The Association of Baseline N-terminal Pro-B-type Natriuretic Peptide With Short and Long-term Prognosis Following Percutaneous Coronary Intervention in Non-ST Segment Elevation Acute Coronary Syndrome With Multivessel Coronary Artery Disease: a Retrospective Cohort Study

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Abstract

Background: Although several studies have shown that N-terminal pro-B-type natriuretic peptide (NT-proBNP) is strongly correlated with coronary artery lesion complexity as well as prognosis in non-ST segment elevation acute coronary syndrome (NSTE-ACS) patients, the prognostic value of NT-proBNP in patients with NSTE-ACS and multivessel coronary artery disease undergoing PCI remains unclear. This study aimed to reveal the relationship between NT-proBNP levels and prognosis among NSTE-ACS patients with multivessel coronary artery disease undergoing successfully percutaneous coronary intervention.

Methods: We consecutively enrolled 1022 patients from January 2010 to December 2014. Patients with a diagnosis of NSTE-ACS with multivessel coronary artery disease and NT-proBNP levels were included. The primary outcome was in-hospital all-cause death. The 3-year follow-up all-cause death was also ascertained.

Results: A total of 12 (1.2%) deaths occurred during hospitalization. The 4th quartile group of NT-proBNP (>1287 pg/ml) had the highest rate of in-hospital all-cause death (4.3%) (P<0.001). Logistic analyses revealed that increasing NT-proBNP was robustly associated with a higher risk of in-hospital all-cause death (adjusted OR: 2.86, 95% CI=1.16-7.03, P=0.022). NT-proBNP had a good ability to predict in-hospital all-cause death (AUC=0.888, 95% CI=0.834-0.941, P<0.001; cutoff: 1568pg/ml). The cumulative event analyses exhibited a statistically significant relationship between a higher level of NT-proBNP and a higher rate of the long-term all-cause death compared with a lower level of NT-proBNP (P< 0.0001).

Conclusions: Increasing NT-proBNP is significant associated with a high risk of in-hospital and long-term all-cause death in NSTE-ACS patients with multivessel coronary artery disease who received percutaneous coronary intervention. NT-proBNP > 1568pg/ml was associated with all-cause, in-hospital death.

Background

Individuals with multivessel coronary artery disease (MCAD) account for approximately 40–70% of patients with NSTE-ACS undergoing coronary angiography (1–3). Currently, percutaneous coronary intervention (PCI) is considered one option for the treatment of MCAD and left main (LM) disease because of its higher procedural success rates and comparable benefits(4–7). However, the incidence of cardiovascular morbidity and mortality after PCI remains high in this population(8, 9). Thus, a biomarker associated with prognosis is useful for identifying high-risk patients.

Several studies have shown that plasma levels of natriuretic peptides such as B-type natriuretic peptide (BNP) and NT-proBNP have a robust relationship with prognosis in patients with NSTE-ACS(10–12). Furthermore, previous studies have demonstrated that increased NT-proBNP levels in patients with NSTE-ACS are independently associated with the presence of more complex and severe coronary lesions(13–15). However, the prognostic value of NT-proBNP in patients with NSTE-ACS and MCAD undergoing PCI
remains unclear. The current study investigated the relationship between NT-proBNP and short-term prognosis in patients with NSTE-ACS and MCAD.

**Methods**

**Study Design**

The cohort was detailed in our previous research(16), and was designed to detect the association between parenteral anticoagulation therapy and clinical outcomes in patients with NSTE-ACS undergoing PCI. In brief, 8197 patients with NSTE-ACS undergoing PCI were enrolled from 5 centres from January 1, 2010 to December 31, 2014. Patients aged 18 years or older who were diagnosed with MCAD, and whose NT-proBNP level was determined on the first day of admission were included, cardiac arrest with return of circulation were included also. MCAD was defined as lesions with $\geq 50\%$ diameter stenosis in the LM artery or $\geq 2$ major coronary vessels with $\geq 50\%$ stenosis. The exclusion criteria were as follows: pregnancy and missing baseline NT-proBNP. They were divided into 4 groups depending on the quartiles of NT-proBNP. Ultrasonic cardiography was conducted after admission, using Simpson's biplane method to calculate the left ventricular ejection fraction (LVEF). The estimated glomerular filtration (eGFR) rate was calculated using the Modification of Diet in Renal Disease equation based on Chinese patients(17). The study protocol was approved by the central ethics committee of Guangdong Provincial People's Hospital, Guangzhou, China. The study was conducted in accordance with the Declaration of Helsinki.

