Severe Cytokine Release Syndrome and Risk of Acute Kidney Injury in Patients With Hematologic Malignancies Undergoing CAR-T Cell Therapy: A Systematic Review and Meta-Analysis

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Introduction

Cytokine Release Syndrome (CRS) is a common complication of Chimeric Antigen Receptor (CAR) T-cell therapy and may contribute to Acute Kidney Injury (AKI) through inflammatory and hemodynamic mechanisms. Understanding the risk of AKI in the context of CRS is clinically important, as it may lead to treatment discontinuation, ICU admission, and worse outcomes.

Objective

To assess whether severe CRS is independently associated with increased risk of AKI in patients with hematologic malignancies undergoing CAR-T cell therapy.

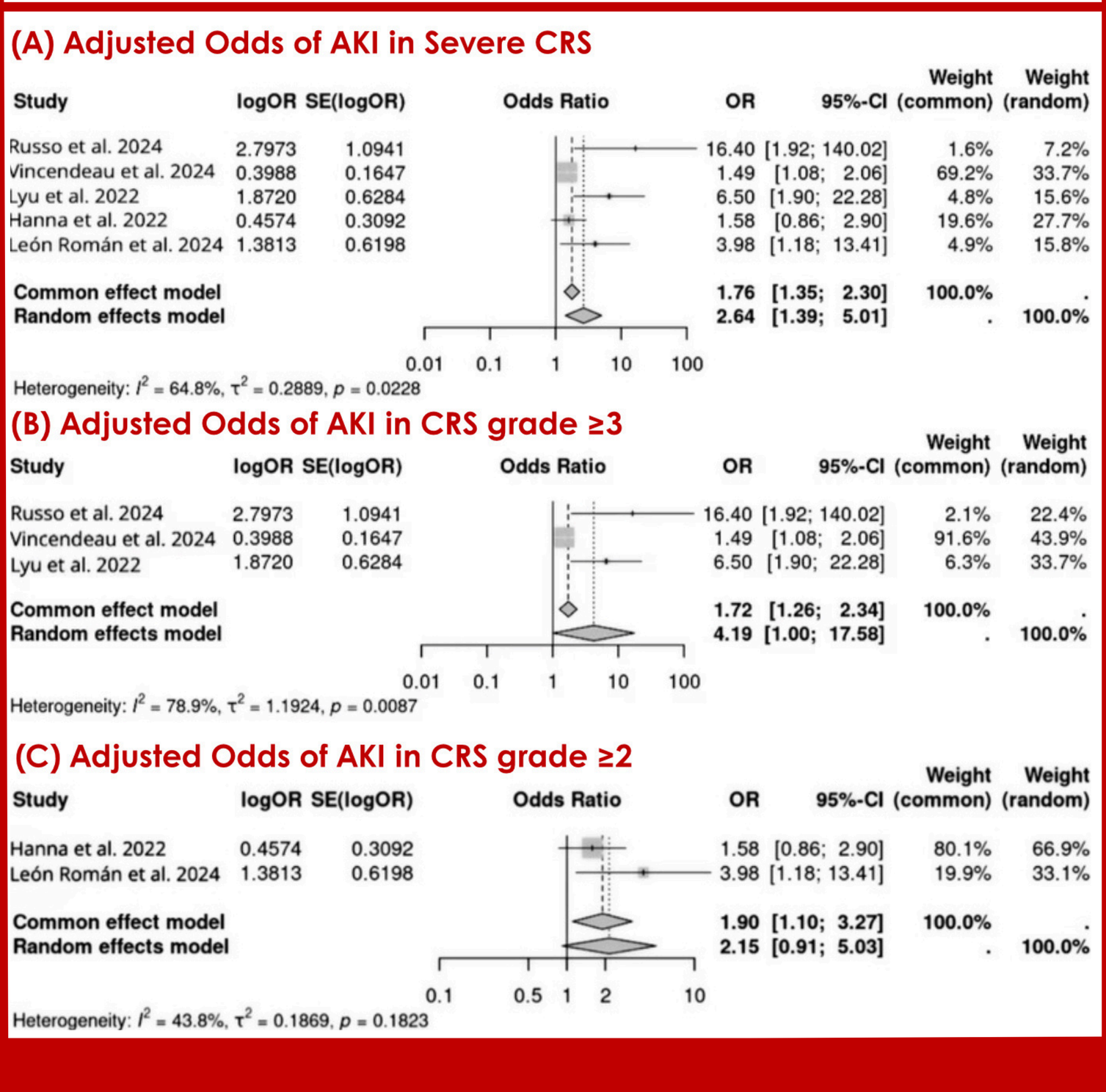
Methods

- We systematically searched PubMed and Google Scholar through May 2025 for studies evaluating the association between severe cytokine release syndrome (CRS) and acute kidney injury (AKI) in patients undergoing CAR-T cell therapy for hematologic malignancies.
- All studies used KDIGO 2012 definitions for AKI and ASTCT criteria for CRS grading.
- For this analysis, severe CRS was defined as CRS grade ≥2.
- A random-effects model was used to calculate pooled adjusted Odds Ratios (aOR) and 95% confidence intervals (CI).
- Subgroup analyses were performed using the CRS severity threshold (grade ≥2 and grade ≥3).
- Heterogeneity was assessed using the I^2 statistic. $p<0.05$ was considered statistically significant.

Results

- **Included Studies:** 5 retrospective cohort studies
- **Follow-up:** 1–12 months
- **Patients:** 613 adults (mean age 58.8 yrs) with hematologic malignancies undergoing CAR-T cell therapy
- **Main Finding:**
  Severe CRS was significantly associated with increased odds of AKI (aOR 2.64; 95% CI 1.39–5.01; p = 0.023, I^2 = 64.8%)
- **Subgroup Analysis:**
  CRS grade ≥3 → Significant association with AKI (aOR: 4.19, 95% CI: 1.00–17.58, p=0.009, I^2 = 78.9%)
  CRS grade ≥2 → No significant association with AKI (aOR: 2.15, 95% CI: 0.91–5.03, p=0.182, I^2 = 43.8%)

Fig 1. Adjusted Odds of AKI in Severe CRS



Conclusions

- Severe CRS is significantly associated with increased risk of AKI in patients with hematologic malignancies undergoing CAR T cell therapy.
- These findings highlight the need for vigilant renal monitoring and supportive care in patients experiencing severe CRS.
- Prospective studies are needed to establish predictive tools and treatment algorithms for CRS-related AKI, ultimately aiming to enhance overall outcomes in CAR-T recipients.

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