Clinical Interventions in Aging

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

# Serum Expression of PDCD4 and ADAM10 in Elderly Patients with Atherosclerotic Acute Myocardial Infarction and Their Combined Predictive Value for Poor Prognosis

Xueliang Pei[1], Facai Cui[2], Yu Chen[3], Zhiyuan Yang[1], Zhouliang Xie[1], Yongjin Wen[1]

[1]Department of Cardiovascular Surgery, Fuwai Central China Cardiovascular Hospital, Zhengzhou, People's Republic of China; [2]Department of Clinical Laboratory, Henan Provincial People's Hospital, Zhengzhou, People's Republic of China; [3]Department of Pathology, Henan Cancer Hospital, Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, People's Republic of China

Correspondence: Xueliang Pei, Email m15515600510@163.com



**Purpose:** To investigate serum programmed cell death factor 4 (PDCD4) and a disintegrin and metalloproteinase 10 (ADAM10) expression in elderly patients with atherosclerotic acute myocardial infarction (AMI) and assess their prognostic value.

**Methods:** A retrospective analysis was conducted on 134 elderly patients with atherosclerotic AMI (disease group) and 110 healthy controls. Serum PDCD4 and ADAM10 levels were measured using ELISA. Based on prognosis, patients were divided into good prognosis (n=79) and poor prognosis groups (n=55). Clinical factors and biomarker levels were compared between groups. Logistic regression identified independent predictors of poor prognosis, and receiver operating characteristic (ROC) curves assessed predictive performance.

**Results:** Serum PDCD4 and ADAM10 levels were significantly higher in AMI patients compared with controls, and further elevated in the poor prognosis group ($P<0.05$). Poor prognosis was also associated with older age, diabetes, STEMI, larger infarct size, anterior wall infarction, higher Killip class and GRACE score, elevated NT-proBNP and hs-CRP, and reduced LVEF ($P<0.05$). Logistic regression confirmed elevated PDCD4 and ADAM10, diabetes, Killip class ≥II, GRACE score ≥140, STEMI, anterior infarction, NT-proBNP increase, and reduced LVEF as independent predictors of poor prognosis ($P<0.05$). ROC analysis showed AUCs of 0.837 for PDCD4, 0.859 for ADAM10, and 0.931 for their combination, with the combined model outperforming either marker alone ($P<0.05$).

**Conclusion:** Serum PDCD4 and ADAM10 are elevated in elderly atherosclerotic AMI patients and independently associated with poor prognosis. Combined detection may provide improved prognostic assessment, although further studies are warranted to validate these findings.

**Keywords:** PDCD4, ADAM10, elderly, atherosclerosis, acute myocardial infarction, prognosis

## Introduction

Acute myocardial infarction (AMI) is a serious cardiovascular event resulting from the rupture of atherosclerotic plaque and subsequent thrombus formation, leading to acute coronary artery occlusion and myocardial ischemic necrosis.[1] In China, with the increasing trend of population aging, the incidence of atherosclerotic AMI in the elderly population continues to rise.[2] The clinical presentation in this group is often complicated by underlying diseases and rapid progression with subtle symptoms, which may delay timely treatment.[3] Furthermore, due to diminished cardiac functional reserve and multi-system degeneration, elderly patients generally experience poorer prognoses, with significantly higher in-hospital mortality and readmission rates compared to younger individuals.[4,5]

Atherosclerosis-related AMI is influenced by multiple risk factors. Traditional risk factors include hypertension, diabetes mellitus, dyslipidemia, smoking, and family history of cardiovascular disease. In recent years, novel factors such as inflammation, oxidative stress, endothelial dysfunction, and genetic susceptibility have been recognized to further increase

Received: 1 July 2025
Accepted: 15 October 2025
Published: 2 December 2025

the risk of AMI and its adverse outcomes.[6] These findings highlight the importance of identifying reliable biomarkers that can capture both traditional and emerging mechanisms to improve risk stratification in elderly AMI patients.

Programmed cell death factor 4 (PDCD4) is a classical tumor suppressor gene first identified in the process of T-cell apoptosis. Its main function is to regulate cell proliferation, differentiation, and apoptosis by inhibiting the activity of the translation initiation factor eIF4A.[7,8] In recent years, studies have revealed that PDCD4 is not only involved in tumorigenesis but also plays an important role in various cardiovascular diseases. For example, it has been reported that PDCD4 is upregulated in myocardial ischemia-reperfusion injury models, where it promotes myocardial cell apoptosis and inflammation, with its expression positively correlated with the extent of myocardial damage.[9] Additionally, PDCD4 may contribute to cardiovascular remodeling by modulating the NF-κB signaling pathway and influencing inflammatory cytokine secretion.[10]

A disintegrin and metalloproteinase 10 (ADAM10) is a zinc-dependent transmembrane protease that plays a pivotal regulatory role in inflammation, cell adhesion, and signal transduction.[11,12] ADAM10 can cleave various receptors and ligands on the cell surface, thus participating in endothelial dysfunction, atherosclerosis development, and plaque instability.[13] Studies have shown that ADAM10 is upregulated in patients with coronary heart disease and heart failure and is closely associated with adverse clinical outcomes.[14] However, its expression characteristics and clinical significance in elderly patients with atherosclerotic AMI have not yet been systematically investigated.

