

Heart failure with reduced ejection fraction of ischaemic and non-ischaemic aetiology

Clinical characteristics, prognosis and factors associated with outcome

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien,
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Avhandlingen baseras på följande delarbeten

- I. Silverdal J, Sjöland H, Bollano E, Pivodic A, Dahlström U, Fu M. Prognostic impact over time of ischaemic heart disease vs. non-ischaemic heart disease in heart failure. *ESC Heart Fail.* 2020;7(1):264-273.
- II. Silverdal J, Sjöland H, Pivodic A, Dahlström U, Fu M, Bollano E. Prognostic differences in long-standing vs. recent-onset dilated cardiomyopathy. *ESC Heart Fail.* 2022;9(2):1294-1303.
- III. Sjöland H, Silverdal J, Bollano E, Pivodic A, Dahlström U, Fu M. Temporal trends in outcome and patient characteristics in dilated cardiomyopathy, data from the Swedish Heart Failure Registry 2003-2015. *BMC Cardiovasc Disord.* 2021;21(1):307.
- IV. Silverdal J, Bollano E, Henrysson J, Basic C, Fu M, Sjöland H. Treatment response in recent-onset heart failure with reduced ejection fraction: non-ischaemic vs ischaemic aetiology. *Accepted for publication in ESC Heart Fail.*

**SAHLGRENSKA AKADEMIN
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Heart failure with reduced ejection fraction of ischaemic and non-ischaemic aetiology

Clinical characteristics, prognosis and factors associated with outcome

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Abstract

BACKGROUND: Ischaemic heart disease (IHD) is common in heart failure (HF) and is often considered to infer a worse prognosis. Following treatment improvements and the increased survival in both IHD and HF, patients are generally older and increasingly multimorbid. The current impact of IHD on mortality in HF and on short-term response to initiated treatment in HF with reduced ejection fraction (HFrEF) is uncertain. Dilated cardiomyopathy (DCM) is one of the most important causes of non-ischaemic HFrEF. Even so, contemporary data on outcomes and prognostic factors are scarce.

AIMS: To evaluate the impact of IHD on mortality in HF over time and on short-term response to initiated treatment in HFrEF. To study the influence of duration on outcomes and comorbid burden in DCM, with further analyses of temporal changes and prognostic factors.

METHODS AND RESULTS: Swedish Heart Failure Registry data were analyzed in the three first studies. *In the first study*, we evaluated the impact of IHD on mortality in 31,000 patients with non-valvular HF during 2000–2012. We found that IHD was associated with higher mortality in the whole cohort, in all age groups, in both men and women, in both HF duration < 6 and ≥ 6 months, and in all groups of left ventricular ejection fraction (LVEF) $< 50\%$. IHD was associated with increased risk during the entire study period. *In the second study*, we studied the characteristics, comorbid burden and outcomes in 3,700 patients with DCM. All outcomes were more frequent in long-standing HF (≥ 6 months) than in recent-onset HF. Irrespective of HF duration, the risk factors for mortality, heart transplantation and HF hospitalizations were: older age, lower blood pressure, lower functional capacity, lower LVEF, left bundle branch block and diabetes. Male sex was adverse in recent-onset HF only, whereas renal dysfunction, atrial fibrillation and loop diuretic use were adverse only in long-standing HF. The age-adjusted number of comorbidities increased with increasing HF duration. *In the third study*, we studied the temporal changes in the clinical characteristics, outcomes and prognostic factors in 7,900 patients with DCM during 2003–2015. Over time, the mean age and the proportion of women increased, LVEF improved, and the patients were less symptomatic. The prevalence of prognostically adverse comorbidities was stable. The risk for one-year mortality and hospitalizations diminished gradually during the study period. *In the fourth study*, we assessed the response to initiated treatment in 317 patients with new-onset HFrEF of ischaemic- and non-ischaemic aetiology hospitalized at the Sahlgrenska University Hospital during 2016–2019. Patients with non-ischaemic aetiology showed a better response over a 28-week follow-up, evaluated with a clinical composite outcome. Re-hospitalizations were half as frequent, and a higher proportion showed improvement in LVEF and a decrease in natriuretic peptides.

CONCLUSIONS: Despite improvements in the treatment of HF and IHD, the latter still entails higher mortality in a broad spectrum of patients with HF and subnormal LVEF. In new-onset HFrEF, the treatment response is better in patients with non-ischaemic- than with ischaemic aetiology. In DCM, longer HF duration is associated with increased comorbidity and worse prognosis. Most known adverse prognostic factors are similar in patients with recent-onset and long-standing HF. During 2003–2015, the overall survival gradually improved, although the changes in the cohort composition and the adverse prognostic factors were small.

KEYWORDS: Heart failure, systolic; Ischemic Heart Disease; Cardiomyopathy, dilated; Prognosis; Mortality; Risk factors