Myeloperoxidase in Atrial Fibrillation – Association with Progression, Origin and Influence of Renin-Angiotensin-System Antagonists

Erik Holzwirth[1], Jelena Kornej[2], Sandra Erbs[1], Danilo Obradovic[1], Andreas Bollmann[2], Gerhard Hindricks[2], Holger Thiele[1], Petra Büttner[1]

[1] Heart Center Leipzig at University Leipzig, Department of Cardiology, Leipzig, Germany
[2] Heart Center Leipzig at University Leipzig, Department of Electrophysiology, Leipzig, Germany

Background

Atrial fibrillation (AF) is the most common cardiac arrhythmia with a lifetime prevalence of roughly 25% and accompanied by a 1.5 to 1.9 fold increased all-cause mortality.

Myeloperoxidase (MPO) is secreted by immune cells especially neutrophils under inflammatory conditions and its serum levels are known to be elevated in patients with atrial fibrillation.[1] Current research suggests its involvement in the fibrotic atrial remodeling[2] which is thought to be both cause and result of AF.

Angiotensin Converting Enzyme Inhibitors or Angiotensin Receptor Blockers (in the following collectively referred to as renin-angiotensin-system antagonists, RAS-A) are commonly used to treat hypertension, a common comorbidity in AF. Beyond that, they are well established in the therapy of heart failure due to their ability to ameliorate cardiac remodeling, a pathological finding shared with AF. Furthermore, RAS-A target, Angiotensin II, has been reported to modulate MPO levels.[1]

Purpose

In this study we investigated circulating MPO levels in progressing AF, compared peripheral and cardiac blood plasma concentrations and analyzed a potential influence of angiotensin-antagonists.

Patients and Methods

Blood was peri-interventionally collected from the femoral vein and from the left atrium in AF patients during catheter ablation (n = 121). Blood from no AF control probands (n=37) was used for comparisons. MPO concentrations were measured using sandwich ELISA and analyzed in AF groups and controls.

	AF (n=121)	Controls (n=37)	p - Value
Age, years	65 (52-78)	59 (43-75)	0.011*
Female, %	47.9	47.4	0.951**
eGFR, ml/min	79 (64-92)	no data	
BMI, kg/m²	29.7 ± 4.9	28.1 ± 6.1	0.093***
Hypertension, %	78.5	71.1	0.342**
Use of RAS-A, %	55.0	56.8	0.754**
paroxysmal AF, %	47.1	-	n.a.
Presence of LVA, %	31	no data	n.a.
Heart frequency	70 (60-88)	68 (60-73)	0.141*
Sinus Rhythm before Procedure, %	51.3	-	n.a.
MPO, ng/ml	27.7 (14.3-66.6)	12.6 (9.9–17.7)	< 0.001*

Abbreviations: n.a. – non applicable, eGFR – estimated glomerular filtration rate, BMI – body mass index, RAS-A – renin-angiotensin-system antagonists, AF – atrial fibrillation, LVA – low voltage areas
* Mann-Whitney U Test, median (IQR) ** Chi Square Test, *** T-Test, mean ± SD

Results

Result 1: MPO is significantly increased in atrial fibrillation.
Result 2: MPO levels are 10-fold higher in left atrial cardiac blood.

