Title
Clinical Evidence of Early Acute Lung Injury Often Precedes the Diagnosis of ALI

Journal
Journal of Intensive Care Medicine, 28(4)

ISSN
0885-0666

Authors
Rackley, Craig R
Levitt, Joseph E
Zhuo, Hanjing
et al.

Publication Date
2013-07-01

DOI
10.1177/0885066612450850

Peer reviewed

Published in final edited form as:
J Intensive Care Med. 2013 ; 28(4): 241–246. doi:10.1177/0885066612450850.

Clinical Evidence of Early Acute Lung Injury Often Precedes the Diagnosis of ALI

Craig R. Rackley, MD[1,2], **Joseph E. Levitt, MD, MS**[3], **Hanjing Zhuo, MPH**[4], **Michael A. Matthay, MD**[5], and **Carolyn S. Calfee, MD, MAS**[6]

[1]Department of Medicine, UCSF, San Francisco, CA

[2]Division of Pulmonary, Allergy, and Critical Care, Duke University Medical Center, Durham, NC

[3]Division of Pulmonary/Critical Care, Stanford University, Stanford, CA, USA

[4]Cardiovascular Research Institute, UCSF, San Francisco, CA

[5]Departments of Medicine and Anesthesia and Cardiovascular Research Institute, UCSF, San Francisco, CA

[6]Departments of Medicine and Anesthesia, UCSF, San Francisco, CA

Abstract

Background—Acute lung injury (ALI) has been primarily defined in patients who require positive pressure ventilation. As a result, the clinical characteristics of patients with early ALI (EALI) prior to the need for mechanical ventilation have not been well characterized. Early identification of patients with ALI and the impending need for positive pressure ventilation could define a study population for trials of novel therapies.

Methods—We analyzed clinical data from 93 patients at 12, 24, and 48 hours prior to the standard diagnosis of ALI. The time of ALI diagnosis was defined when patients were mechanically ventilated and met the 1994 American–European Consensus Conference diagnostic criteria for ALI.

Results—The majority of patients with ALI presented to the hospital more than 24 hours prior to developing ALI. Specifically, 73% presented more than 12 hours prior to diagnosis, and 57% presented more than 24 hours prior to diagnosis. Of patients hospitalized for at least 12 hours prior to ALI diagnosis, 94% had either bilateral infiltrates on chest radiograph, tachypnea, or an oxygen requirement greater than 2 L/min; 79% and 48% had 2 and 3 of these abnormalities, respectively.

Conclusion—The majority of hospitalized patients who are destined to develop ALI demonstrate tachypnea, increased oxygen requirements, and/or bilateral infiltrates on chest radiograph more than 12 hours prior to meeting criteria for diagnosis. Some patients with EALI may be identified prior to meeting diagnostic criteria during a potential therapeutic window.

Corresponding Author: Carolyn S. Calfee, Pulmonary and Critical Care Division, University of California, San Francisco, 505 Parnassus Avenue, Box 0111, San Francisco, CA 94143-0111, USA, carolyn.calfee@ucsf.edu.

Declaration of Conflicting Interests

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Dr Calfee has served on medical advisory boards for Glaxo Smith Kline and Ikaria

Keywords

early acute lung injury; acute respiratory distress syndrome; diagnosis

Introduction

Acute lung injury (ALI) was defined by the American–European Consensus Conference (AECC) in 1994 as the acute onset of hypoxemia (partial pressure of arterial oxygen [PaO_2]/fraction of inspired oxygen [FiO_2] of ≤300) and bilateral infiltrates on chest radiograph without the evidence of left atrial hypertension. Acute respiratory distress syndrome (ARDS) is a more severe form of ALI with a PaO_2/FiO_2 ratio of ≤200.[1] These definitions have subsequently been used to identify patients for clinical trials of therapeutic interventions in the treatment of ALI/ARDS. The diagnostic criteria for ALI/ARDS have been interpreted as requiring a closed ventilatory system for accurate FiO_2 measurements and an arterial blood gas for accurate PaO_2 measurements. As a consequence, most clinical trials in ALI/ARDS over the past 10 years have enrolled only mechanically ventilated patients.[2–10]

Although the consensus definition of ALI/ARDS implies the requirement for positive pressure ventilation, the pathologic processes responsible for ALI clearly predate the development of frank respiratory failure. Identification of patients with incipient ALI may provide a therapeutic window during which preventative interventions could be applied and could be helpful in the design of future clinical trials. Ferguson et al attempted to identify patients with early ALI (EALI) by studying patients with clinical conditions previously linked to ALI such as sepsis, pneumonia, and trauma; however, only 6.5% of patients with these predisposing conditions went on to develop ALI.[11] In another recently published cohort of patients admitted with predisposing conditions for ALI, only 6.8% went on to develop ALI.[12]

