Characterization of cardiac Brain Natriuretic Peptide release in patients with paroxysmal atrial fibrillation undergoing left atrial ablation

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Abstract

Background: Paroxysmal atrial fibrillation (PAF) is associated with elevated levels of Brain Natriuretic Peptide (BNP). The exact cardiac source and implications of this are currently unknown, as are the effects of left atrial ablation on cardiac BNP release. We sought to investigate BNP levels at different cardiac sites in PAF patients before and after left atrial ablation and compare these to a non-AF control cohort.

Methods and Results: 20 PAF patients (52 ± 10 years, 70% males, left ventricular ejection fraction (LVEF) 55 ± 3 %) undergoing ablation were studied, BNP levels were measured at different cardiac sites pre and post ablation and compared to a control cohort undergoing ablation for left lateral accessory pathways (10 patients, 41 ± 11 years, LVEF 55 ± 4%). In both cohorts the coronary sinus (CS) BNP levels were the greatest. The PAF cohort had significantly greater BNP levels than the Control cohort at all sites Pre-ablation and Post-ablation. Ablation of the left atrium was associated with a significant decrease in CS BNP levels (p = 0.05) and trans-cardiac BNP gradient (p = 0.03). This was not observed in the control cohort.

Conclusion: BNP levels are elevated in PAF with the highest levels in the CS. Ablation of the left atrium was associated with an immediate decrease of BNP levels implicating this as the source.

Key words: Ablation, Atrium, Natriuretic Peptides
Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia and creates a large burden to healthcare worldwide (1). Recent advances in management of AF include non-pharmacological therapies such as ablation in the left atrium (2). This procedure typically isolates pulmonary veins electrically and modifies left atrial substrate to potentially cure paroxysmal AF. The impact of this procedure on the cardiac neuro-hormonal system is not completely understood.

Brain Natriuretic Peptide (BNP) is released from the ventricle in heart failure in response to increases in left ventricular pressure and volume (3) and its level in the peripheral venous blood has been associated with morbidity and mortality in heart failure. In patients with AF and normal ventricular function the levels of BNP have also been demonstrated to be elevated, the exact cardiac origin and implications of this are not understood. The origin of BNP in AF may be the atria (4) although this has not been confirmed. Furthermore, decreases in peripheral venous Brain Natriuretic Peptide (BNP) three months after left atrial ablation (5,6) have been observed. The acute effects on chamber specific cardiac BNP production are unknown.

In this study, we sought to characterize the acute effects of ablation on chamber specific BNP levels in AF patients undergoing left atrial ablation to gain insight into the source of production and the acute effect of left atrial ablation.

Methods
**Patient Populations**

Twenty consecutive patients with paroxysmal AF who were undergoing left atrial ablation as part of their AF management were enrolled to participate. Ten consecutive patients who were undergoing ablation of a left lateral accessory pathway via a trans-septal approach served as controls. All patients had normal left ventricular function and were able to give informed consent. Demographic and clinical parameters were collected on each patient. The study was approved by the ethics committee of the University of Western Ontario and London Health Sciences Center, London, Ontario, Canada.

**Ablation Procedure**

Each procedure was performed under general anesthesia or heavy sedation in the post-absorptive state in all patients. The atrial ablation procedure for paroxysmal AF adopted in this study has been published elsewhere (7). In short, a double trans-septal puncture was performed and a circular mapping catheter (Lasso, Biosense Webster, Diamond bar, CA) and 3.5 mm Navistar Thermocool ablation catheter (Biosense Webster, Diamond bar, CA) were passed to the left atrium. A non-fluoroscopic anatomic map (CARTO Biosense Webster, Diamond bar, CA) was then made and merged to a 64 slice CT scan of the left atrium as previously described (8). A wide antral circumferential ablation was performed of both left and right sided pulmonary veins achieving electrical isolation confirmed with the circular mapping catheter. In the control cohort, a single trans-septal puncture was performed and a 4mm radiofrequency ablation catheter (Celcius, Biosense Webster, Diamond bar, CA) was passed to the mitral annulus where
Accessory pathway radiofrequency ablation was performed in the usual way. The ablation times in both cohorts were recorded. Assessment of the left atrial diameter was by echocardiography using the M-Mode cross-sectional atrial diameter in the para-sternal long axis view. Left ventricular ejection fraction was also assessed echocardiographically using a Simpson’s biplane method or gated cardiac blood pool scanning. These assessments were performed within 3 months of the ablation procedure in both cohorts.