In addition to clinical scores such as the Global Registry of Acute Coronary Events (GRACE) score and Killip classification, a variety of biomarkers, including cardiac troponins, B-type natriuretic peptide (BNP), high-sensitivity C-reactive protein (hs-CRP), and growth differentiation factor-15 (GDF-15), have been used to predict prognosis in AMI patients.[15] Nevertheless, the prognostic accuracy of a single biomarker remains limited, underscoring the need for novel molecular markers with complementary mechanisms.

Notably, although PDCD4 and ADAM10 have independent regulatory pathways in cardiovascular injury, both are closely related to oxidative stress, inflammatory responses, and apoptosis, and may synergistically contribute to myocardial damage in the pathogenesis and progression of AMI. Based on this, the present study retrospectively analyzed serum PDCD4 and ADAM10 levels in elderly patients with atherosclerotic AMI, explored their expression patterns and clinical predictive value for poor prognosis, and evaluated the diagnostic efficiency of their combined detection through multivariate logistic regression and ROC curve analysis. The aim is to provide theoretical support and data evidence for risk assessment and precise intervention in elderly patients with AMI.

# Materials and Methods

## Study Subjects

This was a retrospective study that included 134 elderly patients diagnosed and treated for atherosclerotic acute myocardial infarction (AMI) in the Department of Cardiology at our hospital between September 2022 and October 2024, defined as the disease group.

Inclusion criteria: (1) Met the diagnostic criteria for AMI outlined in the 2019 European Society of Cardiology (ESC) Clinical Practice Guidelines for Acute Coronary Syndromes;[16] (2) Age ≥ 65 years, regardless of gender; (3) Diagnosed with atherosclerotic lesions by coronary angiography (CAG), presenting with ≥ 70% coronary artery lumen stenosis or occlusive lesions, excluding AMI caused by non-atherosclerotic factors such as coronary artery spasm or myocardial bridging; (4) Time from first onset to hospital admission <12 h; (5) Complete clinical and follow-up data, including medical history, laboratory tests, imaging results, treatment course, and outcomes; (6) Written informed consent obtained from the patient or their legal representative.

Exclusion criteria: (1) Presence of other acute or chronic systemic diseases such as active or chronic infections, autoimmune diseases, or current immunosuppressive therapy; (2) History of malignancy or current antitumor treatment; (3) Severe hepatic or renal insufficiency; (4) Severe endocrine or metabolic disorders; (5) Underwent PCI or cardiac surgery within 48 h; (6) Severe psychiatric or cognitive disorders; (7) Previously diagnosed with non-atherosclerotic AMI; (8) Recent use of drugs that may affect PDCD4 or ADAM10 expression; (9) Severe arrhythmias that hinder accurate assessment of cardiac function and serum markers.

In addition, 110 age- and gender-matched elderly individuals who underwent health examinations at our hospital during the same period were selected as the control group. All controls had no history of cardiovascular or cerebrovascular diseases, acute inflammation, malignancy, or other major illnesses.

## Grouping Method

Based on the prognosis within six months after discharge, the disease group was further classified through telephone and outpatient follow-up. The following adverse events were recorded: recurrent myocardial infarction, cardiogenic death, hospitalization for heart failure, and severe arrhythmias. The occurrence of any one of these events was considered a poor prognosis. Accordingly, the disease group was divided into: Group A (n=79): Good prognosis; Group B (n=55): Poor prognosis.

## Clinical Data Collection

General and clinical information at admission was collected for all patients, including: Demographic data: age, gender, body mass index (BMI); History of underlying diseases: hypertension, diabetes, smoking history, drinking history; Cardiac function classification: assessed by Killip classification;[17] Electrocardiographic findings: AMI type (STEMI, NSTEMI); Laboratory tests: N-terminal pro-brain natriuretic peptide (NT-proBNP), high-sensitivity C-reactive protein (hs-CRP), left ventricular ejection fraction (LVEF), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), triglycerides (TG), systolic blood pressure (SBP), diastolic blood pressure (DBP); Infarct-related information: infarct size (≥3 leads on ECG), infarct location (anterior wall, inferior wall, anterior septal, others); Scoring system: GRACE score (calculated using data within 24 h of admission).[18]

## Detection of Serum PDCD4 and ADAM10 Levels

Fasting venous blood samples (5 mL) were collected within 24 h of admission. The distribution of sampling time from symptom onset to collection was as follows: 4–6 h (32.1%), 6–9 h (40.3%), and 9–12 h (27.6%). After centrifugation at 3000 r/min for 10 min, serum was separated and stored at –80 °C. The serum levels of PDCD4 (catalog No.: EH2218) and ADAM10 (catalog No.: EH1041) were measured using ELISA kits purchased from Wuhan Fine Biotech Co., Ltd. All samples were independently tested in a blinded manner by two qualified personnel, and the average values were used for statistical analysis. According to the manufacturer's instructions, the intra-assay coefficient of variation (CV) for PDCD4 and ADAM10 was <8%, and the inter-assay CV was <10%, indicating good reproducibility and reliability.