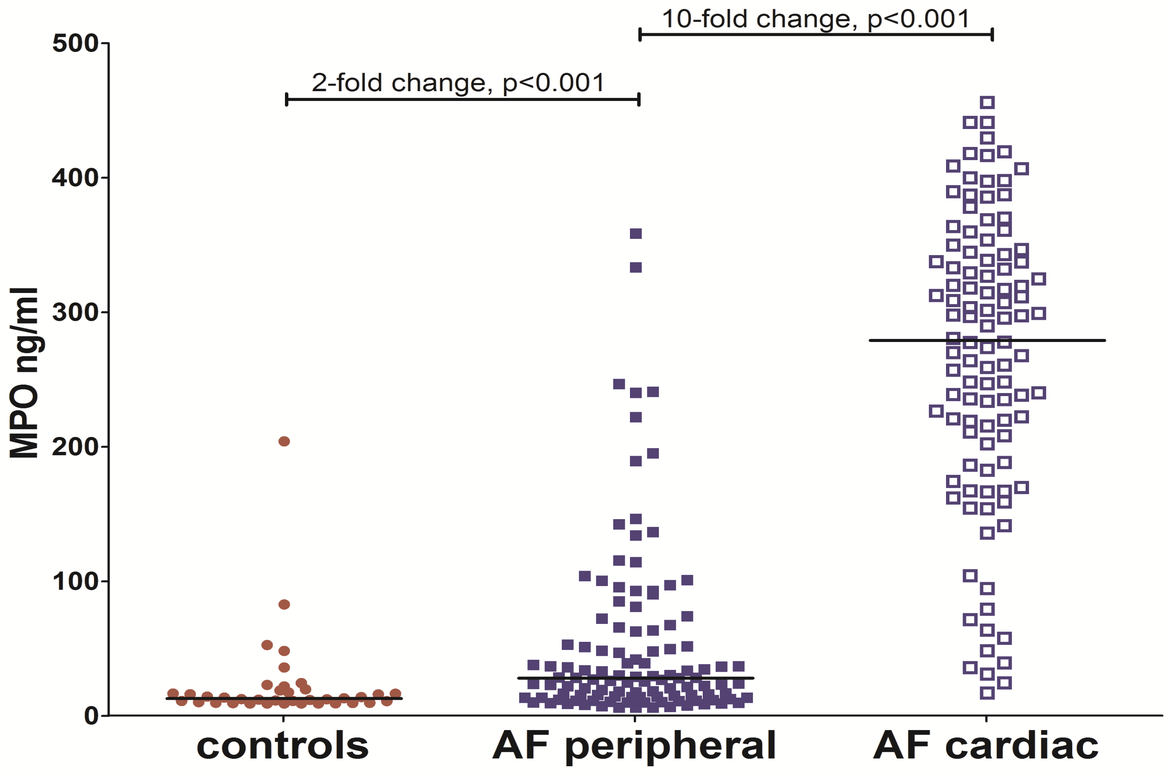

Figure 1: Plasma levels of MPO in controls and paired samples of AF patients from peripheral blood and cardiac blood from the left atrium. Red circles stand for controls; blue squares indicate peripheral blood of patients with AF; clear blue squares indicate cardiac blood of patients with AF.

Result 3: Peripheral and cardiac levels of MPO are similar in paroxysmal and persistent AF and in patients with or without low voltage areas .

