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Development and validation of a long-term prognostic prediction nomogram for ICM on the basis of polymorphism and plasma level of Mfn2

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Research Article

Keywords: Mfn2, Ischemic cardiomyopathy (ICM), Genetic polymorphisms, Prognostic nomogram

Posted Date: November 9th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11306858/v1

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Additional Declarations:
No competing interests reported.

Table 1 and 2 are available in the Supplementary Files section.

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Abstract

Objective: To investigate the association between Mitofusin2 (Mfn2) genotype and its plasma levels with long-term prognosis of ischemic cardiomyopathy (ICM), and to establish and validate a predictive nomogram for long-term prognosis of ICM, thereby providing a theoretical basis for risk assessment of ICM.

Methods: This study included 1092 ICM patients who underwent follow-up at 3, 6, 12, 24, 36, 48, and 60 months after first diagnosed with ICM. Based on follow-up outcomes, patients were categorized into survival and death groups. All patients were randomly divided into a training set (n= 764) and a validation set (n= 328). Univariate Cox regression analysis was performed on the training set. Variables with $P < 0.1$ in univariate analysis underwent Lasso regression analysis. Multivariate Cox regression models were constructed using selected variables by lasso regression analysis.followed performed model validation. Performance was evaluated using ROC curves, calibration curves, and decision curve analysis (DCA).

Results: Multivariate Cox regression analysis revealed that plasma Mfn2 levels, heart rate, serum sodium, treatment with PCI or CABG, beta-blocker use, LVDD, and mutations at SNP loci rs1042842, rs2295281, and rs2236054 were independent predictors of long-term ICM prognosis ($P < 0.05$). The nomogram constructed based

on these findings demonstrated excellent discriminatory ability in both the training and validation cohorts (AUCs: 0.824 [1 year], 0.809 [3 years], and 0.877 [5 years] in the training set; and 0.808 (1 year), 0.767 (3 years), and 0.790 (5 years) in the validation set). The model demonstrated good consistency between observed and predicted values, indicating strong clinical usefulness.

Conclusion: Elevated plasma Mfn2 levels and genetic mutations at rs223605 may represent protective factors influencing long-term prognosis in ICM, whereas mutations at rs1042842 and rs2295281 may constitute risk factors for poor long-term outcomes in ICM.

Highlights

- Elevated plasma Mfn2 levels and genetic mutations at rs223605 may represent protective factors influencing long-term prognosis in ICM
- mutations at rs1042842 and rs2295281 may constitute risk factors for poor long-term outcomes in ICM.
- The prediction model which developed in this study has good clinical usefulness.

Keywords: Mfn2; Ischemic cardiomyopathy (ICM); Genetic polymorphisms; Prognostic nomogram

Introduction

Ischemic cardiomyopathy (ICM) patients have a poor prognosis[1]. Although mortality rates have improved following hospitalization, readmissions and deaths due to adverse cardiovascular events remain common in the early post-discharge period, imposing a significant economic burden on patients and their families[2]，Statistics indicate that 26 million ICM patients worldwide exhibit significant heart failure symptoms, with treatment costs exceeding $30 billion[3]. Despite substantial treatment expenditures, ICM prognosis remains poor, with a 5-year survival rate of only approximately 50% [3]，The primary reason for the high mortality rate in ICM is that ischemic-necrotic cardiomyocytes lack sufficient regenerative and reparative capacity[4]. Cardiomyocytes subjected to prolonged ischemia are prone to developing into quiescent, hibernating, or apoptotic cardiomyocytes, leading to localized fibrotic scar formation and subsequent worsening of heart failure or refractory heart failure[5]，Therefore, Advance assessment and prediction the prognosis of ICM patients，and

Provide individualized treatment to improving the prognosis of ICM patients and reducing their readmission and mortality rates has become an urgent challenge that requires urgent attention.

Mitochondria play a crucial role in the progression of ICM[6]， When mitochondrial function is impaired, it releases large amounts of harmful substances, such as excessive Ca^{2+}, which promotes myocardial cell apoptosis and exacerbates heart failure progression[7]， During ICM, mitochondria employ various intrinsic mechanisms to maintain normal function and exert protective effects, preventing or mitigating these harmful responses[8]. This protective process is achieved through mitochondrial fusion and fission[9]， Mitofusin2 (Mfn2), a transmembrane protein located in the mitochondrial outer membrane, plays a crucial role in mitochondrial fusion and fission, ensuring the normal functioning of mitochondria[10]，Mfn2 not only plays a vital role in mitochondrial fusion and fission but also functions in mitochondrial biochemical reactions and autophagy, maintaining mitochondrial homeostasis [11]。 Therefore, it can be inferred that Mfn2 dysfunction may disrupt normal mitochondrial function, thereby exacerbating the condition of ICM patients.

Our preliminary research indicates that[12] Mfn2 gene mutations and reduced plasma Mfn2 levels correlate with ICM risk. Mfn2 mutations may cause decreased plasma Mfn2 levels, thereby increasing ICM susceptibility. Furthermore, lower plasma Mfn2 levels correlate with more severe ICM progression. Previous studies have reported that Mfn2 gene mutations are associated with hypertension, atherosclerosis, coronary heart disease, and insulin resistance. These conditions are not only risk factors for ICM but also underlying diseases and complications that exacerbate ICM severity. However, no reports exist on the correlation between Mfn2 gene polymorphisms and plasma protein levels with the long-term prognosis of ICM. Therefore, this study aims to establish a prognostic prediction model for ICM, investigate the association between Mfn2 gene polymorphisms and plasma protein levels with long-term ICM outcomes, identify independent predictive factors influencing long-term ICM prognosis, and develop and validate a predictive model capable of accurately forecasting long-term ICM outcomes. This research will provide a theoretical basis for prognosis assessment and personalized treatment strategies for ICM patients.

1. Materials and Methods

Study Design and Subjects

This study adhered to the ethical standards of the Declaration of Helsinki and was approved by the Ethics Committee of the First Affiliated Hospital of Xinjiang Medical

University (Approval No. 20150716-06). All participants provided written informed consent.

