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Original Article

The correlation of the peripheral blood NT-proBNP and NF-κB expression levels with the myocardial infarct area and the post-treatment no-reflow in acute myocardial infarction patients

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Abstract: Objective: To explore the correlation of the peripheral blood NT-proBNP and NF-κB p65 expression levels in the peripheral blood with the myocardial infarct areas on the admission and post-treatment no-reflow of acute myocardial infarction patients. Methods: A total of 124 acute myocardial infarction patients treated in our hospital were placed in an acute myocardial infarction group, 115 patients with stable coronary heart disease were placed in a coronary heart disease group, and 121 healthy people undergoing routine physical examinations were placed in a healthy examination group. After the treatment, the myocardial infarction patients were divided into grade I, grade II, grade III, and grade IV groups according to their Killip heart function classifications. The patients were divided into reflow (thrombolysis in myocardial infarction (TIMI) > grade 2) and no-reflow (TIMI ≤ grade 2) groups according to their flow grades, and into single branch, double branch, and multi-branch groups according to each patient's number of diseased coronary vessels. The Wagner scale scores were used to estimate the infarct areas. All the patients were divided into small area, medium area, and large area groups according to the score results or into good prognosis and poor prognosis groups according to the presence or absence of complications. The amino-terminal pro-brain natriuretic peptide (NT-proBNP) and the nuclear factor-kappa B p65 (NF-κB p65) expression levels in the peripheral blood among the groups were compared. Results: The NT-proBNP and NF-κB p65 expression levels in the peripheral blood were significantly lower in the physical examination and coronary heart disease groups than they were in the acute myocardial infarction group (P<0.001) and were the lowest in the physical examination group (P<0.05). The expression levels were the lowest in the grade I group according to their Killip heart function classification (P<0.001) and increased gradually in each of the grade I to IV groups (all P<0.001). The expression levels were lowest in the single branch group and highest in the multi-branch group (P<0.001). The expression levels were lower in the no-reflow group than they were in the reflow group (P<0.001). The expression levels increased in the large area group compared with the small area and medium area groups (P<0.001). The expression levels were higher in the poor prognosis group than in the good prognosis group (P<0.001). Conclusion: Patients with high peripheral blood NT-proBNP and NF-κB expression levels had increased myocardial infarct areas. The peripheral blood NT-proBNP and NF-κB levels increased in the patients with post-treatment reflow. Therefore, the NT-proBNP and NF-κB expression levels can be used as important indicators for predicting the severity and prognoses of acute myocardial infarction patients.

Keywords: Acute myocardial infarction, NF-κB, reflow, NT-proBNP, infarct area

Introduction

Acute myocardial infarction (AMI) is a common cardiovascular and cerebrovascular disease [1]. Its clinical manifestations include chest pain, which generally scatters to the left shoulder and the back and lasts for about half an hour. Moreover, AMI patients can also be agitated and restless and suffer from hypotension and angina [2]. The main clinical treatment methods for AMI include thrombolysis, medication, and bypass surgery [3, 4]. Amino-terminal pro-brain natriuretic peptide (NT-proBNP), a commonly used biomarker in clinical practice, is able to reflect the cardiac abnormalities. NT-proBNP has a peptide chain length of 76

peptides, no biological activity, and single clearance pathway. Its expression in vivo has a significant correlation with age and increases with age [5]. Measuring one's NT-proBNP level is a commonly used clinical method for diagnosing cardiac insufficiency after myocardial infarction. Nuclear factor-kappa B (NF-κB) was first isolated from lymphocytes. NF-κB exists extensively in organisms and can control many biological processes, including inflammation and apoptosis [6]. NF-κB plays an important role in the inflammatory response and can promote the development of inflammation. A disorder of the NF-κB activation is able to drive pathogenesis [7]. In addition, NF-κB can regulate the expressions of factors in vivo in multiple cardiovascular and cerebrovascular diseases. High levels of NT-proBNP in the peripheral blood of patients suffering from AMI predicts a high risk of left ventricular dilation and left ventricular hypofunction and a high risk of long-term cardiovascular events. The expression levels of NT-proBNP and NF-κB in myocardial infarction and cerebral infarction were investigated in previous studies, and a significantly increased expression level of NF-κB in mice with myocardial infarction was found [8]. However, there are few studies on the correlation of NT-proBNP and NF-κB with myocardial infarct area and post-treatment no-reflow in AMI patients. Therefore, in this study, the correlation was explored by analyzing the expression levels of NT-proBNP and NF-κB p65 in patients with different infarct areas, flow grades, and prognoses.

Materials and methods

General data

A total of 124 AMI patients treated in our hospital from January 2018 to January 2020 were placed in the AMI group, 115 patients with stable coronary heart disease were placed in the coronary heart disease group, and 121 healthy people undergoing physical examinations were placed in the physical examination group. The ages and genders of the patients in the three groups were matched, and no significant differences were found. This study was approved by the Ethics Committee of our hospital.

For the heart function classification, after the treatment, the AMI patients were divided into grade I, grade II, grade III and grade IV groups according to their Killip heart function classifications, with 3, 64, 55, and 2 patients in each group [7].

After the treatment, all patients were divided according to their flow grades into reflow (thrombolysis in myocardial infarction (TIMI) > grade 2) and no-reflow (TIMI ≤ grade 2) groups, with 157 and 82 patients in each group.

According to each patient's number of diseased coronary vessels, the patients were divided into single branch, double branch, and multibranch groups, with 93, 87, and 59 patients in each group.

