



Heart failure risk assessment using biomarkers in patients with atrial fibrillation – Analysis of 32,041 patients from the COMBINE-AF study

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AF and HF



- HF events are the **most common cardiovascular events in patients with AF**
- **Accurate risk assessment for HF** is clinically important and **may enable early treatment**
- **Natriuretic peptides (e.g., NTproBNP)** are the only recommended biomarker for HF risk
- Previous studies studies have highlighted the **association of hs-cTnT and GDF-15 with HF in settings other than AF**

Objectives

To test the ability of **NTproBNP, hs-cTnT & GDF-15** to **improve the prediction of HF outcomes in patients with AF**

Assess the **importance of each biomarkers** in this setting

Methods



COMBINE-AF

Individual patient data meta-analysis
RCTs of DOAC vs. VKA

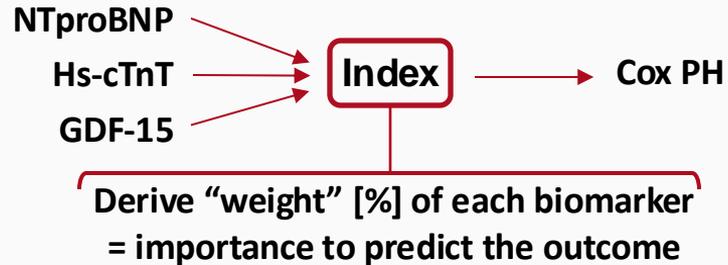
NTproBNP, hs-cTnT,
& GDF-15
available at baseline

32,041 patients

ARISTOTLE, ENGAGE AF-TIMI 48, RE-LY

Median follow-up
26.6 months

- **Composite outcome:** CV death (adjudicated) or hosp. for HF
- **Cox regression & weighted-quantile sum regression analysis**
→ addressing inter-biomarker correlation & ranks biomarkers according to contribution for predicting outcome



- **Adjustment:** sex, age, race, BMI, history of HF, HTN, DM, CAD, AF pattern (paroxysmal vs. persistent/permanent), valvular heart disease, CrCl, & each biomarker

Methods



Individual patient data meta-analysis
RCTs of DOAC vs. VKA

NTproBNP, hs-cTnT,
& GDF-15
available at baseline



32,041 patients

ARISTOTLE, ENGAGE AF-TIMI 48, RE-LY

Median follow-up
26.6 months

Baseline



N = 32,041

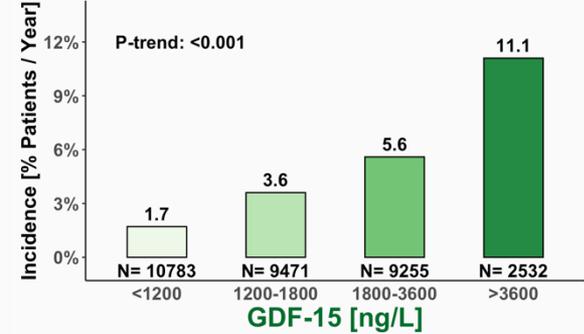
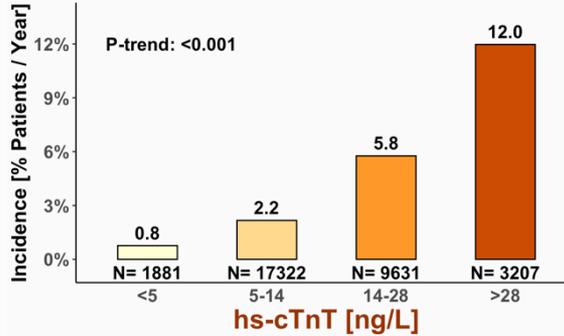
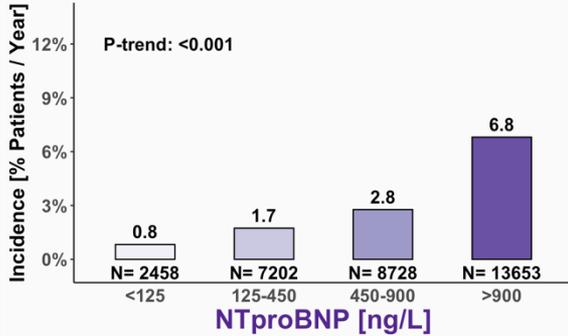
Age	71 (64-77)
Male	63.3%
Parox. AF	23.0%
Heart Failure	41.6%
LVEF \geq 50%	69.1% (N=21,493)
NTproBNP	760 (376-1351)
hs-cTnT	12 (8.1-18.5)
> 14ng/L	40.1%
GDF-15	1,495 (1,060-2,201)

all biomarkers ng/L, median (IQR)

