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Biomarker-Based Heart Failure Risk Stratification In Patients With Atherosclerotic Cardiovascular Disease: Observations From HPS3/TIMI-55-REVEAL

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Disclosures

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Background

- The prevalence of heart failure (HF) is increasing, including in patients with atherosclerotic cardiovascular disease (ASCVD)
- Cardiovascular disease guidelines have placed increasing emphasis on risk-guided HF prevention
- Circulating biomarkers reflecting pathways implicated in HF may improve HF risk assessment in patients with stable ASCVD

Methods

Study Population & Biomarker Testing

- **HPS3/TIMI 55-REVEAL** was a randomized, double-blind, placebo-controlled trial of the CETP inhibitor anacetrapib in patients with stable ASCVD
- We performed a nested prospective biomarker study using blood samples obtained at randomization (n=29,673)
- We measured the following biomarkers (Roche Diagnostics):
 - High-sensitivity troponin T (hsTnT)
 - N-terminal pro-B-type natriuretic peptide (NT-proBNP)
 - Growth differentiation factor-15 (GDF-15)



Methods

Statistical Methods

- We calculated KM event rates of hospitalization for heart failure (HHF) at 4 years post-randomization for each decile of baseline biomarker concentration
- HRs adjusted for covariates of *a priori* clinical relevance to HHF risk (based on a prior analysis from TRA 2P-TIMI 50)
→ age, prior HF, hypertension, diabetes mellitus, eGFR <60, body-mass index, and polyvascular disease
- Discrimination assessed using Harrell's c-index

Results

Hospitalization for Heart Failure

hsTnT

$P_{\text{trend}} < 0.001$

Median concentration (IQR):
 9.8 ng/L (6.9-14.2)

NT-proBNP

$P_{\text{trend}} < 0.001$

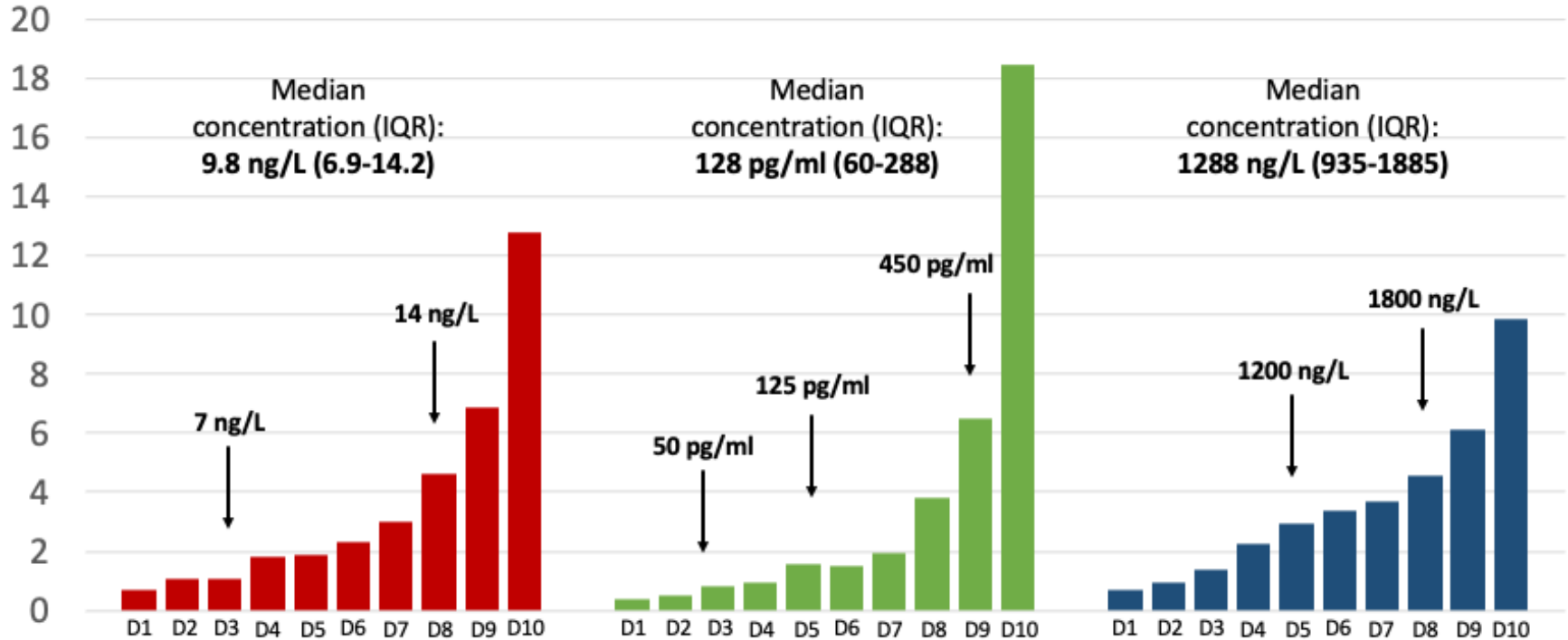
Median concentration (IQR):
 128 pg/ml (60-288)

