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NT-pro BNP as a prognostic indicator for decompensated heart failure in elderly population

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Abstract

Background: As per the updated NICE guidelines, brain (B-type) natriuretic peptide (BNP) is used in the diagnostic criteria and management of heart failure. In this study, we aimed to evaluate the prognostic value of the inactive N-terminal fragment NT-proBNP in an elderly population with decompensated heart failure. **Materials and methods:** We conducted a retrospective observational cohort study of 88 elderly patients who were admitted with decompensated heart failure between September 2023 and April 2024, covering the South Eastern Trust in Northern Ireland. Suspected heart failure admissions were randomly selected to obtain snapshots of each month. Among these admissions, 88 heart failure cases were identified based on echocardiogram findings and NT-proBNP levels obtained at initial admission. The same cohort was followed up for 12 weeks to monitor two specific end points: re-admission with heart failure or death. Heart failure follow-ups were also assessed post-discharge. All cases were categorized into two main cohorts: a heart failure with reduced ejection fraction (HFrEF/EF > 60%) cohort and a heart failure with preserved ejection fraction (HFpEF/EF > 40%) cohort. Prognostic values and all-cause mortality after discharge were assessed for each cohorts via multivariable adjusted Cox regression analysis. Each cohort was further divided into three sub-cohorts based on NT-proBNP value. **Results:** The data analysis showed that patients with NT-proBNP values of >2000 exhibited a mortality rate of 29.1% and a heart failure re-admission rate of 45.6%. Those with rising NT-proBNP values during heart failure follow-up exhibited a re-admission rate of 66.6%, which was much lower than that (33.3%) seen in those with declining NT-proBNP values. **Conclusion:** Our results indicated that higher NT-proBNP levels on admission were predictive of higher mortality and re-admission rates among the elderly population. Furthermore, rising NT-proBNP levels during heart failure follow up were associated with higher mortality and morbidity rates. Therefore, NT-proBNP levels can be used as a prognostic biomarker for elderly patients with heart failure, irrespective of their ejection fraction status.

Keywords: *Heart failure, NT-proBNP, Elderly, Prognostic indicator, Mortality predictor*

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1. Introduction

Brain (B-type) natriuretic peptide (BNP) is a peptide hormone released primarily from the cardiac ventricles in response to myocyte stretch. It is synthesized as an inactive prohormone that is split into the active hormone BNP and the inactive N-terminal fragment NT-proBNP. BNP has several systemic effects, including vasodilation, increased urinary volume and sodium output, and inhibition of the sympathetic nervous and renin–angiotensin–aldosterone systems (Levin *et al.*, 1998).

The prognostic importance of BNP and NT-pro-BNP has been extensively studied in patients with heart failure and acute coronary syndromes, and both markers have been shown to be strong predictors of morbidity and mortality (Tsutamoto *et al.*, 1997). However, neither BNP nor NT-proBNP has been studied as a prognostic indicator among the elderly population. Evaluating BNP as a prognostic indicator of heart failure among the elderly population would enable care providers to plan their treatment and follow-up effectively. Therefore, in this study, we aimed to evaluate the prognostic value of BNP as a predictor of overall outcome in elderly patients with heart failure.

2. Materials and methods

2.1. Study population

We conducted a retrospective observational cohort study of 88 elderly patients who were admitted with decompensated heart failure between September 2023 to April 2024 in Lagan Valley Hospital–Lisburn and Ulster Hospital Dundonald, Northern Ireland. These two major tertiary care and secondary care hospitals, respectively, cover the entire southeastern trust of Norther Ireland, which represents most of the elderly population in the country. Both hospitals have specialized geriatric protocols for elderly care with onsite availability of cardiac services. We assessed 120 patients with suspected heart failure over eight months. The cases were randomly selected as snapshots covering each month. Among these 120 patients, 88 were confirmed to have heart failure based on clinical symptoms, echocardiography findings, and NT-proBNP findings on admission.

We assessed 120 patients with suspected heart failure over eight months. The cases were randomly selected as snapshots covering each month. Among these 120 patients, 88 were confirmed to have heart failure based on clinical symptoms, echocardiography findings, and NT-proBNP findings on admission. Verbal informed consent was obtained from each patient for echocardiography, blood testing, and clinical history and follow-up, as well as for anonymized patient information sharing.

2.2. Baseline measurements

In all patients, a thorough medical history was recorded, including details of any previous myocardial infarction or revascularization, angina pectoris, arterial hypertension, suspected congestive heart failure (defined by symptoms of shortness of breath or leg edema), previous stroke or transient ischemic attacks, diabetes, atrial fibrillation, and any malignancy. This information was obtained from medical records, directly from the patients, or both. Clinical frailty was evaluated for each patient using the Rockwood Clinical Frailty Scale.

Echocardiography findings were evaluated for all the identified cases. Ejection fraction and presence of any regional wall motion abnormalities, valve pathologies, and LV thrombus was documented. NT-proBNP has been measured for majority of the patients as a part of the heart failure work up during hospital admission.

There were no exclusion criteria. The inclusion criteria as follows: >65 years of age or a Rockwood Clinical Frailty Scale score of >4, established acute hospital admission with heart failure, and an NT-proBNP value of >400 ng/L.

