The Effects of Stand-alone Thoracoscopic Left Atrial Appendage Clipping on Blood Pressure and Electrolytes

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Research Article

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Abstract

Background: The natriuretic peptides secreted from the left atrial appendage could affect patients' system homeostasis by antagonizing the renin-angiotensin-aldosterone system. Thus, the epicardial LAA closure may induce unwanted hyponatremia and hypotension cause of isolating the LAA from the circulation. In this study, we aim to explore this phenomenon following stand-alone thoracoscopic LAA clipping and provide a hypothesis of the potential mechanism.

Methods: This was a retrospective, observational study including 27 stroke patients with AF who underwent thoracoscopic LAA clipping. Electrolyte, BP, heart rate, and BNP were measured before the procedure, immediately after the device release, at 1st day, 2nd day postoperation, and 24h before discharge. Fluid amounts were only monitored postoperatively.

Results: There was a significantly acute reduction in serum sodium (mmol/L) at all the timepoints postoperation when compared to baseline. The blood pressure has no significant difference when compared with baseline levels at discharge.

Conclusion: Epicardial LAA clipping induce an acute decrease in serum sodium and MAP postoperation which indicates to the surgeons that the postoperative intake fluid amounts and serum sodium level management should be appropriate. Although the fluctuation of blood pressure of patients was observed perioperative, it has returned to the baseline level till discharge and the accurate and further mechanisms still need more study.

1. Introduction

Atrial fibrillation(AF) is the most common tachyarrhythmia around the world[1]. For patients with non-valvular atrial fibrillation(NVAF), approximately 90% of thrombus are oriented from the left atrial appendage (LAA)[2]and the risk of stroke is five times greater than normal[3]. The procedures that aim to prevent cardiogenic stroke by excluding the LAA from the circulation have been performed for decades. As the derivative of the primitive fetal atrium[4], LAA not only plays an important role in the mechanical circulation but also has neurohormonal function. LAA is the well-known source of atrial natriuretic peptide (ANP) and brain natriuretic peptide(BNP) which are produced in the cardiocytes and secreted into the circulation to affect the patients' systemic homeostasis[5–7]. Cause of the neurohormonal function of LAA mentioned above, the elimination of LAA may induce the change of electrolytes and hemodynamics in NVAF patients.

Maybrook et[8] identified that patients following epicardial LAA closure by Lariat expressed an early and sustained decline in systolic blood pressure, while the serum sodium also expressed an early decline but returned to the baseline during long-term follow-up. Lakkireddy et[9] confirmed this phenomenon as well as reported it wasn't be observed in endocardial LAA occlusion. However, the objects of most former studies were the AF patients who had not suffered ischemic stroke. Furthermore, in the past studies, epicardial

LAA closure procedures were always committed with other cardiac surgery which could affect the postoperative changes of blood pressure and electrolytes a lot. Thus, the objective of this study is to research the changes of electrolytes and hemodynamics following stand-alone thoracoscopic LAA clipping in AF patients with stroke.

2. Methods And Materials

2.1 Patients selection

This is a retrospective, observational study that includes 27 patients with AF who underwent a successful LAA clipping procedure by E-clip(Med-zenith, Beijing) between September 2019 and July 2021 in our institution. The procedure was performed if the patients met the following inclusion criteria: (1) age ≥ 18 years, (2) non-valvular AF, (3) at least one risk factor of embolic stroke (CHADS2 score ≥ 1). (4) poor candidate or unwilling to have long-term oral anticoagulation (OAC) therapy. The procedure would not be operated if the patients met any of the following exclusion criteria: (1) history of pericarditis, (2) history of cardiac surgery, (3) severe pectus excavatum, (4) moderate to large mitral regurgitation, (5) embolic event within the past 30 days, (6) preoperatively renal dysfunction, (7) New York Heart Association class Ⅲ to Ⅳ heart failure symptoms, (8) left ventricular ejection function (LVEF) less than 30%, (9) myocardial infarction within the past 3 months, (10) history of thoracic radiation therapy, (11) myocardial infarction within the last 3 months. Additionally, the patients should also meet the following criteria for the study enrollment: 1. Completely preoperative and postoperative data of electrolyte and hemodynamic; 2. No additional cardiac surgeries were performed simultaneously; 3. No special need for fluid management or diuretic during the perioperative period.