After the treatment, the Wagner scale scores were used to estimate of the patients' infarct areas [8]. According to the estimates, the patients were divided into small area, medium area, and large area groups (≤ 5 score, 6-9 scores, and ≥10 scores), with 89, 94, and 56 patients in each group.

The patients were followed up for 4 weeks after the treatment. They were divided into good prognosis and poor prognosis groups according to the presence or absence of complications such as severe arrhythmia, pump failure, and cardiogenic shock, with 66 and 58 patients in each group [9].

Inclusion and exclusion criteria

Inclusion criteria: The patients in the coronary heart disease group met the diagnostic criteria for stable coronary heart disease. The people in the physical examination group were healthy. The patients in the AMI group met the diagnostic criteria for AMI. The patients or their families signed the informed consent. All the enrolled patients were over 45 years old [10]. Exclusion criteria: Patients with mental disorders, patients with incomplete data, people with a history of heart disease diagnosed through physical examination.

Treatment methods

After their admission to the hospital, the AMI patients underwent conventional treatment like bed rest and oxygen inhalation. Then the optimal drugs and operation method were selected according to the severity of the illness and the location of the infarction. The emergen-

cy percutaneous transluminal coronary interventions (PCI) were performed first on the infarction related artery. Before the surgery, the patients chewed 300 mg of aspirin enteric-coated tablets (Bayer S.p.A) and 300 mg of clopidogrel hydrogen sulphate tablets (Sanofi (China) Investment Co., Ltd., China) and received coronary angiography to determine the locations of their diseased vessels. After the surgery, 4,000 U of low molecular weight heparin (Beijing Science Sun Pharmaceutical Co., Ltd., China) were routinely injected subcutaneously for 12 h for anticoagulation. The patients whose PCI treatment was unsuccessful or who could not undergo PCI for other reasons underwent thrombolytic therapy and cardiac load reducing, such as oxygen inhalation, absolute bed rest and avoiding mood swings, treatments that were beneficial to the patients' recoveries. Alteplase (Boehringer Ingelheim Pharmaceuticals, Germany, approval number: S 20110052) was used for the treatment, with a maximum dose of 100 mg/d. For the patients with a six to twelve-hour onset of symptoms, an initial dose of 10 mg alteplase was injected followed by 50 mg at 60 min later, and the remaining 40 mg were injected at a speed of 10 mg/30 min. For the patients whose onset of symptoms for <6 h, a first dose of 15 mg alteplase was injected followed by 50 mg 30 min later, and the remaining 35 mg were injected within 60 min.

The NT-proBNP expression levels were measured using ELISA

After their admission the patients underwent conventional treatment. After patients were stabilized, they fasted for 8 h overnight, and 4 mL peripheral blood was drawn at 6 am the next day (4 mL fasting peripheral blood was drawn on the same day in the coronary heart disease group and physical examination group). The blood was pipetted into Eppendorf tubes, shaken, and centrifuged for 15 min at 3,000 r/min. The supernatant was obtained. The NT-proBNP content in each group was determined using ELISA assays with an automatic biochemical analyzer (Jinan Tongxin Biological Technology Co., Ltd., China, model: BK-280). The NT-proBNP kit was purchased from the Shanghai Huzhen Industrial Co., Ltd., China. A microplate reader (Shanghai Huanxi Medical Device Co., Ltd., China, model: CA-2,000) was used to determine the optical density (OD) values at a wavelength of 450 nm. The serum was centrifuged for 30 min at 2,000 r/min, and the supernatant was obtained. If the deposition was observed in the above process, centrifugation was performed again. EDTA/citric acid (Zhongliao Biotechnology Co., Ltd., China) was added as an anticoagulant into the plasma and it was left to react for 15 min. The centrifugation was performed as above, and the supernatant was obtained. If the deposition was observed in the above process, the centrifugation was performed again. The operating steps were carried out in accordance with the instructions, and the experiment was performed three times. Then the OD value was measured at a wavelength of 450 nm.

Western blot

The monocytes in the human peripheral blood were isolated using density gradient centrifugation. The venous blood was mixed with 1× Hank's buffered salt solution (HBSS; Yocon Biotechnology Co., Ltd., China) at 1:1 (40 mL). The solution was put into a test tube of 50 mL. Then the solution was mixed with a cell separation liquid (1.077 g/mL, Lymphoprep, Norway) at a volume ratio of 2:1. Then centrifugation was performed for 30 min at 2,000 r/min (1,100 g/min) with the TDL-40L high speed centrifuge (Beckman Coulter Commercial Enterprise (China) Co., Ltd., China). The white mist layer in the middle was pipetted into new tubes. HBSS was added into each tube and mixed, with the volume of HBSS greater than 1 time the volume of the pipetted solution. Then centrifugation was performed for 8 min at 1,100 r/min. The supernatant was discarded. HBSS was added, and the cells were blown out with the pipette. Then the solution was pipetted into new tubes and centrifuged for 8 min at 1,000 r/min. The supernatant was discarded. The remaining solution was mixed, and a small amount of the solution was pipetted into the cell counting chamber for counting. Trypan blue (Beijing Biolab Technology Co., Ltd., China) staining was used to determine the cell activity. If the total number of cells was greater than 1×10^7 cells/mL and the activity was more than 95%, the sample was qualified. The remaining solution was pipetted with a pipette tip of 1 mL into labeled Eppendorf tubes and cryopreserved at -70°C.

