

questionnaire was sent to the 19 academic sites across Canada participating in the FH Canada network. We previously identified 79 cases across the country, and have captured 46 of these cases. Here we describe their medical history, lipid levels, treatments and clinical outcomes. At the time of entry in the Registry, the mean age was 44 +/- 19 years, with a majority of females (54.4%), representing cases across 5 provinces. The average age of diagnosis was 16.4 years, with 67.4% having untreated LDL > 10 mmol/L. Presence of physical markers, such as xanthomas or corneal arcus, were also found in 80.4% and 26.1% of patients, respectively. For lipid-lowering therapy, 52.2% were undergoing LDL-apheresis, 91% were on statins and 41% on PCSK9 inhibitors. 54.3% displayed ASCVD, with 43.5% having aortic stenosis, 15.2% having experienced a myocardial infarction, and 36.9% having undergone one or more coronary artery bypass graft procedures.

CONCLUSION: We plan to use this data at provincial and national levels, helped by the Canadian Organization for Rare Diseases (CORD) and the Réseau Québécois des maladies orphelines (RQMO), to provide HoFH patients access to care, including orphan drugs such as evinacumab, and treatment techniques such as LDL apheresis. This work will provide important new health-related knowledge about the determinants of ASCVD risk and phenotypic manifestations of HoFH in Canada, and examine the quality of life and burden to the healthcare system.

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INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-7 AS A MARKER OF CARDIAC REVERSE REMODELING WITH EMPAGLIFLOZIN: A SECONDARY ANALYSIS OF THE EMPA-HEART CARDIOLINK-6 RANDOMIZED CONTROLLED TRIAL

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BACKGROUND: Reverse cardiac remodeling is believed to contribute to the cardiovascular benefits offered by sodium-glucose transport protein 2 inhibitors (SGLT2i). Given the association between insulin-like growth factor binding protein 7 (IGFBP7) levels and cardiac remodeling, it has been postulated that IGFBP7 may serve as a predictor for individuals who may derive greater benefit from SGLT2i therapy. This exploratory sub-analysis of the EMPA-HEART CardioLink-6 trial examined the association between serum IGFBP7 levels and reverse cardiac remodeling in patients treated with empagliflozin.

METHODS AND RESULTS: The EMPA-HEART CardioLink-6 trial randomized 97 patients with type 2 diabetes and coronary artery disease to either empagliflozin (10 mg/d) or matching placebo for 6 months. The primary outcome was change in left ventricular mass indexed to body surface area (LVMI) from baseline to 6 months as measured by cardiac magnetic resonance imaging. Serum samples collected from patients at baseline were processed for detection of IGFBP7. A

linear model adjusted for baseline characteristics was used to evaluate the relationship between baseline IGFBP7, 6-month change in LVMI, and treatment arm. An adjusted multivariable linear regression model was used to evaluate the association between baseline IGFBP7 and baseline LVMI. Patients with missing covariate data were excluded which resulted in a final analysis set of 74 patients. We observed no association between baseline IGFBP7 levels and change in LVMI, nor was there any significant difference in treatment effect between empagliflozin versus placebo patients (empagliflozin 6-month change in LVMI: 0.25g/m² (95% CI: -0.17 g/m² to 0.67 g/m²) per 1 ng/mL higher IGFBP7 vs. placebo 6-month change in LVMI: 0.07 g/m² (95% CI: -0.21 g/m² to 0.35 g/m²) per 1 ng/mL higher IGFBP7; Pinteraction = 0.49). We also did not detect any association between baseline IGFBP7 and baseline LVMI (P = 0.52). Additional sensitivity analysis assessing the association between IGFBP7 as a categorical variable and 6-month change in LVMI did not reveal any significant interaction (Pinteraction=0.86).

CONCLUSION: Our results suggest that empagliflozin-mediated cardiac reverse remodeling in patients with type 2 diabetes and coronary artery disease is independent of serum IGFBP7 levels. However, given the sample size and short study duration of the EMPA-HEART CardioLink-6 trial, further investigations evaluating whether IGFBP7 levels influence the clinical efficacy of SGLT2i are warranted.

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LEFT VENTRICULAR MASS PREDICTS CARDIAC REVERSE REMODELING IN PATIENTS TREATED WITH EMPAGLIFLOZIN: AN EXPLORATORY SUB-ANALYSIS OF THE EMPA-HEART CARDIOLINK-6 RANDOMIZED CONTROLLED TRIAL

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BACKGROUND: Left ventricular (LV) hypertrophy is associated with an elevated risk for cardiovascular (CV) disease events and all-cause mortality. The CV benefits of sodium-glucose transport protein 2 inhibitors (SGLT2i) have been attributed, in part, to cardiac reverse remodeling. The EMPA-HEART CardioLink-6 study reported that SGLT2 inhibition with empagliflozin was associated with a significant reduction in LV mass indexed to body surface area (LVMI) after 6 months. In this exploratory sub-analysis of the same trial, we evaluated how baseline LVMI may influence cardiac reverse remodeling with empagliflozin.

METHODS AND RESULTS: A total of 97 patients with type 2 diabetes and coronary artery disease were randomized to empagliflozin (10 mg/d) or matching placebo for 6 months. To determine if the impact of empagliflozin on the 6-month change in LVMI was dependent on baseline LVMI, the EMPA-HEART CardioLink-6 cohort was stratified into two groups — baseline LVMI ≥60 g/m² and < 60 g/m². Between-group comparisons were conducted using a linear regression model adjusted for