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RESEARCH LETTER

Increases in Natriuretic Peptides Precede Heart Failure Hospitalization in Patients With a Recent Coronary Event and Type 2 Diabetes Mellitus

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Figure. Geometric mean natriuretic peptide (NP) levels before heart failure (HF) hospitalization (HFH). **Left,** All patients (**top,** B-type NP [BNP]; **bottom,** NT-proBNP [N-terminal prohormone BNP]). Histogram represents number of NP samples available for HFH and control patients by 30-day increments. **Middle,** Patients with no history of HF at randomization (**top,** BNP; **bottom,** NT-proBNP). **Right,** Patients with a history of HF at randomization (**top,** BNP; **bottom,** NT-proBNP).

There were 5% to 7% reductions at week 24 in BNP ($P=0.011$) and NT-proBNP ($P=0.001$) associated with randomization to lixisenatide. These relative reductions did not differ between those who later did and those who did not experience HFH, and the temporal pattern of increases in NP before HFH did not differ by treatment allocation (BNP, $P=0.23$; NT-proBNP, $P=0.08$).

In patients with a recent acute coronary syndrome and type 2 diabetes mellitus, increases in NPs were evident in the months preceding HFH. **It was estimated that patients without a history of HF experienced a progressive increase in NP levels (≈ 3 - to 4-fold),** with accelerated increase during the final 6 months before HFH, whereas patients with a history of HF experienced relatively steady NP levels until ≈ 6 months before HFH, followed by similar increases during the final months. At the time of HFH, patients with and without a history of HF reached comparable NP levels. These changes elucidate important differences between patients with and without a history of HF who experience HFH. These findings suggest that cardiac deterioration is progressing several months before HFH, potentially enabling earlier identification of patients on a trajectory toward HFH. The translation of these observations into guidance on the optimal frequency of NP monitoring or clinically relevant NP changes over specific time intervals for predictive purposes remains to be determined.



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