Transfusion-related acute lung injury in the critically ill: a translational approach
Vlaar, A.P.J.

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Chapter 10

Diagnosing acute lung injury in the critically ill: a national survey among critical care physicians


Abstract

**Background:** Incidence reports on Acute Lung Injury (ALI) vary widely. Insight in diagnostic preferences of critical care physicians when diagnosing ALI may improve identification of the ALI patient population.

**Methods:** Critical care physicians in the Netherlands were surveyed using vignettes involving hypothetical patients and a questionnaire. The vignettes varied in 7 diagnostic determinants based on the North American European Consensus Conference and the Lung Injury Score. Preferences were analyzed by a mixed-effects logistic regression model and presented as odds ratio (OR) with 95% confidence interval.

**Results:** From 243 surveys sent to 30 hospitals, 101 were returned (42%). Odds ratios were as follows: chest X-ray consistent with ALI: OR 1.7(1.3 - 2.3), high Positive End-Expiratory Pressure (PEEP) (15 cmH$_2$O): OR 5.0(3.9 - 6.6), low Pulmonary Artery Occlusion Pressures (PAOP) (< 18 mmHg): OR 4.7(3.6 - 6.1), low compliance (30 ml/cmH$_2$O): OR 0.7(0.5 - 0.9), low PaO$_2$/FiO$_2$ (< 250 mmHg): OR 9.2(6.9 - 12.3), the absence of heart failure: OR 1.2(0.9 - 1.5), presence of a risk factor for ALI (sepsis): OR 1.0(0.8 - 1.3). The questionnaire revealed that critical care physicians with an anesthesiology background differed from physicians with an internal medicine background with regard to hemodynamic variables when considering ALI diagnosis (P< 0.05).

**Conclusions:** Dutch critical care physicians consider the PEEP level, but not the presence of a risk factor for ALI, an important factor to diagnose ALI. Background specialty of critical care physicians influences diagnostic preferences and may account for variance in the reported incidence of ALI.
Introduction

Acute lung injury (ALI) is one of the most important reasons for admittance to an intensive care unit (ICU) and initiation of mechanical ventilation. Because of a lack of specific diagnostic tests, ALI is defined by clinical and radiological criteria. The syndrome can be defined according to criteria from the North American-European Consensus Conference (NAECC), which is most widely used in clinical research, or to the Lung Injury Score (LIS) (table 1). The LIS-based definition scores additional ventilatory criteria, including the compliance of the respiratory system and the level of positive end expiratory pressure (PEEP) and depends less on hemodynamic criteria than the NAECC-based definition.

A wide variance of estimated incidences of ALI has been reported, ranging from 1.5 up to 100 per 100.000 person-years implying that identification of ALI patient populations varies considerably. The wide variance of the incidence of ALI may be caused by individual differences in daily practice of physicians. Critical care physicians may differ in their interpretation of the importance of diagnostic determinants provided by the ALI definitions. It can be hypothesized that the medical background and the level of experience of the critical care physician influences clinical interpretation. Also, the hemodynamic variables of ALI criteria require subjective interpretation, as guidance for the exclusion of patients with hydrostatic pulmonary edema is limited. It has been suggested that echocardiographic findings should be used in determining the nature of bilateral pulmonary infiltrates, but whether echocardiographic findings are used in the practice of diagnosing ALI is not known. Insight in diagnostic preferences of critical care physicians may help to improve identifying the ALI patient population. The aim of this study was to determine which diagnostic determinants are taken into account by critical care physicians when considering the diagnosis ALI, as well as the influence of their medical background on preferences of diagnostic determinants.

Methods

Setting

All Dutch hospitals with an adult ICU department (n=102) were asked to participate in this survey. Surveys were sent to fellows and staff physicians working in the ICU department of the hospitals who agreed to participate. Since the study was a survey conducted among physicians, institutional review board approval was not necessary.
Table 1. Definitions of Acute Lung Injury

**North American European Consensus Conference (NAECC)**
- Acute onset
- PaO2/FiO2 <300 (or <200 ARDS)
- Bilateral infiltrative changes on the chest x-ray
- Absence of hydrostatic pulmonary edema
- Risk factor for ALI present