This was a prospective cohort study. A total of 1092 patients with ICM admitted consecutively to the First Affiliated Hospital of Xinjiang Medical University between January 2016 and December 2018 were enrolled according to inclusion and exclusion criteria（Figure1）. Inclusion criteria: (1) age ⩾ 18 years; (2) significant coronary artery disease characterized by at least one of the following: History of revascularization or myocardial infarction, ⩾75% stenosis of the left main or left anterior descending artery, or ⩾75% stenosis in two or more coronary arteries. (3) Echocardiographic evidence of structural or functional cardiac abnormalities; (4) Exertional dyspnea (NYHA Class II–III) with NT-proBNP ≥125 ng/L. Exclusion criteria included other cardiovascular diseases, acute decompensated heart failure, hemodynamic instability, hepatic/renal insufficiency, and hematologic or autoimmune disorders.

Data Collection and Relevant Definitions

General information, laboratory test results, and cardiovascular disease risk factors were collected for all study subjects. Included white blood cell (WBC), red blood cells (RBC), platelet count (PLT), hemoglobin (HGB), albumin, creatinine (CR), blood urea nitrogen (BUN), total cholesterol (TC), high-density and low-density lipoproteins (HDL-C, LDL-C), triglycerides (TG), serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels, etc. These indices were measured from fasting peripheral venous blood samples collected on the day of admission or the following morning. Collected risk factors included body mass index (BMI), smoking, alcohol consumption, hypertension, and diabetes. Definitions are as follows: Body mass index: Weight (kg) divided by height squared (m^2). Smoker: Individuals with a smoking history of 6 months or longer, or who were still smoking within the past 6 months. Alcohol drinker: Individuals consuming at least 100g of alcohol weekly with a drinking history of 6 months or longer, or who were still drinking within the past 6 months. Hypertension: Individuals with systolic blood pressure ⩾140 mmHg or diastolic blood pressure ⩾ 90 mmHg, based on the 2018 European Society of Cardiology (ESC)/European Society of Hypertension (ESH) guidelines[13]。Diabetes: Individuals

with plasma glucose levels ≥7.1 mmol/L, or plasma glucose levels ≥11.1 mmol/L two hours after ingesting 75g of glucose, or individuals diagnosed with diabetes.

Selecting the Target SNP

The 12 most common single-nucleotide polymorphisms (SNPs) of the Mfn2 gene were identified based on linkage disequilibrium (LD) patterns, using an r^2 ≥ 0.8 and a minor allele frequency (MAF) ≥ 0.05 as selection criteria. The investigation utilized Haploview 4.2 software and the International 1000 Genomes (1000G) database. （Supplementary Figure1） illustrates the LD map for the tagged SNPs.

Genotyping and Plasma Mfn2 Levels

All participants fasted for 12 hours before EDTA-anticoagulated blood collection. RNA and DNA were extracted using TRIzol™: 100 μL of blood was added to 1mL of TRIzol ™, mixed, and stored at -80℃ until analysis.

SNP genotyping was performed using the enhanced multiplex ligation detection reaction (eMLDR) technique (Genesky Biotechnologies Inc., Shanghai, China). Plasma Mfn2 concentrations were quantified utilizing an Mfn2 ELISA kit (mlbio, Shanghai, China).

Outcome Events and Follow-up Content

Follow-up for this study was conducted by specially trained personnel.The outcome event was Cardiogenic death. The time to Cardiogenic death was recorded as the interval from ICM diagnosis to Cardiogenic death. Patient follow-up commenced at the time of initial ICM diagnosis, with subsequent visits scheduled at 3, 6, 12, 24, 48, and 60 months.

Follow-up content included: Determining whether ICM patients experienced Cardiogenic death; if so, recording the time of death and calculating survival duration;Documentation of guideline-compliant medication use following ICM diagnosis, including antiplatelet agents (e.g., aspirin tablets, clopidogrel sulfate tablets/ticagrelor tablets), statins, ACE inhibitors/ARBs, beta-blockers, calcium channel blockers, spironolactone tablets, furosemide tablets, etc.

Statistical Methods

Statistical analysis was performed using SPSS 27.0 and R 4.3.1 software. All subjects

were randomly divided into a training set [764 (0.7)] and a validation set [328 (0.3)], categorized into survival and death groups based on survival status within 5 years. Univariate Cox regression analysis was performed on patient demographics, laboratory results, plasma Mfn2 levels, and genomic data from the training set. $P < 0.05$ was considered statistically significant. To optimize variable selection, Lasso regression analysis was employed. Variables with $P < 0.1$ in univariate analysis were included in Lasso regression for variable selection optimization. Subsequently, variables selected by Lasso regression were incorporated into multivariate Cox regression analysis to establish predictive models and generate nomograms.

Model Validation

Model Validation was assessed through the model's discriminatory power, calibration, and clinical utility. First, a ROC curve was plotted, and the area under the curve (AUC) was calculated to evaluate the model's discriminatory ability[14]. Calibration curves assess model consistency[15]. To evaluate clinical utility, clinical decision curves assess net benefit at different threshold probabilities[16, 17]. Net benefit is measured by subtracting the proportion of false positives from the proportion of true positives, then balancing the relative risk of forgoing intervention against the negative consequences of unnecessary intervention.

2. Results

Among 1092 ICM patients, based on 60-month follow-up results, 544 survived, 472 died, and 76 were lost to follow-up. The 1092 ICM patients were randomly divided into a training set [764 cases (0.7)] and a validation set [328 cases (0.3)].

Univariate Cox Regression Analysis of Clinical Indicators and Genotypes in the Modeling Set

The 764 ICM patients in the modeling cohort were divided into a 5-year survaival group and a 5-year death group based on follow-up outcomes. Univariate Cox regression analysis on clinical data and genotypes at 12 tag SNPs of the Mfn2 gene revealed that： plasma Mfn2 levels, heart rate, hemoglobin, serum sodium, serum albumin levels, LVDD, NT-pro BNP, LVEF, and PCI or CABG treatment， mutations in two SNPs (rs1042842 and rs2295281) were significantly associated with long-term prognosis of ICM ($P < 0.05$) (Supplementary Table1).

Lasso Regression Analysis

To optimize variable selection, indicators with $P < 0.1$ (referencing the dominant model results from the genetic analysis) were selected from the univariate Cox regression

analyses of clinical indicators and genotypes（Table1）. These were incorporated into Lasso regression analysis. Following Lasso regression analysis, the 15 variables were ultimately reduced to 9 variables (Figure2).

