Title:

B-Type Natriuretic Peptide predicts deterioration in functional capacity following lung resection

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Visual Abstract:

Key Question

Does an association exist between peri-operative BNP and post-operative functional limitation in lung resection patients

Key Findings

BNP is associated with subjective and objective markers of functional limitation following lung resection

Take-home message

In lung resection patients, preoperative BNP is a predictor of functional deterioration, and shows potential for use in risk stratification

Abstract:

Objectives:

Following lung resection, there is a decrease in functional capacity and quality of life which is not fully explained by changes in pulmonary function. Previous work demonstrates that B-type Natriuretic Peptide (BNP) is associated with short and long term complications following lung resection, leading to the suggestion that cardiac dysfunction may contribute to functional deterioration. Our aim was to investigate any relationship between BNP and subjective and objective indices of functional deterioration following lung resection surgery.

Methods:

Twenty-seven patients undergoing lung resection had serum BNP measured pre-operatively, on post-operative day (POD)1, POD2, and at two months post-operatively. Functional deterioration was assessed using Six Minute Walk Tests (6MWT) and the Medical Research Council (MRC) dyspnoea scale. ‘Deterioration in functional capacity’ was defined as *either* an increase in MRC dyspnoea score *or* a significant decrease in 6MWT distance.

Results:

BNP increased over time ($p<0.01$) and was significantly elevated on POD1 and POD2 ($p<0.02$ for both). Seventeen patients demonstrated functional deterioration 2-months post-operatively. At all peri-operative timepoints, BNP was significantly higher in patients showing deterioration ($p<0.05$ for all). Pre-operative BNP was predictive of functional deterioration at 2 months with an AUROC of 0.82 ($p=0.01$, CI: 0.65-0.99).

Conclusions:

This study has demonstrated, using subjective and objective measures, that pre-operative BNP is a predictor of functional deterioration following lung resection. BNP may have a role in pre-operative risk stratification in this population, allowing therapy in future to be targeted toward high risk patients with the aim of preventing post-operative cardiac dysfunction.

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Keywords:

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Lung Resection

Risk Stratification

Introduction

Lung cancer remains the leading cause of cancer death worldwide [1]. In suitable patients lung resection offers the best chance of cure; as a result an increasing number of surgeries are being undertaken, contributing to improved survival [2]. Although surgery has a low associated mortality, lung resection leaves patients with a high burden of both short and long term morbidity**.** Functional capacity plays an important role in the physical and social wellbeing of patients with lung cancer; yet unfortunately there is a well-documented decrease in quality of life, functional capacity and exercise tolerance following lung resection [3-5], with as many as 40% of patients reporting disabling dyspnoea [6]. Clinical practice guidelines advocate the use of predicted post-operative (ppo) lung function to predict the risk of post-operative dyspnoea [7-9]. This is calculated by adjusting pre-operative lung function test results to reflect the quantity of lung resected. Predicted post-operative pulmonary function has however been shown to be poorly associated with changes in exercise capacity [10] and quality of life [11] following surgery. This lack of association suggests other factors may be involved in the aetiology of post-operative functional limitation. Several authors have suggested functional impairment may result from cardiac rather than pulmonary limitation [12, 13], and we suggest that B-type Natriuretic Peptide (BNP) may have a role in identifying patients at risk of post-operative functional limitation.

BNP is a 32-amino acid polypeptide released from the cardiac ventricles in response to myocardial stretch and strain. It is easily measurable in plasma in either its active form or an inactive precursor – N-Terminal-pro BNP. BNP increases following lung resection, with the magnitude of increase associated with the amount of lung tissue resected [14]. In non-cardiac surgeries BNP has been shown to be predictive of both short and long term mortality [15, 16]. Furthermore, BNP has been demonstrated to identify patients at risk of both short and long term cardio-pulmonary complications of non-cardiac surgery [17-19], with higher levels of BNP predicting higher complications [15]. These findings have been validated by meta-analysis [20], and consequentially, BNP has been included in both the American Heart Association and

European Society of Anaesthesiology guidelines for assessing peri-operative cardiac risk in patients undergoing non-cardiac surgery [21, 22]. In patients undergoing thoracic surgery, elevated BNP has been associated with increased rates of atrial fibrillation and other cardiac dysrhythmias [23].

There is no previous work comparing BNP to functional capacity in patients undergoing lung resection. Given that impaired functional capacity may be related in part to cardiac function, we hypothesised there would be an association between peri-operative BNP and post-operative functional limitation.

Materials and Methods

This study is an *a-priori* secondary endpoint of a larger observational study using cardiovascular magnetic resonance imaging to investigate right ventricular dysfunction following lung resection (ClinicalTrials.gov: NCT01892800).

Participants

Ethics approval for the study was provided by the West of Scotland Research Ethics Committee (REC Ref: 134/WS/0055) and all participants provided written informed consent. Patients attending for elective lung resection at the Golden Jubilee National Hospital (a tertiary referral hospital providing cardiothoracic surgical services for the West of Scotland) between August 2013 and September 2014 were screened and approached for inclusion. Subjects who were pregnant, participating in any investigational research which could undermine the scientific basis of the study, had contraindications to cardiovascular magnetic resonance or were undergoing; wedge / segmental / sub-lobar lung resection, pneumonectomy, isolated middle lobectomy or thoracoscopic / minimal access lung resection, were excluded. Surgical technique was standardised to a single surgeon performing a postero-lateral muscle sparing thoracotomy and lobectomy with anatomically appropriate lymph node clearance. Anaesthetic technique was standardised and included the use of a volatile agent for anaesthetic maintenance, intra-operative lung protective ventilatory strategies and thoracic epidural blockade for post-operative analgesia.

Measurements

BNP

Blood samples were collected into EDTA test tubes at baseline, immediately post-op, on post-operative days (POD) 1 and 2, and 2 months post-op. Analysis was performed immediately at point of care using the Alere Triage® system (Alere Ltd. Stockport, UK), according to the manufacturer's guidelines. Quality control checks were carried out on the equipment regularly to ensure accuracy in line with the manufacturer's recommendations; the coefficient of variation for BNP measurements was 5%. Patients and clinicians were blinded to BNP results to reduce bias and to prevent BNP results altering patient management.

Functional Capacity

Functional capacity was assessed subjectively using the Medical Research Council (MRC) dyspnoea score, and objectively by Six Minute Walk Test (6MWT). Patients completed MRC dyspnoea scores [24] as an assessment of self-reported functional capacity at baseline, two months post-op and one year post-op. The 6MWT was carried out according to standard guidelines [25] over a 30 metre course by trained respiratory physiologists pre-operatively and 2 months post-operatively. In order to assess any decrease in walk distance a 'minimal important difference' was defined. A decrease in walking distance of 28 metres has been validated as the minimally important difference detected by the 6MWT in a cohort of COPD patients, and, as there has been no minimally important difference defined in a lung resection cohort, this was used in our study [26].

To facilitate integration of subjective and objective assessments of functional capacity, the primary outcome of this study, 'deterioration in functional capacity' was defined as *either* an increase in MRC dyspnoea score of 1 point or more *or* a decrease in walking distance of 28 metres or more. Patients were classed as having ‘deteriorated functional capacity’ if they fulfilled either of these criteria.