2.3. Follow-up

Heart failure medications prescribed upon discharge were documented and categorized as beta blockers, diuretics, dapagliflozin, digoxin, antiplatelets, or anticoagulants. All 88 patients were followed up for 12 weeks after initial hospital discharge. Follow-up pathways were traced through electronic data records, including follow-up with any cardiologist, heart failure nurse, or community-based heart failure care provider.

Any medication changes or additions during follow-up were recorded. Patients who received repeat NT-proBNP were also recorded. Follow-up was monitored in terms of two major end points: heart failure–related death and re-admission due to heart failure.

2.4. Data analysis

All patients were sorted into two main cohorts: a heart failure with reduced ejection fraction (HFrEF/EF > 60%) cohort and a heart failure with preserved ejection fraction (HFpEF/EF > 40%) cohort. Each cohort was again categorized into three main sub-cohorts according to NT-proBNP value on admission: <400 ng/L, 400–2000 ng/L, and >2000 ng/L.

In total, six sub-cohorts were established, and data were analyzed for each sub-cohort. Average age, gender distribution, clinical frailty score, presenting symptoms, and past medical history were listed under demographic distribution data table. Follow-up details, heart failure admissions, and deaths were listed under morbidity and mortality data tables separately.

2.5. NT-proBNP values and end points

The same cohorts were further followed up for 12–15 weeks to monitor the two above-mentioned end points. In addition, whether patients received outpatient heart failure follow-up (e.g., with heart failure nurse, cardiac hub, or cardiology specialist) was also monitored. Repeat BNP values during follow-ups were compared with each patient's initial BNP value and documented as either a "reduction" or "increase." These parameters were again correlated with the aforementioned end points (Tables 3 and 4).

Furthermore, we observed whether there is an increased readmissions or deaths with rising NT-proBNP levels or whether there is decreased readmissions or deaths with declining NT-proBNP values

Categorical variables are reported as frequencies and percentages. Normally distributed continuous variables are presented as means ± standard deviations, whereas non-normally distributed continuous variables are presented medians and interquartile ranges. Student's *t*-test or the Mann–Whitney U test for continuous variables, and the chi squared or Fisher's exact test for categorical variables were used comparison between groups, as appropriate. When needed, the variables were transformed for further analysis.

3. Results

3.1. Demographic characteristics

3.1.1. HFpEF cohort

Patients in the HFpEF cohort were categorized into three sub-cohorts according to NT-proBNP values. In all three sub-cohorts, the majority of patients were male, and most had a Rockwood Clinical Frailty Scale score of 6. The majority of patients presented with shortness of breath, and a minority had evidence of fluid overload.

Data are presented as frequencies (percentages) unless otherwise stated. NYHA II SOB:SD: standard deviation (Tables 1 and 2).

Table 1: Demographic characteristics of HFpEF cohort

NT-proBNP	**<400 ng/L** n = 11	**400–2000 ng/L** **n** = 15	**>2000 ng/L** **n = 27**
Age in years, average (SD)	66.2 (13.7)	80.7 (6.3)	83.3 (8.5)
Sex			
Female	5 (17.2%)	9 (31.0%)	15 (51.7%)
Male	6 (25.0%)	6 (25.0%)	12 (50.0%)

Table 1 (Cont.)			
Clinical Frailty Score			
2	2 (100.0%)	0 (0.0%)	0 (0.0%)
3	2 (50.0%)	1 (25.0%)	1 (25.0%)
4	3 (42.9%)	2 (28.6%)	2 (28.6%)
5	3 (23.1%)	5 (38.5%)	5 (38.5%)
6	0 (0.0%)	7 (38.9%)	11 (61.1%)
7	1 (11.1%)	0 (0.0%)	8 (88.9%)
NYHA II SOB	10(22.2%)	11(24.4%)	24 (53.3%)
Fluid Overload	2(14.3%)	4(28.6%)	8 (57.1%)
Hypertension	2(8.3%)	8(33.3%)	14(58.3%)
Diabetes Mellitus	2(15.4%)	3(23.1%)	8 (61.5%)
Chronic Kidney Disease	0(0.0%)	2(16.7%)	10 (83.3%)
Dyslipidemia	2(40.0%)	2(40.0%)	1 (20.0%)
Coronary Artery Disease	6(33.3%)	5(27.8%)	7 (38.9%)
Cerebrovascular Accident	2(33.3%)	2(33.3%)	2 (33.3%)
Atrial Fibrillation	0(0.0%)	6(33.3%)	12 (66.7%)
Respiratory Diseases	5(29.4%)	5(29.4%)	7 (41.2%)
Malignancy	0(0.0%)	3(25.0%)	9 (75.0%)

Table 2: Demographic characteristics of HFrEF cohort			
NT-proBNP	**<400 ng/L n = 4**	**400–2000 ng/L n = 7**	**>2000 ng/L** n = 24
Age in years, average (SD)	71.3 (10.7)	60.3 (14.1)	77.3 (13.4)
Sex			
Female	1 (8.3%)	3 (25.0%)	8 (66.7%)
Male	3 (13.0%)	4 (17.4%)	16 (69.6%)
Clinical frailty score			
3	1 (100.0%)	0 (0.0%)	0 (0.0%)
4	1 (16.7%)	3 (50.0%)	2 (33.3%)
5	1 (20.0%)	1 (20.0%)	3 (60%)
6	0 (0.0%)	0 (0.0%)	12 (100%)
7	1 (16.7%)	1 (16.7%)	4 (66.7%)
Missing observations	0	2	3