Multivariate Cox Regression Analysis and Scatterplot

Multivariate Cox regression analysis using the above nine variables revealed that plasma Mfn2 levels, heart rate, serum sodium levels, treatment with PCI or CABG, beta-blocker use, LVDD, and mutations at the rs1042842,rs2295281, and rs2236054 SNP sites were independent predictors of long-term prognosis in ICM patients ($P < 0.05$) (Table 2). A clinically applicable visual nomogram was constructed using the nine variables included in the model (Figure 3)

Model Validation

Evaluating Model Discrimination ability

ROC curves were used to assess the model's discriminaton ability in both the training and validation cohorts. In the training cohort, the areas under the ROC curve were 0.824 (1 year), 0.809 (3 years), and 0.877 (5 years).In the validation set, the AUC values were 0.808 (1 year), 0.767 (3 years), and 0.790 (5 years) (Figures 5 A and B), indicating the model possesses good discriminatory ability（Figure4）.

Evaluating Model Consistency

Calibration curves were used to assess model consistency. By developing the calibration curves for the training and validation sets at 1, 3, and 5 years as shown in（Figures 5 A, B, C, and D, E, F), it was observed that the model's predicted values exhibited good consistency with the actual observed values in both the training and validation sets.

Evaluating the Clinical Effectiveness of the Model

DCA curves for 1-year, 3-year, and 5-year periods were constructed in both the training and validation sets (Figure 6) to assess clinical efficacy. The DCA curves demonstrate that this model exhibits good clinical efficacy and can be applied to predict long-term prognosis in ICM patients.

Prognosis Analysis of High-Risk vs. Low-Risk ICM Patients

（1）Using the cutoff value (260.7161) of the total score as the dividing point, all ICM patients were categorized into high-risk and low-risk groups. And developed A scatter plot which illustrates the grouping(Figure 7 A) and survival status(Figure 7 B) of all ICM patients, revealing that the number of deaths within 5 years was higher in the high-

risk group than in the low-risk group.

(2) Survival curves were plotted using the Kaplan-Meier method for both high-risk and low-risk groups to compare 5-year survival rates between high-risk and low-risk ICM patients. Results demonstrated that： a statistically significant difference in 5-year survival rates between the two groups ($P < 0.001$; HR=9.003; 95% CI: 6.720-12.062) (Figure 8 A). The five-year mortality risk for high-risk ICM patients was 9.003 times higher than that for low-risk ICM patients.

(3) Correlation between plasma Mfn2 levels and long-term ICM prognosis: To assess the correlation between plasma Mfn2 levels and long-term prognosis of ICM, we developed a Restricted Cubic Spline (RCS). Results showed that plasma Mfn2 levels were negatively correlated with 5-year mortality in ICM patients ($P < 0.001$), with a linear relationship ($P_{nonlinear} = 0.269$) (Figure 8B).

3. Discussion

This study followed 1092 ICM patients for 60 months, with 544 survivors, 472 deaths, and 76 lost to follow-up. Statistical analysis of relevant data identified factors influencing long-term prognosis in ICM patients. Based on this, a predictive model for long-term prognosis in ICM patients was established and validated. Results revealed that factors influencing long-term prognosis in ICM patients included: using of beta-blocker, heart rate, serum sodium levels, undergoing PCI or CABG, LVDD, plasma Mfn2 levels, and mutations at the Mfn2 gene rs1042842, rs2295281, and rs2236054 SNP sites.

This study first demonstrates that plasma Mfn2 levels correlate with long-term prognosis of ICM patients. For each unit decrease in plasma Mfn2 levels, the 5-year mortality in ICM patients increases by 0.191-fold. Plasma Mfn2 levels may represent a protective factor influencing long-term prognosis of ICM patients. Mfn2 is a transmembrane protein located on the outer mitochondrial membrane[18, 19], while mitochondria serve as vital cellular organelles[20]. Mitochondria comprise two membranes: the outer mitochondrial membrane (OMM) and the inner mitochondrial membrane (IMM), with the space between them termed the intermembrane space[21]. Functioning as cellular powerhouses, mitochondria critically regulate myocardial cell activity[22]. structural abnormalities in mitochondria impair cardiac functions such as pumping blood.Within cells, mitochondria exist in a state of dynamic equilibrium[23]. Mitochondrial dysfunction is closely associated with the onset and progression of various diseases, including diabetes, neurodegenerative disorders, hypertension, heart failure, and others[21].

Abnormal mitochondrial function can exacerbate ICM disease severity [24].The physiological functions of mitochondria in the body include[24]：(1) Energy conversion and supply: Mitochondria serve as the primary site for cellular energy synthesis, particularly during aerobic respiration. Through oxidative phosphorylation, they convert organic compounds like glucose, fatty acids, and amino acids into ATP—the direct energy source required for all cellular activities. Thus, mitochondria are often referred to as the "powerhouse" of the cell[23]，(2) Involvement in cellular metabolism: Beyond energy production, mitochondria mediate diverse metabolic processes including glucose, fatty acid, and amino acid metabolism. These processes are critical for sustaining normal physiological functions.(3) Mitochondria regulate apoptosis: Mitochondria play a pivotal role in the apoptosis process. They control cellular survival by activating apoptosis signaling pathways through regulating transmembrane sites or releasing apoptosis-related proteins. This is vital for maintaining the normal cell life cycle and proper immune system function.(4) Mitochondrial involvement in calcium ion storage and regulation: Mitochondria possess strong calcium ion uptake capacity, serving as buffering compartments for intracellular calcium storage[25]. They also interact synergistically with the endoplasmic reticulum and extracellular matrix to maintain dynamic equilibrium of intracellular calcium concentrations[26]. These mitochondrial functions are vital for normal cellular physiology.As a transmembrane protein located on the outer mitochondrial membrane, Mfn2 influences the progression and development of ICM by regulating these mitochondrial functions[18], thereby impacting ICM prognosis. The specific functions and mechanisms of Mfn2 in mitochondrial regulation are as follows: (1) Modulating mitochondrial fusion and fission by controlling direct contact and material exchange between mitochondria and the endoplasmic reticulum to regulate cellular calcium levels[27].(2) It regulates apoptosis by controlling mitochondrial autophagy for mitochondrial quality control, removing energetically dysfunctional mitochondria while preserving intact, functionally normal mitochondria[27-29]. (3) Mfn2 inhibits the onset and progression of myocardial hypertrophy and heart failure. Given these critical mitochondrial functions, reduced Mfn2 levels in vivo may impair normal mitochondrial function[24, 30].

