Bilateral versus Unilateral Bronchoalveolar Lavage for the Diagnosis of Ventilator-Associated Pneumonia

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Abstract

Background: Ventilator-associated pneumonia (VAP) complicates the clinical course of critically injured intubated patients. Bronchoscopic bronchoalveolar lavage (BAL) represents an invasive and accurate means of VAP diagnosis. Unilateral and blinded techniques offer less invasive alternatives to bronchoscopic BAL. This study evaluated clinical criteria as well as unilateral directed versus bilateral BAL for VAP diagnosis.

Methods: A retrospective chart review of 113 consecutive intubated trauma patients with clinically suspected VAP undergoing unilateral versus bilateral BAL was performed with comparison of positive culture results ($>10^4$ colony-forming units [CFU]/mL). Culture results were compared with chest radiograph (CXR) infiltrates and white blood cell (WBC) count elevation.

Results: Bilateral BAL was more likely to be positive than unilateral BAL (50.4% vs. 25.5%). In 37.1% of bilateral BALs, there was discordance between the sides of positivity or the bacteria isolated. A CXR infiltrate and WBC count elevation did not predict positive BAL.

Conclusions: Clinical indicators of VAP are inaccurate, and bilateral bronchoscopic BAL is more likely than unilateral BAL to provide a positive sample in intubated trauma patients. Techniques that do not sample both lungs reliably should be avoided for diagnosis in this patient population.

VENTILATOR-ASSOCIATED PNEUMONIA (VAP) is the second most common nosocomial infection and is a major cause of morbidity and death in critically injured trauma patients. It can result in prolonged stay in the intensive care unit (ICU), prolonged mechanical ventilation, and higher hospitalization cost [1–4]. Trauma itself is a risk factor for pneumonia in ventilated critically ill patients; however, the diagnosis of VAP is particularly difficult in this patient population [2,5]. Clinical indicators are difficult to interpret in this setting; in particular, the clinical pulmonary infection score (CPIS), which includes temperature, blood leukocyte count, tracheal secretions, oxygenation, and chest radiograph infiltration, is of little diagnostic utility [5–7]. Accurate and timely diagnosis is important for initiating appropriate therapy and avoiding further complications while avoiding unnecessary therapy and potential treatment-associated complications and cost [8].

The use of quantitative cultures of the lower respiratory tract using invasive means of bronchoscopic alveolar lavage (BAL) and protected specimen brushing (PSB) improves the outcomes of patients with suspected VAP [9,10]. However,

several studies of non-trauma patients have suggested that these invasive methods fail to alter antibiotic therapy or improve outcome [11–13]. In addition, invasive sampling methods such as BAL are costly and require specialized training and equipment. Therefore, less-invasive means of sampling the lower respiratory tract, including mini-BAL (without use of a bronchoscope), blind PSB, and blind bronchial sampling (BBS) have been used. Advocates contend that these less-invasive means do not alter diagnostic accuracy. [14–18]. However, these blind methods essentially sample only one lung, and the site of sampling within the lung is unknown. Although some clinicians contend that directed unilateral sampling of the lung suspected to have VAP is as reliable as bilateral sampling [19,20], others argue for single lung sampling because of the high likelihood of concordance between the two lung cultures and the implicit greater risks of bilateral sampling [21]. We undertook this study to determine the diagnostic accuracy of bilateral versus unilateral BAL for VAP in a trauma population.

We hypothesized that bilateral BAL would be more accurate than unilateral examination for VAP diagnosis in the

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trauma population and that standard clinical criteria would not be useful for diagnosis. This study was done during a time when one of the trauma staff performed unilateral BAL directed at the site of suspected VAP on the chest radiograph (CXR).

Patients and Methods

Study population

The University of Wisconsin–Madison Human Subjects Institutional Review Board granted approval for this study. A retrospective chart review was performed on 113 consecutive intubated trauma patients who underwent BAL because of suspected VAP. These patients were identified from a total of 1,546 patients admitted to the University of Wisconsin Hospitals and Clinics Trauma Surgery Service from January 2004 through December 2005. Charts were reviewed for demographic data as well as white blood cell (WBC) count, CXR interpretation, BAL culture, results including side of positive culture and organism isolated, and the timing of BAL collection in relation to the number of days on the ventilator.

