Research Reports in Clinical Cardiology

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

# Clinical Application of PINK1 and ACSL4 Protein Levels in the Acute Myocardial Infarction Patients and Prognosis Evaluation After PCI

Wei Ao[1], Ping Duan[2], Ping Luo[1], Dikai Xiang[1], Qin Wang[1], Yanjiao Ren[1], Qiwei He[1]

[1]Department of Cardiology, Yueyang People's Hospital, Hunan Normal University, Yueyang City, Hunan Province, 414000, People's Republic of China; [2]Department of Cardiology, Shanghai Seventh People's Hospital, Shanghai City, 200000, People's Republic of China

Correspondence: Qiwei He, Department of Cardiology, Yueyang People's Hospital, Hunan Normal University, No. 263 Baling East Road, Yueyanglou District, Yueyang City, Hunan Province, 414000, People's Republic of China, Tel +8615173044525, Email Yueshao1990@163.com



**Objective:** To explore the clinical application of PTEN-induced kinase 1 (PINK1) and acyl-CoA synthetase long chain family 4 (ACSL4) protein levels in patients with acute myocardial infarction (AMI) and the prognosis evaluation after percutaneous coronary intervention (PCI).

**Methods:** 152 AMI patients who underwent PCI at our hospital from October 2021 to February 2023 were selected as the study group. They were divided into a MACE group (31 cases) and a non MACE group (121 cases) based on the major adverse cardiovascular events (MACE) within 28 days after PCI. Additionally, 152 angina pectoris patients admitted during the same period were selected as the control group. Measure and analyze the levels and clinical significance of PINK1 and ACSL4 proteins in all study subjects.

**Results:** The PINK1 protein level in the study group was lower than that in the control group, while the PINK1 protein level in the MACE group was lower than that in the non MACE group ($P<0.05$), while the ACSL4 protein level was the opposite ($P<0.05$); PINK1 expression was negatively correlated with SYNTAX score ($r=-0.602$, $P<0.05$), while ACSL4 expression was positively correlated with SYNTAX score ($r=0.683$, $P<0.05$); Age, LVEF, and ACSL4 were risk factors for poor prognosis in AMI patients after PCI, while PINK1 was a protective factor ($P<0.05$); The combined prediction of PINK1 and ACSL4 for the postoperative prognosis of AMI patients after PCI was superior to the individual detection of PINK1 and ACSL4 ($P<0.05$).

**Conclusion:** The expression levels of PINK1 and ACSL4 are related to the occurrence of AMI, and their combined detection has high predictive power for the prognosis of AMI patients after PCI.

**Keywords:** acute myocardial infarction, PTEN-induced kinase 1, Acyl-CoA synthetase long chain family 4, percutaneous coronary intervention, prognosis

## Introduction

Acute myocardial infarction (AMI) is caused by the acute occlusion of the coronary arteries leading to ischemic myocardial necrosis. In recent years, its incidence rate has shown a rising trend year by year.[1,2] Most AMI is caused by the progress of coronary atherosclerosis, and heart failure in the end stage of AMI is the main cause of disability and death.[3] However, the recent emergence of the novel coronavirus pneumonia can also cause abnormal systemic inflammatory response, atherosclerotic plaque rupture and coagulation system abnormalities, which promote the occurrence of AMI. Percutaneous coronary intervention (PCI) is currently a common clinical treatment for AMI. PCI can reconstruct myocardial blood flow channels, effectively saving ischemic myocardium, thereby reducing the risk of patient death.[4] Statistics show that the treatment rate of PCI for AMI is over 50%, to some extent increasing the survival time of patients. However, some patients experience complications such as myocarditis and heart failure after undergoing PCI,[5,6] severely affecting their health and quality of life. Therefore, finding specific indicators that can diagnose, assess, and predict the prognosis of AMI patients is of great significance. PTEN-induced kinase 1 (PINK1) is a signaling protein.

Received: 28 November 2023
Accepted: 17 May 2024
Published: 4 June 2024

A large number of studies have shown that PINK1 can participate in various intracellular mitochondrial-related signaling pathways, playing a role in regulating mitochondrial energy metabolism, mitochondrial division, and other biological processes. It is closely related to the development of malignant tumors, inflammatory diseases, and other conditions.[7,8] Acyl-CoA synthetase long-chain family 4 (ACSL4), as the key enzyme in the first step of fatty acid degradation metabolism, is primarily related to ferroptosis. Its expression level affects lipid oxide metabolism and intracellular iron accumulation, and is often used to reflect the body's iron metabolism status, which is related to cell damage and the progression of related diseases. Therefore, the expression level of ACSL4 can also be used to diagnose and assess the occurrence and progression of related diseases.[9,10] Based on this, this study measured and analyzed the protein levels of PINK1 and ACSL4 in patients with AMI and analyzed their clinical significance for AMI. In order to improve the accuracy of predicting the prognosis of AMI patients, thereby improving clinical treatment outcomes and patient prognosis.