Table 2 (Cont.)			
Presenting symptoms			
NYHA II SOB	2 (8.3%)	4 (16.7%)	18 (75.0%)
Fluid Overload	0 (0.0%)	0 (0.0%)	6 (100%)
Past medical history			
Hypetension	0 (0.0%)	2 (20.0%)	8 (80.0%)
Diabetes Mellitus	0 (0.0%)	1 (16.7%)	5 (83.3%)
Chronic Kidney Disease	0 (0.0%)	0 (0.0%)	6 (100.0%)
Dyslipidemia	0 (0.0%)	0 (0.0%)	3 (100%)
Coronary Artery Disease	0 (0.0%)	1 (16.7%)	5 (83.3%)
Cerebrovascular Accident	0 (0.0%)	0 (0.0%)	1 (100%)
Atrial Fibrillation	2 (20.0%)	2 (20.0%)	6 (60.0%)
Respiratory Diseases	1 (20.0%)	1 (20.0%)	3 (60%)
Malignancy	0 (0.0%)	0 (0.0%)	3 (100%)

3.1.2. HFrEF cohort

The HFrEF cohort was categorized into sub-cohorts according to NT proBNP values. Similar to the HFpEF cohort, the majority of patients were male, 75% of patients presented with shortness of breath and were diagnosed with heart failure, and 25% of patients presented with evidence of fluid overload. The average Rockwood Clinical Frailty Scale score of the HFrEF cohort was 5.

Data are presented as frequencies (percentages) unless otherwise stated. NYHA II SOB: SD: standard deviation.

3.2. Basic data analysis for end points

Table 3: Data analysis of end points for HFpEF cohort			
	NT Pro BNP 0-400	**NT Pro BNP 400-2000**	**NT Pro BNP >2000**
Mortality			
Alive	10 (91%)	13 (86.6%)	15 (55.6%)
Deceased	01 (9%)	02 (13.3%)	12 (44.4%)
Readmissions			
Yes (including terminal event admission)	02 (18.1%)	03 (33.3%)	19 (74.0%)
No admission	09 (81.8%)	12 (66.6%)	08 (26%)
Heart failure follow up			
Received	05 (45.4%)	08 (61.5%)	05 (35.7%)
Not Received	04 (36.3%)	04 (38.5%)	10 (64.2%)
Not Warranted	02 (18.1%)	0 (0%)	0 (0%)
OP NT ProBNP monitored?			
Yes	1 (11.1%)	03 (38.4%)	02 (35.7%)
No	4 (88.8%)	05 (61.6%)	03 (64.2%)

Table 4: Data analysis of end points for HFrEF cohort

	NT Pro BNP 0-400	NT Pro BNP 400-2000	NT Pro BNP >2000
Mortality			
Alive	3 (75%)	7 (100%)	22 (91.6%)
Deceased	1 (25%)	0%	3 (12.5%)
Readmissions			
Yes (including terminal event admission)	1 (25%)	0%	3 (12.5%)
No admission	3 (75%)	7 (100%)	21 (87.5%)
Heart failure follow up			
Received	4 (100%)	7 (100%)	12 (54.5%)
Not Received	0 (0%)	0 (0%)	6 (27.2%)
Not Warranted	0 (0%)	0 (0%)	4 (18.1%)
NT ProBNP measured?			
Yes	0 (0%)	3 (42.8%)	10 (41.6%)
No	4 (100%)	2 (57.1%)	6 (29.1%)

3.3. NT-proBNP and mortality

The association between NT-proBNP value and mortality was evaluated for both cohorts. In the HFpEF cohort, the sub-cohort with an initial NT-proBNP value of >2000 ng/L on admission demonstrated a high mortality rate of 44% from admission through follow-up. In contrast, the same sub-cohort of the HFrEF cohort exhibited a mortality rate of 8.3%.

The mortality rates of all sub-cohorts were standardized and plotted against NT-proBNP levels. The two sub-cohorts with NT-proBNP values of >2000 demonstrated a mortality rate of 29.1% (Figure 1).