**Data Collection**

The data were obtained in the first interview when the patient was admitted to the hospital. Baseline characteristic data were recorded by the responsible nurse or doctor; the baseline characteristics included demographic data and medical history. The procedural information originated from the catheterization report. All laboratory examinations were conducted during the first 24 hours after admission and before the procedure for all patients, and NT-proBNP was measured using an electrochemiluminescence immunoassay (Roche Diagnostics, Germany). All patients received the drug eluting stent. All interventional strategies were performed at the discretion of the heart team. In-hospital and follow-up assessments were performed by clinic visits or telephone interviews from November 7, 2015 through December 30, 2016.

**Outcomes**

The primary outcome was in-hospital all-cause death. The secondary outcomes were all-cause death during the 3-year follow-up as well as in-hospital major adverse cardiovascular events (MACE), defined as a composite of all-cause death, myocardial infarction and stroke. The definitions of all clinical complications assessed during follow-up were identical to the original registry(16). Death was defined as all-cause deaths regardless cardiac or non-cardiac according to death records. Myocardial infarction was defined as classical symptoms accompanied by elevation of cardiac injury biomarker according to the third Universal Definition of Myocardial Infarction. Any stroke is defined as the presence of a new focal
neurologic deficit thought to be vascular in origin, with signs or symptoms lasting more than 24 hours. A clinical events committee evaluated all clinical outcomes independently.

**Statistical Analysis**

Statistical analysis was performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). Continuous variables are presented as the mean ± standard deviation. Categorical variables are presented as absolute and relative frequencies. Continuous variables were compared between groups using Student’s t-test (parametric variables). Multivariate regression analyses were carried out to evaluate the predictive value of NT-proBNP for different clinical outcomes, which was included as a continuous variable after logarithmic transformation. All the confounders included in the final model were either significant in the univariate analyses or clinical important factors. We included log NT-proBNP, Anaemia, Chronic heart failure, Chronic kidney disease, NSTEMI, LVEF and age to the final model of death analysis, and included log NT-proBNP, Anaemia, Chronic heart failure, chronic kidney disease, NSTEMI, LVEF, age, Diabetes, Myocardial infarction and operation time to the final model of MACE analysis. Receiver-operating characteristic (ROC) curves were used to assess the ability that NT-proBNP discriminates between patients who died and patients who survived during hospitalization. We also used the Youden index to determine the best cutoff of NT-proBNP for predicting all-cause death, and we expected to use this level for further analyses. Cumulative event analyses were performed to compare the long-term prognosis between patients who were divided by the best cutoff level of NT-proBNP. All P values <0.05 were considered statistically significant.

