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# Clinical efficacy of ticagrelor combined with aspirin in patients with coronary heart disease angina pectoris and its effects on NT-ProBNP and CK-MB levels

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**Abstract. – OBJECTIVE: This study aims to explore the clinical efficacy of ticagrelor combined with aspirin in patients with coronary heart disease angina pectoris and the effects on N terminal pro B type natriuretic peptide (NT-ProBNP) and creatine kinase-MB (CK-MB) levels.**

**PATIENTS AND METHODS: A total of 150 patients with coronary heart disease angina pectoris were prospectively analyzed in this study. These patients were admitted to Huaiyin Hospital of Huai'an City from February 2017 to February 2019. The patients were divided into control group and research group according to different treatment methods. The following indicators before and after treatment were observed: therapeutic efficacy, prevalence of adverse reactions, duration and frequency of angina attack, NT-ProBNP and CK-MB levels. Receiver operating characteristic (ROC) curve was used to analyze the predictive value of NT-ProBNP and CK-MB for the curative effect of coronary heart disease angina pectoris.**

**RESULTS: The total effective rate in the research group was higher than that in the control group ($p<0.05$). The prevalence of adverse reactions in the research group was lower than that in the control group ($p<0.05$). The duration and frequency of seizures of the two groups after treatment were lower than those before treatment. The duration and frequency of seizures in the research group were lower than those in the control group ($p<0.05$). The physiological function, physical pain, vital energy score and general health status in the research group were higher than those in the control group ($p<0.05$). The NT-ProBNP and CK-MB levels in both groups after treatment were decreased.**

**CONCLUSION: Ticagrelor combined with aspirin has definite therapeutic effect on patients with coronary heart disease angina pectoris, with low prevalence of adverse reactions. It can significantly reduce the levels of NT-ProBNP and CK-MB, which is worthy of promotion.**

*Key Words:*
Ticagrelor, Aspirin, Coronary heart disease angina pectoris, NT-ProBNP, CK-MB.

## Introduction

Coronary heart disease (CHD) is the leading cause of death worldwide. According to statistics, there were 7.4 million deaths from ischemic heart disease in 2012, which is about one-third of all deaths[1]. Coronary heart disease consists of a wide range of diseases, in which myocardial infarction and angina pectoris are the most common ones. It is estimated that 58% of patients with coronary heart disease have stable angina and the annual mortality rate is between 1.2% and 2.4%. Symptoms of suspected stable angina are common, so accurate diagnosis is often challenging[2-4].

At present, anti-platelet aggregation therapy and statins are the cornerstone of treatment for coronary heart disease angina pectoris[5]. Aspirin is an anti-platelet aggregation drug. Due to the antioxidant stress and endothelial protection, it is currently one of the most widely used drugs in preventing cardiovascular disease. Aspirin can reduce the risk of cardiovascular adverse events and death. Although aspirin is widely used in preventing heart disease, it has little impact on the high-risk population with heart disease. It has been reported that the addition of a second antiplatelet drug to aspirin may inhibit platelets through two different mechanisms, resulting in additional benefits in some clinical situations[6-8]. Ticagrelor, a cyclopentazolium pyrimidine drug, is an inhibitor of platelet activation and aggregation mediated



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by (ADP)$P2Y_{12}$ receptor. It is an effective antiplatelet therapy, which can reduce the prevalence of thrombotic cardiovascular events in patients with acute coronary syndrome (ACS), and help improve the cardiac structure and function of ACS patients after percutaneous coronary intervention (PCI). It may have better effect than aspirin in prevention of recurrent stroke and cardiovascular events in patients with atherosclerotic acute cerebral ischemia[9-11]. However, there have been neither large-scale trials in patients with peripheral arterial disease, nor direct evidence for specific antiplatelet therapy in these patients[5]. N terminal pro B type natriuretic peptide (NT-ProBNP) belongs to the natriuretic peptide family, which is mainly secreted by normal cardiac atrial myocytes. Ventricular B-Type Natriuretic Peptide (BNP) secretion sharply increases in patients with heart failure, suggesting increased ventricular stress and cardiac insufficiency. It is an independent predictor of death in acute decompensated heart failure[12,13]. Creatine kinase-MB (CK-MB) is also a marker of myocardial injury[14,15]. The increase of NT-ProBNP and CK-MB is related to the occurrence of angina pectoris in patients with CHD[16,17], but currently there is no report whether NT-ProBNP and CK-MB can be used as predictors of the efficacy of ticagrelor and aspirin in the treatment of patients with CHD angina pectoris. Therefore, this study analyzed the clinical efficacy of ticagrelor combined with aspirin in patients with coronary heart disease angina pectoris, and compared the effects of combination therapy on NT-ProBNP and CK-MB levels, in order to provide reference for clinical drug medication.