**Blood Sampling**

A luminal coronary sinus catheter and a radial arterial line were used for coronary sinus and peripheral arterial sampling respectively. Sampling from the right ventricle and right atrium was performed via the trans-septal guiding sheaths prior to trans-septal puncture. Peripheral venous sampling was performed via the femoral introducer sheath. Sampling was performed simultaneously from the right ventricle, the right atrium, the peripheral vein, the coronary sinus and the peripheral radial artery. Sampling was then completed from the left atrium after trans-septal puncture within ten minutes of the first sampling. Immediately after left atrial ablation sampling was repeated from the left atrium. Both the trans-septal catheters were removed to the right heart and simultaneous sampling of the right atrium, right ventricle, peripheral femoral vein, coronary sinus and peripheral radial artery was then performed within ten minutes of the left atrial sampling. Sampling for the control cohort was collected in the same manner.

Blood samples were collected into ice-chilled tubes containing an ethylenediaminetetra-acetic acid (EDTA). After centrifugation at 4°C, plasma samples were stored at -70°C until assayed.
Prior to assaying the plasma samples were thawed on ice. The AxSYM BNP Assay (Abbott Diagnostics, Abbott Park, IL, U.S.A.) was employed to measure plasma BNP, this assay uses a micro-particle enzyme immunoassay designed to measure plasma BNP and has been correlated with the point of care TRIAGE Assay (Biosite, San Diego, CA, U.S.A.) (9). Previous research by the current author has demonstrated significant changes in BNP measurements with this assay within 10 minutes of an intervention (10). All levels for BNP are expressed as pictogram per milliliter pg/ml and as absolute levels. The assay is insensitive to BNP levels less than 15 pg/ml and as such a level less than 15 was assigned a value of zero.

A trans-cardiac veno-arterial gradient BNP gradient was calculated as follows:

\[
\text{Trans-cardiac BNP Gradient (pg/ml) = } \text{CS}_{\text{BNP}} (\text{pg/ml}) - \text{LABNP} (\text{pg/ml})
\]

Where \( \text{CS}_{\text{BNP}} \) represents coronary sinus (venous level) BNP level and \( \text{LABNP} \) represents left atrial (arterial level) BNP level.

In addition, a trans-pulmonary veno-arterial BNP gradient was also calculated in the Control and PAF cohorts Pre and Post ablation as follows:

\[
\text{Trans-pulmonary BNP Gradient (pg/ml) = } \text{LABNP} (\text{pg/ml}) - \text{RV}_{\text{BNP}} (\text{pg/ml})
\]

Where \( \text{LABNP} \) represents left atrial (venous level) BNP level and \( \text{RV}_{\text{BNP}} \) represents right ventricular (arterial level) BNP level.
Hemodynamic Measurements

At each sampling time systolic and diastolic blood pressure was recorded in mm/Hg along with heart rate in beats per minute. In addition cardiac rhythm was recorded pre and post ablation.

Statistical Analysis

Data are presented as mean value +/- standard deviation if normally distributed and as median and interquartile range (25th and 75th percentiles) if non-normally distributed, unless otherwise stated. Statistical analysis and graphical presentation was performed using statistical software (SigmaStat, version 2.03, Chicago, Illinois). Within group data was compared using a paired t-test and between group data were compared using an unpaired t-test for normally distributed data. Non-normally distributed unpaired data were analyzed with a Mann-Whitney test and paired non-normally distributed data were analyzed with a Wilcoxon Signed Rank test. Categorical data were compared using a Fisher’s Exact test. Comparisons of data at multiple sites between AF patients and controls were performed using the Wilcoxon Mann-Whitney test with correction for multiple measures by the method of Benjamini and Hochberg (11). A p value of <0.05 was considered statistically significant

Results

Baseline Patient Characteristics and Hemodynamics Pre and Post Ablation
Baseline patient characteristics for both cohorts are listed in Table 1. The paroxysmal AF Cohort of 20 patients had an average age of 52 ± 10 years with 60% males and a left ventricular ejection fraction (LVEF) of 55 ± 3 %. The control cohort of 10 patients had an average age of 41 ± 11 years with 60% males, and a LVEF 55 ± 4%. These groups were well matched with respect to gender and LVEF except the paroxysmal AF cohort was significantly older (p = 0.01). With respect to other demographic parameters not unexpectedly, the PAF cohort had greater prevalence of hypertension, and greater use of Class I and III anti-arrhythmic drugs. Also, left atrial size was larger in the AP diameter, although both groups were in the normal range. Likewise, serum creatinine was slightly higher in the PAF group, likely due to increased age, but well within the normal range.