Table 1. A comparison of the general patient data ($\bar{x} \pm sd$)

Factors	Acute myocardial infarction group (n=124)	Coronary heart disease group (n=115)	Physical examination group (n=121)	χ^2/F (t)	P
Gender				0.550	0.759
Male	71	70	71		
Female	53	45	50		
Previous medical history					
Diabetes	24	29		0.756	0.384
Hypertension	29	23		0.692	0.405
Angina	30	24		0.667	0.414
Others	41	39		0.050	0.823
Time from onset to admission (h)	8.04±3.56	7.67±3.84		0.773	0.440
BMI (kg/m^2)	23.05±3.53	22.97±3.61	22.34±3.48	1.461	0.233
Age (years)	55.3±5.1	55.1±5.1	55.3±5.8	1.972	0.141

Note: BMI: body mass index; BMI = weight (kg)/height (m)^2.

Table 2. Comparison of the NT-proBNP expression and the NF-κB p65 protein levels among the acute myocardial infarction group, the coronary heart disease group, and the physical examination group ($\bar{x} \pm sd$)

Group	n	NT-proBNP (pg/mL)	NF-κB p65
Acute myocardial infarction	124	1321.32±217.36	1.37±0.21
Coronary heart disease	115	976.47±175.14***	0.86±0.15***
Physical examination	121	214.65±43.82***,###	0.41±0.09***,###
F		1463.000	1126.000
P		<0.001	<0.001

Note: Compared with the acute myocardial infarction group, ***P<0.001; compared with the coronary heart disease group, ###P<0.001. NT-proBNP: amino-terminal pro-brain natriuretic peptide; NF-κB: nuclear factor-kappa B.

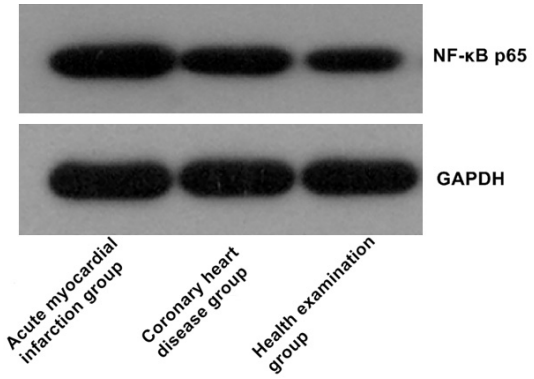

Figure 1. NF-κB p65 protein bands. NF-κB: nuclear factor-kappa B.

The cells were micro-centrifuged for 5 min. The flake precipitate was repeatedly washed with an iced lysis buffer (Cloud-Clone Diagnostic Reagents Institute, China) until the substance floating on the surface was removed (each centrifugation lasted for 5 min at 7,500 g/min). The nuclear flake precipitate was washed with a nuclear buffer (Cloud-Clone Diagnostic Reagents Institute, China) and suspended in distilled water with 50 μL 0.2 mol/L HCl and 0.2 mol/L H_2SO_4. The solution was stored at 4°C overnight, and the cell nucleuses were extracted. The remaining substance was micro-centrifuged for 10 min. The supernatant was mixed with 1 mL iced acetone (Tianjin Jinweier Chemical Co., Ltd., China) and stored at -20°C overnight. The sample was micro-centrifuged for 10 min, rinsed with acetone, dried, and diluted with distilled water. The supernatant sample containing the histone was quantified using the Bradford protein kit (Bio-Rad).

A certain volume of proteins was added into 2× DS gel loading buffers of the same volume. The protein concentration was quantified as 10 g/L. The protein was denaturalized by heating it at 100°C for 5 min and then it was stored at -20°C for subsequent use. The protein was separated electrophoretically in 12-15% polyacrylamide gel (YaoSanMei Environmental Protection Technology, China) at room temperature and transferred to polyvinylidene fluoride

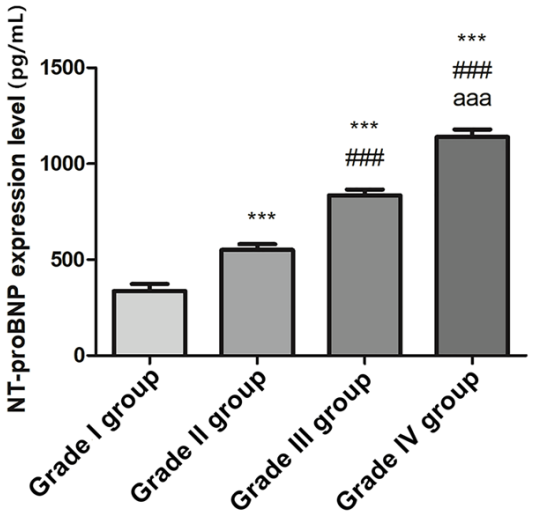

Figure 2. A comparison of the NT-proBNP expression levels among the grade I, grade II, grade III, and grade IV groups. Compared with the grade I group, ***P<0.001; compared with the grade II group, ###P<0.001; compared with the grade III group, aaaP<0.001. NT-proBNP: amino-terminal pro-brain natriuretic peptide.

