Published in final edited form as:

Int J Cardiol. 2015 February 15; 181: 207–212. doi:10.1016/j.ijcard.2014.12.022.

The Impact of Gender and Left Atrial Blood Stasis on Adiponectin levels in Non-valvular Atrial Fibrillation

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Abstract

Background—Obesity is a risk factor for non-valvular atrial fibrillation (NVAF), diabetes mellitus, and hypertension. Adiponectin, a unique biomarker of adipose tissue, has antiinflammatory, insulin-sensitizing, and antiatherogenic properties and is known to be higher in women. The relationship between adiponectin, gender, and thromboembolic risk in atrial fibrillation however is unknown.

Methods—The relationship between gender, adiponectin levels, and echocardiographic measures of blood stagnation and left atrial appendage thrombus (LAAT) was assessed in 209 patients with NVAF (55 women and 154 men; mean age 63 ± 14 years) compared to 70 normal sinus rhythm controls (29 women and 41 men; mean age 64 ± 14 years). Total adiponectin was measured by solid-phase ELISA. Demographic and clinical variables of CHADS₂ and CHA₂DS₂-VASc were collected, and spontaneous echocardiographic contrast (SEC), left atrial appendage emptying velocity (LAAEV) and left atrium volume index (LAVI) were measured prospectively.

Results—Elevated adiponectin was associated with advanced cardiovascular pathology and permanent arrhythmia but only in men with NVAF. In NVAF men, a step-wise increase in adiponectin levels was noted relative to increasing intensity of SEC and decreasing LAAEV. Adiponectin level >16657 ng/ml predicted LAAT (OR: 3.66; 95%CI: 1.21-11.48); $p=0.022$) after adjustment for CHADS₂ score in men but not in women with NVAF.

Conclusions—There is a direct correlation between elevated adiponectin level and the degree of left atrial blood stasis in men but not women with NVAF. High adiponectin levels can be used as an important variable in the prediction of LAAT.

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All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation

Disclosures: The authors report no relationships that could be construed as a conflict of interest

Keywords

atrial fibrillation; left atrial appendage thrombus; adiponectin; gender

INTRODUCTION

Atrial Fibrillation and obesity are growing epidemics and are associated with a high morbidity and mortality.^{1, 2} Obesity is associated with insulin resistance, cardiovascular disease, and risk of developing atrial fibrillation.³ Adiponectin, secreted by adipose cells, is an adipocytokine that is abundantly circulating in plasma in different isoforms and represents a unique blood marker of adipose tissue.⁴ Adiponectin has been shown to have antiinflammatory, insulin-sensitizing effects as well as antiatherogenic properties.⁵ Experiments on adiponectin-knockout mice indicate that adiponectin protects against angiotensin II-induced cardiac fibrosis.⁶ Several studies have shown that men have lower levels of adiponectin compared to women, likely due to testosterone inhibition of adiponectin production.^{7,8} Adiponectin levels are lower in obese individuals, particularly those with visceral adiposity.^{8,9} Levels are also lower in patients with type 2 diabetes mellitus, metabolic syndrome, hypertension, and coronary artery disease.¹⁰⁻¹³

Despite these associations, the relationship between adiponectin and the thromboembolic complications of atrial fibrillation remains unclear. Adiponectin levels were lower in patients developing postoperative atrial fibrillation compared to those who did not develop this dysrhythmia.¹⁴ The thrombotic complications of post-operative atrial fibrillation are known to be very low. Adiponectin levels were directly related to the duration of atrial fibrillation.¹⁵ Levels were higher in patients with persistent compared to paroxysmal atrial fibrillation or normal sinus rhythm (NSR).¹⁵ No consistent relationship has been found between adiponectin levels and left atrial size.^{16,17} Adiponectin levels did not predict stroke or other cardiovascular complications in 918 stably anticoagulated patients with NVAf.¹⁸

The relationship between gender, adiponectin levels, and echocardiographic measures of blood stagnation and left atrial appendage thrombus (LAAT) was assessed in patients with NVAf compared to normal sinus rhythm controls.

