

# The Clinical Relevance and Potential Mechanism of Biomarkers in Elderly Heart Failure Patients

Akademisk avhandling

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av

Alexandra Holmström

Fakultetsopponent:  
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Avhandlingen baseras på följande arbeten:

- I. Holmström A, Sigurjonsdottir R, Edner M, Jonsson Å, Dahlström U, Fu M. **Increased comorbidities in heart failure patients  $\geq 85$  years but declined from  $>90$  years: Data from the Swedish Heart Failure Registry.** *Int J Cardiol.* 2012, *In press*
- II. Holmström A, Petzold M, Fu M. **Re-evaluation of prognostic significance of NT-proBNP in a 5-year follow-up study assessing all-cause mortality in elderly patients  $\geq 75$  years) admitted to hospital due to suspect heart failure.** *Eur Geriatr Med.* 2012, *In press*
- III. Holmström A, Sigurjonsdottir R, Hammarsten O, Gustafsson D, Petzold M, Fu M. **Red blood cell distribution width and its relation to cardiac function and biomarkers in a prospective hospital cohort referred for echocardiography.** *Eur J Intern Med.* 2012, 23(7):604-9.
- IV. Holmström A, Sigurjonsdottir R, Hammarsten O, Petzold M, Gustafsson D, Fu M. **An integrated multiple marker modality is superior to NT-proBNP alone in prognostic prediction in all-cause mortality in a prospective cohort of elderly heart failure patients.** *Manuscript, submitted*



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# The Clinical Relevance and Potential Mechanism of Biomarkers in Elderly Heart Failure Patients

Alexandra Holmström

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

## ABSTRACT

**Aim:** To study the clinical relevance and potential mechanism of biomarkers in elderly heart failure (HF) patients.

**Methods:** A retrospective study was conducted by access to Swedish Heart Failure Registry with focus on HF patients aged  $\geq 85$  years. A secondary study was conducted in our hospital cohort due to acute decompensated HF in elderly patients. A prospective study was conducted in elderly patients referred for echocardiography because of suspected HF.

**Results:** The  $\geq 85$  year group from Swedish Heart Failure Registry was characterized by higher incidence of cardiovascular and non-cardiovascular comorbidities compared with the  $\leq 65$  year group. Compared with the 85-90 year subgroup, the  $>90$  year subgroup had a decline in cardiovascular and non-cardiovascular comorbidities. In the secondary study in elderly patients during hospital admission due to acute decompensated HF, multivariate analysis showed that N-terminal pro-B-type natriuretic peptide (NT-proBNP) was not prognostic predictor for all-cause mortality. However, a subgroup analysis demonstrated that in patients with NT-proBNP  $>8000$  (ng/L), NT-proBNP was the only prognostic predictor for all-cause mortality. In the prospective hospital cohort referred for echocardiography because of suspected HF, red blood cell distribution width (RDW) was higher among patients with HF. In the three multivariate analyses, biomarkers that were prognostic predictors of all-cause mortality were NT-proBNP, cystatin C, RDW, midregional pro-atrial natriuretic peptide (MR-proANP). Finally, when all the variables that were significant in above three multivariate analyses were analyzed in one multivariate analysis the only biomarker that was prognostic predictor of all-cause mortality in elderly HF patients was NT-proBNP. Furthermore, the sensitivity and specificity of the two different multiple marker modalities are higher than NT-proBNP alone.

**Conclusion:** Elderly HF patients had increased cardiovascular and non-cardiovascular comorbidities that declined from  $>90$  years. The prognostic value of NT-proBNP in elderly HF patients has to be interpreted with caution due to higher age and comorbidities. Two different multiple marker modalities incorporating biomarkers were able to improve prognostic prediction compared to NT-proBNP alone.

**Implication:** Our studies strongly suggest that the development of multiple marker models incorporating biomarkers reflecting different pathophysiological pathways might allow for better prognostic prediction in elderly HF patients.

**Keywords:** Heart failure, elderly, biomarkers, comorbidities, mortality

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