HDL-function in atrial fibrillation

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Background

Atrial fibrillation (AF) is the most common sustained arrhythmia in clinical routine and associates with cardio- and cerebrovascular complications, dementia and mortality. AF is a progressing disease resulting in left atrial remodeling which can be detected during catheter ablation as low voltage areas (LVA). Atrial remodeling is underpinned by several pathomechanisms (e.g. fibrosis, hemodynamic alterations, and inflammatory processes) and is triggered by diverse risk factors (age, gender, lifestyle factors, and primary heart disease). Next to those established risk factors alterations in cholesterol levels were controversially discussed as AF risk factors. Recently, it was proposed that HDL function rather than HDL quantity might be associated with cardiovascular disease. HDL and AF are both known to influence the homeostasis of apoptotic, oxidative, and inflammatory processes implicating a potential link.

Purpose

We analyzed prominent metrics of HDL functionality and (HDL) particle distribution in healthy individuals and in AF patients with and without LVA before and following successful therapy.

METHODS

Patients

Patients with AF undergoing catheter ablation (n=93) were free from statins and had no fibrotic heart, kidney, thyroid or liver disease. They were 61.5 +/- 11 years old, 46% female, 53% had paroxysmal AF, 47% had persistent AF, and 18% had left atrial LVA. Blood was collected from femoral vein before catheter ablation. LVA were determined using high-density maps and were defined as potentials <0.5 mV. Follow up examinations were performed 12-18 months following the ablation procedure. Healthy control probands (n=29) were 59 +/- 13 years old and 31% female.

Methods

Cholesterol efflux from J774 macrophages labeled with [3H]cholesterol was measured following 4h incubation with Apo-B-depleted proband serum. Radioactivity in supernatants and cells was then measured by liquid scintillation counting and set into relation with total radioactivity in medium and cells. Commercial kit was used to assess lecithin-cholesterol acyltransferase (Merck, Darmstadt, Germany) in sera according to the manufactures instruction. HDL-particle distribution was measured using NMR spectroscopy.

RESULTS

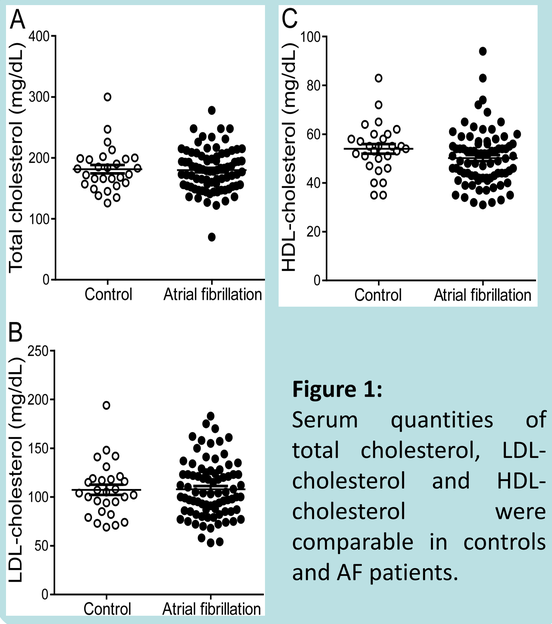

Figure 1: Serum quantities of total cholesterol, LDL-cholesterol and HDL-cholesterol were comparable in controls and AF patients.

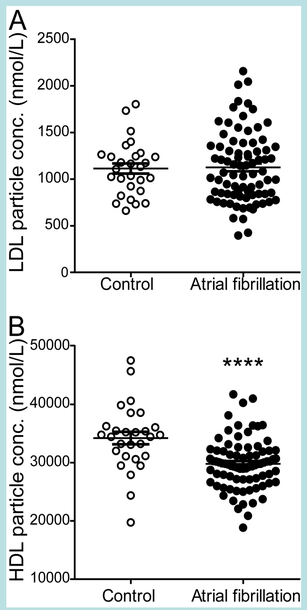

Figure 2: LDL-particle concentration was similar in both groups. HDL-particle concentration was significantly decreased in AF patients.

