CLINICAL STUDY

Interleukin-34 Levels Were Associated with Prognosis in Patients with Acute Myocardial Infarction

Qin Fan,1,2 MD, Rong Tao,1 MD, Hang Zhang,1,2 MD, Hongyang Xie,1,2 MD, Rui Xi,1 MD, Fang Wang,1 MD, Yan Xu,1 MD, Ruiyan Zhang,1,2 MD, Xiaoxiang Yan,1,2 MD and Gang Gu,1 MD

Summary

Inflammatory factors have specific value in acute myocardial infarction (AMI). Our previous studies have identified the prognostic value of interleukin (IL)-34 during chronic heart failure. However, the potential impact of IL-34 on AMI remains unknown.

Serum IL-34 was measured in 287 AMI patients, and they were followed up for the composite endpoint, including cardiovascular death, heart failure hospitalization, recurrent nonfatal myocardial infarction (MI), and nonfatal stroke.

IL-34 levels were significantly associated with the presence of heart failure at baseline and its aggravation after a year. During the five-year follow-up, there was a significant increase in the risk of the composite endpoint (hazard ratio [HR] 1.38 [95% confidence intervals (CI) 1.12-1.70], \( P < 0.01 \)) and cardiovascular death (HR 1.48 [95%CI 1.03-2.27], \( P = 0.03 \)) after full adjustment as IL-34 levels increased.

Higher IL-34 levels in the acute phase were associated with an increased risk of heart failure after MI and poor prognosis.

Key words: Cardiovascular disease, Heart failure, Biomarker

Currently, more patients survive myocardial infarction (MI) owing to improved treatment modalities; however, this has resulted in more candidates for ventricular remodeling and heart failure (HF). It is essential to explore and evaluate the prognostic value of novel biomarkers, including those associated with inflammation and interstitial fibrosis in the risk stratification of post-MI HF.

The immune response and inflammatory process in the post-MI period are regulated by different classes of immune cells, cytokines, and chemokines. Given their importance, secreted inflammation-associated mediators could provide insight into the pathophysiology and prognosis of patients with MI and might serve as biomarkers.

Interleukin (IL)-34, first identified in 2008 with a function resembling that of macrophage colony-stimulating factor (M-CSF), is one type of these cytokines. It plays an important role in the survival and proliferation of monocytes and macrophages, regulating the immune response and inflammation process. As a proinflammatory cytokine, it has also been shown in experimental studies to induce proinflammatory cytokines and chemokines, including IL-6, IL-8, and monocyte chemoattractant protein-1; further mediating the migration and differentiation of monocytes and macrophages. It has also been found to induce profibrotic macrophages to release platelet-derived growth factor, transforming growth factor \( \beta \), and galectin-3, which are associated with HF.

As a secreted cytokine, serum IL-34 is significantly elevated and plays an important part in several inflammatory diseases, including rheumatoid arthritis, Sjogren’s syndrome, and inflammatory bowel disease. Our previous study also demonstrated that IL-34 levels were increased in patients with chronic HF and can serve as a significant predictor of cardiovascular death, HF hospitalization, and all-cause mortality in these patients, especially in the presence of renal dysfunction. Moreover, its levels were markedly elevated, especially in patients with ischemic cardiomyopathy.

However, the prognostic value of IL-34 in AMI, especially regarding the aggravation of HF, is not well understood. Moreover, it is unclear if IL-34 predicts longer term outcomes of MI. Thus, the present cohort study...
aimed to examine the relationship between circulating IL-34 and adverse outcomes in the post-MI period.

Methods

Participants and study design: This prospective cohort study consecutively enrolled eligible patients who underwent coronary artery angiography in the Shanghai Jiao Tong University School of Medicine-affiliated Rui Jin Hospital. Patients were considered for inclusion if they were admitted for a first acute ST-segment elevation (STEMI), according to current definitions. HF was defined as left ventricular ejection fraction (LVEF) ≤ 50% at baseline. Patients without a definite current MI were not included in the study. Moreover, patients with a history of stroke in the four weeks prior to enrollment, with severe concomitant diseases such as malignant disease, serious infections, and autoimmune diseases, with cardiopulmonary arrest on arrival, or who were unwilling to participate were excluded. All patients enrolled were 18 years of age or older.

