#AHA25

# Biomarkers in Cardiac Arrest: An Analysis from the Critical Care Cardiology Trials Network

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# DISCLOSURES

- None

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# BACKGROUND

- Neurological prognostication after cardiac arrest remains challenging despite current clinical tools (clinical exam, brain imaging, EEG, SSEPs)
- Neuron-specific enolase (NSE) is the only established, clinically approved blood-based biomarker for prognostication
- There is an unmet need for better prognostic tools that may be filled by additional biomarkers.
- In an initial exploratory proteomic phase, we identified **kynureninase (KYNU)** as a candidate marker (standard & LASSO regression)
- **KYNU** is a key enzyme in the kynurenine pathway, which has been shown to be triggered by inflammation following cardiac arrest

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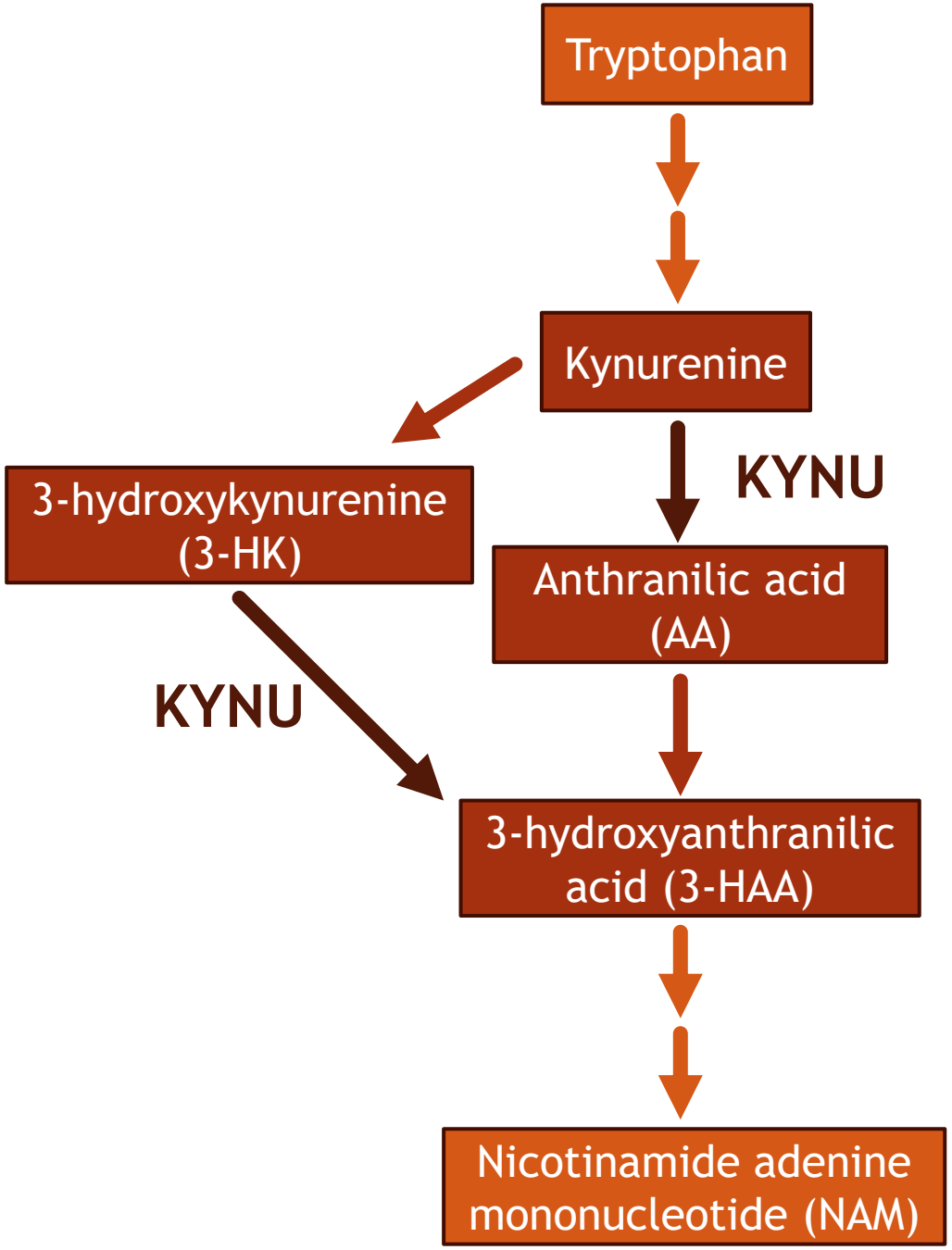
EEG = Electroencephalogram; SSEPs = somatosensory evoked potentials; LASSO = Least Absolute Shrinkage and Selection Operator