**Lung Injury Score (LIS)**

1. Chest x-ray with alveolar consolidation confined to;
   - No quadrant 0
   - 1 quadrant 1
   - 2 quadrants 2
   - 3 quadrants 3
   - 4 quadrants 4

2. PaO2/FiO2
   - ≥ 300 0
   - 225-299 1
   - 175-224 2
   - 100-174 3
   - < 100 4

3. PEEP (when ventilated)
   - ≤ 5 cm H₂O 0
   - 6-8 cm H₂O 1
   - 9-11 cm H₂O 2
   - 12-14 cm H₂O 3
   - ≥ 15 cm H₂O 4

4. Compliance score
   - ≥ 80 ml/cmH₂O 0
   - 60-79 ml/cmH₂O 1
   - 40-59 ml/cmH₂O 2
   - 20-39 ml/cmH₂O 3
   - ≤ 19 ml/cmH₂O 4

**LIS score**

<table>
<thead>
<tr>
<th>Lung Injury</th>
<th>LIS Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>No lung injury</td>
<td>0</td>
</tr>
<tr>
<td>Mild-to-moderate lung injury</td>
<td>0.1-2.5</td>
</tr>
<tr>
<td>Severe lung injury (ARDS)</td>
<td>&gt; 2.5</td>
</tr>
</tbody>
</table>

PaO2/FiO2=arterial oxygen tension to inspired oxygen concentration; PEEP=Positive End-Expiratory Pressure; ARDS= Acute Respiratory Distress Syndrome.
Survey

The survey consisted of three parts: (a) characteristics of the respondent and its ICU; (b) 20 clinical vignettes; (c) questionnaire with questions on hemodynamic variables influencing ALI diagnosing. The survey was introduced with a cover letter, without providing NAECC or LIS definitions for ALI to avoid influencing the physician’s opinion how to diagnose ALI.

Vignettes

To assess clinical physicians’ decision making in diagnosing ALI, vignettes were used. Vignette-based surveys are a well-suited tool to measure practice variation in differential diagnosis. A vignette is a brief, written case history of a fictitious patient. The physicians were asked whether he/she would diagnose this patient as having ALI. The vignette describes case scenarios in which seven factors that determine the presence of ALI are embedded. Each factor has two different levels: the first may indicate ALI, the second can exclude ALI. These factors, which are shown in table 2, were agreed upon during a meeting of critical care physicians (NJ, MS, JG, PS). The levels were embedded in a brief case history (appendix 1). The vignette was tested in a pilot study by 17 critical care physicians for clarity of content. A full factorial design would generate 128 vignettes, which is a number too great to score. Therefore the number of vignettes was reduced using an orthogonal main effects design (SPSS version 15.0). The number of combinations was reduced to 20 from the original 128 possible vignettes. This procedure generates a specific subset of all possible combinations while statistical analysis is still possible of all possible combinations of the factors and their levels.

Table 2. Factors and levels implemented in the vignette used to assess the presence of ALI.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Chest X-ray with bilateral interstitial</td>
<td>Suggestive or not suggestive for pulmonary oedema</td>
</tr>
<tr>
<td>abnormalities</td>
<td></td>
</tr>
<tr>
<td>2. PEEP</td>
<td>5 or 15 cmH2O</td>
</tr>
<tr>
<td>3. PAOP (CVP)</td>
<td>&lt;18 (15) or &gt;20 (18) mmHg</td>
</tr>
<tr>
<td>4. Lung compliance</td>
<td>30 or 60 ml/cmH2O</td>
</tr>
<tr>
<td>5. PaO2/FiO2</td>
<td>&lt;250 or &gt;350 mmHg</td>
</tr>
<tr>
<td>6. History of heart failure</td>
<td>Absent or Present</td>
</tr>
<tr>
<td>7. ALI risk factor</td>
<td>Vascular surgery or Sepsis</td>
</tr>
</tbody>
</table>

PEEP = Positive End-Expiratory Pressure; PAOP = Pulmonary, Artery Occlusion Pressure; CVP = Central Venous Pressure.

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Questionnaire

Next to the 20 vignettes, critical care physicians were questioned using a list of 5 hemodynamic variables. The questions were added because not all diagnostic determinants that may influence the assessment of the physician of the presence or absence of ALI could be taken into account in the vignette. The statements had to be visually scored on a 10 cm line providing a 0% (not taken into account) – 100% (total taken into account) scale.