## Statistical Analysis

All statistical analyses were performed using SPSS 26.0 and graphs were plotted using GraphPad Prism 8. Continuous variables were expressed as ($\bar{x} \pm s$) and compared using the independent-samples *t*-test. Categorical variables were expressed as n (%) and compared using the $\chi^2$ test. Logistic regression was used to identify independent predictors of poor prognosis. A combined prognostic model was constructed by incorporating both PDCD4 and ADAM10 into the multivariate logistic regression equation, and the predicted probability was used for ROC analysis. The predictive performance of each marker and the combined model was assessed by comparing the AUC values using the DeLong test. A P-value <0.05 was considered statistically significant. Sample size was determined based on the principle of ensuring at least 10 outcome events per variable (EPV) included in the regression model, which provided sufficient statistical power.[19] This exploratory design did not involve multiple hypothesis testing across numerous endpoints; therefore, no multiple comparison correction was applied. Potential sources of bias included the single-center retrospective design and lack of external validation, which are discussed in the study limitations.

# Results

## Comparison of Serum PDCD4 and ADAM10 Levels Between the Disease and Control Groups

The serum levels of PDCD4 and ADAM10 in the control group were (18.72±4.63, 1.41±0.36), respectively; in the disease group, the levels were (49.24±12.28, 2.87±0.65), respectively. Compared with the control group, the serum PDCD4 and ADAM10 levels in the disease group were significantly elevated ($P$<0.05), as shown in Figure 1.

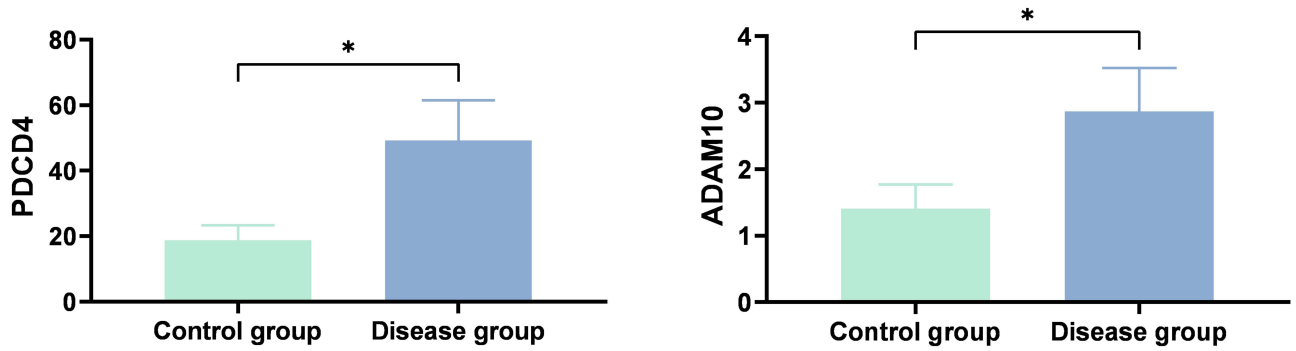


**Figure 1** Comparison of serum PDCD4 and ADAM10 levels between the disease group and control group ($\bar{x} \pm s$, μg/L).
**Notes**: Intergroup comparison, *$P$ < 0.05.

## Comparison of Serum PDCD4 and ADAM10 Levels Between Group A and Group B

The serum levels of PDCD4 and ADAM10 in Group A were (40.53±9.87, 2.38±0.62), respectively; in Group B, the levels were (61.84±16.25, 3.59±0.84), respectively. Compared with Group A, the serum PDCD4 and ADAM10 levels in Group B were significantly higher ($P$<0.05), as shown in Figure 2.

## Univariate Analysis of Factors Affecting Poor Prognosis in Elderly Patients with Atherosclerotic AMI

Univariate analysis showed statistically significant differences between the two groups in terms of age, presence of diabetes, myocardial infarction type, infarct size, infarct location, Killip classification, GRACE score, NT-proBNP, LVEF, and hs-CRP ($P$<0.05), as shown in Table 1.

## Multivariate Logistic Regression Analysis of Factors Affecting Poor Prognosis in Elderly Patients with Atherosclerotic AMI

Using patient prognosis as the dependent variable (good=0, poor=1), potential influencing factors identified in Figure 2 and Table 1 were assigned values (see Table 2) and included in a multivariate logistic regression model. The results showed that elevated PDCD4, elevated ADAM10, diabetes, STEMI type, infarct size involving >3 leads, anterior wall infarction, Killip classification ≥ II, GRACE score ≥ 140, elevated NT-proBNP, and reduced LVEF were independent predictors of poor prognosis ($P$<0.05), as shown in Table 3.