(PVDF) membranes at a constant voltage of 9V (Nrf260 min, H0-130 min). The 5% skimmed milk powder (Shenzhen Lefu Biotechnology Co., Ltd., China) was then diluted with tris buffered saline tween (TTBS; TTC Fog International Limited, China) to seal the PVDF membranes at 4°C overnight (longer than 18 h). The primary antibodies were added separately using an eyedropper, i.e. GAPDH rabbit polyclonal antibody diluted 200 times with TTBS or NF-κB p65 rabbit polyclonal antibody (Zoonbio Biotechnology Co., Ltd., China) diluted 1000 times with TTBS. The membranes were washed three times with TTBS, for 10 min each time. Biotinidase-labeled goat anti-rabbit second antibody (BioVision Corporation) diluted 2,000 times using TTBS was added using an eyedropper and incubated for 1 h at 37°C. The membranes were washed three times with TTBS, for 15 min each time. The membranes were colored with DAB until clear protein bands were observed on the PVDF membranes. After the protein bands were scanned using a gel imaging system, the OD values were analyzed (UVP Bioimaging System). In a parallel operation, each sample was measured twice. The internal reference GAPDH was measured using the same methods to correct errors during the protein quantification and sample loading. The molecular weight and net OD value of the target band were analyzed using the gel image processing system to calculate the relative expression levels of the NF-κB p65 proteins.

Outcome measures

The main outcome measures included the NT-proBNP expression levels and the NF-κB p65 protein expression levels in the peripheral blood of the patients having myocardial infarctions with different flow grades, heart function classifications, and number of diseased coronary vessels. The secondary outcome measures included the NT-proBNP expression levels and the NF-κB p65 protein expression levels in the peripheral blood of the patients having myocardial infarction with different prognoses.

Statistical analysis

All the data were analyzed using SPSS 23.00 statistical software and expressed as the mean ± standard deviation ($\bar{x}$ ± sd). The comparisons among the groups were carried out using one-way analyses of variance and post hoc LSD t tests. The enumeration data were expressed as n/%, and the comparison between groups were done using chi-square tests. P<0.05 indicated a significant difference.

Results

Comparison of the general patient data

There were no significant differences in terms of gender, age, or the other general data among the three groups (P > 0.05, **Table 1**).

The comparisons of the NT-proBNP and NF-κB p65 expression levels among the acute myocardial infarction group, coronary heart disease group and physical examination group

The NT-proBNP and NF-κB p65 expression levels were highest in the acute myocardial infarction group, followed by the coronary heart disease group and the physical examination group (all P<0.001, **Table 2** and **Figure 1**).

Comparison of the NT-proBNP and NF-κB p65 expression levels among the grade I, grade II, grade III, and grade IV groups

The NT-proBNP expression levels in the grade I, grade II, grade III, and grade IV groups were 353.12±39.32, 561.95±46.92, 835.86±189.22 and 1135.42±242.75 pg/mL, respec-

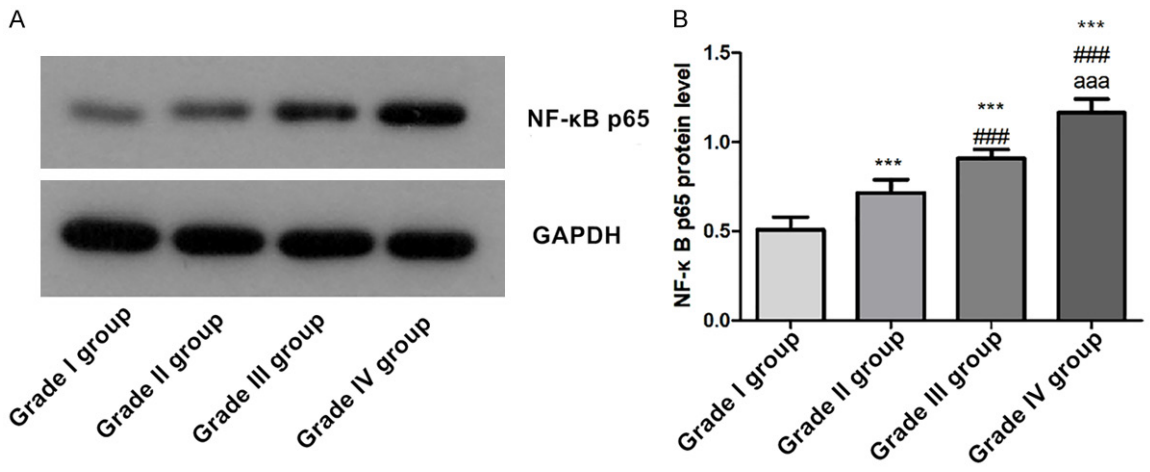

Figure 3. NF-κB p65 protein levels in grade I, grade II, grade III and grade IV groups. A: NF-κB p65 protein bands; B: Comparison of NF-κB p65 protein levels. Compared with the grade I group, ***P<0.001; compared with the grade II group, ###P<0.001; compared with the grade III group, aaaP<0.001. NF-κB: nuclear factor-kappa B.

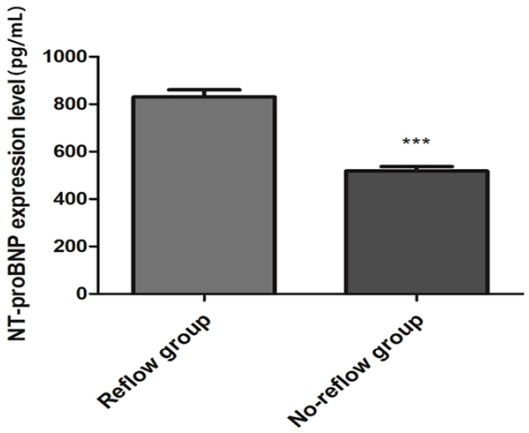

Figure 4. The NT-proBNP expression levels in the reflow group and in the no-reflow group (pg/mL). Compared with the reflow group, ***P<0.001. NT-proBNP: amino-terminal pro-brain natriuretic peptide.

tively, and the NF-κB p65 protein expression levels were 0.54±0.11, 0.76±0.12, 0.88±0.14 and 1.12±0.20, respectively. The NT-proBNP and NF-κB p65 expression levels were increased successively in each group from the grade I group to the grade IV group (all P<0.001, **Figures 2**, **3**).