MATERIALS AND METHODS

Patient recruitment

Study design, patient selection, recruitment, clinical and echocardiographic data collection and assessment have previously been described.¹⁹ Briefly, all patients with NVAf (cases) who had TEE ordered by their primary physician or cardiologist (October 4, 2007 – April 27, 2009) were approached for study participation. Patients were excluded from participated if they had: (1) acute illness, stroke, myocardial infarction or surgery within 30 days; (2) more than moderate heart valvular disease; (3) artificial heart valves; (4) prior unprovoked venous or arterial thrombosis; (5) prior major bleeding unrelated to warfarin therapy; (6) liver disease; (7) active malignancy; or (8) hormonal stimulation (estrogen/progesterone therapy or pregnancy). Control subjects in normal sinus rhythm (NSR) with no prior history

of atrial fibrillation were recruited from the Primary Care Internal Medicine clinic during their annual medical exam. From our original cohort, a subgroup of subjects was randomly sampled for analysis of this study.¹⁹

Evaluation with transesophageal echocardiogram

TEE was performed as previously described.^{20,21} LAAT was defined as an echogenic mass in the appendage or body of the atrium, distinct from the underlying endocardium and pectinate muscles and detected in more than one imaging plane.^{20,21} SEC was defined as a pattern of dynamic “smokelike”, slowly swirling, intracavitary echo-densities imaged with gain settings adjusted to eliminate background noise. SEC was graded as “absent”, “mild”, “moderate”, or “severe” according to the published, echocardiographic criteria.²² LAAEV profiles were measured over 5 consecutive cardiac cycles using pulsed wave Doppler interrogation with the sample volume positioned 1 cm within the orifice of the LAA.²³ The left ventricular ejection fraction (LVEF) was visually estimated. Aortic atherosclerosis severity was defined as “simple” when atheroma thickness was < 4 mm and immobile. “Severe atheroma exceeded 4 mm or contained mobile components.”^{20,21,23} Given the known difficulties in measuring left atrial volume by TEE, LAVI was assessed by transthoracic echocardiography performed within 1 month of the TEE study and calculated by the biplane area-length method.²³ All echocardiographic images were analyzed by the study cardiologist (NA) who was blinded to clinical and laboratory data. Control subjects in NSR did not have evaluations completed with TEE.

Study definitions and event adjudication

Congestive heart failure (CHF) was defined as the presence of clinical symptoms and signs of heart failure within the last three months with or without evidence of LV systolic dysfunction by echocardiography.²⁴ Diabetes mellitus was diagnosed based on the criteria recommended by the American Diabetes Association.²⁵ Stroke, TIA, and systemic embolization were defined by criteria proposed by the American Heart Association.²⁶ Body mass index was evaluated as per the World Health Organization weight categories (normal weight: <25 kg/m²; overweight: 25.0-29.9 kg/m²; obesity: 30-34.9 kg/m²; morbidly obese 35 kg/m²).²⁷ For cases, the presence of atrial fibrillation was confirmed by either electrocardiogram or Holter monitoring. Atrial fibrillation was classified as “paroxysmal”, or “persistent”, or “permanent” in accordance with current guidelines.²⁸ The CHADS₂ and CHA₂DS₂-VASc score was assigned for each case and control.^{24,29}

Sample Collection

For each subject, 20 ml of citrate blood was collected by antecubital venipuncture using a 19 gauge thin-wall “butterfly” needle with a short plastic tube extension. For NVAf patient (cases) scheduled for electric cardioversion or radiofrequency ablation, phlebotomy was uniformly collected prior to the procedure.

Plasma Adiponectin

Adiponectin in plasma was quantitatively determined by the Quantikine Human Total Adiponectin Immunoassay (R&D Systems, Inc. 614 McKinley Place NE, Minneapolis, MN

55413, USA). This assay uses a 4.5 hour solid-phase ELISA method designed to measure total (low, middle, and high molecular weight) human adiponectin. Assay sensitivity was 0.891 ng/mL, intra-assay precision ranged CV: 2.5%-4.7% and inter-assay precision CV: 5.9%-7.9%. All assays were performed in duplicates.

