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Triggering receptors expressed on myeloid cells in pulmonary aspiration syndromes

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Abstract *Objective:* To investigate the potential role of serum and alveolar soluble triggering receptor expressed on myeloid cells (sTREM-1) as a biological marker of pulmonary aspiration syndromes. *Design:* Prospective cohort study. *Setting:* University-affiliated intensive care unit. *Patients:* Seventy-five patients with pulmonary aspiration and 13 controls receiving mechanical ventilation. *Interventions:* Blood and bronchoalveolar lavage (BAL) fluid samples were collected on enrollment. Soluble TREM-1 levels were measured by an enzyme-linked immunosorbent assay. *Measurements and results:* Thirty-eight of 75 participants had documented BAL culture-positive pulmonary aspiration. While circulating levels of sTREM-1 were comparable between those with aspiration syndromes (19.81 ± 12.09 pg/ml) and controls (15.96 ± 11.16 pg/ml) ($p = 0.27$), the alveolar levels of sTREM-1 were higher in patients with culture-positive pulmonary aspiration (344.41 ± 152.82 pg/ml) compared with those culture-negative pulmonary aspiration (142.76 ± 89.88 pg/ml; $p < 0.001$). A cut-off value of 250 pg/ml for alveolar sTREM-1 achieved a sensitivity of 65.8% (95% CI 48.6–80.4) and a specificity of 91.9% (95% CI 78.1–98.2) with an area under the curve of 0.87 (95% CI 0.78–0.94). *Conclusions:* Alveolar sTREM-1 levels can be a potential biomarker for distinguishing BAL culture-positive from BAL culture-negative pulmonary aspiration.

Keywords Aspiration · Pneumonia · sTREM-1 · Bronchoalveolar lavage

Introduction

Pulmonary aspiration is characterized by a constellation of clinical syndromes that develop following inhalation of gastric and oropharyngeal contents into the lower respiratory tract. The term "aspiration pneumonia" has been used to refer to aspiration of oropharyngeal contents into the lung with a resultant bacterial pneumonia, whereas "aspiration pneumonitis" denotes acute lung injury following the inhalation of regurgitated sterile gastric contents [1]. Both conditions are associated with tachypnea, fever, hypoxemia, and radiographic changes on presentation. In the absence of an accurate and a valid marker to distinguish these two entities, the majority of patients with the diagnosis of pulmonary aspiration receive antimicrobial therapy when treatment is indicated only for those with infectious pneumonitis. The pervasiveness of such a practice has contributed at least in part to the increased prevalence of an-

timicrobial resistance in intensive care units and superinfection with multiresistant bacteria [2].

A novel approach to guide antimicrobial therapy is to prescribe antibiotics based on the level of biological markers. Recently, a new family of receptors expressed on myeloid cells [the triggering receptor expressed on myeloid cells (TREM)] has been identified on both human and murine polymorphonuclear neutrophils and mature monocytes [3, 4]. The TREM family members share low sequence homology to each other or to other immunoglobulin superfamily members and are characterized by the presence of a single immunoglobulin-like domain. The cellular expression of TREM-1 is up-regulated following Toll-like receptor activation, with an accompanying increased production of the pro-inflammatory cytokines TNF-α and granulocyte-macrophage colony-stimulating factor [5]. By contrast, TREM-1 is not expressed in samples from patients with noninfectious inflammatory disorders such as psoriasis, ulcerative colitis, or vasculitis caused by immune complexes [5].

Contemporary studies suggest that sTREM-1 in bronchoalveolar lavage [6] and plasma [7, 8] may perform better than CRP and PCT for discriminating between infection and noninfectious conditions. However there are relatively few data available on these markers in patients with aspiration syndromes; therefore, we investigated the utility of plasma and bronchoalveolar levels of sTREM-1 to differentiate between aspiration pneumonia and aspiration pneumonitis.

Methods

Study population

All patients being admitted from the emergency room to the intensive care unit (ICU) between October 2003 and March 2006 with the diagnosis of pulmonary aspiration were considered for enrollment. Some of the patients were part of a previous investigation [9]. The institutional review board approved the study and informed consent was obtained from all participants or their heath care proxy. The inclusion criteria for severe aspiration consisted of all the following criteria: (a) symptoms and signs suggestive of lower respiratory tract pathology (dyspnea, cough, tachypnea, sputum production, or increased alveolar arterial gradient) following a witnessed aspiration; (b) the presence of new radiographic infiltrate; and (c) the need for mechanical ventilation. Patients with severe immunosuppression (solid organ transplantation, steroid therapy of 20 mg/day or more for more than 2 weeks, known HIV, or AIDS-defining criteria), nosocomial aspiration, or who had received antimicrobial therapy within the previous 30 days were excluded. A control group of patients who were intubated for airway protection on hospital admission were also studied. Patients with more than one admission were included only once to ensure independence of observations.