Comparison of the NT-proBNP and NF-κB p65 expression levels in the patients with different TIMI flow grades

The NT-proBNP expression levels in the reflow and no-reflow groups were 835.75±101.87 and 524.13±84.13, respectively, and the NF-κB p65 protein expression levels were 0.79±0.12 and 0.53±0.09, respectively. The expression levels in the no-reflow group were lower than they were in the reflow group (P<0.001, **Figures 4**, **5**).

A comparison of the NT-proBNP and NF-κB p65 expression levels in the patients with different numbers of diseased coronary vessels

The NT-proBNP and NF-κB p65 expression levels were the highest in the multi-branch group, followed by the double branch group and then the single branch group (all P<0.001, **Table 3** and **Figures 6**, **7**).

A comparison of the NT-proBNP and NF-κB p65 expression levels in the patients with different infarct area sizes

The NT-proBNP expression levels in the small area, medium area, and large area groups were 513.87±68.99, 785.54±89.23, and 964.56±125.89 pg/mL, respectively, and the NF-κB p65 protein expression levels were 0.46±0.10, 0.66±0.13, and 0.75±0.14, respectively. The expression levels in the large area group were the highest, followed by the medium area group and then the small area group (all P<0.001, **Figures 8**, **9**).

A comparison of the NT-proBNP and NF-κB p65 expression levels in the patients with different prognoses

The NT-proBNP and NF-κB p65 expression levels in the poor prognosis group were significantly higher than they were in the good prognosis group (P<0.001, **Table 4**; **Figures 10**, **11**).

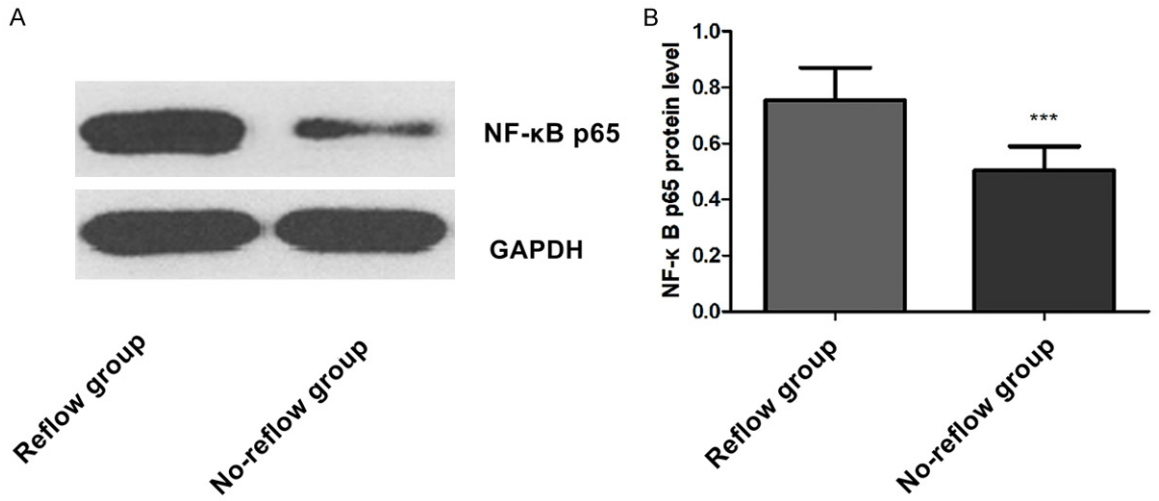

Figure 5. The NF-κB p65 protein levels in the reflow group and no-reflow group. A: NF-κB p65 protein bands. B: A comparison of the NF-κB p65 protein levels. Compared with the reflow group, ***P<0.001. NF-κB: nuclear factor-kappa B.

Table 3. The NT-proBNP and NF-κB p65 expression levels in patients with different numbers of coronary artery branches involved ($\bar{x}$ ± sd)

Number of coronary artery branches involved	n	NT-proBNP (pg/mL)	NF-κB p65
Single	93	843.13±97.75	0.64±0.08
Double	87	1034.33±112.43***,###	0.82±0.11***,###
Multiple	59	1223.08±153.32***,###	0.97±0.13***,###
F		290.300	284.800
P		<0.001	<0.001

Note: Compared with the single branch group, ***P<0.001; compared with the double branch group, ###P<0.001. NT-proBNP: amino-terminal pro-brain natriuretic peptide; NF-κB: nuclear factor-kappa B.

