IN THE NAME OF GOD

Ventilator Induced Kidney Injury

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TABRIZ UNIVERSITY OF MEDICAL SCIENCES

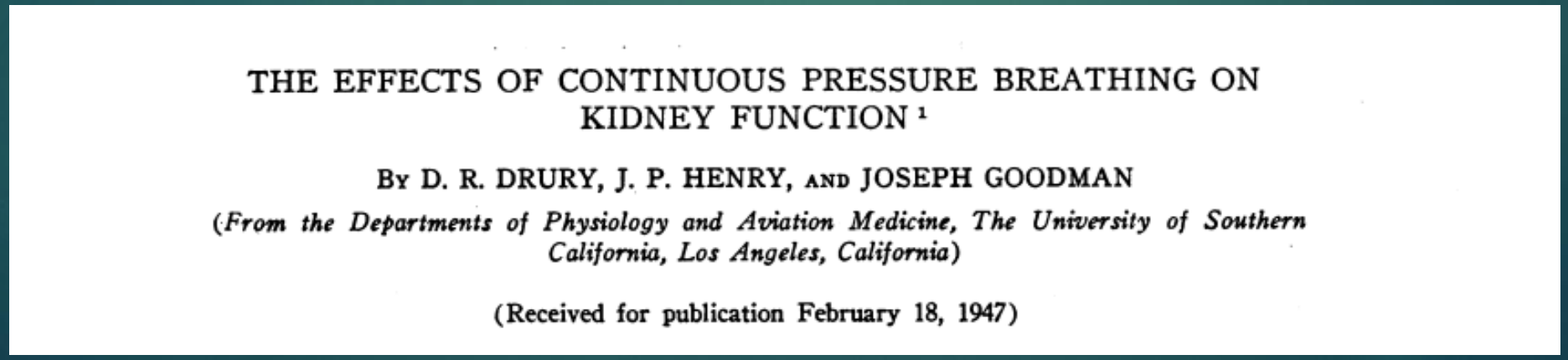
Introduction

- Mechanical ventilation is an independent risk factor for the development of acute kidney injury. AKI affects up to 29% of patients who are mechanically ventilated.
- Conversely, AKI independently doubles the risk of respiratory failure requiring mechanical ventilation.
- As a result, roughly 75% of patients with AKI will be exposed to mechanical ventilation concomitantly during their ICU stay.
- The consequences of combined AKI and the need for mechanical ventilation are severe, as mortality has been shown to increase 4-6-fold compared to AKI or respiratory failure alone.
- Moreover, AKI during mechanical ventilation is associated with prolonged hospitalizations, increased ICU stays, and increased ventilator days.

Vemuri et al., 2022 ; van den Akker et al., 2013

Historical Note

- The use of ventilatory assistance can be traced back to biblical times. However, mechanical ventilators, in the form of negative-pressure ventilation, first appeared in the early 1800s. Positive-pressure devices started to become available around 1900 and today's typical intensive care unit (ICU) ventilator did not begin to be developed until the 1940s.
- Over 75 years ago, Drury et al. demonstrated that increasing levels of continuous positive airway pressure (CPAP) correlated inversely with urea clearance in healthy volunteers (Drury et al., 1947).



THE EFFECTS OF CONTINUOUS PRESSURE BREATHING ON KIDNEY FUNCTION [1]

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OBSERVATIONAL STUDY

OPEN

Association Between Acute Kidney Injury During Invasive Mechanical Ventilation and ICU Outcomes and Respiratory System Mechanics

