

Elevated circulating inflammatory biomarker levels in the SIRT1-NF- κ B-sCD40L pathway in patients with acute myocardial infarction: a case-control study

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ABSTRACT

Background: Inflammation plays a key role in atherosclerosis development and progression. However, the role of novel inflammatory biomarker pathways, namely the SIRT1-NF- κ B-sCD40L, in the etiopathogenesis of human atherosclerosis remains undefined. This study was designed to evaluate the changes and clinical implications of these inflammatory mediators in the plasma of patients with acute myocardial infarction (AMI).

Methods: The peripheral arterial blood of 88 participants (68 patients with AMI and 20 age-matched controls), was drawn prior to performing coronary angiography (CAG). The SIRT1, NF- κ B, and sCD40L plasma levels were quantified using ELISA. Spearman's analysis was used to evaluate the correlation between the three inflammatory markers, while Pearson's test assessed their potential correlation with cardiac troponin T (TNT) levels. Sensitivity, specificity, and area under the ROC curve (AUC) were calculated as measures of diagnostic accuracy.

Results: Patients with AMI showed higher levels of circulating SIRT1, NF- κ B, and sCD40L compared to the age-matched controls ($p < 0.05$). However, the plasma concentrations of these three inflammatory mediators did not differ between the ST-segment elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI) patients. Additionally, in patients with AMI, the SIRT1 level was positively correlated with NF- κ B and sCD40L levels ($p < 0.001$). Likewise, the levels of SIRT1, NF- κ B and sCD40L were positively correlated with TNT levels ($p < 0.001$). More importantly, the ROC analysis showed that the diagnostic accuracy of AMI was significantly higher when NF- κ B or sCD40L level was used in combination with TNT levels ($p < 0.05$).

Conclusions: The levels of the circulating inflammatory biomarkers, including SIRT1, NF- κ B, and sCD40L, were significantly elevated in patients with AMI. These novel biomarkers can improve the diagnostic accuracy of AMI when combined with TNT.

KEY MESSAGES

- AMI is a potentially lethal CAD and is the leading cause of mortality and morbidity worldwide. Inflammation plays a key role in atherosclerosis development and progression. The levels of the circulating novel inflammatory biomarkers, including SIRT1, NF- κ B, and sCD40L, were significantly elevated in patients with AMI.
- The SIRT1 level was positively correlated with NF- κ B and sCD40L levels in patients with AMI.
- The levels of SIRT1, NF- κ B and sCD40L were positively correlated with TNT levels.
- The ROC analysis showed that the diagnostic accuracy of AMI was significantly higher when NF- κ B or sCD40L level was used in combination with TNT levels.
- SIRT1/NF- κ B/sCD40L axis inhibition is a potential new target for AMI treatment.

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1. Introduction

Acute myocardial infarction (AMI) is a potentially lethal coronary atherosclerotic heart disease (CAD) and is the leading cause of mortality and morbidity worldwide [1].

AMI is classified as ST-segment elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI) depending on the ST segment elevation in the electrocardiogram. Outcomes in these patients remain a challenge despite improved diagnostic (high-sensitivity cardiac TNT) and

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treatment modalities, such as primary percutaneous coronary intervention (pPCI) [2]. Risk stratification remains problematic, and the identification of novel predictors is crucial for improved outcomes [2]. Presently, an urgent need for identifying novel biomarkers exists, which aids in early diagnosis, precise risk stratification, and personalized treatment, thereby reducing cardiovascular events and improving prognosis.

Atherosclerosis is a chronic immuno-inflammatory disease that involves lipid accumulation in the large arteries [3,4]. The presence of inflammation plays a crucial role in the etiopathogenesis of atherosclerosis, and inflammatory mediators synergistically facilitate the occurrences of acute events [3,5]. Increased inflammatory activity is associated with the progression of stable coronary disease and a higher risk of AMI [5]. Nevertheless, the role of inflammatory mediators in AMI remains unclear, and thus far, routine measurement of inflammatory markers is not supported by the current international guidelines.

Silence information regulator 2-related enzyme 1 (SIRT1), also known as a longevity factor, is known to delay cardiovascular aging, including the development of atherosclerosis, by inhibiting oxidative stress and inflammation [6–8]. The SIRT1 deacetylation targets are key components of the intracellular inflammatory response [9–11]. However, the association of the SIRT1 plasma levels with AMI requires further elucidation.