Data collection

Demographic data collected included age, gender, comorbid illnesses, and the Charlson index [10]. Clinical data were obtained on ICU admission and comprised clinical symptoms, daily vital signs, laboratory and radiographic data, and the Acute Physiology and Chronic Health Evaluation (APACHE II) score [11]. Chest radiographs were interpreted by the two critical care specialists. Any discrepancy was resolved by consensus. Furthermore, participants were classified based on clinical history into two groups by a health care practitioner blinded to the objectives of the study: aspiration pneumonitis defined as a chemical lung injury resulting from regurgitated gastric contents secondary to decreased level of consciousness (drug overdose, seizure, alcoholic intoxication, or post anesthesia); and aspiration pneumonia defined as the development of new radiographic findings in patients who are at increased risk for oropharyngeal aspiration (neurologic dysphagia, anatomical abnormalities of the upper aerodigestive tract, or disruption of the gastroesophageal junction) [1].

Samples collection

After enrollment, whole-blood C-reactive protein levels were determined using the NycoCard II test kit (Axis-Shield, Oslo, Norway). A fiberoptic bronchoscopy was performed within the first 6 h of presentation prior to antibiotic administration. A soft 13-F-gauge double-sheathed protected catheter (Combicath, Saint-Leu-La-Foret, France) was advanced through the channel of the bronchoscope into a wedged position in a distal bronchus corresponding to the infiltrate on chest X-ray. Distal airways fluid was collected in a suction trap by gentle suction. A standard protected bronchoalveolar lavage was then performed after removal of the inner catheter using three aliquots of 10-ml sterile isotonic saline each. Bronchoalveolar specimens were collected in BD Port-A-Cul (Sparks, Md.) vials and were hand delivered to the microbiology laboratory and processed within 15 min of sampling.

Microbiology

Undiluted and serially diluted samples were plated onto 5% sheep's blood, chocolate, CDC, charcoal-yeast extract agar, and Sabouraud agar. Anaerobic cultures were performed in an anaerobic chamber (Coy Laboratory, Grass Lake, Mich.) fitted with an automatic gas injection system to maintain a constant level of hydrogen gas mix. All cultures were incubated at 37°C under aerobic and

Table 1 Demographics characteristics of the study population

	Pulmonary aspiration ($n = 75$)	Control ($n = 13$)	Significance (p)
Age (years)	57.7 ± 12.6	57.2 ± 15.6	0.6
Gender (F/M)	43/32	7/6	0.9
Nursing home residents	19	2	0.7
Charlson index			0.1
0	17	7	
1–2	36	4	
3–4	18	2	
≥ 5	4	0	
Predisposing factors			
Cerebrovascular accident	23	3	
Neurodegenerative diseases	17	0	
Esophageal dysmotility	2	0	
Drug overdose	25	7	
Seizures	4	1	
Others	4	2	

anaerobic conditions and in CO2-enriched atmosphere. Cultures were evaluated for growth 24, 48, and 72 h later and discarded after 5 days, except for Sabouraud dextrose, which was evaluated at 4 weeks. Plates were assessed for bacterial and fungal growth. The calibrated loop method was used for quantitative culture. All bacterial species isolated by quantitative cultures were identified by standard microbiologic technique. Results of quantitative cultures were expressed as colony-forming units per milliliter (CFU/ml). Infectious etiology of pneumonia was established for a threshold of 10^4 CFU/ml of at least one pathogen for protected BAL (PBAL). The microbiologists reading the Gram-stain slides were blind to the aim of the study during the study period in order to reproduce the conditions of routine practice.