The results of this study indicate that the rs1042842 mutation in the Mfn2 gene is a risk factor affecting the long-term prognosis of ICM. ICM patients carrying the mutant gene have a 3.088-fold higher risk of death within 5 years compared to those with the wild-type gene.rs1042842 is located on exon 19 within the non-coding region of the Mfn2 gene. Although this SNP resides within an exon, its position in the non-coding region means it does not affect amino acid coding, protein structure, or function. However, interactions between SNP sites on the gene may influence the function of other SNPs,

potentially exacerbating ICM severity and increasing mortality risk. Regardless of the specific function of rs1042842, its mutation increases mortality risk in ICM patients. Additionally, this study identified the rs2295281 mutation as another risk factor for long-term ICM prognosis, with ICM patients carrying the mutant allele exhibiting a 2.095-fold higher 5-year mortality risk compared to those with the wild-type allele.rs2295281 is located within intron 8 of the Mfn2 gene. Introns, as non-coding regions, do not contribute to amino acid coding but may influence gene expression regulation and other functions. Similar to rs1042842, mutations at the rs2295281 locus also elevate mortality risk in ICM patients. Collectively, these findings indicate that mutations in both SNPs play a significant role in the long-term prognosis of ICM patients. They not only serve as predictors of ICM onset risk but also function as important indicators for assessing long-term prognosis in ICM patients.

This study further revealed that the rs2236054 mutation acts as a protective factor for long-term ICM prognosis. The 5-year mortality risk for ICM patients carrying the mutant was 0.484 times of those with the wild-genotype. rs2236054 is located in the 5'untranslated region of the Mfn2 gene. This SNP does not participate in amino acid coding and does not affect the structure or function of the Mfn2 protein. However, SNPs at this gene locus may influence the function of other SNPs.The mechanism by which the rs2236054 mutation exerts a protective effect on ICM prognosis may involve: various environmental influences the self-protective system in ICM patients is activated, leading to disruption of the original rs2236054 SNP genotype. Alternatively, the mutation may influence the function of other protective SNPs or antagonize the function of deleterious SNPs.Overall, the rs2236054 mutation may represent the activation of the ICM self-protective system, potentially improving patient prognosis and reducing mortality. Therefore, clinically, mutations at the rs2236054 locus serve as a significant indicator for predicting long-term ICM prognosis.

In summary, this study identified factors influencing long-term prognosis in ICM patients, including: beta-blocker use, heart rate, serum sodium levels, undergoing PCI or CABG, LVDD, plasma Mfn2 levels, and mutations at the Mfn2 gene rs1042842, rs2295281, and rs2236054 SNP loci. Among these, beta-blocker use, heart rate control, revascularization via CABG or PCI, elevated plasma Mfn2 levels, and mutation at the Mfn2 gene rs2236054 site represent protective factors for improving long-term outcomes in ICM patients. Conversely, serum hyponatremia, enlarged LVDD, and mutations at the Mfn2 gene rs1042842 and rs2295281 were identified as risk factors for ICM long-term prognosis. These findings reveal novel biomarkers and genetic targets for predicting ICM long-term outcomes, with the established prognostic model demonstrating good discriminatory power and strong consistency between observed

and predicted values. Despite the promising clinical utility of these results, certain limitations exist: First, this study is a single-center investigation with a limited sample size, necessitating multicenter, large-scale studies to validate the findings. Second, the results have undergone internal validation only and require external validation for further confirmation. Third, although mutations in the Mfn2 gene and plasma Mfn2 levels were found to correlate with long-term ICM prognosis, the specific mechanisms require further elucidation through functional studies.

Conclusion

Elevated plasma Mfn2 levels and genetic mutations at rs223605 may play protective role in long-term prognosis of ICM, whereas mutations at rs1042842 and rs2295281 may result inpoor long-term outcomes in ICM. This findings provide new therapeutic insights for ICM. And the nomogram model which established in this study has good discrimination ability，has strong consists with actual value，and has good clinical usefulness. It can be used in clinic to evaluate the long-term prognosis of ICM, and to improve its prognosis.

Acknowledgments

Not Applicable.

Author contributions

Tuersunjiang Naman and Ailiman Mahemuti performed the experiment，wrote the article. Rukeyaguli Aini , Ayinuer·maihemuti and Ding Yu collected the data and performed the follow-up. Zi-tong Guo performed the statistical analysis and supervised all process.All authors read and approved the final manuscript.

Funding

Tianshan Talent’s medical and health high-level personnel training program (Grant Number:TSYC202401B021)

Data availability statement

The data and materials supporting the findings of this study are available from the first author upon request.

The SNP data used in this study are available at:

https://www.ncbi.nlm.nih.gov/SNP/snp_viewTable.cgi?handle=LXJMU

Declarations

Ethics approval and consent to participate

This study strictly adhered to the Declaration of Helsinki, and all patients and/ or their legal representatives signed informed consent forms. The ethics of this study were reviewed and approved by the Ethics Committee of First affiliated hospital.

Consent for publication

Not applicable

Clinical trial number

Not applicable.

Competing interests

The authors declare no competing interests.