Transcription factor nuclear factor- κ B (NF- κ B) is the central regulator of inflammatory reaction, and its activation is closely related to the pathogenesis of atherosclerosis [12–14]. NF- κ B is involved in numerous pathological processes of atherosclerosis, including foam cell formation, vascular inflammation, vascular smooth muscle cell proliferation, arterial calcification, and plaque progression [12]. Conversely, inhibition of NF- κ B signaling prevents atherosclerosis formation. SIRT1 interacts with NF- κ B p65 and inhibits transcription *via* deacetylation of p65 in response to tumor necrosis factor- α (TNF- α) [15–18]. Thus, the SIRT1/NF- κ B inflammation axis plays a crucial role in the pathogenesis of atherosclerosis.

Soluble CD40 ligand (sCD40L) represents the activation of the CD40-CD40L signaling pathway, and its upregulation accelerates the progression of chronic inflammatory diseases, such as atherosclerosis [19–24]. sCD40L levels are elevated in CAD [25–28], and it has been proposed as a biomarker of atherothrombosis [23,29]. The expression of CD40 is known to be regulated by the SIRT1/NF- κ B pathway [30–33]. The SIRT1-NF- κ B-sCD40L pathway, comprising novel inflammatory biomarkers, may play a crucial role in atherosclerosis development and progression.

Therefore, this case-control study was designed to evaluate the plasma levels of the SIRT1/NF- κ B/sCD40L axis in patients with AMI. Furthermore, the diagnostic specificity and sensitivity of these novel biomarkers for AMI were analyzed and compared with the classic myocardial injury marker cardiac troponin T (TNT).

2. Materials and methods

2.1. Design and population

This case-control study comprised 88 adults participated who were divided into two groups: the AMI group ($n=68$, including STEMI [$n=44$] and NSTEMI [$n=24$] patients), and an age-matched control group ($n=20$) comprising patients without any established cardiovascular disease. The included patients with AMI were recruited at the Second Affiliated Hospital of Shantou University Medical College according to the following inclusion criteria. 1) Patients undergoing AMI Management with or without ST-segment elevation per the ESC guidelines [1,34], i.e. myocardial ischemia with myocardial necrosis, which is defined as cardiac TNT elevation and 2) angiography showing obstructive coronary artery disease. The age-matched control group participants were recruited according to the following inclusion criteria: 1) patients without any established cardiovascular diseases, such as heart failure, previous MI, stroke, or CAD, but presenting with at least one modifiable cardiovascular risk factor, such as smoking habits, hypertension, dyslipidemia, or type 2 diabetes mellitus. The exclusion criteria were: (a) patients with acute and chronic infectious diseases, a history of tumor, or nervous system disorders; (b) patients with acute pulmonary embolism, acute aortic syndrome, peripheral vascular embolism, or stroke; (c) patients with severe liver and kidney failure; (d) those with severe cardiac insufficiency; and (E) patients with a history of recent surgery or trauma.

All individuals provided written informed consent and the study protocol complied with the Declaration of Helsinki. The study was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Shantou University Medical College (permit number: 2018-18).

2.2. Sampling and laboratory analysis

Prior to coronary angiography (CAG), arterial blood samples were collected in clean heparin anticoagulant tubes and centrifuged at 2–8°C for 15 min at 1000 \times g immediately after collection. Subsequently, the separated plasma was centrifuged for an additional 10 min at 10,000 \times g for

complete platelet separation. Lastly, all plasma samples were stored at -80°C for further evaluation.

SIRT1 (Catalog Number Q96EB6, USA R&D Systems, Inc.), NF- κ B (Catalog Number ab176648, USA Abcam Systems, Inc.) and sCD40L (Catalog Number P29965, USA R&D Systems, Inc.) concentrations were assayed using a commercial Human ELISA kit. All samples were subjected to at least three relatively independent repeated experiments.

TNT levels were measured using a sandwich electrochemiluminescence immunoassay in the Department of Laboratory Medicine (Elecsys TNT, Cobas h232 instrument; Roche Diagnostics). Serum creatinine (SCr), blood urea nitrogen (BUN), and blood lipid levels were also analyzed, and the patient's sex and relevant medical history, including smoking, hypertension, and diabetes mellitus, were recorded at admission.

2.3. Statistical analysis

Continuous variables were presented as mean \pm standard deviation (SD) or median (interquartile range, IQR). Between-group comparisons were performed using a student's *t*-test or Mann-Whitney *U*-test. Categorical variables were expressed as numbers and percentages and compared using the Pearson chi-square test or Fisher's exact test. Correlation analysis were performed using Pearson's test or Spearman's test. Data were analyzed using IBM SPSS statistics v.19 software.