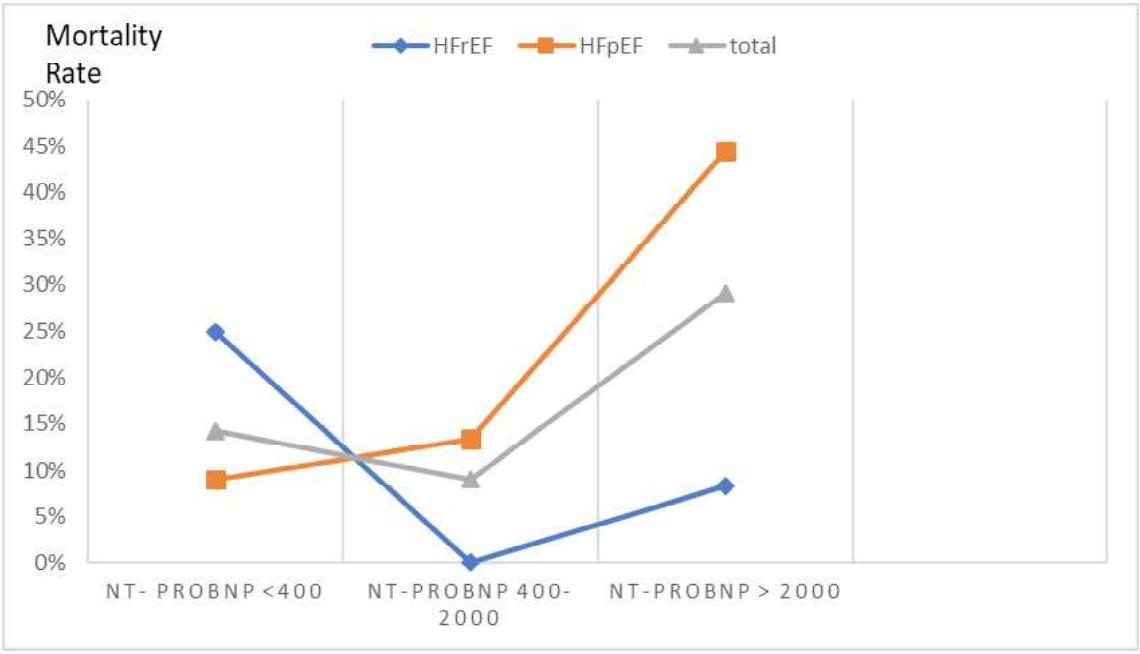

Figure 1: NT-proBNP BNP values and mMortality rates for both HFrEF and HFpEF cohorts

3.4. NT-proBNP and heart failure re-admission

All data from the six sub-cohorts were analyzed in terms of the heart failure re-admission end point. In the HFpEF cohort, the sub-cohort with initial NT-proBNP values of >2000 on admission demonstrated a high readmission rate of 74% during follow-up. In contrast, in the HFrEF cohort, the same sub-cohort exhibited a lower readmission rate of 12.5%, similar to the results of the mortality end point analysis between groups. The data were then statistically standardized for the whole population and plotted against NT-proBNP values. Higher incidence of readmissions and mortality was observed in the patients with rising BNP during the follow-up.

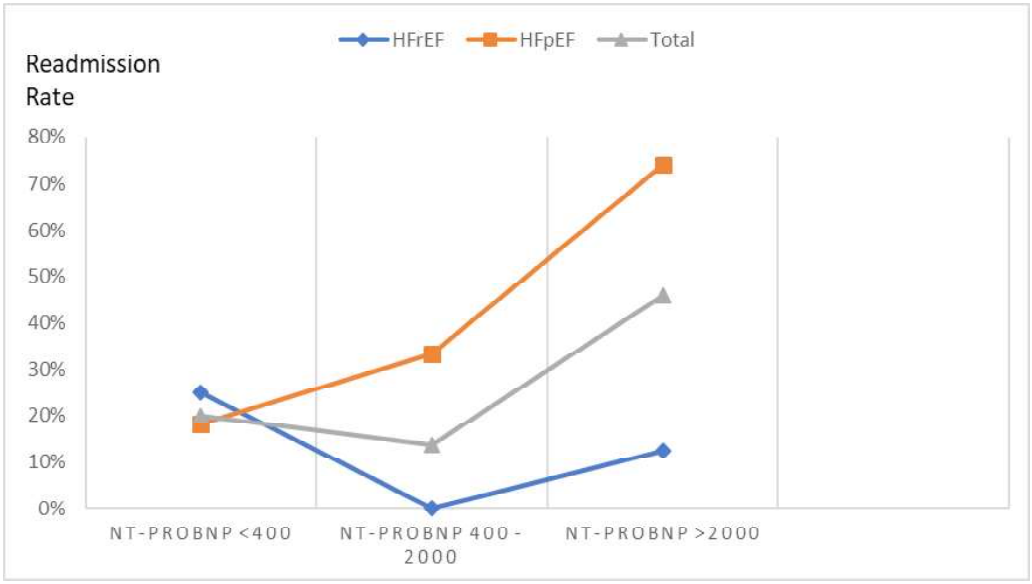

Figure 2: NT-proBNP values and heart failure readmission rates for HFrEF and HFpEF cohorts

3.5. Heart failure follow-up

65.7% (n = 23) of the HFrEF cohort received heart failure follow-up and only 33.7% (n = 18) of the HFpEF cohort received follow-up (Figure 3). Of the patients who received follow-up, 46.3% (n =19) % received a repeat NT-proBNP evaluation either during the follow-up or during a readmission. More than 35% of patients with

