

#### **48. Pre-Diabetes Increases the Risk of Heart Failure Among Patients With Nonvalvular Atrial Fibrillation**

Jia Yi Huang, Gregory Lip, MeiZhen Wu, QingWen Ren, Denise Hung, Stephanie Tse, HungFat Tse, KaiHang Yiu, The University of Hong Kong, Hong Kong

##### **Body**

**Background:** Heart failure (HF) is common in patients with nonvalvular atrial fibrillation (NVAf). Notably, the presence of diabetes increases risk of HF in patients with nonvalvular NVAf. The association between pre-diabetes and risk of HF was nonetheless unexplored in this population. The present study aimed to evaluate whether pre-diabetes was associated with an increased risk of HF in patients with NVAf.

**Methods:** Using a territory-wide electronic health record database, patients with newly diagnosed NVAf from 2010 to 2018 were included to evaluate for risk of HF upon competing risk regression with Cox proportional-hazard model adjustment. Patients were divided into 3 groups according to their baseline glycemic status: (1) type 2 diabetes, (2) pre-diabetes, and (3) normoglycemia. In the pre-diabetes group, the subsequent risk of HF was further evaluated according to the changes of glycemic status at two years following index date.

**Results:** Among 65,994 NVAf patients (mean age 75.7 years, 48.5% female), 10,926 (16.6%) had pre-diabetes, and 27,312 (41.4%) had diabetes at baseline. Over a median follow-up of 7.1 years, 7,203 (26%) normoglycemic patients, 3,168 (29%) pre-diabetic patients, and 8,745 (32%) diabetic patients developed HF (Log rank test,  $P < 0.001$ ). Pre-diabetes was associated with an increased risk of HF compared with normoglycemic patients (subdistribution Hazard Ratio (SHR) = 1.09, 95% confidence interval (CI): 1.04-1.14) and diabetes conferred the highest risk amongst three groups (SHR=1.19, 95%CI: 1.15-1.24). In patients with pre-diabetes at baseline, 873 (8.0%) progressed to diabetes and 1204 (11%) resolved to normoglycemia at 2 years. Compared to those who remained pre-diabetic, patients who progressed to diabetes had a higher risk of HF (SHR = 1.23, 95% CI :1.05-1.44), whereas those who resolved to normoglycemia incurred a lower risk (SHR = 0.80, 95% CI :0.68-0.94).

**Conclusion:** Pre-diabetes was independently associated with an increased risk of HF in patients with NVAf. Pre-diabetic patients who progressed to diabetes at 2 years experienced an increased risk of HF, whereas those who resolved to normoglycemia reduced risk of HF, as compared to those who remained pre-diabetic.

Table 1. Risks of heart failure per 100-person years of follow up.

	Incidence per 100 person-years	Unadjusted HR (95%CI)	p	Model 1 HR (95%CI)	p	Model 2 HR (95%CI)	p
Normal	5.98	Ref		Ref		Ref	
Pre-diabetes	6.52	1.10 (1.05-1.15)	<0.001	1.19 (1.14-1.24)	<0.001	1.09(1.04-1.14)	<0.001
Diabetes	8.16	1.25 (1.21-1.29)	<0.001	1.28 (1.24-1.32)	<0.001	1.19(1.15-1.24)	<0.001

Model 1 adjusted for age, gender.

Model 2 adjusted for age, gender, previous HF, HTN, CKD, CAD, TIA, hyperlipidemia, obesity, NOAC, warfarin, age, stroke, smoking, alcohol.

Table 2. Risks of heart failure at 2 years following AF index date.

	Incidence per 100 person-years	Unadjusted HR (95%CI)	p	Model 1 HR (95%CI)	p	Model 2 HR (95%CI)	p
Progress to normal	7.46	0.78(0.66-0.92)	<0.001	0.76(0.65-0.90)	<0.001	0.80(0.68-0.94)	<0.001
Pre-diabetes	9.48	Ref		Ref		Ref	
Progress to diabetes	11.84	1.59(1.37-1.84)	<0.001	1.51(1.30-1.75)	<0.001	1.23(1.05-1.44)	<0.001

Model 1 adjusted for age, gender.

Model 2 adjusted for age, gender, previous HF, HTN, CKD, CAD, TIA, hyperlipidemia, obesity, NOAC, warfarin, age, stroke, smoking, alcohol.

**Clinical Implications:** These findings highlight the importance of strict blood glucose control in reducing the risk of HF in patients with atrial fibrillation.