
بسم الله الرحمن الرحيم

Predictive value of NT-proBNP on Postoperative Outcome of Isolated Coronary Artery Bypass Patients

Thesis submitted by
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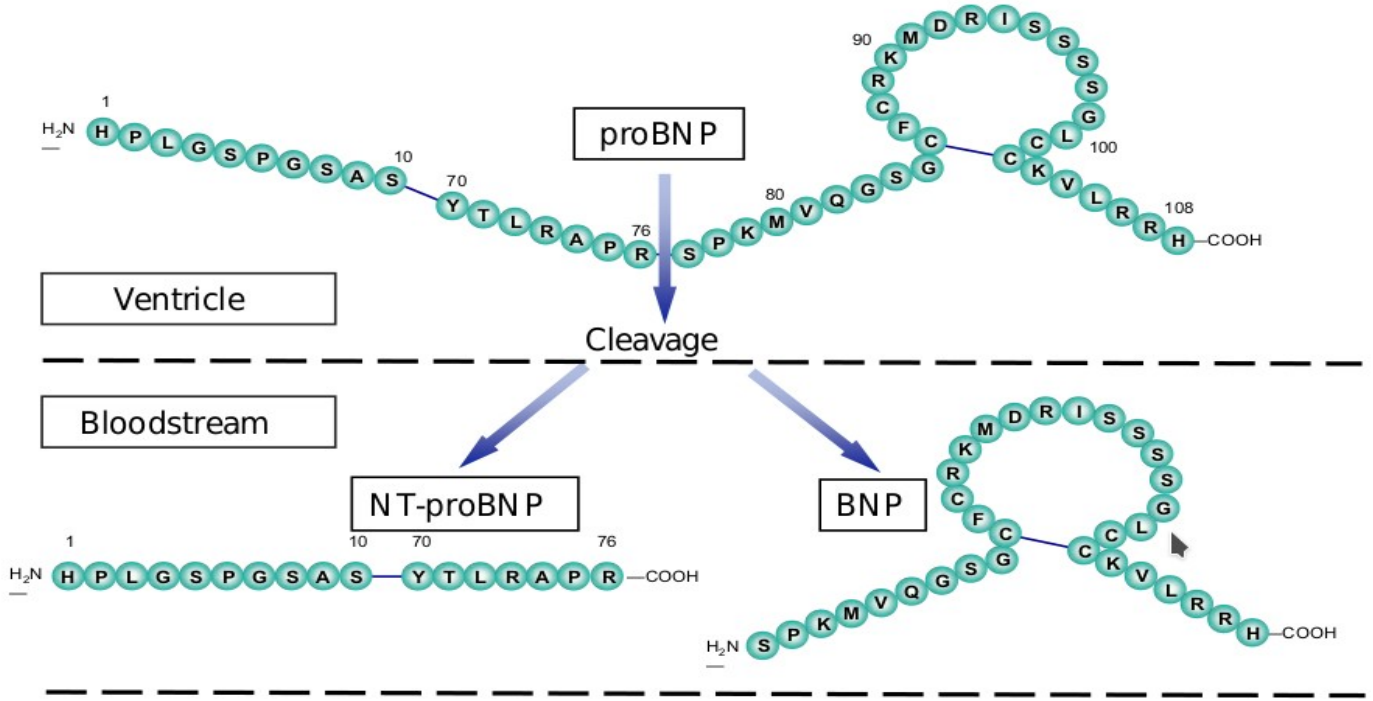
Introduction

- BNP is produced in both atria and ventricles in response to increased myocardial stretch and wall stress.
- Other stimuli for its induction and release include inflammation, activation of the sympathetic nervous system, and the renin-angiotensin-aldosterone system as well as myocardial ischemia.
- Other pathologies such as exacerbated chronic obstructive pulmonary disease, arrhythmias and myocarditis can cause eleveted BNP levels.
- Higher NP levels are associated with: female gender, impaired renal function, and older age.
- BNP induces diuresis, natriuresis, vascular dilatation and inhibition of the sympathetic nervous system reducing cardiac preload and afterload to counteract the detrimental effects of pressure and volume overload seen in HF.