Comorbidities and baseline demographics were collected to assess for confounding factors between groups. Both surgical and anaesthetic technique were standardised.

The sample size was calculated as per the primary objective of the initial study. No separate sample size calculation was carried out for this secondary endpoint.

Statistical methods

Statistical analyses were carried out using SPSS® (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). All variables were visually examined, and normality was tested using the Shapiro-Wilk test. Categorical data are presented as frequency (%) and continuous data are presented as mean (SD) if following a parametric distribution or median (IQR) if following a non-parametric distribution. Changes over time were assessed using the parametric repeated measures ANOVA or the non-parametric Friedman’s test according to data distribution. Post-hoc pairwise comparisons were undertaken using a paired t-test or a Wilcoxon signed rank test. Independent samples t-tests or Mann-Whitney U tests were used to compare independent groups.

Association between continuous variables was assessed using the parametric Pearson’s correlation coefficient and the non-parametric Spearman’s rank order correlation coefficient according to data distribution. The predictive power of BNP to identify deteriorated functional capacity was assessed by examining the area under the Receiver Operating Characteristic curve (AUROC). Youden’s J statistic was used to identify the BNP value with the greatest predictive value. Patients with missing data for one or more parameters were included in the study; however, each individual comparison was made by complete case analysis.

Statistical significance was defined as a p value<0.05. No adjustments were made for multiple comparisons.

Results

Baseline data was collected pre-operatively on 27 patients. Patient demographic data is available in Table 1. All patients were alive at one-year follow up.

Ninety-eight percent (132/135) of planned BNP samples were taken, with three missing at the two month time-point. Samples were missed at the two month time-point due to patients being unwell in other hospitals and therefore being unable to attend for follow-up. Patients returned 90% (73/81) of MRC questionnaires and completed 85% (46/54) of walk tests. Two patients did not attend their 6MWT either pre-operatively or at the two month time-point, and so were excluded from 6MWT analysis.

BNP

BNP increased over time ($p<0.01$, Friedman’s) and was significantly elevated on POD1 and POD2 ($p<0.02$ for both, Wilcoxon Signed Rank Test) before returning to baseline two months post-operatively (Figure 1). There was no association between the number of lung segments resected and the increase in BNP from baseline to peak on POD2 ($r=0.01$ $p=0.96$, Spearman’s).

BNP and Functional Capacity

MRC Scale – subjective functional assessment

Self-reported MRC dyspnoea scores are expressed in Figure 2. There was a significant difference in the distribution of MRC dyspnoea scores over time, with less patients reporting being “not troubled by breathlessness” and more patients reporting functional limitation at both post-operative time-points ($p=0.03$, Friedman’s). No patient reported improvement from baseline on this scale.

BNP on POD1 was significantly associated with MRC scale results 2 months post-operatively ($r=0.56$, $p<0.01$, Spearman’s, Table 2). There was no association between pre-op BNP and post-op MRC scale ($r=0.24$, $p=0.25$).

Six Minute Walk Test – objective functional assessment

Pre-operatively, the median six minute walk distance was 412 metres (360-486), which was unchanged 2 months post-operatively at 420 metres (363-474; p=0.64, Wilcoxon Signed Rank test). This comparison does not however reflect four patients who attended for 6MWT two months post-operatively, but declined to attempt the test due to severe dyspnoea. In total 11 patients (44%) were either unable to walk as a result of severe dyspnoea, or walked at least 28 metres less than baseline and were classified as having 'deteriorated functional capacity' for the purposes of analysis.

Pre-op BNP was higher in patients with a reduced 6MWT distance (p=0.01, Mann-Whitney U). There was a significant negative association between high pre-op BNP levels and low two month post-op 6MWT distances (r=-0.43, p=0.05, Spearman's). POD1 BNP was not associated with two month post-op 6MWT (r=-0.33, p=0.15, Table 2).

Combined functional assessment - Composite of MRC scale and 6 Minute Walk Test

Seventeen patients (68%) demonstrated deteriorated functional capacity two months post-operatively. Within the group showing no functional limitation, there was no change in BNP over time (p=0.34, Friedman's), however in the group demonstrating reduced functional capacity, BNP was significantly increased from baseline on POD1 and POD2 before reducing to baseline levels by 2 months post-operatively (p<0.01, Friedman's test, Figure 3). BNP was higher in the group showing deteriorated functional capacity compared to the group exhibiting no change at all peri-operative time-points, including pre-operatively (p<0.01 for all, Mann Whitney U, Figure 3). There were no differences in baseline demographics (including baseline pulmonary function) between the two groups (Table 1).

Pre-operative BNP was found to be predictive of a deterioration in functional capacity 2 months post-operatively in this cohort, with an AUROC of 0.82 (p=0.01 95% CI: 0.65-0.99, Figure 4). A BNP of 46.5 pg/ml was found to have a sensitivity of 58% and a specificity of 100% to predict deterioration in functional capacity 2 months following surgery. This gives pre-op BNP a Positive Predictive Value (PPV) of 100% and a Negative Predictive Value (NPV) of 53%.

Predicted Post-operative Lung Function

Neither ppo-FEV1 nor ppo-DLCO were associated with MRC scale, 6MWT, or functional deterioration two months post operation (Table 3). There was no difference between ppo-FEV1 or ppo-DLCO when comparing those who suffered functional deterioration with those who did not (p=0.37 and p=0.27 respectively, Independent Samples t-test, Figure 5).

Discussion

The main finding of this study is the observation that BNP is associated with patient reported dyspnoea and 6MWT distance following lung resection, and has predictive ability in identifying patients at risk of deterioration in functional capacity.

As in previous studies, our study demonstrated significant deterioration in functional capacity following lung resection [3, 4]. In addition to significant changes in self-reported breathlessness, it is striking that at 2-months post-operatively, four of the patients presenting for post-operative follow-up declined to perform a 6MWT because they were "too breathless". Our study also echoes the previously reported finding that deterioration in functional capacity was not well associated with changes in predicted post-operative lung function [5].

The observation of poor association between changes in functional capacity and lung function, and the strong association between BNP, a quantitative biomarker of myocardial function and functional capacity adds weight to the hypothesis that cardiac impairment may contribute to limited functional capacity following lung resection. To date, there has been limited study of the influence of cardiac function in determining exercise and functional capacity following lung resection. Okada et al used volumetric pulmonary artery catheters to determine cardiac function in 10 patients undergoing lung resection and demonstrated reduced ejection fraction on exercise post-operatively [27]. Nezu et al performed cardiopulmonary exercise testing in 82 patients undergoing lung resection demonstrating significantly reduced peak oxygen consumption and maximal workload post-operatively[12]. In this group both maximum heart rate and oxygen-pulse were reduced and breathing reserve maintained post-operatively – a pattern of changes suggestive of cardiac limitation.

Whilst previous studies have demonstrated increases in BNP post-operatively following lung resection, the observation that pre-operative BNP is predictive of post-operative exercise function two months later is a novel finding. It is plausible to suggest that BNP may have a future role in pre-operative risk stratification in this population allowing early identification of patients at increased risk of post-operative functional impairment. This could lead to several potential patient benefits:

Firstly, this would serve to better inform the consent process. Recently revised guidelines on lung cancer surgery from the UK National Institute of Heath and Care Excellence (NICE) recommend that patients considered to be at increased risk of *“dyspnoea and associated complications”* should be offered surgical resection “*if they accept the risks”* [28]. Despite this, conventional risk assessment protocols advocated in this guideline or by the British Thoracic Society (BTS) [7], the American College of Chest Physicians (ACCP) [9] and the European Respiratory Society / European Society of Thoracic Surgeons (ERS/ESTS) [8] focus on prediction of post-operative dyspnoea by calculation of predicted post-operative lung function.

