

# HEART FAILURE AND AORTIC STENOSIS

## Factors Influencing Prognosis and Development

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i lokal Arvid Carlsson, Medicinargatan 3, den 20 maj 2021, klockan 09.00, deltagande via länk.

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### Avhandlingen baseras på följande delarbeten

- I. Kontogeorgos S, Thunström E, Johansson MC, Fu M. Heart failure with preserved ejection fraction has a better long-term prognosis than heart failure with reduced ejection fraction in old patients in a 5-year follow-up retrospective study. *Int J Cardiol*, 2017 Apr 1;232:86-92.
- II. Kontogeorgos S, Thunström E, Pivodic A, Dahlström U, Fu M. Prognosis and outcome determinants after heart failure diagnosis in patients who underwent aortic valvular intervention. *Revised and resubmitted ESC Heart Failure*
- III. Kontogeorgos S, Thunström E, Basic C, Hansson PO, Zhong Y, Ergatoudes C, Morales D, Mandalenakis Z, Rosengren A, Caidahl K, Fu M. Prevalence and risk factors of aortic stenosis and aortic sclerosis: a 21-years follow-up of middle-aged men. *Scand Cardiovasc J*. 2020 Apr;54(2):115-123.
- IV. Kontogeorgos S, Thunström E, Lappas G, Rosengren A, Fu M, Lifelong cumulative incidence and predictors of acquired aortic stenosis in a large population of middle-aged men followed for up to 43 years *In manuscript*

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## Factors Influencing Prognosis and Development

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### Abstract

**Background:** An ageing population increases the prevalence of heart failure (HF) and aortic stenosis (AS). Several studies have investigated prognosis and predictors of HF with preserved ejection fraction (HFpEF) compared to heart failure with reduced ejection fraction (HFrEF), with inconsistent results. Valvular heart diseases gain importance in HF aetiology. How often AS occurs with age, the factors that might predict it, how aortic valvular interventions influence outcome of HF remain inadequately studied.

**Methods:** In *the first study* we analysed patients  $\geq 65$  years hospitalised for HF. The 5-year all-cause mortality and prognostic factors were compared between HFpEF and HFrEF. In *the second study*, we created a study cohort consisting of HF with aorta valve intervention due to AS by linking the Swedish Heart Failure Registry with the National Patient Register (NPR) and divided it into two subgroups: AS-HFrEF and AS-HFpEF. For each individual, three matched controls with HF were identified. The outcomes were all-cause and cardiovascular mortality. In *the third study*, we included men who were a part of the ‘Study of Men Born in 1943’ and studied the prevalence and factors predicting AS or aortic sclerosis. In *the fourth study*, we analysed men participating in the Multifactor Primary Prevention Study and identified the outcome (AS) and its associated factors by linking this database to the NPR.

**Results:** In *Paper I*, 5-year mortality was high (67.5%). After adjusting for age, HFpEF had better survival than HFrEF; different factors predicted mortality in HFpEF and HFrEF. In *Paper II*, crude all-cause mortality was 50.3% and no statistically significant differences in all-cause or CV mortality were found between AS-HFpEF and AS-HFrEF or between those with AS-HF and matched HF controls. Prognostic predictors were similar between the two groups, except of diabetes mellitus. In *Paper III*, 2.6% of the individuals developed AS. Body mass index (BMI) correlated with the risk of developing AS after 21 years, whereas BMI and hypercholesterolemia correlated with the development of AS/aortic sclerosis. In *Paper IV*, the cumulative incidence of AS was 3.2%. The factors significantly associated with its development were higher BMI, obesity, cholesterol, arterial hypertension, atrial fibrillation, and smoking.

**Conclusions:** HF has a high mortality, but HFpEF has better prognosis than HFrEF, at least in women. This difference in survival was not apparent if HF developed after AS and subsequent aortic valvular intervention. The cumulative incidence of AS is about 3% and atherosclerotic factors might be involved in its development. These risk factors are modifiable, implying that AS-caused HF could be preventable.

**Keywords:** heart failure, prognosis, predictive factors, aortic stenosis, obesity