- The pro-hormone pre-proBNP, is cleaved into biologically active BNP and the inactive N-terminal-proBNP (NTproBNP), thus they are secreted in equimolar quantites into the circulation.

	Size (KDa)	Half-Life (min)	Normal Ranges Male(pg/mL)	Normal Ranges Female(pg/mL)	Clearance	Biologic Actvity	In vitro Stability at Room Temperature	Biologic Variability(%)
BNP	3.5	21	8.0	13.9	NPR type C, NEPs, meprin-A and dipeptidylpeptidase IV	Active	6h	38
NT-proBNP	8.5	60-120	46.9	64.3	Passively cleared through multiple organs	Inactive	> 3d	28

- BNP has a serum half-life of 20 minutes, whereas NTproBNP has a half-life of 120 minutes causing serum levels of BNP to be significantly lower than those of NTproBNP, despite equimolar secretion.
- Both BNP and NTproBNP are established markers for cardiac failure. NTproBNP is also more stable, which makes its measurement more reliable.

- Changes in hemodynamic parameters (such as left ventricular ejection fraction, EF) and plasma natriuretic peptides (NPs) levels are closely related in patients with cardiovascular diseases.
- NPs assay are useful as a prognostic marker in HF and acute coronary artery syndromes.
- NPs concentrations are independent risk markers for morbidity and/or mortality in patients with acute or chronic HF.
- Both BNP and NTproBNP have been shown to be predictive of adverse outcomes in patients presenting with acute coronary syndrome revealed important prognostic information.

- In patients undergoing cardiac surgery risk adjustment is of paramount importance for clinical audit, benchmarking and research and to identify high-risk patients that may benefit from prophylactic interventions to reduce post-operative adverse outcomes.
- There are many clinical prognostic models such as EuroSCORE. Most of these clinical prognostic scores for cardiac surgery are useful in predicting mortality but not adverse events such as AF or cardiogenic shock requiring IABP.
- Elevated levels of BNP and NT pro-BNP are associated with adverse outcomes in patients undergoing major non-cardiac surgery.

Aim of the study

- to investigate whether preoperative NTproBNP levels are associated with in-hospital mortality and post-operative outcome variables in patients undergoing elective offpump coronary artery bypass grafting.

Patients & Methods

65 consecutive cases registered for elective off-pump coronary artery bypass grafting OPCAB were recruited from 3 cardiothoracic surgery centers in this study constrained by the following inclusion and exclusion criteria

Inclusion criteria

- Patients undergoing elective OPCAB.
- Age group between 18 and 80 years old.

Exclusion criteria

- Patients with signicant valvular heart disease, dilated or hypertophic cardiomyopathy, NYHA III or IV, EF < 40 %, need for inotropic support or intra-aortic balloon pump before surgery
- preoperative atrial fibrillation
- creatinine clearance < 60 ml/min/1.73 m2
- hyperthyoidism and hypothyroidism (serum TSH levels above or below reference ranges respectively. It was measured only upon clinical suspicion.)
- moderate to severe COPD (Shortness of breath at own pace on the level, FEV1 < 80% of predicted, or continuous use of bronchodilators for > 2 weeks).

Study's Procedure and Data Collection

- Beta-blocking agents and statins were given to all patients until the morning of surgery.
- Oral antiplatelets were stopped 5-7 days before surgery
- Euroscore II was calculated.
- Anesthetic and surgical management was not standardized.
- All patients were transferred to the intensive care unit ICU, after conclusion of surgery; intubated and mechanically ventilated.
- The patients were assessed for extubation within 4-8 hours of arrival in the ICU.

Study's Procedure and Data Collection

The following data were collected :

- Full history taking and clinical examination.
- Echocardiography pre-operative.
- Labs:
  - routine pre-operative labs: CBC, coagulation profile, liver and kidney functions test
  - specific: pre-operative NTproBNP
- Calculated of EUROSCORE II
- Data collection to evaluate incidence of complications postoperative ICU stay and till discharge from hospital including:
  - prolonged intubation
  - ischemic stroke
  - timing, duration and dose of inotropic support
  - use of intra-aortic ballon pump
  - myocardial infarction
  - arrhythmias
  - Length of postoperative ICU and hospital stay
  - death

Study's Procedure and Data Collection

Clinical end points

- low output heart failure (inotropic support at second post-operative day, adrenaline > 50ng/kg/min or dobutamine > 10mcg/kg/min at any time and/or need for intra-aortic balloon pump)
- mortality
- arrhythmias
- perioperative myocardial Infarction
- length of ICU
- length of postoperative hospital stay
- prolonged intubation (Intubation more than 24 hours postoperatively and/or reintubation following planned extubation).

