REAL-WORLD RISK OF ACUTE KIDNEY FAILURE AFTER SACUBITRIL/VALSARTAN VS ARB AMONG ADULTS ≥65 WITH HEART FAILURE

RWD 29

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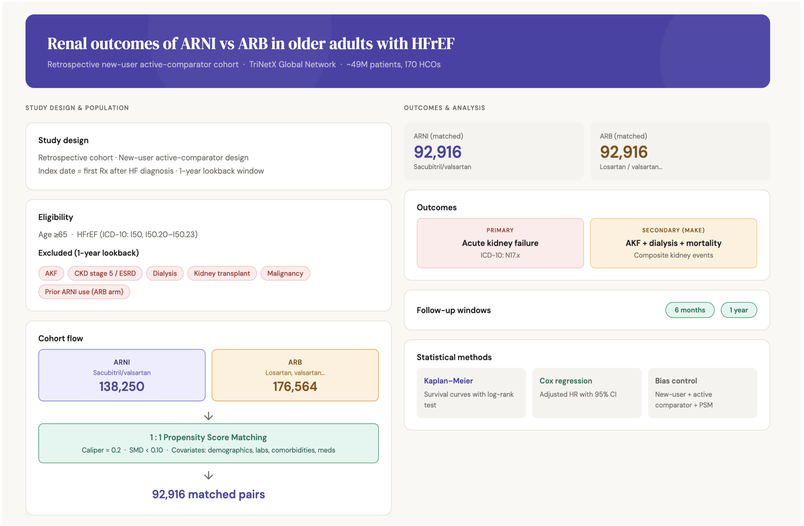
Background

Heart failure and renal dysfunction are deeply interconnected through cardiorenal syndrome, where dysfunction of one organ drives injury in the other. AKI occurs in up to 47% of patients hospitalized with acute decompensated heart failure[1] and affects approximately 20% of HF patients overall, serving as a strong independent predictor of in-hospital and 1-year mortality.[2] This vulnerability is amplified in elderly patients, where reduced renal reserve and comorbidity burden create a high-risk environment for renal events.[3] Although sacubitril/valsartan (ARNI) is guideline-recommended for HFrEF, real-world renal safety data in elderly patients remain limited, and worsening kidney function is a leading cause of dose reduction in clinical practice.[4]

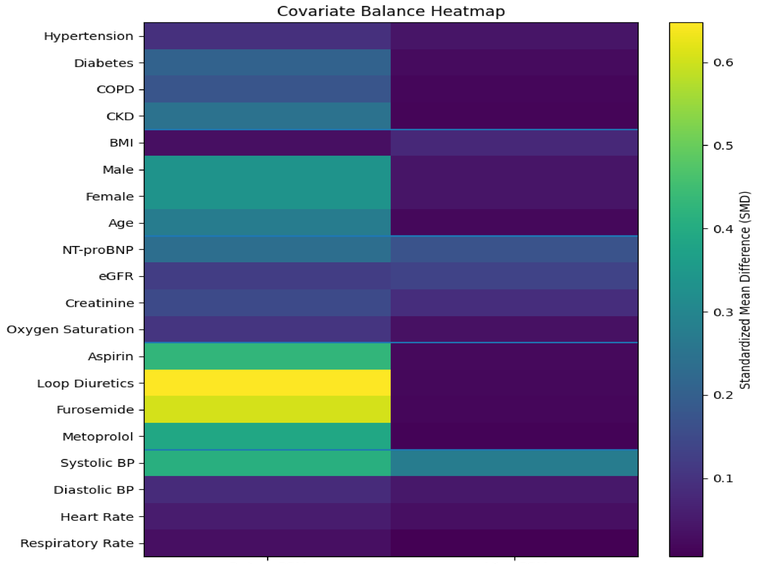
Objective: Comparative renal outcomes between ARNI and ARB in adults aged ≥65 remain unstudied. This study evaluated the real-world risk of acute kidney failure and major adverse kidney events following ARNI versus ARB initiation using a new-user active-comparator design with propensity score matching.