# Research Subjects and Methods

## Research Subjects

In this study, 152 acute myocardial infarction (AMI) patients who underwent PCI in our hospital from October 2021 to February 2023 were enrolled in the study group. Their ages ranged from 50 to 80 years, with an average age of 70.33 ±6.32 years. Inclusion criteria: (1) Meet the related diagnostic criteria for AMI;[11] (2) Nucleic acid tests were performed before admission and the results were negative; (3) First onset of the disease; (4) Indicated for PCI surgery; (5) Both the patient and their families agreed to participate in the study and signed an informed consent form. Exclusion criteria: (1) Those with a history of coronary stent placement; (2) Those with congenital heart disease, myocarditis, and other heart diseases; (3) Patients with functional impairments of vital organs such as lungs, liver, and kidneys; (4) Those with malignant tumors; (5) Those with immune system, blood system, and other systemic diseases. The patient underwent preoperative antiplatelet therapy, angiotensin converting enzyme inhibitors, and statin therapy. Additionally, 152 patients with angina pectoris treated in our hospital during the same period were selected as the control group, both groups tested negative for COVID-19 for SARS-CoV-2. The AMI patients in the study group were further divided into MACE group (31 patients) and non-MACE group (121 patients) based on whether they experienced major adverse cardiovascular events (MACE) within 28 days post-PCI. Among them, there were 2 cases of cardiac death (6.45%), 5 cases of congestive heart failure (16.13%), 6 cases of recurrent angina (19.35%), 8 cases of non fatal recurrent myocardial infarction (25.80%), 5 cases of severe arrhythmia (16.13%), and 5 cases of another revascularization (16.13%). See Figure 1.

## Research Methods

### Data Collection

All participants' age, gender, body mass index (BMI), smoking history, drinking history, hypertension, diabetes, left ventricular ejection fraction (LVEF), SYNTAX score and clinical data such as stent diameter during PCI were collected.

### Determination of PINK1 and ACSL4 Protein Levels

Fasting venous blood (5 mL) was collected from all study subjects on the day after admission, centrifuged at 3500 r/min for 5 minutes, the upper layer serum was collected and stored in a −80°C refrigerator until tested. Total RNA in the serum was extracted using the Trizol reagent (Beijing Quanjinsijin Biotechnology Co., Ltd.), and the purity and concentration of RNA were measured with a spectrophotometer (UV3200, Shanghai Jingke Industry Co., Ltd.). RNA was reverse transcribed into cDNA using the PrimeScript miRNA cDNA Synthesis reverse transcription kit (TaKaRa, Japan). PCR amplification was carried out according to the instructions of the ChamQ Universal SYBR qPCR Master Mix (Catalog number: Q711-02, Takara). The PCR reaction conditions were: denaturation at 95°C for 1 min, 95°C for 15s, 60°C for 1 min, for 40 cycles. GAPDH was used as an internal reference, and the 2-ΔΔCt method was used to calculate the expression levels of PINK1 and ACSL4. The primer sequences are shown in Table 1.