2.2 Data collection

Baseline characteristics were obtained from our institutional patient registry. The data of electrolytes(serum sodium, potassium, glucose), hemodynamics(systolic blood pressure, diastolic blood pressure, heart rate), and BNP level were collected preoperatively, immediately postoperative, on the 1st day postoperative, 2nd day postoperative, and before discharge. We measured the heart rate and blood pressure four times within 24h per time point, then take the average of the data we got. The formula for the mean arterial pressure is MBP=(SBP + DBP*2)/3. Cause of the daily fluid intake and output amounts only be recorded postoperatively, thus we just collected the postoperative intake and output fluid amounts at the following time points: immediately postoperation, 1st day postoperation, 2nd day postoperation, and 24h before discharge.

2.3 Stand-alone thoracoscopic left atrial appendage clipping

The procedure was performed by a new epicardial LAA clipping system called E-lip (Med-zenith, Beijing) which consists of a self-closing clip manufactured by two parallel titanium tubes with elastic nitinol springs covered by braided polyester. Transoesophageal echocardiography (TEE) probe was introduced preoperatively to ensure the absence of thrombi. All patients were placed in the supine position, underwent general anesthesia, and were intubated with a double-lumen endotracheal tube. A standard left-sided minimally invasive thoracoscopic approach was used to successfully introduce the working instruments and device implantation, then a posterior pericardiotomy was performed to exposure LAA. The base of the LAA was measured intraoperatively by the ruler and sized for the appropriate E-clip length (either 35, 40, 45, or 50mm). The position of the device would be confirmed through thoracoscopic vision before the final release of the clip. The device would be repositioned if a residual LAA flow or stump was observed. After the procedure, a chest tube was inserted in the left-sided costodiaphragmatic recess through one of the ports.

2.4 Postoperative care

Patients will be observed in the cardiac care unit, extubated on the same day, and transferred to the ward on the day after tomorrow. Oral anticoagulation and antiplatelet therapy were discontinued after the procedure.

2.5 Statistical analysis

Normally distributed continuous variables are expressed as mean ± SD. Categorical variables were expressed as counts (percentage). Paired t-test was performed to see the differences between baseline continuous variables and those at the variously postprocedure time points. Pearson correlation was used to evaluate the correlation between blood pressure, heart rate, electrolytes, and heart rhythm with BNP levels at different time points. P value < 0.05 was considered statistically significant. SPSS Version 22.0.0.0 (SPSS Inc. Chicago, IL, USA; released 2013) was used for statistical analysis.

3. Results

3.1 Patient Characteristics

Twenty-seven patients who underwent stand-alone thoracoscopic left atrial appendage clipping were included in the analysis. The baseline characteristics are presented in Table 1. The majority of patients were male(N = 21 77.8%) and the mean age for the entire cohort was 66 ± 6.8. The mean body mass index(BMI) among patients was 24.9 ± 3.8kg/m^2. Patients with paroxysmal atrial fibrillation accounted for all patients are 77.8% (N = 21). Preoperative stroke was present in all of the patients. The mean CHADS2 score was 2.7 ± 1.1, and the mean CHA2DS2-VASC score was 3.9 ± 1.3. Hypertension patients(N = 24)accounted for 85.2% of all patients and 92.%(N = 25)percent of patients taking beta-blockers perioperative. In addition, most patients(N = 21, 77.8%) received diuretics during the perioperative period, and 20 of them received furosemide.

Table 1

Baseline clinical characteristics (*N*=27)

Age(years)	66 ± 6.8
Male	21 (77.8%)
BMI(kg/m^2)	24.93 ± 3.76
Atrial fibrillation	
Paroxysmal	21 (77.8%)
Persistent	6 (22.2%)
History of cardiomyopathy	0
Hypertension	24 (88.9%)
Beta blockers use	25(92.6%)
Calcium channel blockers use	11(40.7%)
Diabetes mellitus	6 (22.2%)
History of CVA/TIA	10 (37.0%)
CHADS2 score	2.7 ± 1.1
CHA2DS2-VASc score	3.85 ± 1.3
History of stroke	27 (100%)
On anticoagulation prior-procedure	5 (18.5%)
Any diuretic use	21 (77.8%)
Loop diuretic use	20 (74.1%)
Thiazide diuretic use	1 (4%)