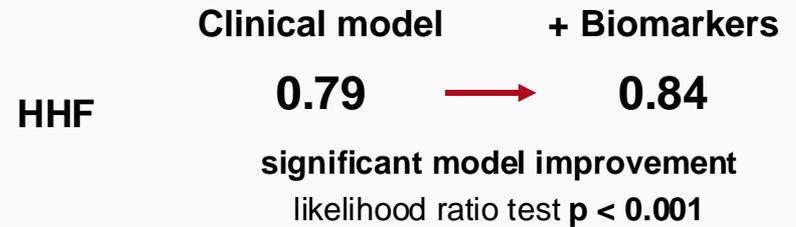
Biomarkers and Outcomes



CV Death / Hospitalization for Heart Failure



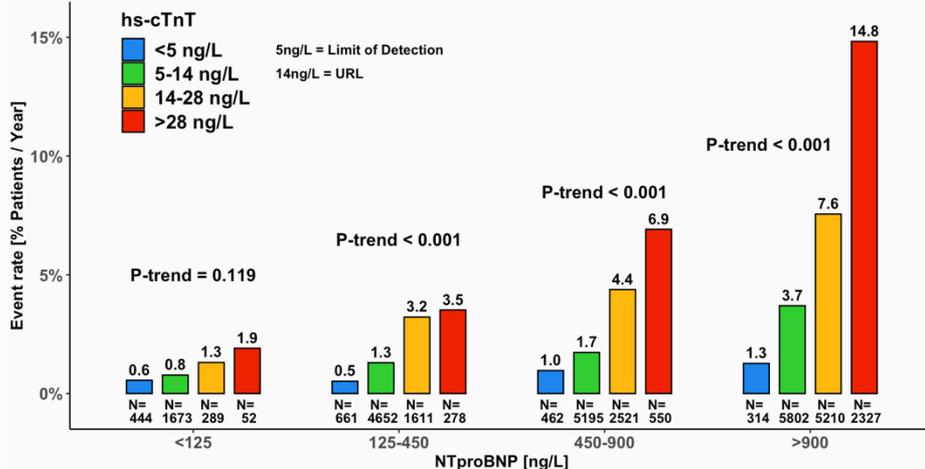
Predictive ability of biomarkers: Model fit by c-Index



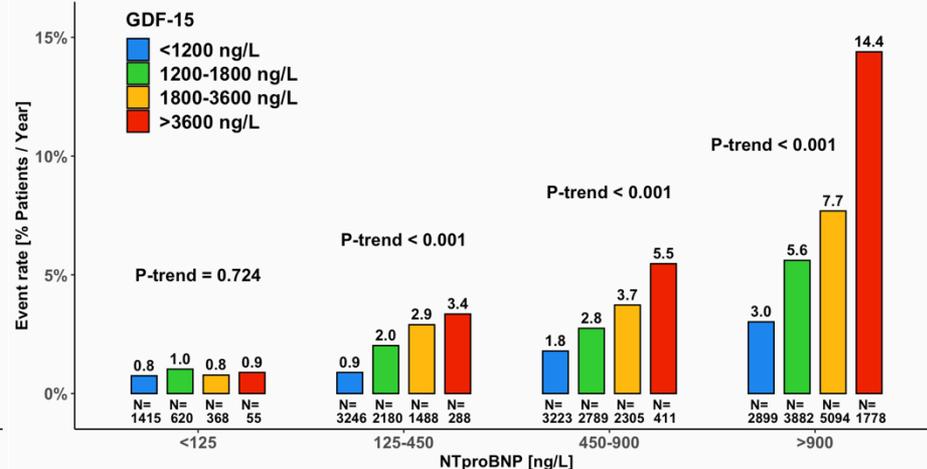
Absolute risk for dual-biomarkers strategy



Cardiovascular Death or Hospitalization for Heart Failure



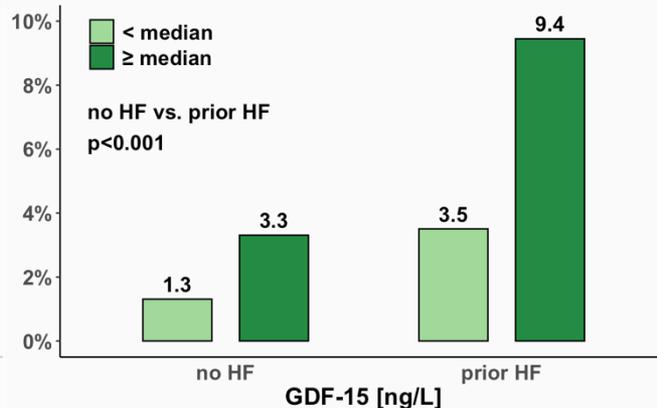
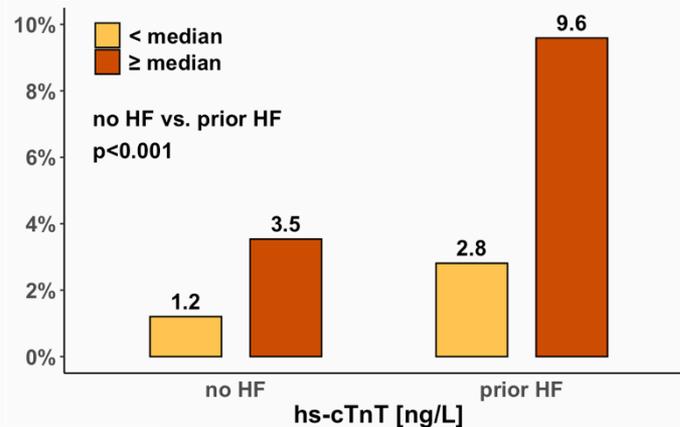
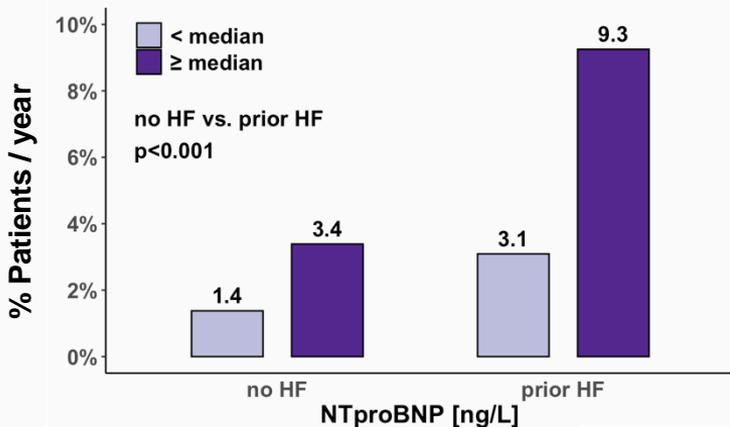
Cardiovascular Death or Hospitalization for Heart Failure



