NT-proBNP, Body Mass Index, and Heart Failure Risk: A Pooled Analysis of SAVOR-TIMI 53, DECLARE-TIMI 58, and CAMELLIA-TIMI 61

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BACKGROUND
- Obesity = well-established risk factor for HF
- NT-proBNP = robust prognostic marker of future HF risk
  → recommended by clinical GLs for HF risk stratification
- NT-proBNP concentrations ↓ in obesity, despite ↑ HF risk
- HF risk as a function of BMI across NT-proBNP categories is incompletely defined, esp. for BMI ≥30 kg/m²

METHODS
- Population = pts enrolled in SAVOR-TIMI 53 (pbo only), DECLARE-TIMI 58 (pbo only for prognostic assoc.), and CAMELLIA-TIMI 61 with available baseline NT-proBNP
- Outcome = Hospitalization for Heart Failure (HHF)
- NT-proBNP was categorized by previously established thresholds (<125, 125-<140, and ≥140 pg/mL)
- Cox regression models were used to examine associations between NT-proBNP and HHF across BMI with adjustment for: age (cont.), sex, HTN, DM, eGFR (cont.), smoking status, established CV dz, prior HF Hx
- Rx interaction of dapagliflozin vs. pbo assessed across relevant categories of BMI and NT-proBNP

RESULTS (Continued)
- Baseline NT-proBNP was ↓ in pts w/ ≥1 BMI with a HHF event (median NT-proBNP for BMI ≥40 vs. <30: 366 vs. 723 pg/mL, p<0.001)
- There was a graded association between ↑ BMI and ↑ rate of HFH within each NT-proBNP group (p-trend<0.001 for each; Fig 1; Table 2) Notably, obese pts w/ a ≤low-level elevation in NT-proBNP (125-<450 pg/mL) had a meaningful absolute risk of HFH over 2y
- Adjusted HRRs also ↑ in a graded fashion w/ each BMI in each NT-proBNP stratum (p-trend<0.001 for each; Fig 2), with a >3-fold ↑ in HFH risk across BMI in those with low-level elevation in NT-proBNP
- All prognostic assoc. were consistent in those w/ and w/o prior HF
- Among pts w/ low-level elevation in NT-proBNP (125-<450 pg/mL) in DECLARE, there was ↑ absolute benefit w/ dapagliflozin vs. pbo at higher BMI (ARR for BMI ≥40 vs. <30: 7.2% vs. 0.8%; Fig 3)
- Only 5% of DECLARE pts w/ NT-proBNP ≥450 pg/mL had BMI≥30 (18% of all events), insufficient to support interaction testing

CONCLUSIONS
For any given range of NT-proBNP, the risk of HFH was significantly higher among those with higher BMI
Obese pts w/ low-level elevation of NT-proBNP (125-<450 pg/mL) had significantly ↑ event rate & HHF
In pts with NT-proBNP 125-<450 pg/mL, dapagliflozin reduced the risk of HFH with a pattern of ↑ ARR and ↑ RRR for HFH as BMI ↑
These findings showcase the importance of considering BMI in interpreting the risk associated with NT-proBNP concentrations for HF risk stratification

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