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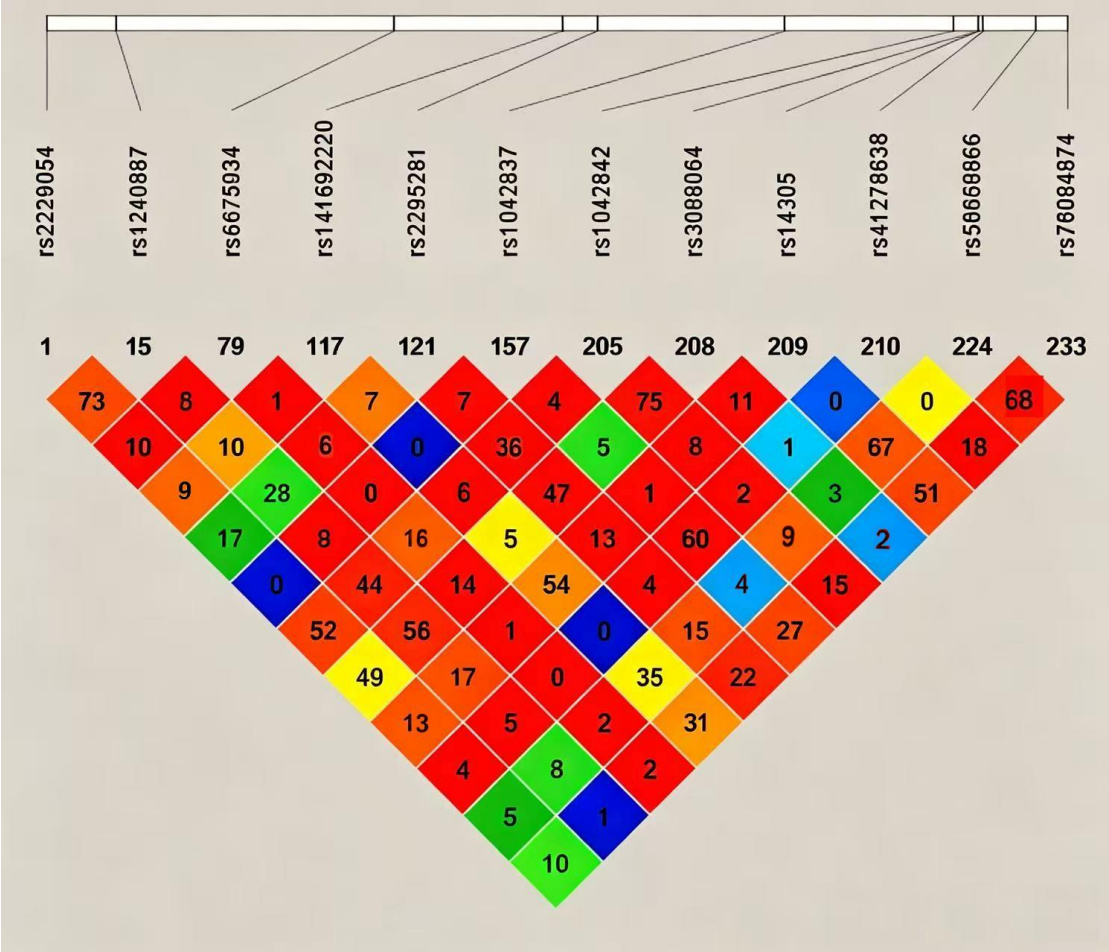
Table legends：

Supplementary Table1： Univariable Cox-regression analysis on all Clinical data and SNPs

Table1： Univariable Cox-regression analysis on Clinical data and SNPs

Table2 Multivariable Cox-regression analysis and establishmen the prognostic model