Measurement of plasma and BAL sTREM-1

Levels of sTREM-1 were determined by enzyme-linked immunosorbent assay, as described previously [12]. Capture antibody of sTREM-1 (R&D, Minneapolis, Minn.) was diluted to 4000 mg/l and distributed in a 96-well plate at a volume of 0.1 ml per well. After overnight incubation, wells were thoroughly washed with a 0.5-g/l solution of Tween in PBS (Merck; pH: 7.2–7.4). Then 0.1 ml of standard concentrations of sTREM-1 (15.1–4000 ng/l; R&D, Minneapolis, Minn.) diluted with reagent diluent (10 g/l BSA in PBS, pH 7.2–7.4, 0.2-μm filtered) serving as a buffer or of serum was added in wells. After incubation for 2 h, wells were washed thrice, and 0.1 ml of one 400 ng/ml dilution of sTREM-1 detection antibody (R&D, Minneapolis, Minn.) was added per well. The plate was then incubated for 2 h, and attached antibodies were signalled by streptavidin. Concentrations of sTREM-1 in each well were estimated by the optical density detected at 450 nm after addition of one 1:1 solution of H_2O_2: tetramethylbenzidine as a substrate (R&D, Minneapolis, Minn.). sTREM-1 concentration was expressed in pg/l. All determinations were performed in duplicate; the inter-day variation of the assay was 5.23%. The lower detection limit was defined by $2 \times$ SD of the blank values (2 pg/ml). Laboratory technicians were unaware of patients' admitting diagnosis or classification.

Statistical analysis

Results were expressed as means $\pm$ SD. Means were compared using Student's t-test for normally distributed variables and the Mann–Whitney test was used otherwise. Proportions were compared using the chi-square test with Yates correction or Fisher's exact test when necessary. Correlation was assessed using Spearman's rank test. Sensitivity, specificity, positive predictive values, and negative predictive values were computed according to standard values. A receiver operator characteristics (ROC) curve was displayed to assess the accuracy of the predictive model. The area under the curve was calculated using the c-index as described previously [13]. All reported p-values are two-tailed. The level of significance was set at 5%.

Table 2 Microbial etiology of pulmonary aspiration

Genus	Number
Streptococcus pneumoniae	1
Staphylococcus aureus	6
Streptococcus sp.	6
Hemophilus influenzae	2
Serratia sp.	2
Escherichia coli	8
Klebsiella pneumoniae	3
Enterobacter sp.	3
Proteus mirabilis	1
Bacteroides fragilis	1
Prevotella species	5
Fusobacterium sp.	1
Peptostreptococcus sp.	4

Results

During the study period, seventy-five patients met the inclusion criteria for enrollment. Twenty-nine patients were excluded because of prior antibiotic treatment. Thirteen patients served as controls. Characteristics of the study population are shown in Table 1. Patients with pulmonary aspiration were comparable in age, gender, and underlying

