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ARTICLE

Regulation of platelet activation and thrombus formation in acute non-ST segment elevation myocardial infarction: Role of Beclin1

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Abstract

This study aims to investigate the mechanism of platelet activation-induced thrombosis in patients with acute non-ST segment elevation myocardial infarction (NSTEMI) by detecting the expression of autophagy-associated proteins in platelets of patients with NSTEMI. A prospective study was conducted on 121 patients with NSTEMI who underwent emergency coronary angiography and optical coherence tomography. The participants were divided into two groups: the ST segment un-offset group ($n = 64$) and the ST segment depression group ($n = 57$). We selected a control group of 60 patients without AMI during the same period. The levels of autophagy-associated proteins and the expression of autophagy-associated proteins in platelets were measured using immunofluorescence staining and Western blot. In NSTEMI, the prevalence of red thrombus was higher in the ST segment un-offset myocardial infarction (STUMI) group, whereas white thrombus was more common in the ST segment depression myocardial infarction (STDMI) group. Furthermore, the platelet aggregation rate was significantly higher in the white thrombus group compared with the red thrombus group. Compared with the control group, the autophagy-related protein expression decreased, and the expression of αIIbβ3 increased in NSTEMI. The overexpression of Beclin1 could activate platelet autophagy and inhibit the expression of αIIbβ3. The results suggested that the increase in platelet aggregation rate in patients with NSTEMI may be potentially related to the change in autophagy. And the overexpression of Beclin1 could reduce the platelet aggregation rate by activating platelet autophagy. Our findings demonstrated that Beclin1 could be a potential therapeutic target for inhibiting platelet aggregation in NSTEMI.

Study Highlights

WHAT IS THE CURRENT KNOWLEDGE ON THE TOPIC?

In NSEMI patients, white thrombus accounts for a proportion. Beclin1 overexpression can activate platelet autophagy and regulate platelet aggregation.

WHAT QUESTION DID THIS STUDY ADDRESS?

This study aims to investigate the mechanism of platelet activation-induced thrombosis in patients with acute non-ST segment elevation myocardial infarction by detecting the expression of autophagy-associated proteins in platelets of patients with non-ST segment elevation myocardial infarction.

WHAT DOES THIS STUDY ADD TO OUR KNOWLEDGE?

This study revealed the presence of red thrombus in a subset of patients with NSTEMI. The proportion of red thrombus was found to be higher in patients with ST segment un-offset.

HOW MIGHT THIS CHANGE CLINICAL PHARMACOLOGY OR TRANSLATIONAL SCIENCE?

The overexpression of Beclin1 can influence platelet aggregation and activation, which may establish a novel cellular and molecular biological foundation for future clinical treatment.

INTRODUCTION

The traditional concept suggests that the pathological basis of acute non-ST segment elevation myocardial infarction (NSTEMI) is a series of changes caused by the stimulation of inflammatory factors, leading to ulceration and rupturing unstable plaques within the coronary arteries. At the same time, platelets at the site of the lesion are activated, leading to adhesion and aggregation, forming platelet-rich thrombi, also known as "white thrombus".[1] However, YasushiIno[1] conducted a study where intravascular images of infarct-related patients with NSTEMI were observed using optical coherence tomography (OCT). The study findings indicated that 27% of the patients exhibited red thrombi, while 39% had white thrombi. There is no consensus on the precise underlying cause of NSTEMI thrombosis. Hence, identifying potential biomarkers and elucidating molecular mechanisms associated with NSTEMI thrombosis is essential to develop more effective and precise diagnostic and therapeutic approaches for NSTEMI.

Platelets play an important role in thrombosis in cardiovascular disease.[2] Therefore, antiplatelet therapy effectively reduces the risk of myocardial infarction and stroke for different types of plaques in the coronary artery. Previous studies have suggested that platelet activation is one of the key factors in cardiovascular thrombosis due to its association with the activation of the local coagulation system, leading to the formation of coronary artery thrombus through a cascade of reactions.[3]

Autophagy is the adaptive response of cells to various pathophysiological conditions. Under the stimulation of various factors, such as hunger, ischemia and hypoxia, and ischemia/reperfusion, autophagy is activated. Autophagy involves the removal of damaged organelles (such as mitochondria) in various pathological conditions, thus preventing the release of apoptotic factors into cells and enhancing cellular resistance against hypoxia. Therefore, it can more effectively preserve the homeostasis of the normal internal environment.[4,5] At the same time, as highly specialized terminal cells, cardiomyocytes rely on autophagy to generate energy and ensure their stability, thereby maintaining normal cardiac function. Therefore, the abnormal autophagy of cardiomyocytes is closely associated with various cardiovascular diseases, including myocardial ischemia/reperfusion injury, myocardial hypoxia, myocardial hypertrophy, cardiomyopathy, and heart failure. Recent studies have demonstrated that platelets, which are non-nucleated cells, also maintain their function through autophagy. Under pathophysiological conditions, the function of platelets is affected by the change in autophagy level. The activation processes, such as adhesion, release, and aggregation, exhibited varying degrees of change.[6]

There are a variety of regulatory factors involved in all aspects of autophagy. Among them, Beclin1 (Becn1), a homolog of yeast autophagy gene Atg6,[7] is widely expressed in various human tissues. It regulates the formation of autophagosomes and promotes its growth and maturation, making it an essential factor in regulating cellular

autophagy levels. At present, studies have shown that the overexpression of Beclin1 can inhibit the occurrence of inflammation after ischemia-reperfusion in acute myocardial infarction.[8] However, the investigation into the role of Beclin1 in regulating autophagy-mediated platelet aggregation and thrombosis remains inconclusive. This study aims to explore the molecular mechanism of platelet aggregation during thrombosis in patients with NSTEMI and explore the role of autophagy key protein Beclin1 in regulating platelet aggregation.