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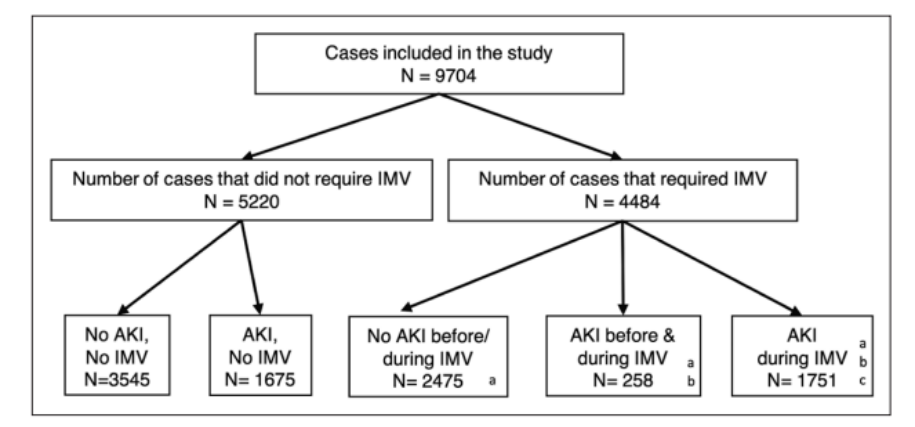
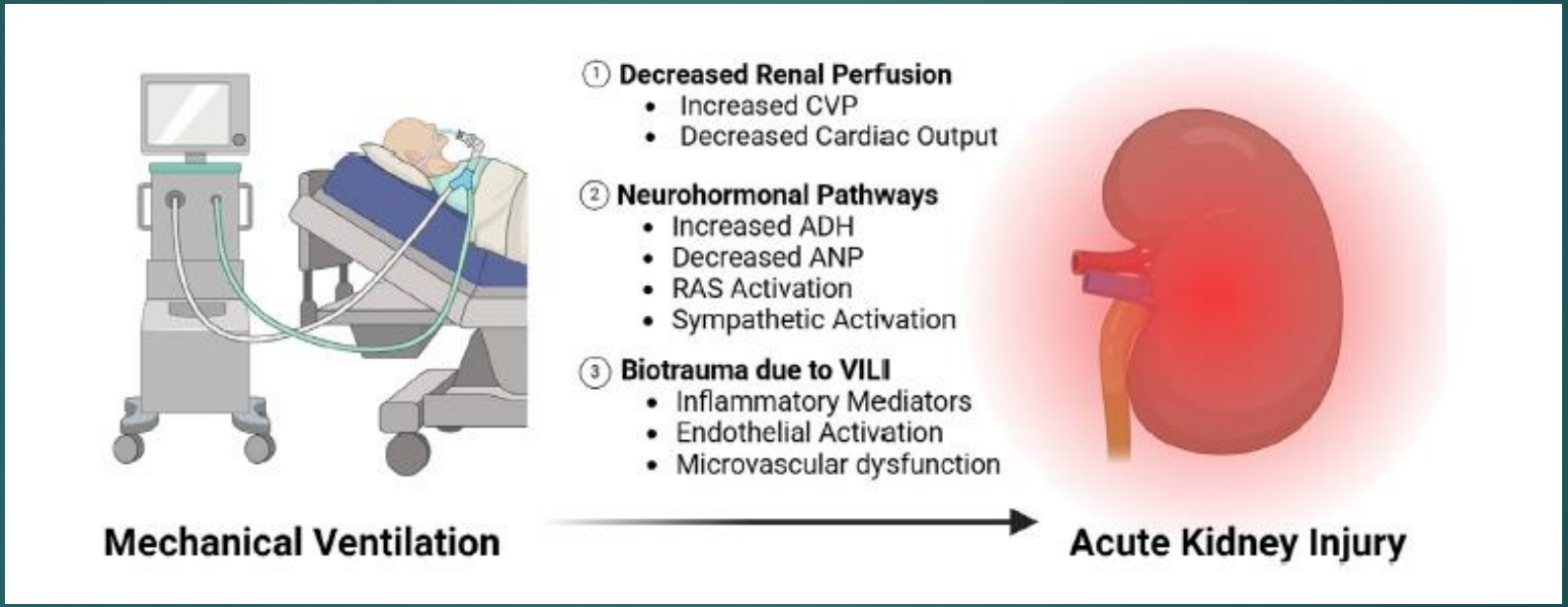
OBJECTIVES: Compare ICU outcomes and respiratory system mechanics in patients with and without acute kidney injury during invasive mechanical ventilation.

DESIGNS: Retrospective cohort study.

- This retrospective cohort study included all adult patients admitted to medical and surgical ICUs at all hospitals sites within the University of California, SanDiego (UCSD) Health System between January 1, 2014, and November 30, 2016.
- We conducted a more recent analysis that found that the incidence of AKI during mechanical ventilation remains incredibly high at 39%.
- Interestingly, our study also found that most AKI cases occurred1–3 days after mechanical ventilation was initiated, which is suggestive of a potential causal relationship.