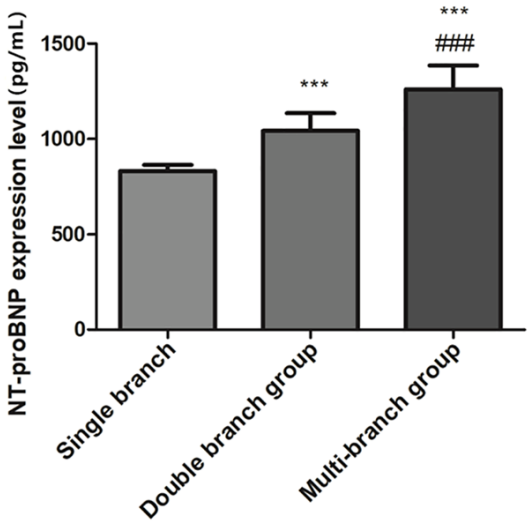

Figure 6. The NT-proBNP expression levels in the single branch, double branch, and multi-branch groups (pg/mL). Compared with the single branch group, ***P<0.001, compared with the double branch group, ###P<0.001. NT-proBNP: amino-terminal pro-brain natriuretic peptide.

Discussion

Cardiovascular diseases are an important and increasingly-common cause of mortality from AMI. Recently, the AMI incidence rate has increased significantly, without any age limit, and great harm has been brought to myocardial infarction patients and their families [11]. Thrombolysis, medication, and bypass surgery are currently the main methods used to treat myocardial infarction and other ischemic heart diseases. Abnormal expression levels of multiple signal factors are found in AMI patients, such as NT-proBNP and NF-κB. Therefore, determining the correlations of the NT-proBNP and NF-κB expression levels with disease development and prognosis has been a focus in recent cardiovascular research [12].

NT-proBNP, a common biomarker of myocardial infarction, plays a significant role in the human body and participates in the excretion of sodi-

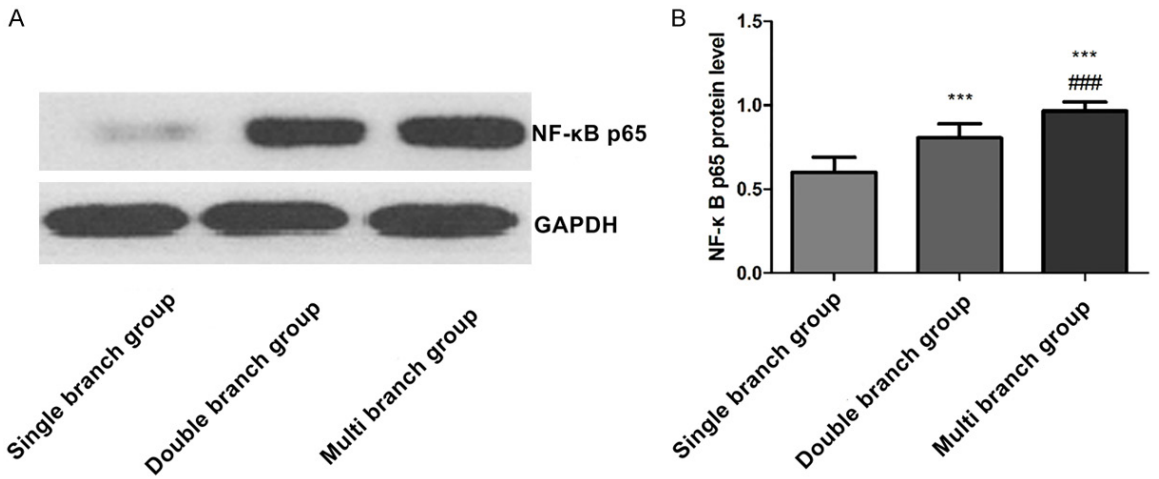

Figure 7. The NF-κB p65 protein levels in the single branch, double branch, and multi-branch groups. A: The NF-κB p65 protein bands. B: A comparison of the NF-κB p65 protein levels. Compared with the single branch group, ***P<0.001, compared with the double branch group, ###P<0.001. NF-κB: nuclear factor-kappa B.

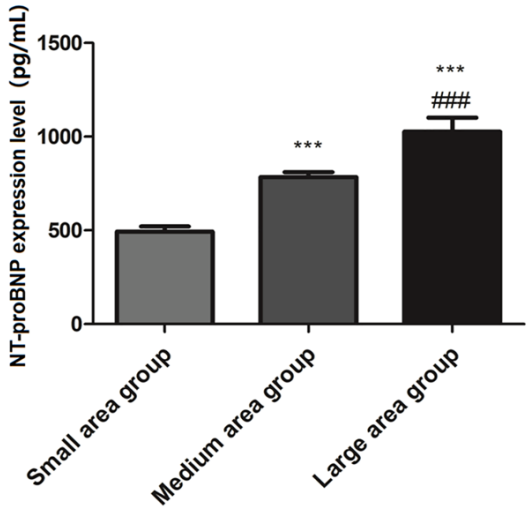

Figure 8. The NT-proBNP expression levels in the small area, medium area, and large area groups. Compared with the small area group, ***P<0.001, compared with the medium area group, ###P<0.001. NT-proBNP: amino-terminal pro-brain natriuretic peptide.

um and urine from the body [13]. NT-proBNP is released into the blood during a myocardial injury, so NT-proBNP expression level in the blood can be measured in in medical clinics to determine whether the patient has cardiac dysfunction [14]. The results in this study showed that the NT-proBNP and NF-κB p65 expression levels in the coronary heart disease group were lower than the corresponding levels in the acute myocardial infarction group. The NT-proBNP and NF-κB p65 expression levels in the grade II, grade III, and grade IV groups were increased compared with the grade I group levels, and the higher flow grades were related to higher expression levels. The expression levels were lower in the no-reflow group than they were in the reflow group. The expression levels were the highest in the multi-branch group, followed by the double branch group and then the single branch group. The expression levels were higher in the large area group than they were in the medium area and small area groups. The expression levels were higher in the poor prognosis group than they were in the good prognosis group. These findings indicate that the NT-proBNP and NF-κB p65 expression levels are positively correlated with the severity of the myocardial infarction. Patients with low flow grades, small infarct areas, reflow, and good prognoses had reduced NT-proBNP and NF-κB p65 expression levels. Patients in a severe condition and with a poor prognosis have significantly increased NT-proBNP and NF-κB p65 expression levels.