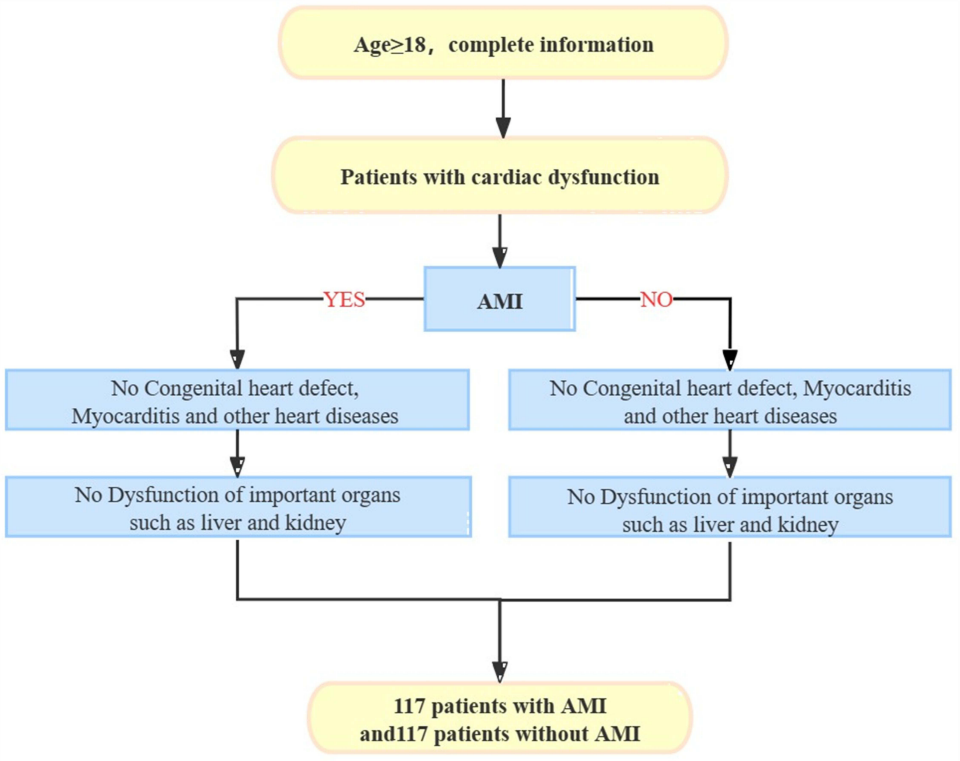


**Figure 1** Case Collection Flowchart.

## Statistical Methods

Categorical data are presented as n (%), and the chi-square test was used for intergroup comparison of categorical data. Measurement data are expressed as ($\bar{x} \pm S$), and the LSD-*t* test was used for comparisons between two groups. The correlation between the expression levels of PINK1 and ACSL4 in serum and SYNTAX score was analyzed by Pearson method. Multivariate logistic regression analysis was applied to evaluate the factors affecting the prognosis of patients with acute myocardial infarction (AMI) after PCI surgery. The predictive ability of serum PINK1 and ACSL4 on the post-PCI prognosis in AMI patients was assessed using the receiver operating characteristic (ROC) curve, and the area under the curve (AUC) was compared using the *Z*-test. $P<0.05$ was considered statistically significant. Data were processed using SPSS 25.0 software.

# Results

## Comparison of PINK1 and ACSL4 Protein Levels Between Two Groups

The study group had lower PINK1 protein levels compared to the control group, while ACSL4 levels and SYNTAX score were also lower than the control group (P<0.05). Refer to Table 2.

**Table 1** Primer Sequences

| Primers | Primer Sequences |
|---|---|
| PINK1 | F:5′-CCATC-CATCTAAGTTCTA-3′ |
| | R:5′-AAGAGTATAGT-GACAAGTA-3′ |
| ACSL4 | F:5'-GAAGGCGGCATTATTAGA-3' |
| | R:5'-ATGTCCGAAGGAGTTGGT-3' |
| GAPDH | F:5'-GGTGAAGGTCGGAGTCAACG-3' |
| | R:5'-CAAAGTTGTCATGGATGACC-3' |

**Table 2** Comparison of PINK1, ACSL4 Protein Levels and SYNTAX Score Between Two Groups ($\bar{x} \pm S$)

| Group | Number of Cases | PINK1 | ACSL4 | SYNTAX Score (Scores) |
|---|---|---|---|---|
| Control group | 152 | 1.02±0.05 | 1.01±0.03 | 18.66±2.49 |
| Study group | 152 | 0.82±0.11 | 1.12±0.26 | 25.90±3.57 |
| *t* | | 20.407 | 5.182 | 20.508 |
| *P* | | <0.001 | <0.001 | <0.001 |

## Correlation Analysis of PINK1 and ACSL4 Levels and Their Correlation with SYNTAX Score

Pearson's analysis indicated that the PINK1 and ACSL4 protein levels in the study group were negatively correlated (r=−0.637, P<0.05). Moreover, PINK1 expression was negatively correlated with SYNTAX score (r=−0.602, P<0.05), while ACSL4 expression was positively correlated with SYNTAX score (r=0.683, P<0.05). See Figure 2 and Table 3.

## Comparison of PINK1 and ACSL4 Protein Levels in AMI Patients with Different Prognostic Outcomes

In the MACE group, the PINK1 protein level was lower than in the non-MACE group, while ACSL4 expression was higher than the non-MACE group ($P$<0.05). Refer to Table 4.

## Analysis of Factors Related to Post-PCI Prognostic Outcomes in AMI Patients

Univariate analysis showed that factors such as gender, BMI, smoking history, alcohol consumption history, hypertension, diabetes, the number of stents implanted during PCI, and stent diameter were not associated with post-PCI prognosis ($P$>0.05). However, there was a statistically significant difference in age and LVEF between the two groups ($P$<0.05). See Table 5.