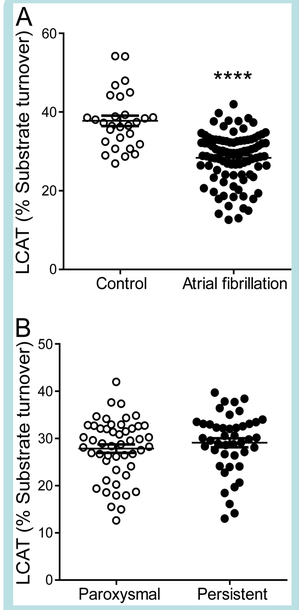

Figure 3: LCAT activity was significantly decreased in AF patients. The type of AF (paroxysmal vs. persistent) had no effect on LCAT activity.

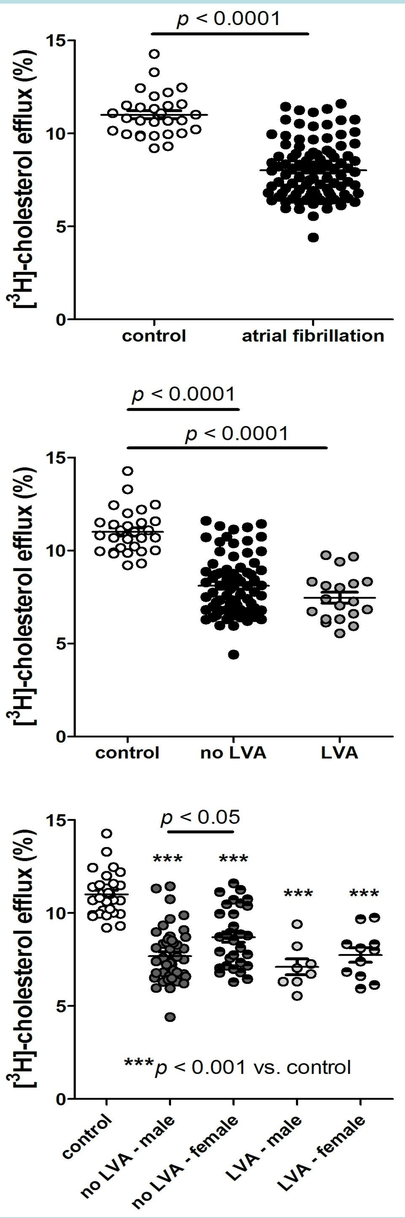

Figure 4: HDL-cholesterol efflux capacity was significantly lower in AF patients compared to controls. By trend efflux capacity was lowest in patients with progressed AF (with LVA). Female AF patients had higher efflux capacities than males.

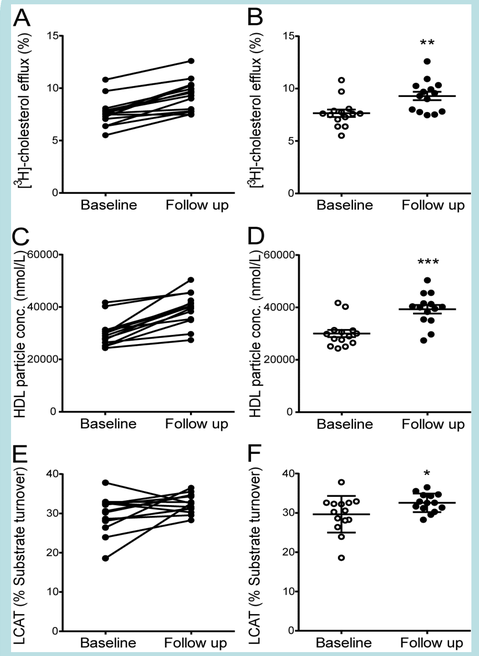

Figure 5: HDL-cholesterol efflux capacity, HDL-particle concentration and LCAT activity were significantly improved one year following succesful catheter ablation therapy.

CONCLUSIONS

The present study is the first to demonstrate that alterations in HDL functionality and composition are associated with atrial fibrillation in general and may partially also associate with AF progression. Successful AF therapy was found to associate with improved HDL functionality.

We conclude that HDL-dysfunctionality is a characteristic of atrial fibrillation and assume a contribution to AF related processes and associated risk.

Contact
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COI: All authors declare that no conflict of interest exists.