Values are mean ± SD or n (%)

CVA: cerebrovascular accident, TIA: transient ischemic

3.2 Changes of electrolytes and hemodynamics

Table 2 shows the outcomes of electrolytes, eGFR, blood pressure and heart rate data measured at the predefined time points. The mean preoperative serum sodium level(Fig. 1A) was 142.6 ± 2.6mmol/L and decreased immediately after the procedure (138.8 ± 2.5mmol /L ($P < 0.001$)). Sodium levels at 1st day and 2nd day postprocedure were 139.0 ± 3.2mmol/L and 138.4 + 2.7mmol/L, respectively ($P < 0.001$ at both time points when compared to baseline). At hospital discharge, although sodium level presented the trend of recovery (138.6 ± 2.8mmol/L), still significantly lower than the preoperative sodium level (P <

0.001). A significant increase in glucose(Fig. 1C) was observed immediately after operation (9.5 ± 2.4 VS. 4.9 ± 1.0 (P < 0.001)), then the glucose level expressed the decreased trend up to discharge, but the glucose level were significantly lower than the baseline at each time points postoperative (P < 0.001). When patients who were suffering from diabetes mellitus were excluded from the analysis, mean glucose values were still significantly different from baseline at all the time points postoperative (P < 0.001). The level of serum potassium(Fig. 1B) presented a similar trend with glucose, but the postoperative fluctuation of potassium was not statistically significant when compared with the baseline.

Table 2
Electrolyte and hemodynamic data

	Baseline	**Immediately**	**1st day post**	**2nd day post**	**Discharge**
Electrolytes					
Na+ (mmol/L)	142.6 ± 2.7	138.8 ± 2.5(P < 0.001)	139 ± 3.2 (P < 0.001)	138.4 ± 2.7 (P < 0.001)	138.6 ± 2.8 (P < 0.001)
K+ (mmol/L)	3.9 ± 0.28	4.1 ± 0.6 (P > 0.05)	4.3 ± 1.4 (P > 0.05)	4.2 ± 0.5 (P < 0.05)	4.0 ± 0.3 (P > 0.05)
eGFR(mL/min/1.7 [illegible])	93.4 ± 16.9	97.1 ± 14.1 (P > 0.05)	93.6 ± 17.9 (P > 0.05)	84.3 ± 22.9 (P = 0.029)	92.0 ± 15.3 (P > 0.05)
Glu(mmol/L)	4.9 ± 1.0	9.5 ± 2.4 (P < 0.001)	9.2 ± 2.8 (P < 0.001)	7.8 ± 1.5 (P < 0.001)	7.0 ± 1.7 (P < 0.001)
Hemodynamics					
Heart rate	72.7 ± 7.8	90.1 ± 20.8 (P < 0.001)	97.7 ± 14.3 (P < 0.001)	103.3 ± 13.8 (P < 0.001)	79.86 ± 8.2 (P < 0.001)
SBP(mmHg)	121.4 ± 9.7	131.2 ± 12.6 (P < 0.001)	122.3 ± 9.3 (P > 0.05)	118.7 ± 13.3 (P > 0.05)	120.5 ± 11.2 (P > 0.05)
DBP(mmHg)	78.0 ± 5.7	79.0 ± 8.2 (P > 0.05)	71.6 ± 9.1 (P < 0.001)	75.4 ± 9.6 (P > 0.05)	80.1 ± 6.9 (P > 0.05)
MAP (mmHg)	92.3 ± 5.6	96.5 ± 8.7 (P = 0.012)	88.4 ± 7.3 (P = 0.005)	87.5 ± 7.8 (P = 0.002)	93.4 ± 7.9 (P > 0.05)
Values are mean ± SD. p values are relative to the baseline values.					
eGFR: estimated glomerular filtration rate					
SBP: systolic blood pressure DBP: diastolic blood pressure MAP: mean arterial pressur					