**Results**

**Baseline Characteristic**

Of the 1022 patients who met the final criteria, 118 (11.5%) patients were female, and the average age was 65.8 (standard difference:10.5, ranged from 33 to 90). All were Han nationality. We identified 585 patients older than 65 in total. Variables were compared by baseline NT-proBNP quartile values. The baseline characteristics are presented in Table 1. Patients with high NT-proBNP were older, with lower body weight, had higher heart rates and more frequently had NSTEMI, chronic kidney disease, anaemia diabetes and stroke than low NT-proBNP patients. Chronic heart failure, prior MI, prior PCI and lower LVEF were more frequent in higher NT-proBNP quartiles. Furthermore, most of the treatment variables exhibited insignificant differences among the different NT-proBNP groups except for the time to procedure.
| Baseline characteristics | NT-proBNP (Q1 < 96 pg/ml) N = 257 | NT-proBNP (96 pg/ml < Q2 < 328 pg/ml) N = 255 | NT-proBNP (328 pg/ml < Q3 < 1287 pg/ml) N = 255 | NT-proBNP (Q4 > 1287 pg/ml) N = 255 | P value |
|--------------------------|-------------------------------------|-----------------------------------------------|-----------------------------------------------|-------------------------------------|---------|
| **General characteristics** |                                      |                                               |                                               |                                     |         |
| Mean age (SD), y          | 61.02 ± 10.11                       | 65.05 ± 10.25                                | 66.94 ± 10.45                                | 70.09 ± 8.90                       | < 0.001 |
| Age ≥ 65y, No. (%)        | 103(40.1)                           | 134(52.5)                                    | 158(62.0)                                    | 190(74.5)                          | < 0.001 |
| Female, No. (%)           | 61(23.7)                            | 53(20.8)                                     | 72(28.2)                                     | 76(29.8)                           | 0.076   |
| Weight, mean (SD), kg     | 68.29 ± 11.59                       | 67.47 ± 12.29                                | 65.91 ± 13.49                                | 62.28 ± 13.89                      | < 0.001 |
| Heart rate, mean (SD), bpm| 74.38 ± 10.27                       | 72.79 ± 10.77                                | 75.15 ± 12.69                                | 80.66 ± 16.02                      | < 0.001 |
| LVEF, mean (SD), %        | 67.60 ± 5.09                        | 65.21 ± 7.55                                 | 59.59 ± 11.10                                | 49.85 ± 14.66                      | < 0.001 |
| Anaemia, No. (%)          | 49(19.1)                            | 65(25.5)                                     | 98(38.4)                                     | 148(58.0)                          | < 0.001 |
| Serum creatinine level, mean (SD), µmol/dL | 0.93 ± 0.25                      | 0.99 ± 0.26                                  | 1.10 ± 0.48                                  | 1.60 ± 1.60                        | < 0.001 |
| **Disease type, No. (%)** |                                      |                                               |                                               |                                     |         |
| NSTEMI                    | 44(17.1)                            | 64(25.3)                                     | 83(32.5)                                     | 126(49.4)                          | < 0.001 |
| Unstable angina           | 213(82.9)                           | 189(74.7)                                    | 172(67.5)                                    | 129(50.6)                          | NA      |
| **eGFR, mL/min/1.73 m²**  |                                      |                                               |                                               |                                     |         |
| Mean (SD),                | 88.77 ± 23.41                       | 82.22 ± 23.63                                | 76.04 ± 27.49                                | 59.53 ± 25.68                      | < 0.001 |
| ≤ 60 mL/min/1.73 m², No. (%) | 27(10.5)                           | 42(16.5)                                     | 68(26.7)                                     | 133(52.2)                          | < 0.001 |

Abbreviations: NT-proBNP, N-terminal pro-B-type natriuretic peptide; Q, quartile; NSTEMI, non–ST-segment elevation myocardial infarction; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; NA, not applicable; LM, left main; LAD, left anterior descending; LCX, left circumflex; RCA, right coronary artery.
| Baseline characteristics | NT-proBNP (Q1 < 96 pg/ml) N = 257 | NT-proBNP (96 pg/ml < Q2 < 328 pg/ml) N = 255 | NT-proBNP (328 pg/ml < Q3 < 1287 pg/ml) N = 255 | NT-proBNP (Q4 > 1287 pg/ml) N = 255 | P value |
|--------------------------|----------------------------------|---------------------------------|---------------------------------|----------------------------------|---------|
| Current smoker           | 74(28.8)                         | 71(27.8)                        | 80(31.4)                        | 69(27.1)                         | 0.726   |
| Hypertension             | 169(65.8)                        | 183(71.8)                       | 171(67.1)                       | 183(71.8)                        | 0.316   |
| Diabetes                 | 89(34.6)                         | 80(31.4)                        | 92(36.1)                        | 120(47.1)                        | 0.002   |
| Cardiac arrest           | 0(0.0)                           | 0(0.0)                          | 1(0.4)                          | 1(0.4)                           | 0.570   |
| Chronic heart failure    | 18(7.0)                          | 21(8.2)                         | 46(18.0)                        | 107(42.0)                        | < 0.001 |
| Myocardial infarction    | 23(8.9)                          | 28(11.0)                        | 67(26.3)                        | 74(29.0)                         | < 0.001 |
| Percutaneous coronary intervention | 64(24.9) | 42(16.5) | 35(13.7) | 49(19.2) | 0.009   |
| Coronary artery bypass surgery | 2(0.8)   | 3(1.2)  | 2(0.8)  | 4(1.6)  | 0.796   |
| Stroke                   | 8(3.1)                           | 23(9.0)                         | 32(12.5)                        | 35(13.7)                         | < 0.001 |

**Treated lesion, No. (%)**

|                | LM     | LAD    | LCX    | RCA    |
|----------------|--------|--------|--------|--------|
|                | 25(9.7)| 161(62.6)| 92(35.8)| 120(46.7)|
|                | 31(12.2)| 170(66.9)| 117(46.1)| 120(47.2)|
|                | 35(13.8)| 168(66.4)| 121(47.8)| 102(40.3)|
|                | 36(14.2)| 163(64.4)| 99(39.1)| 101(39.9)|
| P value        | 0.402  | 0.730  | 0.017  | 0.181  |