Secondly, with greater understanding of the mechanisms of post-operative cardiac dysfunction, it may be possible to implement targeted strategies to reduce BNP and therefore risk pre-operatively. Alternatively, it may be possible to use BNP (alone or in concert with, for example, exercise testing) to stratify patients at increased risk of post-operative functional impairment to a peri-operative therapeutic pathway seeking to prevent post-operative cardiac dysfunction.

Current ESA/ESC guidelines recommend considering using BNP to obtain prognostic information in high risk patients prior to non-cardiac surgery [21], yet the potential role of natriuretic peptides in aiding peri-operative decision making in patients undergoing lung resection is unclear. There is no discussion of BNP in either BTS[7], ACCP[9] or ERS/ESTS[8] guidelines which specifically concern pre-operative assessment of patients undergoing lung resection.

With BNP previously having been demonstrated to be predictive of the risk of early post-operative complications [19] and long term survival following non-cardiac surgery [16], and now in the current study to be predictive of longer term functional limitation, we suggest further work is required to explore the potential utility of BNP in the pre-operative assessment of patients undergoing lung resection.

This study found that a BNP level of 46.5 pg/ml had the greatest sensitivity and specificity to predict deterioration in functional capacity in lung resection patients. This level of BNP however is lower than what is classically considered to be pathological; we believe this cut-off value allows identification of patients with sub-clinical cardiac dysfunction who are ‘at-risk’ of post-operative cardiac dysfunction, and that the further insult of lung resection is the precipitant that leads to functional deterioration. Previous work in other populations has demonstrated that similarly modest BNP values are predictive of left ventricular systolic and diastolic dysfunction [29, 30].

Limitations

As this study was an *a-priori* secondary endpoint of another study no power calculation was performed. Sample size was relatively modest and this study may therefore have lacked the statistical power to detect meaningful changes between time-points and associations between variables. Similarly, the reported ‘positive findings’ would benefit from validation in a larger patient cohort. As discussed, and an inherent risk in all observational research of this type, there was a small amount of missing data in our study; a small proportion of this was due to patients being too ill to undergo scans or partake in walking tests, and this may have acted as a potential source of confounding. This is mitigated in part however by the patients who were unwilling to perform post-operative 6MWT due to breathlessness being classified in the analysis as having suffered a significant deterioration in functional capacity. There was no quantification of the impact that pain had on patient dyspnoea.

Additionally our participants were limited to a single tertiary cardiothoracic referral centre, and as such results may not be as applicable to other patient cohorts. Whilst the study population appeared to typify the 'normal' West of Scotland thoracic surgical population, these patients may bear a differing burden of comorbidity to those elsewhere. Finally, all of our patients received an open lung resection, and less invasive surgery such as VATS may yield differing results.

Conclusion

This study has demonstrated that preoperative BNP is as a predictor of functional deterioration following lung resection. Using both subjective and objective measures of functional capacity, pre-op BNP levels were shown to be predictive of post-operative functional deterioration, so strengthening their potential for use in peri-operative risk stratification in this population.

FUNDING

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COMPETING INTERESTS

None

ETHICS APPROVAL

West of Scotland research ethics committee (134/WS/0055)

Figures and legends:

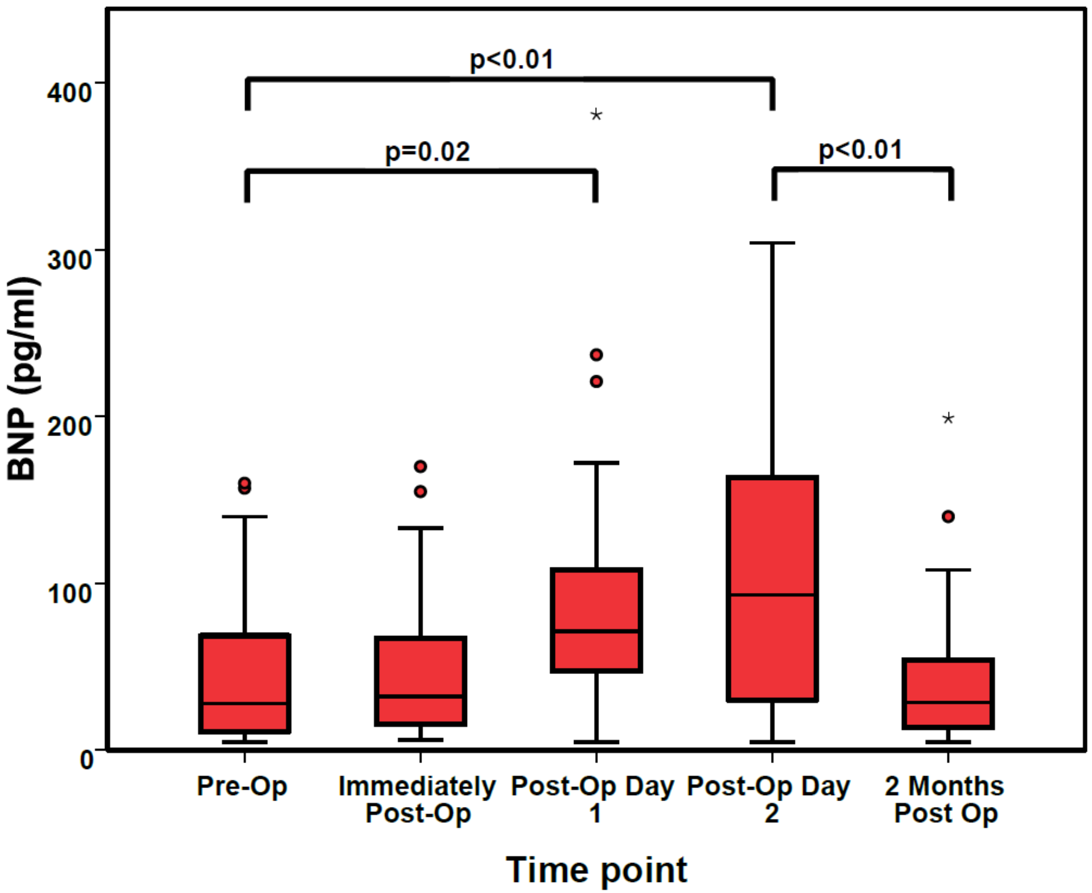

Figure 1 – Change in BNP levels throughout the peri-operative period.
Change over time assessed via Friedman's test ($p<0.01$), pair-wise comparisons between timepoints assessed via Wilcoxon Signed Rank Test.