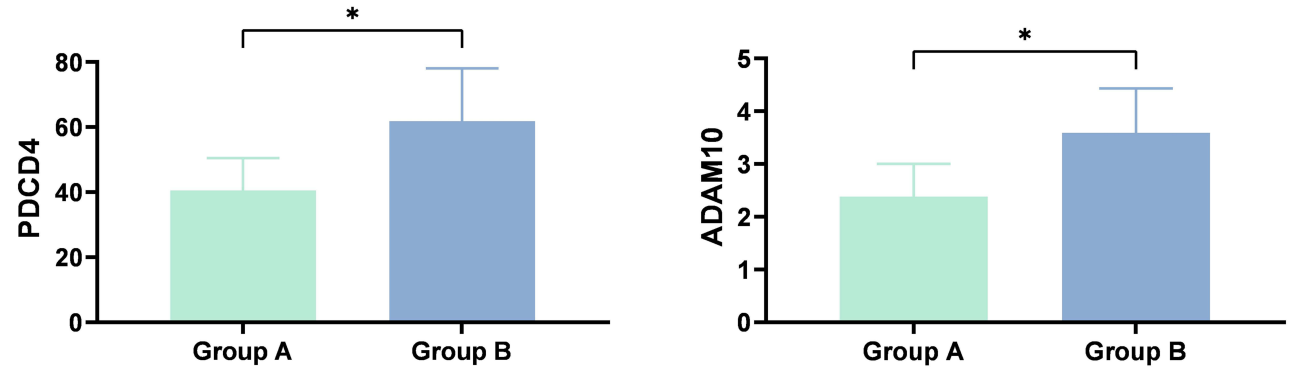


**Figure 2** Comparison of serum PDCD4 and ADAM10 levels between Group A and Group B ($\bar{x} \pm s$, μg/L).
**Notes**: Intergroup comparison, *$P$ < 0.05.

**Table 1** Univariate Analysis of Factors Affecting Poor Prognosis in Elderly Patients with Atherosclerotic AMI ($\bar{x} \pm s$, n[%])

| Variable | Prognosis | | $t/x^2$ | *P* |
|---|---|---|---|---|
| | Group A (n=79) | Group B (n=55) | | |
| Male | 46 (58.23) | 34 (61.82) | 0.173 | 0.676 |
| Age (years) | 69.42±5.31 | 73.15±5.86 | 3.832 | < 0.001 |
| BMI (kg/m$^2$) | 23.76±2.45 | 24.19±2.37 | 1.012 | 0.313 |
| Smoking history | 38 (48.10) | 26 (47.27) | 0.008 | 0.924 |
| Alcohol history | 10 (12.66) | 7 (12.73) | 0.000 | 0.992 |
| Hypertension | 42 (53.16) | 32 (58.18) | 0.330 | 0.565 |
| Diabetes | 19 (24.05) | 31 (56.36) | 14.474 | < 0.001 |
| Type of MI (STEMI) | 31 (39.24) | 43 (78.18) | 19.885 | < 0.001 |
| Infarct size >3 leads | 22 (27.85) | 39 (70.91) | 24.244 | < 0.001 |
| Infarct location | – | – | 22.640 | < 0.001 |
| Anterior wall | 32 (40.51) | 45 (81.82) | – | – |
| Inferior wall | 29 (36.71) | 7 (12.73) | – | – |
| Others | 18 (22.78) | 3 (5.45) | – | – |
| Killip class ≥ II | 14 (17.72) | 34 (61.82) | 27.426 | < 0.001 |
| GRACE score > 140 | 13 (16.46) | 32 (58.18) | 25.310 | < 0.001 |
| SBP (mmHg) | 138.26±18.21 | 142.63±20.15 | 1.307 | 0.193 |
| DBP (mmHg) | 76.28±9.45 | 75.53±8.74 | 0.465 | 0.642 |
| TC (mmol/L) | 4.52±1.12 | 4.48±1.15 | 0.201 | 0.840 |
| TG (mmol/L) | 1.67±0.75 | 1.74±0.78 | 0.522 | 0.602 |
| LDL-C (mmol/L) | 2.65±0.73 | 2.72±0.76 | 0.536 | 0.592 |
| HDL-C (mmol/L) | 1.14±0.24 | 1.12±0.22 | 0.490 | 0.624 |
| NT-proBNP (pg/mL) | 1286.54±546.27 | 2213.78±619.35 | 9.146 | < 0.001 |
| LVEF (%) | 56.47±6.92 | 48.63±7.84 | 6.106 | < 0.001 |
| hs-CRP (mg/L) | 8.91±2.63 | 11.74±3.32 | 5.496 | < 0.001 |

**Table 2** Variable Assignment Table

| Independent Variable | Assignment Method |
|---|---|
| PDCD4 | Original value |
| ADAM10 | Original value |
| Age | Original value |
| Diabetes | No = 0, Yes = 1 |
| Type of MI | NSTEMI = 0, STEMI = 1 |
| Infarct size | ≤3 leads = 0, >3 leads = 1 |
| Infarct location | Non-anterior = 0, Anterior = 1 |
| Killip class | < II = 0, ≥ II = 1 |
| GRACE score | < 140 = 0, ≥ 140 = 1 |
| NT-proBNP | Original value |
| LVEF | Original value |
| hs-CRP | Original value |

## Predictive Diagnostic Value of Serum PDCD4 and ADAM10 Alone and in Combination for Poor Prognosis

ROC curve analysis showed that the AUC values for PDCD4, ADAM10, and their combined prediction of poor prognosis were 0.837, 0.859, and 0.931, respectively. The AUC for the combined diagnosis was superior to the individual markers (Z_combined–PDCD4 = 3.653, $P<0.05$; Z_combined–ADAM10 = 3.239, $P<0.05$), as shown in Table 4 and Figure 3.