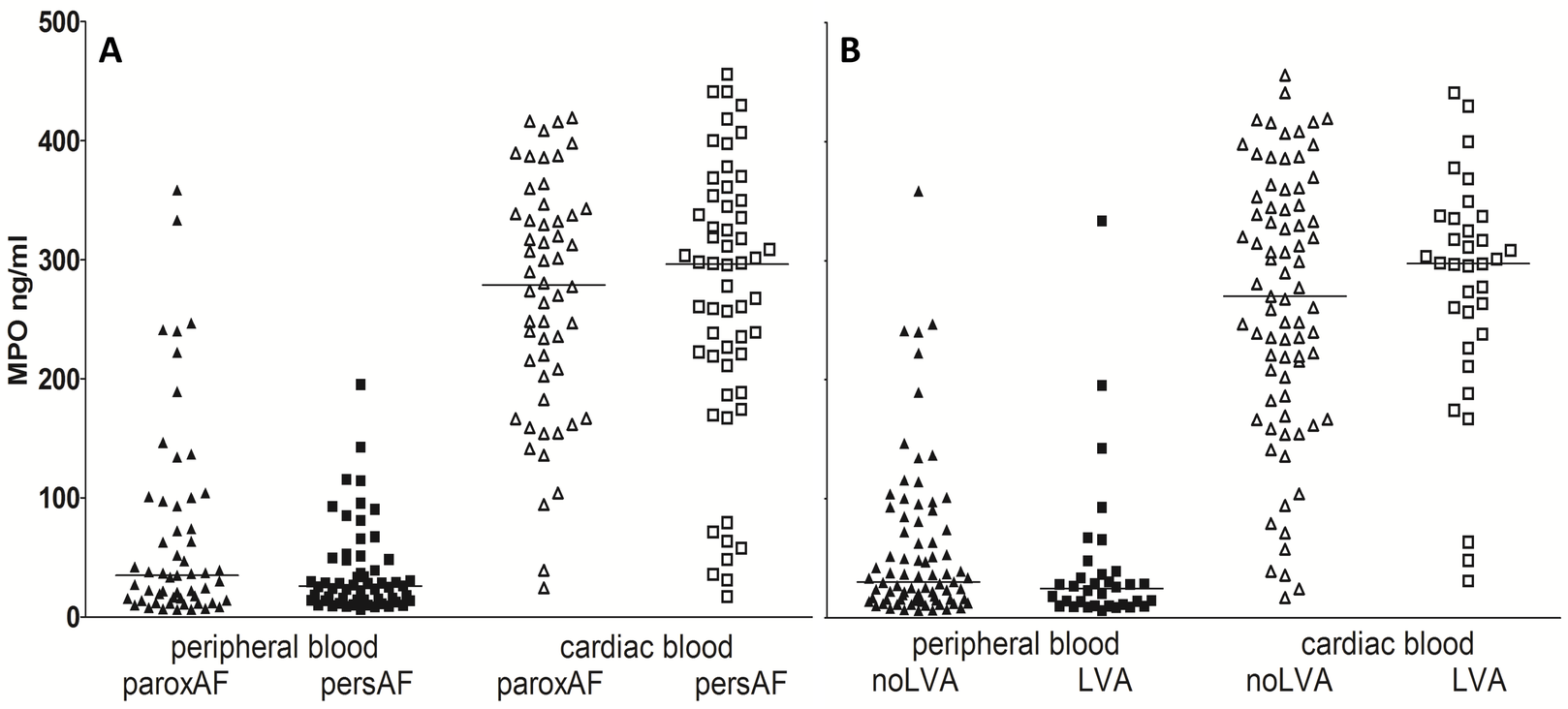

Figure 2: MPO ng/ml level in **A** patients with paroxysmal atrial fibrillation (paroxAF) (indicated by triangles) and patients with persistent atrial fibrillation (persAF) (indicated by squares) in peripheral blood (filled symbols) and cardiac circulation (clear symbols). **B** in patients with atrial fibrillation but no detectable left atrial low voltage areas (noLVA) (indicated by triangles) and patients with detectable low voltage areas (LVA) (indicated by squares) in peripheral blood (filled symbols) and cardiac circulation (clear symbols). No differences in MPO concentration in peripheral or cardiac blood were detected (Mann-Whitney-U Test, p>0.05)

Result 4: Peripheral MPO ng/ml concentrations in AF patients using (n=65) or not using (n=51) RAS-A (Mann-Whitney-U Test, p<0.05)

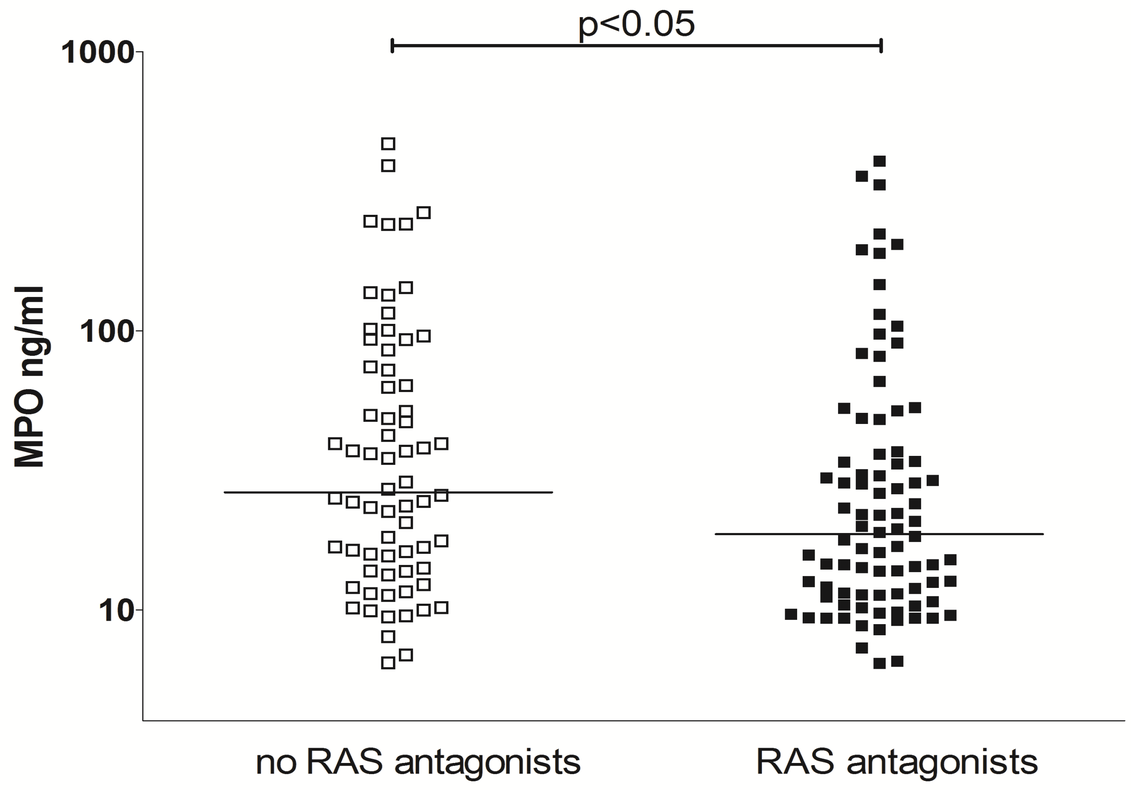

Figure 3. Peripheral MPO ng/ml concentrations in AF patients using (n=65) or not using (n=51) RAS-A (Mann-Whitney-U Test, p<0.05).

Conclusions

The pro-fibrotic enzyme MPO is generally elevated in AF patients irrespective of AF progression stage. Left atrial MPO levels in AF patients are ten fold increased relative to its peripherally collected counterpart suggesting its direct origination from the atria which further supports the notion of AF being a local inflammatory disease.

The usage of RAS-A resulted in lowered MPO levels among AF patients. Interestingly, this effect was only observable in peripheral blood samples but not in atrial blood. Further studies investigating the underpinning mechanisms and possible therapeutical implications are necessary.

References

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Contact: Petra Büttner
Petra.buettner@medizin.uni-leipzig.de
Department of Internal Medicine/ Cardiology, Heart Center Leipzig at University of Leipzig

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