We reported that 33% of patients identified in the emergency department with acute bilateral opacities on chest radiograph went onto develop ALI requiring mechanical ventilation.[13] In this cohort, we defined EALI as acute bilateral radiographic abnormalities not exclusively due to heart failure and an oxygen requirement of more than 2 L/min. These criteria were 73% sensitive and 79% specific for predicting progression to ALI. However, what remains unknown is how many patients with ALI initially meet criteria for EALI and, more broadly, what fraction of patients with ALI could be detected earlier in their clinical course.

Our objectives were to study a cohort of patients with ALI enrolled at a single tertiary care medical center in order to (1) determine the time course of the appearance of physiologic or radiographic abnormalities prior to meeting diagnostic criteria for ALI and (2) determine which of these patients meet criteria for EALI at some point preceding their ALI diagnosis. In addition, we sought to determine whether particular patient characteristics were associated with the tempo of progression to ALI with frank respiratory failure.

Methods

Study Population

Data were obtained from patients who met the AECC diagnostic criteria for ALI[1] within 48 hours of being treated with mechanical ventilation and were prospectively enrolled in an observational cohort at a single academic medical center in San Francisco, CA, over a 5-year period from 2003 to 2008. Exclusion criteria included age less than 18 years, pregnancy, severe chronic lung disease, congestive heart failure, or a myocardial infarction

or pulmonary embolism within 30 days prior to enrollment. We excluded patients who developed ALI more than 48 hours after endotracheal intubation, since 1 of the objectives of the study was to identify early predictors of progression to ALI prior to intubation. The study protocol was approved by the University of California, San Francisco Institutional Review Board (CHR# H2811-31929), and all participants or their surrogates provided informed consent.

Data Collection

Data on demographic characteristics, comorbidities, diagnosis, and physiologic data were collected at the time of study enrollment. Data were retrospectively collected on respiratory rate, oxygen requirements, and chest radiographs for up to 72 hours prior to meeting formal diagnostic criteria for ALI. Additionally, we collected microbiologic and transfusion data for each patient during the 72 hours prior to diagnosis.

Respiratory rate and oxygen requirement data were taken from the patients' charts, and the highest value in each time interval (12–24, 24–48, and 48–72 hours prior to diagnosis of ALI) was recorded. Oxygen requirements were classified dichotomously as either ≤2 or >2 L/min, based on prior work by our group showing that this cutoff was predictive of the subsequent development of ALI.[13] Chest radiographs were reviewed by 2 experienced clinicians and qualified as having bilateral opacities if opacities were present bilaterally and were not thought to be solely due to atelectasis or effusions.

Statistical Analysis

Statistical analysis was performed using SAS 9.1 (Cary, NC). Categorical variables were analyzed by chi-square test. Continuous variables were analyzed by *t* tests for normally distributed data and Wilcoxon rank sum tests for nonnormally distributed data. Linear models were used to analyze the association of patient characteristics and clinical risk factor for ALI with tempo of development of ALI. Statistical significance for all variables was set at a *P* value of <.05.

Results

We identified 93 patients with ALI who met our inclusion criteria, and all these patients were included in the statistical analysis. Baseline characteristics of these patients are displayed in Table 1. Of note, the cohort was well balanced with respect to gender, racial, and ethnic diversity. No patients had trauma as a risk factor for ALI, as the university hospital from which this cohort was drawn is not a trauma center. Severity of disease was high, with a mean Acute Physiology And Chronic Health Evaluation II score of 23.5, and mortality in the cohort was 29%.

The majority of patients with ALI (73%) presented to the hospital at least 12 hours prior to diagnosis, and 57% presented more than 24 hours prior to diagnosis. However, a substantial fraction of patients (27%) either had ALI at the time of hospital presentation or developed ALI within 12 hours of arrival. Table 2 depicts the number of patients hospitalized at each time point during the 48 hours prior to diagnosis of ALI and the number of those patients with evidence of early respiratory insufficiency (bilateral infiltrates on chest radiograph, respiratory rate greater than 20, and/or greater than 2 L/min of oxygen requirement). At each time point, nearly half of patients who were hospitalized had all 3 clinical abnormalities, and only a small minority of patients had no clinical evidence of incipient ALI. In total, 66% of hospitalized patients who progressed to develop ALI had at least 2 of the 3 clinical abnormalities 48 hours prior to receiving mechanical ventilation and meeting the diagnostic criteria for ALI.