MATERIALS AND METHODS

Study population and design

As a prospective study, this study continuously included 121 patients with acute NSTEMI who met the inclusion and exclusion criteria. These patients underwent emergency coronary angiography and OCT during emergency coronary artery treatment at Henan People's Hospital between July 1, 2021, and April 30, 2023. At the same time, 60 healthy volunteers without a history of acute myocardial infarction or prior use of antiplatelet medications were enrolled. The age range of the healthy volunteers was limited to 18–80 years. The statistical data were recorded secretly, and the medical history and blood samples were collected within 2 h. The definition of NSTEMI is established based on the 2018 ESC guidelines. The results of ECG, coronary angiography, and OCT were collected in detail. Two researchers read and evaluated all the ECG and coronary angiography data. In case of any disagreement, a third experienced interventional physician in our hospital will provide judgment and reach a consensus. All the OCT data are read and analyzed by professional software provided by two experienced cardiologists in our hospital. In case of any disagreement between the two parties, a third professional analysis engineer intervenes to reach a mutual agreement. Based on the results of ECG, the participants were categorized into two groups: the ST segment depression (STDMI) group, which included individuals with ST segment depression in two or more consecutive leads (precordial lead ≥2 mm, limb lead ≥1 mm), and the ST segment un-offset (STUMI) group, which comprised individuals with either no significant change in ST segment or a level of depression that did not meet the criteria for the STDMI group. Based on the results obtained from OCT, NSTEMI patients were divided into two groups: the white thrombus group and the red thrombus group. This study was approved by the Medical Ethics Committee of the People's Hospital of Zhengzhou University. All patients in the group provided informed consent and signed relevant documents.

Inclusion and exclusion criteria of patients in the NSTEMI group

Inclusion criteria for the study were as follows: (1) patients with a definite diagnosis of NSTEMI; (2) patients who underwent emergency percutaneous coronary intervention (PCI) and had confirmation of coronary artery thrombus through OCT examination during the procedure; (3) patients aged between 18 and 80 years; (4) patients' medical records in the group showed no significant deficiencies and all key test parameters were acceptable.

Exclusion criteria: (1) To eliminate the effect of ischemia-reperfusion time on thrombus composition, this study excluded patients with imaging time longer than 180 min from symptom onset to OCT catheter insertion; (2) To eliminate the effect of previous antiplatelet drugs on the actual platelet aggregation rate, patients who received long-term P2Y12 receptor antagonists or loading dose and intravenous thrombolysis were excluded in this study; (3) OCT examination was not performed during the operation; (4) malignant arrhythmias; (5) severe infectious diseases; (6) severe hepatorenal insufficiency; (7) cachexia; (8) poor quality of OCT imaging.

Analysis of infarct-related intravascular thrombus components in patients with NSTEMI by OCT

In OCT images, the irregular mass/floc image attached to or floating on the surface of the vascular lumen is generally defined as a thrombus. Thrombus can be divided into three types based on their optical properties: (1) Red thrombus (mainly composed of red blood cells): strong attenuation, often shows high back reflection; (2) white thrombus (mainly composed of platelets): uniform optical signal, weaker attenuation than red thrombus, often shows low back reflection; (3) mixed thrombus: optical signal is often between red thrombus and white thrombus, or both exist in a similar proportion.

Platelet collection and platelet aggregation rate detection

Further details are provided in Text S1.

Western blot and immunofluorescence and RT-PCR

Further details are provided in Text S2.

Lentivirus transfection

Beclin1 overexpressed lentivirus strain was used to transfect platelets. Platelets were cultured in a six-well plate coated with bovine fibrinogen (Solarbio, Beijing), and the lentivirus containing Beclin1 gene and the new culture medium of lentivirus vector carrying green fluorescence (Shanghai Genechem Co., Ltd.) were replaced the next day. The lentivirus user manual stated that the platelets were transfected stably for 6–8 h. Subsequently, an equivalent volume of fresh growth medium was added to each group to sustain the culture. Puromycin (Thermo Science, A1113802) was added for further screening. Two days post-transfection, the samples were observed using a fluorescence microscope (Olympus, Tokyo, Japan). The acquired images were subsequently analyzed to observe the efficiency of lentivirus transfection.

Statistical analysis

The statistical analysis software used in this study was IBM SPSS28.0 software. The resulting data is expressed as mean ± standard deviation (Mean ± SD). An independent samples *t*-test was utilized to compare the two groups when the data met the normal distribution assumptions and variance homogeneity. A rank sum test was employed in cases of non-normal distribution or unequal variances. A one-way ANOVA was conducted for group comparisons and a test for homogeneity of variances between groups. The LSD method was applied to test for variance homogeneity, whereas Dunnett's ST3 method was used in unequal variances.

RESULTS

Baseline population

Table S1 demonstrates significant differences in age ($p = 0.003$), gender ($p = 0.002$), body mass index (BMI) ($p < 0.0001$), history of diabetes ($p < 0.0001$), type of infarction-related vessels, and preoperative TIMI grade between the two groups. There was no statistically significant difference in the "Door to balloon time" between the two groups. In the STUMI group, the infarct-related vessels were predominantly located in the left circumflex branch (LCX) ($p < 0.0001$), with TIMI 0 grade ($p = 0.006$), while in the STDMI group, they were observed with TIMI 3 grade ($p = 0.024$).

Comparison of thrombus types in patients with different types of NSTEMI

Red and white thrombi in infarct-related arteries of patients with NSTEMI were observed under OCT, as shown in Figure 1. The STUMI group exhibited a higher prevalence of red thrombus, while the STDMI group exhibited a higher prevalence of white thrombus, and a statistically significant difference was found between the two groups (Table S2) ($p < 0.0001$).