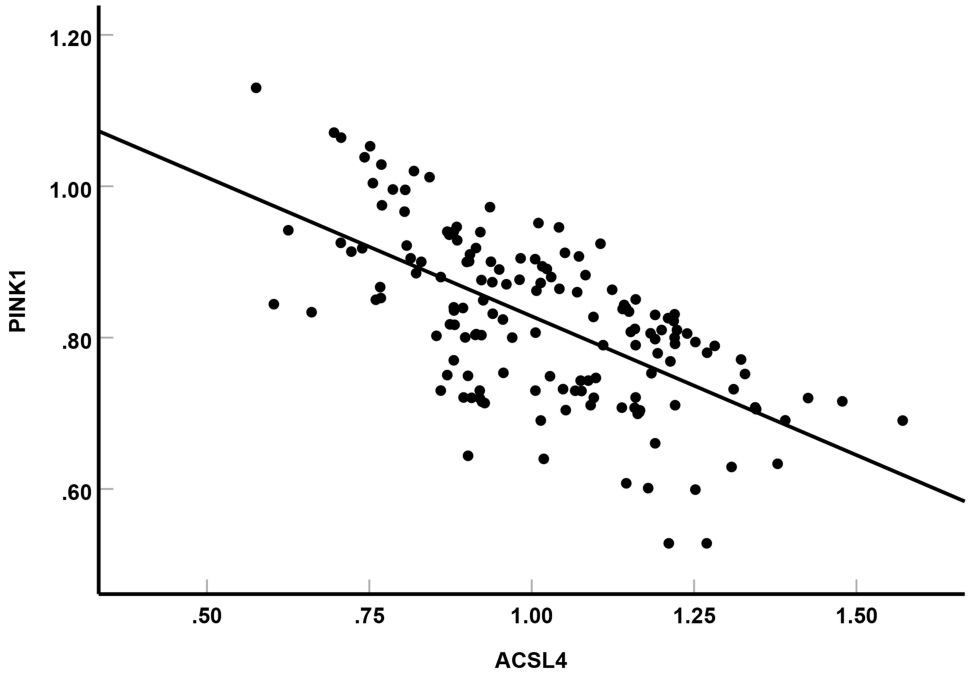


**Figure 2** Correlation analysis of PINK1 and ACSL4 protein levels.

**Table 3** Correlation Analysis Between PINK1 and ACSL4 Protein Levels and SYNTAX Score

| | SYNTAX Score (Scores) | |
|---|---|---|
| | *r* | *P* |
| PINK1 | −0.602 | <0.001 |
| ACSL4 | 0.683 | <0.001 |

**Table 4** Comparison of PINK1 and ACSL4 Protein Levels in Acute Myocardial Infarction Patients with Different Prognosis States ($\overline{x} \pm S$)

| Group | Number of Cases | PINK1 | ACSL4 |
|---|---|---|---|
| MACE group | 31 | 0.71±0.07 | 1.33±0.33 |
| Non MACE group | 121 | 0.85±0.12 | 1.07±0.24 |
| *t* | | 6.220 | 4.958 |
| *P* | | <0.001 | <0.001 |

**Table 5** Analysis of Relevant Factors Affecting the Prognosis of Patients with Acute Myocardial Infarction [$\overline{x} \pm S/n(\%)$]

| Index | Number of Cases | MACE Group (n=31) | Non MACE Group (n=121) | $\chi^2/t$ | *P* |
|---|---|---|---|---|---|
| Age (years) | | | | | |
| <65 | 71 | 9 (12.68) | 62 (87.32) | 4.889 | 0.027 |
| ≥65 | 81 | 22 (27.16) | 59 (72.84) | | |
| Gender | | | | | |
| Male | 90 | 17 (18.89) | 73 (81.11) | 0.308 | 0.579 |
| Female | 62 | 14 (22.58) | 48 (77.42) | | |
| BMI (kg/m$^2$) | | | | | |
| <22 | 54 | 11 (20.37) | 43 (79.63) | 0.000 | 0.996 |
| ≥22 | 98 | 20 (20.41) | 78 (79.59) | | |
| Smoking history | | | | | |
| Yes | 78 | 14 (17.95) | 64 (82.05) | 0.590 | 0.442 |
| No | 74 | 17 (22.97) | 57 (77.03) | | |
| Drinking History | | | | | |
| Yes | 108 | 25 (23.15) | 83 (76.85) | 1.742 | 0.187 |
| No | 44 | 6 (13.64) | 38 (86.36) | | |
| Hypertension | | | | | |
| Yes | 98 | 19 (19.39) | 79 (80.61) | 0.172 | 0.678 |
| No | 54 | 12 (22.22) | 42 (77.78) | | |
| Diabetes | | | | | |
| Yes | 44 | 7 (15.91) | 37 (84.09) | 0.767 | 0.381 |
| No | 108 | 24 (22.22) | 84 (77.78) | | |
| LVEF (%) | | 58.44±6.39 | 54.22±5.62 | 3.626 | <0.001 |
| Number of stents implanted | | | | | |
| Single pieces | 92 | 19 (20.65) | 73 (79.35) | 0.010 | 0.922 |
| Multiple pieces | 60 | 12 (20.00) | 48 (80.00) | | |
| Support diameter (mm) | | 3.17±0.61 | 3.22±0.72 | 0.355 | 0.723 |

