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

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av

Constantinos Ergatoudes

Fakultetsopponent:
Docent Krister Lindmark
Institutionen för folkhälsa och klinisk medicin, Umeå universitet, Umeå

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

*J Card Fail.* 2018;24:594-600

*Submitted*
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Constantinos Ergatoudes

Department of Molecular and Clinical Medicine, Institute of Medicine, 
Sahlgrenska Academy, University of Gothenburg, Sweden

ABSTRACT

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

Aims: To identify characteristics associated with improved or worsened prognosis in patients with estab- 
lished 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 differ- 
ent 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 ≤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 ≥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 ≥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) ≥25ng/L and high-sensitivity C-reactive protein (hs-CRP) >3mg/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%) devel- 
oped 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 pa-
tients 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 mid-
dle-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