## Patients and Methods

### General Information

A total of 150 patients with coronary heart disease angina pectoris were prospectively analyzed in this study. These patients were admitted to our hospital from February 2017 to February 2019, and were divided into control group and research group according to different treatment methods. Their age ranged from 35 to 60 years old, and the average age was (54.54±10.23) years old. 72 cases in the control group were treated with aspirin enteric-coated tablets, and 78 cases in the research group were treated with ticagrelor on the basis of the control group.

**Inclusion criteria:** (1) patients diagnosed as coronary heart disease angina pectoris[12]; (2) patients without arrhythmia; (3) patients without major coagulopathy; (4) patients without atrioventricular block; (5) patients who obeyed the doctor's advice and did not quit this study halfway; (6) patients in the study group received dual antiplatelet therapy.

**Exclusion criteria:** (1) patients combined with other infectious diseases; (2) patients combined with other serious organ diseases; (3) patients with severe liver and kidney dysfunction; (4) patients with drug allergy; (5) patients with previous mental illness.

This study was approved by the Hospital Ethics Committee. All patients and their families signed the informed consent.

### Treatment Methods

Both groups were given angiotensin-converting enzyme inhibitors, β-blockers, diuretics, statins, bed rest, and reasonable diet. The control group was treated with aspirin enteric-coated tablets (Bayer S.p.A. imported drug registration number: H20160684) for the first time with 300 mg.po, and the next day with 75 mg.po.qd. The research group was given ticagrelor (AstraZeneca AB imported drug registration number: H20120486; London, UK) for the first time with 180 mg.po on the basis of the control group, and the second day with 90 mg.po.bid. The course of treatment is half a year.

### Observation Indicators

The observation indicators included therapeutic efficacy, prevalence of adverse reactions, duration and frequency of angina pectoris attack before and after treatment. The quality of life before and after treatment was evaluated. The levels of NT-ProBNP and CK-MB in serum were compared before and after treatment. ROC curve was used to analyze the predictive value of NT-ProBNP and CK-MB for the curative effect of coronary heart disease angina pectoris.

### Evaluation Criteria of Clinical Effect

Clinical efficacy evaluation criteria[13]: markedly effective (normal ECG and symptoms significantly reduced or disappeared); effective (duration and frequency of attacks reduced and symptoms significantly alleviated); invalid (no significant

changes in symptoms and signs). Total efficiency = (markedly effective + effective)/total number * 100%.

### Comparing the Quality of Life Before and After Treatment

SF-36 scale[14] was used to evaluate the quality of life of patients 1 day before treatment and 1 day after treatment. Each dimension was 100 points. The higher the score, the higher the quality of life.

### Detection of NT-ProBNP and CK-MB Levels in Serum Before and After Treatment

The fasting venous blood was taken 1 day before treatment, 1 day after the end of treatment, and 3 months after treatment. NT-proBNP was detected by chemiluminescent method, and CK-MB was determined by immunolabeling with CK-MB kit (Xinfan Technology Co., Ltd., Nanjing, China). Beckman Olympus 5800 was purchased from Beckman Coulter (Brea, CA, USA).

### Statistical Analysis

The Statistical Product and Servise Solution (SPSS) 19.0 (IBM Corp., Armonk, NY, USA) was used. Counter data were expressed by rate, and the rate was compared by $\chi^2$ test. Measurement data were expressed as mean±standard deviation (mean±SD). The *t*-test was used for comparison between the two groups. Paired *t*-test was used before and after treatment. ROC curve was used to analyze NT-ProBNP and CK-MB in the prediction of coronary heart disease angina pectoris. $p<0.05$ was statistically significant.

## Results

### General Information

There were no significant differences in gender, age, BMI, smoking, and drinking history between the two groups ($p>0.05$) (Table I).

### Evaluation of Clinical Efficacy

The total effective rates of control group and research group were 73.61% and 94.87%, respectively, so the total effective rate of research group was higher than that in the control group ($p<0.05$) (Table II).