**Drug eluting stent type, No. (%)**

|                | First generation | Second generation |
|----------------|------------------|-------------------|
|                | 122(53.0)        | 108(47.0)         |
|                | 131(60.4)        | 86(39.6)          |
|                | 132(62.6)        | 79(37.4)          |
|                | 144(74.6)        | 49(25.4)          |
| P value        | < 0.001          | NA                |

Abbreviations: NT-proBNP, N-terminal pro-B-type natriuretic peptide; Q, quartile; NSTEMI, non–ST-segment elevation myocardial infarction; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; NA, not applicable; LM, left main; LAD, left anterior descending; LCX, left circumflex; RCA, right coronary artery.
In-hospital Outcomes

A total of 12 (1.2%) all-cause deaths occurred in the hospital. Patients with NT-proBNP > 1287 pg/ml had the highest all-cause death (4.3% highest vs 0.0% lowest, p < 0.001, Table 2). Patients in the highest quartile of NT-proBNP had the highest in-hospital MACE (6.3% highest vs 0.8% lowest, p < 0.001), while there were no significant difference in in-hospital stroke or myocardial infarction between the different groups (Table 2). Higher NT-proBNP was associated with higher a risk of in-hospital all-cause death (univariate: OR: 3.06, 95% CI: 1.77–5.28, P < 0.001; multivariate: adjusted OR: 2.86, 95% CI: 1.16–7.03, P = 0.022) (Table 3). Additionally, there was also a significant relationship between increasing NT-proBNP and a higher risk of in-hospital MACE (adjusted OR: 2.09, 95% CI: 1.35–3.23, P = 0.001) after adjusting for confounders. The discrimination analyses showed that NT-proBNP is sufficient in predicting in-hospital all-cause death (Fig. 1). The area under the curve of the ROC is 0.888 (95% CI: 0.834–0.941, P < 0.001). The best cutoff of the NT-proBNP for predicting in-hospital death was 1568 pg/ml (sensitivity: 91.7%, specificity: 78.5%).

Table 2
Clinical outcomes of different baseline NT-proBNP levels

| In-hospital outcomes | NT-proBNP (Q1 < 96 pg/ml) N = 257 | NT-proBNP (96 pg/ml < Q2 < 328 pg/ml) N = 255 | NT-proBNP (328 pg/ml < Q3 < 1287 pg/ml) N = 255 | NT-proBNP (Q4 > 1287 pg/ml) N = 255 | P value |
|----------------------|-----------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------|---------|
| All-cause death      | 0(0.0%)                           | 0(0.0%)                                       | 1(0.4%)                                       | 11(4.3%)                          | < 0.001 |
| stroke               | 0(0.0%)                           | 0(0.0%)                                       | 2(0.8%)                                       | 3(1.2%)                           | 0.142   |
| Myocardial infarction| 2(0.8%)                           | 0(0.0%)                                       | 2(0.8%)                                       | 3(1.2%)                           | 0.434   |
| MACE                 | 2(0.8%)                           | 0(0.0%)                                       | 4(1.6%)                                       | 16(6.3%)                          | < 0.001 |