The systolic blood pressure (SBP)(Fig. 2A) increased immediately postoperation when compared with baseline (131.2 ± 12.6 VS. 121.4 ± 9.7 (P < 0.001)), then decreased to 122.3 ± 9.3 and 118.7 ± 13.3 on the 1st day 2nd day postoperative, respectively. However, both time points were not statistically significant when compared with baseline(P > 0.05). Before discharge, the mean SBP value was still lower than the baseline but was not statistically significant (120.5 ± 11.2 VS. 121.4 ± 9.7(P > 0.05)). Diastolic blood pressure (DBP) (Fig. 2B)significantly decreased on the 1st day postoperative, and return to baseline at hospital discharge

The mean arterial pressure (MAP) expressed a similar but more obvious trend with SBP and DBP Fig. 2. A significant increase was observed immediately after operation (96.5 ± 8.7 VS. 92.3 ± 5.6 (P = 0.012)). The MAP at 1st day (88.4 ± 7.3) and 2nd (87.5 ± 7.8) postoperative were significantly lower than the baseline (P = 0.005 and P = 0.002 when compared with baseline respectively). The MAP had returned to baseline (93.4 ± 7.9 VS. 92.3 ± 5.6 (P > 0.05)) before discharge. Heart rates were significantly elevated at all the time points postprocedure and show the trend of recovery on the hospital discharge. Table 2

3.3 Change of BNP and daily postprocedure fluid amounts

The trend of BNP is similar to glucose and potassium Table 3. The mean BNP level was 232.0 ± 128.6 mmol/L on the preoperation. BNP levels on the 1st day and 2nd day postoperative were 408.0 ± 239.4 and 433.1 ± 190.0mmol/L, respectively (P = 0.024 and P = 0.029 when compared to preoperation). BNP presented the trend of recovery (355.9 ± 270.6 VS. 232.0 ± 128.6 (P > 0.05)) on the hospital discharge. There are no significant changes in fluid amounts postoperative.

Table 3
B-type Natriuretic Peptides and fluid amounts

	Baseline	Immediately	1st day post	2nd day post	Discharge
BNP (mmol/L)	232.0 ± 128.6	239.0 ± 130.9 (P > 0.05)	408.0 ± 239.4 (P = 0.024)	433.1 ± 190.0 (P = 0.029)	355.9 ± 270.6 (P > 0.05)
Fluid amounts					
Intake (ml)	-	2037.2 ± 738.2	1689.6 ± 693.4 (P = 0.12)	1567.3 ± 628.5 (P = 0.031)	1850.5 ± 525.3 (P = 0.30)
Output (ml)	-	2132 ± 281.9	2075.1 ± 365.4 (P = 0.52)	1779.2 ± 444.9(P < 0.001)	1764.8 ± 512.2 (P = 0.011)
ΔFluid (ml)	-	-91.1 ± 711.9	-299.0 ± 829.5(P = 0.37)	-137.8 ± 658.0 (P = 0.82)	78.5 ± 738.1 (P = 0.48)
Values are mean ± SD. p values of BNP and Fluid amounts are respectively relative to the baseline and immediately postoperation values.					
Intake: patients’ daily infusion postoperative Output: patients’ daily urine amounts postoperative ΔFluid: equal to the Intake fluid amounts minus output fluid amounts.					

3.4 Relationship between neurohormonal effects and electrolytes and hemodynamics

Pearson correlation analysis was performed to see if there was any relationship between the resultant neurohormonal effects of LAA clipping and electrolytes and hemodynamics postprocedure. We found no significant correlation between heart rates and the BP (systolic or diastolic), MAP, or electrolytes level at any of the respective, pre-defined time points.

4. Discussion

LAA is the derivative of the primitive fetal atrium, aside from known electrical and mechanical/reservoir properties[4,10], the current studies have also shown the LAA has important neurohormonal function[4,6,7]. LAA is a well-known source of Atrial natriuretic peptide (ANP) and approximately 30% of total ANP is stored in the LAA within ANP-producing granulocytes. The secretion of ANP and BNP is stimulated by various factors and the most sensitive of which is the distention in the LAA wall[12,13]. After being secreted into the circulation from the heart, ANP and BNP produce diuretic, natriuretic, and hypotensive activity via affecting the vessel, kidney, and functionally antagonizing the renin-angiotensin-aldosterone system (RAAS) [14,15]. In the patients with heart failure, the increase of ANP and BNP induce natriuresis and diuresis resulting in the normalization of sodium levels and blood pressure. However, in a non-heart failure state, serum ANP and BNP elevation can induce hyponatremia and unwanted hypotension[16].

