity and differences related to specimen preparation. Paired BAL and BB results allow comparison within the same patient and reduce case-mix distortion.^{8–11}

Direct comparisons also show that procedural sequence and cellular yield can influence the information provided by bronchial cytology specimens.^{12–14} These findings support the use of complementary sampling when clinically appropriate. However, diagnostic yields vary by preparation method, lesion characteristics, and clinical spectrum. Paired data for histologically confirmed ADC and SCC remain limited, particularly from local centers. By comparing BAL and BB within the same patient, a paired design minimizes case-mix distortion and provides a direct assessment of subtype-specific performance. This study therefore evaluated the subtype-specific performance of BAL, BB, and their combined use against histopathology.

Method

This retrospective paired diagnostic-accuracy study reviewed patients who underwent BAL, BB, and lung biopsy at the Department of Anatomical Pathology, Prof. dr. Chairuddin Panusunan Lubis Teaching Hospital, Medan, between January 2023 and June 2024. Eligible patients had paired BAL and BB cytology results and histopathological confirmation of ADC or SCC. Cases with incomplete records were excluded. The unit of analysis was the patient, and each patient contributed paired BAL and BB results. BAL, BB, and biopsy were obtained during the same bronchoscopy session as part of the institution's integrated diagnostic protocol. Cytology specimens were processed and reported earlier than biopsy specimens because of their shorter processing time; however, the retrospective records did not consistently document the exact intraprocedural sequence of BAL, BB, and biopsy for every case.

The extracted variables were age group, sex, final histopathological subtype, and the cytology category reported for each sampling method. BAL and BB were the two index tests. Their results were analyzed as paired observations. This permitted direct comparison within the same selected population without double counting patients.

Cytology preparations consisted of air-dried direct smears stained with Giemsa; liquid-based cytology was not used. The BAL and BB cytology slides were re-evaluated by a pathologist blinded to the final histopathological diagnosis before cytologic-histopathological correlation. Histopathology, stained with hematoxylin and eosin, served as the reference standard. Cytology categories were interpreted in line with current respiratory cytology reporting systems. For each target subtype, a cytologic diagnosis of the same subtype was classified as positive. Benign, atypical, suspicious, inadequate, and alternative-subtype cytology results were classified as non-positive for that target subtype. For the combined strategy, a result was positive when either BAL or BB assigned the target subtype. Sensitivity and subtype-specific specificity were calculated from 2×2 tables with exact Clopper–Pearson 95% CIs. The alternative histopathological subtype was the non-target group; therefore, the study does not estimate specificity for cancer versus non-cancer detection.^{15–18} The study is reported in accordance with STARD 2015.¹⁹

For sensitivity, a true positive was a concordant cytologic subtype assignment. Any non-concordant cytology result among cases with the same reference subtype was a false negative. For subtype-specific specificity, a true negative was the absence of the target-subtype assignment among cases with the alternate reference subtype. Exact intervals were selected because several cells had small counts or zero false-positive observations.

The protocol was approved by the Health Research Ethics Committee of Universitas Sumatera Utara. The approval number was 719/KEPK/USU/2025. The study population was the retrospectively identified cohort described above. Results are reported in aggregate.

Result

Thirty-eight patients had paired BAL and BB results and histopathological confirmation. ADC accounted for 21 cases (55.3%) and SCC for 17 cases (44.7%). The cohort was predominantly male. The largest age group was 60–69 years (Table 1).

Table 2 presents the diagnostic performance of each strategy. BAL identified 20 of 21 ADC cases, whereas BB identified 16. In contrast, BB identified 16 of 17 SCC cases, whereas BAL identified 8. Combining BAL and BB did not identify additional ADC cases beyond BAL or additional SCC cases beyond

Table 1. Characteristics of The Study Cohort

Characteristic	n	%
Age, years		
40–49	3	7.9
50–59	14	36.8
60–69	20	52.6
70–79	1	2.6
Sex		
Male	32	84.2
Female	6	15.8
Reference standard		
Lung adenocarcinoma	21	55.3
Squamous cell carcinoma	17	44.7

Discussion

This paired study showed different sensitivity profiles for BAL and BB. BAL had higher sensitivity for ADC, while BB had higher sensitivity for SCC. The combined strategy matched the better single test for each subtype: it improved SCC detection relative to BAL alone but did not exceed BB, and it did not improve ADC detection beyond BAL. Therefore, these data support complementary sampling rather than a claim that combination testing universally improves sensitivity.

The absence of cross-subtype cytologic assignments produced a point estimate of 100% for subtype-specific specificity in this preselected malignant cohort. This result warrants caution. For ADC, the non-target group comprised only 17 SCC cases; for SCC, it

Table 2. Subtype-specific Diagnostic Performance of BAL and BB Against Histopathology

Target subtype	Index test	TP/FN	TN/FP	Sensitivity, % (95% CI)	Specificity,* % (95% CI)
ADC (n = 21)	BAL	20/1	17/0	95.2 (76.2–99.9)	100.0 (80.5–100.0)
ADC (n = 21)	BB	16/5	17/0	76.2 (52.8–91.8)	100.0 (80.5–100.0)
ADC (n = 21)	BAL + BB	20/1	17/0	95.2 (76.2–99.9)	100.0 (80.5–100.0)
SCC (n = 17)	BAL	8/9	21/0	47.1 (23.0–72.2)	100.0 (83.9–100.0)
SCC (n = 17)	BB	16/1	21/0	94.1 (71.3–99.9)	100.0 (83.9–100.0)
SCC (n = 17)	BAL + BB	16/1	21/0	94.1 (71.3–99.9)	100.0 (83.9–100.0)

BAL, bronchoalveolar lavage; BB, bronchial brushing; ADC, adenocarcinoma; SCC, squamous cell carcinoma; TP, true positive; FN, false negative; TN, true negative; FP, false positive; CI, confidence interval. *Specificity is subtype-specific, with the alternative subtype as the non-target group.