Table 1. Comparison of the clinical characteristics between patients with AMI and adults with cardiovascular risk factors (age-matched controls).

Variables	AMI group (<i>n</i> = 68)	Age-matched control group (<i>n</i> = 20)	<i>P</i> -value
Age (mean \pm SD) (year)	62.94 \pm 11.42	60.55 \pm 9.89	0.40
Gender, male, <i>n</i> (%)	45.00 (66.20)	9.00 (45.00)	0.09
Cardiovascular risk factors, <i>n</i> (%)			
Diabetes mellitus	16.00 (23.50)	3.00 (15.00)	0.54
Hypertension	46.00 (67.65)	11.00 (55.00)	0.29
Current smoker	40.00 (58.80)	8.00 (40.00)	0.14
Laboratory values [mean (IQR)]			
TC (mmol/l)	5.12 (4.36–6.00)	4.70 (4.24–5.50)	0.18
TG (mmol/l)	1.51 (0.99–1.88)	1.53 (1.03–1.96)	0.61
HDL-C (mmol/l)	1.10 (0.94–1.26)	1.16 (0.99–1.44)	0.14
LDL-C (mmol/l)	3.47 (2.80–4.07)	3.23 (2.73–3.85)	0.35
Apo-A1 (g/l)	1.24 (1.12–1.34)	1.33 (1.21–1.44)	0.07
Apo-B (g/l)	0.96 (0.81–1.14)	0.85 (0.77–1.05)	0.09
BUN (mmol/l)	5.68 (4.04–6.62)	4.60 (3.68–5.54)	0.08
SCr (μ mol/l)	95.89 (77.60–104.40)	81.41 (69.98–93.30)	0.04
Hs-CRP (mg/l)	14.86 (2.81–15.49)	3.89 (0.45–4.63)	0.02
TNT (ng/l)	326.50 (60.75–1361.25)	<40.00	<0.001

Abbreviations: Apo-A1: apolipoprotein A1; Apo-B: apolipoprotein B; BUN: blood urea nitrogen; HDL-C: high-density lipoprotein-cholesterol; Hs-CRP: high-sensitivity C reaction protein; LDL-C: low-density lipoprotein-cholesterol; SCr: serum creatinine; TC: total cholesterol; TG: triglycerides; TNT: troponin T.

MedCalc 16.8.4 statistical software was used to analyze the diagnostic accuracy of the factors by drawing the receiver operating characteristic curves (ROC) and area under the ROC curve (AUC), and the 95% confidence interval (CI) was described. The DeLong test was used to compare the AUCs. A *P* value of <0.05 indicated statistical significance.

3. Results

3.1. Participants characteristics

The 88 inpatients were divided into an AMI group (*n* = 68, including STEMI [*n* = 44] and NSTEMI [*n* = 24]) and an age-matched control group (*n* = 20) based on clinical data and CAG results. The clinical characteristics and biochemical parameters of the participants are shown in Table 1 and Supplementary Material. Patients with AMI showed higher TNT (326.50 [60.75–1361.25] vs. <40 ng/L, $p < 0.001$), Hs-CRP (14.86 [2.81–15.49] vs. 3.89 [0.45–4.63] mg/mL, $p = 0.02$) and SCr (95.89 [77.60–104.40] vs. 81.41 [69.98–93.30] μ mol/L, $p = 0.04$) levels compared to the age-matched control group. There were no significant differences in age, sex, smoking history, presence of hypertension and diabetes mellitus, and blood lipid level between the two groups ($p > 0.05$).

3.2. Circulating SIRT1, NF- κ B, and sCD40L levels

Compared with the age-matched controls, patients with AMI showed higher circulating levels of SIRT1 (60.03 \pm 4.80 vs. 36.44 \pm 1.32 ng/ml, $p = 0.0097$; Figure 1A), NF- κ B (331.20 \pm 54.81 vs. 186.80 \pm 43.71 pg/ml, $p < 0.0001$; Figure 1B), and sCD40L (131.30 \pm 17.30 vs. 47.63 \pm 4.61 pg/ml, $p = 0.0108$; Figure 1C). These results are consistent with the changes in Hs-CRP, which is a key inflammatory factor in atherosclerotic cardiovascular diseases. However, a subgroup analysis showed no difference in the plasma concentrations of these three inflammatory mediators between the STEMI and NSTEMI patients ($p > 0.05$, Figure 2). It is worth noting that compared with the age-matched controls, the levels of circulating inflammatory biomarker levels in the SIRT1-NF- κ B-sCD40L pathway were significantly elevated both in STEMI and NSTEMI patients ($p < 0.05$, Figure 2).