In our study, we observed that the SBP increased immediately postoperation, then return to the baseline level on the 1st day postoperative, and have no significant difference with the baseline at discharge. DBP showed the familiar trend with SBP, except only increased a little immediately postoperation. The outcomes of patients undergoing the E-clip procedure we observed are different from the past studies about the changes of BP in the patients following on others epicardial left atrial appendage closure[8,17]. Maybrook et[8] announced that LAA exclusion through LARIAT suture delivery device results in an early and persistent decrease in systolic BP, Maybrook et[8] observed a significant reduction of systolic BP (mmHg) at 24 h (113.3 ± 16.0; $p < 0.0001$) and 72 h (119.0 ± 18.4 mmHg; $p < 0.0001$) post-LARIAT when compared with pre-LARIAT BP (138.2 ± 21.3). The reduction in systolic BP persisted at 6-month follow-up (128.8 ± 17.3; $p = 0.0005$). In the study that included 38 patients who underwent epicardial LAAE, about blood pressure change following epicardial LAA exclusion, Turagam et[18] also observed a significant decrease in SBP both at 3-month follow-up, and it's worth noting that compared to the baseline level(137.50 mmHg), SBP was significantly decreased immediately postoperation(115.40 mmHg). In our study, the E-clip procedure was performed in patients thoracoscopically which means there was no extracorporeal circulation, and no sternotomy was performed in operation. Furthermore, as mentioned above, the procedure of epicardial LAAC includes closure, suture ligation, stapling, and excision. The different procedures lead to different physiological changes in LAA postoperation, in our study, the LAA in the patients who underwent the E-clip procedure will present with situ ischemic necrosis and fibrosis. Compared with the studies which mixed multiple kind procedures of epicardial LAAC into one group, and performed other cardiac surgery procedures simultaneously, the outcome we observed in our study may represent the blood pressure changes of patients undergoing stand-alone thoracoscopic left atrial appendage clipping by E-clip more accurate. Based on the phenomenon we observed, we hypothesized that stand-alone thoracoscopic left atrial appendage clipping may not result in a long-term decrease in blood pressure, but long-term follow-up is needed to prove this perspective. It should be noted that although the blood pressure of patients following the epicardial LAAC had returned to baseline at discharge, the acute decline of MAP was commonly observed among most patients. This fluctuation of the mean arterial pressure we observed in the study is significant, and the maximum reduction is 27 mmHg within 48 hours postoperative, which suggest surgeons should be more cautious on the postoperative fluid management and beware of all kinds of complications due to the lack of organ perfusion caused by an intense decrease in mean arterial pressure.

In our study, the acute decline of serum sodium was commonly observed among most patients which were also pronounced in past studies[8,18,19]. Remarkably, Holmes etl[10] observed that among the AF patients after epicardial LAA closure by Lariat, the average serum sodium level decreased by 4.98 ± 3.74mmol/L within 48 hours postprocedure; and there were 32 patients (52.4%) decreased ≥ 4mmol/L, and 6 patients (9.8%) decreased ≥ 10 mmol/L. In our study, a more significant decrease was observed: the average serum sodium level decreased by 5.65 ± 2.61 mmol/L within 48 hours postprocedure, and there were 13 patients (61.9%) who decreased ≥ 4mmol/L, and 3 patients (14.29%) decreased ≥ 10 mmol/L. As a common postoperative complication, hyponatremia could induce severe central nervous system dysfunction including headache, nausea, lethargy, disorientation, or depressed reflexes[20]. Additionally, the cerebral edema induced by rapid and significant fluctuations in serum sodium levels can lead to serious complications including seizures, coma, brain damage, and brain-stem herniation due to cerebral edema[20]. The predictable decline of serum sodium, we observed, secondary to the stand-alone thoracoscopic left atrial appendage clipping, could elucidate the early, unexplained postoperative serum sodium decline and may obviate further expensive and unnecessary investigation. Through our study, we suggest that for patients with pre-existing hyponatremia or who are on diuretics, the postoperative fluid management should be appropriate or reduce the use of diuretics, otherwise, it may prolong the hospital stay of patients.