Effect of autophagy on platelet activation

To further investigate the association between platelet autophagy and aggregation, the platelet proteins extracted from the healthy control and NSTEMI groups were detected by Western blot. The results showed that the expression of autophagy-associated protein Beclin1 and LC3II/LC3I in different types of myocardial infarction group was lower than that in the healthy control group (Figure 2b,c), while the expression of P62 protein and platelet activation-related protein αIIbβ3 (αIIbβIII) was higher than that in the healthy control group (Figure 2d). The expression of αIIbβ3 in the STDMI group was higher than in the STUMI group (Figure 2e). After pre-treating platelets with common autophagy inhibitors 3-methylpurine (3-MA) and chloroquine (CQ), the levels of P62 and αIIbβ3 were further increased (Figure 3d,e), and the levels of Beclin1 and LC3II/LC3I were further decreased (Figure 3b,c). These results suggest that the blockage of autophagy may aggravate platelet activation in NESTEMI.

Beclin1 regulates platelet activation in NSTEMI by regulating autophagy

To further confirm that if the recovery of autophagy could inhibit platelet aggregation, we observed the effect of Beclin1 overexpression (Len-Beclin1) on platelet activation in patients with different acute myocardial infarctions. Firstly, we utilized a lentivirus strain overexpressing Beclin1 to transfect platelets. The transfection efficiency of the lentivirus was assessed using the immunofluorescence method (Figure S1A). Western blot (Figure S1C,D, $p = 0.0068$) and RT-PCR (Figure S1B, $p = 0.0016$) method was used to observe the changes of Beclin1 in each group after Beclin1 overexpression lentivirus transfection. Then the expression of Beclin1

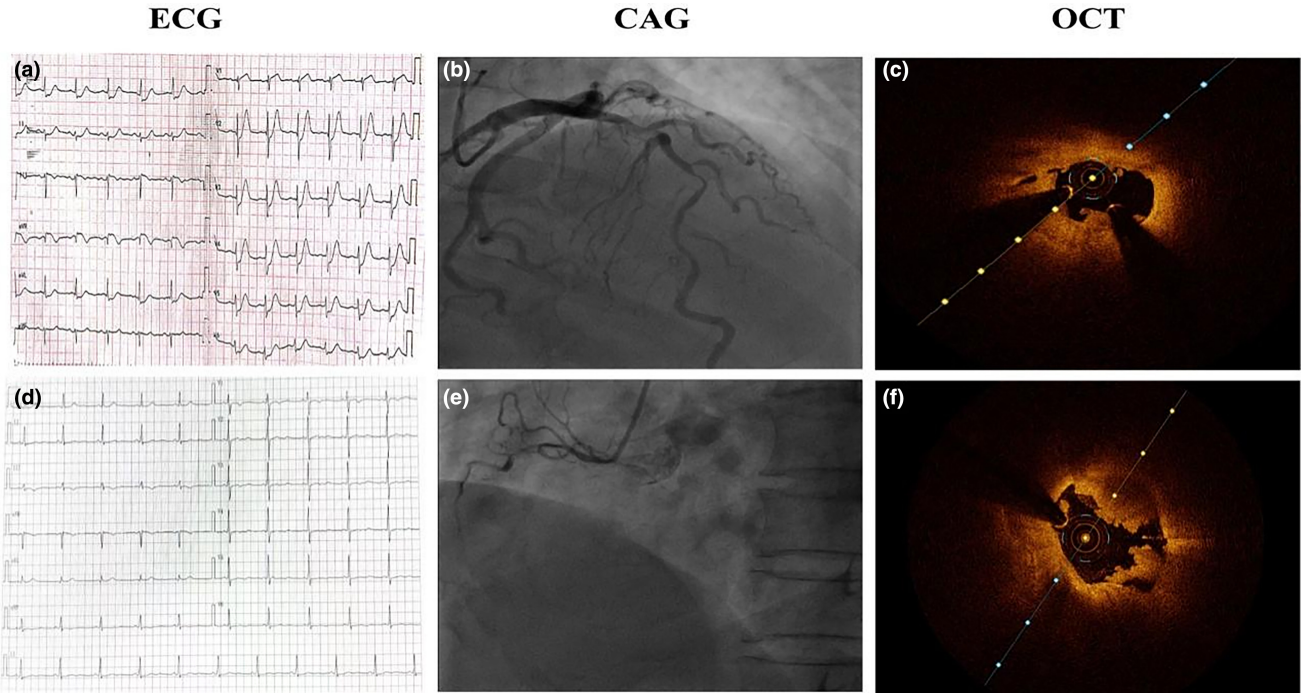

FIGURE 1 OCT characteristics of different thrombus types in NSTEMI patients. (a) Electrocardiogram of STDMI patient; (b) coronary angiography of STDMI patient; (c) pre-PCI coronary OCT image of STDMI patient, with visible white thrombus; (d) electrocardiogram of STUMI patient; (e) coronary angiography of STUMI patient; (f) pre-PCI coronary OCT image of STUMI patient, with visible red thrombus; PCI, percutaneous coronary intervention.

and its downstream autophagy-related proteins and the expression of platelet activation-related protein αIIbβ3 were observed. Western blot results demonstrated that overexpression of Beclin1 upregulated LC3II/LC3I expression (Figure 4c), downregulated P62 expression (Figure 4b), and inhibited the expression of αIIbβ3 in platelets of STUMI and STDMI (Figure 4e).