BB. No cytology result assigned ADC to an SCC reference case or SCC to an ADC reference case.

For ADC reference cases, BAL yielded 20 concordant malignant ADC results and 1 benign result; BB yielded 16 concordant malignant ADC results, 4 benign results, and 1 suspicious result. For SCC reference cases, BAL yielded 8 concordant malignant SCC results, 6 benign results, 2 inadequate results, and 1 atypical result. BB yielded 16 concordant malignant SCC results and 1 benign result. Thus, the observed difference between BAL and BB arose predominantly from false-negative or indeterminate cytology rather than cross-subtype assignment.

The widest CIs occurred for BAL sensitivity for SCC. This estimate was based on 17 SCC cases. Specificity estimates were also imprecise. Their non-target groups contained only 17 or 21 cases.

comprised 21 ADC cases. The corresponding exact CIs are wide, and these values describe discrimination between two known histological subtypes, not specificity for detecting lung cancer in an unselected population with benign disease, other lung tumors, or metastatic malignancy. Cytologic pitfalls and non-neoplastic mimics can also resemble malignancy in routine practice, which this restricted cohort was not designed to represent.^{20,21}

The differential performance is biologically plausible because bronchoscopic specimens may capture tumors differently according to lesion location, airway accessibility, cellular exfoliation, and specimen quality. SCC more commonly arises in central or proximal bronchi, where an accessible endobronchial lesion can be directly sampled by brushing and may yield abundant tumor cells. In contrast, ADC more often presents as a peripheral parenchymal lesion beyond the reach of conventional brushing; malignant cells ex-

foliated into distal airways and alveolar spaces may therefore be recovered by BAL.^{2,6} These are general anatomic and biologic considerations rather than lesion-specific observations in the present cohort. Guidance on sampling and cytopathology emphasizes the effects of specimen acquisition, triage, and adequacy on diagnostic and downstream use.²²⁻²⁴ The present study did not document lesion visibility, lesion location, or adequacy in a way that permits attribution of the observed pattern to any specific procedural factor. Differences from published estimates should therefore be interpreted cautiously because comparators vary in population, technique, and cytologic preparation.

The finding that BAL was more sensitive for ADC and BB for SCC should be regarded as an empirical pattern in this cohort. It is not a procedural rule for every lesion. The result reinforces the value of obtaining and interpreting all available specimens in context. When both procedures are performed, reporting each specimen separately may be more informative than an unqualified overall cytology result.

Clinically, concordant cytologic subtype assignment may provide useful preliminary information when tissue acquisition is being planned or reviewed. In an accessible central lesion suspicious for SCC, BB may be prioritized to optimize direct sampling, whereas BAL may be particularly informative for a peripheral or parenchymal lesion suspicious for ADC. These considerations should be applied only when technically appropriate and should not be interpreted as a procedural rule for every lesion. When both sample types are submitted, reporting BAL and BB separately may be more informative than an unqualified overall cytology result. A negative, atypical, suspicious, or inadequate cytology result should not exclude malignancy or replace tissue confirmation. Specimen triage must also anticipate molecular and other ancillary testing when clinically indicated.²⁵⁻²⁷ Testing pathways that incorporate programmed death-ligand 1 assessment, reflex molecular testing, and appropriate tissue acquisition illustrate why cytology results must be interpreted within a multidisciplinary diagnostic strategy.²⁸⁻³⁰

Several limitations require emphasis. This was a retrospective single-center study with only 38 patients and a restricted spectrum of two histologically confirmed tumor subtypes. Selection of patients who underwent both cytology procedures and biopsy

may introduce verification and spectrum bias. The study did not assess lesion site or visibility, detailed sampling technique, interobserver reproducibility, or whether cytology readers were blinded to other clinical information. The small non-target groups produced wide CIs for specificity, and the design cannot estimate specificity for lung cancer versus benign disease. These findings should therefore be interpreted as subtype-specific performance in this selected cohort.

Conclusion

Among histologically confirmed ADC and SCC cases, BAL showed higher sensitivity for ADC. BB showed higher sensitivity for SCC. Combined testing matched rather than exceeded the better individual test for each subtype. BAL and BB can provide complementary preliminary cytologic information, but histopathological confirmation remains necessary for definitive diagnosis and management.

Declarations

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Competing interests

The authors declare no competing interests.

Author contributions

All authors contributed to study planning, data collection, cytologic and histopathological assessment, analysis, drafting, and critical revision of the manuscript. All authors approved the final manuscript.

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