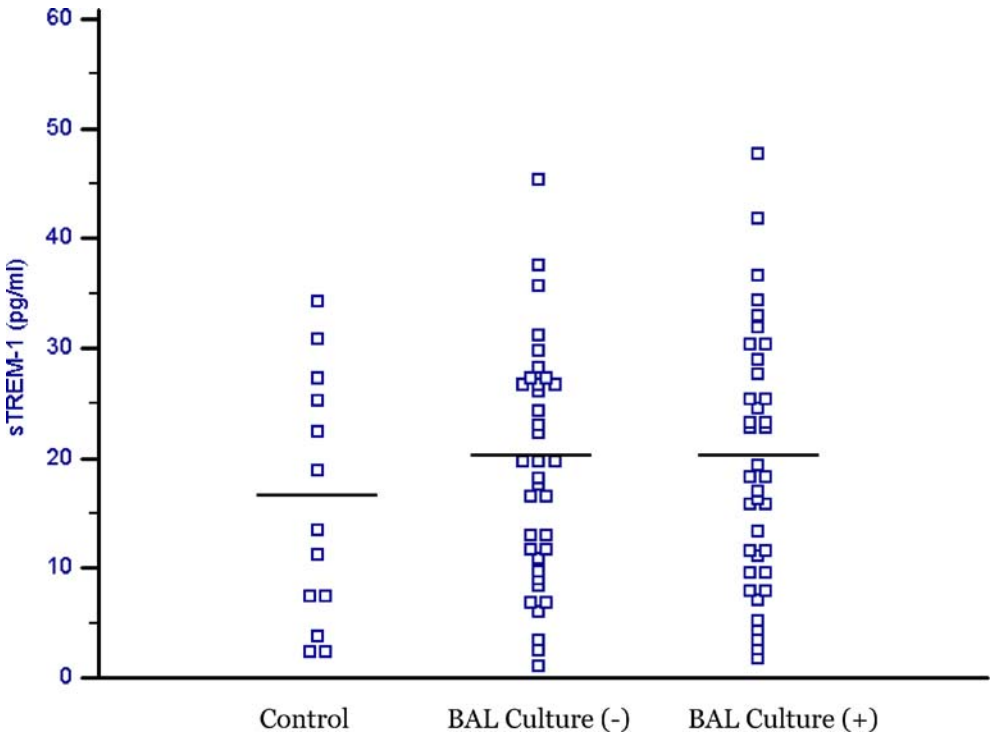

Fig. 1 Plasma levels of sTREM-1 measured in 38 patients with BAL culture-positive pulmonary aspiration, 37 patients with BAL culture-negative pulmonary aspiration, and 13 controls. *Horizontal bars* represent the mean values of sTREM-1

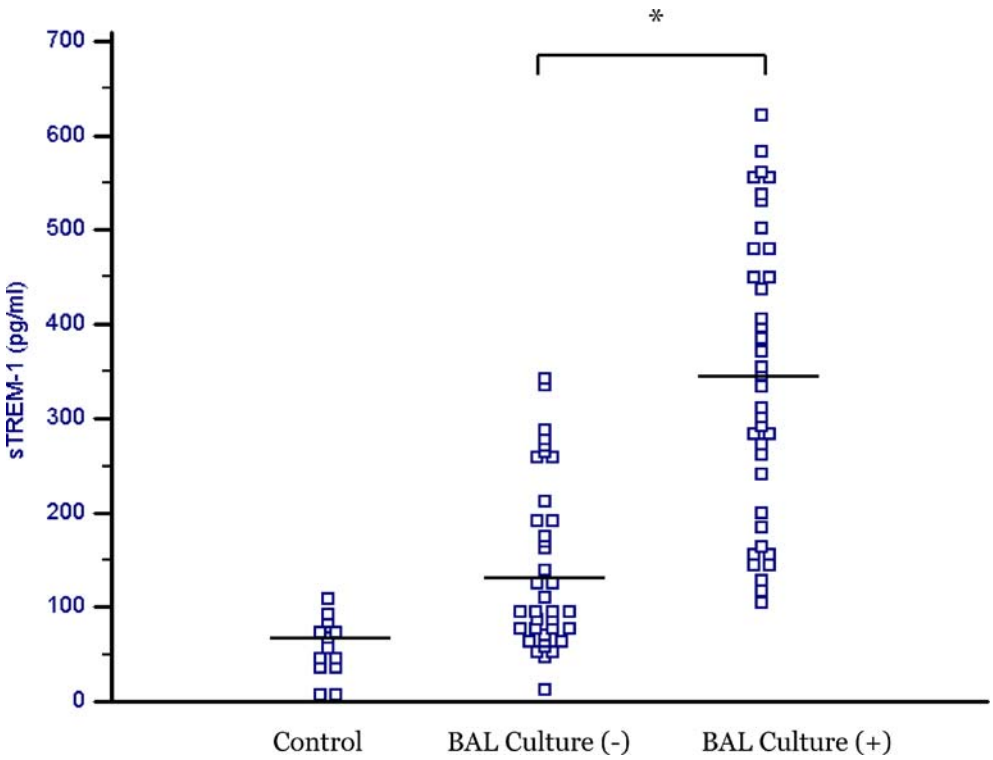

Fig. 2 Alveolar levels of sTREM-1 measured in 38 patients with BAL culture-positive pulmonary aspiration, 37 patients with BAL culture-negative pulmonary aspiration, and 13 controls. *Horizontal bars* represent the mean values of sTREM-1. *Asterisk* indicates statistical significance

comorbidities compared with the control group. Drug overdose (33%), cerebrovascular accidents (31%), and neurodegenerative diseases (23%) accounted for the majority of the underlying causes of pulmonary aspiration.

An infectious etiology for pulmonary aspiration was documented in 38 (51%) of the 75 patients. Overall, 43 organisms were isolated from cultures of the bronchial samplings (Table 2). Gram-negative enteric bacilli (40%) accounted for the predominant organisms followed by anaerobic bacteria (26%), streptococcal species (14%), and *Staphylococcus aureus* (14%). Three patients had polymicrobial infections: *Enterobacter cloacae* and *Bacteroides fragilis*; *Escherichia coli* and *Fusobacterium* sp; and *Escherichia coli, Enterobacter cloacae*, and *Peptostreptococcus* sp.