### Adverse Reactions

In the control group, there were 6 cases of myocardial infarction, 1 case of stroke, 7 cases of unstable angina pectoris, and 1 case of heart failure. There was no serious adverse reactions, such as cardiovascular death, and the total prevalence of adverse reactions was 20.83%. In the research group, there were 2 cases of myocardial infarction, 0 case of stroke, 2 cases of unstable angina pectoris, and 0 case of heart failure. There was no serious adverse reactions, such as cardiovascular death, and the total prevalence of adverse reactions was 5.13%. So the total prevalence of adverse reactions in the research group was lower than that in the control group ($p<0.05$) (Table III).

### Duration and Frequency of Angina Pectoris Before and After Treatment

There was no significant difference in the duration and frequency of seizures between the two groups before treatment ($p>0.05$). After treatment, the duration and frequency of seizures in both groups were lower than those before treatment ($p<0.05$). After treatment, the duration and frequency of seizures in the research group were lower than those in the control group ($p<0.05$) (Figure 1).

### Comparison of Quality of Life Before and After Treatment in both Groups

Physiological function, physical pain, vitality score and general health status of patients in the research group were higher than those of the control group ($p<0.05$). There was no difference in social function and emotional function between the two groups ($p>0.05$) (Table IV).

### Detection of NT-ProBNP and CK-MB Levels in Serum Before and After Treatment

The levels of NT-ProBNP and CK-MB in the third month after treatment were lower than those prior to treatment ($p<0.05$), while the levels of NT-ProBNP and CK-MB after treatment were lower than those prior to treatment and 3 months after treatment ($p<0.05$) (Figure 2).

### The Predictive Value of NT-ProBNP and CK-MB in the Treatment of Coronary Heart Disease Angina Pectoris

Area under curve (AUC), critical level, sensitivity and specificity of coronary heart disease angina pectoris predicted by NT-ProBNP were 0.751, 59.432, 91.30 and 63.78, respectively. AUC,

**Table I.** General Information.

| | Control group (n = 72) | Research group (n = 78) | $\chi^2/t$ | p |
|---|---|---|---|---|
| Gender [n (%)] | | | 0.135 | 0.713 |
| Male | 40 (55.56) | 41 (52.56) | | |
| Female | 32 (44.44) | 37 (47.44) | | |
| Age | | | 0.472 | 0.492 |
| < 50 | 25 (34.72) | 23 (29.49) | | |
| ≥ 50 | 47 (65.28) | 55 (70.51) | | |
| BMI (kg/m$^2$) | 23.18 ± 1.01 | 23.21 ± 1.43 | 0.147 | 0.883 |
| Smoking [n (%)] | | | < 0.001 | 0.978 |
| Yes | 46 (63.89) | 50 (64.10) | | |
| No | 26 (36.11) | 28 (35.90) | | |
| Drinking [(%)] | | | 0.004 | 0.947 |
| Yes | 41 (56.94) | 44 (56.41) | | |
| No | 31 (43.06) | 34 (43.59) | | |
| Place of residence [n (%)] | | | 0.600 | 0.439 |
| City | 35 (48.61) | 33 (42.31) | | |
| Rural | 37 (51.39) | 45 (57.69) | | |
| Past medical history | | | | |
| Hypertension [n (%)] | | | 0.002 | 0.966 |
| Yes | 51 (70.83) | 55 (70.51) | | |
| No | 21 (29.17) | 23 (29.49) | | |
| Diabetes mellitus | | | 0.028 | 0.867 |
| Yes | 48 (66.67) | 53 (67.95) | | |
| No | 24 (33.33) | 25 (32.05) | | |
| COPD | | | 0.247 | 0.619 |
| Yes | 34 (47.22) | 40 (51.28) | | |
| No | 38 (52.78) | 38 (48.72) | | |
| Stroke history | | | 0.404 | 0.525 |
| Yes | 25 (34.72) | 31 (39.74) | | |
| No | 47 (65.28) | 47 (60.26) | | |
| Place of residence [n (%)] | | | 0.600 | 0.439 |
| City | 35 (48.61) | 33 (42.31) | | |
| Rural | 37 (51.39) | 45 (57.69) | | |
| Past medical history | | | | |
| Hypertension [n (%)] | | | 0.002 | 0.966 |
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| No | 38 (52.78) | 38 (48.72) | | |
| Stroke history | | | 0.404 | 0.525 |
| Yes | 25 (34.72) | 31 (39.74) | | |
| No | 47 (65.28) | 47 (60.26) | | |

critical level, sensitivity and specificity of coronary heart disease angina pectoris predicted by CK-MB were 0.858, 61.794, 91.30 and 66.14, respectively (Table V and Figure 3).