Mechanisms of AKI due to mechanical ventilation



Mechanisms of AKI due to mechanical ventilation

1. The systemic hemodynamic effects of positive pressure ventilation.

- An increase in intrathoracic pressure during mechanical ventilation led to decreases in venous return and cardiac output, which led to a decrease in renal perfusion.
- positive pressure also impacts renal perfusion through increased central venous pressure (CVP) and venous congestion. Renal perfusion pressure is equal to mean arterial pressure (MAP)–CVP. Therefore, as CVP is increased with positive pressure ventilation, renal perfusion will be decreased fora given MAP (Sun et al., 2022).

Mechanisms of AKI due to mechanical ventilation

2. Activation of Neurohormonal pathways

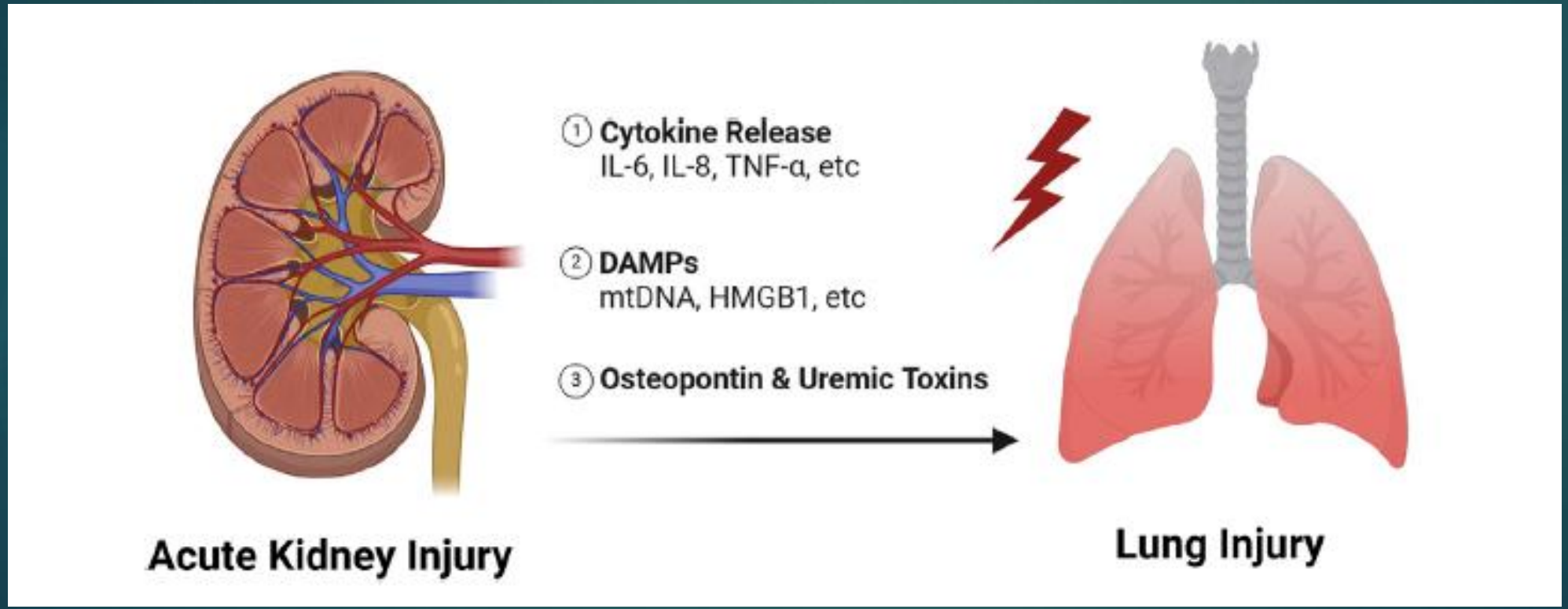
- Neurohormonal pathways activated by positive pressure breathing have also been implicated in the alterations in kidney function that occur during mechanical ventilation.
- Fewell and Bond were among the first to implicate these mechanisms by showing that renal denervation prior to positive pressure ventilation improved urine output and GFR (Fewell and Bond, 1979).
- In subsequent studies, activation of the renin angiotensin system (RAS) (Kaczmarczyk et al., 1992),
- increased release of antidiuretic hormone (ADH) (Bark et al., 1980; Farge et al., 1995),
- decreases in atrial natriuretic peptide (ANP) (Ramamoorthy et al., 1992) were found to occur during mechanical ventilation in both human and animal models.