GDF-15

$P_{\text{trend}} < 0.001$

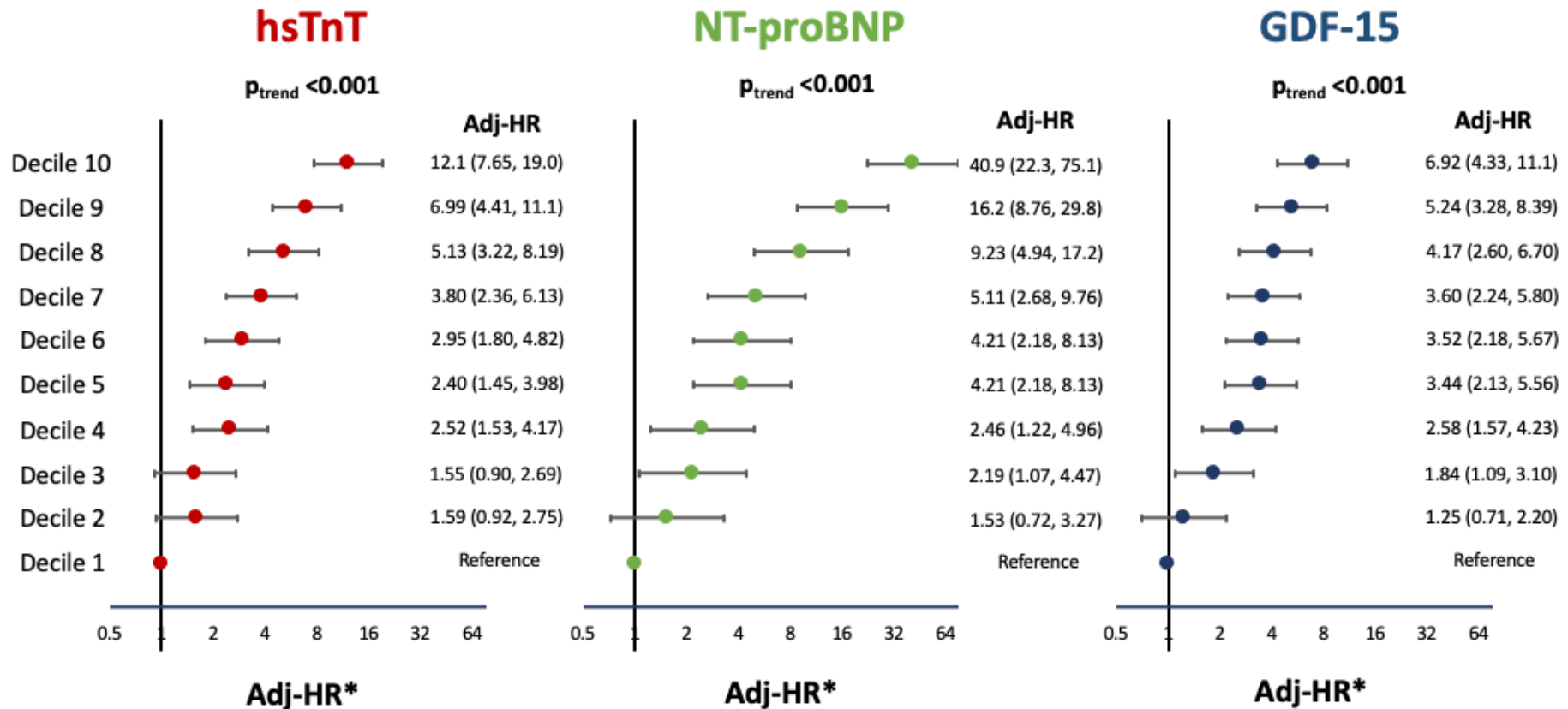
Median concentration (IQR):
 1288 ng/L (935-1885)

