Atrial fibrillation
Treatment, associated conditions and quantification of symptoms

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorsexamen framläggs till offentligt försvar i Hörsal E04, ingång R-1, Biomedicinhuset, Norrlands universitetssjukhus, fredagen den 15 september, kl. 13:00.
Avhandlingen kommer att försvaras på svenska.

Fakultetsopponent: Professor Juhani Koistinen, Medicinska fakulteten, Åbo universitet, Åbo, Finland.
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**Abstract**

**Background:** Atrial fibrillation (AF) is the most prevalent cardiac arrhythmia. There is a need for new pharmacological treatment strategies since the current antiarrhythmic drugs have a modest efficacy and may have severe side effects. Cardioversion (CV) of AF offers an opportunity to study related conditions in sinus rhythm (SR) and during AF. Since catheter ablation of AF is a symptomatic treatment, it is important to have tools for measurement of arrhythmia-related symptoms.

**Aims:** To evaluate the effect of atorvastatin on maintaining SR after CV of persistent AF. To assess if high-sensitivity C-reactive protein (hsCRP) predicts the recurrence of AF after CV in a population randomized to treatment with either atorvastatin or placebo. To quantify the symptomatic effect of left atrial catheter ablation of AF. To assess if the restoration of SR by CV, in a population with persistent AF, affects sleep apnea.

**Methods:** Paper I: A total of 234 patients were randomized to treatment with either high dose atorvastatin or placebo prior to CV. Paper II: In a pre-specified substudy which included 128 of the patients in study I, hsCRP was analyzed before and after CV. Paper III: Umea 22 Arrhythmia Questions (U22) is a questionnaire that quantifies paroxysmal tachycardia symptoms. A total of 105 patients underwent first-time pulmonary vein isolation and answered U22 forms at baseline and follow-up 304 (SD 121) days after ablation. Paper IV: Polysomnography was performed before and after CV in 23 patients with persistent AF scheduled for elective CV.

**Results:** Paper I: An intention-to-treat analysis with the available data, by randomization group, showed that 57 (51%) in the atorvastatin group and 47 (42%) in the placebo group were in SR 30 days after CV (OR 1.44, 95%CI 0.85–2.44, P=0.18). Paper II: HsCRP did not significantly predict recurrence of AF at 30 days. However, after adjusting for treatment with atorvastatin, hsCRP predicted the recurrence of AF (OR 1.14, 95% CI 1.01–1.27). Six months after CV, hsCRP at randomization predicted recurrence of AF in both univariate analysis (OR 1.30, 95% CI 1.06–1.60) and in multivariate logistic regression analysis (OR 1.33, 95% CI 1.06–1.67). Paper III: The U22 scores for well-being, arrhythmia as cause for impaired well-being, derived time-aspect score for arrhythmia, and discomfort during attack detected relevant improvements of symptoms after the ablation. U22 showed larger improvement in patients undergoing only one procedure than in patients who later underwent repeated interventions. Paper IV: Obstructive sleep apnea occurred in 17/23 patients (74%), and central sleep apnea in 6/23 patients (26%). Five patients had both obstructive and central sleep apnea. SR at follow-up was achieved in 16 patients. The obstructive apnea-hypopnea index, central apnea-hypopnea index, and the number of patients with obstructive or central sleep apnea did not differ before and after restoration of SR.

**Conclusions:** Atorvastatin is not a treatment option with regards to maintaining SR after CV in patients with persistent AF. HsCRP was associated with AF recurrence 1 and 6 months after successful CV of persistent AF. U22 quantifies the symptomatic improvement after AF ablation with adequate internal consistency and construct validity. Both obstructive and central sleep apneas are highly prevalent in patients with persistent AF. Obstructive sleep apneas are unaffected by the CV of AF to SR.

**Keywords**

Atrial fibrillation, cardioversion, atorvastatin, high-sensitivity C-reactive protein, symptoms, sleep apnea.