Medical information and samples were collected at discharge, which was set as baseline. All subjects underwent echocardiography at baseline and one year after recruitment and were followed up to time of the long-term endpoints. A medical history and concomitant cardiac medications were obtained at baseline. Patients were followed up prospectively by direct contact, telephone communication, and chart review in order to record mortality, HF hospitalizations, and other adverse events.

Informed consent was obtained from each patient before data collection. The study was approved by the Institutional Ethics Committee of the Rui Jin Hospital affiliated to the Shanghai Jiao Tong University School of Medicine (Shanghai, China). The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in the a priori approval by the institution’s human research committee.

Outcomes: All subjects were followed up until death or to the last visit. The primary endpoint was major adverse cardiovascular events (MACE), defined as the composite of cardiovascular death, hospitalization for HF, recurrent nonfatal MI, and nonfatal stroke. All events were documented during planned clinic assessments every six months, with deaths identified mainly by a review of medical records and through direct contact with the patients’ family. Moreover, the date of the event was recorded and information explaining the cause was obtained. Generally, follow-up data were available for 96.8% of the included patients and 264 patients were able to undergo echocardiography one year after enrollment.

IL-34 measurement: Collected blood samples were centrifuged, within 30 minutes, at 2,000 rpm for 20 minutes to obtain serum. Serum IL-34 was measured using a human IL-34 Quantikine ELISA kit (D3400; R&D Systems, MN, USA), according to the manufacturer’s protocol.

Echocardiography: Echocardiography was performed both at baseline and one year after enrollment. Left ventricular end-systolic diameter (LVESd), left ventricular end-diastolic diameter (LVEDd), and left atrial diameter (LAd) were measured for each subject using M-mode echocardiography. The simplified two-plane Simpson method was used to calculate LVEF in the two-dimensional apical four-chamber and two-chamber views.

Other clinical examination: All demographic and clinical characteristics were recorded at baseline through face-to-face interviews, including information regarding medical history and details regarding concomitant diseases and major combined medications. Physical examination, echocardiography, and routine laboratory tests were performed on the same day. Estimated glomerular filtration rate (eGFR) was calculated by the Modification of Diet in Renal Disease equation. Body mass index (BMI) (kg/m²) was calculated using height and weight measured at baseline. The Gensini score system was used to quantify the degree of each vascular lesion via coronary angiography.

Statistical analysis: Data were first tested for distribution normality using the Kolmogorov-Smirnov test. Continuous data are expressed as the mean ± standard deviation (SD) and were compared using the independent Student t-test or one-way analysis of variance test, where appropriate, if normally distributed. Nonparametric data were log-transformed to a normal distribution for further analysis. The chi-squared test or Fisher’s exact test was used to compare categorical variables where appropriate.

The association between variables was tested using simple and multivariable linear regression models. Logistic regression models were used to estimate the predictive value of IL-34 for HF at baseline, as continuous variables, ordinal variables, and categorical data. Odds ratios (ORs) were presented unadjusted, adjusted for age and sex (model 1), and adjusted for age, sex, BMI, history of hypertension, history of diabetes mellitus (DM), log high-sensitivity C-reactive protein (hsCRP), Gensini score, eGFR, and medication (model 2). During follow-up, patients were censored at the time of the first MACE, at the time they were lost to follow-up, or at the end of the data analysis. The Kaplan-Meier (KM) method and log-rank test were used to compare survival after MI according to IL-34 levels. The association of IL-34 levels with MACE, as well as with cardiovascular death, was assessed using Cox proportional hazards regression models. Hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated using standardized increments of natural log-transformed IL-34 levels and levels of IL-34, both as ordinal and as categorical data. Univariate and multivariable models were used; first adjusted for age and sex; and then for the full model including age, sex, BMI, history of hypertension, history of DM, hemoglobin, eGFR, low-density lipoprotein (LDL), hsCRP, NT-pro-brain natriuretic peptide (NT-proBNP), LVEF, Killip classification, coronary artery Gensini score, number of diseased vessels, the way of revascularization, number of implanted stents, and medication.

The cutoff value of IL-34 (84.21 pg/mL), which best predicted MACE in all patients, was estimated using receiver operating characteristics (ROC) curves. The KM method and Cox regression models were also used to compare between patients below and above the cutoff value. C-statistic analyses including several conventional risk factors with and without IL-34 were also performed to determine the prognostic value of IL-34 for risk stratifi-
cation among patients with AMI.

All statistical analyses were performed using SPSS software (version 20.0; SPSS, Inc., Chicago, IL, USA). *P* < 0.05 was considered statistically significant and the significance was two-tailed.