Figure



Supplemetary Figure1: Linkage disequilibrium（LD）map of SNPs of the Mfn2 gene

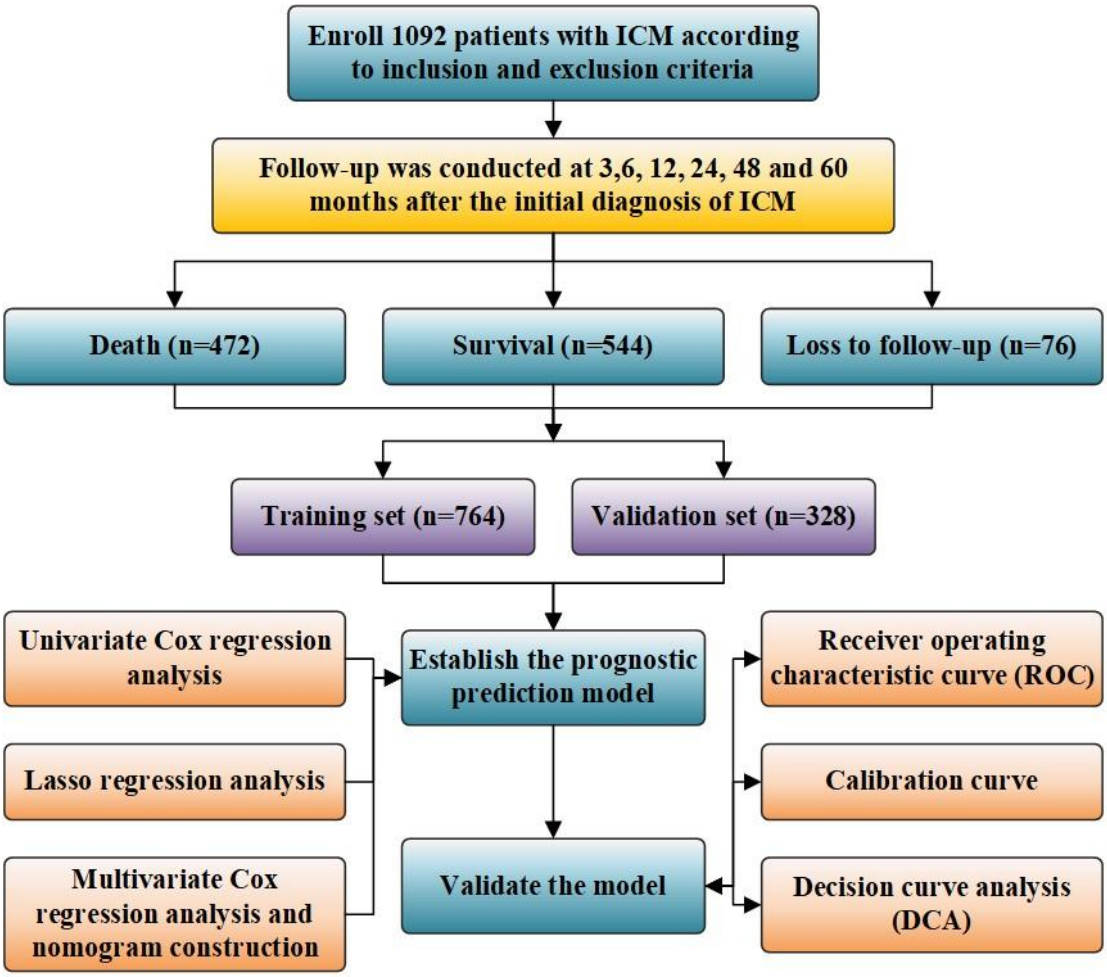


Figure1： Flowchart of this study

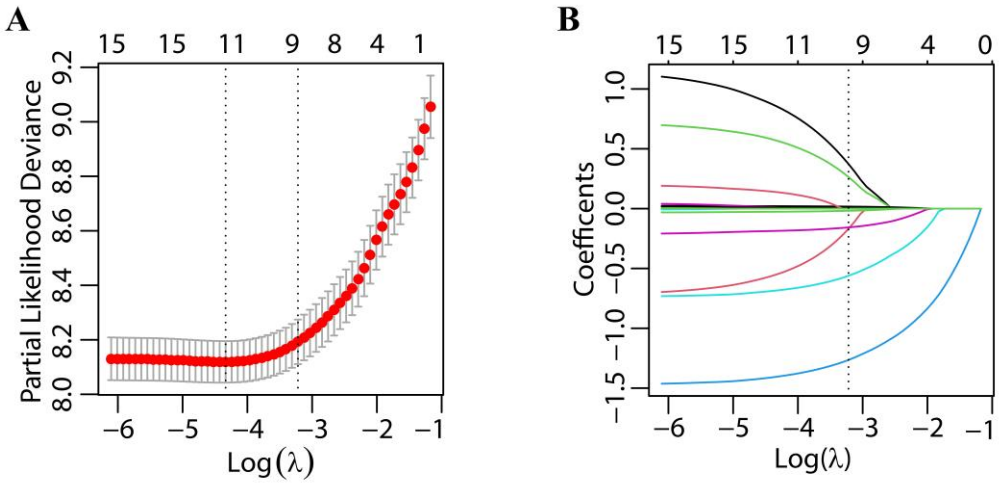


Figure2： Selected features based on the LASSO model. (A) 10-fold cross-validation was carried out to select the tuning parameter (λ) based on the LASSO model based on

the minimum criteria. The C-index was plotted versus log(λ). Dotted vertical lines were drawn at the optimal values by using the minimum criteria and the 1 standard error of the minimum criteria (1-SE criteria). (B) LASSO coeffcient profles of the 9 features, a coeffcient profle plot was produced against the log(λ) sequence. Vertical line was drawn at the value selected using 10-fold cross-validation, where optimal λ resulted in nonzero coeffcients.

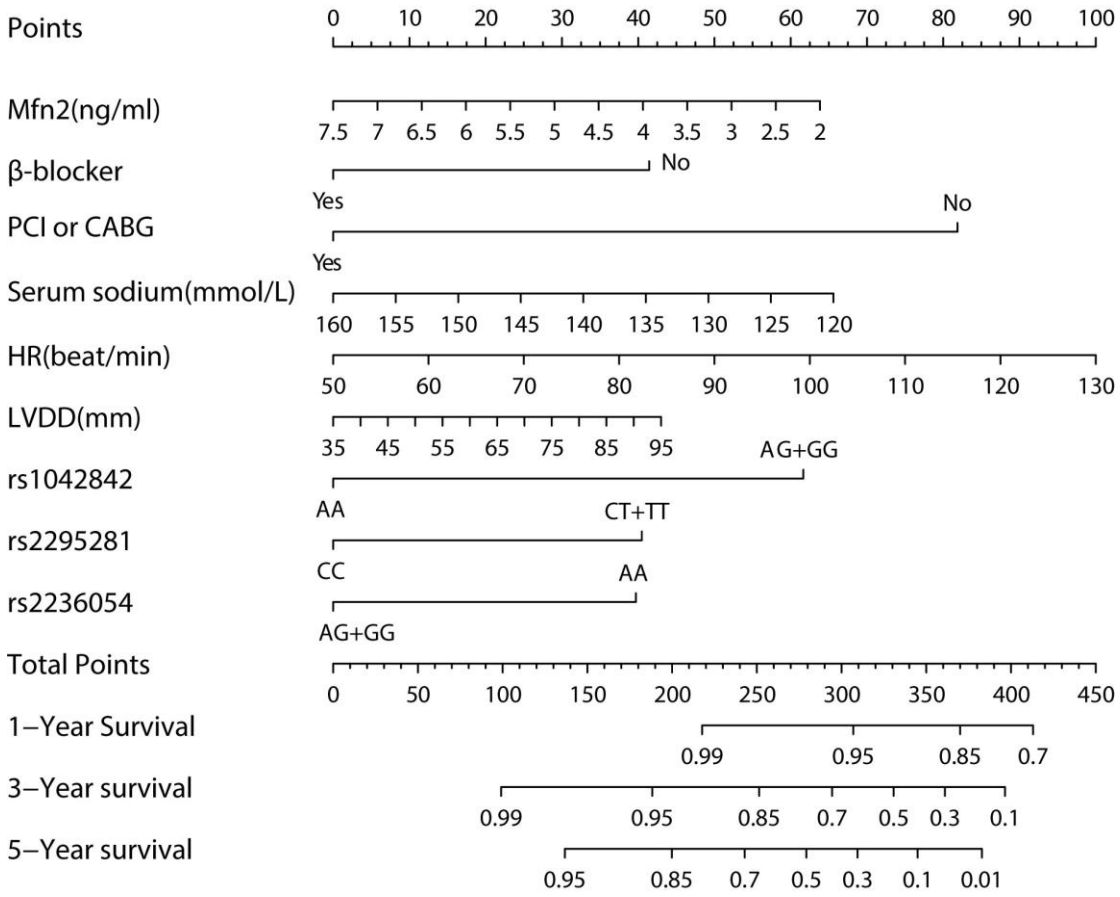


Figure3： Nomogram for evaluating the survival rate of ICM.

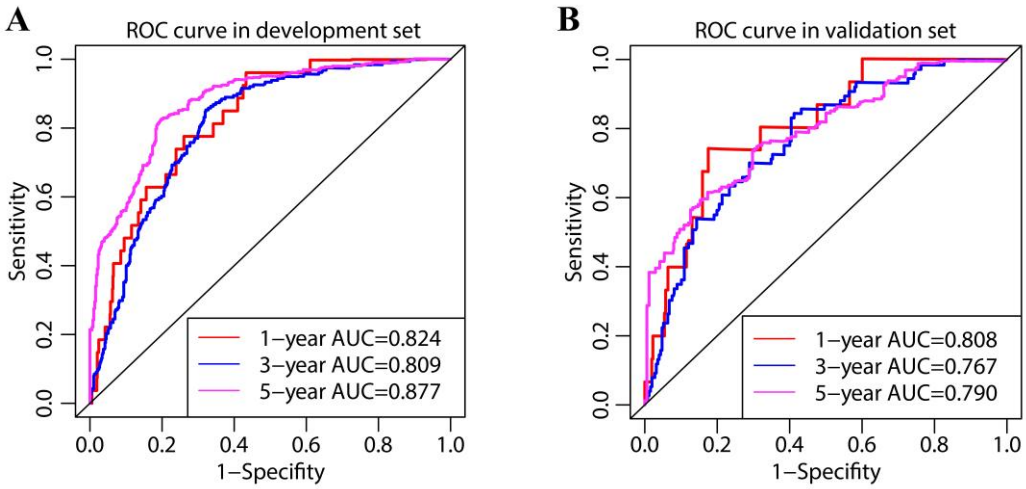


Figure 4: Receiver operating curve（ROC） of 1-year, 2-year, 3-year in the training set (A) and validation set (B).

