

Relationship between cardiac biomarkers and major adverse cardiovascular events in DECLARE-TIMI 58

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Background

- Biomarkers of hemodynamic stress and myocardial injury are associated with the risk of CV death and heart failure (HF) in patients with atherosclerotic cardiovascular disease (ASCVD).
- Here, we explore the association between cardiac biomarkers (NT-proBNP and hsTnT) and ASCVD outcomes in patients with type 2 diabetes (T2DM).

Methods



- Nested biomarker study in DECLARE-TIMI 58
- Patients with T2DM and either multiple risk factors (MRF) (~60%) or established ASCVD (~40%)
- Serum levels of NT-proBNP and hsTnT (Roche Diagnostics) were measured in all patients with available blood samples at randomization (n = 14,565) in the TIMI Biomarker Laboratory
- **Primary Endpoint:** Major adverse cardiovascular events (MACE, i.e., the composite of myocardial infarction, ischemic stroke, and CV death)
- Multivariable adjusted Cox models & Spline regression models

Baseline Biomarker Concentrations

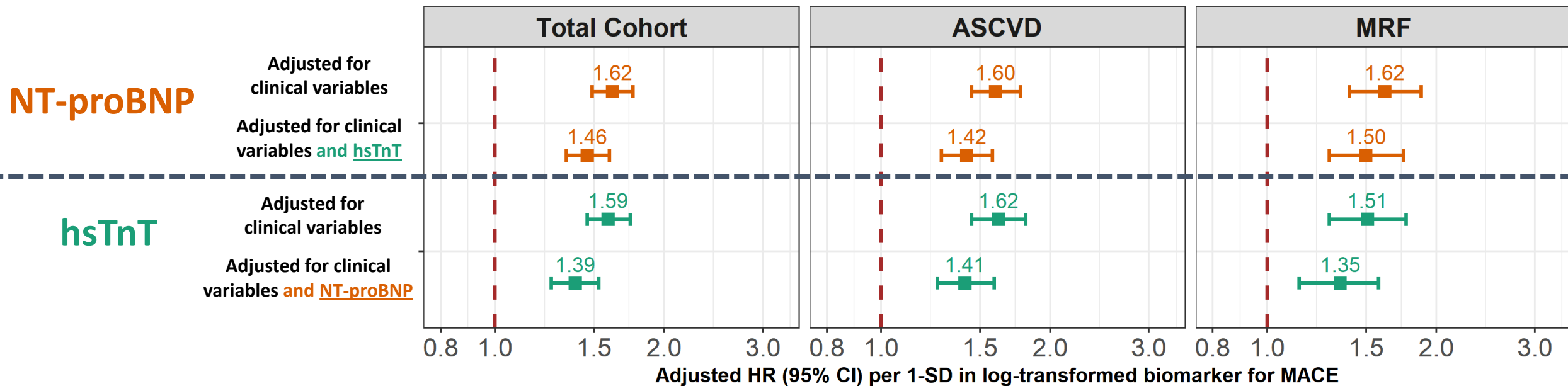
	NT-proBNP				hsTnT		
	N	Median (IQR)	>125 pg/ml	≥450 pg/ml	Median, IQR	≥6 ng/L	≥14 ng/L
Total Population	14,565	75 (35 - 165)	33%	8%	10.2 (6.9-15.5)	82%	30%
ASCVD	5,972	106 (48-241)	44%	13%	11.6 (7.7-17.7)	86%	38%
MRF	8,590	61 (30-122)	24%	5%	9.3 (6.4-14.0)	79%	25%

Baseline characteristics by biomarker quartiles

	NT-proBNP		hsTnT	
	Q1	Q4	Q1	Q4
Age (yrs)	61	66	62	66
Duration of diabetes (yrs)	10	12	10	13
ASCVD (%)	28	58	32	52
Prior HF (%)	3	23	5	18
Baseline eGFR (ml/min/1.73m ²)	93	82	94	80

All P-trend <0.05

Relationship between cardiac biomarkers and MACE within the placebo arm



Clinical covariates: Adjusted for age, sex, race, smoking, baseline eGFR, BMI, T2DM duration, insulin use, history of CAD, MI, ischemic stroke, PAD, HF, dyslipidemia & hypertension

