The Role of Bronchoalveolar Lavage in COVID-19 Diagnoses and Management

Edie Zhang[1], Shuman Liu MD[2], Rosemary C. She, MD[2]
Keck School of Medicine, [1]Department of Pathology, Los Angeles, CA, USA

Background

In the diagnosis of SARS-CoV-2, nasopharyngeal swabs (NPS) from the upper respiratory tract are primarily used for polymerase chain reaction (PCR) testing. The lower airway is not considered a primary sample site, though COVID-19 can cause severe lower airway disease. The use of bronchoalveolar lavage (BAL), a targeted way of sampling alveolar contents through bronchoscopy-directed saline delivery and recollection, can allow for assessment of disease stage and responsiveness to therapy [1]. Additionally, studies have shown inconsistencies between SARS-CoV-2 results in NPS and BAL samples as the disease progresses from the periphery to within the lungs [2,3]. As such, the utility of BALs, particularly in the background of SARS-CoV-2 management, warrants further exploration. This study aims to evaluate the clinical and diagnostic role of bronchoalveolar lavage in diagnosing and managing COVID-19.

Materials and Methods

- This was a retrospective chart review of patients admitted to Keck Medical Center from March 1st, 2020, to April 29th, 2021, who had both NPS and BAL samples collected and tested for SARS-CoV-2 RNA.
- Four patient groups were were designated by PCR results: (A) NPS+BAL+, (B) NPS+BAL-, (C) NPS-BAL+, and (D) NPS -BAL-.
- Data were collected from medical and laboratory records including admission reason, BAL indication, date of symptom onset if applicable, turnaround time of RT-PCR results, cycle threshold (Ct) values for positive BAL samples, and patient status upon discharge.
- Due to the study size, statistical analyses were largely descriptive. The student t-test, one-way ANOVA, and post-hoc Tukey HSD test were applied for between-group comparisons. A p-value of <0.05 was considered significant.

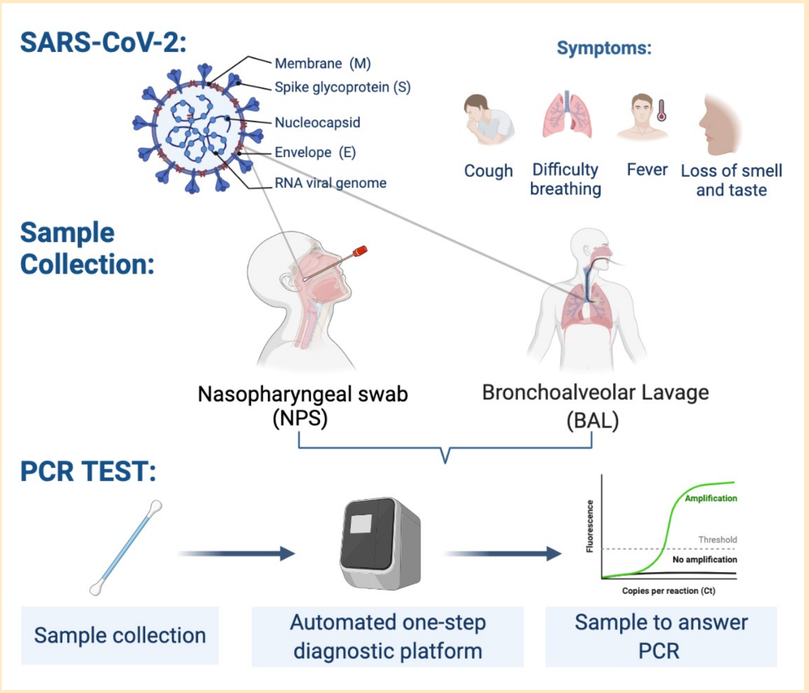

Figure 1: Infographic of collection and processing methods for NPS and BAL samples. Viral components of SARS-CoV-2 and associated symptoms of COVID-19 are also included.