Statistics

The means and standard deviations for continuous variables and distributions for frequency of categorical variables were summarized using descriptive statistics. (SPSS version 15.0).

A mixed-effects logistic regression model was used to determine whether the levels of diagnostic determinants for ALI clustered within each respondent assessment of the 20 vignettes. Mixed-effects logistic regression models can be used to predict discrete outcome variables when observations are correlated. Therefore, the respondent was included in the model as a random effect parameter (corresponding to individuals drawn at random from a population) and the factor levels as fixed parameters. The mixed-effects logistic regression model showed to be a significant better model then the “naive” multivariable logistic regression model (difference in log likelihood Chi² 47.16, df 1, \(p < 0.001\)) (Statistics version 10.1, Statacorp).

The levels of diagnostic determinants in favor of ALI diagnosis were coded as 1 (PaO₂/FiO₂ < 250 mmHg, chest X-ray consistent with interstitial abnormalities suggestive for pulmonary edema, high PEEP (15 cmH₂O), low pulmonary artery occlusion pressure (< 18mmHg), low compliance (30 ml/cmH₂O), no history of heart failure present, risk factor for ALI present). Therefore, odds ratio’s and their 95% confidence intervals above 1 are supportive for a diagnosis of ALI.

The scores on the statements (visual analogue scale) are given as means ± standard error. Differences between medical specialty were analyzed using ANOVA analysis followed by Bonferroni post test. A \(p\) value of < 0.05 was taken as statistically significant.

Results

Thirty hospitals participated in this study. Of the 243 questionnaires sent, 101 were returned (response rate 42%). Characteristics of the responding critical care physicians showed that 38% of the critical care physicians had an anesthesiology background specialty while 57% had an internal medical background specialty.
More than 50% of the responding critical care physicians had 10 years or less of working experience. Forty-two percent of the respondents worked in an academic hospital while 58% of the respondents worked in a referral hospital.

**Vignette**

The impact of the determinants in ALI diagnosing is depicted in figure 1. The odds ratios were as follows; chest X-ray abnormalities consistent with ALI: OR 1.7 (1.3 - 2.3), high PEEP (15 cmH2O): OR 5.0 (3.9 - 6.6), low pulmonary artery occlusion pressure (< 18mmHg): OR 4.7 (3.6 - 6.1), low compliance (30 ml/cmH2O): OR 0.7 (0.5 - 0.9), low PaO2/FiO2 (< 250 mmHg): OR 9.2 (6.9 - 12.3), the absence of heart failure: OR 1.2 (0.9 - 1.5), the presence of a risk factor for ALI (sepsis): OR 1.0 (0.8 - 1.3). Teaching hospitals did not differ from referral hospitals in the use of clinical factors to diagnose ALI.

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**Table 3.** Characteristics of the participating physicians and centers in the survey.

<table>
<thead>
<tr>
<th>Function</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fellow</td>
<td>15%</td>
</tr>
<tr>
<td>Critical care specialist</td>
<td>78%</td>
</tr>
<tr>
<td>Specialist with other background</td>
<td>7%</td>
</tr>
</tbody>
</table>

**Medical specialty**

<table>
<thead>
<tr>
<th>Medical specialty</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicine</td>
<td>57%</td>
</tr>
<tr>
<td>Anesthesiology</td>
<td>38%</td>
</tr>
<tr>
<td>Other</td>
<td>5%</td>
</tr>
</tbody>
</table>

**Sex**

<table>
<thead>
<tr>
<th>Sex</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>69%</td>
</tr>
<tr>
<td>Female</td>
<td>31%</td>
</tr>
</tbody>
</table>

**Age (SD)**

- 42±7

**Experience (years)**

<table>
<thead>
<tr>
<th>Experience (years)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5</td>
<td>44%</td>
</tr>
<tr>
<td>6-10</td>
<td>28%</td>
</tr>
<tr>
<td>11-20</td>
<td>20%</td>
</tr>
<tr>
<td>20+</td>
<td>8%</td>
</tr>
</tbody>
</table>