# BACKGROUND

- **KYNU** catalyzes conversion of kyn to anthranilic acid
- The kyn pathway is the main route for tryptophan catabolism
  - Pathway has important role in inflammation and immune responses
- **3-HAA** is correlated with deleterious outcomes in CV disease
  - Neurotoxic activity

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# METHODS

- Admissions to the Levine Cardiac Intensive Care Unit (CICU) at Brigham and Women's Hospital (Boston, MA) between 2017 and 2020 were enrolled in a biorepository with admission blood sampling
- KYNU was assayed using the Olink Proximity Extension Assay (PEA) [neurology panel] among 150 patients with cardiac arrest and available controls without presenting cardiac arrest (N=81)
- In addition, NSE was measured using the R&D Systems ELISA
- In-hospital neurological outcome was assessed using the modified Rankin score (mRS) through structured chart review by investigators blinded to the investigational biomarker results

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# RESULTS: Study Cohort

| | Cardiac Arrest | Control | p-value |
|---|---|---|---|
| Age, years | 66 (21-89) | 71 (21-89) | 0.38 |
| Female Sex | 34.0% | 39.5% | 0.71 |
| Out-of-Hospital Arrest | 51.3% | N/A | - |
| Shockable Rhythm | 57.3% | N/A | - |
| Targeted Temperature Control | 33.3% | N/A | - |
| Shock | 70% | 0% | - |

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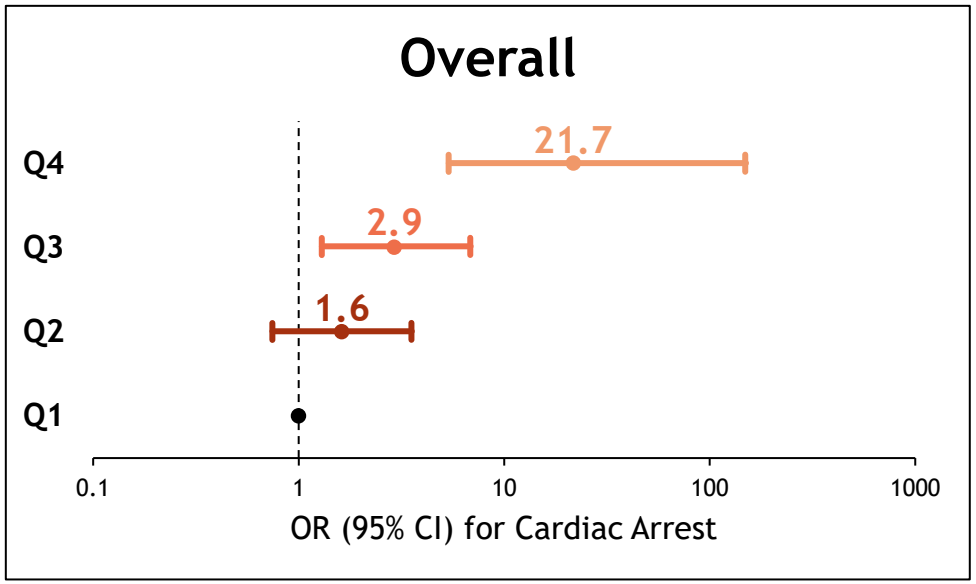
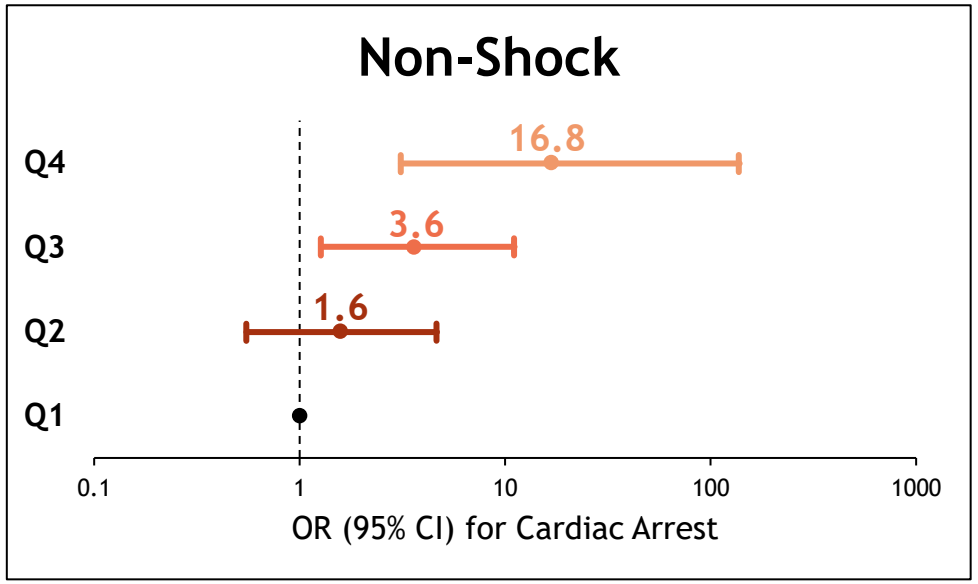
# RESULTS: Cardiac Arrest