**Table 3** Multivariate Logistic Regression Analysis of Poor Prognosis in Elderly Patients with Atherosclerotic AMI

| Factor | *β* | *SE* | *Wald* $x^2$ | *OR* | 95% CI | *P* |
|---|---|---|---|---|---|---|
| Elevated PDCD4 | 0.684 | 0.192 | 12.690 | 1.981 | 1.357–2.891 | <0.001 |
| Elevated ADAM10 | 0.602 | 0.201 | 8.983 | 1.826 | 1.229–2.715 | 0.003 |
| Diabetes | 0.977 | 0.357 | 7.497 | 2.658 | 1.311–5.390 | 0.006 |
| STEMI type | 1.434 | 0.461 | 9.659 | 4.196 | 1.693–10.401 | 0.002 |
| Infarct size >3 leads | 1.328 | 0.452 | 8.651 | 3.773 | 1.557–9.141 | 0.003 |
| Anterior wall infarction | 1.162 | 0.478 | 5.902 | 3.197 | 1.258–8.125 | 0.015 |
| Killip class ≥ II | 1.217 | 0.414 | 8.626 | 3.377 | 1.507–7.565 | 0.003 |
| GRACE score ≥ 140 | 1.176 | 0.402 | 8.580 | 3.241 | 1.483–7.084 | 0.003 |
| Elevated NT-proBNP | 0.001 | 0.0003 | 11.845 | 1.043 | 1.002–1.102 | 0.001 |
| Reduced LVEF | −0.072 | 0.022 | 10.706 | 0.931 | 0.891–0.973 | 0.001 |

**Table 4** Predictive Diagnostic Value of Serum PDCD4 and ADAM10 Alone and in Combination for Poor Prognosis

| Indicator | Cut-off Value | AUC | 95% CI | Sensitivity (%) | Specificity (%) |
|---|---|---|---|---|---|
| PDCD4 | 51.54 μg/L | 0.837 | 0.763–0.872 | 76.49 | 79.62 |
| ADAM10 | 2.90 μg/L | 0.859 | 0.811–0.907 | 80.13 | 76.59 |
| Combined | – | 0.931 | 0.864–0.963 | 85.25 | 83.46 |

## Discussion

This study focused on elderly patients with atherosclerotic AMI and explored the differences in serum PDCD4 and ADAM10 expression levels and their combined predictive value for poor prognosis. The results showed that both PDCD4 and ADAM10 levels were significantly elevated in AMI patients, especially in those with poor outcomes, and were independent risk factors for prognosis. The AUC value of the combined detection was higher than that of individual indicators, suggesting its potential clinical value in prognostic assessment.

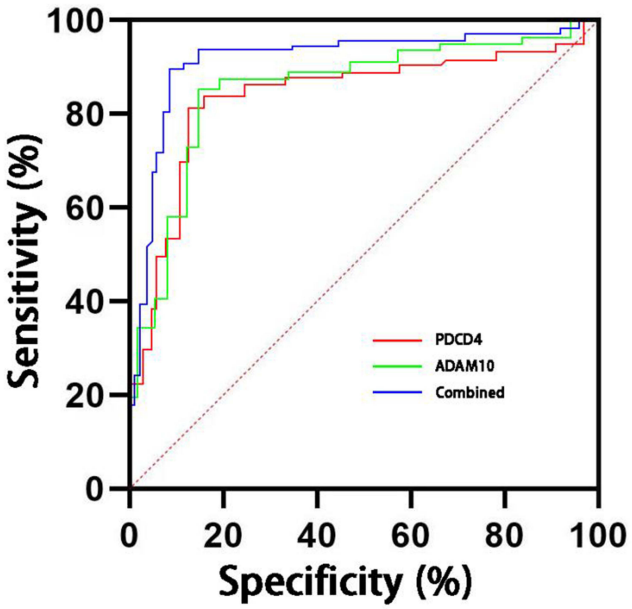


**Figure 3** ROC curves for PDCD4, ADAM10 alone and in combination for predicting poor prognosis.

PDCD4 was initially identified as a tumor suppressor gene, but recent studies have found that it also plays an important role in cardiovascular diseases, particularly in relation to apoptosis, oxidative stress, and inflammatory responses.[20,21] Studies have shown that PDCD4 can promote cardiomyocyte apoptosis by inhibiting the PI3K/Akt/mTOR signaling pathway.[22,23] Under the condition of myocardial ischemic necrosis following AMI, upregulation of PDCD4 expression may exacerbate myocardial cell death in the lesion area, thereby leading to left ventricular remodeling and deterioration of cardiac function. In addition, PDCD4 can activate the NF-κB pathway to promote the release of pro-inflammatory cytokines such as IL-6 and TNF-α, increasing local myocardial inflammation and accelerating plaque instability and reperfusion injury.[24,25] The findings of this study support the above viewpoints: PDCD4 expression was significantly increased in AMI patients, particularly in the poor prognosis group, indicating that it is not only involved in the pathological process but may also serve as an important prognostic predictor. Therefore, PDCD4 may become a potential molecular marker for evaluating myocardial injury severity and prognosis after AMI.

As a member of the metalloproteinase family, ADAM10 not only participates in plaque formation and destabilization in the cardiovascular system but also influences the progression of atherosclerosis and the occurrence of acute events by regulating intercellular adhesion, inflammatory responses, and vascular remodeling.[26,27] Mechanistically, ADAM10 can cleave multiple key molecules such as Notch1, VE-cadherin, and TNF-α precursors, disrupt the vascular endothelial barrier, induce endothelial cell apoptosis, activate macrophages, and promote matrix degradation, ultimately leading to plaque rupture and AMI.[28,29] Moreover, some studies have found that elevated ADAM10 expression is also closely related to myocardial fibrosis and heart failure, suggesting its long-term role in cardiac remodeling after AMI.[30,31] This study confirmed that ADAM10 levels were significantly elevated in AMI patients, especially in those with poor prognosis, which may indicate its association not only with acute events but also with long-term decline in cardiac function.