Figure 1 demonstrates the percentages of all patients with clinical abnormalities at each time point prior to diagnosis. Among hospitalized patients, an increased oxygen requirement and tachypnea were more prevalent at 12 hours prior to diagnosis than bilateral infiltrates on chest radiograph. Specifically, at 12 hours prior to diagnosis, 78% of hospitalized patients required more than 2 L/min of oxygen and 79% had respiratory rates recorded greater than 20, whereas only 64% had bilateral infiltrates. An elevated oxygen requirement was also the earliest abnormality to develop in hospitalized patients, with 73% of hospitalized patients requiring greater than 2 L/min of oxygen 48 hours prior to diagnosis compared to only 61% and 54% that had elevated respiratory rates or bilateral infiltrates on chest radiograph, respectively.

In our prior work, we found a median time from initial chest radiograph with bilateral infiltrates to progression to ALI was 22 hours (interquartile range [IQR] 10–43 hours).[13] In the current cohort, we found that the median time from the first qualifying chest radiograph to progression to ALI was 9.5 hours (IQR 0.2–32.7 hours) for all patients. In the subset of patients not intubated at the time they first had a qualifying chest radiograph (n =59), the median time to progression to ALI was 23 hours (IQR 5.8–78.4 hours), which corroborates our prior results.[13]

We also evaluated the number of patients who met EALI criteria (acute bilateral radiographic abnormalities not due exclusively to heart failure and an oxygen requirement of more than 2 L/min)[13] at each time point prior to diagnosis of ALI. Among patients who had presented to the hospital, EALI criteria were met by 59% at 12 hours, 51% at 24 hours, and 49% at 48 hours prior to diagnosis of ALI.

We tested a number of clinical characteristics to determine whether any were predictive of a rapid progression from initial presentation with a qualifying chest radiograph to diagnosis of ALI. In both unadjusted and multivariate analyses, sepsis as a clinical risk condition for ALI was associated with more rapid progression to ALI when compared to all other patients with ALI who did not have sepsis as their primary clinical risk condition for ALI (P =.02 in univariate model; P =.03 in multivariate model, Table 3). The median time elapsed between first abnormal chest radiograph and the diagnosis of ALI in patients with sepsis was 4.4 hours (IQR 0.1–13.0 hours). Pneumonia, aspiration, or other clinical risk conditions were not associated with a more rapid progression to ALI. Age was predictive of a slower progression to ALI with each additional year of age adding 1.5 hours to the time from initial qualifying chest radiograph to the diagnosis of ALI (P =.02). Other clinical characteristics including gender, race, ethnicity, use of alcohol, blood transfusions, presence of a chronic disease, and positive microbiologic cultures were not associated with the tempo of progression to ALI (Table 3).

Discussion

Most therapeutic interventions that initially demonstrated promise for the treatment of ALI/ARDS have not demonstrated a benefit in large clinical trials.[14,15] Patients in the very early stages of ALI before severe diffuse alveolar damage has occurred may derive more benefits from therapeutic interventions and may thus represent a promising target population for future clinical trials of novel therapies. We conducted a retrospective analysis of patients who ultimately developed ALI to determine whether they displayed early signs of ALI prior to meeting diagnostic criteria for ALI. We found that most patients with ALI presented at least 24 hours prior to diagnosis, and many patients had abnormalities associated with EALI as much as 48 hours prior to diagnosis, indicating that there is clearly a window of time prior to diagnosis in which many patients could potentially be identified and treated.

Overall, hypoxemia appears to be the earliest abnormal clinical parameter that we evaluated in the early identification of ALI. It would be expected that chest radiographs would lag behind hypoxemia in the early stages of ALI, and a slight increase in respiratory rate may not exceed the threshold of 20 breaths/min that we evaluated. Alternatively, respiratory rate may not always be recorded accurately in the medical record and thus may be a less sensitive indicator of early respiratory failure. Additionally, oxygen requirement is a parameter being measured several times per day in the hospital setting and, therefore, may reflect changes in status more acutely, whereas chest radiographs may only be obtained on admission and with a major change in clinical status.