Currently, it's generally believed that changes in RAAS caused by changes in ANP and BNP following epicardial LAAC induce fluctuations in homeostasis. However, the specific changes of ANP and BNP postoperative and the actual mechanism of perioperative changes in homeostasis are still unclear. In our study, although BNP was only measured in some patients, it still showed a trend that was different from past studies[21,22,23]. In addition, a significant increase in glucose was observed among most of the patients, while Lakkureddy et[9] announced that insulin significantly increased in patients who underwent epicardial LAAC procedure at 24 hours postoperation and 3 months follow-up when compared with the baseline level. But interestingly, there was no significant change in glucose at 24 hours postoperation and 3 months follow-up.

4.2 Study limitations

There are several important limitations of the study. This is a single-center study with all the inherent limitations of retrospective and observational studies. The study is also limited by sample size. First and foremost, cause of lack of long-term follow-up data, thus it is unclear whether the aforementioned changes are long-term or temporary. In addition, the direct and real-time measurement of the level of ANP and the expression of the RAAS system was not performed, and the sample size of the BNP level is small. Consequently, we can only make a hypothesis and infer the relation based on the data we collected. Besides, the changes mentioned above about electrolytes and hemodynamics are susceptible to diuretics use, fluid management, and patients' psychological factors. Therefore, more studies are needed to explain the accurate and further mechanism.

5. Conclusion

Stand-alone thoracoscopic Left atrial appendage clipping results in the acute decline of serum sodium and means arterial pressure. These findings have important clinical implications that the surgeons should pay more attention to the patient's electrolyte and fluid level following the epicardial left atrial appendage clipping, and provide early data for the studies about postprocedure neurohormone and RAAS-related changes secondary to epicardial left atrial appendage clipping. In addition, although the fluctuation of blood pressure of patients was observed perioperative, it has returned to the baseline level till discharge which indicates stand-alone thoracoscopic left atrial appendage clipping may not affect the blood pressure at long-time follow-up. The point mentioned above were hypothesized based on the data we collected, thus the accurate and further mechanisms still need more study.

List Of Abbreviations

LAA	Left atrial appendage
LAAC	Left atrial appendage closure
BP	Blood pressure
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
MAP	Mean arterial pressure
NP	Natriuretic peptide
ANP	Atrial natriuretic peptide
BNP	Brain natriuretic peptide
AF	Atrial fibrillation
NVAF	Non-valvular atrial fibrillation
TEE	Transoesophageal echocardiography
BMI	Body mass index
RAAS	Renin-angiotensin-aldosterone system

Declarations

6.1 Availability of data and materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request

6.2 Competing interests

This study has no conflict of interest.

6.3 Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

6.3 Authors' contributions

Yiming Chen, MD, performed the data analyses and wrote the manuscript; Dong Xu, MD, Ph.D.contributed to the conception of the study and helped perform the analysis with constructive discussions.

6.4 Acknowledgements

Not applicable

6.5 Consent for publication

Not applicable

7 Ethics declarations

This is a retrospective, observational study that was conducted on already available data; and we have checked with the ethical committee of Beijing Tiantan hospital to make sure the ethical approval is not needed in this study and complying with the requirements of China.