Chest radiograph interpretation and white blood cell count determination

A CXR was taken just prior to the BAL and reviewed and interpreted by a staff radiologist. The WBC counts were determined from venous blood drawn within 24 h prior to bronchoscopic BAL. These samples were processed by the clinical laboratory at our institution.

Bronchoalveolar lavage collection and processing

Patients who were suspected clinically to have VAP underwent bronchoscopic BAL specimen collection on the day the VAP was suspected. Bronchoscopy and BAL collection was performed by surgical residents in post-graduate years 2–5 under the direct supervision of the attending surgeon. Prior to bronchoscopy, patients were oxygenated with 100% oxygen, and vital signs were monitored closely throughout the procedure. Patients were sedated deeply, had appropriate analgesia, and were paralyzed before the procedure. For collection of the BAL specimen, a flexible fiberoptic bronchoscope was advanced via the endotracheal tube into the bronchus intermedius for right-sided collections and just distal to the upper-lobe take-off for left-sided collections. Sixty milliliters of sterile saline was injected followed by aspiration into a sterile trap within 5 sec with an attempt at collecting a minimum of 10 mL per sample. On average, 10–15 mL of effluent was sent for analysis. During the time of this study, one of our trauma surgery staff was attempting unilateral BAL directed at the site of suspected VAP on CXR, while the rest of our trauma surgery staff was performing bilateral BALs regardless of CXR findings. For bilateral BALs, the bronchoscope was not sterilized; however, the effluent from the initial side was aspirated until there was air return, thereby leaving minimal residual volume in the aspiration channel of the bronchoscope. The effluent was collected in separate traps and sent to the laboratory as separate specimens. Samples were maintained at room temperature. Quantitative cultures were processed by the microbiology laboratory according to a standard protocol. A quantitative threshold of $>10^4$ colony-forming units (CFU)/mL was considered a positive BAL in

this study. This value did not reflect that chosen to institute antibiotic therapy, as antibiotics were administered routinely for $\geq 10^5$ cfu/mL and individualized for samples with values $>10^4$ but $<10^5$.

Bilateral and unilateral BAL analysis

Bilateral BALs were reviewed for side of positive culture as well as for organisms isolated. Unilateral BALs were also reviewed for positive cultures and organisms isolated and were analyzed by side (right, left, or unspecified). Bilateral and unilateral BAL were compared for positivity by the χ^2 test. Correlation between CXR air-space disease and BAL positivity was determined by χ^2 analysis for patients receiving bilateral BALs only, as unilateral BALs obviously did not analyze both lungs. The correlation between WBC count and BAL positivity also was determined by χ^2 analysis. Bilateral and unilateral BAL were compared for monomicrobial isolation and polymicrobial isolation as well as organisms by the Student *t*-test with significance at $p < 0.05$.

Results

Patient demographics and BAL numbers

From January 2004 to December 2005, 1,546 patients were admitted to the Trauma Surgery Service at the University of Wisconsin Hospital and Clinics. Of these, 113 consecutive intubated patients who were suspected to have VAP underwent a BAL for diagnosis (total of 170 BALs). Nearly all patients (98%) were admitted after blunt trauma, the average age was 41.3 ± 17.0 years, and the majority (76%) were male. The average hospital stay for these patients was 28.6 ± 16.0 days. The majority (65%) were discharged to a rehabilitation facility or nursing home, whereas 24% were discharged home and 5% to another hospital, and 5% died. The total number of BAL procedures was 170 with 47 collected unilaterally directed at the site of suspected pneumonia, and 123 collected bilaterally.

