EDITORIAL

Kidney-lung Crosstalk in Determining the Prognosis of Acute Kidney Injury Phenotypes in Acute Respiratory Distress Syndrome Patients

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Organ crosstalk is a salient feature in a critically ill patient. A significantly high mortality is associated with acute respiratory distress syndrome (ARDS). Acute respiratory distress syndrome associated systemic inflammatory response (SIRS) leads to lung injury and this also has significant effects on cardiovascular, renal, and neurologic function.[1] In almost 50% of the patients, ARDS leads to acute kidney injury (AKI), the most common extra-pulmonary organ dysfunction. In patients with ARDS the risk of mortality is significantly increased with the development of AKI.[2] The risk factors for the development of AKI[3] in critically ill patients are co-morbidities like immune suppression, chronic heart disease, chronic liver disease, hematologic malignancies, diabetes mellitus (DM), presence of shock, ARDS, increased age, and others.

There are multiple pathogenetic factors that lead to the development of AKI in ARDS patients but the mechanism of renal injury in ARDS is yet to be understood completely. In ARDS patients, poor lung compliance leads to the development of high intra thoracic pressure which leads to the reduction of cardiac output. Subsequently, the renal perfusion also becomes inadequate. Hypoxemia, hypercarbia, and systemic acidosis develop due to gas exchange abnormalities. Hence, there is alteration of renal vascular resistance and renal perfusion pressure which results in AKI.[4] Damage to the alveolar capillary membrane occurs from sub-optimal ventilator management strategy and this potentiates an inflammatory response and the multi system organ failure (MSOF) becomes worsened. Ventilator-induced lung injury (VILI) affects renal integrity due to the compromised hemodynamics and altered neuro-humoral mechanisms.[5] It was observed in the ARMA trial that the low tidal volume lung protective ventilatory strategy with optimized positive end-expiratory pressure (PEEP) and limited plateau pressure led to lesser incidences of renal failure.[6] An increase in diuresis and renal resistive indices has been noticed when permissive hypercapnia has been targeted during the management of ARDS.[7] Ultimately, the glomerular filtration rate (GFR) is reduced and subsequently, AKI develops after about 48 hours of ARDS. Urine output is decreased and markers of kidney injury like BUN, and creatinine are elevated. However, this change in the level of the biomarkers occurs after the onset of the renal injury. The renal stress can be identified by multiple novel biomarkers before the initiation of functional change and this aids in the identification of at risk kidneys.[8] Few examples are plasma or urinary neutrophil gelatinase-associated lipocalin (NGAL), urinary kidney injury molecule 1 (KIM-1), urinary tissue inhibitor of metalloproteinase-2 (TIMP-2), and insulin-like growth factor-binding protein 7 (IGFBP7), and others. In subclinical AKI, structural kidney injury occurs without a rise in creatinine.

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There are multiple complications associated with AKI that may have considerable effects on the lungs. The traditional complications of AKI are electrolyte derangements, uremia, and fluid overload; with poor oxygenation.[9] These complications are amenable to renal replacement therapy (RRT). Non-traditional complications of AKI are often not correctable by RRT and lead to a mortality of up to 60%. These include inflammatory lung injury, cardiac dysfunction, and immune paralysis. A continuous liaison needs to be maintained between the nephrologists and intensivists while deciding upon the key therapeutic approach of a critically ill patient with AKI and ARDS as regards the optimization of fluid balance, achievement of euvolemia and avoidance of hypophosphatemia while on RRT. The critically ill patients with AKI experience delayed weaning from mechanical ventilation. The presence of both these complications in the patients infected with novel SARS-CoV-2 virus had also been associated with a poor prognosis. The presence of AKI complicating ARDS in critically ill patients is an important factor that contributes to increased mortality. However, heterogeneity exists within the clinical syndrome of AKI and therefore, the management protocol needs to be individualized and optimized.[10] The patho-physiologic mechanisms of individual sub-groups of AKI is unique.[11] Hence, clinical outcome might be affected if all these sub-groups are combined into a common entity.