**Hospital**

<table>
<thead>
<tr>
<th>Hospital</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Academic</td>
<td>42%</td>
</tr>
<tr>
<td>Non-Academic</td>
<td>58%</td>
</tr>
</tbody>
</table>

**ICU capacity (CI 95%)**

<table>
<thead>
<tr>
<th>ICU=Intensive Care Unit</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilated beds</td>
<td>16 (13.6-18.4)</td>
</tr>
<tr>
<td>Non-ventilated beds</td>
<td>2.3 (1.6-2.9)</td>
</tr>
</tbody>
</table>

(table 3). More than 50% of the responding critical care physicians had 10 years or less of working experience. Forty-two percent of the respondents worked in an academic hospital while 58% of the respondents worked in a referral hospital.
Questionnaires

Hemodynamic factors that may be considered when diagnosing ALI were measured with the Visual Analogue Scale (VAS) and presented in table 4. Critical care physicians with an anesthesiology background differed from critical care physicians with an internal medicine background when considering ALI diagnosis. Both the presence of a valve dysfunction and a diastolic dysfunction (as measured by E/A ratio) was more often taken into account by critical care physicians from anesthesiology origin (p< 0.05).

Table 4. Relative importance of factors that are taken into account when diagnosing ALI by a visual analogue scale.

<table>
<thead>
<tr>
<th>Statements</th>
<th>Percentage taken into account</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Cardiac output estimated by PAC</td>
<td>Overall Anesthesiology Internal Medicine</td>
</tr>
<tr>
<td>2. Left ventricle function estimated by echocardiography</td>
<td>26 (3) 22 (4) 27 (4)</td>
</tr>
<tr>
<td>3. E/A ratio estimated by echocardiography</td>
<td>40 (3) 45 (5) 35 (4)</td>
</tr>
<tr>
<td>4. Valvular dysfunction present</td>
<td>33 (3) 38 (5) 26 (3)*</td>
</tr>
<tr>
<td>5. 24 hours fluid balance</td>
<td>43 (3) 52 (5) 33 (3)†</td>
</tr>
</tbody>
</table>

Data are represented as mean percentage (SE). Data present percentage that physicians take a factor into account when considering ALI (0—not taken into account, 100=always taken into account). PAC =Pulmonary Artery Catheter; E/A =diastolic dysfunction (Early diastolic filling velocity / Atrial filling velocity). *p< 0.05, † p< 0.001 anesthesiology vs. internal medicine, ANOVA analysis with Bonferroni post test.

Figure 1. Preferences for diagnostic determinants for acute lung injury (ALI). Data are presented for each factor level separately as odds ratios (OR) and 95% confidence interval (95%CI). Abbreviations; AAA=Abdominal Aortic Aneurysm; PAOP=Pulmonary Artery Occlusion Pressure.
Diagnosis

This national survey assessed the relative importance of diagnostic determinants for critical care physicians when diagnosing ALI in their patients. Of the respiratory determinants, PaO$_2$/FiO$_2$ and PEEP level are considered important determinants in diagnosing ALI, whereas pulmonary artery occlusion pressure and results of chest X-ray are considered less important. The history of heart failure, level of compliance or presence of a risk factor for ALI had no impact on diagnosing ALI. The medical background specialty of critical care physicians influenced preferences of hemodynamic diagnostic determinants.

Besides PaO$_2$/FiO$_2$, the application of high PEEP levels in mechanical ventilation had a strong preference. Current practice of mechanical ventilation of critically ill patients indicates that PEEP is increasingly applied. It is probable that critical care physicians recognize that PEEP aids in keeping the alveoli open, resulting in better oxygenation. The application of PEEP may even result in excluding a patient from fulfilling the definition of ALI according to NAECC criteria, despite worsening of the pulmonary condition of the patient. However, the optimal PEEP level in ALI is unknown. There is no strong evidence that high PEEP is beneficial in ALI patients.

We do not argue that patients with a high PEEP level have ALI. Our data however, suggest that patients ventilated with a high level of PEEP may be diagnosed as ALI in clinical practice. In accordance, a prior descriptive study showed that critical care physicians diagnose ALI more frequent then predicted by NAECC criteria. Our finding of a strong diagnostic preference of high PEEP in diagnosing ALI may influence implication of results from intervention trials in ALI patients identified by NAECC criteria, which may be applied to a different patient population.