This study, based on the assessment of the individual predictive abilities of PDCD4 and ADAM10, further validated the clinical value of their combined application in prognostic prediction. ROC curve analysis showed that the AUC for the combined prediction of poor prognosis by PDCD4 and ADAM10 was 0.931, significantly higher than the individual AUCs of 0.837 and 0.859, indicating a notable improvement in predictive accuracy and sensitivity. The cutoff values derived from ROC analysis may serve as preliminary reference thresholds for identifying high-risk patients in clinical practice. Clinicians could consider patients exceeding these thresholds as candidates for intensified monitoring or early intervention, although further prospective validation is needed to confirm optimal clinical decision-making. This improvement may stem from the complementary roles of the two in the pathophysiology of AMI: PDCD4 primarily reflects the degree of inflammation and cell death, while ADAM10 is involved in vascular injury and plaque stability. Therefore, combined detection enables a comprehensive assessment of the entire disease course and multiple pathways in AMI patients. Notably, the predictive performance of PDCD4 and ADAM10 compares favorably with established biomarkers such as NT-proBNP, hs-CRP, and troponin, providing additive prognostic value. Combined measurement may thus enhance risk stratification beyond conventional markers, especially when integrated with clinical scoring systems like GRACE.[32] In the future, the construction of a multi-factor prognostic scoring model incorporating traditional cardiovascular indicators such as NT-proBNP and hs-CRP may provide decision-making support for individualized treatment of AMI.

In addition to PDCD4 and ADAM10, this study also identified GRACE score ≥ 140, Killip classification ≥ II, STEMI type, anterior wall infarction, infarct size involving >3 leads, reduced LVEF, elevated NT-proBNP, and presence of diabetes as independent risk factors for poor prognosis. These findings are generally consistent with existing guidelines and previous studies.[33–35] Among them, the GRACE score, as one of the most commonly used risk assessment tools for AMI patients, integrates multiple indicators such as blood pressure, heart rate, creatinine level, and Killip classification, and can effectively predict in-hospital mortality and long-term adverse cardiovascular events; Killip classification reflects the severity of acute heart failure and indicates the compensatory capacity of left heart function; NT-proBNP and LVEF further confirm cardiac function status from the perspectives of myocardial structure and ventricular load; the importance of infarct location and size has also been confirmed, especially anterior wall infarction and extensive infarction (involving >3 leads), which often suggest a large infarct area, poor cardiac function recovery, and high risk of malignant arrhythmia or cardiogenic shock. Additionally, patients with diabetes tend to have more severe underlying vascular lesions, more active inflammatory responses, and poorer tolerance to reperfusion, making them more prone to poor outcomes.

Although this study has certain representativeness and practical significance, it still has the following limitations: (1) This is a single-center retrospective study with a relatively small sample size and potential selection bias; (2) Longitudinal observation of the dynamic changes in serum PDCD4 and ADAM10 was not conducted, lacking temporal information; (3) The impact of differences in treatment strategies (eg, PCI, medication adherence) on prognosis was not analyzed, which may affect the generalizability of the conclusions; (4) The study lacks in vitro mechanistic experiments to verify the pathways involved. Future research should include multicenter, large-sample prospective studies, combined with myocardial tissue samples and animal models, to further explore the specific roles of PDCD4 and ADAM10 in myocardial injury and repair after AMI from a mechanistic perspective, and evaluate their feasibility as therapeutic targets.

## Conclusion

This study systematically assessed the relationship between serum levels of PDCD4 and ADAM10 and prognosis in elderly patients with atherosclerotic AMI, clearly demonstrating that both are independent risk factors for poor prognosis. Moreover, their combined detection shows higher predictive efficacy than individual markers. This finding provides a novel molecular basis and theoretical support for establishing a multi-molecule, multi-dimensional prognostic evaluation system for AMI. From the perspective of clinical practice, the detection methods for PDCD4 and ADAM10 (ELISA) are convenient, relatively low-cost, and highly applicable. Furthermore, integrating PDCD4 and ADAM10 measurements into existing risk scoring systems (eg, GRACE) or validating their use in prospective clinical trials could facilitate clinical translation, improve early risk stratification, and optimize intervention timing in AMI patients.

## Abbreviations

PDCD4, programmed cell death factor 4; ADAM10, a disintegrin and metalloproteinase 10; AMI, acute myocardial infarction; ELISA, Enzyme-linked immunosorbent assay; CCK-8, Cell Counting Kit-8; ELISA, Enzyme Linked Immunosorbent Assay; ROC, Receiver operating characteristic; NT-proBNP, N-terminal pro–B-type natriuretic peptide; LVEF, left ventricular ejection fraction; hs-CRP, high-sensitivity C-reactive protein; STEMI, ST-segment elevation myocardial infarction; AUC, area under the curve; ESC, European Society of Cardiology; CAG, coronary angiography; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides; SBP; systolic blood pressure; DBP, diastolic blood pressure.

## Data Sharing Statement

All the results are presented in the article. Further inquiries can be directed to the corresponding authors.

