Independent predictors of heart failure in patients with type 2 diabetes and chronic kidney disease: modeling from the CREDENCE trial

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Background: SGLT2 inhibitors have been shown to reduce hospitalization for heart failure (HHF). We sought to determine independent baseline predictors for HHF specifically in a population with type 2 diabetes and chronic kidney disease (CKD).

Methods: CREDENCE randomized 4401 participants with type 2 diabetes and CKD to canagliflozin 100 mg versus placebo. We evaluated the baseline clinical and demographic factors using multivariate regression modeling to identify the independent predictors of HHF.

Results: Overall, 230 participants (89 canagliflozin; 141 placebo) had at least 1 HHF event. Canagliflozin reduced the incidence of HHF compared with placebo (4.0% vs 6.4%; HR 0.61; 95% CI 0.47–0.80). Participants with HHF events postrandomization were older (65.8 vs 62.9 y), and had a longer duration of diabetes (17.4 vs 15.7 y), higher prevalence of prior HF (30.4% vs 14.0%), higher urinary albumin:creatinine ratio (1347 vs 904 mg/g), lower estimated glomerular filtration rate (51.5 vs 56.4 mL/min/1.73m^2), and higher prevalence of prior cardiovascular disease (65.7% vs 49.6%) compared to those without HHF. Independent predictors of HHF are shown in the Table.

Conclusions: HHF is common in patients with type 2 diabetes and CKD. Canagliflozin reduces HHF by 39% compared with placebo. Higher urinary albumin:creatinine ratio was the most potent predictor of HHF and should be part of patient risk assessment.

Table 1. Baseline Predictors of HHF*

Parameter	Chi-square	HR (95% CI)	P value
Log UACR (1 unit increase)	36.0	2.95 (2.07, 4.21)	<0.001
Age (1 year increase)	17.0	1.04 (1.02, 1.06)	<0.001
Prior heart failure (Yes/No)	16.7	1.93 (1.41, 2.65)	<0.001
Loop diuretic (Yes/No)	9.6	1.79 (1.24, 2.57)	0.002
Peripheral arterial disease (Yes/No)	8.5	1.71 (1.19, 2.45)	0.004
Diastolic BP (1 mmHg increase)	6.7	0.98 (0.97, 1.00)	0.01
Glycated hemoglobin (1% increase)	6.5	1.14 (1.03, 1.27)	0.01
Insulin (Yes/No)	5.9	1.56 (1.09, 2.22)	0.02
Prior myocardial infarction (Yes/No)	4.9	1.58 (1.05, 2.36)	0.03
Body mass index (1 kg/m^2 increase)	4.2	1.02 (1.00, 1.04)	0.04
Randomization to canagliflozin (vs. placebo)	12.9	0.61 (0.47–0.80)	<0.001

UACR, urinary albumin:creatinine ratio; BP, blood pressure. *Multivariate models adjusted for randomization.