Effect of platelet activation on thrombosis in patients with NSTEMI

To further investigate the effect of platelet activation in patients with different thrombus types of NSTEMI, the platelets of the red thrombus group and white thrombus group of NSTEMI patients were stained with αIIbβ3 by immunofluorescence to visualize platelet activation, and subsequently observed and analyzed. Simultaneously, we analyzed the average platelet aggregation rates induced by arachidonic acid (AA) and collagen (COL) in various groups. The results demonstrated a significantly higher average platelet aggregation rate in the white thrombus group compared with the red thrombus group (Table S3) ($p < 0.0001$). Immunofluorescence analysis showed that the level of platelet activation in the white thrombus group was higher than that in the red thrombus group (Figure 5).

Effect of Beclin1 on platelet activation in NSTEMI patients with different thrombus types

Next, to further explore the regulatory mechanism of Beclin1 on platelet activation in different types of thrombus. Different groups of platelets were transfected with Beclin1 lentivirus. The impact of lentivirus on αIIbβ3 protein expression and platelet aggregation rate was observed after transfection. Similarly, we analyzed the average platelet aggregation rates induced by AA and collagen (COL) in each groups. The overexpression of Beclin1 could reduce platelet aggregation rate to a certain extent (Figure 6b,c). The Western blot results demonstrated lower expression of the lentivirus genome αIIbβ3 protein in lentiviruses carrying Beclin1 overexpression (Len-Beclin1) compared with the lentivirus-negative control group (Len-Vector) (Figure 6g). And compared with the white thrombus group, the expression of αIIbβ3 protein was inhibited more significantly in the red thrombus group (Figure 6g). The results of

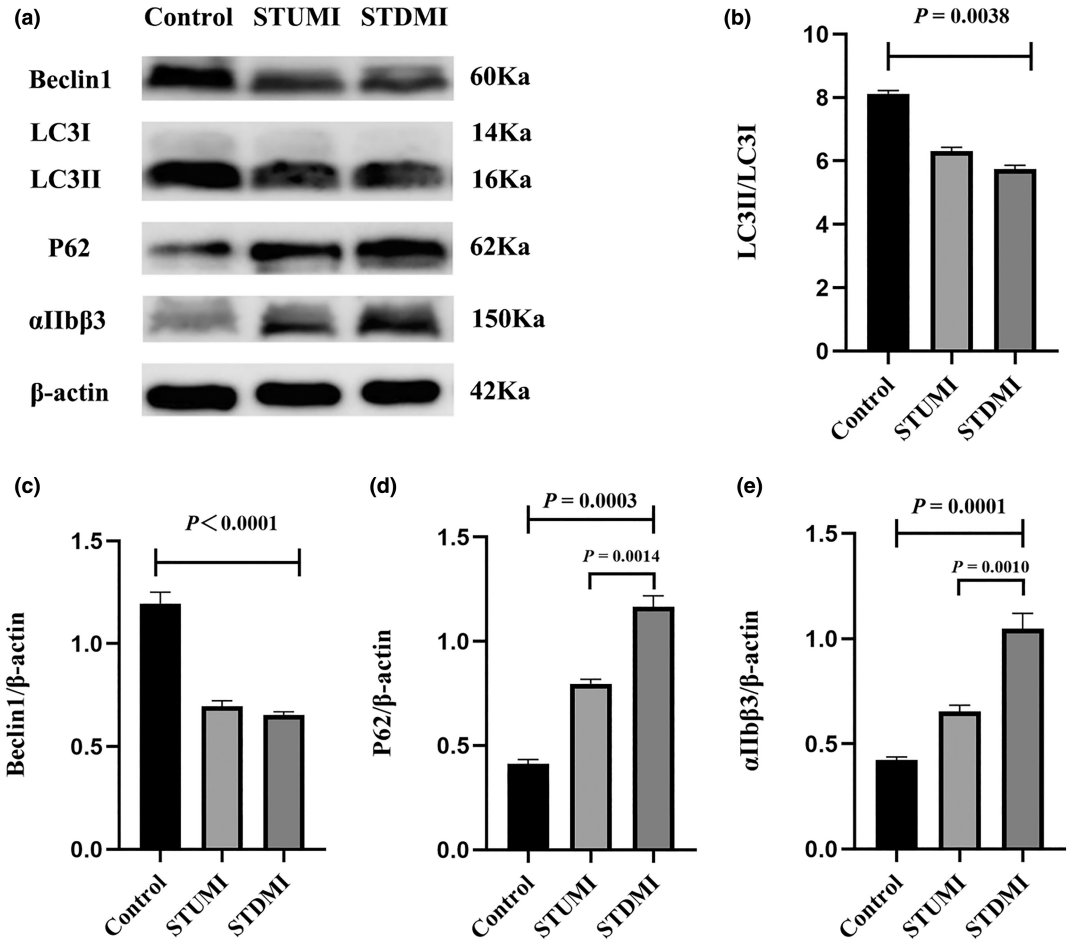

FIGURE 2 The relationship between autophagy and platelet activation. (a) Western blot analysis of Beclin1 (c), LC3II/LC3I (b), P62 (d), and αIIbβ3 (e) protein expression and densitometric analysis in platelets from patients with different types of acute myocardial infarction. Data are represented as mean ± SD ($n = 3$); $p < 0.05$ indicates a statistical difference.

immunofluorescence were consistent with those of Western blot (Figure 6a).