Ablation times, measurement of blood pressure and heart rate in both the left atrial ablation and control cohorts are presented in Table 2. There were no significant differences (p > 0.05) in blood pressure and heart rates pre and post ablation between the control and PAF cohort. Ablation Times in both cohorts were as follows, PAF cohort 2619 ± 1022 seconds, versus, Control 349 ± 258 seconds; p < 0.001. Two patients in the PAF cohort were in atrial fibrillation prior to ablation all other patients in the cohort were in sinus rhythm at the time of ablation. Each patient in the PAF cohort except the two in atrial fibrillation at the time of ablation had not suffered a symptomatic paroxysm for at least 48 hours prior to the ablation. All patients in the control cohort were in sinus rhythm and did not suffer AF. No patient in the control group had suffered a symptomatic paroxysm of SVT for at least 48 hours prior to ablation. SVT was however induced in all patients prior to ablation.

Assessment of BNP levels
PAF Cohort Pre and Post ablation compared with Control Cohort Pre and Post Ablation

The site specific BNP levels in both the control and PAF cohort for both pre and post ablation are presented and compared in Table 3. Compared to the control cohort, the PAF cohort had significantly greater (p < 0.05) site specific comparisons of BNP levels at all sites prior to ablation. Post ablation the PAF cohort had significantly greater site specific comparisons of BNP levels (p < 0.05) except for the right ventricular level (p = 0.10) and right atrial level (p = 0.06) which were greater but not significantly so.

A comparison of BNP values at all sites in both cohorts Pre ablation demonstrated the Pre-ablation CS (Coronary Sinus) BNP level in the PAF cohort was significantly greater (p < 0.001) than all other sites measured in both cohorts. A comparison of all sites in both cohorts Post ablation demonstrated the post ablation CS BNP level in the PAF cohort was significantly greater (p < 0.001) than levels at all other sites.

PAF Cohort: Pre versus Post Ablation

Before ablation, in the PAF cohort, the highest BNP levels were measured in the CS 181 (104-614) pg/ml. A comparison of the BNP levels at all the six sites pre-ablation demonstrated that CS BNP was significantly greater (p = 0.001) than all other sites. CS BNP levels decreased after ablation (Pre 181 (104-614) pg/ml, Post 142 (81-274) pg/ml; p= 0.05)(Figure 1). After ablation, the highest BNP levels were measured in the CS 142 (81-274) pg/ml and a comparison of BNP
levels at all six sites post ablation also demonstrated that the CS BNP level was significantly greater (p < 0.001) than all other sites measured. Otherwise, chamber specific BNP levels showed a non-significant decrease post ablation.

Control Cohort: Pre versus Post Ablation

In the control cohort comparison of BNP levels measured at all six sites pre ablation demonstrated that the CS BNP level was significantly greater than all other sites (p= 0.005) however post ablation a comparison of all sites were not significantly different from each other. In addition, BNP levels did not significantly change (p > 0.05) pre versus post ablation in the CS (Figure 1) or at other sites measured.

Transcardiac and Trans-pulmonary BNP Gradients

The trans-cardiac BNP gradients pre versus post ablation for the PAF Ablation cohort decreased significantly: Pre AF Ablation 253 ± 329 pg/ml, Post AF Ablation 172 ± 334 pg/ml, p Value = 0.03 . In the Control cohort the trans-cardiac gradient pre versus post ablation approached significance: Pre-Ablation BNP 41 ± 45 pg/ml, Post-Ablation BNP 25 ± 39 pg/ml, p = 0.08. The comparison of trans-cardiac BNP gradient between the PAF cohort and the Control cohort revealed the trans-cardiac BNP gradient was significantly higher in the PAF cohort compared with the Control cohort pre (p = 0.01) and post ablation (p = 0.003).