Hospitalization for HF at 4 years



Results

Hospitalization for Heart Failure



*Adjusted for age, h/o HF, DM, polyvascular disease, eGFR <60, BMI, HTN



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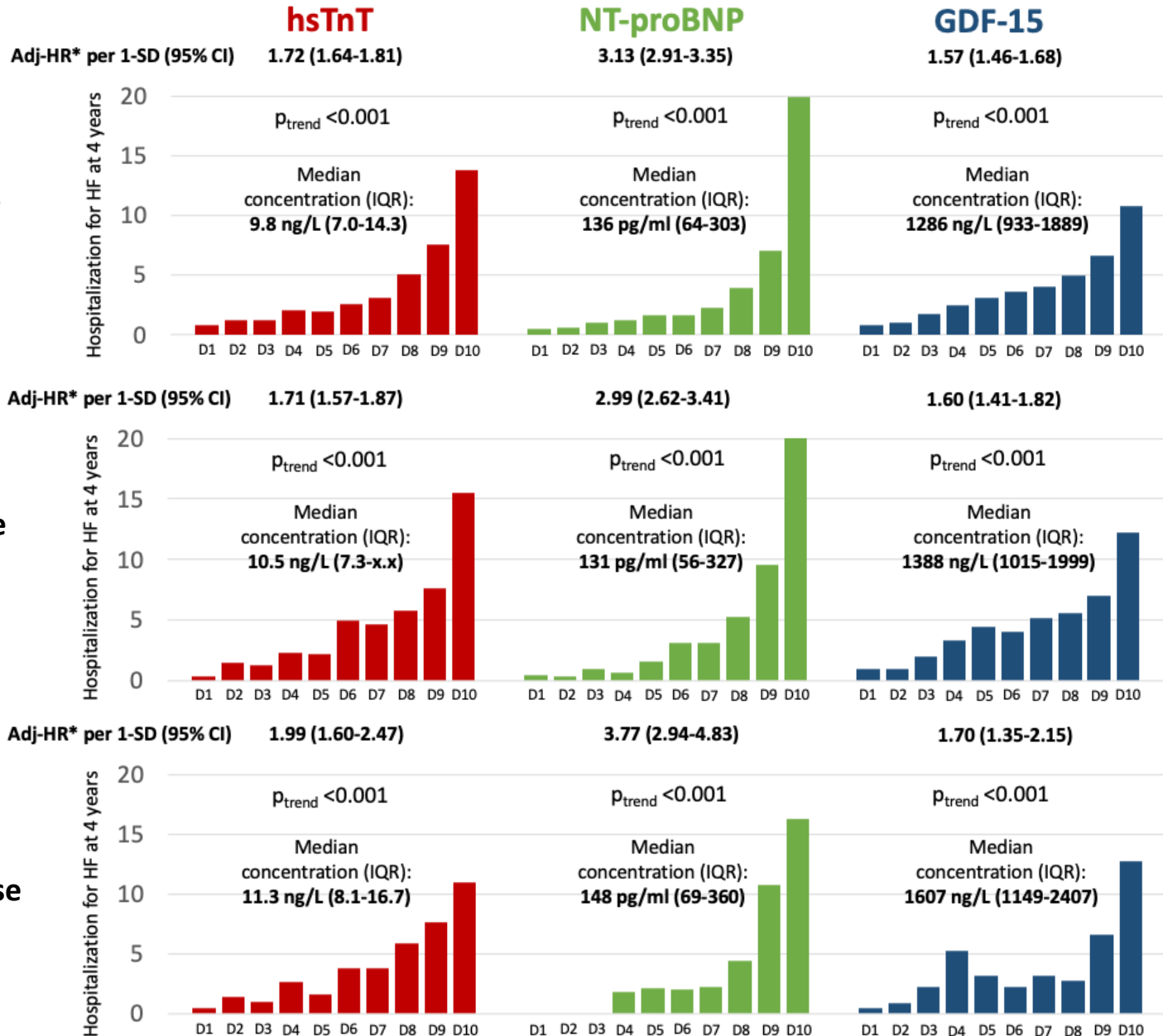
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Subgroups

**Coronary Heart Disease
(n=25,974)**

**Cerebrovascular Disease
(n=6,615)**

**Peripheral Arterial Disease
(n=2,350)**





Results

- When added to a multivariable Cox regression model of clinical risk indicators,* these 3 biomarkers significantly improved the prognostic performance of the model:

C-index 0.74 → C-index 0.85 (p<0.001)

- The gradients of HHF risk were consistent in patients randomized to anacetrapib vs. placebo (no interaction)

*Clinical risk indicators: age, prior HF, hypertension, diabetes mellitus, eGFR <60, body-mass index, and polyvascular disease





Conclusions

- In patients with stable ASCVD, biomarkers of myocardial injury, hemodynamic stress, and oxidative stress provide incremental information for the prediction of HHF
 - ❑ Continuous graded relationship
 - ❑ Independent and additive to major clinical risk factors
 - ❑ Consistent across ASCVD subtypes
- Future studies should address whether these patients are more likely to benefit from emerging HF preventive therapies