Abbreviation: MACE: major adverse cardiovascular events; NT-proBNP: N-terminal pro-B-type natriuretic peptide
|                      | Univariate analysis | Multivariate analysis |
|----------------------|---------------------|-----------------------|
|                      | OR      | 95% C.I. | P     | OR      | 95% C.I. | P     |
| All-cause death      |         |         |       |         |         |       |
| log NT-proBNP        | 3.06    | 1.77 ~ 5.28 | < 0.001 | 2.86    | 1.16 ~ 7.03 | 0.022 |
| Anaemia              | 9.43    | 2.05 ~ 43.27 | 0.004 | 4.63    | 0.49 ~ 43.41 | 0.179 |
| Chronic heart failure| 3.14    | 0.99 ~ 10.01 | 0.053 | 0.88    | 0.20 ~ 3.93 | 0.865 |
| Chronic kidney disease| 3.98  | 1.25 ~ 12.64 | 0.019 | 1.96    | 0.33 ~ 11.5 | 0.458 |
| NSTEMI               | 3.15    | 0.99 ~ 10.01 | 0.051 | 3.07    | 0.56 ~ 16.90 | 0.198 |
| LVEF                 | 0.96    | 0.92 ~ 1.00 | 0.037 | 1.00    | 0.95 ~ 1.05 | 0.990 |
| age                  | 1.04    | 0.98 ~ 1.11 | 0.170 | 2.86    | 1.16 ~ 7.03 | 0.436 |
| MACE                 |         |         |       |         |         |       |
| log NT-proBNP        | 1.98    | 1.47 ~ 2.68 | < 0.001 | 2.09    | 1.35 ~ 3.23 | 0.001 |
| Anaemia              | 2.72    | 1.15 ~ 6.42 | 0.023 | 1.09    | 0.37 ~ 3.18 | 0.875 |
| Chronic heart failure| 1.28    | 0.47 ~ 3.51 | 0.633 | 0.39    | 0.11 ~ 1.36 | 0.139 |
| Chronic kidney disease| 2.86  | 1.23 ~ 6.68 | 0.015 | 1.73    | 0.58 ~ 5.19 | 0.326 |
| NSTEMI               | 1.27    | 0.53 ~ 3.07 | 0.589 | 0.74    | 0.26 ~ 2.11 | 0.571 |
| LVEF                 | 0.98    | 0.95 ~ 1.01 | 0.130 | 1.01    | 0.97 ~ 1.05 | 0.617 |
| age                  | 1.04    | 0.99 ~ 1.08 | 0.096 | 1.00    | 0.95 ~ 1.05 | 0.940 |

Abbreviations: NT-proBNP, N-terminal pro-B-type natriuretic peptide; NSTEMI, non–ST-segment elevation myocardial infarction; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular events.
|                          | Univariate analysis | Multivariate analysis |
|--------------------------|---------------------|-----------------------|
|                          | OR  | 95% C.I. |  P   | OR  | 95% C.I. |  P   |
| Diabetes                 | 1.41| 0.60 ~ 3.30 | 0.425| 0.92| 0.34 ~ 2.51 | 0.868|
| Myocardial infarction    | 1.64| 0.63 ~ 4.25 | 0.308| 0.81| 0.25 ~ 2.70 | 0.736|
| operation time 24–72 h (Reference is 24 h) | 0.93| 0.33 ~ 2.62 | 0.884| 0.82| 0.23 ~ 2.90 | 0.758|
| operation time > 72 h (Reference is 24 h) | 1.46| 0.54 ~ 3.98 | 0.456| 1.62| 0.52 ~ 5.03 | 0.406|

Abbreviations: NT-proBNP, N-terminal pro-B-type natriuretic peptide; NSTEMI, non–ST-segment elevation myocardial infarction; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular events.

**Long-term Outcomes**

All the 1022 patients completed the 3-year follow-up. Death was recorded in 121 (11.8%) patients. The long-term all-cause death was compared between patients with baseline NT-proBNP ≤ 1568 pg/ml and patients with baseline NT-proBNP > 1568 pg/ml. The patients with the higher level of NT-proBNP had a significant higher long-term event rate compared with the patients with the lower level of NT-proBNP (P < 0.0001) (Fig. 2).

**Discussion**

This study finds that patients who presented with the NT-proBNP level more than 1287 pg/ml had the highest rate of both in-hospital all-cause death and MACE. In addition, we determined a cutoff of 1568 pg/ml as the best value to evaluate in-hospital death. During the 3-year follow-up, the patients with higher levels of NT-proBNP (more than 1568 pg/ml) had a higher frequency of all-cause death.

The current study showed the relationship between increased NT-proBNP levels and adverse outcomes in NSTE-ACS patients with MCAD. However, the pathophysiological mechanism behind the association between ischaemia and NT-proBNP elevation is still unknown. Previous studies have reported that myocardial ischaemia could cause transient and permanent increase in wall stress, myocardial tension, and then induce BNP neurohormone release from the ventricular myocardium(18–20). Furthermore, several studies (20–22) have also shown that ventricular BNP gene expression is upregulated by myocardial hypoxia, and provoking an increase in plasma concentrations of NT-proBNP. In addition, the level of NT-proBNP is strongly related to cardiac function and can be used for the detection of left ventricular (LV) systolic and diastolic dysfunction(23, 24). An immediate increase in plasma BNP levels occurs after myocardial ischaemia(9, 25) and before the elevation of traditional myocardial necrosis
markers. Meanwhile, the magnitude of BNP level increase is proportional to the severity of myocardial ischaemia(26). In this study, patients with NT-proBNP levels greater than 1287 pg/ml presented with the highest level of LV dysfunction (the mean LVEF was 49.85 ± 14.66). Therefore, it could be speculated that higher levels of NT-proBNP at admission are the result of both myocardial ischaemia before the index event and the index event itself. Another mechanism for NT-proBNP elevation in patients with acute coronary syndromes is the permanently elevated levels of NT-proBNP reflecting ventricular dysfunction or heart failure before the index event. It is interesting that patients in the group of NT-proBNP > 1287 pg/ml were near-normal LVEF (49.85%±14.66%), it could be surmised that these patients with form of diastolic dysfunction, as previous study found that NT-proBNP plasma levels were increased in patients with diastolic dysfunction(27).