3.3. Correlation between SIRT1, NF- κ B, and sCD40L levels

The results of the Spearman's correlation analysis showed that SIRT1 levels were correlated with NF- κ B ($r = 0.58$, $p < 0.001$; Figure 3A) and sCD40L ($r = 0.38$,

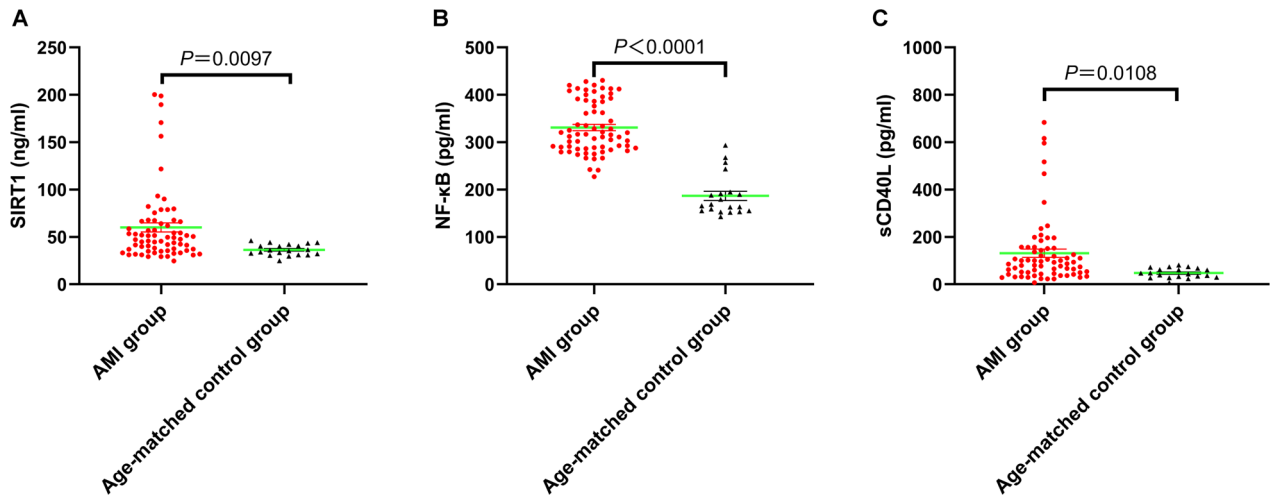


Figure 1. Comparison of the circulating levels of the SIRT1/NF-κB/sCD40L axis between AMI patients and age-matched controls using student's *t*-test. (A). SIRT1, (B). NF-κB, and (C). sCD40L.