Lab and sample analysis methods

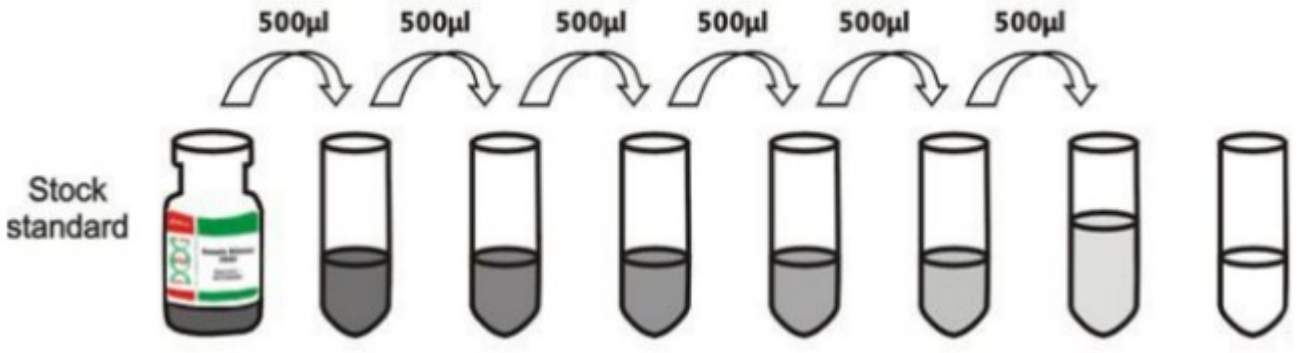
- Venous samples for measuring NT-proBNP were collected on the day of surgery before induction.
- Samples were sent for analysis at critical care department laboratories, Cairo University hospitals.
- EDTA samples were collected and plasma samples were stored in deep freezer till measured once.
- Lab staff were blinded to the clinical conditions
- and clinicians were blinded to the preoperative NTproBNP sample results.

Lab and sample analysis methods

- We used ELISA immunoassay technique that allows in vitro quantitative determination of human NTproBNP concentrations in serum, plasma and biological fluids.

- ELISA (Enzyme-Linked Imuunosorbent Assay) is based on the competitive binding enzyme immunoassay technique. The microtiter plate provided in the kit has been pre-coated with an antibody specific to NTproBNP. During the reaction, NTproBNP in the sample or standard competes with a fixed amount of biotin-labeled for sites on a precoated monoclonal antibody (Ab) specific to NTproBNP.

