Association of acute kidney injury defined with the AKIN criteria and poor outcome in acute respiratory distress syndrome patients
Mohamed H. Saleh, Mohamed O. Elghonemi

Background Few studies have reported the deleterious association between acute respiratory distress syndrome (ARDS) and acute kidney injury (AKI). We aimed to evaluate the association of AKI and poor outcome in ARDS patients and whether this association is related to fluid overload or not.

Patients and methods Sixty-four patients diagnosed with ARDS and had been mechanically ventilated were enrolled. AKI was diagnosed using the Acute Kidney Injury Network criteria. Patients were stratified into two groups according to the degree of renal impairment. All data were statistically analyzed.

Results The mean age of the studied patients was 47.23 ±10.12 years; 33 (51.6%) were men. In group 2, the follow-up Lung Injury Severity Score and length of hospital stay were significantly higher compared with group 1: 3.33±0.74 points and 19.11±6.37 days versus 2.84±0.57 points and 12.38±4.21 days (P<0.004 and <0.001, respectively). Also, they had higher need to use vasoactive (VA) agents, 21 (55.3%) versus 6 (23.1%) (P=0.019). In-patient mortality was significantly correlated with the need to use VA agents and higher cumulative fluid balance (R=0.394 and 0.24, P=0.001 and 0.05, respectively). The need to use VA agents was the only independent predictor of mortality (odds ratio=4.18, P=0.022).

Conclusion AKI as defined on the basis of the Acute Kidney Injury Network criteria is associated with poor outcome in ARDS patients.

Egypt J Bronchol 2017 11:327–331
© 2017 Egyptian Journal of Bronchology

Keywords: acute kidney injury, Acute Kidney Injury Network criteria, acute respiratory distress syndrome

Patients and methods

This study was a prospective observational study carried out on 64 patients admitted to the Critical Care Department of Cairo University and diagnosed with ARDS from March to December 2014. The study has been approved by our local ethical committee. According to the Berlin Criteria, ARDS was defined by timing (within 1 week of clinical insult or onset of respiratory symptoms); radiographic changes (bilateral opacities not fully explained by effusions, consolidation,
or atelectasis); origin of edema (not fully explained by cardiac failure or fluid overload); and severity on the basis of the PaO2/FiO2 ratio on 5 cm of continuous positive airway pressure [13]. All patients underwent a full clinical examination and laboratory investigation including assessments of blood gases and lactate levels. Acute Physiology and Chronic Health Evaluation II (APACHE II) and Lung Injury Severity (LIS) Scores were calculated upon admission. The LIS score was reassessed 1 week after admission for all patients.

All patients received mechanical ventilation through a commercially available ventilator (Puritan–Bennett®) in the volume-controlled mode. Tidal volume was set to be 6–8 ml/kg. Predicted body weight in kg was calculated from the following formula: 2.3[height (inches)-60] +45.5 for women or 50 for men. The respiratory rate was set up to 35 breaths/min to deliver the expected minute ventilation requirement (generally, 7–10 ml/kg), which was higher in group 2 compared with group 1 (2.8±3.1 vs. -1.2±2.88 l, P=0.02), patients in both groups had comparable general characteristic data (Table 1). In group 2 patients, 15 (23.3%) and 12 (18.7%) patients had AKIN grades 2 and 3, respectively. Patients in group 2 had worse outcome parameters compared with those in group 1 as the follow-up LIS and length of hospital stay were significantly higher in group 2 compared with group 1 patients: 3.3±0.7 points and 12±6.3 days versus 2.8±0.5 points and 12±4.1 days (P=0.004 and 0.001, respectively). Also, they had a higher need to use vasoactive (VA) agents, 21 (77.7%) patients versus 17 (45.9%) patients, and spent more days on mechanical ventilation, 14.1±4.5 versus 8.5±3.7 (P=0.019 and <0.001, respectively) (Table 2).

In the studied patients, in-patient mortality occurred in 30 (46.9%) patients, and it was significantly higher in the patients in group 2: 18 (66.7%) versus 12 (32.4%) (P=0.019). (Table 3) shows a comparison of surviving patients.

**Results**

The mean age of the studied patients was 47.23±10.12 years; 33 (51.6%) were men. The mean PaO2/FiO2, and LIS score on admission were 169.95±31 and 3.06±0.54, respectively. Apart from cumulative fluid balance, which was higher in group 2 compared with group 1 (2.8±3.1 vs. -1.2±2.88 l, P=0.02), patients in both groups had comparable general characteristic data (Table 1). In group 2 patients, 15 (23.3%) and 12 (18.7%) patients had AKIN grades 2 and 3, respectively. Patients in group 2 had worse outcome parameters compared with those in group 1 as the follow-up LIS and length of hospital stay were significantly higher in group 2 compared with group 1 patients: 3.3±0.7 points and 19±6.3 days versus 2.8±0.5 points and 12±4.1 days (P=0.004 and 0.001, respectively). Also, they had a higher need to use vasoactive (VA) agents, 21 (77.7%) patients versus 17 (45.9%) patients, and spent more days on mechanical ventilation, 14.1±4.5 versus 8.5±3.7 (P=0.019 and <0.001, respectively) (Table 2).

In the studied patients, in-patient mortality occurred in 30 (46.9%) patients, and it was significantly higher in the patients in group 2: 18 (66.7%) versus 12 (32.4%) (P=0.019). (Table 3) shows a comparison of surviving patients.

