

Risk Factors and Predictors of Heart Failure: from Incidence to Prognosis

Akademisk avhandling

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av

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Avhandlingen baseras på följande delarbeten

I. Barywani SB, Ergatoudes C, Schaufelberger M, Petzold M, Fu ML. Does the target dose of neurohormonal blockade matter for outcome in Systolic heart failure in octogenarians?
Int J Cardiol. 2015;187:666-72

II. Ergatoudes C, Schaufelberger M, Andersson B, Pivodic A, Dahlström U, Fu M. Non-cardiac comorbidities and mortality in patients with heart failure with reduced vs. preserved ejection fraction: a study using the Swedish Heart Failure Registry.
Clin Res Cardiol. 2019;108:1025-33

III. Ergatoudes C, Thunström E, Hansson PO, Morales D, Mandalenakis Z, Rosengren A, Zhong Y, Caidahl K, Fu M. Natriuretic and Inflammatory Biomarkers as Risk Predictors of Heart Failure in Middle-Aged Men From the General Population: A 21-Year Follow-Up.
J Card Fail. 2018;24:594-600

IV. Ergatoudes C, Hansson PO, Svärdsudd K, Rosengren A, Thunström E, Caidahl K, Pivodic A, Fu M. Incidence rates and risk factors of heart failure: comparing two cohorts of middle-aged men born 30 years apart.
Submitted

**SAHLGRENKA AKADEMIN
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ABSTRACT

Background: Heart failure (HF) is a major public health problem affecting at least 26 million people worldwide and one of the leading causes of disability and death.

Aims: To identify characteristics associated with improved or worsened prognosis in patients with established HF and to study factors associated with higher risk for the incidence of HF in the general population.

Methods and Results: This thesis consists of four papers. Paper I was designed to study the impact of different dose levels of beta-blockers (BBs) and angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin II receptor blockers (ARBs) on long-term mortality in elderly patients with HF with reduced ejection fraction (EF). The study cohort included 184 HF patients aged ≥ 80 years with EF $\leq 40\%$. The target ACEI/ARB dose was associated with reduced all-cause mortality compared to $<50\%$ of target dose. There were no significant differences in survival between the different BB doses. In Paper II, a comparison of the prevalence and prognostic contribution to mortality of non-cardiac comorbidities was conducted between HF patients with EF $<50\%$ and $\geq 50\%$. Data from the Swedish Heart Failure Registry between May 2000 and December 2012 were used. Stroke, anemia, gout, and cancer were all associated with higher mortality in both phenotypes with similar impact, whereas diabetes, renal failure, and liver disease had a higher impact in patients with EF $<50\%$. Pulmonary disease was more prominent in patients with EF $\geq 50\%$. In Paper III, the predictive value of different biomarkers for HF incidence was examined. The study cohort was a randomly selected sample of men born in 1943 who were followed up over 21 years. N-terminal pro B-type natriuretic peptide (NT-proBNP) $\geq 25\text{ng/L}$ and high-sensitivity C-reactive protein (hs-CRP) $>3\text{mg/L}$ at age 50 years were associated with higher odds of incident HF. Paper IV studied and compared risk factors and incidence of HF in middle-aged men born 30 years apart. The study population consisted of a sample of men born in 1943 (described in Paper III) and a similar sample of men born in 1913. The impact of different factors on the risk of developing HF was examined. Eighty men born in 1913 (9.4%) and 42 men born in 1943 (5.3%) developed HF during follow-up with an adjusted hazard ratio comparing the two cohorts of 0.46 (95% confidence interval 0.28–0.74, $p=0.002$). In both cohorts, higher body mass index, higher diastolic blood pressure, treatment for hypertension, and onset of atrial fibrillation, ischemic heart disease, or diabetes mellitus were associated with higher risk of HF. Higher heart rate was associated with an increased risk only in men born in 1913, whereas higher systolic blood pressure, smoking, higher glucose, higher cholesterol, and physical inactivity were associated with an increased HF risk in men born in 1943. The relative importance of atrial fibrillation as a risk factor decreased, whereas that of systolic blood pressure and physical inactivity increased in men born in 1943 compared with men born in 1913.

Conclusions: Titration to the target ACEI/ARB dose is beneficial with respect to mortality in elderly patients with HF. Non-cardiac comorbidities contribute significantly to mortality in both HF phenotypes with some notable differences. NT-proBNP and hs-CRP have a predictive value for the incidence of HF in middle-aged men. The incidence of HF in middle-aged men has decreased during the past 30 years and, in the meantime, the risk profile for HF has also changed.

Keywords: Heart failure, prognosis, characteristics, risk factors, incidence, prediction