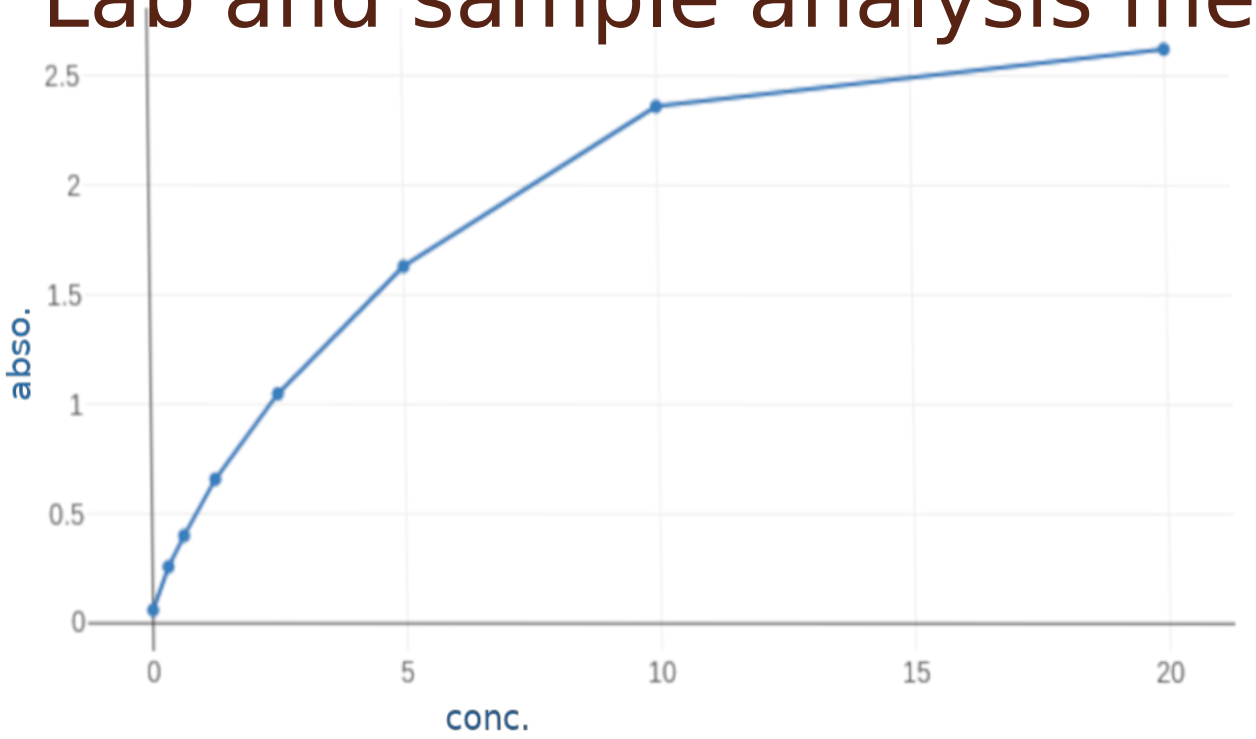
Lab and sample analysis methods



- Standard was reconstituted with 1 ml of sample diluent. This produces a stock standard of 20ng/mL.

- The undiluted standard serves as high standard concentration (20ng/mL) and the sample diluent serves as zero standard concentration.

Lab and sample analysis methods



- A curve is plotted with serial standard dilutions log graph, plotting the mean absorbance for each standard on the X-axis against the concentration on the Y-axis and draw a best fit curve through the points on the graph.
- The concentration of NTproBNP in the samples is then determined by plotting the OD (optical density) of the samples on the standard curve.