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Figures

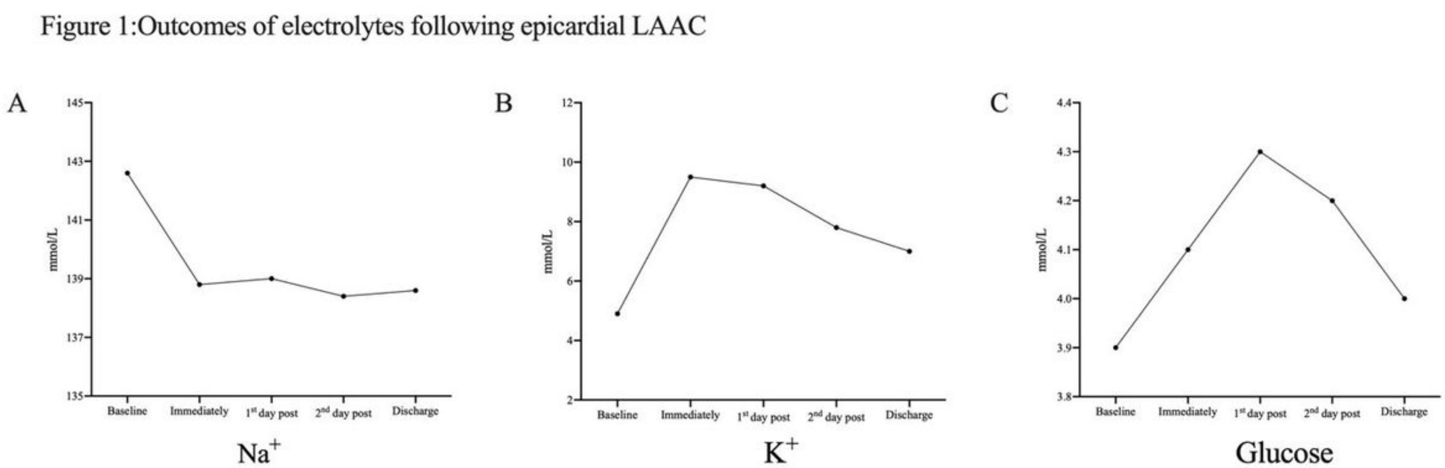

Figure 1

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Figure 2:Outcomes of blood pressure following Epicardial LAAC

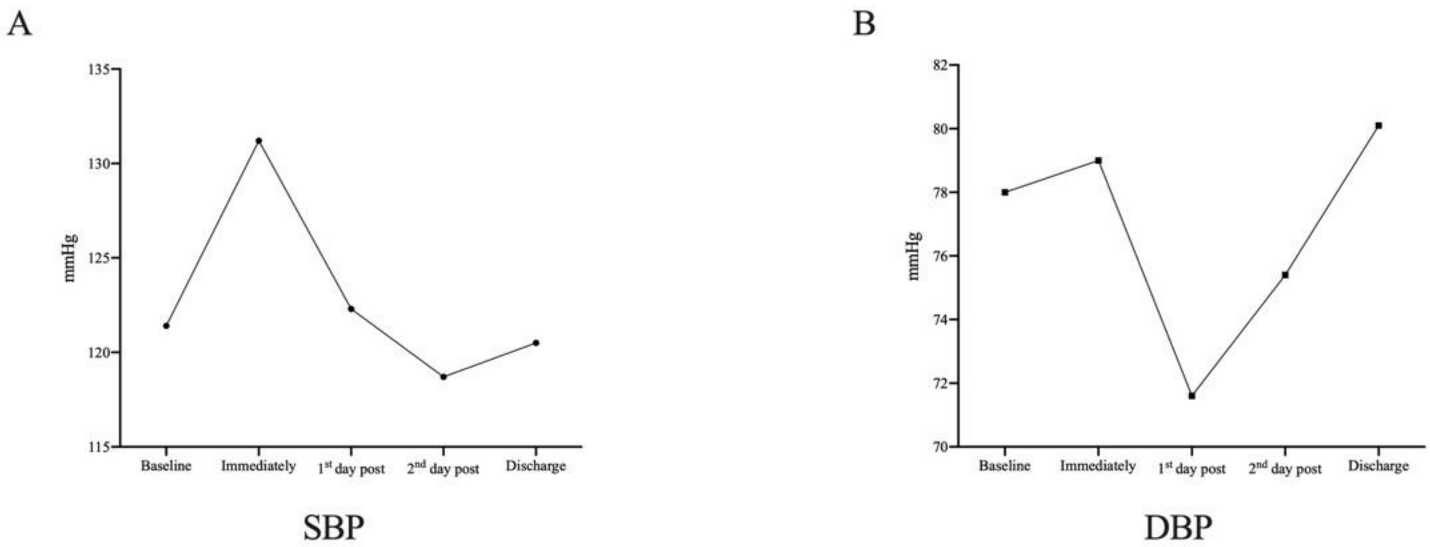

Figure 2

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