

Cardiac Neuroendocrine Function: A new opportunity for targeted chronic therapies

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Background

- Heart failure is a preeminent medical problem accounting for nearly 6 million US hospitalizations each year and is projected to cost the healthcare system \$53 Billion by the year 2030 (1). Additionally, hypertension, one of the leading drivers of heart failure, already costs the US healthcare system \$79 billion annually (2). Current treatment strategies for the management of heart failure and hypertension are lacking. A recent study, Left Atrial Appendage (LAA) Homeostasis, published in the Journal of the American College of Cardiology demonstrated hormonal signaling changes following left atrial occlusion (LAAO) device placement (3). Follow up long term studies have demonstrated persistent long term impacts on multiple endocrine signaling pathways following LAAO (4). Additionally, a recent study in the European Heart Journal for Cardiovascular imaging demonstrated significant variation in cardiac remodeling following diagnosis of hypertension that varied by sex, ethnicity, and BP control (5).

Objective

The objective of this poster is to examine new evidence on cardiac endocrine signaling and how this might be used with new imaging modalities to generate novel treatments for hypertension and heart failure.

Methods

LAA Homeostasis

77 Patients in a single center study
38 Patients epicardial closure
39 Patients endocardial
Patient's blood samples collected

LAA Homeostasis 2

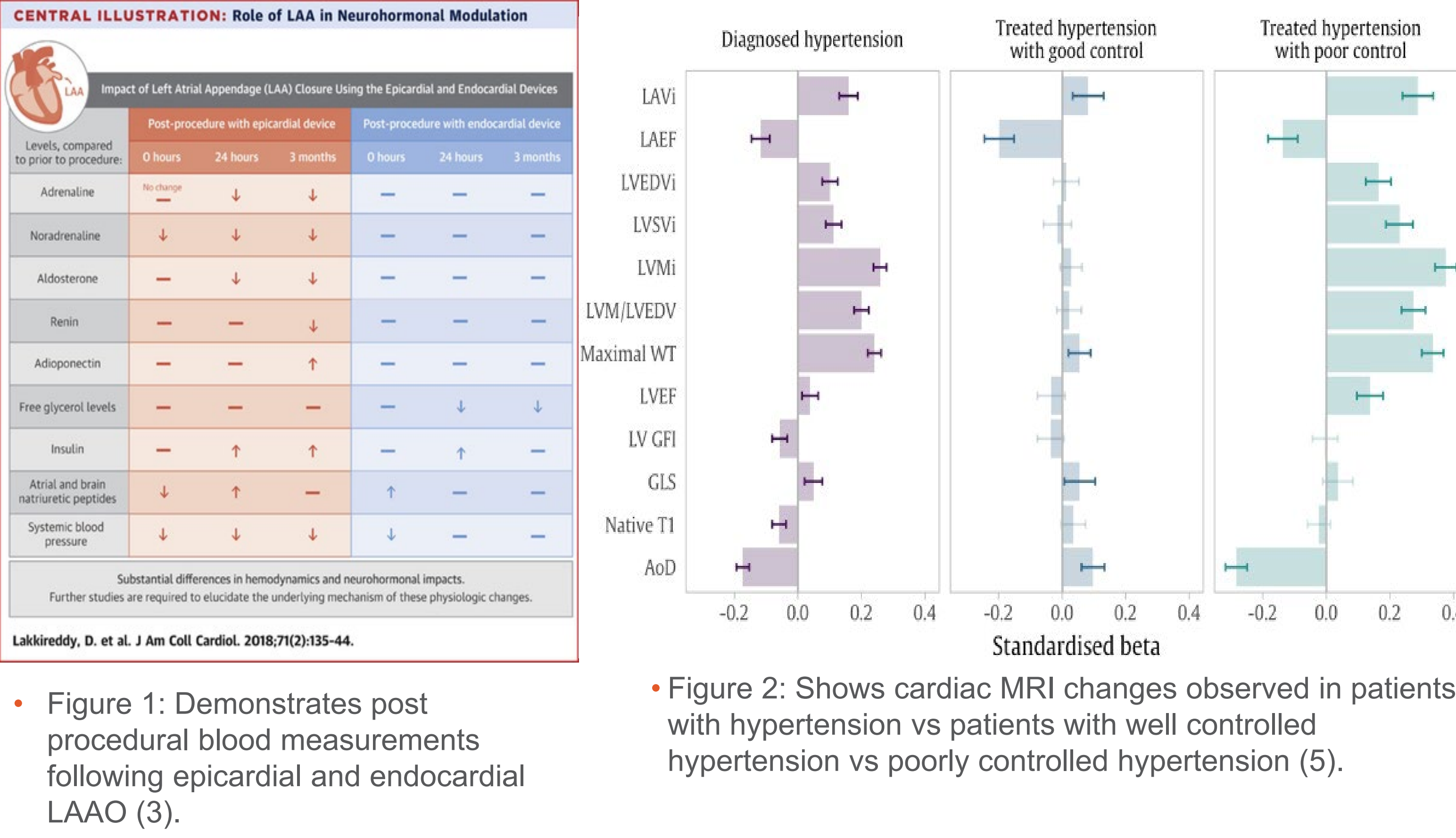
Prospective single center study, 60 patients with long standing A-Fib treated with LARIAT
Patient's blood samples collected