**Table 6** Multivariate Logistic Regression Analysis of Relevant Factors Affecting the Prognosis of Patients with Acute Myocardial Infarction

| Index | β | SE | Wald | *P* | OR | 95% CI |
|---|---|---|---|---|---|---|
| Age | 0.572 | 0.222 | 6.641 | 0.010 | 1.772 | 1.147~2.738 |
| LVEF | 0.638 | 0.292 | 4.776 | 0.029 | 1.893 | 1.068~3.355 |
| PINK1 | −0.612 | 0.186 | 10.844 | 0.001 | 0.542 | 0.376~0.780 |
| ACSL4 | 0.452 | 0.207 | 4.775 | 0.029 | 1.572 | 1.048~2.359 |

## Multivariate Logistic Regression Analysis on Factors Affecting the Prognosis of AMI Patients Post-PCI

Taking the post-PCI prognostic status in AMI patients as the dependent variable (MACE=1, non-MACE=0) and using age (≥65 years=1, <65 years=0), LVEF (actual value), PINK1 (actual value), and ACSL4 (actual value) as independent variables, logistic regression analysis showed that age, LVEF, and ACSL4 are risk factors for poor prognosis in AMI patients, while PINK1 acts as a protective factor ($P$<0.05). Refer to Table 6.

## Analysis of the Predictive Ability of PINK1 and ACSL4 for Prognostic Status in AMI Patients

ROC curve analysis indicated that the AUC for predicting the prognostic status of AMI patients by PINK1 and ACSL4 alone were 0.800 and 0.772, respectively. The combined detection AUC was 0.872, which was superior to either PINK1 or ACSL4 alone (ZCombination of the two-PINK1=2.228, ZCombination of the two-ACSL4=3.010, P=0.022, 0.002). See Figure 3 and Table 7.

# Discussion

Acute myocardial infarction (AMI) is primarily caused by sudden myocardial ischemia and hypoxia due to coronary artery abnormalities. It has a higher incidence rate among the elderly population. AMI has a rapid onset and severe condition; therefore, its clinical treatment outcomes tend to be poor. Both the disability and mortality rates among

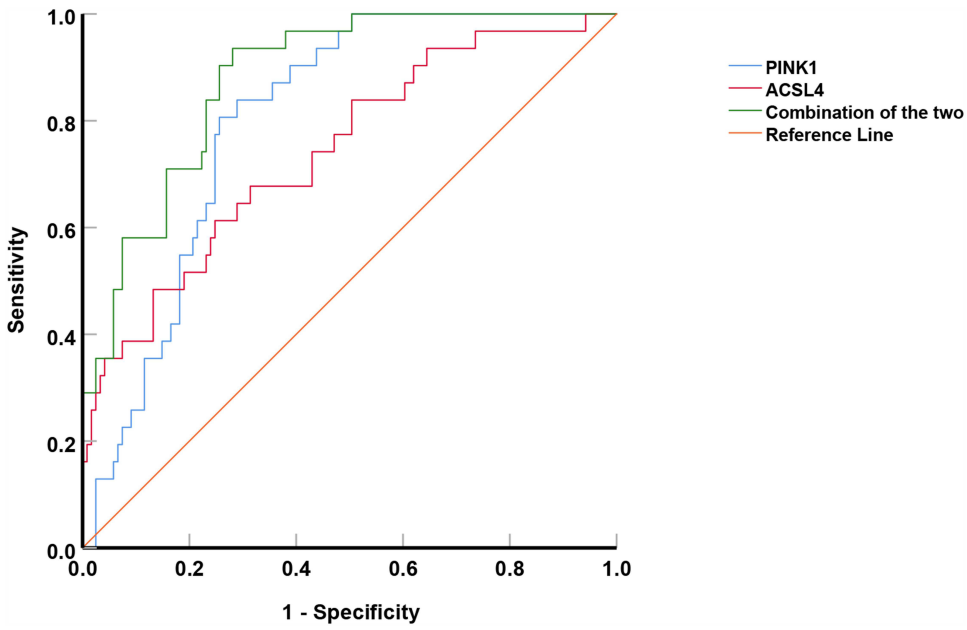


**Figure 3** Receiver operating characteristic of PINK1 and ACSL4 in predicting the prognosis of patients with acute myocardial infarction.