DISCUSSION

Based on the traditional perspective,[9,10] ST segment elevation myocardial infarction (STEMI) commonly signified complete coronary artery occlusion due to red thrombus formation, primarily composed of red blood cells. NSTEMI frequently results from incomplete coronary artery occlusion caused by a white thrombus, primarily composed of platelets. Previous studies have revealed that the occlusion or non-occlusion of infarct-related vessels was not definitive in both STEMI and NSTEMI. Additionally, the type of thrombus found in infarct-related vessels was not consistently red or white thrombus.[11,12] In recent years, there have been increasing studies on the types of infarction-related intravascular thrombus and the factors influencing thrombosis in patients with acute myocardial infarction. By studying patients with myocardial infarction, Quadros et al.[13] found that compared with red thrombus, patients with white thrombus had a smaller coronary artery diameter, reduced overall thrombus volume, and shorter symptomatic ischemia time. Johanne Silvain et al.[14] discovered that the sole independent predictor of thrombus composition was the duration of ischemia. They suggested this might be due to the close correlation between platelet and fibrin content and the duration of ischemia. Jia et al.[15] found that compared with STEMI, NSTEMI patients were more likely to have plaque erosion, with a greater occurrence of white thrombus at the infarction site. Only a few industry studies have conducted preliminary research on the types of intracoronary thrombus in NSTEMI. This study utilized OCT to observe the thrombus types in infarct-related vessels among patients with NSTEMI. We found that red thrombus was more common in patients with STUMI, while white thrombus was more common in patients with STDMI, which indicated that there seemed to be some relationship between ST segment and thrombus types. But other influencing factors (like age, gender etc.) still could not be excluded. Considering that there were still few studies on the

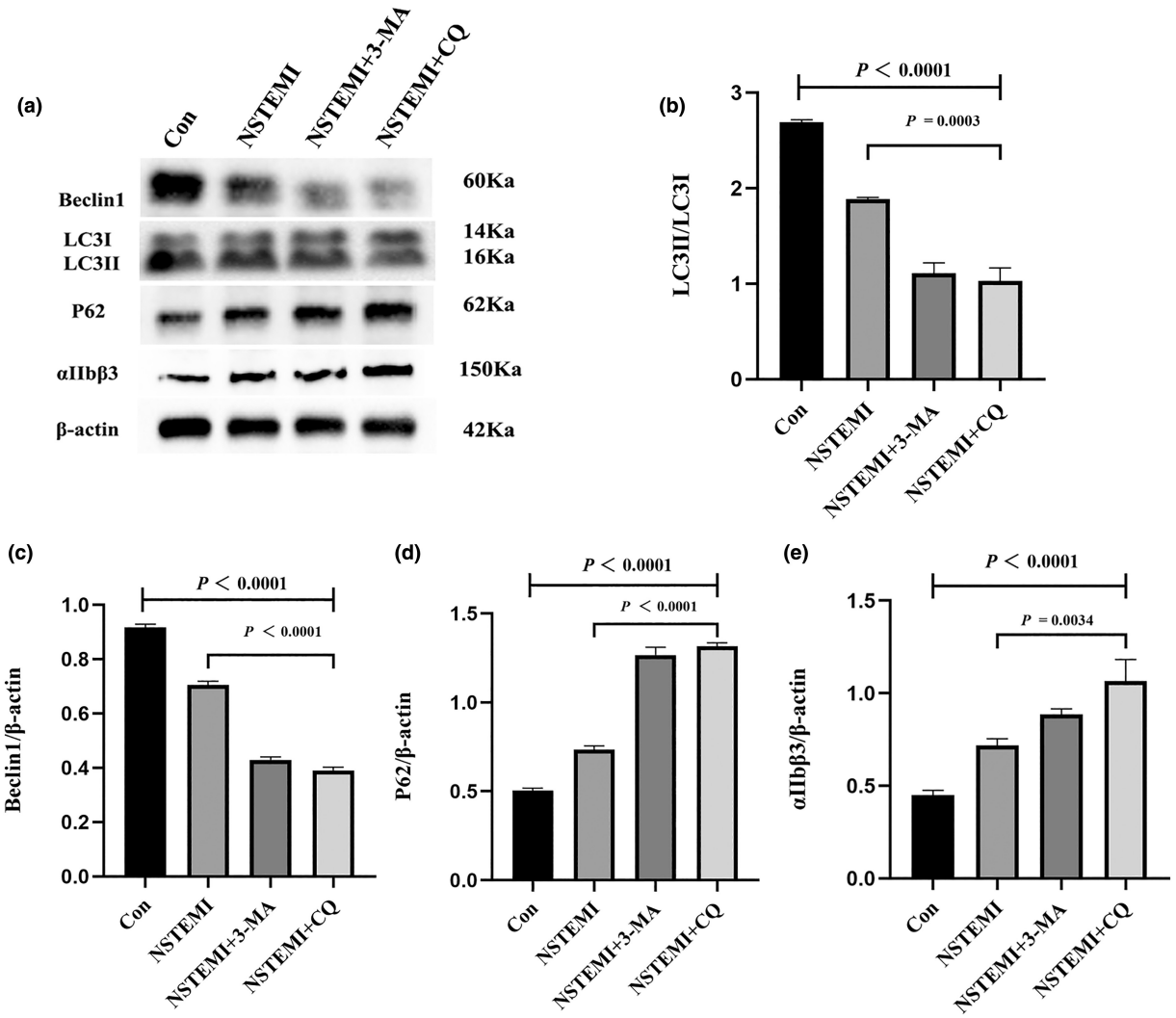

FIGURE 3 3-methylpurine (3-MA) and chloroquine (CQ) further promote platelet activation. After the application of 3-MA and CQ (a), the levels of P62 (d) and αIIbβ3 (e) were further increased, and the levels of Beclin1 (c) and LC3II/LC3I (b) were further decreased. Western blot analysis data are represented as mean ± SD ($n = 3$); $p < 0.05$ indicates a statistical difference.

influencing factors of NSTEMI thrombus types, its specific mechanism could need to be further discussed in the future.