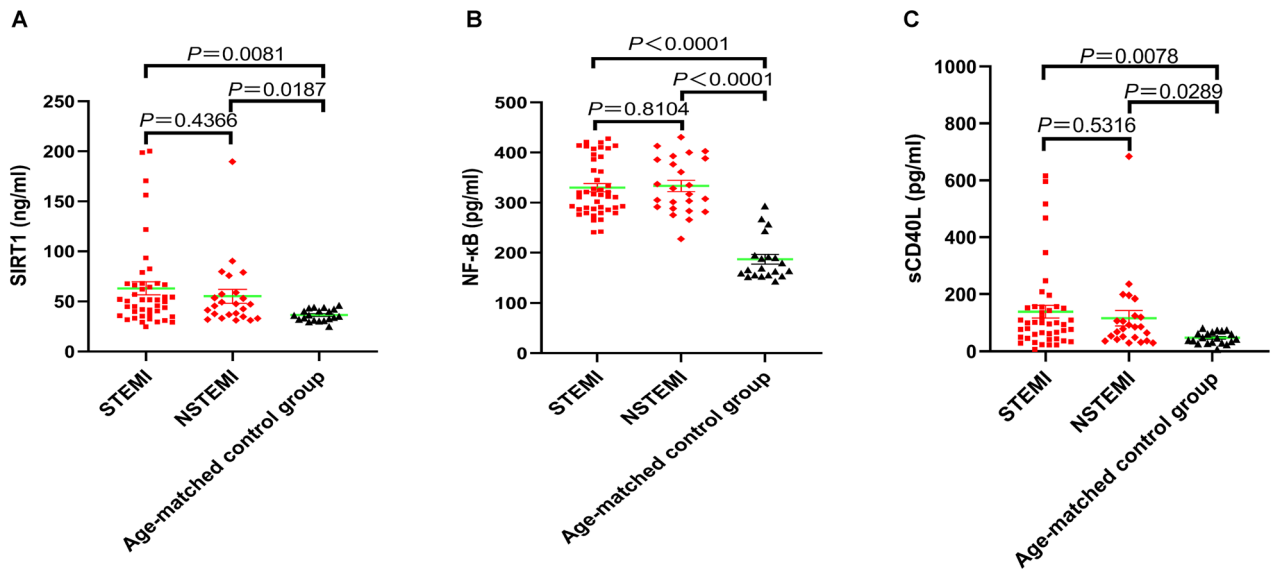


Figure 2. Subgroup analysis of the plasma concentrations of the SIRT1/NF-κB/sCD40L axis using ANOVA combined with student's *t*-test. (A). SIRT1, (B). NF-κB, and (C). sCD40L.

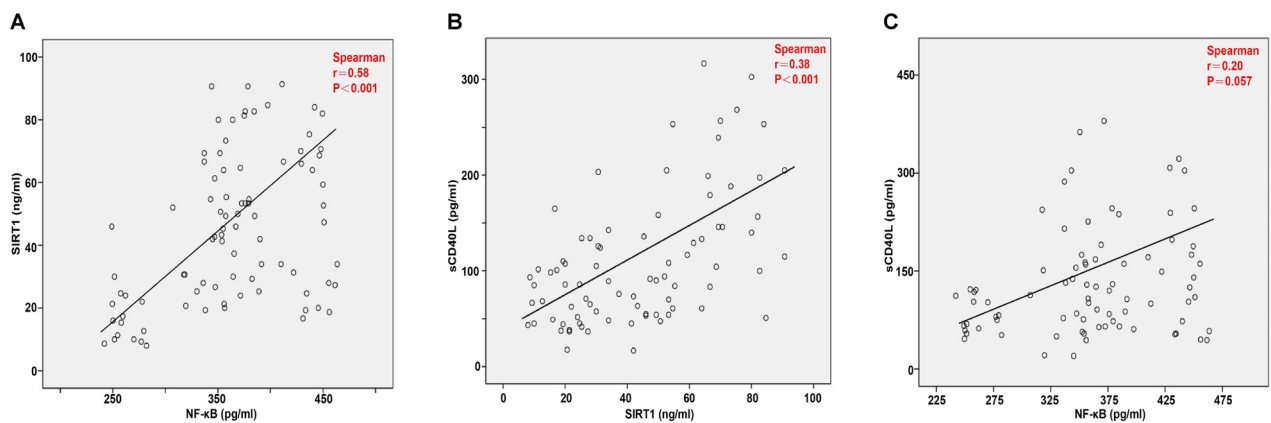


Figure 3. Correlation analysis between the concentration of the three factors of the SIRT1/NF-κB/sCD40L axis using spearman's rank correlation analysis. (A). between SIRT1 and NF-κB, (B). between SIRT1 and sCD40L, (C). between NF-κB and sCD40L.

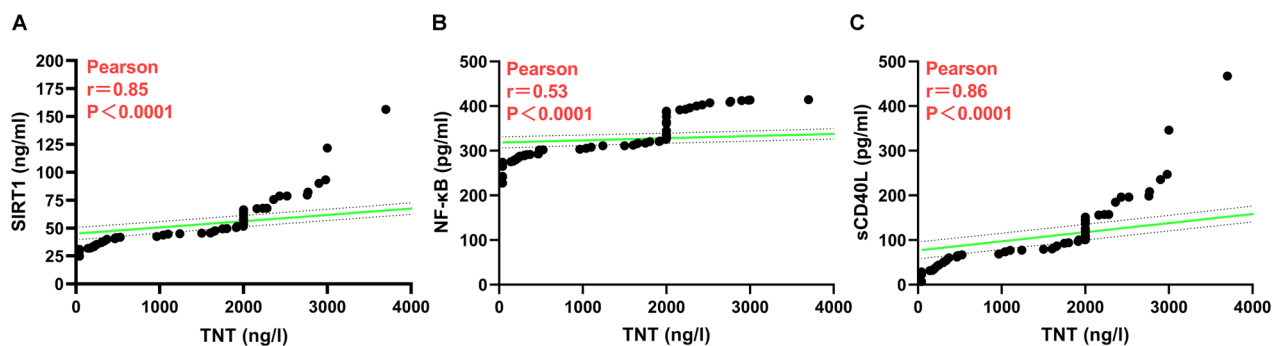


Figure 4. Correlation analysis of the SIRT1/NF- κ B/sCD40L axis with TNT levels using Pearson's correlation analysis. (A). between SIRT1 and TNT, (B). between NF- κ B and TNT, (C). between sCD40L and TNT.