Hypertension by cardiovascular phenotype

39,095 participant data examined for cardiac MRI metrics and stratified analyses based on sex, ethnicity and BP control performed

- LAA Homeostasis:** Found initial postprocedural data indicating structural heart changes are linked to changes in neuroendocrine signaling as well as changes in blood pressure
- LAA Homeostasis 2:** Demonstrated postprocedural neurohormonal changes and showed that they persist long term. Also demonstrated that blood pressure changes are maintained long term
- Hypertension by Cardiovascular Phenotype:** Showed objective imaging data which indicates structural changes on cardiac MRI are linked to management of hypertension. Also showed phenotypic variability of structural changes based on ethnicity and sex.

Results

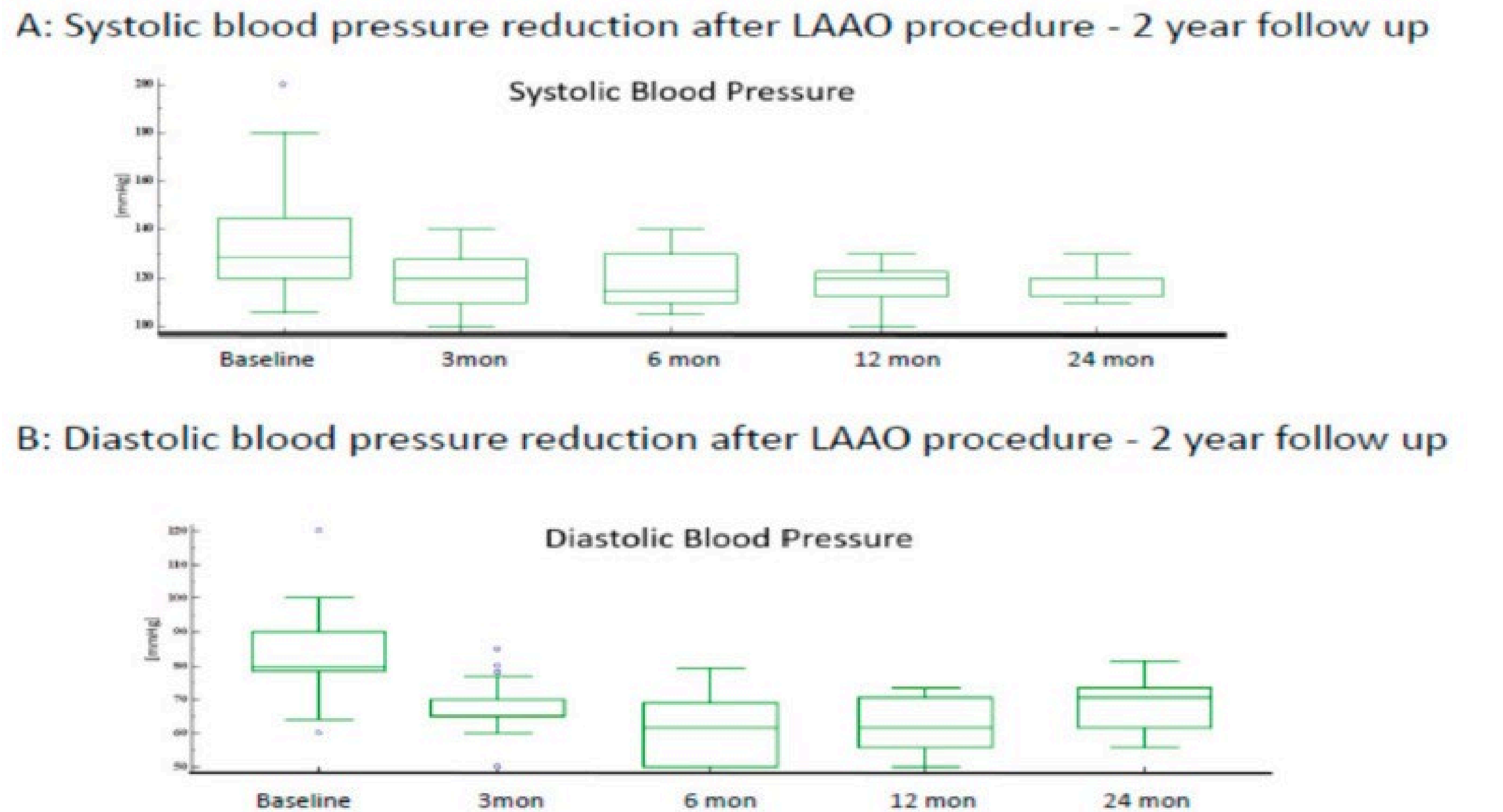


Changes in electrolytes, natriuretic peptide, and adrenergic markers after LAAC compared to baseline.

Factor	24 h	7 Days	1 Month	3 Months	6 Months	12 Months	24 Months
NT-proANP	↑	↓	↓	↓	-	-	-
NT-proBNP	-	-	-	-	-	↓	↓
Adrenaline	-	-	↓	↓	↓	↓	↓
Noradrenaline	↓	↓	↓	↓	↓	↓	↓
Aldosterone	-	-	-	-	↓	↓	↓
Plasma renin activity	-	↓	↓	↓	↓	↓	↓
Vasopressin	↓	↓	↓	↓	↓	↓	↓
Endothelin	↑	↑	↑	↑	↑	↑	↑

All values compared to baseline levels, - no change, ↑ increased level, ↓ decreased level.

- Figure 3: Demonstrates post procedural blood measurements following epicardial LAAO in a new cohort followed for an extended period up to 24 months (4).



- Figure 4: Shows blood pressure changes pre and post epicardial LAAO (4). As you can see not only is there an initial change in blood pressure following procedure but that change persists even 2 years later.

Discussion

