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Risk factors for heart failure in the ACE trial population

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Background and aims: Heart failure (HF) is a deadly complication of type 2 diabetes but little is known about its incidence and recurrence in patients with coronary heart disease (CHD) and impaired glucose tolerance (IGT). We used Acarbose Cardiovascular Evaluation (ACE) trial data to identify baseline variables predictive of hospitalization for HF (hHF) or cardiovascular (CV) death in this Chinese population with CHD and IGT randomised to acarbose or placebo. As ACE showed a non-significant 11% hHF first event relative reduction with acarbose, compared with placebo (P=0.48), we have assessed the impact on recurrent hHF.

Materials and methods: We defined a composite hHF and CV death endpoint (to account for competing risk of death) and determined independent risk factors for it using a Cox proportional hazards model. Participants were censored at hHF, CV death or end of follow-up. The 16 baseline variables evaluated included age, sex, body mass index (BMI), smoking, plasma creatinine, prior CV events, fasting and 2-hour post load glucose, and HbA_{1c}. Those with a univariate composite endpoint association (P<0.1) were considered for inclusion in the multivariable model, with P<0.05 required for retention. The Anderson-Gill model, a generalization of the Cox proportional hazards model, was used to analyse recurrent hHF events.

Results: The 6522 ACE participants were mean (SD) 64.2 (8.0) years old, BMI 25.4 (3.1) kg/m^2, with the majority male (73%) and were followed for median five years. Significant independent hHF/CV death risk factors were: age, plasma creatinine, prior HF, prior stroke, prior myocardial infarction (MI) and prior atrial fibrillation (AF) (Table). There was a numerical 9% relative reduction in the first occurrence of hHF/CV death with acarbose, compared with placebo (Hazard ratio [HR] 0.91, 95% CI 0.74-1.11, P=0.34). Of 138 patients that had ≥1 episode of adjudicated hHF, 40 (0.6 %) experienced ≥1 recurrent events (94 events in total), a mean rate of 3.35 (1.71) over five years, and no significant effect seen with acarbose (HR 1.19, 95% CI 0.92-1.55, P=0.19).

Conclusion: In Chinese patients with CHD and IGT, those at higher risk of hHF/CVD were older with higher plasma creatinine values, prior MI, AF, HF and stroke. Allocation to acarbose 50mg TID was associated with a numerical 9% reduction in hHF/CV death.

Risk Factors for Hospitalization for Heart Failure or CV death

	Univariate Analyses		Multivariable Analysis	
Variable	**Hazard Ratio (95% CI)**	**P-value**	**Hazard Ratio (95% CI)**	**P-value**
Age (years)	1.07 (1.06-1.09)	<0.0001	1.06 (1.05-1.08)	<0.0001
BMI (Kg/m^2)	0.96 (0.93-0.99)	0.011	...	0.62
eGFR (ml/min/1.73m^2)	0.98 (0.98-0.98)	<0.0001	...	0.44
Plasma creatinine (µmol/L)	1.02 (1.02-1.03)	<0.0001	1.02 (1.01, 1.02)	<0.0001
Sex (vs. Female)	0.70 (0.55-0.90)	0.005	...	0.73
Prior Heart Failure (vs. none)	3.82 (2.82-5.16)	<0.0001	2.28 (1.67-3.13)	<0.0001
Prior myocardial infarction (vs. none)	1.65 (1.35-2.01)	<0.0001	1.71 (1.39-2.09)	<0.0001
Prior unstable angina (vs. none)	0.65 (0.52-0.80)	<0.0001	...	0.59
Prior Stroke (vs. none)	1.98 (1.47-2.67)	<0.0001	1.53 (1.13-2.08)	0.0065
Prior atrial fibrillation (vs. none)	2.64 (1.89-3.69)	<0.0001	1.62 (1.15-2.29)	0.0062

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Disclosure: **C.A.B. Scott:** None.