$p < 0.001$; Figure 3B) levels. Notably, the correlation between NF- κ B and sCD40L levels was not significant ($r = 0.20$, $p = 0.057$; Figure 3C).

3.4. Correlation of SIRT1, NF- κ B and sCD40L levels with TNT levels

As shown in Figure 4, the results of Pearson's correlation analysis showed that SIRT1 ($r = 0.85$, $p < 0.0001$; Figure 4A), NF- κ B ($r = 0.53$, $p < 0.0001$; Figure 4B) and sCD40L ($r = 0.86$, $p < 0.0001$; Figure 4C) levels were positively correlated with TNT levels. The above results indicate that the elevated levels of these inflammatory cytokines contribute to the diagnosis of AMI.

3.5. Diagnostic accuracy of TNT alone and in combination with NF- κ B and sCD40L

For evaluating the usefulness of these inflammatory mediators as potential biomarkers for identifying patients with AMI, ROC curves were constructed. In Figure 5, the AUCs of NF- κ B and sCD40L for predicting AMI occurrence were 0.97 (95% CI: 0.92–0.99) and 0.76 (95% CI: 0.66–0.85), respectively. The AUCs for these two inflammatory mediators were > 0.75 ; thereby suggesting their utility as biomarkers. Compared with the AUC of TNT (0.95, 95% CI: 0.88–0.99), the laboratory gold standard for diagnosing AMI, NF- κ B showed comparable sensitivity and specificity to TNT (Z-score: 0.85, $p = 0.39$); however, the diagnostic value of sCD40L was significantly lower than TNT (Z-score: 3.36, $p = 0.0008$).

The results of the logistic regression analysis showed that compared with using TNT alone, NF- κ B combined with TNT (NF- κ B+TNT) had a significantly increased AUC (0.99, 95% CI: 0.96–1.00; $p = 0.0107$), thereby indicating a higher diagnostic value of NF- κ B+TNT than that of TNT alone. Similarly, the AUC (0.99, 95% CI: 0.93–0.99; $p = 0.0240$) of sCD40L combined with TNT (sCD40L+TNT) was also significantly increased

compared to TNT alone, suggesting a higher diagnostic value of sCD40L+TNT compared to TNT alone.

4. Discussion

To the best of our knowledge, the present study is the first to explore the changes in the circulating inflammatory mediators SIRT1, NF- κ B, and sCD40L levels in patients with AMI. Three important findings were noted in this study. 1) the plasma concentrations of SIRT1, NF- κ B, and sCD40L were measured before pPCI and their levels were significantly increased compared to the age-matched controls. 2) SIRT1 changes were positively correlated with NF- κ B and sCD40L level changes; nevertheless, the correlation between the NF- κ B and sCD40L levels was statistically insignificant. 3) The levels of SIRT1, NF- κ B and sCD40L were positively correlated with TNT levels. 4) NF- κ B and TNT had comparable sensitivity and specificity, and their combination significantly improved the diagnostic value of AMI. The inflammatory mediators comprising the SIRT1/NF- κ B/sCD40L axis have possible use as novel biomarkers for AMI, and targeted regulation of this axis may reduce acute cardiovascular event incidences and improve patient prognosis.