Sub-phenotyping aids in prognostic enrichment (i.e., different outcomes based on a particular sub-phenotype) and predictive

enrichment (i.e., different responses to treatment). A significant part of individualized approach to the management of AKI is the prognostic enrichment. Identification and employment of precision therapeutics (i.e., predictive enrichment) is the target of sub phenol tying a diverse and complex disorder. There are different ways of sub-phenotyping in AKI, like clinical sub-phenotypes based on serum creatinine (SCr) trajectory or biomarker-based sub-phenotypes.[12] Till date, there have not been many studies that deal with the outcomes of patients with ARDS associated with AKI based on the different sub-phenotypes of AKI. Besides, there is also a lack in substantial and robust data regarding the early identification of AKI sub-phenotypes in ARDS patient within 48 hours of invasive mechanical ventilation (IMV).

Among all the scoring systems to predict ARDS mortality, the DRONE score is unique in that it is the only scoring system that incorporates the significant parameter of DP, i.e., driving pressure (Pplat, PEEP), oxygenation [quantified by the ratio of partial pressure of arterial oxygen to the fraction of inspired oxygen (PaO_2/FiO_2)] and nutritional assessment with the modified nutrition risk in the critically ill (mNUTRIC) score).[13] Many authors have described the multiple aspects of DP in terms of mortality predictor in ARDS, a surrogate to lung stress, a marker of VILI, a useful tool in optimal PEEP titration, and a marker of ARDS severity.[14] The modified nutrition risk in the critically ill (mNUTRIC) score includes the patient's parameters such as age, acute physiology and chronic health evaluation II (APACHE II) score, sequential organ failure. The DRONE score ≥4 could be a reliable predictor of mortality at 48 hours in ARDS patients receiving IMV. Each point increase in the DRONE score can increase the mortality by 5.43 times in ARDS patients receiving IMV.

In a study by Kellum et al.,[15] renal recovery in critically ill patients has been classified into five groups. These included early and late sustained reversal, relapsing AKI with and without complete renal recovery, and never-reversed AKI. Diverse long-term outcomes have been ascribed to these groups. Non-recovery following AKI occurs in about 40% of cases and it is associated with a guarded prognosis. There was an incidence of high mortality after 1 year in the patients who had not recovered at hospital discharge (59%) as compared to those who had recovered late. However, late recovery (i.e., after day 7) commonly occurs in more than half of the patients.

The current single-center observational study was conducted on 266 ARDS patients on invasive mechanical ventilation (IMV), to determine the sub-phenotypes of AKI associated with ARDS. Sub-phenotyping was done based on the serum creatinine (SCr) trajectories from day 1 to day 5 of IMV into resolving (sub-phenotype-1) or non-resolving (sub-phenotype-2) AKI. In the study, 222 patients were included for data analysis out of which 141 patients (63.51%) had AKI. The incidence of sub-phenotype-2 AKI among the ARDS cohort was 35.13% and was significantly higher among the non-survivors (87.7%). Acute kidney injury Sub-phenotype-1 had higher median day 1 SCr than sub-phenotype-2 but lower levels by day 3 and day 5 of IMV. The median time of survival was 8 days in AKI sub-phenotype-2 versus 45 days in AKI with sub-phenotype. The classification of patients into AKI or non-AKI categories in ARDS patients based on the severity may not predict outcomes, rather sub-phenotyping based on serum creatinine trajectories is the reliable predictor. The DRONE score ≥ 4 within 48 hours of IMV also predicted the sub-phenotype-2 AKI among ventilated ARDS patients.

To conclude, increased mortality has been observed in patients with AKI developing respiratory complications and that signifies a co-relation between AKI and ARDS. There exists a bidirectional relationship as AKI can develop in mechanically ventilated patients with ARDS. However, larger multi-centric studies focusing on ARDS-AKI cross talk is the need of the hour. Clinicians need to consider the complexity of organ interactions during the management of critically ill patients with these interrelated conditions.