The trans-pulmonary BNP gradient did not significantly alter in the PAF cohort or the Control cohort pre versus post ablation: Pre AF Ablation 11 ± 32 pg/ml, Post AF Ablation 26 ± 66
pg/ml, p Value = 0.4 and the Control cohort: Pre-Ablation BNP -8 ± 28 pg/ml, Post-Ablation BNP -10 ± 27 pg/ml, p = 0.6. The trans-pulmonary BNP gradient post ablation was significantly higher in the PAF cohort compared with the Control cohort (p = 0.013), however the pre ablation trans-pulmonary gradients were not significantly different between cohorts (p= 0.14).

Discussion

In this study we demonstrated elevations in BNP levels in patients undergoing left atrial ablation for PAF as compared to those with SVT, with the most elevated levels in the coronary sinus. In addition, we demonstrated an immediate acute significant decrease in coronary sinus BNP levels and trans-cardiac BNP gradient post ablation of the left atrium, suggesting the atria as the likely source of the BNP. The exact origin and cause of elevated BNP levels observed in PAF patients with normal systolic left ventricular function remains unknown. Previous research has demonstrated acute decreases in peripheral venous BNP at day 1 and up to 3 months after AF ablation (12) and suggested that BNP levels after ablation may be a marker for successful outcome (13). These studies along with the current study suggest a possible association with BNP and the pathogenesis of PAF. Further research is needed to establish an exact cause and effect. It may be that BNP release is initiated by factors such as mechanical strain in the atria and the ventricle, potentially associated with the atrial fibrillation and/or concomitant diastolic dysfunction. Accordingly, it has been demonstrated that BNP gene expression is stimulated by mechanical strain in animal models (14). The release of BNP in AF abates when the arrhythmia is
terminated such as after electrical cardioversion (15;16) implying an arrhythmia specific induction of BNP release.

Elevated BNP in AF patients has also been demonstrated in non-heart failure patients in a sub-study of the Breathing Not Properly study and the authors suggested higher levels >200 pg/ml should be utilized as a cut off for the diagnosis of heart failure in AF patients (17). This disparity was not demonstrated in the same study in heart failure patients where AF was not an independent discriminator of BNP level (18). A study by Rossi et al (19) corroborated this finding demonstrating that left ventricular function was the main determinant of BNP levels and not AF in a heterogeneous heart failure population. BNP in chronic AF patients with preserved left ventricular function however has been correlated to left atrial volume index and left ventricular mass index and AF duration (20). Our current study also establishes the association of paroxysmal atrial fibrillation with normal left ventricular systolic function with increased BNP. The site specific measurements in this study also provide insight as to BNP release in PAF. In the non-failing heart the source of BNP is believed to be in the atrium (4) and BNP mRNA has been found in the left atrial wall (21). Ablation of the left atrium was not associated with an acute increase in left atrial BNP levels as may have been expected with release secondary to cytolysis from ablation. The current data suggest BNP levels in PAF are driven by the coronary sinus level and release into the coronary sinus is acutely decreased with radiofrequency ablation of left atrial tissue implicating the atria and not the ventricles as the source of BNP in PAF. Hemodynamics measured did not differ significantly pre and post ablation between the cohorts however the changes in BNP observed with radiofrequency ablation in the PAF cohorts may have resulted from affects of radiofrequency ablation on secondary (non-atrial) sites which were not assessed.
The coronary sinus drains the left ventricle and hence values in the coronary sinus increase with heart failure \(^{(22)}\). The increased production of BNP in heart failure would appear to be secondary to induced ventricular production \(^{(23)}\). The coronary sinus also drains the lateral and posterior left atrium and the left atrial appendage \(^{(24)}\) and these areas of the left atrium drained by the coronary sinus may be responsible for elevated levels of BNP observed.