Laurenz Jaberg et al. demonstrated that plasma NT-proBNP is a strong predictor of outcome in patients undergoing acute LM coronary artery stenting; however, this was a retrospective study, and NT-proBNP was measured only in 71 ACS patients with LM disease at hospital admission(11). Our study extended this interaction to patients with NSTE-ACS and MCAD, another population at high risk of ischaemia. MCAD predisposes to a more severe and extensive myocardial ischaemia, which results in higher levels of NT-proBNP.

Nevertheless, NT-proBNP still exhibited a robust association with death after adjusted LVEF in the current study. Previous studies have demonstrated that the association between NT-proBNP and death was not linked to LVEF(28, 29). Furthermore, previous studies have demonstrated that the level of NT-proBNP is associated not only with myocardial ischaemia in coronary heart disease, but also with all kinds of cardiac pathological conditions, such as the activation of the renin-angiotensin-aldosterone system(30). Previous studies have shown that tissue hypoxia induces the release of BNP in the absence of LV dysfunction(31). In this population, patients with higher levels of NT-proBNP at admission have a greater extent of myocardial ischaemia because of more severe coronary lesions and express subclinical LV dysfunction, possibly consequent to the effects of chronic repetitive ischaemia on the myocardium(32, 33). All these mechanisms could result in poor prognosis and an increased risk of death. However, the exact mechanism underlying the connection between NT-proBNP and death needs to be studied further.

Limitations

The current study still has some limitations. Firstly, although great efforts were taken, we still could not adjust for all the potential confounders because of the retrospective study design. And the impact of treatment changes over time cannot be determined. Secondly, we could not determine the exact cause of death due to an unavailability of first-hand clinical documents, which is the reason why it is difficult for us to determine the causal relationship between death and increasing NT-proBNP. Thirdly, because the persistent monitoring of in-hospital NT-proBNP was deficient, we could not determine a relationship between NT-proBNP level changes and prognosis. Detailed studies are warranted.

Conclusion
A high level of NT-proBNP at admission is associated with a higher risk of in-hospital all-cause death among NSTE-ACS patients with MCAD who received PCI. NT-proBNP more than 1568 pg/ml is a reasonable cutoff value that is associated with in-hospital and long-term all-cause death.

**List Of Abbreviations**

BNP: B-type natriuretic peptide; eGFR: estimated glomerular filtration; LM: left main; LV: left ventricular; LVEF: left ventricular ejection fraction; MACE: major adverse cardiovascular events; MCAD: multivessel coronary artery disease; NT-proBNP: N-terminal pro-B-type natriuretic peptide; NSTE-ACS: non-ST segment elevation acute coronary syndrome; PCI: percutaneous coronary intervention; ROC: Receiver-operating characteristic;

**Declarations**

**Ethics approval and consent to participate**

The study protocol was approved by the central ethics committee of the Guangdong General Hospital, Guangzhou, China. [No. GDREC201610H(R1)] The requirement for informed consent was waived because it is a retrospective observational study and patient records and information were anonymized and de-identified prior to analysis.

**Consent for publication**

This manuscript does not include any individual person's data.

**Availability of data and materials**

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

**Competing interests**

The authors declare that they have no competing interests.

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**Authors’ contributions**
HW, JL and CY: Methodology, Project administration, CP and DC: Formal analysis and Software, FH, ZL, GW, JL and WX: Data curation, Resources, HW, CP and LY: Writing- Original draft preparation. LJ, LW and GZ: Visualization, Investigation. CJ and TN: Supervision, Validation, HP: Conceptualization, Funding acquisition and Writing- Reviewing and Editing. All authors have read and approved the manuscript. This manuscript has not been published or presented elsewhere in part or in entirety and is not under consideration by another journal.

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Figures
Figure 2

Cumulative event analysis during follow-up between patients with high and low levels of NT-pro BNP (cutoff: 1568 pg/ml).