Although compliance is severely compromised in ALI, critical care physicians rated this parameter to be of no importance in diagnosing ALI. This finding, which is in accordance with an earlier survey study on diagnosing ALI, may be explained by the emphasis on the beneficial effect of application of PEEP on oxygenation in research on mechanical ventilation. Also, compliance is calculated from the change in volume relative to a change in applied pressure and requires interpretation of ventilatory settings, rather then mere application of a PEEP level. Not all ventilators display compliance on the monitor which may result in under appreciation of this variable. Notably, although considered a hallmark of ALI, the finding of interstitial abnormalities on the chest X-ray was not a strong preference when considering ALI. Physicians may recognize that application of PEEP increases radiographic translucency, thereby diminishing interstitial abnormalities.

The presence of an appropriate risk factor is mandatory in the current NAECC definition. In this study, an admission diagnosis of sepsis, which is frequently accompanied by lung injury, was not scored in favor of the diagnosis ALI. An
explanation for this finding is tempting. We speculate that the diversity of the diseases that can cause ALI may result in ignoring established risk factors. Alternatively, physicians may only be interested in the presence or absence of ALI at a given moment and not in the cause.

We found that medical specialty background of critical care physicians influenced preferences of diagnostic determinants to diagnose ALI. Hemodynamic variables were considered more important by critical care physicians with anesthesiology as their background specialty. This may be explained by a difference in emphasis on hemodynamic monitoring during anesthesiology residency compared to internal medicine residency. The ability of cardiothoracic anesthesiologists to perform echocardiography, may contribute to a preference of hemodynamic variables estimated by this technology. Differences in medical background of critical care physicians may be a source of variance in identifying ALI patient populations. We propose that background specialty of critical care physicians is taken into consideration when ALI criteria are applied in future clinical trials.

The survey design of this study has several limitations. Firstly, although vignettes have been recognized as a valid tool to assess preferences in clinical practice, we can not rule out a discrepancy between physician’s practice of ALI diagnosing and their answers to vignettes with hypothetical patients. Secondly, diagnostic determinants influencing ALI diagnosis are many. A vignette survey is limited to a number of determinants to generate an optimal number of vignettes which respondents can adequately evaluate. We chose determinants which are accepted characteristics of the syndrome ALI. Lastly, although surveys were returned from all participating centers, the response rate of individual critical care physicians was disappointing. However, assuming that the opinions of critical care physicians are consistent within one centre, the results of this study reflects the opinion of Dutch critical care physicians on what factors are considered important in the diagnosis of ALI.

Conclusion

In conclusion, this survey on the practice of diagnosing ALI shows that critical care physicians consider the level of PEEP an important determinant in diagnosing ALI. Clinical risk factors are not considered when diagnosing ALI. The medical background specialty of critical care physicians influenced preferences of diagnostic hemodynamic determinants, which may contribute to variance in the estimated ALI patient population. These findings provide insight in the practice of ALI diagnosis.
Appendix 1.

Example Vignettes

1. A male patient of 55 years old is admitted to the ICU because of sepsis. The patient is mechanically ventilated.
   • No history of heart failure
   • PaO$_2$/FiO$_2$ <250 mmHg
   • PEEP 15 cmH$_2$O
   • Lung compliance 30 ml/cmH$_2$O
   • Chest X-ray shows bilateral interstitial abnormalities suggestive for pulmonary oedema
   • Pulmonary Artery Occlusion Pressure <18 mmHg

Does this patient have Acute Lung Injury? Yes/No

2. A male patient of 55 years old undergoes elective correction of an abdominal aneurysm. During surgery, the patient received 2 units of red blood cells and 1000 ml colloid infusion. The patient is 4 hours post surgery and is mechanically ventilated on the ICU.
   • History of heart failure
   • PaO$_2$/FiO$_2$ >350 mmHg
   • PEEP 5 cmH$_2$O
   • Lung compliance 60 ml/cmH$_2$O
   • Chest X-ray shows bilateral interstitial abnormalities not suggestive for pulmonary oedema
   • Pulmonary Artery Occlusion Pressure >20 mmHg

Does this patient have Acute Lung Injury? Yes/No
Reference List