Comparison of clinical and radiographic presentations of patients with and without documented bacterial infections is summarized in Table 3. There was no significant difference between the two groups in terms of body temperature, leukocyte counts, and degree of hypoxemia. Although bilateral interstitial infiltrates were more notably observed in those with negative BAL cultures, there was no specific radiographic pattern that would indicate the presence of a lower respiratory tract infection.

Bacteria on Gram staining were identified in 29 of the 38 patients with culture-positive pulmonary aspiration and in 11 of the 37 patients with culture negative ($p < 0.001$). When comparing the final diagnosis with the presence or absence of bacteria on Gram stain, sensitivity, specificity, positive predictive values, and negative predictive values were, respectively, 87, 81, 83, and 86%, respectively. When assessing the degree of qualitative agreement (congruent or incongruent) between Gram stain and

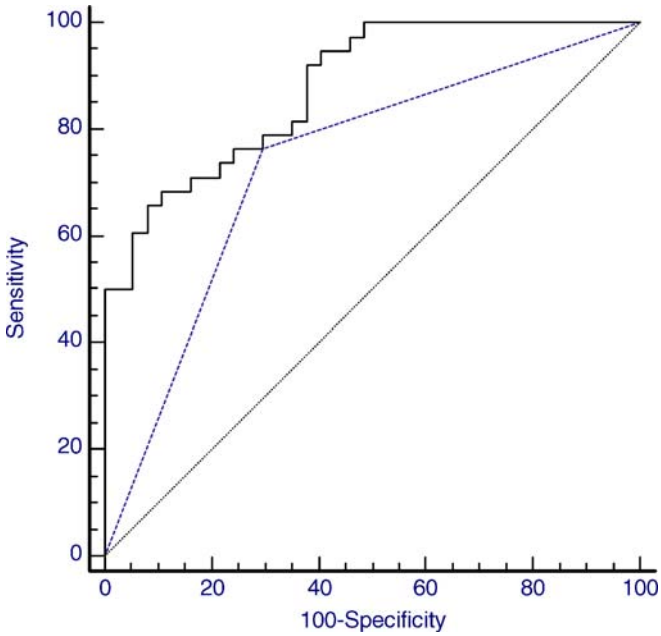

Fig. 4 Comparison of receiver operator characteristics curves for various cut-offs of bronchoalveolar lavage sTREM-1 values [*continuous line*; area under the curve (AUC) = 0.87] and bronchoalveolar lavage Gram stain (*dotted line*; AUC = 0.73)