**Results**

**Baseline characteristics:** A total of 287 AMI patients who had coronary angiography were enrolled in the present study, the mean patient age was 62.76 ± 12.29 years and 87.8% of patients were male. The median IL-34 level was 77.58 (IQR 54.59-124.52) pg/mL. All patients were separated into three groups according to the tertiles of the IL-34 levels: tertile 1, < 64.27 pg/mL; tertile 2, 64.27 ≤ IL-34 < 109.62 pg/mL; and tertile 3, ≥ 109.62 pg/mL. The baseline characteristics are presented in Table I, including the clinical and laboratory characteristics.

At baseline, higher IL-34 levels were associated with increased age, worse renal function, more severe inflammatory condition, and poorer general condition. IL-34 increased age, worse renal function, more severe inflammation. Serum IL-34 levels were significantly elevated in patients with and without DM (103.61 ± 112.40 versus 117.99 ± 131.09 pg/mL, *P* = 0.93), and between those patients with and without hypertension (116.51 ± 123.32 versus 117.99 ± 131.09 pg/mL, *P* = 0.93), and between those patients with and without DM (103.61 ± 112.40 versus 122.52 ± 130.62 pg/mL, *P* = 0.25).

**IL-34 was significantly associated with the presence and severity of cardiac dysfunction in AMI patients:** In all patients at baseline, those with higher IL-34 levels were more likely to develop ventricular enlargement and cardiac dysfunction (Table I), as indicated by echocardiography parameters. Those with higher IL-34 levels also tended to belong to the higher levels of Killip classification. Serum IL-34 levels were significantly elevated in patients with cardiac dysfunction than in those without (130.62 pg/mL versus 94.72 pg/mL, *P* < 0.01) (Figure 1A).

Simple linear regression analysis showed that higher IL-34 levels were significantly correlated with higher NT-proBNP (*r* = 0.29, *P* < 0.01), LVEDd (*r* = 0.15, *P* = 0.01), LVEFd (*r* = 0.15, *P* = 0.01), and LAd (*r* = 0.17, *P* = 0.01), as well as with lower LVEF (*r* = −0.15, *P* = 0.01). Logistic regression analysis further demonstrated the independent predictive value of IL-34 for cardiac dysfunction in patients with AMI. Univariate and multivariable analyses indicated that patients with higher IL-34 had an unadjusted OR of 1.52 (95% CI 1.17-1.98, *P* < 0.01) and a fully adjusted OR of 1.32 (95% CI 1.03-1.78, *P* = 0.03) per 1 SD increase of the log-transformed variable. Moreover, as a categorical variable, the highest tertile of IL-34 level revealed a significantly increased risk for HF (OR 2.32 [95% CI 1.15-4.71], *P* = 0.02), compared with the lowest tertile in the fully adjusted model including age, sex, BMI, history of hypertension, history of DM, log hsCRP, Gensini score, eGFR, and medication (Table II).

Furthermore, among AMI patients, 264 (91.99%) patients were able to undergo echocardiography one year after enrollment. Baseline IL-34 levels were significantly correlated with a decrease in LVEF (*r* = −0.24, *P* < 0.01; Figure 1B), using the follow-up measurement minus baseline parameter, implying its association with aggravation of HF.

**AMI patients with higher IL-34 levels tended to have a worse prognosis:** During the first five years of follow-up (median follow-up of 3.26 [IQR 2.62-3.76] years), 82 (28.9%) patients in the AMI group experienced MACE (15 in IL-34 tertile 1, 29 in tertile 2, and 38 in tertile 3), which consists of cardiovascular death, hospitalization for HF, recurrent nonfatal MI, and nonfatal stroke (Figure 1C). Among these outcomes, more patients died from cardiovascular disease in the patient sample with higher IL-34 levels. The increase in the risk of sudden death and death from the aggravation of HF was statistically significant (Figure 1D).