- Higher KYNU concentrations significantly associated with presentation with cardiac arrest
- Strong graded relationship across KYNU quartiles with cardiac arrest in patients overall and among subgroup without cardiogenic shock

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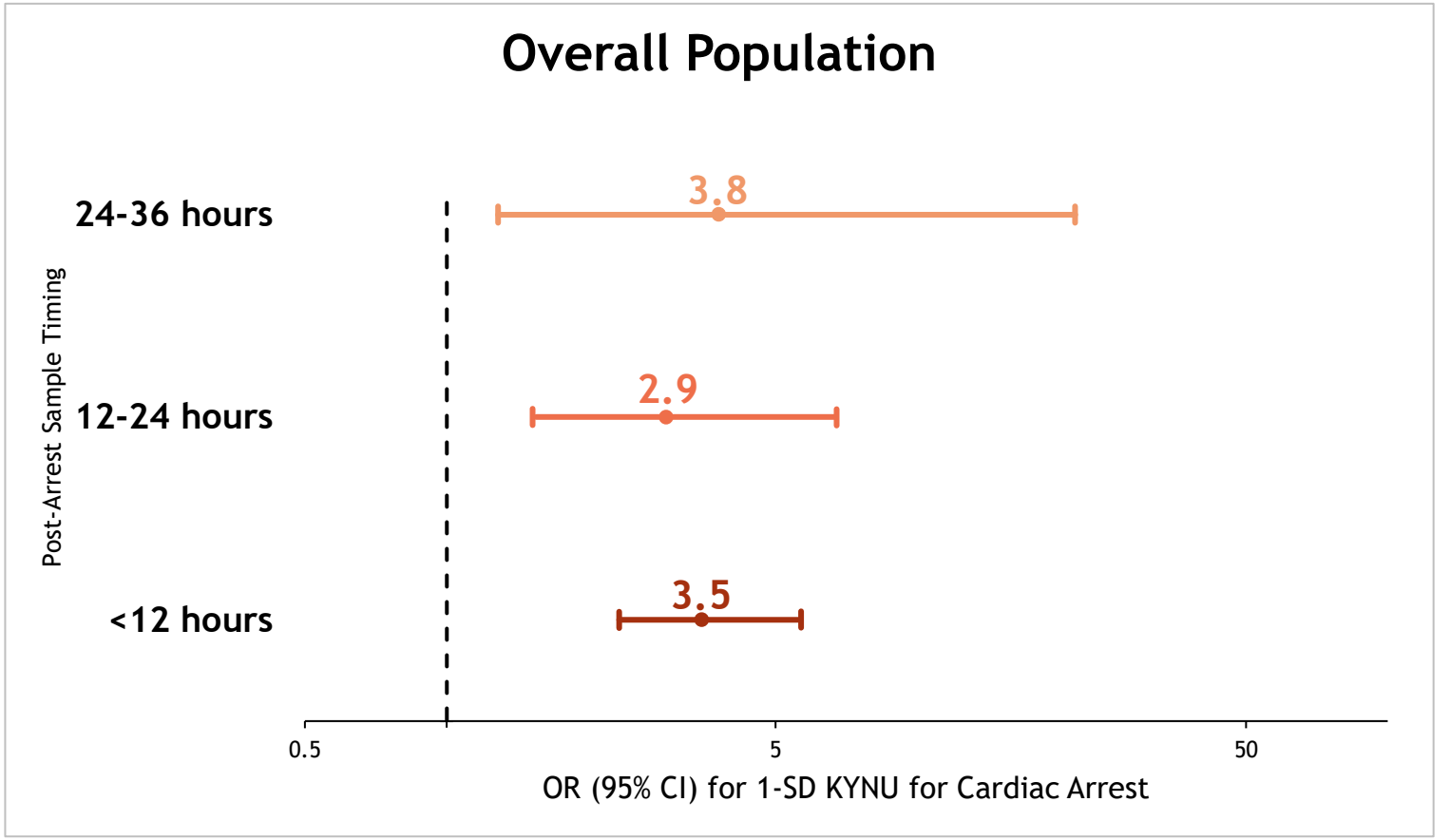
Association between KYNU and presenting cardiac arrest adjusted for age, sex, BMI, eGFR, and NSE