As one of the primary constituents of thrombus, platelets have a significant association with thrombosis by participating in its initiation and enlargement process.[16] In the pathological state, the excessive release of platelet factors can lead to abnormal platelet aggregation which could induce excessive thrombosis, particularly the formation of intra-arterial thrombus and microthrombus.[17] Therefore, antiplatelet therapy is crucial in preventing and treating thrombotic diseases.[18,19] It has been found[20] that one of the prerequisites of cardiovascular thrombotic events is the activation of platelets. And several studies[21-23] have confirmed that platelet activation involves multiple signaling pathways. Among these pathways, integrin αIIbβ3 (αIIbβIII), a receptor found on the platelet membrane, was highly abundant and crucial in the entire process of platelet activation. Platelet activation was only triggered when αIIbβ3 bound to fibrinogen, enhancing each agonist's activation effect to its respective receptor. Therefore, this protein served as the final pathway for platelet activation. In this research, we found that compared with the red thrombus group, patients in the white thrombus group had more significant activation of αIIbβ3 and its platelet aggregation rate was higher. In addition, we also found that the expression of αIIbβ3 in platelets of STDMI patients was significantly higher than that of STUMI patients. Maybe this could also explain why white thrombus is more common in STDMI. However, which signaling pathway might regulate the activation of αIIbβ3 still needs further exploration.

Recent studies have revealed the presence of autophagy in platelets.[24,25] It maintains its normal physiological function through autophagy. Autophagy is the primary mechanism of cell degradation, enabling cells to survive starvation and other stress conditions by promoting the isolation and

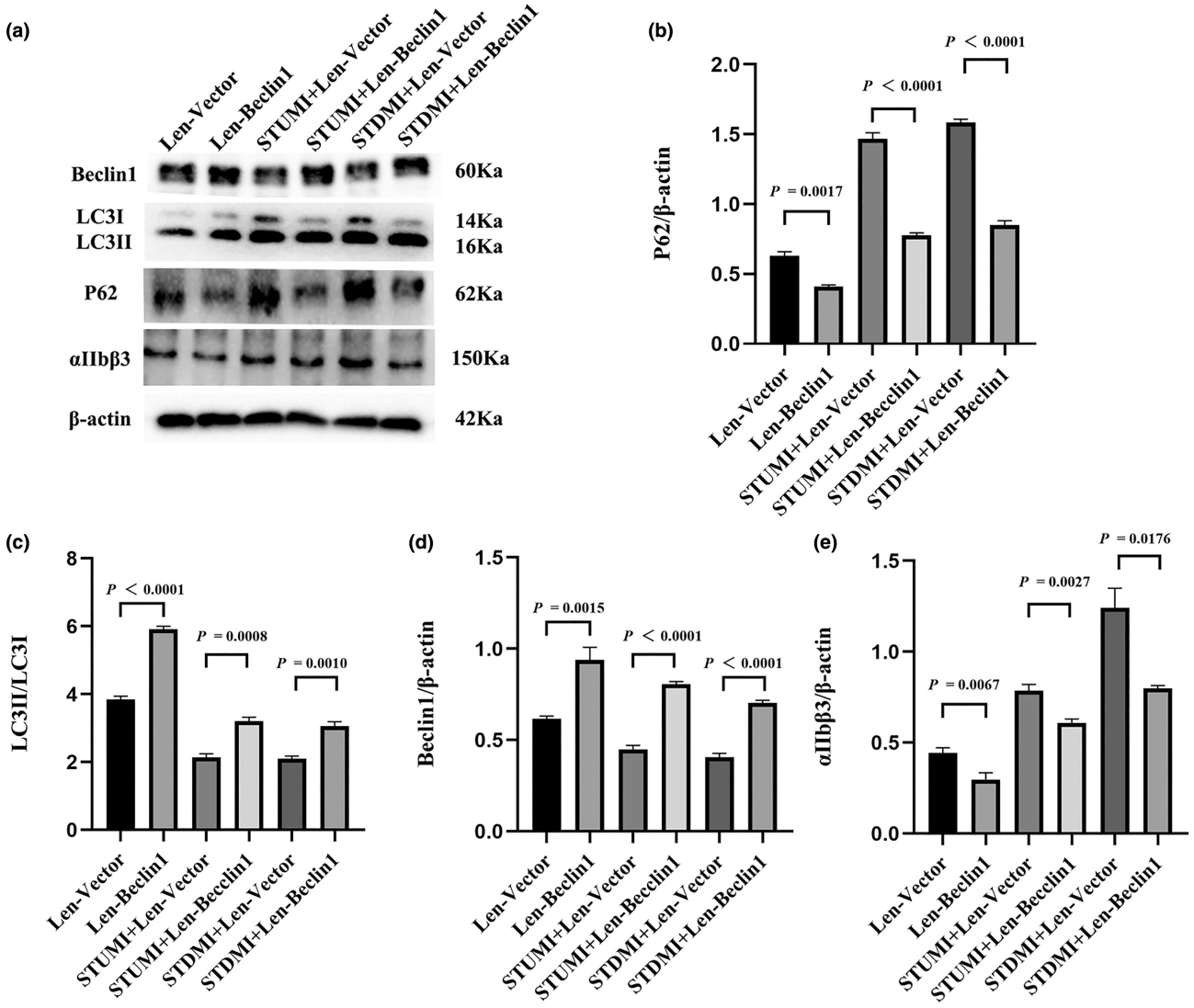

FIGURE 4 The regulatory role of Beclin1 overexpression on platelet activation in patients with NSTEMI. The effect of Beclin1 overexpression on platelet activation in patients with different types of NSTEMI (a), Western blot analysis of Beclin1 (d), LC3II/LC3I (c), P62 (b), and αIIbβ3 (e) protein expression and densitometric analysis in platelets from patients with different types of acute myocardial infarction. Data are mean ± SD ($n = 3$). Compared with the control group, Beclin1 overexpression upregulated the expression of LC3II/LC3I in platelets in different groups and downregulated the expression of P62, while the activity of αIIbβ3 was inhibited. $p < 0.05$ indicates a statistical difference.