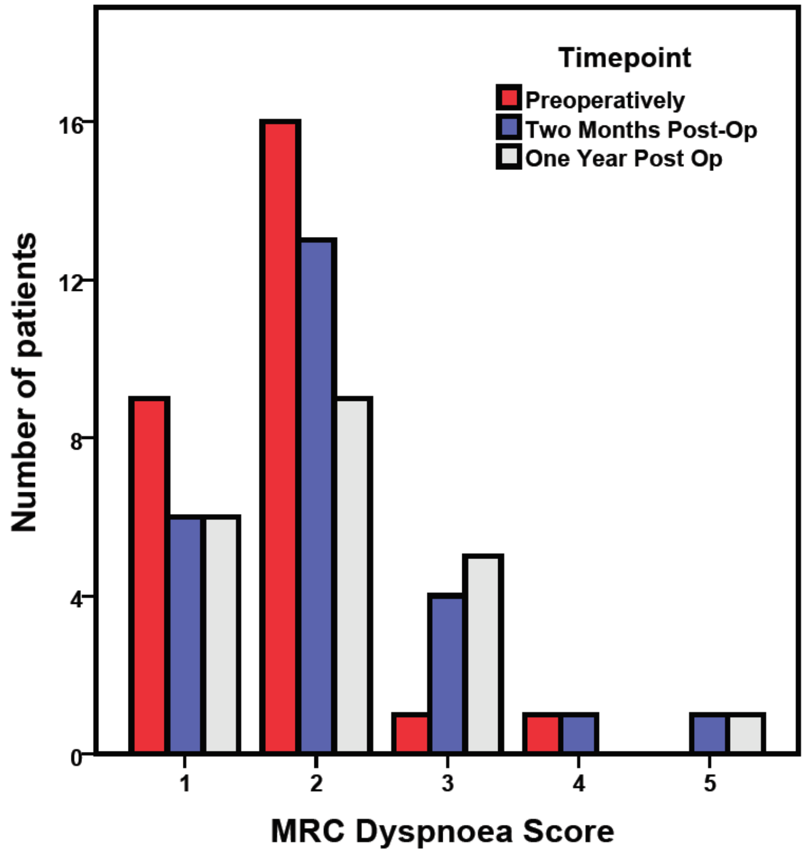

Figure 2 - Change in MRC dyspnoea scores over time.

Change over time **p=0.03** (Friedman's test).
MRC Score (35): 1 - Not troubled by breathlessness except on strenuous exercise. 2 - Short of breath when hurrying on the level or walking up a slight hill. 3 - Walks slower than most people on the level, stops after a mile or so, or stops after 15 minutes walking at own pace. 4 – Stops for breath after walking about 100 yds or after a few minutes on level ground. 5 – Too breathless to leave the house, or breathless when undressing.

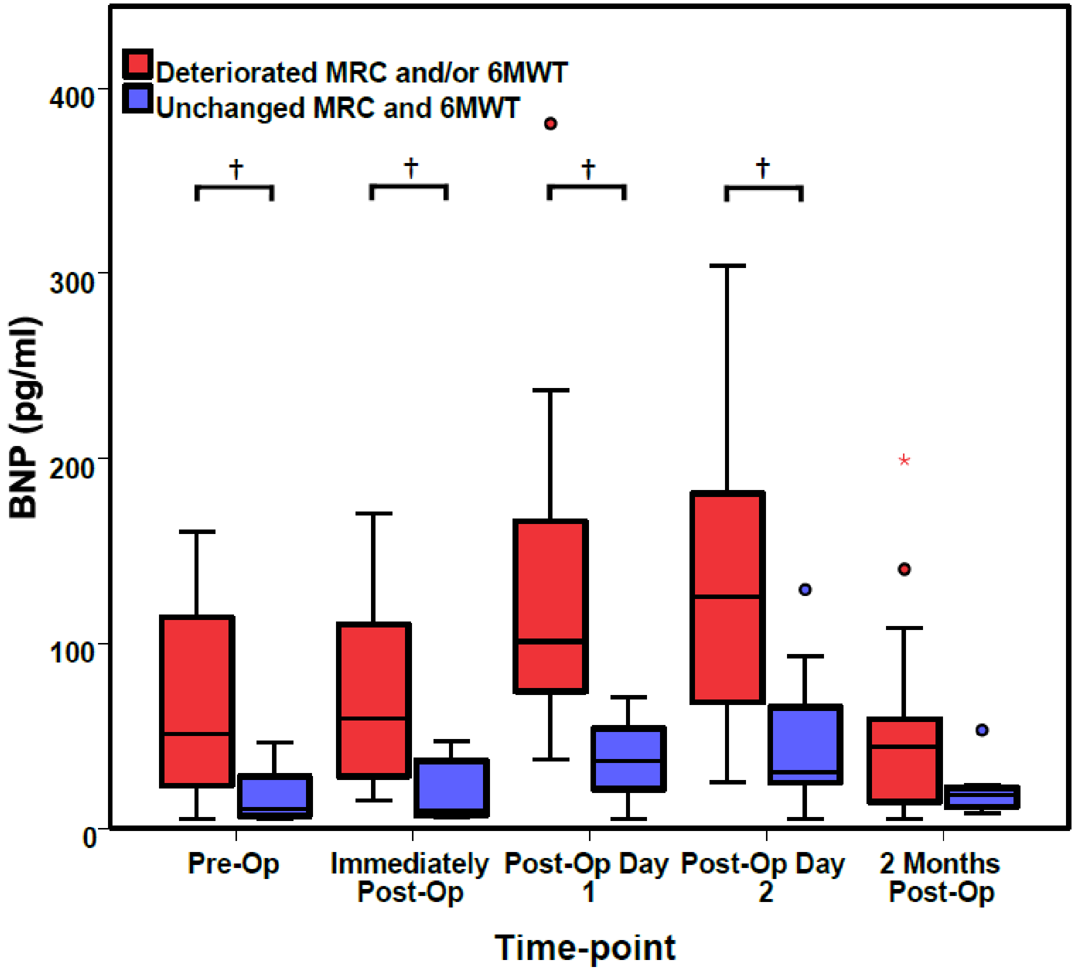

Figure 3 - Comparison of BNP levels between patients with deteriorated and unchanged functional capacity post-operatively. Change over time in patients showing functional deterioration – p<0.01 (Friedman's). Change over time in patients showing no functional deterioration – p=0.03 (Friedman's). Comparisons between groups carried out using Mann Whitney U Tests - † signifies p<0.01.