Culture results

The outcomes of both the bilateral and unilateral BALs are depicted in Figure 1. Of the 123 bilateral BALs, 46 (37.4%) had positive cultures from both sides, with 39 of these cultures yielding the same organisms from both sides, and the remainder having different organisms in the left and right lungs. Of the 123 bilateral BALs, 16 (13.0%) were positive on one side only with a predilection for right-sided positivity (11 vs. 5). This meant that 23 of the 62 (37.1%) of the bilateral BALs were discordant for either the side of positivity or the bacteria isolated. Of the 47 unilateral BALs, 34 (72.3%) did not have directionality specified in the chart, whereas 5 (10.6%) were right-sided, and 8 (17.0%) were left-sided. Overall, unilateral directed BALs were positive in 25.5% of cases, whereas bilateral BALs were positive in 50.4% of cases, a difference that is statistically significant ($p < 0.01$).

Correlation between BAL culture results, CXR findings, and WBC count

No correlation was found between the presence or location of air-space disease on CXR and the probability of a positive BAL ($p = 0.44$). The contingency table for the side of air-space disease and the side of BAL positivity in patients receiving a

FIG. 1. Bronchoscopic alveolar lavage outcomes.

bilateral BAL is depicted in Table 1. Only 32 (26.0%) of the total CXRs were in concordance (16 bilaterally positive+16 bilaterally negative) with BAL culture results. Forty patients who had no findings of air-space disease on CXR underwent bilateral BAL, and of these, 26 (60%) had positive BAL culture results. There also was no correlation between an elevated WBC count ($>10,500$ WBC/mm³) and the likelihood of a positive BAL ($p=0.63$). Of the 170 BALs performed, 106 patients had an elevated WBC count at the time of BAL, with only 47 (49.2%) of those BALs being positive. Furthermore, 61 patients had a normal WBC count, with 30 (49.2%) of these patients having positive BAL results.

Bacterial isolates from bilateral versus unilateral BAL

Monomicrobial growth was more likely in patients receiving a bilateral BAL (33.3%) versus unilateral BAL (10.6%) ($p < 0.001$). There was no difference between bilateral and unilateral BAL in the likelihood of polymicrobial growth. The bacterial isolates from the unilateral and bilateral BALs are depicted in Table 2. We saw no significant differences in the species of bacteria isolated from bilateral and unilateral BAL.

The bacterial isolates from patients receiving BALs were classified according to time on the ventilator, and this is depicted in Figure 2, along with the overall percentages of bacterial isolates. Over time, there was a shift toward gram-

negative bacterial infections as the number of ventilator days increased.

Discussion

Accurate and timely diagnosis of VAP in critically injured trauma patients is of utmost importance for preventing associated morbidity and death [22, 23]. Common clinical indicators of VAP are difficult to interpret in this patient population, and invasive means of sampling the lower respiratory tract have been found to be more sensitive and specific than non-invasive diagnostic studies [24]. At our institution, BAL is the primary invasive means for diagnosing VAP. However, bronchoscopy requires advanced training and special equipment and is not readily available at some centers. Recently, equipment capable of obtaining samples from the lower respiratory tract without direct vision or localization has been marketed [14, 17, 18, 25]. In addition, some investigators have attempted directed invasive measures for the side of suspected pneumonia to simplify diagnosis by decreasing intervention time and simplifying microbiologic analysis [21].

Our data demonstrate that bilateral sampling of the lower respiratory tract with BAL increases the likelihood of

TABLE 2. BACTERIAL ISOLATES FROM BILATERAL AND UNILATERAL BRONCHOALVEOLAR LAVAGE FLUID

	Unilateral (n = 47)(%) ^a	Bilateral (n = 123)(%)	P value
<i>Staphylococcus aureus</i>	6 (13)	16 (13.0)	1.00
<i>Enterobacterium</i>	4 (8.5)	16 (13.0)	0.60
<i>Haemophilus</i> spp.	3 (6.4)	15 (12.2)	0.40
<i>Pseudomonas</i> spp.	3 (6.4)	8 (6.5)	1.00
<i>Streptococcus pneumoniae</i>	0	9 (7.3)	0.06
<i>Acinetobacter</i>	0	4 (3.3)	0.58
Methicillin-resistant <i>S. aureus</i>	0	2 (1.6)	1.00
<i>Streptococcus</i> spp.	0	2 (1.6)	1.00
Other	1 (2.1)	8 (6.5)	0.45