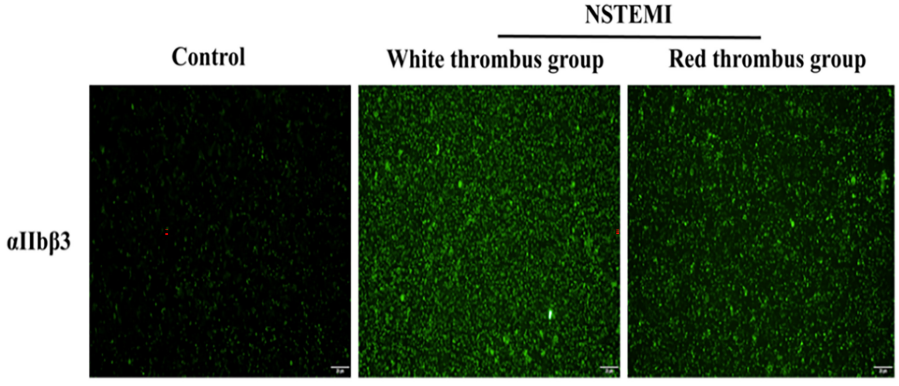

FIGURE 5 Effect of platelet activation on thrombosis in patients with NSTEMI. Compared with the healthy control group, platelet activation was significant in NSTEMI patients, while platelet activation in the white thrombus group was more evident than in the red thrombus group in NSTEMI patients.