Results

Table 1: Patient characteristics overall and by SARS-CoV-2 detection status

Characteristic	All (N=154)	Population by SARS-CoV-2 detection status				
		NPS+ and/or BAL+				
		All NPS+ and/or BAL+ (n=65)	NPS+/BAL+ (n=34)	NPS+/BAL– (n=26)	NPS-/BAL+ (n=5)	NPS–/BAL– (n=89)
Median age (range), years	59 (23–88)	61 (23–87)	64 (30–87)	57 (23–77)	66 (27-71)	58 (25–88)
Male, n (%)	92 (59.7)	39 (60.0)	19 (55.9)	16 (61.5)	4 (80.0)	53 (59.6)
Female, n (%)	62 (40.3)	26 (40.0)	15 (44.)	10 (38.5)	1 (20.0)	36 (40.4)
Median time between admission and discharge, days	24	24	25	24	18	24
Died during study period, n (%)	67 (43.5)	36 (55.4)	19 (55.9)	14 (53.8)	3 (60.0)	31 (34.8)
Co-morbidities, n (%)						
Hypertension	74 (48.1)	40 (61.5)	20 (58.8)	17 (65.4)	3 (60.0)	34 (38.2)
Cardiovascular disease	61 (39.6)	24 (36.9)	12 (35.3)	9 (34.6)	3 (60.0)	37 (41.6)
Diabetes	55 (35.7)	28 (43.1)	13 (38.2)	12 (46.2)	3 (60.0)	27 (30.3)
Malignancy	35 (22.7)	6 (9.2)	4 (11.7)	2 (7.7)	0	29 (32.6)
CNS disease	32 (20.8)	15 (23.1)	5 (14.7)	9 (34.6)	1 (20.0)	17 (19.1)
Kidney disease	34 (22.1)	13 (20.0)	7 (20.6)	5 (19.2)	1 (20.0)	21 (23.6)
Morbid obesity	33 (21.4)	10 (15.4)	5 (14.7)	4 (15.4)	1 (20.0)	23 (25.8)
Lung disease	43 (27.9)	17 (26.2)	9 (26.5)	6 (23.1)	2 (40.0)	26 (29.2)
Liver disease	22 (14.3)	9 (13.8)	4 (11.8)	3 (11.5)	2 (40.0)	13 (14.6)
GI disease	20 (13.0)	3 (4.6)	1 (2.9)	2 (7.7)	0	17 (19.1)
Rheumatic/autoimmune disease	18 (11.7)	8 (12.3)	6 (17.6)	1 (3.8)	1 (20.0)	10 (11.2)
COVID-19 therapies, n (%)*						
Steroids	47 (30.5)	45 (69.2)	28 (82.4)	16 (61.5)	3 (60.0)	0
Remdesivir	29 (18.8)	28 (43.1)	19 (55.9)	8 (30.8)	2 (40.0)	0
Tocilizumab	25 (16.2)	21 (32.3)	14 (41.2)	7 (26.9)	2 (40.0)	2 (2.2)
Convalescent plasma	16 (10.4)	13 (20.0)	11 (32.4)	4 (15.4)	0	1 (1.1)
HCQ	13 (8.4)	11 (16.9)	8 (23.5)	3 (11.5)	1 (20.0)	1 (1.1)
Antibiotics, n (%)	59 (38.3)	55 (84.6)	33 (97.1)	19 (73.1)	5 (100.0)	2 (2.2)
Chest Radiograph Findings, n (%)						
Diffuse or bilateral opacities	124 (80.5)	52 (80.0)	31 (91.2)	16 (61.5)	5 (100.0)	72 (80.9)
Focal or unilateral opacities	17 (11.0)	5 (7.7)	3 (8.8)	2 (7.7)	0 (0)	12 (13.5)
Other or no findings	13 (8.4)	8 (12.3)	0 (0)	8 (30.8)	0 (0)	5 (5.6)
Mean time from symptom onset to BAL, days (SD)	21 (1.73)	27 (2.02)	24 (1.76)	35 (4.51)	13 (2.08)	14 (2.61)
Bacterial culture performed, n	141	57	30	22	5	84
Positive bacterial culture, n (%)	47 (33.3)	29 (50.9)	15 (50.0)	11 (50.0)	3 (60.0)	17 (20.2)
Fungal culture performed, n	88	26	13	9	4	62
Positive fungal culture, n (%)	12 (13.6)	8 (30.8)	5 (38.5)	2 (22.2)	1 (20.0)	4 (6.5)
Median Cycle Threshold (Ct) Values	32.0	32.0	29.2	N/A	32.8	N/A
ARDS diagnosis, n (%)	87 (56.5)	52 (80.0)	32 (94.1)	15 (57.7)	5 (100.0)	35 (39.3)