Furthermore, higher IL-34 levels were significantly associated with an increased risk for MACE (*P* < 0.01; Figure 1E) and cardiovascular death (*P* < 0.01; Figure 1F) using KM curves and log-rank tests. Both univariate and multivariable Cox proportional hazard models further indicated the prognostic value of IL-34, as a continuous variable, and when divided into tertiles. Higher IL-34 levels were independently associated with the risk for MACE (HR 1.38 [95% CI 1.12-1.70] per SD, *P* < 0.01), as a continuous log-transformed variable, adjusted for the full model including age, sex, BMI, NT-proBNP, and various conventional influencing factors (Table III). Moreover, when the IL-34 level was divided into tertiles, there was a two-fold increased risk (HR 2.62 [95% CI 1.41-4.87], *P* < 0.01) in the fully adjusted model for MACE in tertile 3 compared to tertile 1 (HR 1.99 < 0.01). Higher IL-34 levels were also significantly associated with the risk for cardiovascular death. When fully adjusted, the prognostic value remained significant when IL-34 was analyzed as a log-transformed continuous variable (HR 1.48 [95% CI 1.03-2.27], *P* = 0.03) (Table III).

**The cutoff value of IL-34 in risk stratification after AMI:** Moreover, the cutoff value for IL-34 levels in AMI patients that best predicted MACE was calculated as 84.21 pg/mL. Within the AMI groups, the event rate was 19.5% in patients with IL-34 levels below the cutoff value, while 39.4% patients with IL-34 levels above the cutoff value experienced MACE (*P* < 0.01). The KM survival curves and log-rank test demonstrated a significant difference between the two patient groups (Figure 2A). Moreover, compared with those patients below the cutoff value, patients in the higher group had an increased risk of both MACE (HR 2.12 [95% CI 1.33-3.38], *P* < 0.01) and cardiovascular death (HR 3.06 [95% CI 1.19-7.90], *P* = 0.02) in the fully adjusted model in the Cox regression analyses (Table III).

In order to evaluate the prognostic value of IL-34 for improvement of risk stratification, an increment in the C-
statistic analyses was performed in AMI patients. Adding IL-34 to the multivariable hazards model markedly increased the prognostic value of conventional risk factors (area under the ROC curve 0.76 [95%CI 0.69-0.82] versus 0.70 [95%CI 0.63-0.77], \( P = 0.04 \); Figure 2B).
short-term LVEF decrease, as assessed by echocardiography, as well as a long-term risk for MACE and cardiovascular death, which augments existing knowledge and risk prediction models, demonstrating a significant clinical value.

Firstly, in the present study, in patients with AMI, those with higher IL-34 levels had an increased risk for post-MI cardiac function deterioration, further leading to poorer long-term prognosis after adjustment for age, sex, and several influencing factors, including NT-proBNP and hsCRP. Our previous study reported that serum IL-34 levels were correlated with the presence and severity of chronic ischemic HF and were prognostic for cardiovascular death and HF re-hospitalization in patients with chronic HF, proving the relationship between IL-34 and cardiac function. It is also of clinical value that adding IL-34 to conventional prediction models could improve their prognostic ability. Based on several studies, it is reasonable to speculate that IL-34 could, directly and indirectly, affect cardiac function; this therefore reflects the severity of HF, and could act as a mediator of cardiac injury, repair, and remodeling in the post-MI period.

Cardiac injury and remodeling in the post-MI period consist of the immune response, interstitial fibrosis, and ventricular dysfunction. IL-34 may contribute to ischemic myocardial injury and repair owing to its function as a regulator of immunity and the inflammation process; thus influencing prognosis.

Furthermore, our present study indicated a significant direct relationship between IL-34 levels and cardiac enlargement and dysfunction, both at baseline and after one year. Higher IL-34 levels were also associated with the higher rate of death due to aggravation of HF. Serum IL-34 levels tended to be higher in chronically hepatitis C virus-infected patients with high fibrosis stages than in those patients with lower fibrosis stages and healthy control participants, associated with markers indicating the severity of fibrosis, which may be applicable to fibrosis of the heart. In basic studies, IL-34 could promote CC chemokine receptor 1 (CCR1) and CCR5, as well as interferon-γ production, by NK cells, further affecting the process of fibrosis. It has also been demonstrated that IL-34 can induce profibrotic macrophages to release platelet-derived growth factor, transforming growth factor β (TGF-β), and galectin-3. Galectin-3 is also an important marker of HF, especially cardiac fibrosis, and is related to increased HF risk and mortality, predicting poor outcomes with clinical value. As a result, considering that serum IL-34 could predict HF aggravation, it may affect cardiac function as an inflammatory factor mediating cardiac fibrosis through a TGF-β and galectin-3-associated pathway. However, the direct effect of IL-34 on remodeling post-MI and the underlying mechanisms of this direct effect still need to be explored.