Statistical Analysis

Demographic, clinical and echocardiographic characteristics and adiponectin levels were compared between cases and controls. Continuous variables (mean $\pm$ standard deviation) were compared between groups using a two-sample t-test. Categorical variables (%) were compared using Pearson's Chi-square test for independence. Ordinal variables (%; median with quartiles) were compared using Wilcoxon rank-sum test. Area under the curve (C-index) for adiponectin levels is presented as a receiver operating characteristic (ROC) curve using logistic regression models. Using the cut-point determined by ROC curve, adiponectin levels were dichotomized according to whether the circulating levels were under or over the calculated threshold. This dichotomy for adiponectin levels was assessed into the logistic models to explore the overall predictive value of adiponectin [OR (95% CI), P-value] upon the development of LAAT. This was also done without the dichotomy for adiponectin levels.

RESULTS

Patient Population

Demographic and clinical characteristics, separately by gender, are presented for 209 NVAf patients and for 70 NSR controls (Table 1). More NVAf patients had hypertension [132 (63%) vs 33 (49%), $p=0.0339$] and took warfarin [164 (78%) vs 1 (2%), $p<0.0001$] compared to NSR controls. Of the NVAf cases, female patients were older and more likely to be morbidly obese compared to men. The distribution of all other demographic and clinical variables was similar between genders for both cases and controls. For the case – control comparison, there was no significant difference in either the mean CHADS₂ or CHA₂DS₂-VAsC scores. For patients with NVAf (cases) however, the mean CHADS₂ ($p=0.0531$) and CHA₂DS₂-VAsC scores (<0.001) were higher in women compared to men reflecting older age of women and, for the latter tool, the scoring methodology that gives one point for female gender. Detailed information of demographic and clinical characteristics for cases and controls can be found in the Supplement.

Within NVAf cases, 79% had non-permanent atrial fibrillation and 62% had this arrhythmia for more than one year. Markedly enlarged left atrium (LAVI >60 mL/m²) was observed in 19% and severely decreased LAEEV (<25 cm/s²) in 27% of cases. SEC was assessed as moderate in 24% and severe in 15% of NVAf patients who had adequate echocardiographic image quality. Simple (<4 mm) atheroma within thoracic aorta were found in 120 (59%) and complex (>4 mm) in 12 (6%) of evaluated NVAf patients. Apart from the left ventricular ejection fraction which was higher in women (58.9 ± 8.1 vs 53.4 ± 12.1 , $p=0.002$), echocardiographic findings were evenly distributed among male and female cases. Detailed information on echocardiographic characteristics of NVAf cases by gender can be found in the Supplement.

The distribution of adiponectin levels in NVAf cases and NSR controls relative to demographic and clinical characteristics is summarized in Table 2. For both cases and controls, adiponectin levels varied by age, female gender, and increasing BMI. Adiponectin levels were greater in NVAf patients with known heart failure and increasing CHADS₂ and CHA₂DS₂-VASc scores. Beyond these demographic and clinical variables there were no differences in adiponectin levels. Adiponectin levels did not differ by anticoagulant, antiplatelet or statin therapy.

The impact of gender on adiponectin levels in relation to atrial fibrillation characteristics and echocardiographic findings are presented in Table 3. In men, adiponectin levels increased with permanent atrial fibrillation, worsening ejection fraction and left atrial appendage emptying velocity, increased SEC intensity, as well as the existence of left atrial appendage thrombus and burden of thoracic aortic atherosclerosis. In contrast, there was no relationship between left atrial and ventricular function, measures of atrial blood stagnation or thoracic aortic atherosclerosis and adiponectin levels in women with NVAf.