Methods



Result

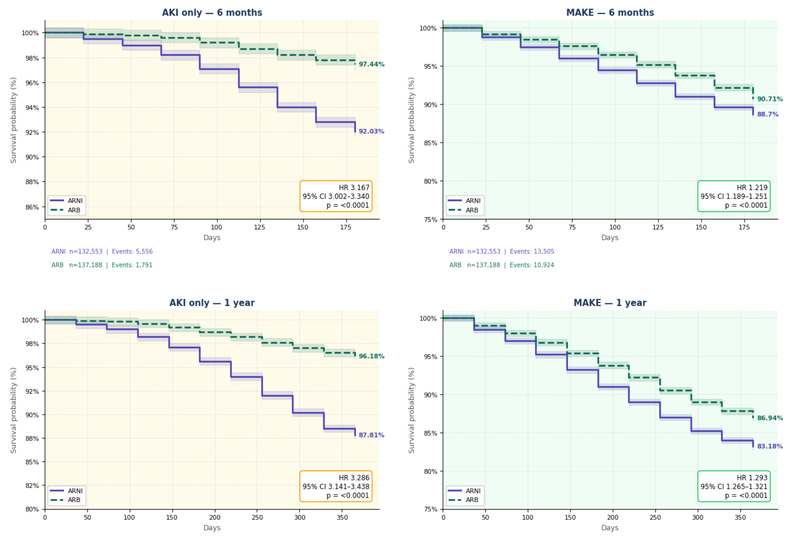
Figure 1. Visualizing Covariate Balance: ARNI vs. ARB Cohorts



Result

Figure 2. KM Curves for Survival Analysis

Kaplan-Meier analysis of renal outcomes in elderly HFrEF: acute kidney failure vs major adverse kidney events



Result

After 1:1 propensity score matching (92,916 pairs) and exclusion of pre-existing AKF, the analytic cohorts comprised 78,322 ARNI and 85,429 ARB users.

Primary outcome — Acute kidney failure: ARNI use was associated with significantly higher AKF risk at both follow-up periods. At 6 months, survival free from AKF was 92.03% (ARNI) versus 97.44% (ARB) (HR 3.167; 95% CI 3.002–3.340; p=0.0053), widening at 1 year to 87.81% versus 96.18% (HR 3.286; 95% CI 3.141–3.438; p=0.0016). Kaplan–Meier curves demonstrated early and sustained divergence from the index date, with the hazard ratio increasing from 3.167 at 6 months to 3.286 at 1 year.

Secondary outcome — MAKE composite: At 6 months, survival free from MAKE was 88.70% (ARNI) versus 90.71% (ARB) (HR 1.219; 95% CI 1.189–1.251; p<0.0001), with consistent findings at 1 year (HR 1.293; 95% CI 1.265–1.321; p<0.0001). The substantially attenuated MAKE hazard ratios compared with isolated AKF suggest partial attribution to outcome ascertainment differences, with the composite capturing the shared cardiorenal mortality burden across both groups.

Conclusion

1. In elderly HFrEF patients aged ≥65 years, sacubitril/valsartan (ARNI) was associated with a significantly higher risk of acute kidney failure compared with ARB across all follow-up periods (6 months to 5 years), with hazard ratios increasing monotonically from 3.167 to 3.610 (all p<0.0001).
2. Kaplan-Meier curves demonstrated early and sustained divergence from the index date, with the survival gap widening progressively over time suggesting a cumulative renal risk associated with ARNI initiation in this population.
3. When evaluated using a MAKE composite outcome, hazard ratios were substantially attenuated (HR 1.219 at 6 months; HR 1.293 at 1 year), reflecting the shared cardiorenal mortality burden inherent to elderly HFrEF patients independent of drug class.
4. Propensity score matching achieved excellent covariate balance across all observed covariates (all SMD <0.10), supporting the internal validity of the comparison.
5. Given the inherent cardiorenal vulnerability of elderly HFrEF patients, these findings underscore the importance of individualized therapy, baseline renal function assessment, and close monitoring of eGFR following ARNI initiation.

References

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