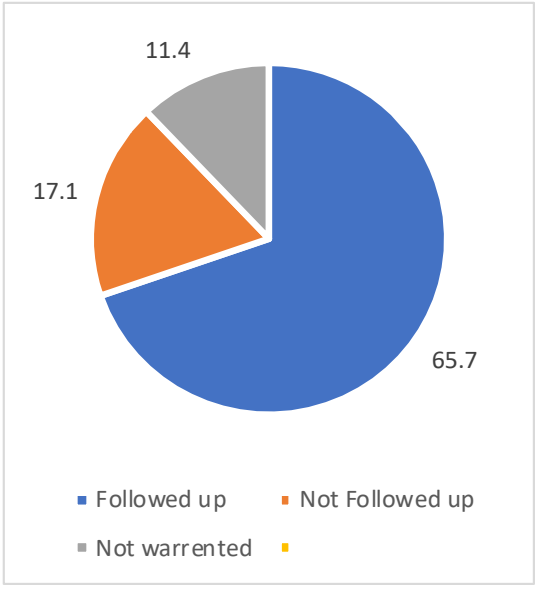

Figure 3: Follow-up rates for HFrEF

moderately high NT-proBNP (400-2000)–38.4% (n = 3) for the HFpEF cohort and 42.8% (n = 3) for the HFrEF cohort-received repeat NT-proBNP evaluation during follow-up. Sub-cohorts with NT-proBNP values of >2000 demonstrated similar repeat BT-proBNP evaluation rates during follow-up: 37.5% (n = 6) for the HFpEF cohort and 41.6% (n = 10) for the HFrEF cohort.

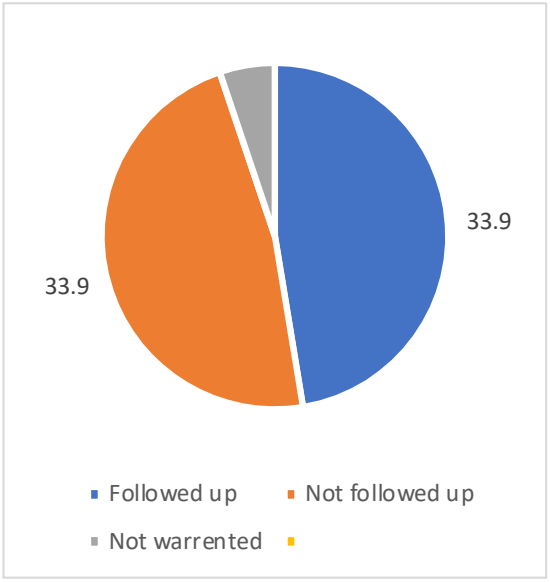

Figure 4: Follow up rates for HFpEF cohorts

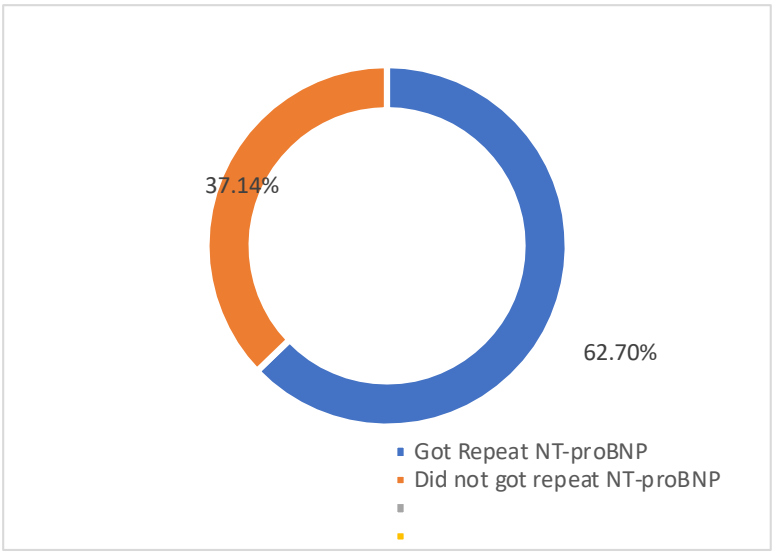

Figure 5: Follow-up NT-proBNP evaluation rates for total study sample

The data analysis was further extended to determine whether patients exhibited declining or rising NT-proBNP values during heart failure follow-up, compared the BNP reduction rate with the re-admissions in HFpEF and HFrEF cohorts.

During follow-up, nine patients exhibited rising NT-proBNP values, of which six were re-admitted due to heart failure exacerbation, representing a 66.6% re-admission rate for patients with rising NT-proBNP values. Of the 12 patients who exhibited declining NT-proBNP values during follow-up, only four were re-admitted with heart failure exacerbation, representing a 33.3% re-admission rate for patients with declining NT-proBNP values, as seen in Figure 7