For NVAf males, a step-wise increase in adiponectin levels was noted relative to increasing intensity of SEC (Figure 1). In contrast, adiponectin levels were elevated across the spectrum of SEC in women with NVAf and were not different compared to controls. Similar results were noted when comparing adiponectin levels and left atrial appendage emptying velocity when stratified by gender (Figure 2).

A positive pairwise correlation between adiponectin level and age ($p < .0001$) and left atrial volume index ($p = 0.0335$) was found. A negative correlation was noted with weight ($p = 0.0002$) and left atrial appendage emptying velocity ($p = 0.0014$). Details of pairwise correlations between continuous demographic and echocardiographic variables and adiponectin levels are available in the Supplement.

Receiver operating characteristic (ROC) curves were generated using adiponectin levels for the prediction of LAAT among male and female cases. Using the cut-point determined by ROC curves, adiponectin levels were dichotomized and logistic modeling was used to explore the overall predictive value of adiponectin [OR (95% CI), P-value] to identify LAAT. For cases, the best adiponectin cut-off for predicting this endpoint was 16657 ng/ml (AUC 0.66, $p = 0.019$). This cut-off concentration showed a sensitivity of 0.53 and specificity of 0.78. The area under the ROC curve for predicting the presence of a LAAT in NVAf men (AUC 0.75, $p = 0.0017$) gave again 16657 ng/ml adiponectin concentration with sensitivity of 0.57 and specificity of 0.84. When constructing the ROC curve for LAAT prediction in NVAf women, no significant cut-off point for adiponectin concentration was found (AUC 0.59, $p = 0.760$). Adiponectin level above 16657 ng/ml was associated with LAAT by univariate logistic regression in men (Odds Ratio (OR): 6.78; 95% CI: 2.16-22.42; $p = 0.0012$) but not in women (OR: 1.08 95% CI: 0.13-7.14; $p = 0.930$). After adjustment for age and CHADS₂ score, adiponectin level >16657 ng/ml remained an independent predictor for LAAT in men with NVAf (OR: 3.66; 95% CI: 1.21-11.48; $p = 0.022$). However, adiponectin level higher than 16657 ng/ml lost its independent prediction for LAAT in NVAf men when left atrial appendage emptying velocity was added to this model (OR: 2.32; 95% CI: 0.38-15.53; $p = 0.3540$).

DISCUSSION

The major finding of this study is a gender related difference in adiponectin levels among patients with NVAF. In our patients with NVAF, adiponectin levels were nearly 1.5 fold greater in women. Amongst the normal controls, these levels were nearly 2 fold greater in women. To our knowledge, this is the first study to demonstrate a direct correlation between adiponectin and the degree of left atrial blood stasis in men but not women with NVAF. A progressive increase of adiponectin level was observed in NVAF men with the advanced atherosclerosis of thoracic aorta, decreased left ventricular systolic function, decreased left atrial appendage emptying velocity, progressive intensity of SEC, and development of LAAT. Adiponectin levels exceeding 16657 ng/ml independently predicted the presence of LAAT after adjustment for age and CHADS₂ score yet only in men. After adjusting for left atrial appendage emptying velocity, the predictive power for identifying LAAT was lost suggesting that adiponectin may be a surrogate for left atrial blood stasis in men.

Whereas adiponectin has anti-inflammatory, anti-atherogenic⁵, anti-fibrotic⁶ and anti-thrombotic effects³⁰, elevated adiponectin observed with worse cardiovascular pathology and increased thromboembolic propensity could represent reactive response. It is unlikely however, that adiponectin protective properties are capable of completely ameliorating these pathologic processes. Factors responsible for both atherogenesis and atrial fibrillation are known to be multifactorial and pervasive. It is therefore reasonable to hypothesize that adiponectin is responsive to the disease process much like brain natriuretic peptide is responsive to heart failure. Several possible mechanisms could be suggested to explain gender related differences in adiponectin reactivity. First, there is a different metabolism of this adipocytokine in men; adiponectin is known to be governed at least in part by testosterone^{7,8}. Second, adiponectin level varies by adipose location which could be different in women compared to men³¹. In women, omental adipocytes are known to be smaller than subcutaneous cells independently of BMI³². Fat cell size was found to be an important determinant of adipogenic gene expression regulating metabolic activity³³. Third, whereas adiponectin levels are high in women, it is possible that further elevations may not be useful. Fourth, adiponectin could be a reactive metabolic regulator in men but constitutive in women and therefore does not vary by disease severity. Lastly, compare to men, the number of female cases was smaller and possibly not sufficient to observed significant differences. Further studies with more female cases may be necessary to confirm our findings. It needs to be emphasised, that despite gender differences in adiponectin reactivity, the prevalence of LAAT was similar for men and women.