Stratification by prior Heart Failure



CV Death / Hospitalization for Heart Failure



Weighted Quantile Sum Regression Analysis

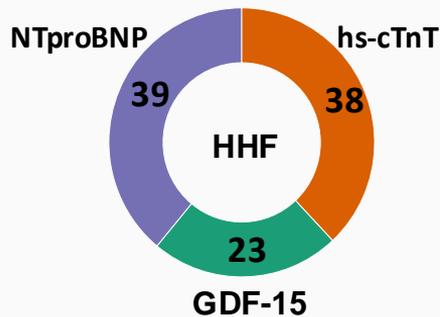
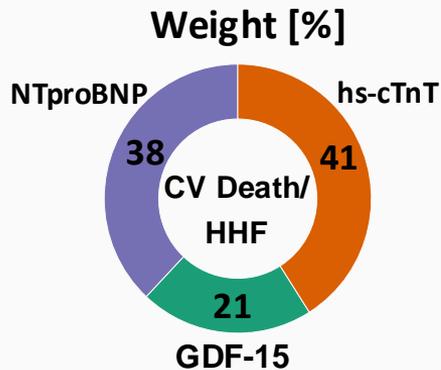


→ Address inter-biomarker correlation & rank contribution (weight) to predict the outcome

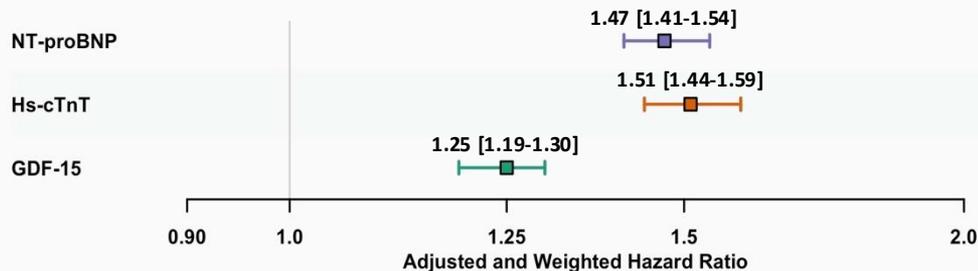
Correlation
NTproBNP
with...

hs-cTnT
 $r=0.40$
 $p<0.001$

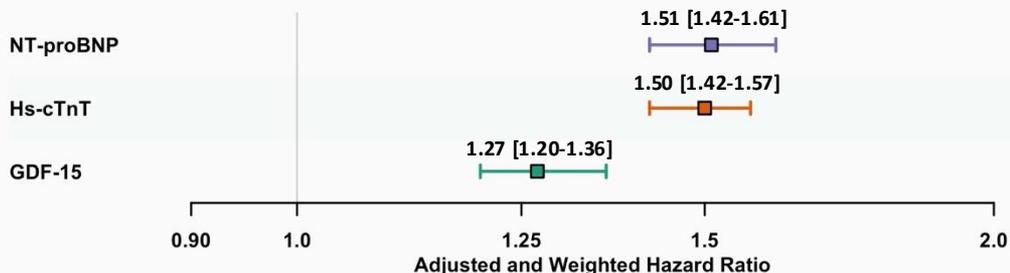
GDF-15
 $r=0.36$
 $p<0.001$



Cardiovascular Death or Hospitalization for Heart Failure



Hospitalization for Heart Failure



Conclusion



- **NTproBNP, hs-cTnT, and GDF-15** are **independently** associated with **HF outcomes** and improve HF risk assessment beyond clinical variables.
- This association is found in patients **with or without established HF** at baseline.
- Performance **to predict HF: hs-cTnT ~ NTproBNP > GDF-15.**

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Conclusion



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Heart Failure Risk Assessment Using Biomarkers in Patients With Atrial Fibrillation

Analysis From COMBINE-AF

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