Our PAF and control cohorts were well matched with respect to factors such as gender, body mass index and LVEF known to affect peripheral venous BNP. Factors that were different between the cohorts included: age, left atrial size, incidence of hypertension, renal function and usage of anti-arrhythmic drugs. To our knowledge there is currently no data to associate Class I and III anti-arrhythmic drugs directly with alterations in cardiac BNP release. With respect to the age difference, an eleven year age difference in mean ages can be associated with an increase in peripheral venous BNP levels. The increase has been demonstrated only to be in the order of 1.4 fold per 10 years \(^{(25)}\) and is very unlikely to account for the greater differences observed between the cohorts in the current study. Advanced age predicts elevated BNP levels and is believed secondary to increased diastolic dysfunction and poorer renal function \(^{(26)}\). The differences in renal function in the current study are both within normal range and are most likely age related.

Deterioration in renal function predominantly affects pro-BNP, which is exclusively cleared by the kidney and its clearance is affected during chronic renal disease \(^{(27)}\) which is not characteristic of our cohorts. The significant increase in left atrial size (to upper limits of normal) and incidence of hypertension in the AF cohort in comparison to the control cohort are both typically associated with AF and potentially may account for the differences in BNP observed in this study as both may be associated with diastolic heart dysfunction. We did not formally
quantify diastolic dysfunction in our current study however it may be inferred in the AF cohort by the increased left atrial size in comparison to the control cohort and along with the greater incidence of hypertension. Previous research has associated AF with diastolic heart dysfunction which was observed to resolve when sinus rhythm was restored with catheter ablation (28;29). As alluded to earlier it is currently unclear which is the precipitant or antecedent. Again the observed decrease in cardiac BNP release post ablation in this study implies the source of increased BNP in diastolic heart dysfunction maybe the atria. The magnitude of difference observed in the AF is also similar to trans-cardiac gradients albeit differently measured observed in aortic stenosis patients with diastolic dysfunction (30).

The trans-cardiac and trans-pulmonary BNP gradient estimations are novel measurements of BNP cardiac release and pulmonary BNP metabolism. Trans-cardiac BNP gradient has been used previously by the current author to assess differences in cardiac BNP release in heart failure subjects in sinus rhythm and AF in response to exercise (31), however to our knowledge trans-pulmonary BNP gradients have not been used to assess a PAF cohort and Control cohort in such a manner. BNP may be metabolized in the lung by Tissue Neutral Endopeptidases and BNP receptors on the pulmonary vasculature and as such may contribute to elevated BNP levels observed in pulmonary conditions and hypoxic states (32;33). The clinical validity of trans-cardiac and trans-pulmonary levels in the current setting does require further research; however the trans-cardiac gradient in particular would appear to be the best acute assessment of cardiac BNP release. Predominantly studies of the physiological effects on cardiac BNP release have assessed peripheral venous BNP which introduces the potential for interference from possible non-cardiac sources, inability to gauge acute changes accurately and no allowance for effects of peripheral
BNP clearance and metabolism. In two previous studies (34;35) in heart failure patients, the transcardiac BNP gradient has been assessed and it is from some of these data (35) that the ventricular source of BNP in heart failure has been inferred.

Limitations

In both our Control and PAF cohorts we do not have constant electrocardiographic documentation of heart rhythm in the 48 hours prior to the procedure and as such cannot exclude asymptomatic paroxysms prior to ablation affecting the initial BNP levels. The assay we employed in this study measures acute change in BNP levels over minutes to hours unlike the pro-BNP assay. The acute sensitivity of the assay to changes in BNP level however would serve to limit the effect of preceding arrhythmias. In addition, preceding arrhythmias are unlikely to have affected the change in BNP levels in response to ablation observed in this study.

Conclusions

Our findings demonstrate the source of BNP in PAF patients with normal systolic ventricular function is structures drained by the coronary sinus, most likely the left atrium, and that therapies such as radiofrequency ablation of the left atrium can acutely decrease cardiac BNP release.

Conflict of Interest Disclosures: None
References:


Table 1: Demographic Parameters in PAF versus Control Cohort

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PAF Cohort</th>
<th>Control Cohort</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>52 ± 10</td>
<td>41 ± 11</td>
<td>0.01</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>55 ± 3</td>
<td>55 ± 4</td>
<td>0.92</td>
</tr>
<tr>
<td>Male</td>
<td>14/20</td>
<td>7/10</td>
<td>1.0</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>30 ± 5</td>
<td>27 ± 6</td>
<td>0.14</td>
</tr>
<tr>
<td>Class III AAD</td>
<td>4/20</td>
<td>1/10</td>
<td>0.64</td>
</tr>
<tr>
<td>Class I AAD</td>
<td>12/20</td>
<td>1/10</td>
<td>0.02</td>
</tr>
<tr>
<td>Hypertension</td>
<td>9/20</td>
<td>0/10</td>
<td>0.01</td>
</tr>
<tr>
<td>Left Atrial Size (mm)</td>
<td>39 ± 6</td>
<td>30 ± 2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine (mmol/L)</td>
<td>86 ± 15</td>
<td>70 ± 5</td>
<td>0.003</td>
</tr>
</tbody>
</table>