**Table II.** Clinical efficacy [n (%)].

| | Control group (n = 72) | Research group (n = 78) | $\chi^2$ | p |
|---|---|---|---|---|
| Markedly effect | 25 (34.72) | 32 (41.03) | 0.631 | 0.427 |
| Effective | 28 (38.89) | 42 (53.85) | 3.365 | 0.067 |
| Invalid | 19 (26.39) | 4 (5.13) | 13.040 | < 0.001 |
| Total | 53 (73.61) | 74 (94.87) | 13.040 | < 0.001 |

**Table III.** Prevalence of adverse reactions.

| | Control group (n = 72) | Research group (n = 78) | $\chi^2$ | p |
|---|---|---|---|---|
| Myocardial infarction | 6 (8.33) | 2 (2.56) | 2.468 | 0.116 |
| Apoplexy | 1 (0.67) | 0 (0.00) | 1.091 | 0.296 |
| Unstable angina | 7 (9.72) | 2 (2.56) | 3.401 | 0.065 |
| Cardiovascular death | 0 (0.00) | 0 (0.00) | 0.000 | 0.000 |
| Heart failure | 1 (0.67) | 0 (0.00) | 1.091 | 0.296 |
| Total | 15 (20.83) | 4 (5.13) | 8.348 | 0.004 |

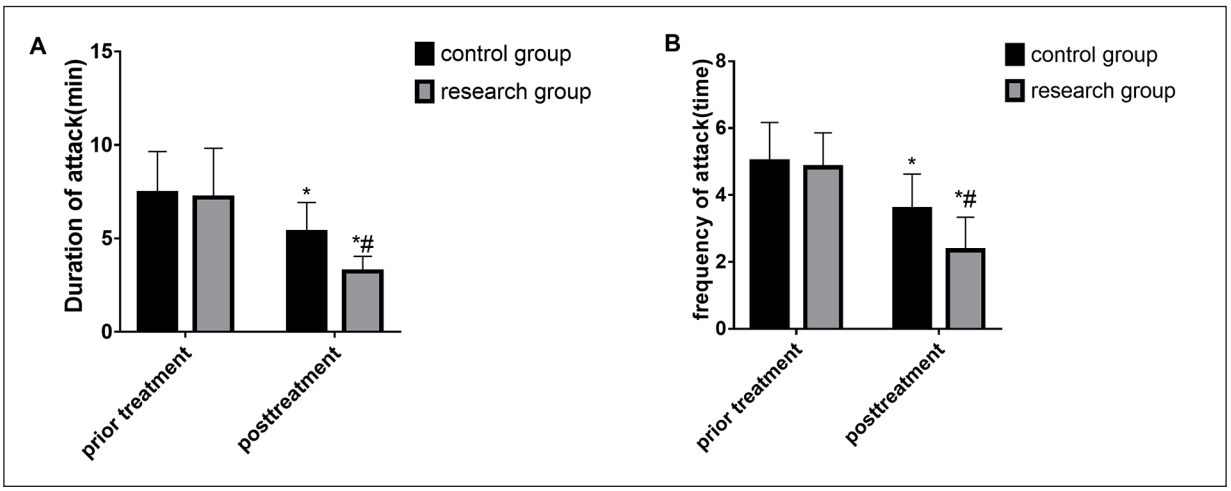


**Figure 1.** Duration and frequency of angina pectoris before and after treatment. **A,** The duration of each attack of angina pectoris. **B,** The number of attack of angina pectoris per week. *Compared with that prior to treatment ($p<0.05$); #Compared with the control group after treatment ($p<0.05$).

## Discussion

Coronary heart disease angina pectoris is a critical stage of ischemic heart disease accompanied by thrombosis and intermittent embolism, and is associated with high-risk myocardial infarction and sudden death. It is caused by rupture of atherosclerotic plaque and subsequent activation of platelets[15]. Therefore, anti-platelet therapy is needed.