As previously observed^{34,35}, NVAF patients with heart failure had increased adiponectin levels. In our study however, adiponectin levels did not correlate with other stroke risk factors including diabetes mellitus, hypertension, and vascular disease. Furthermore, adiponectin levels did not differ by antithrombotic therapy including warfarin or antiplatelet medications. An impact of statin therapy on adiponectin levels^{32,33} could not be verified by our results.

CONCLUSIONS

We identified a gender related difference in adiponectin levels among patients with NVAf. We found a direct correlation between adiponectin and the degree of left atrial blood stasis in men but not women. NVAf man had progressive increase of adiponectin level with decreasing left atrial appendage emptying velocity, progression of intensity of SEC and development of LAAT. Atrial fibrillation is a heterogeneous disease which varies by clinical characteristics including the propensity for embolization. High adiponectin levels can now be added as an important variable in the prediction of LAAT in this disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgement of grant support

This work was supported by CR 17896 grant from the Department of Internal Medicine, Mayo Clinic and statistical support was provided by an internal grant from the Mayo Clinic Division of Cardiology. Research support also was funded, in part, by a training grant from the National Institutes of Health, National Heart, Lung and Blood Institute (K12HL83141) in vascular medicine (KPC) and by Mayo Foundation. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Figure 1. Relationship between adiponectin and spontaneous echocardiography contrast (SEC) and left atrial appendage thrombus (LAAT) of nonvalvular atrial fibrillation (NVAf) compared to control subjects with normal sinus rhythm (NSR) by genders. Measures are presented as mean and confidence intervals.

Figure 2.

Relationship between adiponectin and left atrial appendage emptying velocities (cm/s) in nonvalvular atrial fibrillation (NVAf) patients compared to control subjects with normal sinus rhythm (NSR) by genders. Measures are presented as mean and confidence intervals.

Table 1

Demographic and clinical characteristics of non-valvular atrial fibrillation (NVAF) patients (cases) and normal sinus rhythm (NSR) controls.

Variable	NVAF Patients			NSR Controls		
	Female (N=55)	Male (N=154)	P	Female (N=29)	Male (N=41)	P
Age, years (mean $\pm$ SD)	68.1 $\pm$ 11.1	60.9 $\pm$ 14.0	0.0007	65.4 $\pm$ 14.2	63.4 $\pm$ 14.3	0.4922
65-74 years, n (%)	17 (31%)	41 (27%)	0.0274	9 (32%)	8 (20%)	0.4530
75, n (%)	16 (29%)	23 (15%)	0.0207	8 (29%)	11 (28%)	0.9229
Female, n (%)						
Body Mass Index (mean $\pm$ SD)	30.6 $\pm$ 8.6	30.4 $\pm$ 5.6	0.8264	30.0 $\pm$ 7.5	30.1 $\pm$ 6.3	0.9593
Body Mass Index Categories			0.0160			0.4087
< 25 kg/m ²	15 (27%)	23 (15%)		10 (35%)	10 (24%)	
25.0-29.9 kg/m ²	17 (32%)	57 (37%)		5 (17%)	14 (34%)	
30.0-34.9 kg/m ²	6 (11%)	42 (28%)		6 (21%)	9 (21%)	
35 kg/m ²	17 (32%)	32 (21%)		8 (28%)	8 (20%)	
Congestive Heart Failure, n (%)	17 (32%)	43 (28%)	0.6742	4 (14%)	8 (20%)	0.5391
Hypertension, n (%)	38 (69%)	94 (61%)	0.2879	16 (57%)	17 (43%)	0.2337
Diabetes Mellitus, n (%)	8 (15%)	22 (14%)	0.9624	6 (21%)	10 (25%)	0.7317
Stroke/TIA prior, n (%)	12 (22%)	20 (13%)	0.1185	3 (11%)	2 (5%)	0.3788
Vascular Diseases, n (%)	16 (29%)	39 (25%)	0.5861	4 (14%)	8 (20%)	0.5277
CHADS ₂ mean $\pm$ SD	1.87 $\pm$ 1.6	1.44 $\pm$ 1.3	0.0531	1.38 $\pm$ 1.4	1.21 $\pm$ 1.4	0.6078
CHA ₂ DS ₂ -VASc)mean $\pm$ SD	3.8 $\pm$ 2.1	2.16 $\pm$ 1.9	<0.001	2.82 $\pm$ 1.8	1.61 $\pm$ 1.55	0.0037