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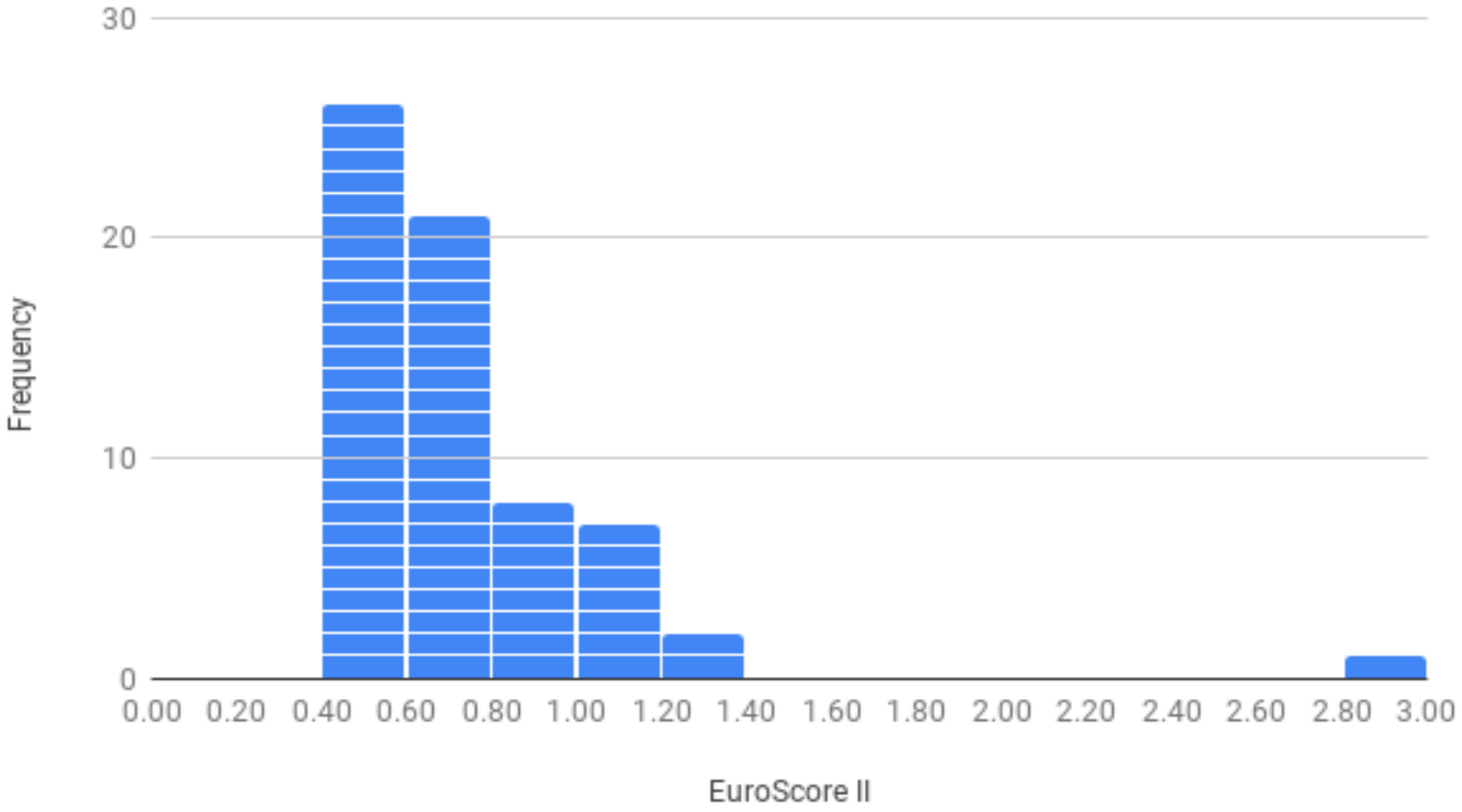
Results