BMI Body Mass Index, AAD Anti-Arrhythmic Drugs, LVEF Left Ventricular Ejection Fraction

Table 2: Blood Pressure and Heart Rate PAF ablation Cohort versus Control Cohort

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre Ablation PAF</th>
<th>Pre Ablation Control</th>
<th>p Value</th>
<th>Post Ablation PAF</th>
<th>Post Ablation Control</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP mm/Hg</td>
<td>110 ± 20</td>
<td>116 ± 20</td>
<td>0.92</td>
<td>116 ± 24</td>
<td>114 ± 27</td>
<td>0.92</td>
</tr>
<tr>
<td>DBP mm/Hg</td>
<td>68 ± 13</td>
<td>69 ± 13</td>
<td>0.92</td>
<td>71 ± 18</td>
<td>73 ± 12</td>
<td>0.75</td>
</tr>
<tr>
<td>MAP mm/Hg</td>
<td>79 ± 13</td>
<td>81 ± 20</td>
<td>0.84</td>
<td>85 ± 18</td>
<td>93 ± 20</td>
<td>0.48</td>
</tr>
<tr>
<td>HR Beats/min</td>
<td>75 ± 24</td>
<td>73 ± 9</td>
<td>0.83</td>
<td>80 ± 19</td>
<td>74 ± 17</td>
<td>0.26</td>
</tr>
</tbody>
</table>

PAF Paroxysmal Atrial Fibrillation, SBP Systolic Blood Pressure, DBP Diastolic Blood Pressure, MAP Mean Arterial Pressure, HR Heart Rate
**Table 3:** Cardiac Brain Natriuretic Peptide Levels Measured Pre & Post Ablation in Control and Paroxysmal Atrial Fibrillation Cohort*

<table>
<thead>
<tr>
<th>Site Level (pg/ml)</th>
<th>Pre-PAF</th>
<th>Pre-Control</th>
<th>P Value</th>
<th>Post-PAF</th>
<th>Post-Control</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral Vein</td>
<td>77 (35-126)</td>
<td>17 (0-48)</td>
<td>0.03</td>
<td>70 (40-113)</td>
<td>21 (4-53)</td>
<td>0.047</td>
</tr>
<tr>
<td>Radial Artery</td>
<td>83 (37-134)</td>
<td>10 (0-56)</td>
<td>0.03</td>
<td>78 (46-140)</td>
<td>12 (0-68)</td>
<td>0.02</td>
</tr>
<tr>
<td>Right Atrium</td>
<td>67 (39-120)</td>
<td>25 (0-52)</td>
<td>0.046</td>
<td>78 (33-121)</td>
<td>37 (18-52)</td>
<td>0.06</td>
</tr>
<tr>
<td>Left Atrium</td>
<td>85 (42-122)</td>
<td>30 (0-63)</td>
<td>0.04</td>
<td>80 (37-133)</td>
<td>23 (0-56)</td>
<td>0.04</td>
</tr>
<tr>
<td>Right Ventricle</td>
<td>84 (35-123)</td>
<td>21 (0-54)</td>
<td>0.05</td>
<td>69 (33.5-110)</td>
<td>36 (19-76)</td>
<td>0.10</td>
</tr>
<tr>
<td>Coronary Sinus</td>
<td>181 (104-614)</td>
<td>58 (18-99)</td>
<td>0.005</td>
<td>142 (81-274)</td>
<td>56 (14-78)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*Data presented as median and interquartile range (25th and 75th percentiles)

PAF Paroxysmal Atrial Fibrillation

**Figure Legend:**

**Figure 1:** BNP levels Pre and Post Ablation (median) in the CS of PAF Cohort (solid line) and in the CS levels of the Control Cohort (broken line)

* p = 0.05
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