Acute and Stable Ischemic Heart Disease

INCREASED RISK OF SEVERE HYPOGLYCEMIC EVENTS BEFORE AND AFTER CARDIOVASCULAR EVENTS IN TYPE 2 DIABETES: VALIDATION OF A NOVEL CONCEPT

Moderated Poster Contributions
Acute and Stable Ischemic Heart Disease Moderated Poster Theater, Poster Hall, Hall F
Sunday, March 17, 2019, 1:30 p.m.-1:40 p.m.

Session Title: Special Considerations in High-Risk ACS Patients: Insights From Observational Studies
Abstract Category: 03. Acute and Stable Ischemic Heart Disease: Therapy
Presentation Number: 1027-11

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Background: Severe hypoglycemic events (SHEs) in type 2 diabetes (T2D) are associated with an increased risk of subsequent cardiovascular (CV) events. A reverse relationship, however, in which nonfatal CV events are associated with a subsequent increased SHE risk has been demonstrated in TECOS. We sought to validate this novel bidirectional relationship using EXSCEL data.

Methods: Time-dependent associations were examined between SHEs and subsequent CV events or all-cause mortality (ACM) in a post hoc analysis of 14,752 EXSCEL participants with T2D, and between nonfatal CV events and subsequent SHEs, in both partial and fully adjusted models.

Results: Participants with (versus without) SHEs were on average older, with longer diabetes duration and lower estimated glomerular filtration rate, and were more frequently non-White, insulin treated, and had prior CV or heart failure events. SHEs were not associated with once-weekly exenatide therapy, compared with placebo (hazard ratio 1.13, 95% CI 0.94-1.36, P=0.18). In fully adjusted models, SHEs increased the risk of ACM, CV death and hospitalization for heart failure (hHF), whilst non-fatal MI, non-fatal stroke and hHF all increased subsequent risk of SHEs (Table).

Conclusion: A robust bidirectional association between SHEs and subsequent risk of CV events, and between nonfatal CV events and subsequent risk of SHEs, was confirmed, suggesting a "frail" T2D sub-phenotype with increased susceptibility to both SHEs and CV events.

	Total (events *per* 100 pyrs)		Adjusted for selected clinical factors*		Full adjustment†	
CV event after a severe hypoglycemic event (SHE)						
Event	Before or without SHE	After SHE	HR (95% CI)	p	HR (95% CI)	p
MACE	1694 (3.8)	50 (5.8)	1.43 (1.08, 1.91)	0.013	1.19 (0.89, 1.60)	0.230
All-cause death	1036 (2.1)	55 (5.5)	2.06 (1.57, 2.71)	<0.001	1.83 (1.38, 2.42)	<0.001
CV death	691 (1.4)	32 (3.2)	1.84 (1.28, 2.62)	0.001	1.60 (1.11, 2.30)	0.012
MI	943 (2.1)	33 (3.8)	1.68 (1.18, 2.39)	0.004	1.32 (0.92, 1.90)	0.131
Stroke	398 (0.9)	7 (0.8)	0.84 (0.40, 1.78)	0.652	0.77 (0.36, 1.63)	0.488
Hospitalization for HF	424 (0.9)	26 (2.9)	2.88 (1.92, 4.33)	<0.001	2.09 (1.37, 3.17)	0.001
Severe hypoglycemic event after a CV event						
Preceding event	Before or without CV event	After CV event	HR (95% CI)	p	HR (95% CI)	p
Nonfatal MI or stroke	430 (0.9)	36 (1.7)	2.50 (1.75, 3.56)	<0.001	2.04 (1.42, 2.93)	<0.001
Nonfatal MI	438 (0.9)	28 (1.8)	2.52 (1.70, 3.74)	<0.001	2.02 (1.35, 3.01)	0.001
Nonfatal stroke	455 (0.9)	11 (1.8)	2.56 (1.40, 4.70)	0.002	2.30 (1.25, 4.23)	0.007
Hospitalization for HF	448 (0.9)	18 (3.1)	4.40 (2.70, 7.15)	<0.001	3.24 (1.98, 5.30)	<0.001

*Clinical adjustment factors are age, sex, race, weight, current smoking, and randomized treatment.
†Covariates included for full adjustment are age, sex, race, ethnicity, HbA1c, NYHA class, current smoking, randomized treatment, MI, cardiovascular disease, stroke, ≥50% stenosis in carotid artery, atrial fibrillation or flutter, SBP, DBP, heart rate, height, BMI, eGFR, diabetes duration, baseline insulin, time dependent insulin use during the trial, chronic respiratory disease, amputation, diabetic neuropathy, and foot ulcers. Models for hypoglycemia also adjust for baseline beta blockers and sulfonylurea.