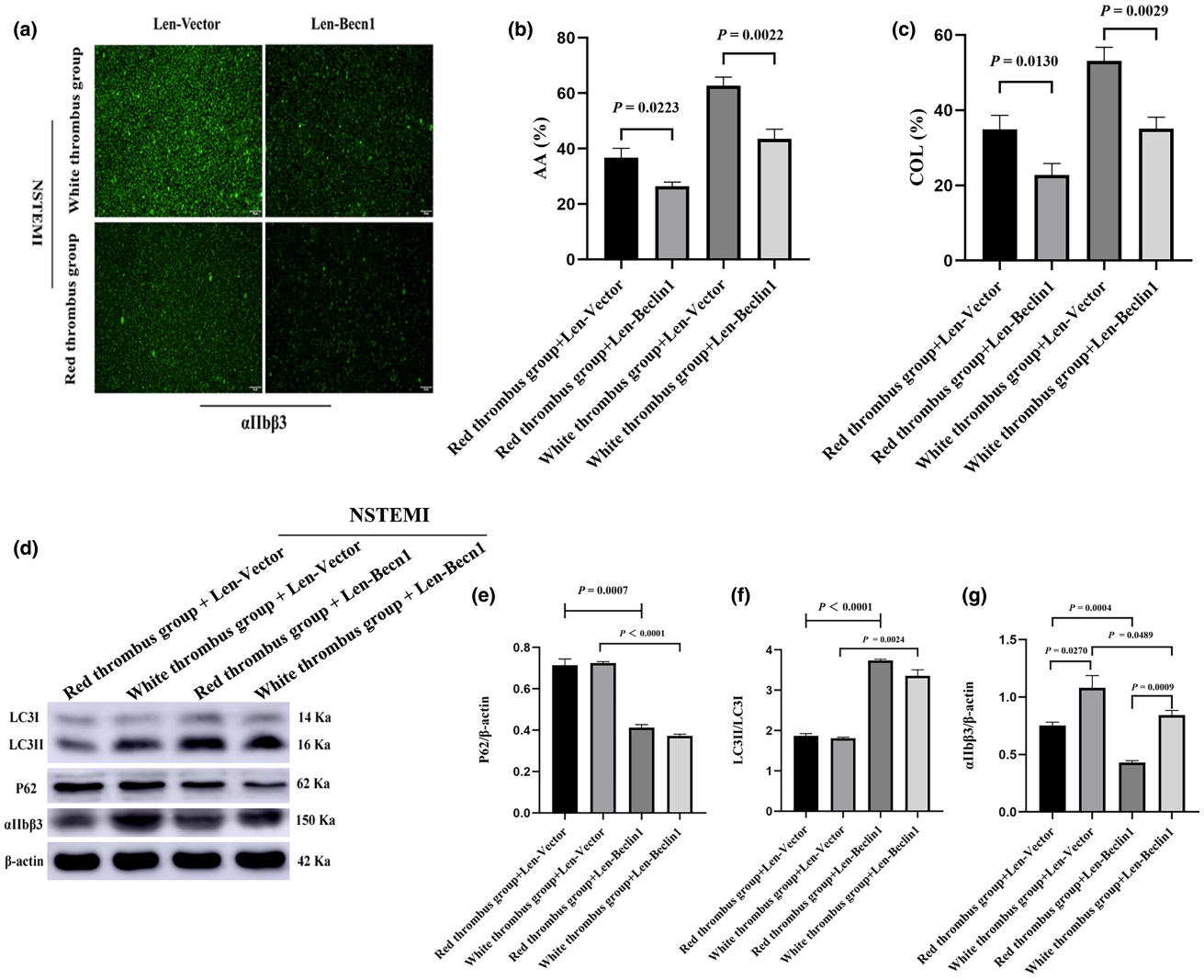

FIGURE 6 The regulatory role of Beclin1 on platelet activation in NSTEMI patients with different types of thrombi. (a) Platelets transfected with Beclin1 overexpression lentivirus significantly inhibit the expression of αIIbβ3 compared with the Len-Vector group, and the inhibition is more significant in the red thrombus group than in the white thrombus group. (b, c) The average platelet aggregation rates induced by arachidonic acid (AA) and collagen (COL) in each groups. Compared with the Len-Vector group, the platelet aggregation rate in the Len-Beclin1 group decreased significantly. (d) The effect of Beclin1 overexpression on platelet activation in different thrombus types in NSTEMI. Beclin1 overexpression upregulates the expression of LC3 (f) in platelets in different groups and downregulates the expression of P62 (e), while the activity of αIIbβ3 (g) is inhibited, more significantly in the red thrombus group than in the white thrombus group. Data are represented as mean ± SD ($n = 3$), $p < 0.05$ indicates statistical difference.

degradation of many cytoplasms, damaged organelles (such as mitochondria), and protein aggregates.[26] Simultaneously, autophagy can moderately enhance cellular tolerance to hypoxia, thereby protecting cells from damage caused by changes in external conditions.[3] Ouseph et al.[27] found that platelet aggregation was significantly inhibited, and essential processes such as hemostasis and thrombosis were also affected after conditional knockout of the key autophagy gene Atg7 in platelets. Zhou et al. found that PPAR γ can inhibit platelet activation due to the inhibition of mitochondrial autophagy mediated by the FOUNDC-1 pathway. The inhibition of mitochondrial autophagy alleviates cardiac inflammation and protects against microcirculatory damage resulting from ischemia-reperfusion.[6] The myocardial infarction area of FUNDC-1 knockout rats was smaller, and the platelet P-selectin and aggregation rate were lower than those of the wild type, and these differences were not influenced by time. The experimental results showed that platelet mitochondrial autophagy could protect cardiomyocytes from hypoxia-reperfusion injury.[28] As autophagy might be crucial in platelets' activation, aggregation, adhesion, and even overall thrombus formation, we detected the level of platelet autophagy in each group. The results showed that compared with healthy controls, the expression of autophagy-related gene proteins Beclin1 and LC3II/LC3I in platelets of patients with different types of NSTEMI was downregulated, while the expression of P62 and αIIbβ3 protein was upregulated. This indicated that platelet activation

in NSTEMI was accompanied by the depression of autophagy, especially in patients with STDMI. So was there some correlation between the two? To further verify this conjecture, we pre-treated platelets with commonly used autophagy inhibitors 3-methyladenine (3-MA) and chloroquine (CQ) and found that the levels of autophagy-related proteins LC3II/LC3I and Beclin1 were further inhibited, while the level of P62 was further elevated. In contrast, the expression of αIIbβ3 protein was further enhanced. These results suggested that the blockage of autophagy might aggravate platelet activation in NESTEMI.

As one of the earliest mammalian autophagy-related proteins, Beclin1 (Becn1) plays an important role in the autophagy process and is closely related to the occurrence and progression of various diseases.[29,30] Previous studies have found that Beclin1 plays an important protective role in cardiomyocytes against ischemia-reperfusion injury.[31,32] However, the role of Beclin1 in regulating intracoronary thrombosis during platelet activation remains unclear. In this study, we constructed Beclin1 overexpression lentivirus to transfect platelets, aiming to induce platelet autophagy activation and investigate its impact on platelet activation in NSTEMI. We initially assessed transfection efficiency by monitoring green fluorescence emitted by the lentivirus. Subsequently, we evaluated mRNA and protein expression levels of Beclin1 to confirm successful infection. Next, Beclin1 overexpression lentivirus was introduced into distinct groups. The findings of this study demonstrated that Beclin1 overexpression effectively heightened platelet autophagy levels in NSTEMI. Notably, when compared with the Len-Vector group, the Len-Beclin1 group exhibited significantly reduced levels of αIIbβ3. Moreover, in patients presenting diverse thrombus types, Beclin1 overexpression not only markedly attenuated αIIbβ3 expression but also mitigated platelet aggregation rates. Particularly noteworthy was the observation that αIIbβ3 protein expression was notably suppressed in the red thrombus group compared with the white thrombus group. Our results suggested a correlation between various thrombus types and platelet aggregation in NSTEMI, potentially regulated by autophagy. The overexpression of Beclin1 appears to inhibit platelet activation and aggregation by activating platelet autophagy to a certain degree. Nevertheless, the precise molecular mechanisms governing thrombosis, platelet activation, and autophagy in NSTEMI remain elusive and warrant further investigation.

CONCLUSION

In summary, the findings of this study revealed the presence of red thrombus in a subset of patients with NSTEMI. The proportion of red thrombus was found to be higher in patients with ST segment un-offset. Among different types of thrombus populations, the average platelet aggregation rate was higher in patients with white thrombus than in patients with red thrombus. There is a relationship between Beclin1-mediated autophagy and platelet activation and aggregation in various thrombosis forms. The overexpression of Beclin1 can influence platelet aggregation and activation, which may establish a novel cellular and molecular biological foundation for future clinical treatment, presenting Beclin1 as a potential therapeutic target.

AUTHOR CONTRIBUTIONS

L.M. and W.S. wrote the manuscript. Y.C., S.D. and W.S. designed the research. Y.C., S.D., W.S., L.M., J.L., H.W., Z.D., Q.H., and Y.K. performed the research. L.M. and J.L. analyzed the data.

FUNDING INFORMATION

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests for this work.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

ETHICS STATEMENT

The present study was approved by the Medical Ethics Committee of Henan Provincial People's Hospital (approval no. 2020-158).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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