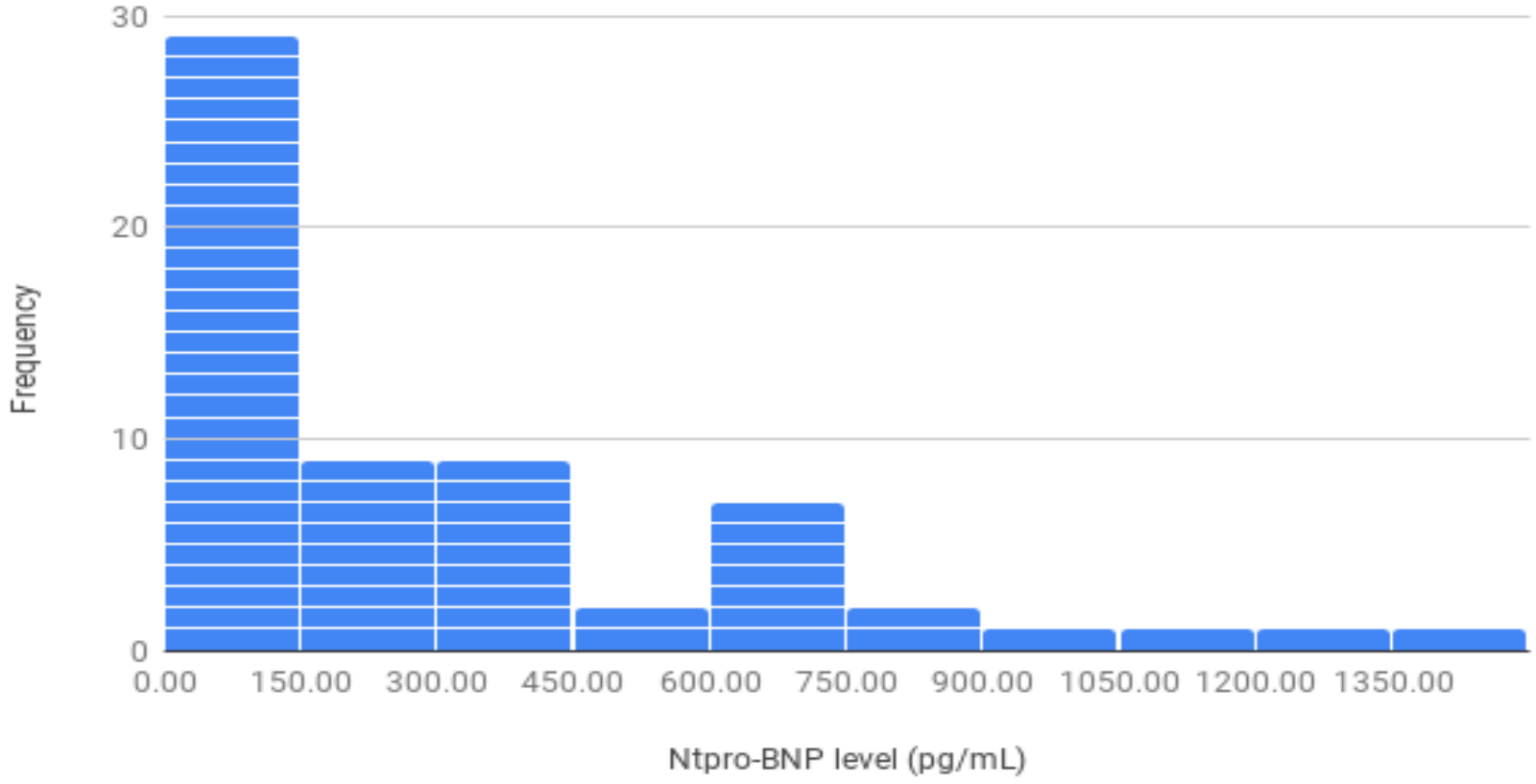
Demographics and Risk Factors

- *Sixty-five patients were recruited*
- *The average age was* 57.62 ±7.21
- 56 (86.15%)were males
- 10 (15.38%) had diabetes mellitus
- 42 (64.62%) were hypertensive
- only one had peripheral vascular disease



- *preoperative ejection fraction averaged 50.91±8.13*
- *EuroscoreII averaged 0.76±0.34. Its median was 0.68(0.50-2.94) with IQR [0.55-0.82]*

Preoperative NTproBNP Levels



	Mean	*Standard Deviation*	*Median*	*Min*	1st quartile	3rd quartile	*Max*
NTBNP (pg/mL)	312.41	*329.93*	*160*	*10*	80	397.5	*1440*

Postoperative Outcome

	Count(%)
low CO	5(7.7)
arrhythmia	4(6.2)
perioperative MI	4(6.2)
prolonged vent	3(4.6)
Delayed Recovery	1(1.5)
mortality	2(3.1)

- *mean ICU stay was 3.37±0.84 days*
- *mean hospital stay was 6.38±1.3 (3-12) days*

Relation between NTproBNP and Outcome

Complication	pre-operative NTproBNP (pg/mL) mean±SD		
	No	Yes	P-value
Low output heart failure	*296.84±329.75*	*490±307.97*	*0.168.*
Arrhythmia	*306.37±333.77*	*400±292.91*	*0.462.*
perioperative MI	*303.79±331.23*	*437.5±326.22*	*0.397.*
Prolonged ventilation	*300.33±330.69*	*550±244.33*	*0.121.*
Delayed neurological recovery	*300.65±319.29*	*1030*	*0.129.*
Mortality	*306.33±331.15*	*495±318.19*	*0.306*

Relation between NTproBNP and Outcome

		NTBNP
ICU stay	Correlation Coefficient	*-.022-*
	P value	*0.861*
	N	*65*
in-hospital stay	Correlation Coefficient	*-.017-*
	P value	*0.896*
	N	*65*

Conclusion

- Our study didn’t show significant correlation between pre-operative NTproBNP and post-operative heart failure, arrhythmias, perioperative myocardial infarction, length of ICU stay, prolonged intubation, hospital stay or mortality.

- This is likely due to the low incidence of complications and low NTproBNP levels secondary to favorable outcomes in our patients given that they had very low risk factors.

Thank You