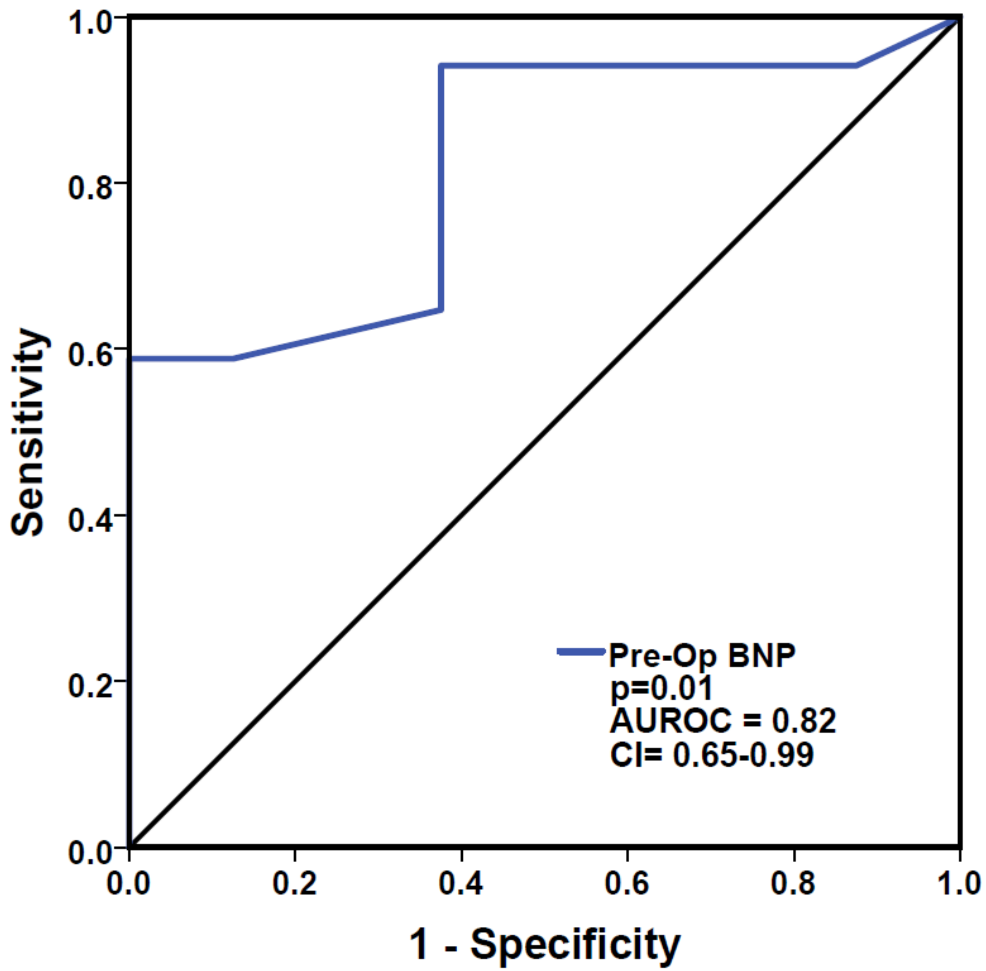

Figure 4 - ROC curve assessing ability of pre-operative BNP to predict Functional Deterioration 2 months post-operatively.

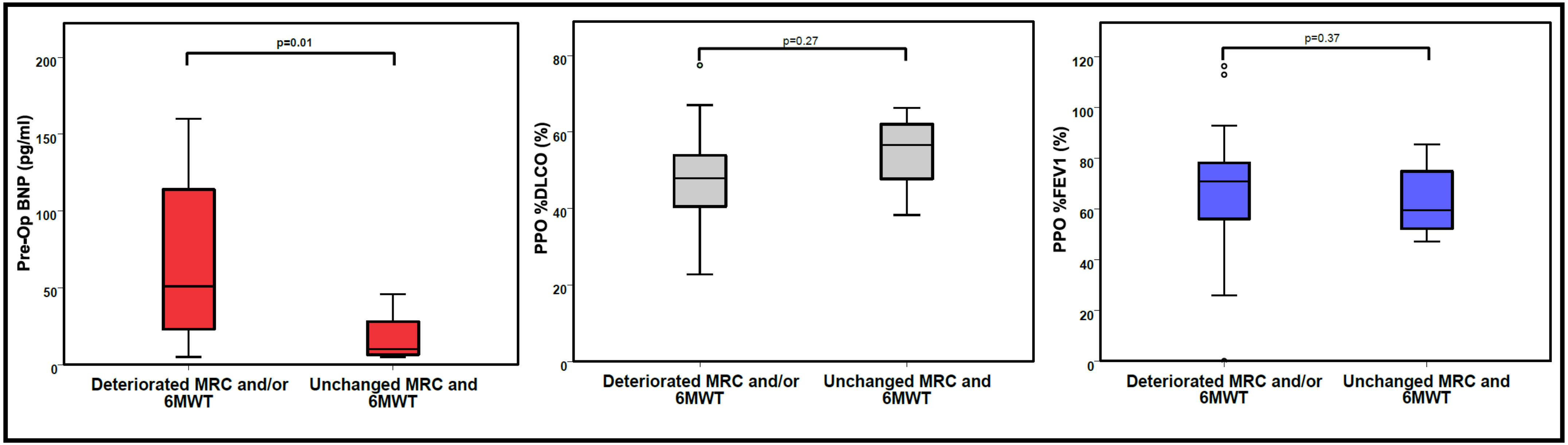

Figure 5 - Difference in BNP, predicted post-operative%FEV1, and predicted post-operative-DLCO between group showing functional deterioration, and group showing no functional deterioration.
Differences measured using independent samples t-test or Mann-Whitney U test.

Tables

Table 1 – Baseline Demographics.

Differences assessed using independent samples t-tests, Mann-Whitney U tests, or Fisher's exact test.

	All Patients n=27	Functional Deterioration n=17	Unchanged Functional Capacity n=8	p value
Age	65.5±9.6	68.8±7.6	59±11.1	0.34
Male Gender	10(37%)	5(29%)	4(50%)	0.39
BMI	26.08±3.89	25.61±3.96	26.19±3.39	0.73
Smoking Status:				
- Current Smoker	13(48%)	9(53%)	4(50%)	-
- Ex-Smoker	12(44%)	7(41%)	3(38%)	-
- Never smoked	2(7%)	1(6%)	1(13%)	-
Pack Years	38±22	37±24	38±19	0.95
FEV1 % Predicted	84±30	88±35	80±17	0.57
PPO FEV1 (%)	68±21	72±24	63±14	0.37
FEV1/FVC Ratio (%)	64±18	72(50-75)	60 (55-76)	1
DLCO (mmol/kPa/min)	5.16±1.74	4.67±1.62	5.98±1.75	0.08
PPO DLCO (%)	51±12	49±13	55±10	0.27
Thoracoscore	0.78(0.52 - 0.83)	0.66(0.51-0.93)	0.57(0.42-0.8)	0.32
Pre-Op LVEF (%)	58(57-63)	60(54-65)	57(56-59)	0.53
Past Medical History				
- History of Cancer	7(26%)	5(29%)	2(25%)	1
- COPD	6(22%)	4(24%)	2(25%)	1
- Hypertension	9(33%)	4(24%)	3(38%)	0.64
- Heart Disease	6(22%)	3(18%)	2(25%)	1
- Obesity	2(7%)	1(6%)	0(0%)	1
- PVD	5(19%)	2(12%)	1(13%)	1
Number of segments resected	5 (3-5)	5 (3-5)	4 (3-5)	0.63
Type of resection				
- Pneumonectomy	1(4%)	1(6%)	0(0%)	-
- Upper Lobectomy	16(59%)	11(65%)	4(50%)	-
- Lower Lobectomy	6(22%)	2(12%)	3(38%)	-
- Extended Upper Lobectomy	1(4%)	1(6%)	1(13%)	-
- Extended Lower Lobectomy	3(11%)	2(12%)	0(0%)	-
Pathology				

- Primary Lung Cancer	24(89%)	16(94%)	6(75%)	-
- Metastatic Malignancy	1(4%)	1(6%)	0(0%)	-
- Benign Disease	2(7%)	0(0%)	2(25%)	-
Critical Care Stay (hours)	47.23 (29.21-53.47)	47.15 (28.7-51.25)	53.13 (29.5-71.45)	0.37
Hospital Stay (days)	8(7-11)	8(7-10.5)	9(7.25-19.5)	0.44

BMI: Body Mass Index; FEV1: Forced Expiratory Volume in 1 second; PPO: Predicted Post Operative; FVC: Forced Vital Capacity; DLCO: Diffusion capacity of the lung for carbon monoxide; LVEF: Left Ventricular Ejection Fraction**;** COPD: Chronic Obstructive Pulmonary Disease; PVD: Peripheral Vascular Disease.