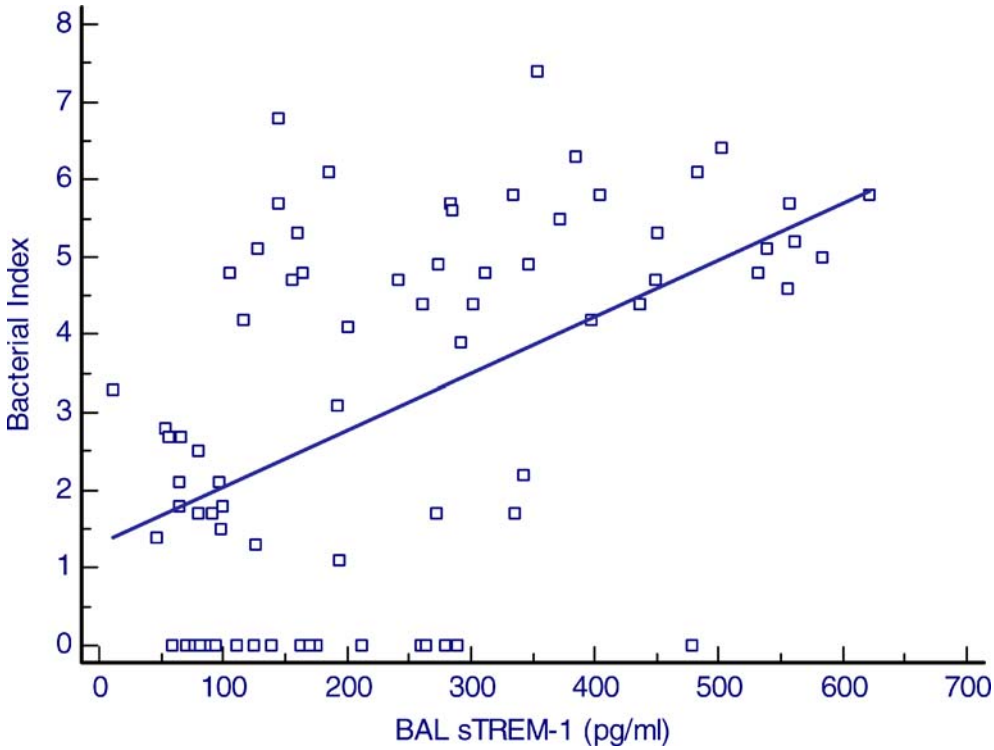

Fig. 3 Scatter plot between the bacterial index ($\log_{10}$CFU/ml) and the bronchoalveolar lavage sTREM-1 levels ($r = 0.51$; $p < 0.001$)

quantitative cultures, the correlation was congruent in 63% (47 of 75) and incongruent in 37% (28 of 75).

Although C-reactive protein levels were significantly greater among patients with pulmonary aspiration (84 ± 39 mg/l for culture-positive pulmonary aspiration and 77 ± 34 mg/l for culture-negative pulmonary aspiration) when compared with controls (24 ± 36 mg/l; $p < 0.001$), these levels were comparable between the pulmonary aspiration groups irrespective of the BAL cultures ($p = 0.32$).

Using clinical history to define pulmonary aspiration, an infectious etiology for pulmonary aspiration was present in 31 (69%) of the 45 patients admitted with aspiration pneumonia while 7 (23%) of the 30 patients with aspiration pneumonitis had a potential pathogen isolated from the lower respiratory tract.

sTREM-1 values in plasma and BAL fluid

The levels of circulating sTREM-1 were comparable between the control group (15.96 ± 11.16 pg/ml) and those with culture-positive pulmonary aspiration (19.91 ± 12.03 pg/ml) and culture-negative pulmonary aspiration (19.46 ± 11.47 pg/ml; $p = 0.23$ and $p = 0.44$, respectively; Fig. 1). In contrast, the levels of sTREM-1 were higher in bronchoalveolar lavage fluid from patients with culture-positive pulmonary aspiration (344.41 ± 152.82 pg/ml) and culture-negative pulmonary aspiration (142.76 ± 89.88 pg/ml) compared with controls (57.13 ± 30.28 pg/ml; $p < 0.001$ for both; Fig. 2). More importantly, the levels for BAL sTREM-1 were significantly higher in patients with culture-positive pulmonary aspiration than those with culture-negative pulmonary aspiration ($p < 0.001$). For those patients classified as aspiration pneumonia, BAL sTREM-1 levels were also elevated compared with the BAL sTREM-1 levels of patients with aspiration pneumonitis (296.0 ± 165.38 vs. 148.35 ± 107.54 pg/ml, respectively; $p < 0.001$). There was no correlation between the severity of hypoxemia and BAL sTREM-1 levels or between the bacterial species and BAL sTREM-1 levels; however, a significant association was observed between microbial density expressed as bacterial index ($\log_{10}$, CFU/ml) and the levels of BAL sTREM-1 ($r = 0.51$; $p < 0.001$; Fig. 3).

The predictive ability of BAL sTREM-1 to differentiate between culture-positive pulmonary aspiration and culture-negative pulmonary aspiration was assessed using the ROC curve. The areas under the ROC curves for alveolar sTREM-1 and BAL Gram stain were, respectively,

Table 3 Clinical characteristics of patients with pulmonary aspiration. *APACHE*, Acute Physiologic and Clinical Health Evaluation; *EA*, endotracheal aspirates; *PBAL*, protected bronchoalveolar lavage

