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ORIGINAL RESEARCH

The Prognostic Value of Platelet-to-Lymphocyte Ratio and Tricuspid Regurgitation Velocity in Patients with Light-Chain Myocardial Amyloidosis

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Purpose: To explore the prognostic value of inflammatory indexes and novel echocardiographic parameters in light-chain myocardial amyloidosis (AL-CA) patients.

Methods: We retrospectively collected clinical, laboratory, electrocardiography and echocardiographic parameters of patients. The prognostic value of inflammation indexes and echocardiographic parameters was assessed, and the association of inflammation indexes with cardiac function and the type of light chain (AL) was analyzed.

Results: In total, 83 biopsy-proven AL-CA patients were studied (age: 61.42±10.7 years; 68.7% male). The inflammation indexes [PLR (Platelet-to-Lymphocyte ratio), NLR (Neutrophil-to-Lymphocyte ratio), NMLR ((Neutrophil+Monocyte)-to-Lymphocyte ratio), SIRI ((Monocyte × Neutrophil)-to-Lymphocyte ratio), SII ((Platelet × Neutrophil)-to-Lymphocyte ratio), (all $P<0.001$)] and echocardiographic parameter TRV (Tricuspid Regurgitation Velocity), ($P=0.005$) were significantly higher in deceased patients compared with survivors. Multivariate COX regression analysis indicated that PLR, TRV, Lymphocyte (LYM) and Left Ventricular Ejection Fraction (LVEF) were independent outcome predictors. The PLR, TRV, and the combined indicator (PLR+TRV) showed great value in predicting short-term prognosis. The likelihood ratio $\chi 2$ test showed that PLR and TRV added predictive values to the Mayo04, Mayo12, and Euro15 models. The Spearman correlation analysis demonstrated a positive correlation between the inflammation indexes and New York Heart Association (NYHA) class, Mayo04 stage, Mayo12 stage, and Euro15 stage. Additionally, the NLR ($P<0.001$), NMLR ($P=0.002$), SIRI ($P=0.029$), and SII ($P<0.001$) were higher in Lambda than in Kappa light-chain patients.

Conclusion: Our study revealed that PLR and TRV were valid predictors of short-term survival in AL-CA, and the levels of several inflammation indexes correlated with the severity of cardiac involvement and AL subtype.

Keywords: light-chain myocardial amyloidosis, inflammatory index, tricuspid regurgitation velocity, prognosis

Introduction

AL amyloidosis is a fatal disease characterized by monoclonal plasma cell hyperplasia and deposition of insoluble fibrils formed by immunoglobulin light chains in various organs. In approximately two-thirds of AL amyloidosis, there is cardiac impairment at diagnosis, which is a major determinant of prognosis. The overall survival (OS) was estimated at 1.3 years from diagnosis for patients with AL-CA.[1] Patients with symptoms of heart failure (HF) have a fulminant disease course with a median survival of approximately 3–4 months.[2,3] Thus, early identification of patients with poorer prognosis may serve clinicians in timely tailoring treatment regimes and focusing on achieving cardiac remission as soon as possible.

Several parameters of cardiac morphology and function have been described for the risk assessment of AL-CA. Some biomarkers, such as cardiac troponin-T (cTnT), N-terminal pro-B-type natriuretic peptide (NT-pro-BNP),[4] and serum-free light chain difference (dFLC),[5] have been incorporated into the prognostic staging system of AL-CA. Other clinical markers and imaging parameters, including von Willebrand Factor (vWF),[6] soluble suppression of tumorigenicity2 (sST2),[7] higher E/A ratio, increased left ventricular wall thickness and decreased fractional shortening on echocardiography,[8] higher extracellular volume (ECV),[9] and late gadolinium enhancement (LGE) on cardiac magnetic resonance examination (CMR),[10] have been demonstrated

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to be predictors of prognosis in AL-CA. Nonetheless, the accuracy of certain indicators (eg, cTnT, NT-pro-BNP) assays may be affected by renal insufficiency.[11,12] Although CMR is clinically valuable in diagnosis and prognosis, it is not available to all patients because of limitations in the availability of facilities and patient tolerance (eg, patients with metal implantations or patients with claustrophobia). In addition, some imaging parameters merely mirror localized cardiac involvement and do not adequately capture the overall condition of the body.