Table 2

Association between BNP and measures of functional deterioration.

Associations assessed via Pearson's or Spearman's correlation coefficients. Statistically significant results are highlighted in **bold.**

BNP	**6MWT two months Post-Op**		**MRC Scale two months Post-Op**	
	r	**p value**	**r**	**p value**
Pre-Op BNP	**-0.43**	**0.05**	0.24	0.25
POD1 BNP	-0.33	0.15	**0.57**	**0.01**
POD2 BNP	-0.01	0.38	0.33	0.11

Table 3

Association between predicted post-operative-lung function and measures of functional deterioration.

Associations assessed via Pearson's or Spearman's correlation coefficients. PPO, predicted post-operative; FEV_1, forced expiratory volume in 1 second; DLCO, diffusing capacity for carbon monoxide.

	6MWT two months Post-Op		MRC Scale two months Post-Op		Combined Functional Assessment two months Post-Op	
	r	**p value**	**r**	**p value**	**r**	**p value**
PPO FEV_1	0.09	0.7	-0.18	0.38	-0.12	0.57
PPO DLCO	-0.03	0.9	-0.27	0.19	0.26	0.21

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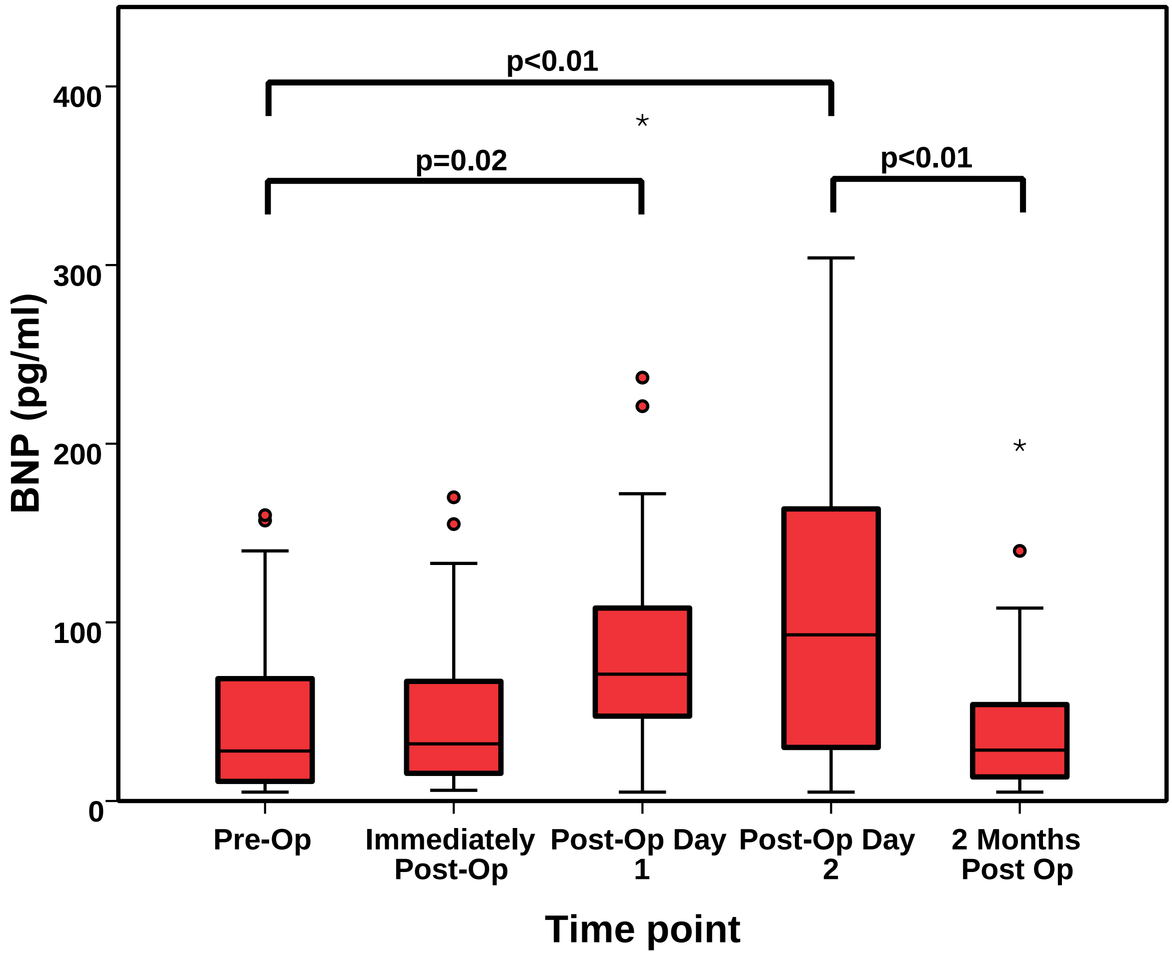
Figure 1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p=0.02
p<0.01
400
300
200
100
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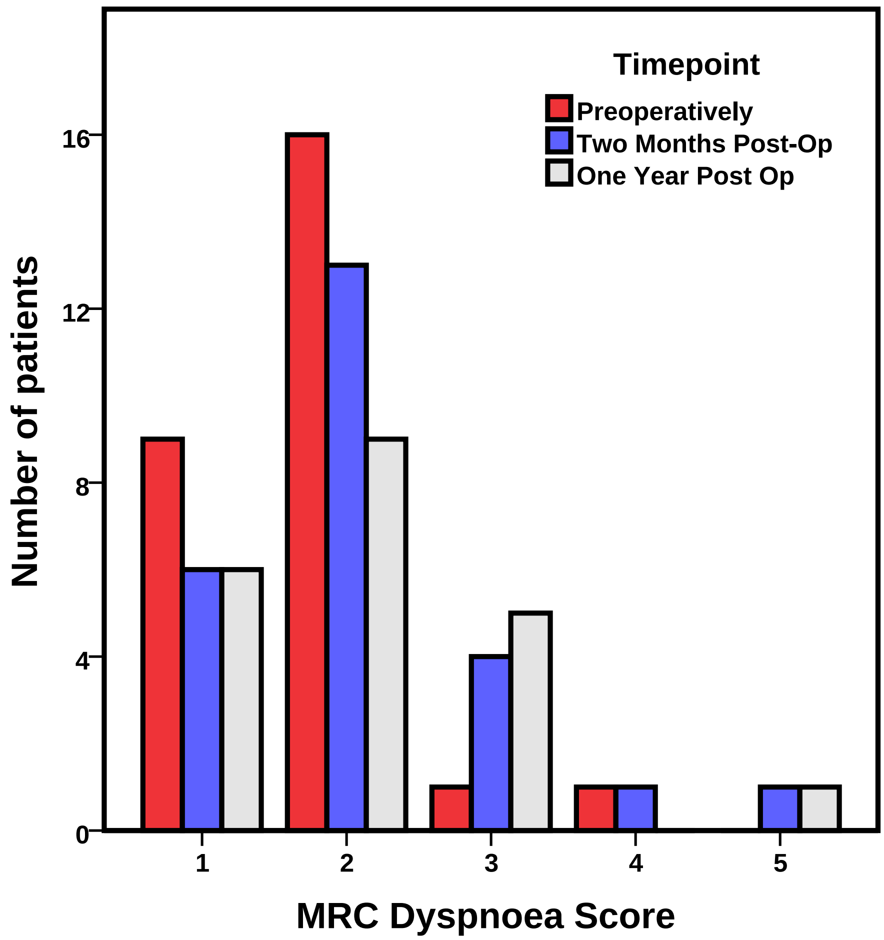
BNP (pg/ml)
Pre-Op
Immediately Post-Op
Post-Op Day 1
Post-Op Day 2
2 Months Post Op
Time point