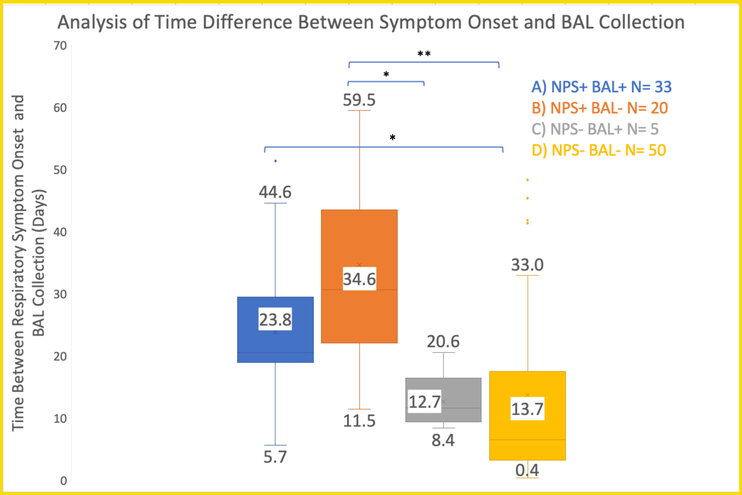

Figure 4: Comparison of time difference in days between respiratory symptom onset and first BAL sample collection. Not all patients had documented respiratory symptoms for analysis. Group A obtained BALs significantly later than Group D (*p<0.05) and Group B obtained BALs significantly later than both Group C (p<0.05) and Group D (p<0.01). Statistical analysis was performed using one-way ANOVA with post-hoc Tukey HSD.

Discussion

- A higher proportion of NPS+ patients with BAL+ test results received COVID-19 therapies and antibiotics compared with those with BAL-test results, which may indicate more severe disease in this population.
  - BAL+ COVID-19 patients were also more likely than BAL- COVID-19 patients to have an ARDS diagnosis (p<0.01).
  - NPS+ and BAL+ patients were more likely than NPS+ and BAL- patients to have diffuse or bilateral chest radiographic opacities (p<0.01).
  - However, there was no significant difference in the all-cause mortality rate in the BAL+ and BAL- subgroups.
- Twelve patients had SARS-CoV-2 and aspergillus co-infections, 10 of whom (83.3%) died during the study period. This supports other observations of high mortality rate among patients with COVID-19 associated invasive pulmonary aspergillosis.
  - NPS+ or BAL+ patients were more likely to have cultures positive for Aspergillus co-infections than NPS- and BAL- patients (p<0.05).
- Although Ct values in BAL specimens were not associated with patient mortality in this study, they have been associated with viral load and disease severity [4].
- Time from symptom onset to BAL testing was significantly shorter in Group A than D (p<0.05) and in Group B than C (p<0.05) and D (p<0.01) most likely due to clinical urgency. Providers may have ordered BAL earlier if patients presented with symptoms concerning for COVID-19 but did not test positive on NPS.
- BALs remained positive ranging from 19.9 to 51.7 days after symptom onset compared to NPS samples that remained positive from 3.3 to 32.1 days. This is consistent with the prolonged duration of PCR positivity in many COVID-19 patients.

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