Table 2

Adiponectin Level by demographic characteristics in normal sinus rhythm (NSR) controls and non-valvular atrial fibrillation (NVAF) cases.

Variable	Adiponectin, ng/ml [median (IQR)]			
	NVAF patients (N=209)	P	NSR Controls (N=70)	P
Age, years		<0.0001		0.0521
< 65	9178 (6478-13497)		9729 (3914-14716)	0.8633
65 - 74	11422 (6641-16822)		11759 (5494-16558)	0.9853
75 years	16668 (10090-22591)		13682 (9688-23837)	0.9661
Gender		<0.0001		0.0301
Female	13895 (10090-22591)		14229 (10116-20617)	0.7893
Male	9379 (6080-14968)		7701 (3881-13680)	0.8577
Body Mass Index Categories		0.0265		0.0010
< 25 kg/m ²	14029 (10017-19479)		16854 (10539-23899)	0.1807
25.0-29.9 kg/m ²	10482 (7187-16810)		13674 (6136-20840)	0.4526
30.0-34.9 kg/m ²	9176 (5844-13236)		9688 (2883-11866)	0.2783
35 kg/m ²	11369 (6595-15710)		7233 (4854-12555)	0.719
Congestive Heart Failure		0.0002		0.7449
Yes	13091 (8812-20047)		8889 (3329-20288)	0.2463
No	9688 (6389-15128)		11812 (6502-16320)	0.1225
Hypertension		0.3259		0.3884
Yes	11369 (6655-17297)		10088 (5402-15374)	0.5352
No	9688 (7387-15028)		13386 (6524-19946)	0.2057
Coronary Artery Disease		0.4319		0.2406
Yes	11136 (7899-16487)		7651 (3812-13682)	0.2626
No	10516 (6857-16374)		12559 (6737-18537)	0.2785
Diabetes Mellitus		0.4478		0.1684
Yes	10915 (5574-15215)		6407 (3090-14614)	0.5781
No	10609 (7294-11657)		12419 (7391-19558)	0.3722
Stroke/TIA, prior		0.4395		0.3100
Yes	12769 (7281-19555)		18681 (6210-27416)	0.3334
No	10354 (6999-15602)		11401 (6136-15903)	0.8200

