Gender-dependent regulation of FABP4 and leptin according to atrial fibrillation burden

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Aims: Adiposity plays a key role in the pathogenesis of atrial fibrillation (AF). Its associated proteins are differentially released between male and female. FABP4 and leptin are mediators in adipose tissue-inflammatory effects. Our aim was to study their gender differential behavior on mechanisms associated with AF progression.

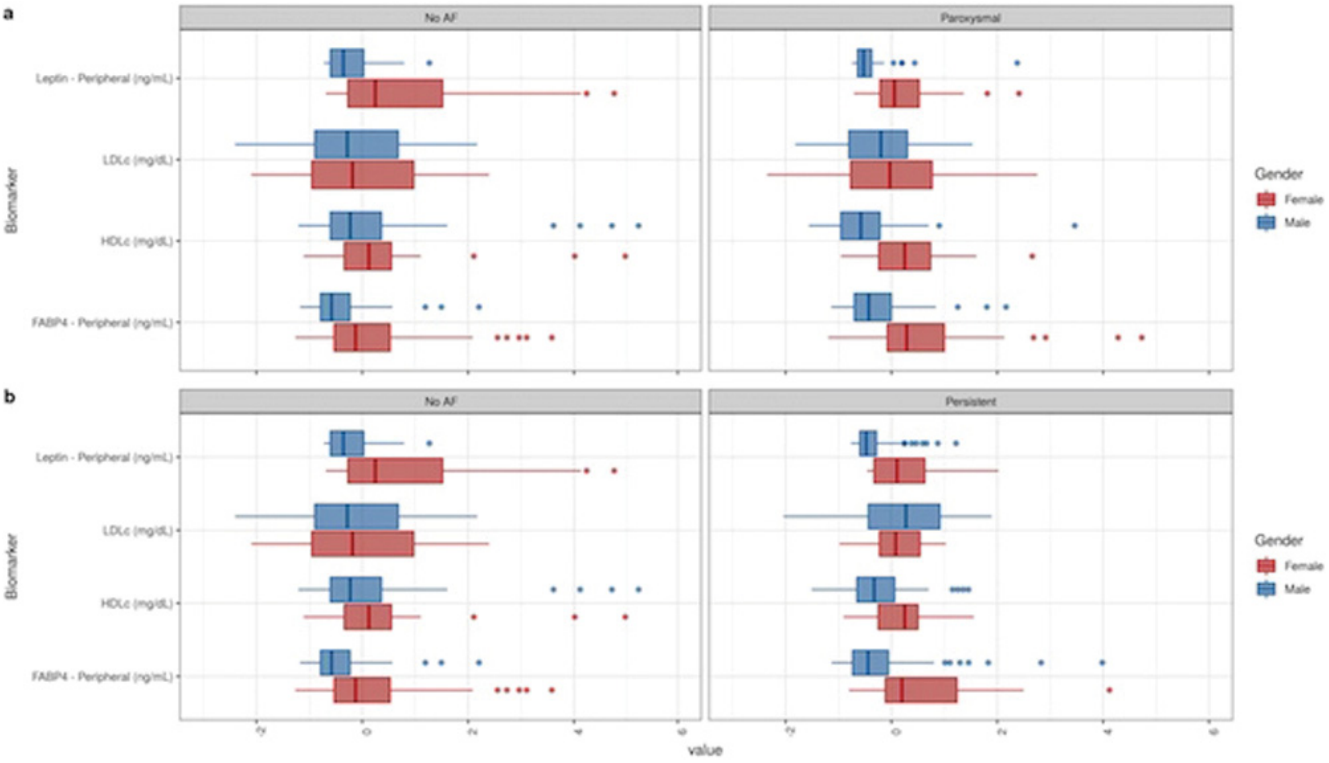
Methods and results: Two independent cohorts were analyzed: A) patients referred for AF catheter ablation (n=217) and patients with suspected coronary artery disease referred for a CT scan (without previous history of AF) (n=105). Protein levels were determined by multiplex fluorometric immunoassay. Gene mRNA expression was analyzed by real time polymerase chain reaction. Correlation between biomarkers was explored with heatmaps and Kendall correlation coefficients. Logistic regression and random forest model determined the best predictors of AF recurrence after catheter ablation. Our results showed: 1) a distinctive profile according to gender, with an increment of FABP4 levels in women (20±14, 29±18 and 31±17 ng/mL; p=0.007) and a decrease of leptin levels in men (22±15, 13±16 and 13±11 ng/mL; p=0.001) among control, paroxysmal and persistent AF groups, respectively; 2) sex differences regarding inflammatory profile, oxidative stress and autonomic indirect markers in AF; 3) a prominent role of adipokines to discriminate AF recurrence after ablation. In persistent AF, FABP4 was the best predictor (LR coefficient 1.067, 95% CI 1–1.14, p=0.046).

Conclusion: The major finding of the present study is the sex differences of FABP4 and leptin according to AF burden. The relationship of these adipokines with oxidative stress, inflammatory and autonomic indirect markers might explain part of the mechanisms underlying the AF perpetuation.

Table 1

	Women			Men		
	COEFF.	SE	p	COEFF.		SE p
(Intercept)		−1.69	0.092		−2.62	0.009
Age	0.181	2.23	0.027	0.217	3.30	0.001
BMI	0.215	2.41	0.017	0.246	3.12	0.002
AFpresence/control	0.232	2.81	0.006	0.129	1.80	0.074
Leptin	0.147	1.65	0.101	0.261	3.28	0.001

Box plots represents median and interquartile range of adipokines and lipoproteins. Regarding gender: a) no history of AF vs paroxysmal AF. b) no history of AF vs persistent AF.



Adipokines regarding Gender & AF burden