In this study, total effective rate of the control group was 73.61%, and that of the research group was 94.87%. So total effective rate of the research

**Table IV.** Quality of life score.

| Test items | Detection time | Control group (n = 72) | Research group (n = 78) | t | p |
|---|---|---|---|---|---|
| Physiological function | Prior Treatment | 64.64 ± 10.34 | 65.29 ± 10.25 | 0.386 | 0.700 |
| | Post Treatment | 71.42 ± 6.43* | 82.45 ± 11.21* | 7.974 | |
| Somatic pain | Prior Treatment | 66.92 ± 11.54 | 67.23 ± 11.96 | 0.161 | 0.872 |
| | Post Treatment | 75.34 ± 8.35* | 89.12 ±11.25* | 8.462 | |
| Vitality score | Prior Treatment | 66.14 ± 13.75 | 65.44 ± 13.24 | 0.318 | 0.751 |
| | Post Treatment | 77.23 ± 5.63* | 89.12 ± 9.37* | 9.324 | |
| General health status | Prior Treatment | 69.52 ± 11.52 | 68.76 ± 12.53 | 0.386 | 0.700 |
| | Post Treatment | 78.63 ± 6.23* | 91.02 ± 8.45* | 10.150 | |
| Emotional function | Prior Treatment | 72.24 ± 10.32 | 72.14 ± 10.93 | 0.058 | 0.954 |
| | Post Treatment | 74.12 ± 9.34 | 74.31 ± 10.39 | 0.117 | 0.907 |
| Social function | Prior Treatment | 81.34 ± 12.83 | 82.37 ± 12.53 | 0.497 | 0.620 |
| | Post Treatment | 81.95 ± 12.27 | 82.67 ± 12.82 | 0.351 | 0.726 |

*Note:* *Compared with prior treatment, $p < 0.05$.

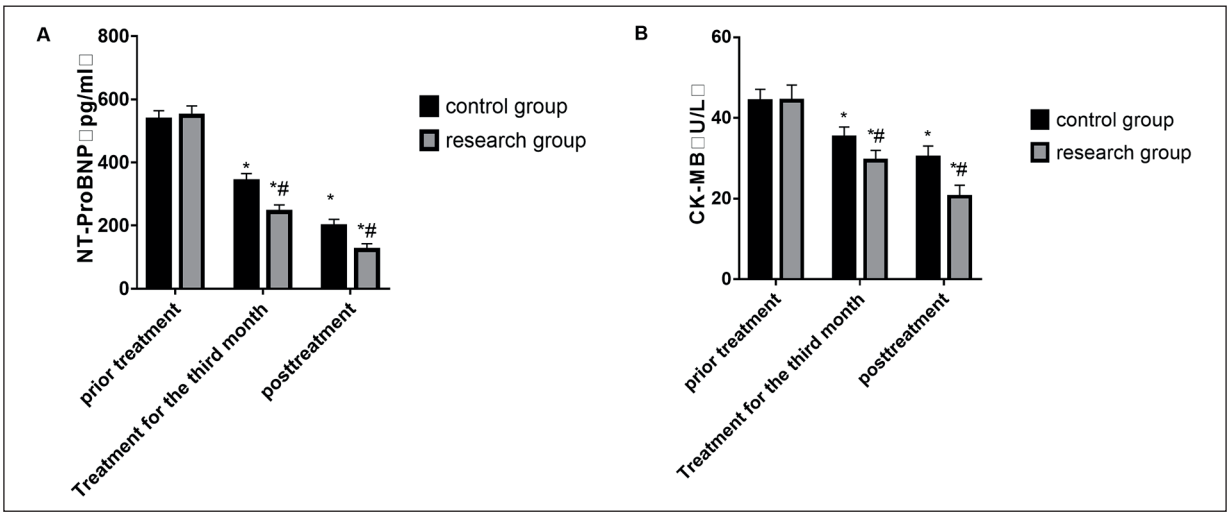


**Figure 2.** Detection of NT-ProBNP and CK-MB levels in serum before and after treatment. **A,** Detection of NT-ProBNP levels prior and after treatment. **B,** Detection of CK-MB levels prior to and after treatment. *Compared with that prior to treatment ($p<0.05$); #Compared with the control group after treatment ($p<0.05$).