Mechanisms of AKI due to mechanical ventilation

3. inflammatory crosstalk between the injured lung and kidney

- In a landmark study, Imai et al. demonstrated that serum from rabbits who developed ventilator induced lung injury (VILI) due to high tidal volume ventilation caused renal tubule cell apoptosis in vitro and in healthy rabbits in vivo (Imai et al., 2003).
- These findings provided a direct link between systemic inflammatory mediators generated by lung injury and downstream renal consequences (i.e., biotrauma).
- Subsequent studies from our group and others found that VILI leads to
- endothelial inflammation (Hepokoski et al., 2017) and
- microvascular dysfunction in the kidney (Choi et al., 2003).

Mechanisms of lung injury due to AKI



Prevention and Treatment of AKI in Patients on Mechanical Ventilation

1. Choosing optimal ventilator settings: Low Tidal Volume

- The current approach to ventilator management is based on the 2000 Acute Respiratory Distress Syndrome Network (ARDSNet) trial which showed that patients with ARDS treated with open lung protective ventilation (low tidal volumes and high PEEP) had an increase in survival and renal failure free days.
- The seminal trial of 861 subjects with ALI/ARDS randomized patients to receive tidal volumes of 12 or 6 ml/kg of ideal body weight in order to determine the effect of lower tidal volumes on mortality. The trial was stopped early when mortality was found to be lower in the low tidal volume group (31 vs. 39.8%, p = 0.007).

Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med 2000;342: 1301–1308.

Prevention and Treatment of AKI in Patients on Mechanical Ventilation

1. Choosing optimal ventilator settings:PEEP

- While low tidal volume ventilation is clearly renal protective, there is some controversy regarding the optimal PEEP.
- As reviewed above, pre-clinical and clinical studies have suggested that high PEEP induces renal dysfunction, yet other studies have
- shown no correlation between risk of AKI and PEEP (van den Akker et al., 2013; Almonacid-Cardenas et al., 2023; Basse et al., 2023).
- More recently, studies have shown that the driving pressure (plateau pressure-PEEP), which accounts for lung compliance, is a better predictor of patient outcomes than tidal volume or PEEP alone (Amato et al., 2015).
- However, the relationship between driving pressure and AKI has not been clearly established, and the optimal PEEP vs. driving pressure remains to be established.
- For now, low tidal volume ventilation with 6–8 cc/kg based on ideal body weight is universally employed for most patients, but optimal lung and kidney protective ventilator settings are likely not “one size fits all”.
- Studies focused on determining precision, patient-specific ventilator settings are ongoing (Beitler et al., 2022)

Prevention and Treatment of AKI in Patients on Mechanical Ventilation

2. counteracting the systemic hemodynamic effects of positive pressure via a combination of fluids and vasopressors.

- The amount of fluids vs. vasopressors and the optimal vasopressors for kidney protection have not been clearly established.
- Furthermore, the Fluids and Catheters Treatment Trial (FACTT) in 2006 showed that patients treated with a conservative fluid management strategy spent fewer days requiring mechanical ventilation, in addition to a non-significant trend towards lower dialysis requirements (Wiedemann et al., 2006).
- In terms of the type of fluid management, evidence suggests that balanced crystalloids decrease the need for renal replacement therapy or persistent renal dysfunction (Semler et al., 2018).

Prevention and Treatment of AKI in Patients on Mechanical Ventilation

2. counteracting the systemic hemodynamic effects of positive pressure via a combination of fluids and vasopressors.

- Norepinephrine is considered the first line vasopressor in adult critically ill patients,
- but recent studies have suggested that combination vasopressors, such as β-agonists with angiotensin II (Tumlin et al., 2018), may improve renal outcomes.
- The impact of specific vasopressors alone and in combination remains an active area of investigation.
- As noted previously, increasing CVP due to mechanical ventilation has a deleterious impact on renal perfusion and increasing CVP is associated with AKI (Sun et al., 2022). It is tempting to suggest that patients on mechanical ventilation should have a higher MAP goal to counteract the effects of high CVP.
- However, there is a paucity of data to support this notion currently and maintaining a MAP greater than 65 mmHg is generally believed to provide adequate renal perfusion.