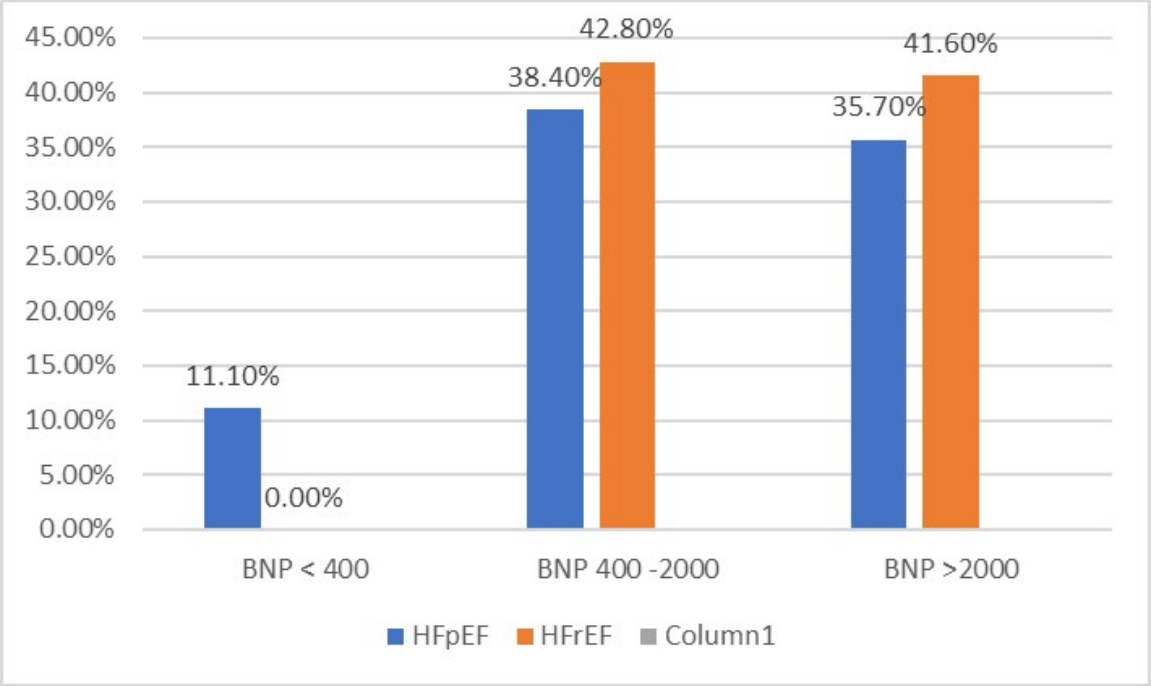

Figure 6: Follow-up NT-proBNP evaluation rates for sub-cohorts

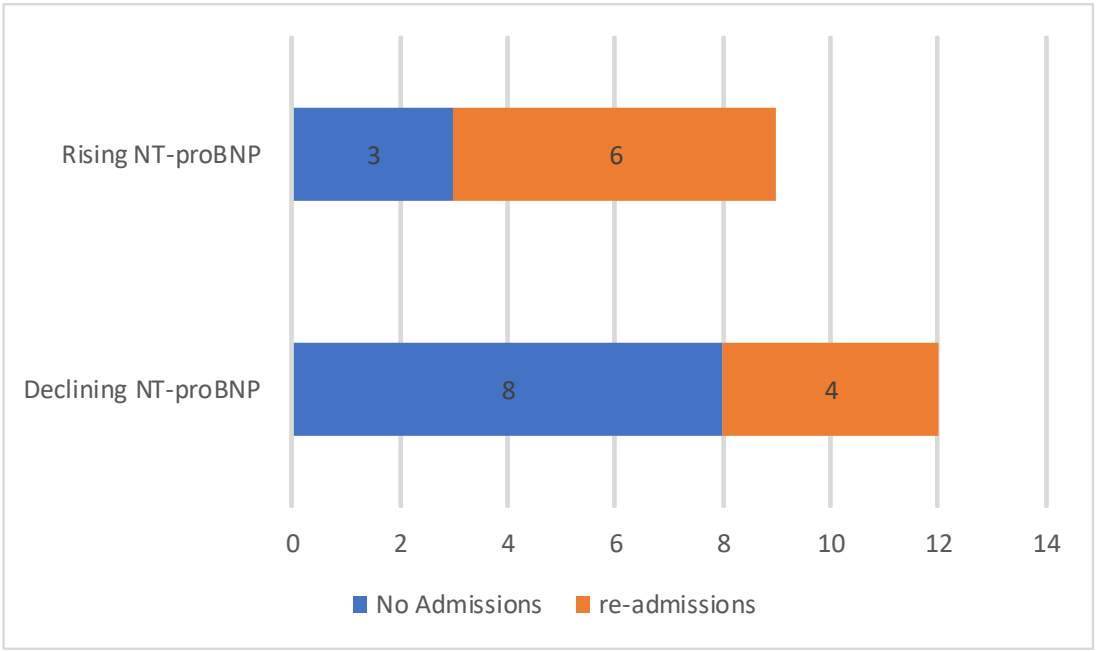

Figure 7: Association between changes in NT-proBNP value and re-admission rate

3.6. Statistical power

We re-categorized all the data according to NT-proBNP values. Area under the receiver operating curve (AUROC) was calculated for each cohort to measure the natriuretic peptide's performance in predicting heart failure mortality at first admission screening. Multiple logistic regression was then performed for the total study sample to determine whether NT-proBNP was predictive of mortality in heart failure, as seen in Figure 8. AUROC was 0.478 for the total study sample, indicating that NT-proBNP values can be used as a prognostic biomarker for predicting mortality in elderly heart failure patients

