

# Studies of Risks Associated with Atrial Fibrillation.

Akademisk avhandling

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av

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This thesis is based on the following papers:

- I Olsson LG, Swedberg K, Lappas G, Stewart S, Rosengren A. Trends in stroke incidence after hospitalization for atrial fibrillation in Sweden 1987 to 2006.  
*Manuscript*
- II Olsson LG, Swedberg K, Lappas G, Stewart S, Rosengren A. Trends in mortality after hospitalization for atrial fibrillation in Sweden 1987 to 2006.  
*Manuscript*
- III Swedberg K, Olsson LG, Charlesworth A, et al. Prognostic relevance of atrial fibrillation in patients with chronic heart failure on long-term treatment with beta-blockers: results from COMET.  
*Eur Heart J 2005;26:1303-8.*
- IV Olsson LG, Swedberg K, Ducharme A, et al. Atrial fibrillation and risk of clinical events in chronic heart failure with and without left ventricular systolic dysfunction: results from the candesartan in heart failure-assessment of reduction in mortality and morbidity (CHARM) program.  
*J Am Coll Card 2006;47:1997-2004.*

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## STUDIES OF RISKS ASSOCIATED WITH ATRIAL FIBRILLATION

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### Abstract:

**Aim:** To investigate temporal trends in the risk of mortality and stroke associated with incident atrial fibrillation (AF) in Sweden. To investigate the risk of morbidity and mortality associated with prevalent and incident AF in patients with chronic heart failure with preserved (CHF-PEF) or reduced left ventricular ejection fraction (CHF-REF) enrolled in two large randomised trials.

**Methods:** In Papers I and II, we utilized Swedish National Hospital Discharge Registry linked with the cause-specific death registers. The hospital discharge registry has been in operation since the 1960s and has operated on a nation-wide basis since 1987. From this source all patients discharged from a Swedish hospital with a first diagnosis of AF were collected, and data regarding age, gender and registered comorbidities were obtained and compared by 5-year periods. Paper III utilized data from the Carvedilol Or Metoprolol European Trial (COMET). Paper IV utilized data from the Candesartan in Heart failure-Assessment of Reduction in Morbidity and mortality (CHARM) programme.

**Results:** The incidence of ischemic strokes up to 3-years after a first diagnosis of AF was 11.6% 1987-1991 (period 1) and 9.6% 2002-2006 (period 4), corresponding to a 17.5% relative decrease, the decrease mainly occurred during 1997-2001 (period 3), with small changes before and thereafter. The incidence of hemorrhagic strokes was 1.0% period 1 and 1.3% period 4, a 37.2% relative increase. The total number of strokes thus declined during the observation period. The decline in the total stroke incidence in AF patients was higher than that seen in the rest of the Swedish population. 3-year mortality was 34% during period 1 and 26% period 4, corresponding to a 23% relative decrease in mortality during the observation period. Patients diagnosed with any of previous stroke, chronic heart failure, acute coronary syndrome and diabetes mellitus had high but declining 3-year mortality rates during the observation period, regardless of age and sex. Patients without the prespecified comorbidities had lower case-fatality, especially in younger patients, but improvements in survival were smaller. Patients with CHF and AF had an increased risk of mortality and morbidity compared to patients in sinus rhythm, regardless of LVEF at baseline. Patients with CHF-REF had the highest absolute morbidity and mortality in CHARM trial, but patients with CHF-PEF had higher relative increase in morbidity and mortality with AF. New onset AF during the follow-up was a strong predictor of mortality and morbidity in both studies, regardless of baseline LVEF.

**Conclusions:** Patients discharged from a Swedish hospital with a first diagnosis of atrial fibrillation had moderate decreases in stroke incidence and mortality during a 20 year observation period. Although treatment and management of AF and its associating conditions, have improved dramatically during the last 30 years, AF is still associated with an excess morbidity and mortality. Even when patients with important comorbidities are excluded from the analysis, there is a considerable mortality among patients with AF. In a prespecified analysis of two large randomized trials with CHF and AF, AF was associated with increased morbidity and mortality both when present and when occurring during study follow-up, regardless of baseline EF.

**Keywords:** Atrial fibrillation, stroke, ischemic, hemorrhagic, mortality, temporal trends, ejection fraction, preserved, chronic heart failure, new onset, cohort study, randomised controlled trial.

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