It is appropriate to use NT-proBNP to determine clinical myocardial infarction, heart failure and other heart diseases [15]. If any pressure is implemented on the heart, the myocardial cells will secret NT-proBNP. Therefore, using NT-proBNP detection in patients without any clinical manifestations or electrocardiographic abnormalities, cardiac abnormality can be found early, and the corresponding treatment

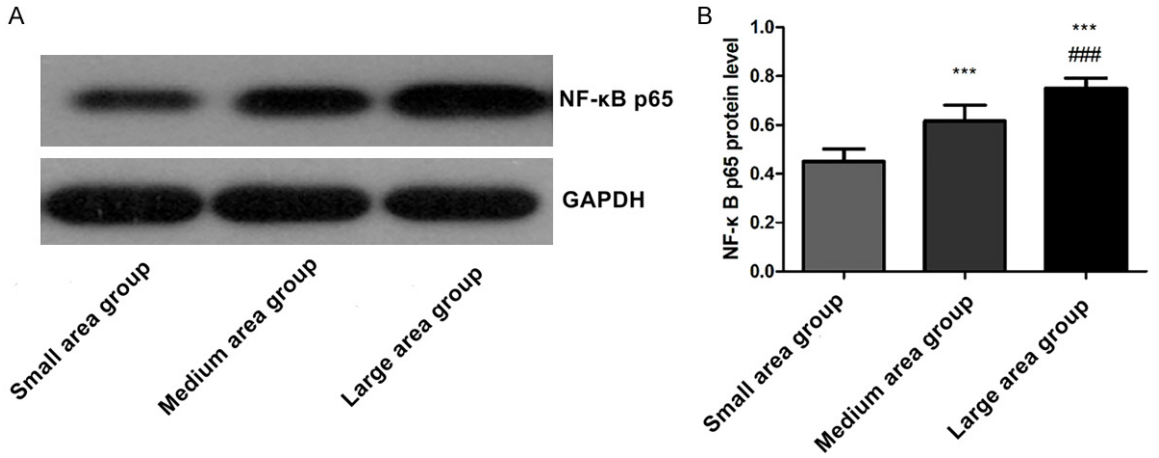

Figure 9. The NF-κB p65 protein levels in the small area, medium area, and large area groups. A: NF-κB p65 protein bands, B: Comparison of the NF-κB p65 protein levels. Compared with the small area group, ***P<0.001; compared with the medium area group, ###P<0.001. NF-κB: nuclear factor-kappa B.

Table 4. The NT-proBNP and NF-κB p65 expression levels in the poor prognosis and good prognosis groups ($\bar{x}$ ± sd)

Group	n	NT-proBNP (pg/mL)	NF-κB p65
Good prognosis	66	354.75±42.11	0.51±0.07
Poor prognosis	58	532.88±51.97***	0.62±0.10***
t		29.270	9.972
P		<0.001	<0.001

Note: Compared with the good prognosis group, ***P<0.001. NT-proBNP: amino-terminal pro-brain natriuretic peptide; NF-κB: nuclear factor-kappa B.

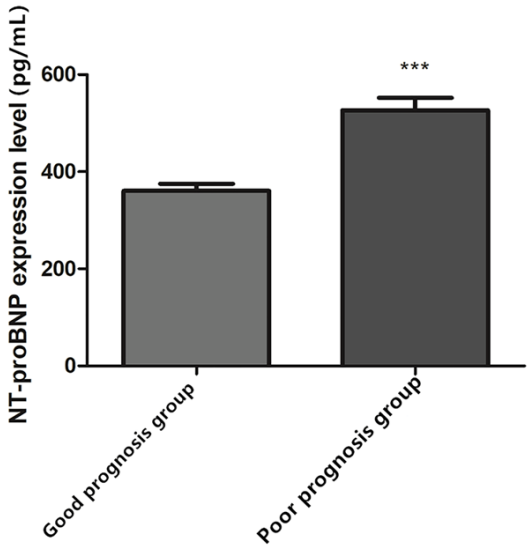

Figure 10. The NT-proBNP expression levels in the poor prognosis and good prognosis groups. Compared with the good prognosis group, ***P<0.001. NT-proBNP: amino-terminal pro-brain natriuretic peptide.

can be carried out to increase the treatment effectiveness rate and decrease the possibility of the disease worsening. The NT-proBNP expression levels vary with different diseases, and the NT-proBNP levels secreted by the myocardial cells are different in severe myocardial infarctions and mild ventricular pressure anomalies [16]. Therefore, the early detection of the NT-proBNP expression levels after onset can help determine the risk assessments of patients' conditions. The NT-proBNP content was significantly high in the elderly patients with AMI and increased significantly with an increase in heart function classification [17]. One study confirmed that the serum NT-proBNP level has correlations with the left ventricular ejection fraction, the left ventricular end systolic volume, and the left ventricular end diastolic volume, suggesting that NT-proBNP is associated with ventricular hypertrophy and cardiac dysfunction [18].