Secondly, as an inflammatory cytokine, IL-34 has been shown to induce proinflammatory cytokines and chemokines, including IL-6, IL-8, and the chemokine ligand CCL2, in human whole blood, additionally causing a deterioration of the patient’s general condition. These proinflammatory cytokines could induce IL-34 and vice versa. It has been demonstrated that a significant relationship exists between immune response and inflammation in the post-MI period, which affects prognosis, including cardiovascular death and HF. IL-34 was correlated with hsCRP among AMI patients in our study, and among all causes of cardiovascular death, the event rate of sudden death was also significantly higher in patients with higher IL-34, showing that IL-34 may affect the prognosis post-MI by taking part in the inflammatory process. IL-34 also plays a part in inflammatory disease by stimulating mononuclear phagocyte adhesion to the endothelium, via angiogenesis, and through macrophage recruitment, which may be one of the mechanisms underlying the exacerbation of cardiac dysfunction and adverse outcomes. The investigation of the function of IL-34 in inflammation is likely to provide new insight into clinical practices beyond traditional inflammatory biomarkers in patients with MI.

Thirdly, we found a significant correlation between serum IL-34 and renal dysfunction in patients with AMI, which was in accordance with the results of our previous studies that indicated the predictive value of IL-34 for renal dysfunction in HF and its prognostic value, especially in those with chronic kidney disease. Studies have demonstrated that IL-34 can stimulate the proliferation of myeloid cells in the bone marrow and kidney, directly af-

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**Table 1.** Baseline Characteristics of Patients with Acute Myocardial Infarction by Tertiles of Serum IL-34 (continued)

| Medications | IL-34 < 64.27 pg/mL (n = 96) | 64.27 ± IL-34 < 109.62 pg/mL (n = 96) | IL-34 ≥ 109.62 pg/mL (n = 95) | P value |
|-------------|-----------------------------|--------------------------------------|-------------------------------|---------|
| ACEI/ARB    | 67 (69.8)                   | 71 (74.0)                            | 66 (69.5)                     | 0.75    |
| B-blocker   | 81 (84.4)                   | 90 (93.8)                            | 75 (78.9)                     | 0.01    |
| Nitrates    | 42 (43.8)                   | 41 (42.7)                            | 43 (45.3)                     | 0.94    |
| Statin      | 91 (94.8)                   | 83 (86.5)                            | 78 (82.1)                     | 0.02    |
| CCB         | 8 (8.3)                     | 14 (14.6)                            | 8 (8.4)                       | 0.27    |

Data are presented as mean ± standard deviation (SD) or n (%). ACEI indicates angiotensin-converting enzyme inhibitor; AMI, acute myocardial infarction; ARB, angiotensin receptor blocker; BMI, body mass index; BUN, blood urea nitrogen; CABG, coronary artery bypass grafting; CCB, calcium channel blocker; CKD, chronic kidney disease; HDL, high-density lipoprotein; hsCRP, high sensitivity C reactive protein; IL-34, interleukin-34; LAd, left atrium diameter; LDL, low-density lipoprotein; LVEDd, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESd, left ventricular end-systolic diameter; NT-proBNP, N-terminal pro-brain natriuretic peptide; PCI, percutaneous coronary intervention; and WBC, white blood cell.
A: Comparison of serum IL-34 between AMI patients with and without HF. B: Simple linear regression analysis of log IL-34 and change in LVEF, which was defined as follow-up LVEF minus baseline LVEF, calculated using the simplified two-plane Simpson method by echocardiography. C: Comparison of the event rate of each adverse event according to serum IL-34 tertiles in the AMI group, including MACE, cardiovascular death, HF hospitalization, nonfatal re-myocardial infarction, and nonfatal stroke. D: Comparison of the event rate of each cause of cardiovascular death according to serum IL-34 tertiles. E, F: Kaplan-Meier curves for MACE (E) and cardiovascular death (F) according to the tertiles of IL-34.

Figure 1. Association of serum interleukin-34 levels with the presence of heart failure (HF) and adverse outcomes in patients with acute myocardial infarction. A: Comparison of serum IL-34 between AMI patients with and without HF. B: Simple linear regression analysis of log IL-34 and change in LVEF, which was defined as follow-up LVEF minus baseline LVEF, calculated using the simplified two-plane Simpson method by echocardiography. C: Comparison of the event rate of each adverse event according to serum IL-34 tertiles in the AMI group, including MACE, cardiovascular death, HF hospitalization, nonfatal re-myocardial infarction, and nonfatal stroke. D: Comparison of the event rate of each cause of cardiovascular death according to serum IL-34 tertiles. E, F: Kaplan-Meier curves for MACE (E) and cardiovascular death (F) according to the tertiles of IL-34.

