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Study links increasing severity of heart failure with increased risk of developing diabetes

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New research published in *Diabetologia* (the journal of the European Association for the Study of Diabetes) shows that increasing severity of heart failure is associated with an increased risk of developing diabetes. The study is by Dr Malene Demant, Department of Cardiology, Copenhagen University Hospital Gentofte, Copenhagen, Denmark, and colleagues.

A previous study by the same authors has shown an increased risk of diabetes in patients with heart failure following a heart attack, but this new research aimed to analyse all patients with heart failure regardless of whether or not they had had a heart attack.

The study followed all Danish patients discharged from hospitalisation for first-time heart failure in 1997-2010, without prior use of oral diabetes drugs, until a claimed prescription for oral diabetes drugs, death, or 31 December 2010. The severity of each patient's heart failure was estimated via the dose of drugs (loop-diuretics) used to treat their condition.

In total, 99,362 patients were included and divided into five loop-diuretic dose groups: Group 1: 30,838 (31%) used no loop diuretics; Group 2, 24,389 (25%) used 40 mg or less per day; Group 3, 17,355 (17%) used 40-79 mg/day; Group 4, 11,973 (12%) used 80-159 mg/day; and Group 5 14,807 (15%) used 160 mg or more per day. A total of

7,958 patients (8%) developed diabetes.

Loop-diuretic dosages were associated with an increased risk of developing diabetes in a dose-dependent manner. The increased risk of developing diabetes for groups 2-5 versus group 1 (the reference group) was 2.06 times for group 2, 2.28 for group 3, 2.88 for group 4, and 3.02 for group 5. Thus patients in the group with the most severe heart failure (group 5) were three times more likely to develop diabetes than those with the least severe (group 1).

Patients who were also being treated with ACE inhibitors (angiotensin-converting-enzyme inhibitors) had a less pronounced increase in diabetes risk across all groups. The authors suggest this could be due to blockage of the neurohumeral axis, or improving cardiac function, or both. The clinical implications of this finding still need to be determined, say the authors.

In total, 62,565 (63%) patients died during the study period. Patients who developed diabetes were 16% more likely to die than those who did not develop diabetes. Increasing severity of heart failure, was, not surprisingly, also associated with further risk of death, with an increased risk in groups 2-5 compared with group 1: 14% for group 2; 17% for group 3; 29% for group 4 and 45% for group 5.

Dr Demant says: "From an epidemiological perspective, the poor prognosis associated with diabetes in patients with heart failure has confused researchers for 35 years. Even after adjustment for risk factors such as coronary artery disease and abnormal blood fats, several studies have over the years reported diabetes to be consistently associated with increased mortality."

She adds: "Our data add important insights to the understanding of the mechanisms underlying this poor prognosis, because it might be that the

sickest patients are those who develop diabetes. Thus, diabetes may, in part, be a marker of heart failure severity in addition to being a causal risk factor for mortality in heart failure cohorts."

While the study does not explicitly examine mechanisms for the above effects, the authors discuss several possibilities, such as patients with heart failure having decreased cardiac output and thereby diminished oxygen, glucose and insulin distribution to peripheral muscular tissue which may lead to increased insulin resistance as well as decreased insulin release; lack of physical activity in those with the most severe heart failure, and also potential side effects of loop-diuretic drugs.

The authors conclude: "This study, based on nationwide data, suggests an increased risk of development of diabetes in patients with heart failure, with increasing loop-diuretic dosage used as a proxy for heart failure severity. It emphasises the need to monitor and treat patients with heart failure to prevent diabetes development. Future strategies for heart failure management should include increased awareness of risk of diabetes in patients with severe heart failure."

Provided by Diabetologia

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