Figure 2


Timepoint
Preoperatively
Two Months Post-Op
One Year Post Op
Number of patients
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4
8
12
16
1
2
3
4
5
MRC Dyspnoea Score

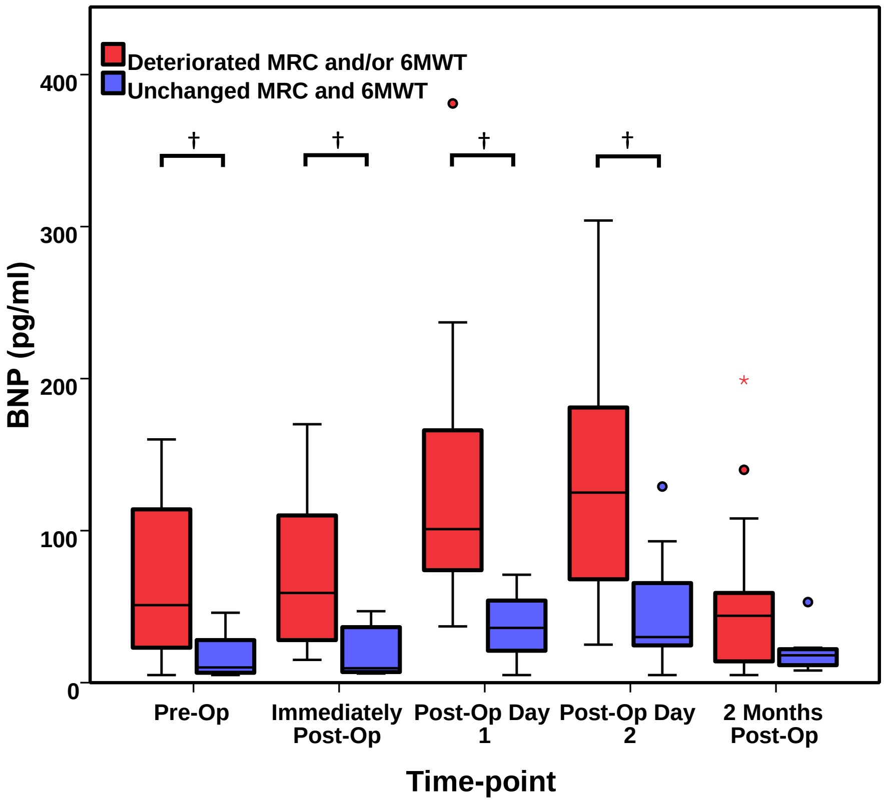

Deteriorated MRC and/or 6MWT
Unchanged MRC and 6MWT
†
†
†
†
*
400
300
200
100
0
BNP (pg/ml)
Pre-Op
Immediately Post-Op
Post-Op Day 1
Post-Op Day 2
2 Months Post-Op
Time-point

Figure 4 Click here to access/download;Figure;ICVTS Figure 4.pdf

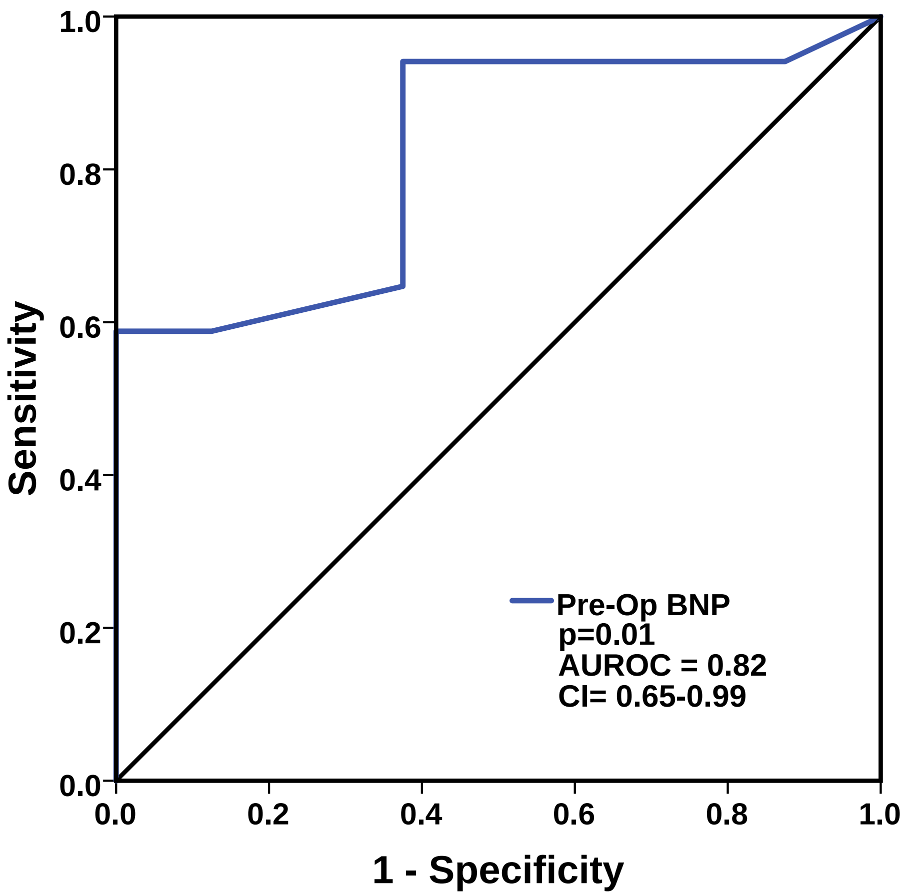
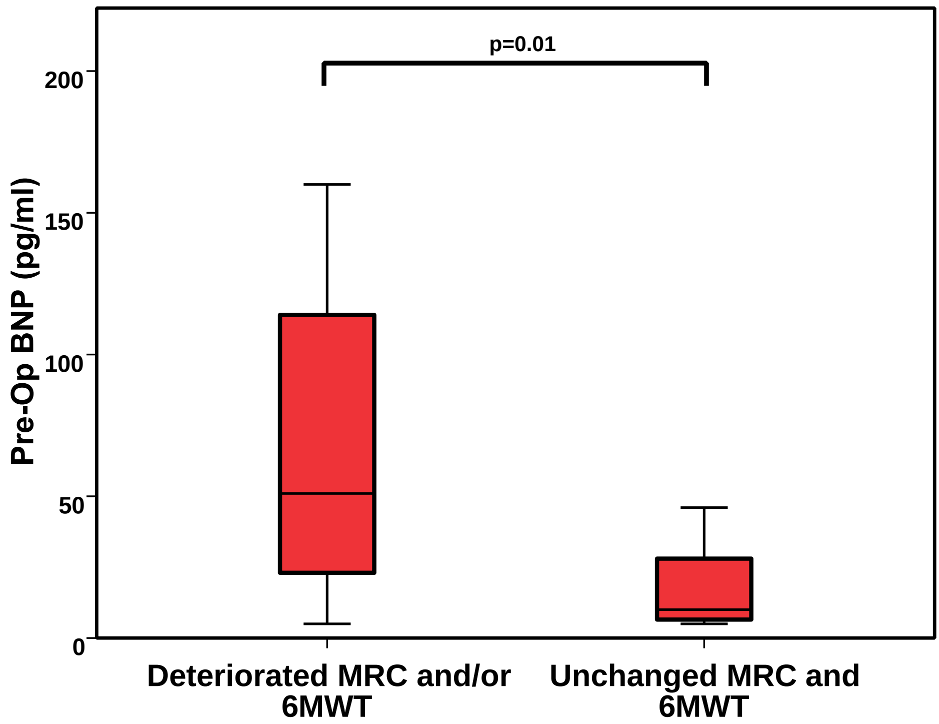