We have previously described a clinical syndrome of EALI defined by hospital admission with bilateral opacities on the chest radiograph, the absence of clinical evidence of isolated left atrial hypertension, and the need for greater than 2 L/min of supplemental oxygen. Patients presenting to the emergency department with bilateral infiltrates on chest radiograph were followed to determine how many would develop ALI with the intention of defining a population with EALI.[13] Bilateral infiltrates on chest radiograph had a specificity of only 33% and an unknown sensitivity for predicting progression to ALI. Evaluating chest radiographs as the sole screening tool may be insufficient to detect the majority of patients with early evidence of ALI. In this study, we found that only 63% of hospitalized patients had bilateral infiltrates on the chest radiograph greater than 12 hours prior to diagnosis and only 59% met the proposed diagnostic criteria for EALI.

Using the clinical risk condition as a screening tool would appear to be a very sensitive screening test. All the patients in our study were given a diagnosis that Ferguson et al had identified as a clinical risk condition for ALI.[11] Previously, Hudson et al demonstrated that 79% of patients with ARDS had a known clinical risk condition for the development of ARDS[16]; thus, using clinical risk condition as a screening tool likely has a sensitivity of 79% or greater. However, it has been shown that only 6% to 17% of patients identified with a clinical risk condition at time of hospitalization go on to develop ALI.[11,12,17] Therefore, using a clinical risk condition alone would not be a feasible method for selecting patients for preventative or early therapeutic interventions trials.

Trillo-Alvarez et al presented a novel ALI prediction score (the Lung Injury Prediction Score [LIPS]) that scores patients using 17 variables including clinical risk conditions for ALI as well as risk modifiers. They demonstrated that an initial elevated oxygen requirement (>4 L/min or FiO_2 of >.35) was predictive of progression to ALI and had a sensitivity of 68%.[17] It is likely that lowering the threshold of oxygen requirement to the levels used in our study would further increase this sensitivity. The overall performance of the LIPS tool was modest with a sensitivity of 69%, a specificity of 84%, and a positive predictive value of only 24%. These findings were later validated in a larger multicenter prospective cohort.[12] One limitation of the LIPS is the large number of variables needed to calculate the score, which may make it a cumbersome tool for routine clinical use. Furthermore, its relatively low positive predictive value may preclude its use as an enrollment tool for clinical trials of therapies that carry a significant risk of adverse effects.

Our study also has some limitations. First, our cohort did not include patients with trauma as a risk factor for ALI. It is therefore unclear how our parameters would perform in this population. Our study was conducted in a single center, which may limit the broader applicability of our results, although it is reassuring that our data largely validate our prior work at Stanford University Medical Center.[13] The retrospective collection of the clinical variables we analyzed is limited by the accuracy of data recorded within patients' charts. Additionally, a major limitation is our inability to calculate the specificity of an increased oxygen requirement or respiratory rate in this cohort, since only patients that developed ALI

were studied. Finally, we note that 27% of patients either had ALI on hospital presentation or developed ALI within 12 hours of arrival; thus, identification of patients prior to progression to ALI will not always be feasible.

In conclusion, the most significant finding from our study is that many patients who progress to develop ALI show signs of EALI well before they develop respiratory failure and the need for positive pressure ventilation. This population may be particularly amenable to treatment strategies that focus on the prevention of frank respiratory failure and avoidance of the need for mechanical ventilation. Our findings support the feasibility and rationale for developing accurate and timely screening tools to identify this cohort of patients. Computerized screening tools have demonstrated a significant improvement in the identification of patients with ALI.[18–20] We are seeking to identify patients at risk of ALI at an even earlier stage, and it is likely that a similar electronic screening tool might aid in selecting these patients at the earliest possible time point. A multicenter study prospectively evaluating the positive predictive value of using the need for supplemental oxygen, an elevated respiratory rate and bilateral infiltrates on the chest radiograph to identify patients with EALI prior to the need for mechanical ventilation should be conducted in order to more definitively define a population for future interventional studies.

Acknowledgments

Authors would like to thank Dana McClintock, MD, and Magda Cepkova, MD.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Dr Calfee was supported by HL090833 and by the Flight Attendant Medical Research Institute, and by NIH/NCRR/OD UCSF-CTSI Grant Number KL2 RR024130. Dr Matthay was supported by HL 51856. Dr Levitt was supported by 5K23HL091334-02.