**Table 7** Analysis of Predictive Efficacy of PINK1 and ACSL4 in Predicting the Prognosis of Patients with Acute Myocardial Infarction

| Variable | AUC | Cut-off value | 95% CI | Sensitivity (%) | Specificity (%) | Youden index |
|---|---|---|---|---|---|---|
| PINK1 | 0.800 | 0.77 | 0.727~0.860 | 80.65 | 74.38 | 0.550 |
| ACSL4 | 0.772 | 1.18 | 0.697~0.836 | 77.42 | 71.07 | 0.484 |
| Combination of the two | 0.872 | - | 0.808~0.921 | 90.32 | 70.25 | 0.605 |

patients are high, which significantly impacts the quality of life for the patients and their families.[12,13] Currently, the commonly used Percutaneous Coronary Intervention (PCI) procedure can quickly restore blood flow to the occluded artery, reduce the infarcted area, thereby relieving the ischemic state of the myocardium in AMI patients, playing a vital role in reducing the short-term mortality rate of AMI. However, some patients may experience ventricular remodeling after PCI, with related nerves activated, increased inflammation response, leading to complications such as pneumonia and heart failure, which can also pose a threat to patients' health.[14,15] At present, T-ProBNP, GDF15 and other biomarkers commonly used in clinical practice are susceptible to multiple factors such as autoimmune system disorders and inflammation, and the prediction accuracy is low.[16] Therefore, it is particularly important to find specific factors that can assist in diagnosis and prediction of the prognosis of patients with acute myocardial infarction. In view of such patients and conditions, this study mainly discussed the expression levels of PINK1 and ACSL4 in patients with acute myocardial infarction and their clinical significance, aiming to improve the early diagnosis rate of acute myocardial infarction, predict the prognosis of patients after PCI, and provide intervention to improve the therapeutic effect and prognosis of patients. As relevant studies have shown that there is a significant difference in postoperative mortality between PCI performed during non-working hours and normal working hours, all patients included in this study were performed PCI by doctors who were on duty that day or had the operation time and doctors determined in advance.

PINK1 is an essential member of the serine/threonine kinase family. Relevant studies have shown that abnormal expression of PINK1 can disrupt mitochondrial structure and function, subsequently affecting the onset and progression of various diseases, including tumors.[17] In this study, the protein level of PINK1 in the study group of AMI patients was lower than that of the control group ($P<0.05$). Furthermore, the PINK1 protein level in the MACE group, who experienced cardiovascular adverse events within 28 days post-PCI, was also lower than that in the non-MACE group ($P<0.05$), and PINK1 expression was negatively correlated with SYNTAX score ($r=-0.602$, $P<0.05$). These results indicate that PINK1 is not only related to the onset of AMI but its expression level is also correlated with the prognostic status of patients after PCI. This might be because a decrease in PINK1 expression can impair mitochondrial autophagy function, increasing mitochondrial activity, activating endothelial cell oxidation and stress, mediating cellular damage, apoptosis, and other physiological processes, leading to complications such as heart failure and myocarditis, thereby affecting the patient's prognostic status.[18,19] These preliminary results suggest that PINK1 might serve as a specific factor for diagnosing AMI and predicting post-PCI prognostic outcomes.