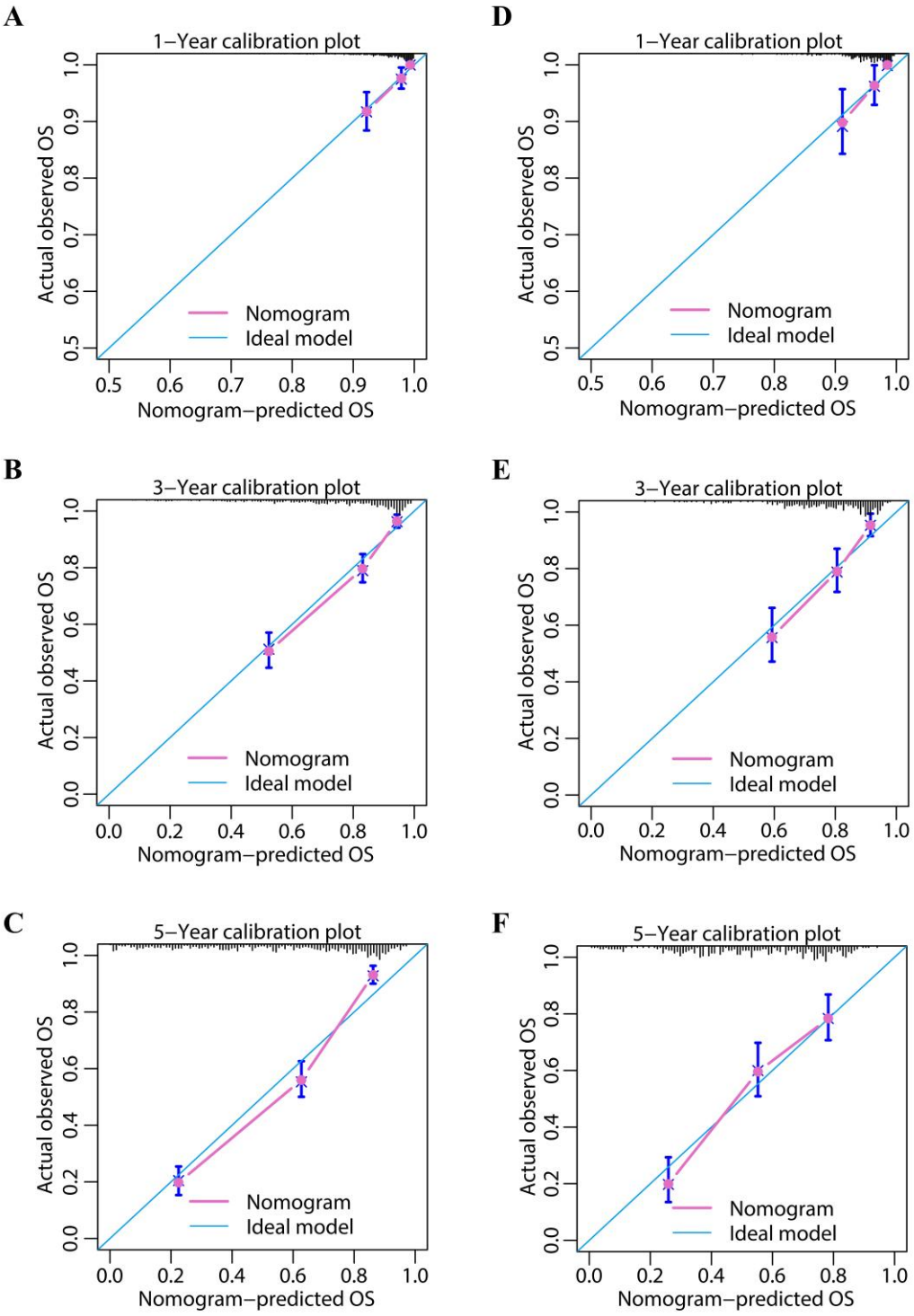


Figure 5: Calibration plot for the nomogram. (A–C): Calibration plot for the 1-year survival (A), 3-year survival (B) and 5-year survival (C) in the training set. (D–F): Calibration plot for the 1-year survival (D), 3-year survival (E) and 5-year survival (F)