## Ethics Statement

The research protocol was approved by the Ethics Committee of Fuwai Central China Cardiovascular Hospital (No. 2024-105). All experiments and procedures were performed according to the Declaration of Helsinki (as revised in 2013).

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Disclosure

The authors report no conflicts of interest in this work.

## References

1. Krittanawong C, Khawaja M, Tamis-Holland JE, Girotra, S, Rao, SV . Acute Myocardial Infarction: Etiologies and Mimickers in Young Patients. *J Am Heart Assoc*. 2023;12(18):e029971. doi:10.1161/JAHA.123.029971

2. Jiang GH, Wang DZ, Zhang H, et al. [Epidemiological characteristics of pre-hospital mortality due to acute myocardial infarction from 1999 to 2016 in Tianjin city]. *Zhonghua yu fang yi xue za zhi*. 2020;54(1):99–103. Wolof. doi:10.3760/cma.j.issn.0253-9624.2020.01.018
3. Lindahl B, Mills NL. A new clinical classification of acute myocardial infarction. *Nat Med*. 2023;29(9):2200–2205. doi:10.1038/s41591-023-02513-2
4. Jacoby RM, Nesto RW. Acute myocardial infarction in the diabetic patient: pathophysiology, clinical course and prognosis. *J Am Coll Cardiol*. 1992;20(3):736–44. doi:10.1016/0735-1097(92)90033-j
5. Yan H, Wu X, He Y, Staub D, Wen X, Luo Y. Carotid intraplaque neovascularization on contrast-enhanced ultrasound correlates with cardiovascular events and poor prognosis: a systematic review and meta-analysis. *Ultrasound Med Biol*. 2021;47(2):167–176. doi:10.1016/j.ultrasmedbio.2020.10.013
6. Wu Z, Wang D, Tang C. Urinary sodium-potassium ratio as a genetic predictor of myocardial infarction. *Coron Artery Dis*. 2025;36(7):561–568. PMID: 40326438. doi:10.1097/MCA.0000000000001532
7. Wang Q, Yang HS. The Impact of Pdcd4, a Translation Inhibitor, on Drug Resistance. *Pharmaceuticals (Basel)*. 2024;17(10):1396. doi:10.3390/ph17101396
8. Matsuhashi S, Manirujjaman M, Hamajima H, Ozaki, I. Control Mechanisms of the Tumor Suppressor PDCD4: Expression and Functions. *Int J Mol Sci*. 2019;20(9):2304. doi:10.3390/ijms20092304
9. Zhang J, Luo CJ, Xiong XQ, et al. MiR-21-5p-expressing bone marrow mesenchymal stem cells alleviate myocardial ischemia/reperfusion injury by regulating the circRNA_0031672/miR-21-5p/programmed cell death protein 4 pathway. *J Geriatric Cardiol*. 2021;18(12):1029–1043. doi:10.11909/j.issn.1671-5411.2021.12.004
10. Li C, Sun Y, Jiang C, et al. Porcine circovirus type 2 infection activates NF-κB pathway and cellular inflammatory responses through circPDCD4/miR-21/PDCD4 axis in porcine kidney 15 cell. *Virus Res*. 2021;298:198385. doi:10.1016/j.virusres.2021.198385
11. Shahid S, Ikeda A, Layana MC, Bartlett, JD. ADAM10: Possible functions in enamel development. *Front Physiol*. 2022;25(13):1032383. doi:10.3389/fphys.2022.1032383
12. Ou L, Huang W, Zhang T, Xu D, Kong D, Meng Y. Circular RNA circ_0114876 regulates osteoarthritis through upregulating ADAM10 via targeting miR-1227-3p. *Transpl Immunol*. 2023;77:101747. doi:10.1016/j.trim.2022.101747
13. Huner Yigit M, Atak M, Yigit E, Topal Suzan Z, Kivrak M, Uydu HA. White tea reduces dyslipidemia, inflammation, and oxidative stress in the Aortic Arch in a model of atherosclerosis induced by atherogenic diet in ApoE knockout mice. *Pharmaceuticals*. 2024;17(12):1699. doi:10.3390/ph17121699
14. Yao Y, Sun W, Sun Q, et al. Platelet-derived exosomal MicroRNA-25-3p inhibits coronary vascular endothelial cell inflammation through Adam10 via the NF-κB signaling pathway in ApoE(-/-) mice. *Front Immunol*. 2019;10:2205. doi:10.3389/fimmu.2019.02205
15. Aydin S, Ugur K, Aydin S, Sahin, I, Yardim, M, et al. Biomarkers in acute myocardial infarction: current perspectives. *Vasc Health Risk Manag*. 2019;17(15):1–10. doi:10.2147/VHRM.S166157
16. Saraste A, Barbato E, Capodanno D, et al. Imaging in ESC clinical guidelines: chronic coronary syndromes. *Eur Heart J Cardiovasc Imaging*. 2019;20(11):1187–1197. doi:10.1093/ehjci/jez219
17. Şeker T, Türkoğlu C, Akkuş O, Gür M. The relationship between visible thrombus aspiration material with no-reflow and in-hospital mortality ratio in patients with anterior ST-elevation myocardial infarction treated with primary percutaneous coronary intervention. *Turk Kardiyoloji Dernegi Arsivi*. 2019;47(2):95–102. doi:10.5543/tkda.2019.49940