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References

1. Bautista E, Arcos M, Jimenez-Alvarez L, García-Sancho MC, Vázquez ME, Peña E, et al. Angiogenic and inflammatory markers in acute respiratory distress syndrome and renal injury associated to A/H1N1 virus infection. Exp Mol Pathol 2013;94(3):486–492. DOI: 10.1016/j.yexmp.2013.03.007.
2. Liu KD, Glidden DV, Eisner MD, Parsons PE, Ware LB, Wheeler A, et al. Predictive and pathogenetic value of plasma biomarkers for acute kidney injury in patients with acute lung injury. Crit Care Med 2007;35(12):2755–2761. PMID: 18074478.
3. Darmon M, Clec'h C, Adrie C, Argaud L, Allaouchiche B, Azoulay E, et al. Acute respiratory distress syndrome and risk of AKI among critically ill patients. Clin J Am Soc Nephrol 2014;9(8):1347–1353. DOI: 10.2215/CJN.08300813.
4. Husain-Syed F, Slutsky AS, Ronco C. Lung-kidney cross-talk in the critically ill patient. Am J Respir Crit Care Med 2016;194(4):402–414. DOI: 10.1164/rccm.201602-0420CP.
5. Hepokoski M, Englert JA, Baron RM, Crotty-Alexander LE, Fuster MM, Beitler JR, et al. Ventilator-induced lung injury increases expression of endothelial inflammatory mediators in the kidney. Am J Physiol Renal Physiol 2017;312(4):F654–F660. DOI: 10.1152/ajprenal.00523.2016.
6. Acute Respiratory Distress Syndrome Network; Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, et al. 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. DOI: 10.1056/NEJM200005043421801.
7. Darmon M, Schortgen F, Leon R, Moutereau S, Mayaux J, Di Marco F, et al. Impact of mild hypoxemia on renal function and renal resistive index during mechanical ventilation. Intensive Care Med 2009;35(6):1031–1038. DOI: 10.1007/s00134-008-1372-5.
8. Bellomo R, Kellum JA, Ronco C, Wald R, Martensson J, Maiden M, et al. Acute kidney injury in sepsis. Intensive Care Med 2017;43(6):816–828. DOI: 10.1007/s00134-017-4755-7.
9. Park BD, Faubel S. Acute kidney injury and acute respiratory distress syndrome. Crit Care Clin 2021;37(4):835–849. DOI: 10.1016/j.ccc.2021.05.007.
10. Bhatraju PK, Mukherjee P, Robinson-Cohen C, O'Keefe GE, Frank AJ, Christie JD, et al. Acute kidney injury sub phenotypes based on creatinine trajectory identifies patients at increased risk of death. Crit Care 2016;20(1):372. DOI: 10.1186/s13054-016-1546-4.
11. Vaara ST, Bhatraju PK, Stanski NL, McMahon BA, Liu K, Joannidis M, et al. Sub phenotypes in acute kidney injury: A narrative review. Crit Care. 2022;26(1):251. DOI: https://doi.org/10.1186/s13054-022-04121-x.
12. Ostermann M, Zarbock A, Goldstein S, Kashani K, Macedo E, Murugan R, et al. Recommendations on acute kidney injury biomarkers from the acute disease quality initiative consensus conference: A consensus statement. JAMA Netw Open 2020;3(10):e2019209. DOI: https://doi.org/10.1001/jamanetworkopen.2020.19209.
13. Todur P, Nileshwar A, Chaudhuri S, Thejesh S. Incidence, Outcomes, and Predictors of sub-phenotypes of acute kidney injury among

acute respiratory distress syndrome patients: A prospective observational study. Indian J Crit Care Med 2023;27(10):724–731.
14. Aoyama H, Yamada Y, Fan E. The future of driving pressure: A primary goal for mechanical ventilation? J Intensive Care 2018;6:64. DOI: https://doi.org/10.1186/s40560-018-0334-4.
15. Kellum JA, Sileanu FE, Bihorac A, Hoste EA, Chawla LS. Recovery after acute kidney injury. Am J Respir Crit Care Med 2017;195(6):784–791. DOI: 10.1164/rccm.201604-0799OC.