# RESULTS: Timing of Sampling

- KYNU maintains association with cardiac arrest even when measured early (<12h)

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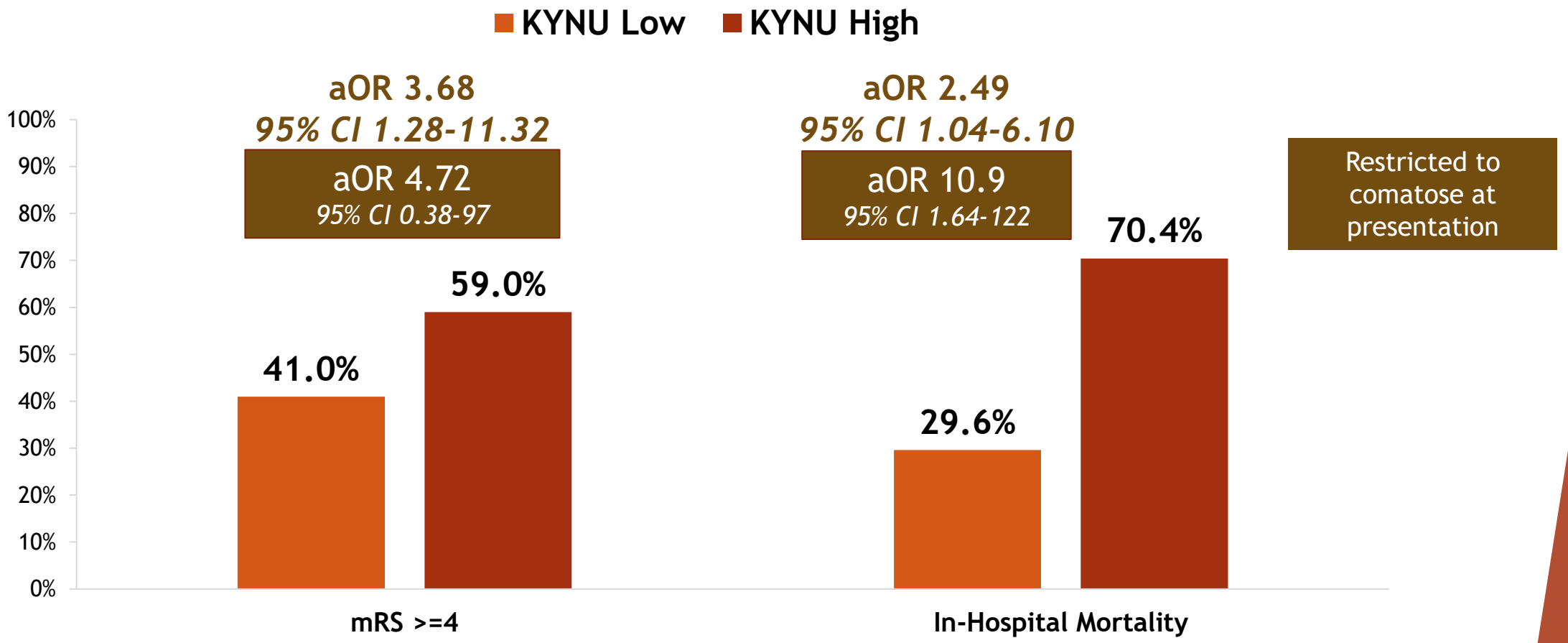
# RESULTS: mRankin and Mortality

- High KYNU associated with ~4-fold odds of poor neurological outcome at discharge (mRS≥4)
- Higher KYNU concentrations (>median) significantly associated with in-hospital mortality




aOR = adjusted OR; Analyses adjusted for age, sex, BMI, eGFR, and NSE

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# CONCLUSIONS

- Cardiac arrest is associated with higher KYNU concentrations among LCU patients, including early after presentation
- Among cardiac arrest patients, higher KYNU concentrations are associated with worse disability or death by hospital discharge
- KYNU is a candidate biomarker for neurological prognostication following cardiac arrest

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