The expression level of ACSL4 is mainly associated with ferroptosis. An increase or decrease in ACSL4 activity can influence the metabolism of lipid peroxides and the accumulation of iron within cells, disrupting intracellular oxidative-reductive balance, triggering cell death, and subsequently playing a regulatory role in the onset and progression of diseases in multiple systems such as the kidneys.[20] Some researchers have found that knocking out the ACSL4 gene can inhibit iron-deficiency anemia in mice, reduce inflammation and macrophage infiltration in the kidneys,[21] and a low expression level of ACSL4 can enhance tumor ferroptosis, improve anti-tumor immunity, and is closely related to the survival rate of cancer patients.[22] Based on this, this study also measured and analyzed the expression level and clinical significance of ACSL4. The results showed that the ACSL4 level in the study group was lower than the control group ($P<0.05$), and the ACSL4 expression level in the MACE group was higher than the non-MACE group ($P<0.05$). Moreover, the correlation analysis results showed that the expression of ACSL4 was positively correlated with SYNTAX score ($r=0.683$, $P<0.05$). It is speculated that this is mainly due to the increase and decrease of ACSL4 activity, which can affect the metabolism of lipid oxides and the accumulation of intracellular iron, disrupt the intracellular redox balance, trigger cell death, and thus affect the prognosis of patients with related diseases. All these

results indicate that both ACSL4 and PINK1 are related to the onset and progression of acute myocardial infarction, and they play opposing roles. This study further analyzed the factors related to the post-PCI prognostic status of AMI patients. The results showed that there were statistically significant differences in age and LVEF between the two groups ($P<0.05$). Combined with the results of multifactorial Logistic regression analysis, age, LVEF, and ACSL4 were risk factors for adverse prognosis in AMI patients, while PINK1 was a protective factor ($P<0.05$). This is primarily because older patients have weaker immunity, drug resistance, and recovery capabilities, making them more susceptible to postoperative complications leading to adverse outcomes. The LVEF level can reflect heart function. Due to cardiac remodeling post-AMI, there is left ventricular cavity dilation. Excessive dilation can lead to left ventricular systolic and diastolic dysfunction, resulting in cardiovascular adverse events such as heart failure.[23] Finally, using the ROC curve, we analyzed the predictive efficacy of PINK1 and ACSL4 on the post-PCI prognostic status of AMI patients. The results showed that the cutoff values for predicting the prognosis of acute myocardial infarction patients after PCI using PINK1 and ACSL4 are 0.77 and 1.18, which are the critical values for predicting the patient's prognosis. This study also found that the combined detection of PINK1 and ACSL4 is superior to individual detection and had a higher predictive efficacy for the post-PCI prognosis of AMI patients.

In conclusion, the expression levels of PINK1 and ACSL4 are related to the onset of acute myocardial infarction. Their combined detection has a higher predictive efficacy for the post-PCI prognosis of AMI patients. However, as this study only observed the prognosis of patients within 28 days after surgery, follow-up will continue to be conducted to observe the survival status of patients within the next one to five years, and case collection will continue to verify the results of this study. At the same time, the specific impact mechanisms of PINK1 and ACSL4 on acute myocardial infarction and the prognosis after PCI will be further explored.

## Data Sharing Statement

Data is available from the corresponding author on request.

## Ethics Approval and Consent to Participate

The study involving human participants were reviewed and approved by the Ethics Committee of Yueyang People's Hospital, Hunan Normal University (Ethical approval number:20220617) and with the 1964 Helsinki Declaration. Written informed consent to participate in this study was provided by all participants.

## Funding

No funding was provided for this research.

## Disclosure

The authors declare no conflicts of interest in this work.

## References

1. Arora S, Stouffer GA, Kucharska-Newton AM, et al. Twenty year trends and sex differences in young adults hospitalized with acute myocardial infarction. *Circulation*. 2019;139(8):1047–1056. doi:10.1161/CIRCULATIONAHA.118.037137
2. Gulati R, Behfar A, Narula J, et al. Acute myocardial infarction in young individuals. *Mayo Clin Proc*. 2020;95(1):136–156. doi:10.1016/j.mayocp.2019.05.001
3. Ong S-B, Hernández-Reséndiz S, Crespo-Avilan GE, et al. Inflammation following acute myocardial infarction: multiple players, dynamic roles, and novel therapeutic opportunities. *Pharmacol Ther*. 2018;186:73–87. doi:10.1016/j.pharmthera.2018.01.001
4. Chen L, Han L, Luo J. Selection of percutaneous coronary intervention in elderly patients with acute myocardial infarction in tertiary hospital. *Medicine*. 2019;98(29):e16544. doi:10.1097/MD.0000000000016544
5. Yang Q, Wang Y, Liu J, et al. Invasive management strategies and antithrombotic treatments in patients with Non-ST-segment-elevation acute coronary syndrome in China: findings from the improving CCC project (Care for cardiovascular disease in China). *Circulation*. 2017;10(6):e004750.
6. Mancone M, Cavalcante R, Modolo R, et al. Major infections after bypass surgery and stenting for multivessel coronary disease in the randomised SYNTAX trial. *EuroIntervention*. 2020;15(17):1520–1526. doi:10.4244/EIJ-D-19-00208
7. Lunati A, Lesage S, Brice A. The genetic landscape of Parkinson's disease. *Rev Neurol*. 2018;174(9):628–643. doi:10.1016/j.neurol.2018.08.004
8. Truban D, Hou X, Caulfield TR, et al. PINK1, parkin, and mitochondrial quality control: what can we learn about parkinson's disease pathobiology? *J Parkinsons Dis*. 2017;7(1):13–29. doi:10.3233/JPD-160989