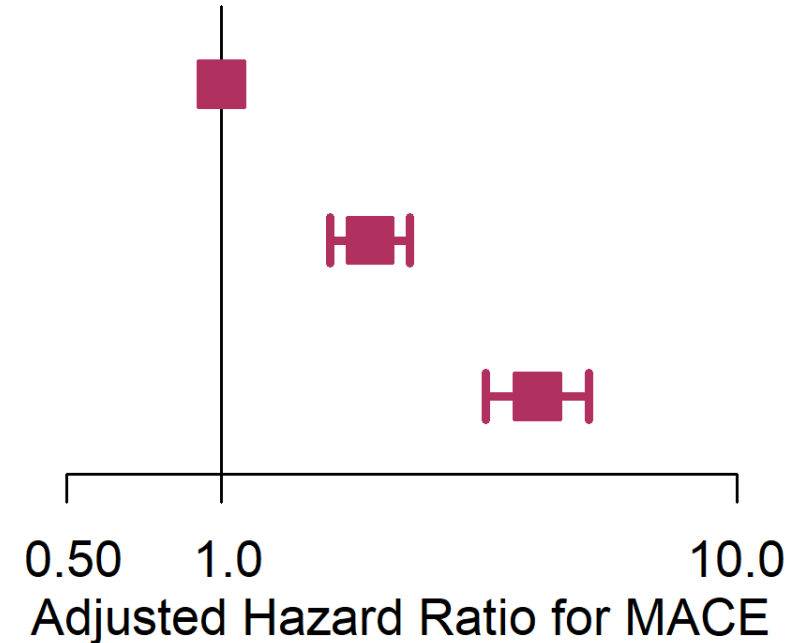
Multimarker Analysis



Biomarker Cut-Off
 hsTnT ≥ 14 ,
 NT-proBNP ≥ 450

Multimarker Analysis Adj. HR (95% CI)

0 Biomarkers Elevated	Reference
1 Biomarker Elevated	1.94 (1.62-2.32)
Both Biomarkers Elevated	4.10 (3.26-5.16)

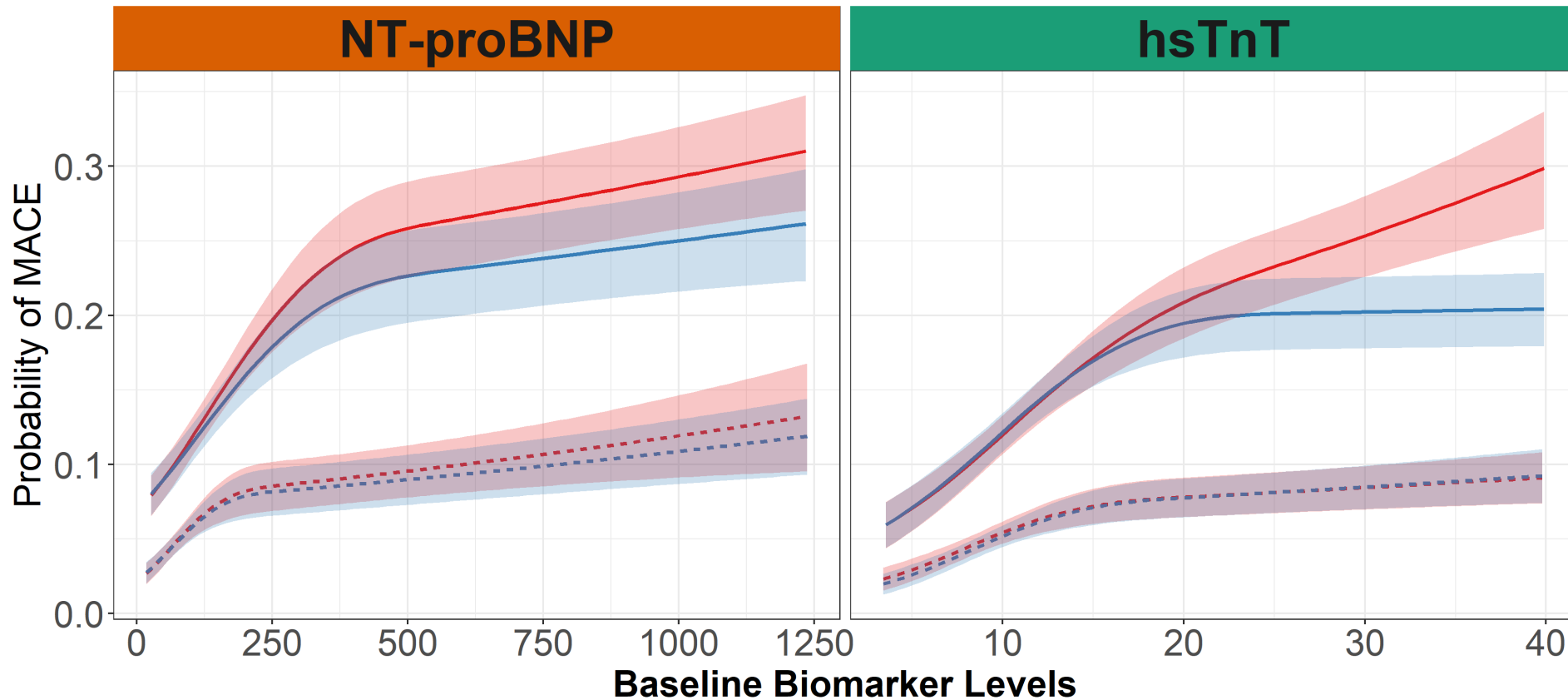


Adjusted for age, sex, race, smoking, baseline eGFR, BMI, T2DM duration, insulin use, history of CAD, MI, ischemic stroke, PAD, HF, dyslipidemia & hypertension

Risk of MACE by baseline biomarker levels and stratified by treatment arm



Subgroup — ASCVD — MRF **Treatment** — Placebo — Dapagliflozin



Conclusion

- **In patients with T2DM both with and without ASCVD, higher baseline NT-proBNP or hsTnT levels identified patients at increased risk of MACE.**
- **The difference in MACE rates between dapagliflozin and placebo tended to be more pronounced in ASCVD patients with higher baseline NT-proBNP or hsTnT levels.**