SIRT1 is a nicotinamide adenine dinucleotide (NAD⁺) dependent class III deacetylase [35,36]. The biological effects of SIRT1, such as longevity regulation, delaying cardiovascular aging, including atherosclerosis formation, by inhibiting oxidative stress and inflammation, can be attributed to its deacetylation function [6–8,35,36]. SIRT1 is downregulated in atherosclerotic plaques in patients and atherosclerotic animal models [37–40]. Overexpression of SIRT1 (endothelial cell-specific) is protective against atherosclerosis [41]; however, SIRT1 knockdown (smooth muscle cell-specific) has shown increased atherosclerosis formation in *ApoE* knockout mice [38]. Treatment of *ApoE* knockout mice with SRT3025, a small molecule activator of SIRT1,

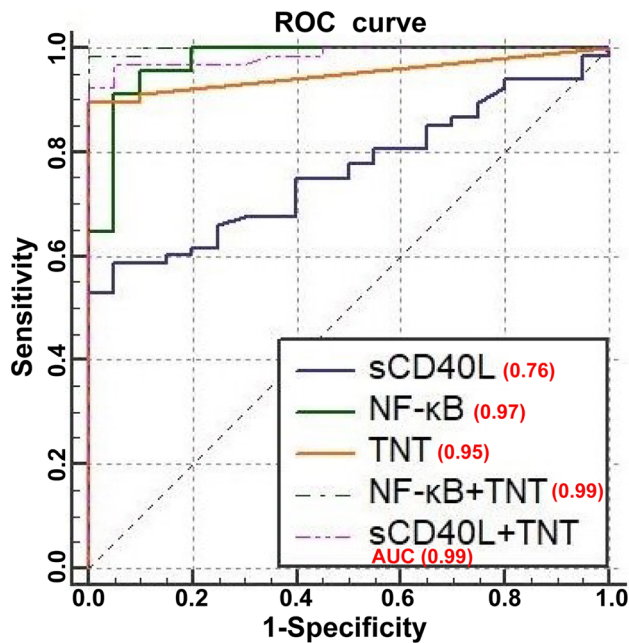


Figure 5. Receiver operating characteristic (ROC) curves of potential biomarkers for the diagnosis of AMI. The ROC analysis and area under the ROC curve (AUC) are shown for NF-κB and sCD40L alone and combined with TNT.

showed significant atherosclerosis reduction [42]. However, transgenic mice with systemically overexpressed SIRT1 showed more severe dyslipidemia and atherosclerosis when put under an atherogenic diet [43]. This indicates that SIRT1 can have anti-atherosclerotic and pro-atherosclerotic effects. In the present study, the circulating SIRT1 level was significantly increased in patients with AMI. However, this result is in contrast to that of Breitenstein et al. who found reduced SIRT1 expression in the peripheral blood monocytes of patients with CAD [39]. These differences may be attributed to the different types of CAD, and AMI belongs to a type of unstable CAD. Previous studies have confirmed that inflammation, oxidative stress, and aging can increase SIRT1 expression [44–46], which could be a compensatory mechanism against the adverse effects of ischemia. Additionally, heart-specific overexpression of SIRT1 in mice showed that moderate expression (up to 7.5-fold) of SIRT1 retards aging and protects the heart from oxidative stress, whereas high levels (12.5-fold) of SIRT1 increase oxidative stress and apoptosis [45]. This indicates that SIRT1's cardioprotective effect is related to its expression level in the heart.

SIRT1 interacts with the NF-κB p65 and inhibits the transcription of p65 through deacetylation [15–18]. NF-κB is a central regulator of inflammatory reaction, and its activation is closely related to the pathogenesis of atherosclerosis [12–14]. Furthermore, it is involved in all stages of atherosclerosis, including early

atherosclerotic lesion formation, plaque progression, and advanced atherosclerosis [14]. NF-κB promotes the expression of multiple proinflammatory (*TNF-α*, *IL-1β*, and *IL-6*) and proadhesive genes (*MCP1*, *ICAM-1*, and *VCAM-1*) in endothelial cells [12–14], thereby inducing endothelial dysfunction, which is a crucial initial factor in early atherosclerotic lesion formation. Recently, Karunakaran et al. reported that RIPK1 primarily drives NF-κB-dependent inflammation activation in early atherosclerotic lesion formation [47]. Conversely, studies on *ApoE* knockout mice have shown that endothelial cell-specific inhibition of NF-κB reduces and stabilizes atherosclerotic plaques [48,49]. Furthermore, clinical NF-κB1 promoter gene polymorphism or mutation has been reported to be closely related to CAD susceptibility and prognosis [50–52]. Subsequent meta-analyses further supported this conclusion [53,54], suggesting that the NF-κB signaling pathway, *via* its pro-inflammatory mechanisms, is related to CAD pathogenesis and progress. Consistent with these results, we found that the NF-κB plasma concentration in patients with AMI was higher than that in the age-matched controls. The results of Spearman's correlation analysis showed that the SIRT1 level was positively correlated with NF-κB. The levels of SIRT1 and NF-κB were positively correlated with TNT levels. Moreover, NF-κB and TNT were found to have comparable sensitivity and specificity and their combination could significantly improve the diagnostic accuracy of AMI.