<table>
<thead>
<tr>
<th>Table 1 General characteristics of the studied patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
</tr>
<tr>
<td>-------------</td>
</tr>
<tr>
<td>(n=37)</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Sex (female)</td>
</tr>
<tr>
<td>DM</td>
</tr>
<tr>
<td>HTN</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
<tr>
<td>PaO2/FiO2</td>
</tr>
<tr>
<td>APACHE II</td>
</tr>
<tr>
<td>LIS 1</td>
</tr>
<tr>
<td>Cumulative fluid balance</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD or n (%). APACHE II, Acute Physiology and Chronic Health Evaluation II; DM, diabetes mellitus; FIO2, fraction of inspired oxygen; HTN, hypertension; LIS, Lung Injury Severity Score; PaO2, arterial partial oxygen pressure, *P value < 0.05.
and nonsurviving patients. Although it was not significant, we noted that the cumulative fluid balance was more positive in nonsurviving patients as opposed to a more negative fluid balance in those who survived. Spearman’s correlation showed that in-patient mortality was significantly correlated with the need to use VA agents and cumulative fluid balance, but not admission/follow-up LIS or length of hospital stay (Table 4).

Univariate regression analysis showed that positive cumulative fluid balance is an independent predictor of higher follow-up LIS and length of hospital stay, but not for the need to use VA agents or mortality (Table 5).

In multivariate analysis, AKIN grade was not an independent predictor of in-patient mortality and nonsurviving patients. Although it was not significant, we noted that the cumulative fluid balance was more positive in nonsurviving patients as opposed to a more negative fluid balance in those who survived. Spearman’s correlation showed that in-patient mortality was significantly correlated with the need to use VA agents and cumulative fluid balance, but not admission/follow-up LIS or length of hospital stay (Table 4).

Univariate regression analysis showed that positive cumulative fluid balance is an independent predictor of higher follow-up LIS and length of hospital stay, but not for the need to use VA agents or mortality (Table 5).

In multivariate analysis, AKIN grade was not an independent predictor of in-patient mortality (odds ratio=0.797 and P=0.549). The need to use VA agents was the only independent predictor of mortality in our cohort (odds ratio=4.18 and P=0.022).

Discussion

There is growing evidence pointing to deleterious interactions between lung dysfunction and renal impairment in critically ill patients [3]. This study found a higher incidence of AKI in ARDS patients and its contribution toward poor outcome in these patients as our results indicate that 42% of ARDS patients developed significant renal impairment, that is, AKIN grades 2 and 3 during their hospital stay. Also, development of significant renal impairment was associated with increased mortality, in addition to other poor outcome parameters such as length of hospital stay, need to use VA agents, and number of days on mechanical ventilation. Multivariate regression analysis showed that AKI was not an independent predictor of mortality in our cohort.

The reciprocal risk of AKI and lung dysfunction in critically ill patients was similarly reported by Clemens et al. [15]. Unlike our study, they also reported that both AKI and ARDS are independent risks for subsequent death. This can probably be attributed to the different type of patients in their study; they studied burn patients.

The ARDSNet investigators [10] and Darmon et al. [16] reported an increased risk of development...
of AKI in ARDS patients. Similarly, many investigators reported that biotrauma induced by mechanical ventilation with the subsequent release of inflammatory cytokines not only affects the lung but also leads to further systemic inflammation with subsequent kidney and other organ dysfunction [10,11,17]. However, these studies did not clearly evaluate the influence of development of AKI on the patients’ outcome.

A recent meta-analysis suggested that both ARDS and mechanical ventilation were associated with a three-fold increase in the risk of AKI [18]. The studies included in this analysis were focused on specific types of patients such as trauma [19], postlung transplant [20], malignant [21], and advanced liver cell failure patients [22]. Thus, the general applicability of the findings is unclear.

In our results, positive cumulative fluid balance was an independent predictor of poor outcome parameters such as follow-up LIS score and length of hospital stay, but not in-patient mortality. This observation may postulate the possible mechanism of the association between AKI and poor outcome in our cohort. We believe that this observation could have therapeutic implications in the management of AKI in ARDS patients. In line with these results, a randomized, multicenter study [2] evaluated a strategy of fluid restriction in ARDS patients. Unlike our study, they excluded patients with renal failure. However, their results similarly showed that a conservative strategy significantly improved oxygenation in patients and decreased the number of days with mechanical ventilation, but did not influence mortality at 60 days. However, Prowle et al. [23] limiting the beneficial effect of fluid restriction in ARDS patients to whom the pulmonary edema is more pronounced but not in less severe form of lung injury. Moreover, they reported that fluid restriction may lead to tissue hypoperfusion with and renal injury. Seethala et al. [24] reported that higher volume of early fluid administration was associated with the development of ARDS, meaning that higher cumulative fluid balance is not only a predictor of outcome in ARDS patients but could also be a causative factor in septic patients.

Our results also showed that the need to use VA agents was the only independent predictor of mortality in our cohort. This confirms previous study results of Boyle et al. [25], who reported that the use of vasopressors was one of the predictors of mortality in their cohort.

Conclusion

AKI is associated with poor outcome in ARDS patients. Higher cumulative balance with subsequent volume overload could possibly be a poor prognostic factor.

In addition to a small sample size, this study had many limitations. As this was an observational study, we did not evaluate the influence of different AKI therapeutic modalities on the outcome in ARDS patients. Also, the value of early renal replacement therapy in these patients was not assessed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References


Ranieri VM, Giunta F, Suter PM, Slutsky AS. Mechanical ventilation as a mediator of multisystem organ failure in acute respiratory distress syndrome. JAMA 2000; 284:43–44.