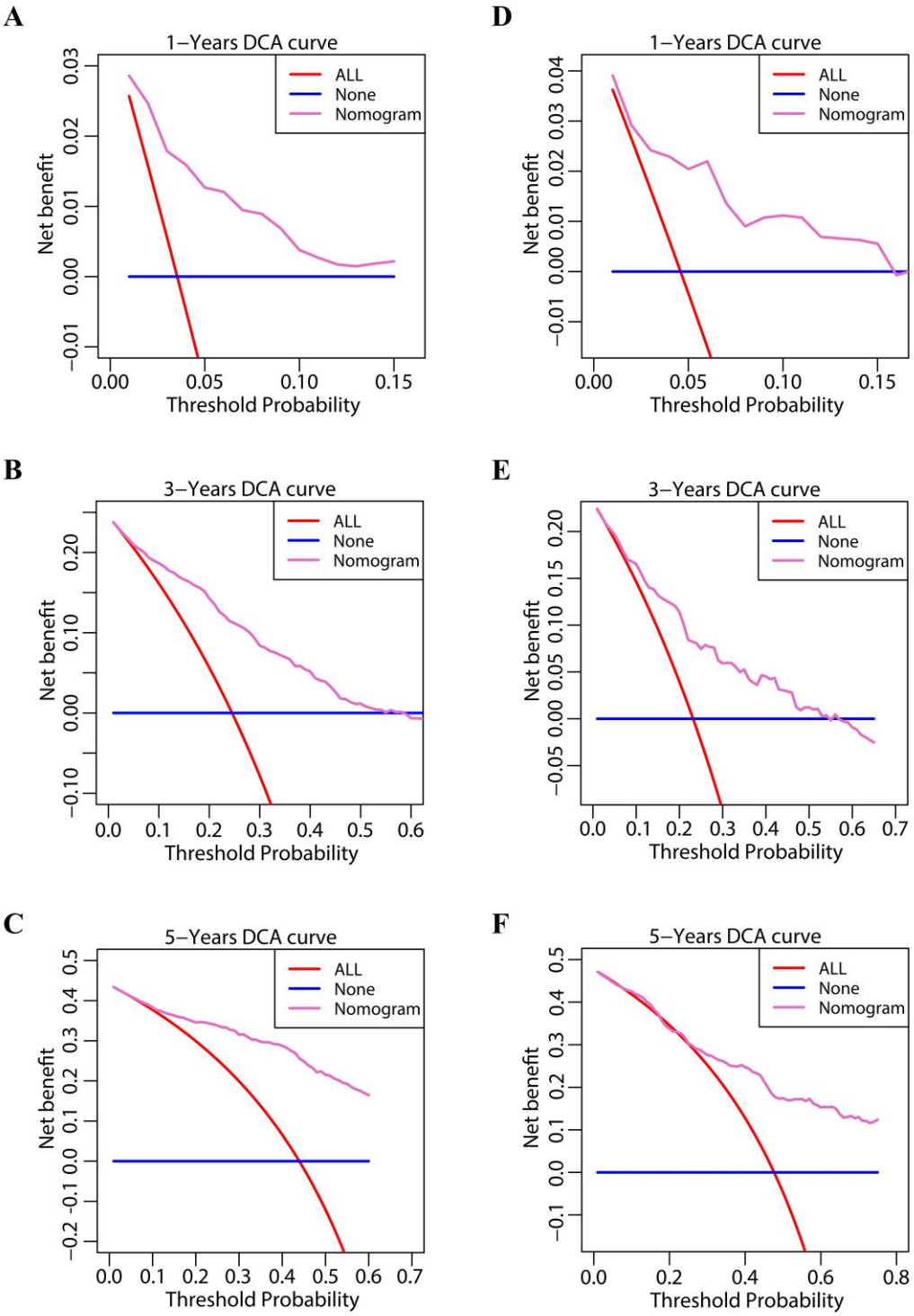


Figure 6: Decision curve analysis of the nomogram. (A–C): Decision curve analysis of the nomogram for 1-year (A), 3-year (B) and for 5-year (C) in the training set. (D–F): Decision curve analysis of the nomogram for 1-year (D), 3-year (E) and for 5-year (F)

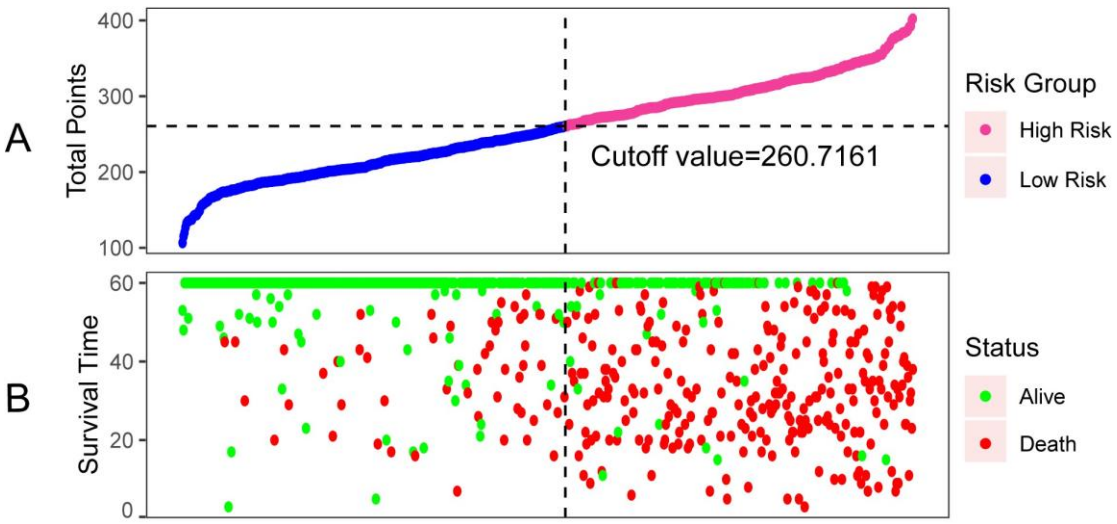


Figure 7: Division and distribution of patients according the risk and statues. (A) Division of high and low risk group according to the cutoff value of total point of nomoscore. (B) Distribution of survival status of high and low risk patients.

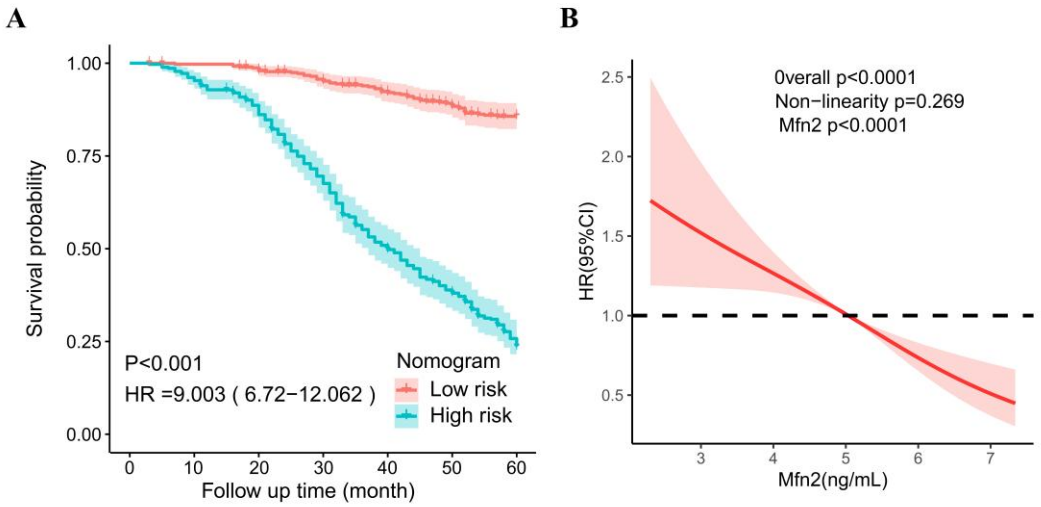


Figure 8:(A) Survival curve showing high- and low-risk group patients of ICM. (B)Dose–response relationship between plasma Mfn2 level and prognosis of ICM (restricted cubic spline)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryTable1.docx
- Table1.docx
- Table2.docx