The expression of CD40 can be regulated by the SIRT1/NF-κB pathway [30–33]. sCD40L represents the activation of the CD40-CD40L signaling pathway, and its upregulation can accelerate chronic inflammatory disease progress [23]. Accumulating evidence indicates that the CD40-CD40L system plays a crucial role in atherosclerosis occurrence and development [19–24]. The effect of CD40L on the size of atherosclerotic lesions remains controversial in animal models [55]. Some studies have shown that blocking CD40L *via* gene knockout or antibodies, can reduce the lesion size [56–58]; whereas, other studies found no effect on the lesion size [59,60]. Fortunately, recent studies have confirmed that CD40L cell-specific knockout can reduce experimental atherosclerosis. Bosmans et al. found that myeloid-specific CD40-deficient reduces atherosclerosis by preventing macrophage pro-inflammatory polarization [61]. Additionally, T cell-specific and dendritic-cell-specific CD40L deficiency also reduces atherosclerosis in mice [29]. Nevertheless, platelet-specific CD40L deficiency has not been found to have any effect on atherosclerotic plaque burden and is only involved in atherothrombosis [29]. These newly recent consistently confirm that CD40L has cell-specific roles in atherosclerosis.

Likewise, the clinical correlation between sCD40L and atherosclerosis remains controversial. sCD40L is elevated in CAD [25–28], and its levels are significantly higher in patients with acute coronary syndrome than in patients with stable angina [62]. Moreover, the sCD40L level is positively correlated with multi-vessel lesions and high-burden thrombus formation in the coronary artery [63]. Nevertheless, some studies found no correlation between sCD40L and CAD. de Lemos et al. found a negligible correlation between sCD40L and hyperlipidemia and no correlation between sCD40L and subclinical atherosclerosis [64]. Notably, a study published by Gergeri et al. found no correlation between sCD40L levels and 1-year cardiovascular mortality [65]. The significant correlation between sCD40L levels and cardiovascular mortality was only identified in a subgroup analysis of patients with CAD and heart failure with preserved ejection fraction [65]. Briefly, most of the existing clinical studies have shown that the sCD40L level is closely related to CAD, especially in acute cardiovascular events and unstable atherosclerotic plaques. sCD40L has been considered as a biomarker of atherothrombosis [23,29], which may be attributed to its key role in platelet activation and thrombosis [66,67]. Consistent with the above results, the present study also found that the sCD40L plasma levels were significantly elevated in patients with AMI. The results of the Spearman's correlation analysis showed that the SIRT1 level was positively correlated with sCD40L. Moreover, the levels of sCD40L were positively correlated with TNT levels. The diagnostic accuracy of sCD40L alone is lower than that of TNT. However, a combination of sCD40L and TNT had significantly improved diagnostic value.

This had some limitations. Firstly, to rule out the effect of iodine-containing contrast agents on inflammatory mediators, this study only selected peripheral arterial blood samples from subjects before CAG and did not dynamically observe changes in the SIRT1/NF- κ B/sCD40L axis. Secondly, due to strict screening, the sample size was relatively small, and this was a single-center study. Therefore, it is necessary to establish a large sample database; conduct multicenter, randomized, controlled trials; and obtain more data to form an evaluation consensus.

5. Conclusion

To the best of our knowledge, this study is the first to demonstrate that the levels of circulating inflammatory biomarkers of the SIRT1/NF- κ B/sCD40L axis were significantly elevated in patients with AMI. The levels of

SIRT1, NF- κ B and sCD40L were positively correlated with TNT levels. When combined with TNT, these novel biomarkers can improve the diagnostic accuracy of AMI. Targeted regulation of inflammatory mediators or blocking related pathways can reduce cardiovascular events in patients with AMI, thereby improving patient prognosis. Therefore, SIRT1/NF- κ B/sCD40L axis inhibition is a potential new target for AMI treatment.

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Ethics approval and consent to participate

The study was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Shantou University Medical College (permit number: 2018-18). All subjects provided a written consent form.

Consent for publication

Not applicable.

Authors' contributions

C. Chen and W. Yu designed this program. M. Zheng and W. Wang conducted the data collection and analysis. M. Zheng produced the manuscript which was checked by W. Yu. All authors read and approved the final manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

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

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