References

1. Bernard GR, Artigas A, Brigham KL, et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. Am J Respir Crit Care Med. 1994; 149(3 Pt 1):818–824. [PubMed: 7509706]
2. Liu KD, Levitt J, Zhuo H, et al. Randomized clinical trial of activated protein C for the treatment of acute lung injury. Am J Respir Crit Care Med. 2008; 178(6):618–623. [PubMed: 18565951]
3. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000; 342(18):1301–1308. [PubMed: 10793162]
4. The ARDS Network. Ketoconazole for early treatment of acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. JAMA. 2000; 283(15):1995–2002. [PubMed: 10789668]
5. Meduri GU, Golden E, Freire AX, et al. Methylprednisolone infusion in early severe ARDS: results of a randomized controlled trial. Chest. 2007; 131(4):954–963. [PubMed: 17426195]
6. Mercat A, Richard JC, Vielle B, et al. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. JAMA. 2008; 299(6):646–655. [PubMed: 18270353]
7. Randomized placebo-controlled trial of lisofylline for early treatment of acute lung injury and acute respiratory distress syndrome. Crit Care Med. 2002; 30(1):1–6. [PubMed: 11902249]
8. Spragg RG, Lewis JF, Walmrath HD, et al. Effect of recombinant surfactant protein C-based surfactant on the acute respiratory distress syndrome. N Engl J Med. 2004; 351(9):884–892. [PubMed: 15329426]

9. Steinberg KP, Hudson LD, Goodman RB, et al. Efficacy and safety of corticosteroids for persistent acute respiratory distress syndrome. N Engl J Med. 2006; 354(16):1671–1684. [PubMed: 16625008]
10. Brower RG, Lanken PN, MacIntyre N, et al. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. N Engl J Med. 2004; 351(4):327–336. [PubMed: 15269312]
11. Ferguson ND, Frutos-Vivar F, Esteban A, et al. Clinical risk conditions for acute lung injury in the intensive care unit and hospital ward: a prospective observational study. Crit Care. 2007; 11(5):R96. [PubMed: 17784960]
12. Gajic O, Dabbagh O, Park PK, et al. Early identification of patients at risk of acute lung injury: evaluation of lung injury prediction score in a multicenter cohort study. Am J Respir Crit Care Med. 2011; 183(4):462–70. [PubMed: 20802164]
13. Levitt JE, Bedi H, Calfee CS, Gould MK, Matthay MA. Identification of early acute lung injury at initial evaluation in an acute care setting prior to the onset of respiratory failure. Chest. 2009; 135(4):936–943. [PubMed: 19188549]
14. Levitt JE, Matthay MA. Treatment of acute lung injury: historical perspective and potential future therapies. Semin Respir Crit Care Med. 2006; 27(4):426–437. [PubMed: 16909376]
15. Calfee CS, Matthay MA. Nonventilatory treatments for acute lung injury and ARDS. Chest. 2007; 131(3):913–920. [PubMed: 17356114]
16. Hudson LD, Milberg JA, Anardi D, Maunder RJ. Clinical risks for development of the acute respiratory distress syndrome. Am J Respir Crit Care Med. 1995; 151(2 Pt 1):293–301. [PubMed: 7842182]
17. Trillo-Alvarez C, Cartin-Ceba R, Kor DJ, et al. Acute lung injury prediction score: derivation and validation in a population based sample. Eur Respir J. 2011; 37(3):604–609. [PubMed: 20562130]
18. Azzam HC, Khalsa SS, Urbani R, et al. Validation study of an automated electronic acute lung injury screening tool. J Am Med Inform Assoc. 2009; 16(4):503–508. [PubMed: 19390095]
19. Herasevich V, Yilmaz M, Khan H, Hubmayr RD, Gajic O. Validation of an electronic surveillance system for acute lung injury. Intensive Care Med. 2009; 35(6):1018–1023. [PubMed: 19280175]
20. Koenig HC, Finkel BB, Khalsa SS, et al. Performance of an automated electronic acute lung injury screening system in intensive care unit patients. Crit Care Med. 2011; 39(1):98–104. [PubMed: 20959782]