9. Doll S, Proneth B, Tyurina YY, et al. ACSL4 dictates ferroptosis sensitivity by shaping cellular lipid composition. *Nat Chem Biol*. 2017;13(1):91–98. doi:10.1038/nchembio.2239
10. Stoyanovsky DA, Tyurina YY, Shrivastava I, et al. Iron catalysis of lipid peroxidation in ferroptosis: regulated enzymatic or random free radical reaction? *Free Radic Biol Med*. 2019;133:153–161. doi:10.1016/j.freeradbiomed.2018.09.008
11. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). *J Am Coll Cardiol*. 2018;72(18):2231–2264. doi:10.1016/j.jacc.2018.08.1038
12. Jones DA, Wright P, Alizadeh MA, et al. The use of novel oral anticoagulants compared to vitamin K antagonists (warfarin) in patients with left ventricular thrombus after acute myocardial infarction. *Eur Heart J Cardiovasc Pharmacother*. 2021;7(5):398–404. doi:10.1093/ehjcvp/pvaa096
13. Cheng P, Han H, Chen F, et al. Amelioration of acute myocardial infarction injury through targeted ferritin nanocages loaded with an ALKBH5 inhibitor. *Acta Biomater*. 2022;140:481–491. doi:10.1016/j.actbio.2021.11.041
14. Park M-W, Kim CJ, Kim M-C, et al. A prospective, multicentre, randomised, open-label trial to compare the efficacy and safety of clopidogrel versus ticagrelor in stabilised patients with acute myocardial infarction after percutaneous coronary intervention: rationale and design of the TALOS-AMI trial. *EuroIntervention*. 2021;16(14):1170–1176. doi:10.4244/EIJ-D-20-00187
15. Ma L, Pan Y, Wu Z, et al. Effect of tegretol on oxidative stress, serum inflammatory factors, and left ventricular function in AMI patients after emergency PCI. *Comput Math Methods Med*. 2022;2022:8929058. doi:10.1155/2022/8929058
16. Tokarek T, Dziewierz A, Plens K, et al. Percutaneous coronary intervention during on- and off-hours in patients with ST-segment elevation myocardial infarction. *Hellenic J Cardiol*. 2021;62(3):212–218. doi:10.1016/j.hjc.2021.01.011
17. Yin K, Lee J, Liu Z, et al. Mitophagy protein PINK1 suppresses colon tumor growth by metabolic reprogramming via p53 activation and reducing acetyl-CoA production. *Cell Death Differ*. 2021;28(8):2421–2435. doi:10.1038/s41418-021-00760-9
18. Zhao C, Chen Z, Xu X, et al. Pink1/Parkin-mediated mitophagy play a protective role in cisplatin induced renal tubular epithelial cells injury. *Exp Cell Res*. 2017;350(2):390–397. doi:10.1016/j.yexcr.2016.12.015
19. Durga Devi T, Babu M, Mäkinen P, et al. Aggravated postinfarct heart failure in type 2 diabetes is associated with impaired mitophagy and exaggerated inflammasome activation. *Am J Pathol*. 2017;187(12):2659–2673. doi:10.1016/j.ajpath.2017.08.023
20. Li J, Cao F, Yin H-L, et al. Ferroptosis: past, present and future. *Cell Death Dis*. 2020;11(2):88. doi:10.1038/s41419-020-2298-2
21. Wang Y, Zhang M, Bi R, et al. ACSL4 deficiency confers protection against ferroptosis-mediated acute kidney injury. *Redox Biol*. 2022;51:102262. doi:10.1016/j.redox.2022.102262
22. Liao P, Wang W, Wang W, et al. CD8+ T cells and fatty acids orchestrate tumor ferroptosis and immunity via ACSL4. *Cancer Cell*. 2022;40(4):365–378.e6. doi:10.1016/j.ccell.2022.02.003
23. Ortiz VD, Türck P, Teixeira R, et al. Carvedilol and thyroid hormones co-administration mitigates oxidative stress and improves cardiac function after acute myocardial infarction. *Eur J Pharmacol*. 2019;854:159–166. doi:10.1016/j.ejphar.2019.04.024