18. Xiang L, Cheng YP, Wang J, Wu YN, Chen R. [Effects of obstructive sleep apnea syndrome on myocardial work and prognosis in patients with acute myocardial infarction]. *Zhonghua yi xue za zhi*. 2023;103(48):3946–3953. Danish. doi:10.3760/cma.j.cn112137-20230401-00525
19. Peduzzi P, Concato J, Kemper E, et al. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol*. 1996;49(12):1373–1379. doi:10.1016/S0895-4356(96)00236-3
20. Zhu J, Wang Q, Zheng Z, et al. MiR-181a protects the heart against myocardial infarction by regulating mitochondrial fission via targeting programmed cell death protein 4. *Sci Rep*. 2024;14(1):6638. doi:10.1038/s41598-024-57206-8
21. Wang Y, Gao C, Zhou K, Liu W, Zhang Y, Zhao Y. MicroRNA-532-5p-programmed cell death protein 4 (PDCD4) axis regulates angiotensin II-induced human umbilical vein endothelial cell apoptosis and proliferation. *Microvasc Res*. 2021;138:104195. doi:10.1016/j.mvr.2021.104195
22. Zheng Y, Zhao P, Lian Y, Li S, Chen Y, Li L. MiR-340-5p alleviates oxygen-glucose deprivation/reoxygenation-induced neuronal injury via PI3K/Akt activation by targeting PDCD4. *Neurochem Int*. 2020;134:104650. doi:10.1016/j.neuint.2019.104650
23. Sugiura T, Nawaz S, Ferrell BE, Yoshida T. Induced pluripotent stem cells: a new dawn for the treatment of ischemic cardiomyopathy. *Innov Discov*. 2024;1(4):31. doi:10.53964/id.2024031
24. Yu L, Yang Y, Wang J, et al. PDCD4 promotes inflammation/fibrosis by activating the PPAR-γ/NF-κB pathway in mouse atrial myocytes. *Mol Med Rep*. 2024;30(5). doi:10.3892/mmr.2024.13333
25. Abdel-Salam OME, Abd El Baset M, Omara EA, Sleem AA. Protection by L-arginine against epinephrine-induced arrhythmia and cardiotoxicity. *Innov Discov*. 2024;1(2):12. doi:10.53964/id.2024012
26. Qian Z, Huang Y, Yang N, et al. miR-34a-5p/MARCHF8/ADAM10 axis in the regulation of vascular endothelial cell dysfunction and senescence. *Mech Ageing Dev*. 2025;225:112060. doi:10.1016/j.mad.2025.112060
27. Fu Q, Tang Y, Peng J, et al. miR-520d suppresses rapid pacing-induced apoptosis of atrial myocytes through mediation of ADAM10. *J Mol Histol*. 2021;52(2):207–217. doi:10.1007/s10735-020-09938-w
28. Guo D, Huang F, Xue R, et al. A Disintegrin and Metalloproteinase 10 (ADAM10) is essential for oligodendrocyte precursor development and myelination in the mouse brain. *Mol Neurobiol*. 2023;60(3):1675–1689. doi:10.1007/s12035-022-03163-0
29. Ivaldo C, Passalacqua M, Furfaro AL, et al. Oxidative stress-induced MMP- and γ-secretase-dependent VE-cadherin processing is modulated by the proteasome and BMP9/10. *Sci Rep*. 2023;13(1):597. doi:10.1038/s41598-022-27308-2
30. Selejan SR, Linz D, Tatu AM, et al. Sympathoadrenergic suppression improves heart function by upregulating the ratio of sRAGE/RAGE in hypertension with metabolic syndrome. *J Mol Cell Cardiol*. 2018;122:34–46. doi:10.1016/j.yjmcc.2018.08.003
31. Klapproth E, Witt A, Klose P, et al. Targeting cardiomyocyte ADAM10 ectodomain shedding promotes survival early after myocardial infarction. *Nat Commun*. 2022;13(1):7648. doi:10.1038/s41467-022-35331-0
32. Symum H, Van Handel M, Sandul A, et al. Testing trends and co-testing patterns for HIV, hepatitis C and sexually transmitted infections (STIs) in Emergency departments. *Prev Med Rep*. 2024;44:102777. doi:10.1016/j.pmedr.2024.102777

33. Chen Q, Su H, Yu X et al. The stress hyperglycemia ratio improves the predictive ability of the GRACE score for in-hospital mortality in patients with acute myocardial infarction. *Hellenic J Cardiol*. 2023;70(1):36–45. doi:10.1016/j.hjc.2022.12.012
34. Tan X, Wang XY, Xu S et al . Identification of Cardiometabolic Protein Biomarkers for Acute Myocardial Infarction Using Olink Proteomics. *J Inflamm Res*. 2025;22(18):2629–2646. doi:10.2147/JIR.S495784
35. Ji C, Song F, Huang X, Qu X, Qiu N, Zhu J. [Comparison of the predictive value of the modified Cadillac, GRACE and TIMI risk scores for the risk of short-term death in patients with acute ST segment elevation myocardial infarction after percutaneous coronary intervention]. *Zhonghua Wei Zhong Bing ji Jiu Yi Xue*. 2023;35(3):299–304. Dutch. doi:10.3760/cma.j.cn121430-20220727-00696