group was significantly higher than that of the control group, suggesting that the combined use of ticagrelor and aspirin was more effective than the use of aspirin alone. According to Dobesh et al[16], as a new type of $P2Y_{12}$ inhibitor, ticagrelor has rapid inhibition of platelets, stronger action and better therapeutic effect. This is consistent with our results, indicating that its efficacy is better. Moreover, the duration and frequency of seizures before and after treatment were also counted. It was found that the duration and frequency of seizures after treatment in the research group were lower than those in the control group, suggesting that ticagrelor combined with aspirin could better alleviate the pain of patients than aspirin alone, and further shows that the curative effect is better. In our study, the prevalence of total adverse reactions in the research group was significantly lower than that in the control group, suggesting that the research group has higher safety. Johnston et al[17] mentioned that ticagrelor could prevent recurrent stroke and cardiovascular events in ischemic patients more effectively than aspirin, and had a higher safety in study of the role of ticagrelor and aspirin in acute stroke and transient ischemic attack[18]. Moreover, according to statistics, ticagrelor has been widely used in elderly patients with ST-segment elevation myocardial infarction since 2011. Compared with patients treated with clopidogrel in the same conditions, patients treated with ticagrelor had lower mortality and adverse events after one year, while the bleeding rate was similar. These findings all emphasized higher safety and effectiveness of ticagrelor[19]. We can see that the quality of life of patients treated with ticagrelor combined with aspirin is significantly improved by the SF-36 scale, which indicates that combination therapy can better improve the quality of life and reduce the pain of patients for the disease.

BNP (BNP and NT-ProBNP) belongs to the natriuretic peptide family, which is mainly secreted by normal cardiac atrial myocytes. The rapid increase of ventricular BNP secretion in patients with heart failure suggests increased ventricular stress and cardiac insufficiency. It is an independent predictor of death in acute decompensated heart failure[20,21]. CK-MB is also a marker of

**Table V.** Predictive value of NT-ProBNP and CK-MB in the treatment of coronary heart disease angina pectoris.

| | AUC | Critical level | 95% CI | Sensitivity % | Specificity % |
|---|---|---|---|---|---|
| NT-ProBNP | 0.751 | 59.432 pg/ml | 0.6754-0.82692 | 91.30 | 63.78 |
| CK-MB | 0.858 | 61.794 U/L | 0.7927-0.9224 | 91.30 | 66.14 |

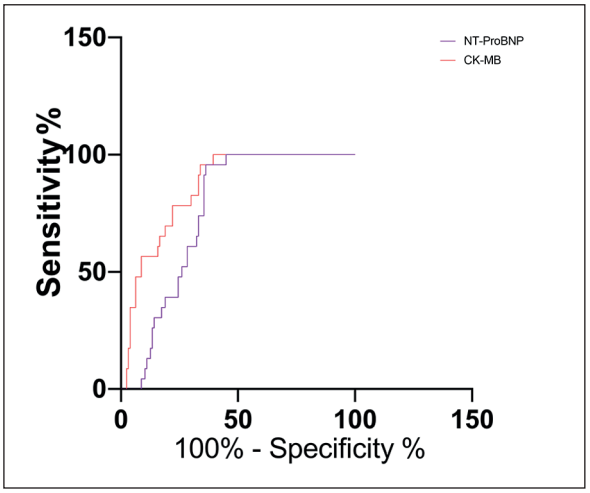


**Figure 3.** Predictive value of NT-ProBNP and CK-MB in the treatment of coronary heart disease angina pectoris. AUC of NT-ProBNP and CK-MB for predicting coronary heart disease angina pectoris were 0.751 and 0.858, respectively.

myocardial damage[22,23]. In this work, the levels of myocardial markers in the control group and the research group decreased, but the level in research group was significantly lower than that in the control group. This indicates that the serum markers of central muscle injury are significantly reduced after treatment with ticagrelor combined with aspirin. Many researches have shown that antiplatelet drugs and vasodilators can alleviate myocardial injury[24], indicating that the combined therapy is better than the therapy in the control group. This work also analyzed the predictive value of NT-ProBNP and CK-MB for the treatment of coronary heart disease angina pectoris. The results suggest that the AUC of NT-ProBNP and CK-MB for predicting coronary heart disease angina pectoris are 0.751 and 0.858, respectively, and the sensitivity is 91.30%, indicating the predictive value of both markers for coronary heart disease angina pectoris.

Although ticagrelor is more effective and faster in anti-platelet aggregation, its role and mechanism in the prevention of microvascular dysfunction is not clear[24]. This study did not explore this direction, and we would like to start from this direction in the next investigation, in order to better understand the clinical medication.

## Conclusions

In summary, ticagrelor combined with aspirin has a good therapeutic effect on patients with coronary heart disease angina pectoris, with low prevalence of adverse reactions and high safety. It can significantly reduce the levels of NT-ProBNP and CK-MB, which is worthy of promotion.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

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