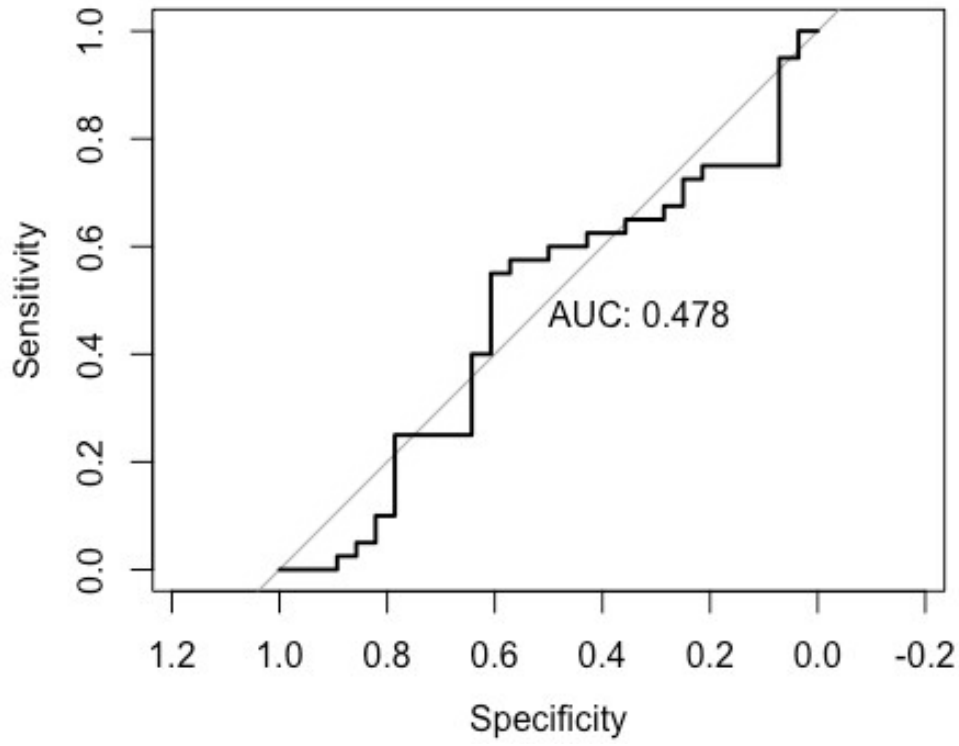

Figure 8: Receiver operating characteristic curve for specificity and sensitivity of NT proBNP (for the total study sample)

Kaplan–Meier curves and log rank analysis were used to compare the cumulative incidence of the primary end point between HFpEF and HFrEF groups, as seen in Figures 9 and 10. The Kaplan–Meier curves for both cohorts demonstrated that survival probability decreased as NT-proBNP levels increased (*p*-values of 0.29 and 0.018 for the HFpEF and HFrEF cohorts, respectively).