- LAA Homeostasis and the follow up Homeostasis 2 trials both provide data indicating long term structural changes from LAAO with epicardial closure technique modifies systemic levels of neurohormones and blood pressure levels. These hormonal changes persist for at least 24 months based on this trial data and result from an as of yet undiscovered neurohormonal cardiac signaling pathway (3).
- The Hypertension by Cardiovascular Phenotype paper demonstrated that hypertension is strongly associated with cardiac MRI findings indicative of worsening cardiac function. Furthermore, the data demonstrated significant abatement in changes following treatment of hypertensive (5). Sub-group analysis further demonstrated that the cardiac structure difference vary between groups based on sex and ethnicity (5).

Conclusion

- The LAA Homeostasis 1 and 2 papers data clearly demonstrate that cardiac regulation of endocrine signaling operates not only through stretch receptor activation but also via long lasting changes following ligation and fibrosis of cardiac tissue. Additionally, LAA Homeostasis 2 demonstrated that following epicardial ligation of the left atrial appendage long term blood pressure measurements significantly decreased and remained decreased. Furthermore, the data from the European Heart Journal shows that diagnosis and poor control of hypertension is associated with worsening imaging markers for heart failure while improved blood pressure control is associated with improved markers and in some cases near normalization of observed structural changes. This data indicates that more research into identifying specific endocrine signaling pathways of the heart may yield novel treatments for heart failure and hypertension. Additionally, this data demonstrates the utility of new imaging modalities to identify groups which may benefit from more aggressive treatment strategies.

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