Variable	Adiponectin, ng/ml [median (IQR)]			
	NVAF patients (N=209)	P	NSR Controls (N=70)	P
Vascular Disease, prior		0.4090		0.3095
Yes	11990 (7999-15941)		6315 (3115-17431)	0.2822
No	10425 (6666-16719)		12212 (7252-16899)	0.3208
Antiplatelet Therapy, n (%)		0.5487		0.7849
Yes	10245 (6645-14593)		10108 (4333-17381)	0.7889
No	11124 (7730-17597)		12419 (6578-17909)	0.7526
Warfarin Therapy, n (%)		0.8983		0.2572
Yes	10662 (6932-16054)		2396 (2396-2396)	0.1986
No	9955 (7155-17711)		11866 (6407-17340)	0.6481
Statin Therapy, n (%)		0.4437		0.2776
Yes	10268 (6369-17854)		6950 (3345-16051)	0.3728
No	10742 (7413-15783)		12559 (7507-18393)	0.2257
CHADS ₂		0.0104		0.6230
0	8921 (6827-12922)		10564 (5225-15719)	0.5558
1	10333 (6478-14814)		12646 (7233-19257)	0.2202
2	13001 (8074-19681)		10128 (5402-19829)	0.6297
CHA ₂ DS ₂ -VASC		0.0005		0.2197
0	7996 (5289-9955)		7619 (4331-13110)	0.8394
1	9330 (6310-12922)		13386 (7507-15657)	0.1619
2	12358 (8089-19504)		12279 (6320-19946)	0.9591

IQR, interquartile range

Table 3

Adiponectin levels in women and men with non-valvular atrial fibrillation (NVAF) by echocardiographic characteristics.

Variable	Adiponectin, ng/ml [median (IQR)]		P
	Female (N=55)	Male (N=154)	P
Duration of atrial fibrillation			0.2232
< 48 hours	NA	8310 (3179-17704)	0.2236
48 hours to <7 days	15179 (13494-42618)	9364 (5103-15471)	0.0196
1 week to 4 weeks	14610 (11292-35124)	12232 (6850-25605)	0.4706
>1 month to <12 months	11408 (9409-12688)	9764 (5148-17672)	0.6872
1 year	14984 (10034-23763)	9232 (6139-12903)	<0.0001
Type of Atrial Fibrillation			0.8657
Non-permanent	13494 (10078-20812)	8923 (5873-13255)	0.0413
Permanent	16040 (10515-23230)	11572 (6865-19137)	<0.0001
LVEF 40%			0.1667
No	14527 (10313-23230)	8921 (5896-13901)	0.0263
Yes	9409 (8491-10312)	12111 (7863-19763)	<0.0001
Left Atrial Volume Index			0.3630
<30	14610 (8950-20798)	12567 (6558-18520)	0.1925
30 to <40	15122 (10813-26704)	9527 (7627-14990)	0.6723
40 to <60	12982 (9429-16904)	8694 (4783-13318)	0.0024
60	14169 (9043-21440)	8746 (6714-12382)	0.0522
Aortic Atheromatous Disease			0.0215
None	14610 (9429-22591)	9002 (4846-12682)	0.050
Simple (<4 mm)	13494 (10445-24083)	8890 (6139-15941)	0.0019
Complex (>4 mm)	11656 (10146-29593)	13112 (10970-23008)	0.0010
Left Atrial Appendage Emptying Velocity			0.8552
75	11936 (7893-25966)	6590 (4127-10435)	0.0005
50 to <75	18687 (15124-25426)	9418 (6358-14442)	0.0038
25 to <50	13695 (11250-19534)	8179 (5637-11572)	0.0018
<25	12668 (9409-18447)	12111 (8971-19329)	0.0002
Spontaneous Echo Contrast			0.7195
			0.0002

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Variable	Adiponectin, ng/ml [median (IQR)]			
	Female (N=55)	P	Male (N=154)	P
None	10685 (7647-25251)		8345 (4962-12837)	0.0030
Mild	14169 (11337-16159)		7813 (4799-12010)	0.0004
Moderate	15757 (9920-26358)		10555 (5896-15704)	0.0240
Severe	19051 (11661-23484)		10742 (8240-20845)	0.2114
Left Atrial Appendage Thrombus		0.7705		0.0005
No	14169 (10256-21257)		8921 (5867-13482)	<0.0001
Yes	10181 (7080-26389)		17246 (9970-20485)	0.7093

IQR, interquartile range