In addition, many renal markers can predict adverse outcomes such as mortality and HF severity post-MI. For example, eGFR and Cystatin C were identified as prognostic biomarkers in MI, independent of traditional risk factors. The correlation between IL-34 and these renal markers in our study, along with its influence on renal function, which is essential during the post-MI process. Therefore, IL-34 may affect post-MI kidney function, which could, in turn, cause deterioration in cardiac function, forming a vicious circle.

Moreover, our previous study demonstrated that among HF patients, IL-34 levels were significantly associated with the presence and severity of coronary artery disease. Interestingly, in the present study, IL-34 levels were not significantly associated with the severity of coronary artery disease calculated by the Gensini score in
Firstly, this was an observational cohort study. Although IL-34 is analyzed as a log transformed continuous variable, an ordinal variable divided according to tertiles of IL-34, and a categorical variable using the lowest tertile as reference. Model 1: adjusted for age and sex and Model 2: adjusted for age, sex, body mass index, history of hypertension, history of diabetes mellitus, log hsCRP, Gensini score, eGFR and medication. As a continuous variable, OR is shown as per 1 SD. AMI indicates acute myocardial infarction; eGFR, estimated glomerular filtration rate; HF, heart failure; hsCRP, high sensitivity C reactive protein; IL-34, inter leukin 34; OR, odds ratio; and SD, standard deviation.

In the present cohort, IL-34 elevation showed a marked adverse prognosis, including cardiovascular death, first time HF hospitalization, recurrent myocardial infarction or stroke. Model 1: adjusted for age and sex and Model 2: adjusted for age, sex, body mass index, history of hypertension, history of diabetes mellitus, hemoglobin, eGFR, LDL, hsCRP, NT-proBNP, LVEF, Killip classification, coronary artery Gensini score, number of diseased vessel, the way of revascularization, number of implanted stents and medication. As a continuous variable, HR is shown as per 1 SD. AMI indicates acute myocardial infarction; eGFR, estimated glomerular filtration rate; HR, hazard ratio; hsCRP, high sensitivity C reactive protein; IL-34, inter leukin 34; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular events; NT-proBNP, N-terminal pro-brain natriuretic peptide; and SD, standard deviation.

In all, the above results suggest that IL-34 might be involved in the post-MI process by influencing immune response and inflammation, cardiac remodeling, and renal function, leading to HF and poor prognosis, especially during the acute phase.

There are several limitations to the present study. Firstly, this was an observational cohort study. Although we used a rational adjustment model consisting of known post-MI risk factors, we could not exclude residual confounding. Moreover, the results need to be validated in larger cohort studies with different environmental and genetic backgrounds to further determine the predictive and prognostic value of IL-34 in those patients with AMI. Serial evaluations of IL-34 levels at different time points in the post-MI period might be complementarily used in the future to assess the specificity and efficiency of IL-34 as a diagnostic or prognostic biomarker. In addition, it seems necessary to clarify the specific mechanism underlying the function of IL-34 during the process of post-MI cardiac dysfunction.

Conclusions

In the present cohort, IL-34 elevation showed a markedly adverse prognosis, including cardiovascular death, over a long follow-up period among patients with AMI and was associated with the presence and aggravation of HF in the post-MI period. The measurement of IL-34 during the acute phase could be considered a part of contemporary approaches for risk stratification and may be used as a novel biomarker and predictor of a poor prognosis.
Conflicts of interest: The authors declare that they have no conflict of interest.

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Disclosure

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Figure 2. The cutoff value of serum interleukin-34 levels for risk stratification in patients with acute myocardial infarction. A: Kaplan-Meier curves for MACE in patients with serum IL-34 level below and above the cutoff value. Differences between groups were analyzed with the log-rank test. B: Receiver operating characteristic curves for multivariable analyses, including risk factors with and without IL-34 as predictors of MACE in AMI patients. The risk factors included age, sex, body mass index, history of hypertension, history of diabetes mellitus, hemoglobin, eGFR, LDL, hsCRP, NT-proBNP, LVEF. Killip classification, coronary artery Gensini score, number of diseased vessel, the way of revascularization, number of implanted stents, and medication.
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