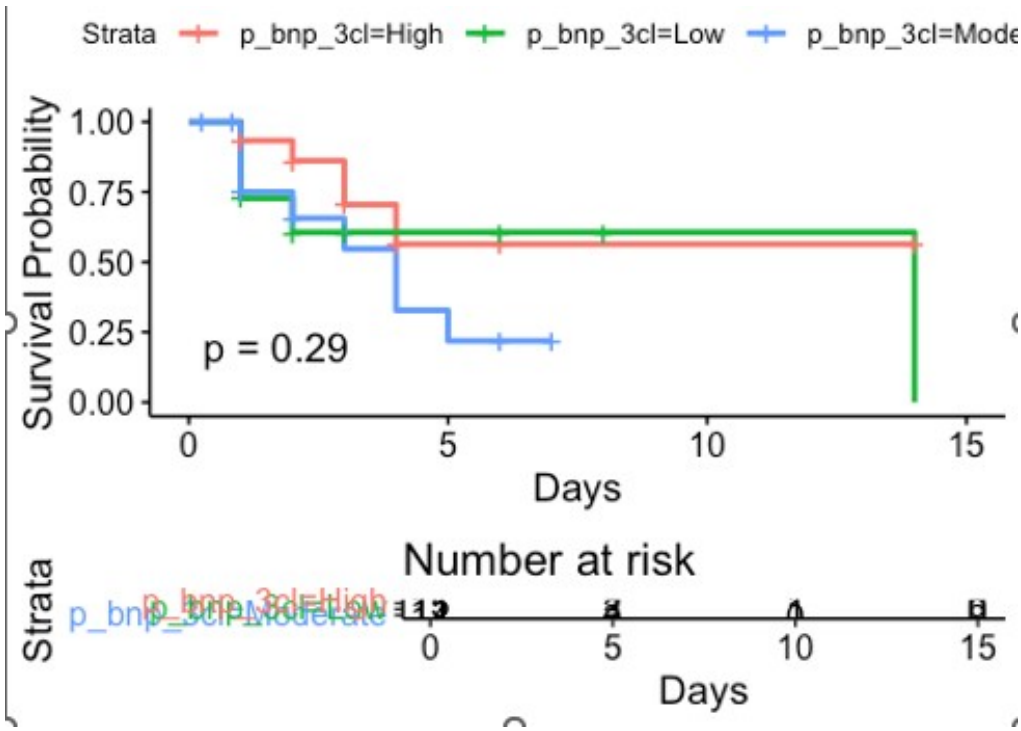

Figure 9: Kaplan-Meier curve for HFpEF cohort

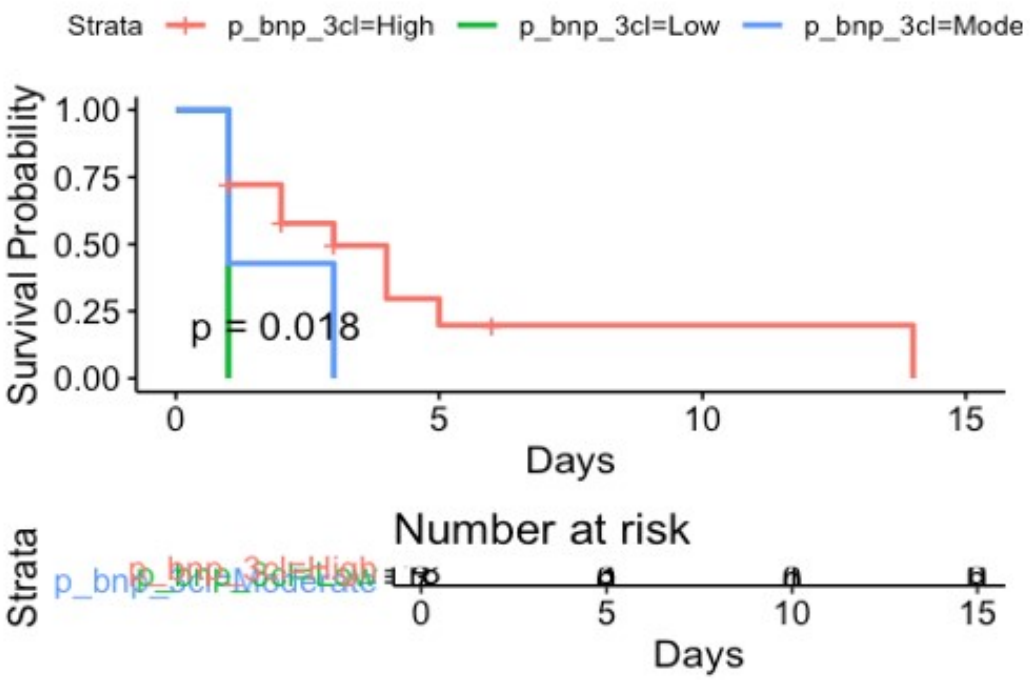

Figure 10: Kaplan–Meier curve for HFrEF cohort

In this study, the null hypothesis is that NT-proBNP cannot be used as a prognostic indicator for elderly patients with heart failure. The *p*-values for both cohorts were less than this significance level, hence the null hypothesis was rejected.

4. Discussion

In this cohort study, two major heart failure cohorts were analyzed for specific end points under six main sub-cohorts. Our data analysis showed that whose with NT-proBNP values of >2000 exhibited a mortality rate of 29.1% and a heart failure re-admission rate of 45.6%. Those with rising NT-proBNP values during heart failure follow-up exhibited a re-admission rate of 66.6%, which was much lower than that (33.3%) among those with declining NT-proBNP values. Based on the statistical power of the study, NT-proBNP can be used as a prognostic marker for mortality in elderly patients with heart failure irrespective of their ejection fraction.

5. Study limitations

This study did have some limitations. The data collection was done randomly to obtain snapshots of each month of the study period. The initial approach used for data collection included screening patients who had inpatient echocardiography for heart failure, with the assumption that all heart failure admissions received inpatient echocardiography. However, this selection process may have missed some patients.

Other factors that can cause high NT-proBNP values were not evaluated in this study. However, the documented demographic characteristics included most of these factors, and the results were standardized. Data on body mass index, serum creatinine levels, and sepsis were not collected, as it was challenging to access these data sets. In the future, we hope to carry out a separate study to extensively analyze these factors.

The mortality and re-admission records we obtained were analyzed to determine the causes for mortality and re-admissions. Some patients had other associated causes of mortality beyond heart failure, such as sepsis, Acute Kidney Injury (AKI) on Chronic Kidney Disease (CKD) and cardiorenal syndrome. Most of the re-admissions were actual heart failure re-admissions, but a minority of patients presented with respiratory conditions that could have exacerbated existing heart failure, such as pneumonia or infective exacerbation of chronic obstructive pulmonary disease. The presence of other associated conditions in addition to heart failure that contributed to mortality and re-admission was an unavoidable limitation in this study. Finally, our follow-up was done over 12-15 weeks, but it would be ideal if it could be extended further.

6. Conclusion

Our results provided satisfactory statistical evidence that higher NT-proBNP values on admission were a good predictor of mortality and re-admission among the elderly population. Furthermore, rising NT-proBNP levels during heart failure follow-up were associated with higher mortality and morbidity rates. Therefore, NT-proBNP level can be used as a prognostic biomarker for elderly patients with heart failure, irrespective of their ejection fraction status. Monitoring NT-proBNP levels in all heart failure cases could be beneficial to prevent mortality and morbidity, as heart failure medications can then be optimized prior to episodes of heart failure decompensation.

Acknowledgment

We would like to acknowledge all our mentors and existing literature that aided in the completion of this study. We confirm that ethical committee approval was sought where necessary and is acknowledged by the team whenever needed.

Funding and ethical approval

We have started the initial project as hospital-based series of audits. These audits were carried out multiple cycles and the data collection was done retrospectively. Informed verbal consent was taken from the patients prior to the data collection. Since the nature of the data collection for the audits were used in this publication, this publication was exempt from receiving ethical approval as per the guidance by the research ethics board in Northern Ireland.

No funding was received to this project as this was carried out as audit cycles initially.

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