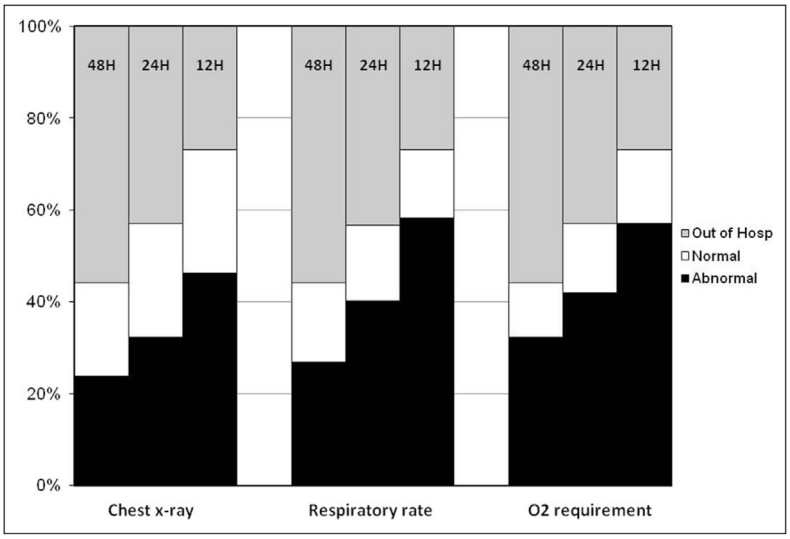

Figure 1.
Percentage of patients with early clinical abnormalities (bilateral infiltrates on the chest radiograph, respiratory rate >20/min, or oxygen requirement greater than 2 L/min) at each time point prior to diagnosis.

Table 1

Clinical Characteristics of the Acute Lung Injury Cohort (n=93)

Baseline Characteristics	Mean ± SD or n (%)
Age, years	59 ± 17
Female gender	44 (47)
Race	
Caucasian	62 (67)
African American	8 (9)
Asian/Pacific Islander	19 (20)
Other	4 (4)
Hispanic ethnicity	13 (14)
Comorbidities at ICU admission	
Acute hepatic failure	8 (9)
Cirrhosis	15 (16)
End stage renal disease	2 (2)
Immunosuppression	18 (19)
Metastatic cancer	2 (2)
Lymphoma	3 (3)
Hematologic malignancy	5 (5)
AIDS	3 (3)
Acute kidney injury	17 (18)
Clinical risk condition for ALI	
Sepsis	25 (27)
Pneumonia	41 (44)
Aspiration	22 (24)
Other	5 (5)
On day of diagnosis	
SAPS II	47 ± 15
APACHE II	24 ± 7
APACHE III	92 ± 42
In hospital mortality by diagnosis	1 (20)
Sepsis	5 (22)
Pneumonia	16 (40)
Aspiration	5 (23)
Other	1 (13)
Overall mortality	27 (29)

Abbreviations: SAPS II, Simplified Acute Physiology Score II; APACHE II and III, Acute Physiology And Chronic Health Evaluation II and III; SD, standard deviation; ICU, intensive care unit.

Table 2

Hospitalized Patients With Abnormalities Consistent With Early Respiratory Insufficiency at Each Time Point Prior to Diagnosis of ALI

Number of Clinical Abnormalities[a]	48 Hours	24 Hours	12 Hours
0/3	7 (17%)	5 (9%)	4 (6%)
1/3	7 (17%)	12 (23%)	10 (15%)
2/3	11 (27%)	14 (26%)	22 (32%)
3/3	16 (39%)	22 (42%)	32 (47%)
Total patients admitted to hospital	41	53	68

Abbreviation: ALI, acute lung injury.

[a]Clinical abnormalities: acute onset of bilateral infiltrates on chest radiograph, respiratory rate greater than 20, and/or greater than 2 L of oxygen requirement.

Table 3

Multivariate Analysis of Risk Factors for Time to Progression of ALI

Risk Factor	Relative Difference (hours)	95% CI	*P* Value
Age	1.5	0.2–2.7	.02
Sepsis	−46	−89–−3	.03
Female gender	19	−19–57	.32
Race			
Caucasian	0		
Asian	−28	−79–23	.28
Black	5	−64–75	.88
Other	−42	−124–39	.30
Alcohol use[a]	31	−10–73	.14
Blood transfusions[b]	−5	−47–38	.82
Chronic disease[c]	17	−22–57	.39
Positive culture[d]	−21	−60–18	.28
Smoker (current)	−33	−83–18	.20
Smoker (former)	−44	−98–10	.11

Abbreviations: ALI, acute lung injury; CI, confidence interval; APACHE II, Acute Physiology And Chronic Health Evaluation II.

[a]Reported alcohol consumption greater than or equal to 1 drink per day.

[b]Transfusion of blood products, including red blood cells, platelets, or fresh frozen plasma, within 72 hours prior to diagnosis of ALI.

[c]As defined in the APACHE II scoring system, the presence of liver cirrhosis, congestive heart failure (New York Heart Association class IV), chronic hemodialysis, or severe immunosuppression.

[d]Any positive microbiologic culture from any source taken within 72 hours prior to diagnosis of ALI.