TABLE 1. CONTINGENCY TABLE FOR CORRELATING CHEST RADIOGRAPHS AND BILATERAL BRONCHOALVEOLAR LAVAGE FINDINGS

<i>Side of radiographic infiltrate</i>	<i>Side of positive BAL culture (%)^a</i>				
	<i>Right</i>	<i>Left</i>	<i>Bilateral</i>	<i>Negative</i>	<i>Total</i>
Right	0	1 (9.1)	6 (54.6)	4 (36.4)	11
Left	1 (4.6)	0	6 (27.3)	15 (68.2)	22
Bilateral	6 (12.0)	2 (4.0)	16 (32.0)	26 (52.0)	50
Negative	4 (10.0)	2 (5.0)	18 (45.0)	16 (40)	40
Total	11	5	46	61	123

^aPercentages are expression of site of positive lavage culture for given radiographic infiltrate.

^aPercentages are specific organisms isolated from fluid. Fisher exact test used to determine p value.

FIG. 2. Bronchoscopic alveolar lavage findings according to duration of ventilation.

obtaining positive BAL specimens compared with unilateral sampling. This is particularly important, as our study and others have shown that the presence or absence of infiltrates on chest radiograph have no correlation with BAL culture results [6,26]. Bronchoscopic unilateral-directed BAL directed at the site of pneumonia suspected radiographically therefore results in missed diagnoses of VAP, as well as potentially incomplete antibiotic therapy. This is evident when looking at the breakdown of positive bilateral BAL culture results in our study showing 16 of the 62 positive cultures having only one side positive with an additional 7 cases resulting in different bacteria isolated from either side. Unilateral sampling via noninvasive technique likely results in similar decreases in accuracy and inappropriate therapy. Additionally, bilateral BAL in our study resulted in a higher percentage of monomicrobial growth, likely reflecting more accurate diagnosis than unilateral BAL.

Clinical indicators and scores are notoriously poor predictors of a positive VAP diagnosis in trauma patients [5]. In our study, we demonstrated that in regard to CXRs, the presence of an infiltrate did not predict a positive BAL culture; on the other hand, the absence of infiltrate did not predict a negative BAL culture. This lack of predictive value is likely attributable to the presence of pulmonary contusion in trauma patients, as well as the systemic inflammatory response to trauma that can result in indirect pulmonary inflammation. The other clinical parameter investigated in this study, WBC, also was shown to have no predictive value for the diagnosis of VAP. Again, the systemic inflammatory response to trauma can result in elevated WBC, and the presence of other infectious or inflammatory events can cloud the picture further [27].

Finally, we confirmed the results of several previous studies illustrating that the causative organisms of VAP shift from predominantly gram-positive to gram-negative bacteria as the duration of ventilation increases [28,29].

There are several limiting factors to our study. We did not measure duration of ventilation or VAP resolution for these

patients and do not know if the increased sensitivity of bilateral BAL resulted in a decrease in morbidity, antibiotic use, or pneumonia recurrence. Additionally, we used fever, leukocytosis, and absence of another obvious infection site as clinical indicators of potential pneumonia. Finally, only one staff member performed unilateral-directed BAL, whereas the other trauma staff performed the bilateral BALs. This may have resulted in differences in technique affecting our results. However, the importance in our results rests in the differences between sides in the bilateral BAL group and the potential for missed or inaccurate BAL cultures.

Whereas no gold standard for the diagnosis of VAP has been established, invasive sampling of the lower respiratory tract under conditions of suspected VAP is considered the most sensitive and specific [30–32]. A BAL is a common invasive modality associated with a low rate of complications. Despite the retrospective data in this study of critically ill trauma patients, we contend that bilateral BAL sampling results in a higher diagnostic accuracy than unilateral sampling when using BAL as a tool to institute or avoid antibiotic treatment. We agree with others that classical clinical criteria of chest radiography, fever, and WBC count are less desirable. Unilateral BAL directed at the site of suspected pneumonia as well as diagnostic modalities fail to sample both lungs and are therefore likely less to be accurate for this patient population. These results and recommendations may be applicable to other critically ill ventilated patients as well.

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