Interplay Between Heart Failure Events, New-Onset Diabetes, and Finerenone in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

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BACKGROUND/OBJECTIVE

- Diabetes is a major risk factor for HF, but whether HF events contribute to new-onset diabetes is less understood.
- HF events trigger neurohormonal, and metabolic stress, potentially leading to insulin resistance and dysglycemia.
- Finerenone reduces new-onset diabetes in HFmrEF/HFpEF, but the mechanisms remain uncertain.
- We aimed to study:
  - The association between HF events and new-onset diabetes.
  - Whether reductions in HF events mediate finerenone's benefits on diabetes incidence in the FINEARTS-HF trial.

METHODS

FINEARTS-HF: global RCT of finerenone vs. placebo in HFmrEF/HFpEF.

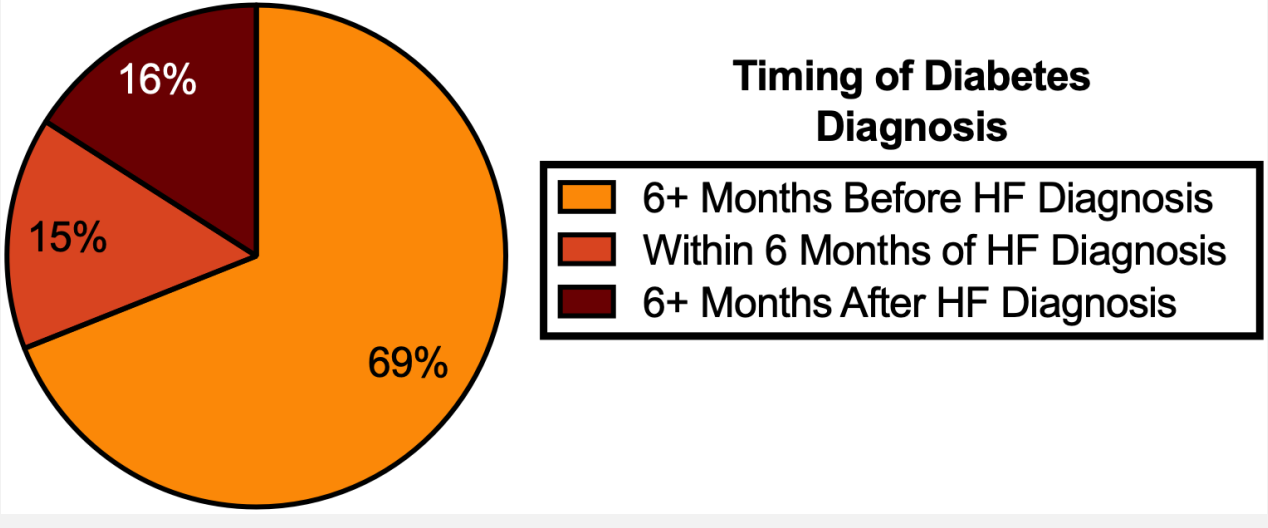
- Temporal relationship between HF diagnosis and self-reported diabetes at baseline.
- Trajectories in HbA1c around worsening HF events (repeated-measures regression, restricted cubic splines).
- Cox models comparing incidence of diabetes after vs. before HF events.
- Cox models assessing whether the reduction in HF events with finerenone accounted for its effect on new-onset diabetes.

- **New-onset diabetes:** ≥2 HbA1c ≥6.5% *or* new glucose-lowering therapy (excluding SGLT2i).
- **HF event:** hospitalization or urgent visit.

RESULTS

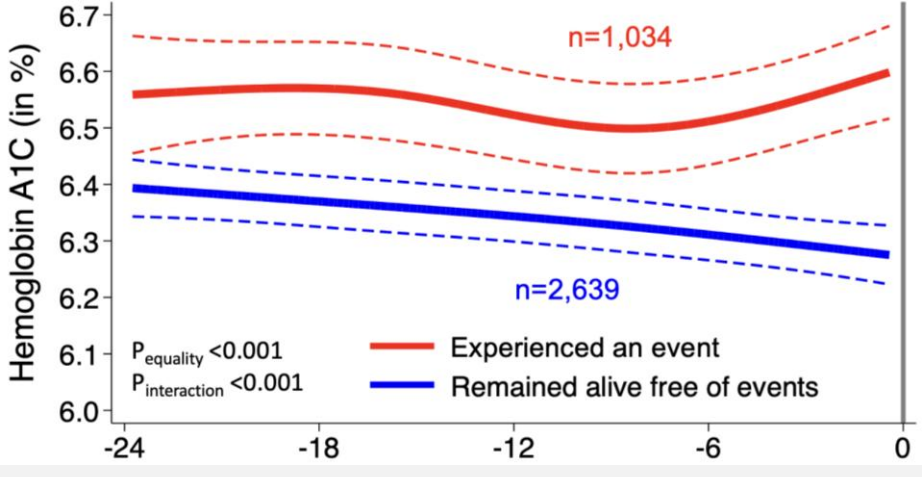
- 6,001 participants enrolled in FINEARTS-HF. 2,439 (40.6%) had diabetes at baseline. Among them, the relative timing of diabetes and HF diagnoses could be determined in 2,412 patients.

