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Phenotypic features of patients with Type 2 diabetes at increased risk of severe hypoglycemic events occurring before or after cardiovascular events

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Aims: To characterize patients with severe hypoglycemic events (SHEs) requiring third-party assistance occurring before or after adjudicated cardiovascular (CV) events (CVEs) in the exenatide study of cardiovascular event lowering (EXSCEL).

Methods: Baseline clinical characteristics for participants with SHEs occurring before CVEs were compared with those with SHEs occurring after nonfatal CVEs, and with those without SHEs or CVEs. Time-dependent associations were examined bidirectionally between SHEs and CVEs in both partial and fully adjusted models.

Results: Of 14,752 participants in the intention-to-treat population (73.1% with established CV disease), 466 (3.2%) experienced SHEs, with no significant difference between once-weekly exenatide and placebo assignment over 3.2 years median follow-up. In total, 116 of these participants had CVEs, 66 after and 50 before SHEs. Both groups with co-existent SHEs and CVEs showed similar characteristics, and were "5 years older than those without, had 5 years longer diabetes duration, were twice as likely to have chronic kidney disease stage 3, more frequently had established CV disease, heart failure (HF) and pre-study CVEs, with higher use of CV medications and insulin ('80% of participants). Participants with SHEs before CVEs showed 97%, 41% and 46% baseline prevalence for CVEs, HF history and CKD3, respectively. In fully adjusted models, SHEs increased the risk of CV death and hospitalization for HF (hHF), whilst nonfatal MI, nonfatal stroke and hHF all increased subsequent risk of SHEs.

Conclusions: Patients at dual risk of SHEs and CVEs appear to represent a "frail" phenotype, regardless of the order in which they occur.

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