	BAL (+) culture ($n = 38$)	BAL (–) culture ($n = 37$)	Significance (p)
Glasgow Coma Scale	9.4 ± 2.3	8.1 ± 2.5	0.03
Body temperature (°F)	99.1 ± 4.3	98.9 ± 3.4	0.78
Blood leukocytes count (mm^{-3})	16.4 ± 7.4	15.8 ± 4.9	0.65
PAO_2/FIO_2 (mmHg)	212.1 ± 54.1	220.4 ± 70.2	0.58
APACHE II score	28.5 ± 4.6	27.2 ± 6.6	0.33
Radiographic pattern			0.13
Unilobar infiltrate	22 (58)	14 (38)	
Mulitlobar infiltrate	16 (42)	23 (62)	
EA Gram stain (+)	33 (87)	22 (59)	0.02
PBAL Gram stain (+)	29 (76)	11 (29)	< 0.001
CRP (mg/l)	84 ± 39	77 ± 34	0.32
Duration of MV	8.2 ± 6.7	6.4 ± 4.8	0.02
ICU length of stay	12.1 ± 9.2	7.9 ± 5.6	0.04
Mortality rate	35%	14%	0.07

Table 4 Clinical characteristics of patients based on BAL sTREM-1 threshold

	sTREM-1 ≤ 250 ($n = 40$)	sTREM-1 > 250 ($n = 35$)	Significance (p)
Glasgow Coma Scale	8.2 ± 2.4	8.9 ± 2.8	0.25
Body temperature (°F)	98.2 ± 4.6	99.6 ± 3.1	0.12
Blood leukocytes count (mm^{-3})	15.8 ± 7.0	16.4 ± 5.6	0.73
PAO_2/FIO_2 (mmHg)	221.0 ± 63.6	212.3 ± 57.4	0.54
APACHE II score	26.4 ± 5.6	29.5 ± 5.4	0.08
Radiographic pattern			0.72
Unilobar infiltrate	16 (40)	20 (57)	
Multilobar infiltrate	24 (60)	15 (43)	
CRP (mg/l)	74 ± 31	86 ± 42	0.18
Duration of MV	6.8 ± 5.0	8.0 ± 6.3	0.06
ICU length of stay	8.3 ± 5.9	11.6 ± 8.7	0.09
Mortality rate	18%	31%	0.3

0.87 (95% CI 0.78–0.94) and 0.73 (95% CI 0.62–0.83; $p = 0.034$; Fig. 4). Using a cut-off value of 250 pg/ml, the sTREM-1 achieved a sensitivity of 65.8% (95% CI 48.6–80.4) and a specificity of 91.9% (95% CI 78.1–98.2). In comparison, the AUC for the plasma sTREM-1 was 0.51 (95% CI 0.39–0.62; $p < 0.001$). We should note that the accuracy of the endotracheal aspirate Gram stain was significantly lower than the BAL Gram stain in determining culture-positive pulmonary aspiration. Although the endotracheal Gram stain achieved a sensitivity of 94.7% (95% CI 82.2–99.2), the specificity was only 24.3% (95% CI 11.8–41.2) with an AUC of 0.59.

Outcome

The crude mortality rate of pulmonary aspiration in patients with positive BAL cultures was higher than those with BAL-negative (35 vs. 14%) cultures, although the difference did not reach statistical significance ($p = 0.07$). The duration of mechanical ventilation and ICU length of stay were, however, significantly longer for those with positive BAL cultures (Table 3) than their counterparts. When the study population was categorized according to sTREM-1 levels (Table 4), we were unable to delineate any clinical characteristics or outcome that would separate those with sTREM-1 $\leq$250 pg/ml from those with BAL sTREM-1 $>$250 pg/ml.

Discussion

The ability to distinguish aspiration pneumonia from aspiration pneumonitis remains one of the most difficult challenges in the care of patients with aspiration syndromes. Established clinical criteria with new or progressive infiltrates on chest radiography, fever, leukocytosis or leukopenia are of limited diagnostic value in differentiating these two entities. The new finding of this study highlights the fact that measuring levels of sTREM-1 in bronchoalveolar fluid might be a useful biological marker to identify BAL culture-positive pulmonary aspiration.

Over the past few years, there have been several attempts to establish criteria that would distinguish aspiration pneumonia from aspiration pneumonitis, but none of the proposed models has been proven to be highly accurate. Based on a cohort of hospitalized nursing home patients, Mylotte and colleagues [14] developed an algorithm aimed at assisting health care providers in the management of aspiration syndromes. The model relied on two clinical criteria: a history of gastric aspiration and presence of radiographic infiltrate. Although the model was validated subsequently in a separate group of patients [15], the study had several limitations that would seriously limit its reproducibility. In contrast to our study, where an aggressive approach for identifying offending pathogens was performed, the etiologic diagnosis in the studies by Mylotte and coworkers [14, 15] was not established; thus, cases of aspiration pneumonia could be easily misclassified as aspiration pneumonitis. Moreover, 23% of patients with aspiration pneumonitis in our series had evidence of bacterial infection that would have been missed if clinical criteria were the sole discriminating factor.