A previous study showed that NF-κB has a significant correlation with the expressions of the inflammatory mediators and with the immune response. NF-κB transcribes and regulates numerous disease factors and participates in multiple cardiovascular and cerebrovascular diseases [19]. Inflammation signals are transferred first into the cell membranes and then increase the NF-κB activity through I-κB kinase and other pathways in the cells for specific recognition. Gene transcription and regulation

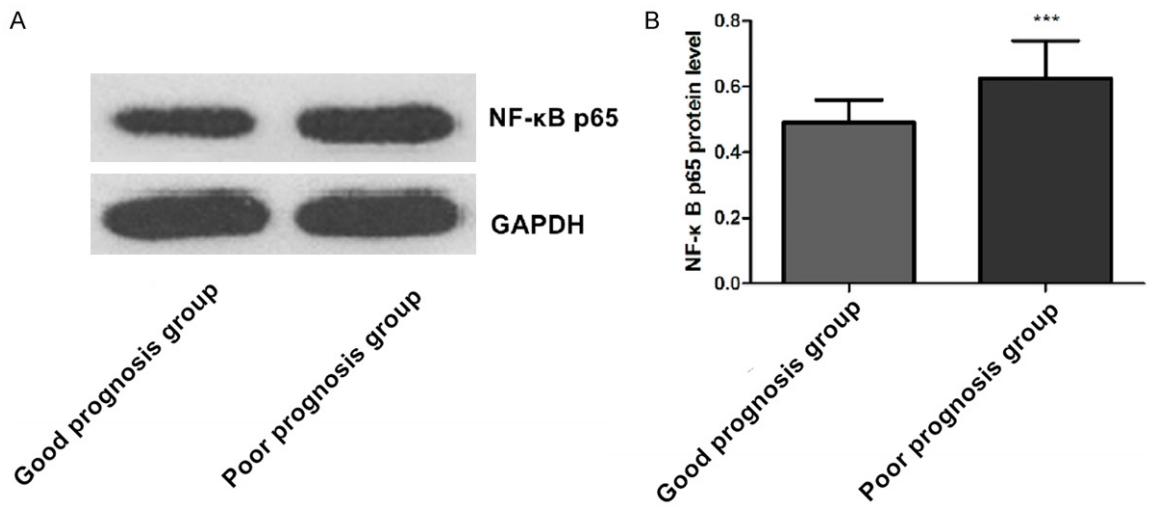

Figure 11. The NF-κB p65 protein levels in the poor prognosis and good prognosis groups. A: NF-κB p65 protein bands, B: A comparison of the NF-κB p65 protein levels. Compared with the good prognosis group, ***P<0.001. NF-κB: nuclear factor-kappa B.

occur, causing inflammatory injuries. NF-κB is a protein with multiple transcriptional regulation effects, and the NF-κB signaling pathway-mediated inflammatory response, cell proliferation and differentiation, cell apoptosis, and the immune response play important roles in the pathological process of ventricular remodeling after AMI [20]. NF-κB is a powerful antioxidant in the body and a key factor for regulating various oxidative stress injuries in cells. A decrease in the NF-κB expression level has multiple biological functions, such as anti-inflammation, anticancer, apoptosis inhibition, and maintaining the cellular oxidation-antioxidation balance [21]. In vitro cell experiments show that NF-κB plays an important role in anti-oxidative stress injuries and in the anti-apoptosis of myocardial cells. When NF-κB activity decreases, the myocardial cells' anti-apoptosis, anti-inflammatory, and antioxidant abilities increase accordingly. If the NF-κB activity is activated, the cells become vulnerable to inflammatory factors and oxidants [22]. Patients with high NF-κB levels have a high incidence rate of no-reflow during intervention operations, suggesting that NF-κB might be an independent risk factor for no-reflow in the coronary arteries. NF-κB is a member of the inflammatory factor family, and intervention using statins can significantly reduce the occurrence of no-reflow, confirming the role of NF-κB activation in the occurrence of no-reflow [23]. An animal experiment showed that the NT-proBNP and NF-κB p65 expression levels in rats with large myocardial infarct areas were significantly higher than they were in rats with small myocardial infarct areas, indicating that the NT-proBNP and NF-κB p65 expression levels can directly affect the severity of myocardial infarction [24]. The NF-κB expression level in patients with 3 or more diseased vessels increases significantly, and their conditions become more severe. The NF-κB expression levels are higher in patients with higher heart function classifications and are significantly negatively correlated with prognosis after the treatment, i.e. patients with poor prognoses have high NF-κB expression levels and poor treatment effects [25]. The results in this study are similar to the above study results.

There were some shortcomings in this study. Overall physical examinations were not carried out in all the patients, so the effect of other disease factors (infections, other cardiovascular and cerebrovascular diseases, etc.) could not be excluded, and this might bias the results to some extent. More experimental methods should be used in future studies to provide more favorable experimental evidence for the detection and treatment of AMI.

In conclusion, the NT-proBNP and NF-κB expression levels can significantly reflect AMI patients' conditions and increase as the disease progresses. Patients with high NT-proBNP and NF-κB expression levels have large myocardial infarct areas and increased post-treatment no-

reflow. Therefore, the NT-proBNP and NF-κB expression levels are important and can be used as indicators for predicting the occurrence of no-reflow after acute myocardial infarction.

Disclosure of conflict of interest

None.

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