Figure 5a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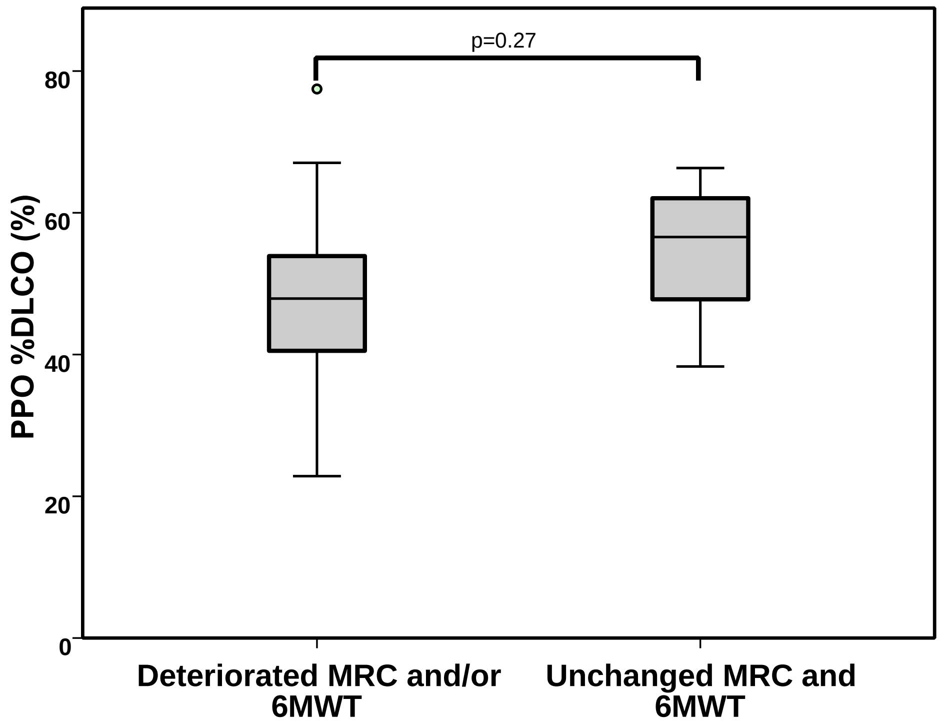
200
150
100
50
0
Pre-Op BNP (pg/ml)
Deteriorated MRC and/or 6MWT
Unchanged MRC and 6MWT

Figure 5b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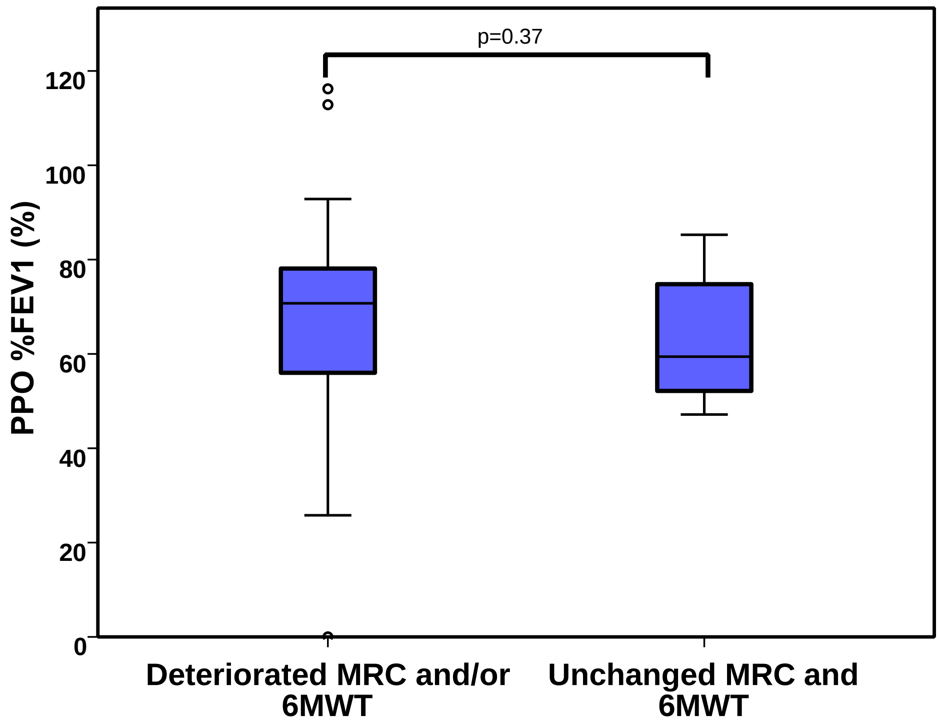
80
60
40
20
0
PPO %DLCO (%)
Deteriorated MRC and/or 6MWT
Unchanged MRC and 6MWT

Figure 5c



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PPO %FEV1 (%)
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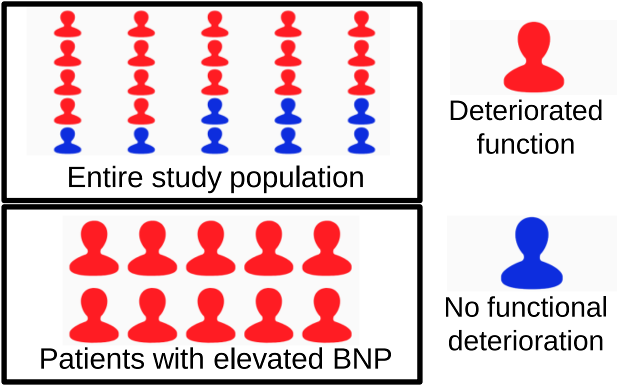
100
80
60
40
20
0
Deteriorated MRC and/or 6MWT
Unchanged MRC and 6MWT

BNP predicts deterioration in functional capacity following lung resection



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