Relative Timing of Diabetes and HF Diagnoses, at Baseline

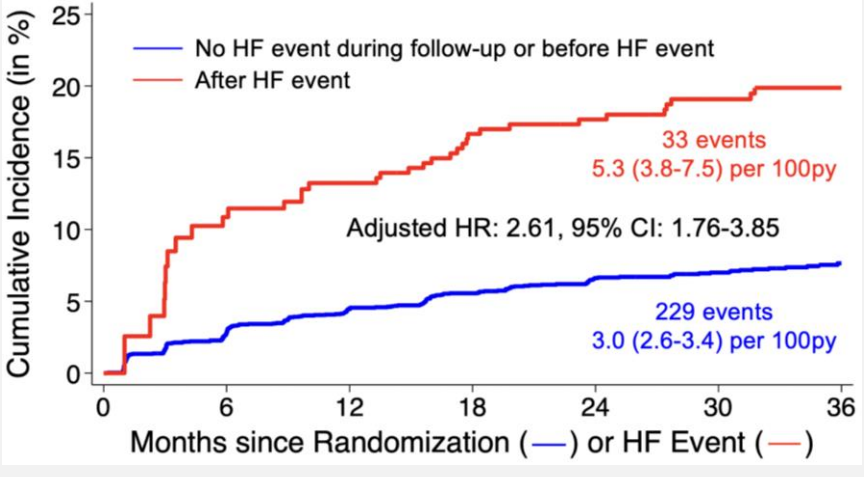


RESULTS

HbA_{1c} Trajectory Before Worsening HF Events

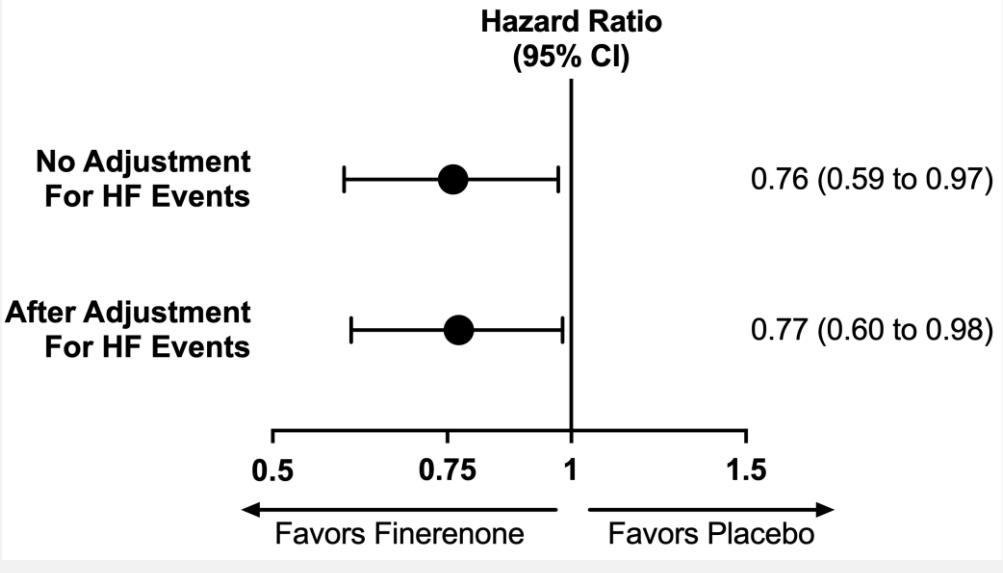


Incidence of Diabetes After Worsening HF Events



Adjusted hazard ratio (and 95% CI) adjusted for age, sex, LVEF, eGFR, BMI, systolic blood pressure, geographic region, log-transformed NT-proBNP, NYHA class, treatment arm, and baseline β-blocker, ACEi, ARB, and ARNi use.

Effect of Finerenone on New-Onset Diabetes



Both models were adjusted for baseline HbA_{1c} and stratified by geographic region and LVEF (<60%, ≥60%).

Discussion

- Diabetes often precedes HF, but ~1 in 3 cases occurs after or around HF onset → need for diabetes screening in HF.
- HbA1c rises in months preceding HF events, suggesting worsening insulin resistance.
- HF events associated with a >2-fold higher risk of new-onset diabetes → supports a bidirectional relationship between HF and diabetes.
- Finerenone reduced new-onset diabetes independent of HF event reduction.

Limitations & Conclusions

- **Limitations:**
  - possible misclassification of event (diabetes and HF) timing,
  - residual confounding,
  - limited generalizability.

- **Conclusion:**
  HF events may accelerate the development of diabetes. Benefits of finerenone on new-onset diabetes appeared independent of its effects on HF events.

Manuscript available soon in *Diabetes Care*