Heart failure (HF) and type 2 diabetes (T2D) are important causes of hospitalizations and mortality. Heart failure is two and five times more common in diabetic men and women, respectively, and associated with a worse prognosis than age-matched non-diabetics. The ACCORD trial (NCT000006260) tested the impact of intensive vs. standard glucose-lowering treatment (target HbA1c <6.0% vs. 7.0%-7.9%) on cardiovascular events in T2D patients (median baseline HbA1c 8.1%). We further explored the treatment effects on hospitalization or death due to heart failure (hdHF).

### Methods

Rates of hdHF were compared by treatment arms across genders, as well as by gender across treatment arms in secondary analyses of publicly available patient-level data from the ACCORD trial.

- We report event rates as Kaplan-Meier estimates and hazard ratios (95% CI) at 2.5, 5, and 7 years (end-of-trial).
- Multivariate analysis was used to adjust for age, gender, race, body mass index (BMI), established cardiovascular disease (CVD), previous HF, baseline HbA1c, use of insulin, sulfonylureas, or thiazolidinediones (TZDs), duration of T2D, estimated glomerular filtration rate (eGFR), and current smoking status.

### Results

#### Table 1. Characteristics of the subjects at baseline.

<table>
<thead>
<tr>
<th></th>
<th>Men (N=6289)</th>
<th>Women (N=3932)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥65 yr</td>
<td>1132 (18%)</td>
<td>1133 (28%)</td>
</tr>
<tr>
<td>BMI ≥30 (Kg/m²)</td>
<td>1831 (9%)</td>
<td>1836 (9%)</td>
</tr>
<tr>
<td>Duration of T2D ≥10 yr</td>
<td>1551 (49%)</td>
<td>1674 (39%)</td>
</tr>
<tr>
<td>Established CVD</td>
<td>1279 (41%)</td>
<td>1289 (41%)</td>
</tr>
<tr>
<td>Previous HF</td>
<td>382 (13%)</td>
<td>347 (13%)</td>
</tr>
<tr>
<td>HbA1c ≥8%</td>
<td>274 (9%)</td>
<td>276 (9%)</td>
</tr>
<tr>
<td>Age ≥65 years, BMI ≥30, CVD</td>
<td>593 (22%)</td>
<td>590 (22%)</td>
</tr>
<tr>
<td>Age ≥65 years, BMI ≥30, CVD</td>
<td>569 (22%)</td>
<td>557 (22%)</td>
</tr>
<tr>
<td>Age ≥65 years, BMI ≥30, CVD, previous CVD</td>
<td>625 (23%)</td>
<td>625 (23%)</td>
</tr>
</tbody>
</table>

During a median follow-up of 4.9 years, hdHF events occurred in:

- 4.7% (298/6299) of men vs. 3.7% (146/3952) of women (p = 0.013 by Fisher’s exact test);
- 4.7% (148/3145) with intensive vs. 4.8% (150/3154) with standard treatment arms in men (p = 0.953); and
- 4.2% (84/1969) with intensive vs. 3.2% (62/1983) with standard treatment arms in women (p = 0.077).

Comparing men to women, the rate of hdHF events:

- increased with intensive treatment in men after 3.5 years (Fig. 1A), but the difference was not significant between genders across the entire observation period (p=0.428 by log-rank test); and
- significantly decreased with standard treatment arms in women across the entire study (p=0.007) (Fig. 1B).

Comparing intensive to standard glucose-lowering treatment, the rate of hdHF events:

- did not differ significantly at any time point in men (p=0.974) (Fig. 2B);
- was non-significantly higher in women (p=0.077) (Fig. 2A); and
- exhibited no gender by treatment interaction (p=0.150).

Significant risk factors for hdHF included:

- age ≥65 years, BMI ≥30 kg/m², CVD, previous HF, baseline HbA1c ≥8%, insulin use, eGFR ≤60 mL/min, current smoking in the entire population;
- age ≥65 years, CVD, previous HF, baseline HbA1c ≥8%, insulin use, current smoking in men; and
- age ≥65 years, BMI ≥30 kg/m², CVD, previous HF, eGFR ≤60 mL/min in women.

### Conclusion

- Women with type 2 diabetes tended to have an increased risk of hdHF events with intensive vs. standard glucose-lowering treatment in the ACCORD trial. No such difference was observed among men.
- This hypothesis-generating secondary analysis, without adjustments for multiple comparisons, warrants confirmatory studies.
- The findings call attention to the importance of outlining gender differences in treatment responses in clinical trials.

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**DISCLOSURES:** NONE

**DISCLAIMER:** The contents of this poster are solely the responsibility of the authors, and do not represent the official views of the NIH, the FDA, Howard University, or Ohio State University. These analyses were conducted on publicly available data from BioLINCC.