Several biological markers have been introduced recently in an effort to improve the diagnostic accuracy of infectious pneumonitis such as C-reactive protein, procalcitonin, proinflammatory markers, and sTREM-1 with varying degrees of accuracy. In our investigation, we did not find any association between initial plasma C-reactive protein levels and severity of illness or the type of aspiration syndromes irrespective of the BAL cultures. Previous investigators have also shown that C-reactive protein values did not correlate well with severity of illness [16], as these scores are weighted heavily by age and serve primarily to predict mortality. Similarly, levels of C-reactive protein were comparable between patients suspected of aspiration pneumonia and aspiration pneumonitis [15]. Because C-reactive protein is a nonspecific marker of inflammation rather than infection, it was not surprising to note that it provided no potential role in the delineation of pulmonary aspiration syndromes.

Recently, the diagnostic value of sTREM-1 has been demonstrated both in pneumonia [6] and sepsis [8]. The presence of sTREM-1 in the bronchoalveolar lavage fluid was more accurate than any clinical findings or laboratory values including the clinical pulmonary infection score and procalcitonin in identifying the presence of bacterial pneumonia (likelihood ratio, 10.4; sensitivity, 98%; specificity, 90%). When sTREM-1 was used to differentiate the presence of pneumonia from its absence, the area under the ROC curve was 0.93. Using a similar approach, two other studies [12, 17] have confirmed the role of alveolar sTREM-1 as a reliable marker of pneumonia and especially VAP, but its sensitivity is not 100% and some false-negative results can be observed, as with other biologic markers of bacterial infection. Our study extends these findings to the syndromes of pulmonary aspiration by demonstrating elevated alveolar levels of sTREM-1 levels in patients with BAL culture-positive compared with cases with BAL culture-negative pulmonary aspiration. One notable observation is the lower sensitivity of sTREM-1 determination compared with the study by Gibot and colleagues [6]. This could be attributed to data homogeneity reflected in our inclusion criteria, which were limited to patients with witnessed pulmonary aspiration while excluding ventilator and nosocomial pneumonia. Another possibility would be a variance in the type and source of antigen standards used to measure BAL sTREM-1. Notwithstanding this, BAL sTREM-1 provided a higher accuracy than available markers for detection of pulmonary aspiration [18].

Our findings do not support the use of plasma levels of sTREM-1 in the management of the pulmonary aspiration syndromes. These findings are corroborated by a recent study of patients with ventilator-associated pneumonia where plasma levels did not differ significantly from controls at study entry or during the course of the study [12]. The fact that circulating levels of sTREM-1 levels were lower than those in the alveolar fluid obtained from patients with pulmonary aspiration argues against the possibility that increased levels in the lung compartment stem from increased permeability of the alveolocapillary membrane. We should indicate that we did not obtain serial plasma levels on our patients and thus we cannot exclude the possibility that plasma levels might rise on subsequent days due to acute lung injury or superimposed nosocomial infection.

Our study has several limitations. It was conducted at a single large academic medical center with enrollment criteria strictly limited to pretreated patients, and therefore our results may not apply to other clinical settings. But unlike the etiology of nosocomial pneumonia, where the predominance of pathogens can vary between and within the same institution, the microbiology of pulmonary aspiration reflects an endogenous infection and thus a predictable one. Secondly, the sTREM-1 assay does not determine the causative organism and thus should not preclude the clinician from performing microbiological studies when possible. Thirdly, it is plausible that elevation of alveolar sTREM-1 might have preceded the detection of bacterial load in the significant range resulting in decreased sTREM-1 specificity. Fourthly, the classification of aspiration syndromes into aspiration pneumonia and aspiration pneumonitis is arbitrary and based on expert opinion, and there is every reason to believe that both entities are not mutually exclusive; however, this is the first study, to our knowledge, to validate these definitions by obtaining cultures of the lower respiratory tract.

Conclusion

In conclusion, our results suggest that alveolar sTREM-1 may be useful in separating infectious from noninfectious pulmonary aspiration. Although very promising, the usefulness of measuring sTREM-1 in clinical practice has to be determined prospectively in dedicated studies.

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