Inflammation indexes are novel biomarkers that provide an overview of the overall inflammatory state. They are calculated by integrating various cell subgroups, including platelets, neutrophils, monocytes, and lymphocytes.[13] Consequently, they are more concise, widely available, affordable, and can be applied for routine use in laboratories with limited resources for disease evaluation. In recent decade, a series of inflammation indexes have emerged as robust indicators for prognostic prediction in cancers and cardiovascular diseases.[14,15] The association of inflammation indexes with AL-CA requires further investigation. In addition, echocardiography, as a brief, non-irradiating, and noninvasive technique, is being increasingly investigated. The clinical value of more relevant imaging parameters is expanding, and their prognostic value in AL-CA warrants further exploration. Hence, the aim of this investigation was to explore the prognostic value of inflammatory indexes and echocardiographic parameters in cohorts with AL-CA, as well as the correlation of inflammatory indexes with the AL subtype and the severity of cardiac involvement.

Method

Study Population

In total, 83 patients with confirmed AL-CA admitted to Beijing AnZhen Hospital, Capital Medical University, between January 2018 and October 2024 were enrolled in this retrospective study. The inclusion criteria were as follows: (1) positive cardiac biopsy for CA or (2) a tissue biopsy demonstrating AL amyloid deposits with unexplained thickened Left ventricle wall thickness and elevated NTpro-BNP.[16] All patients had no history of other cardiomyopathies or myocardial infarction on admission or during follow-up. Demographic and clinical data were collected from patients with AL-CA electronic health records.

Clinical Evaluation and Laboratory Data

The clinical and laboratory parameters involved in the interpretation included the following categories: general information of the patients; baseline complete blood cell counts, biochemical examination indicators, myocardial injury markers, AL phenotype, serum involved/non-involved free light chain ratio (iFLC/niFLC) and difference (dFLC), electrocardiographic manifestations, and echocardiographic parameters. AL-CA was further classified into kappa isoforms and lambda isoforms based on the type of immunoglobulin light chain involved.[17]

Definition of Inflammation Indexes

PLR (Platelet-to-Lymphocyte ratio), NLR (Neutrophil-to-Lymphocyte ratio), NMLR [(Neutrophil+Monocyte)-to-Lymphocyte ratio], SIRI [(Monocyte × Neutrophil)-to-Lymphocyte ratio], and SII [(Platelet × Neutrophil)-to-Lymphocyte ratio] were defined, respectively.

Definition of Other Organs Involvement

Other organs involvement was categorized based on the 2005 consensus criteria.[18] The definitions are as follows: (1) Kidney: Daily urine collection: proteinuria >0.5 g/day; (2) Liver: Alkaline phosphatase activity >1.5 upper reference range; (3) nervous system: clinical symptoms: sensorimotor, symmetrical, peripheral neuropathy of the lower extremities; (4) gastrointestinal tract: direct biopsy confirmation of the presence of amyloid deposits in conjunction with clinical symptoms; (6) Lung: Biopsy confirmation of the presence of amyloids in conjunction with clinical symptoms; X-ray showing interstitial lesions in the lungs; (7) tongue and skin: biopsy confirmation of the presence of amyloids.[18]

Cardiac Function Staging Criteria

Based on the Mayo04 staging criteria, patients were classified into stage I, II, or III according to whether they had 0, 1, or 2 of the following findings: NT-proBNP≥332 ng/L, cTnT≥0.035 ug/L.[4] Patients were classified as having Mayo12 stage I, II, III, or IV disease according to whether they had 0, 1, 2, or 3 of the following findings: NT-proBNP≥1800 ug/L, cTnT≥0.025 μg/L, and a difference between involved and uninvolved serum free light-chain concentrations (dFLC) ≥180 mg/L.[5] Besides, the Euro15 (European 2015, a modified version of the Mayo04 model) further stratifies Mayo04 stage III into stages IIIa and IIIb based on NT-proBNP levels <8500 ng/L (stage IIIa) and NTpro-BNP levels >8500 ng/L (stage IIIb).[19,20] According to the cardiac function classification criteria defined by the NYHA in 1928, patients were categorized as NYHA class I, II, III, or IV.[21]

Follow Up

All patients were followed up or via telephone before recording follow-up data. The final follow-up date was October 1, 2024. The endpoint event was defined as all-cause death, and the follow-up time was defined as the time from diagnosis to the last follow-up or death.

Statistical Analysis

Continuous variables are presented as means ± standard deviations (SDs) or medians (interquartile ranges, IQRs) and were compared using *T*-tests or Wilcoxon rank-sum tests when appropriate. Categorical variables were expressed as frequencies and percentages and were compared using the chi-square test or Fisher's exact test when appropriate. Univariate Cox regression analyses were performed to identify independent predictors of mortality. Variables exhibiting a significance threshold of $p<0.05$ and relevant variables were incorporated into the multivariate Cox regression analysis. Possible collinearity among candidate predictors was assessed using variance inflation factors (VIF) with a threshold equal to 10. To avoid statistical coupling of variables, separate multivariable models were performed that excluded parameters derived from one another. Prognostic factors for overall survival (OS) were identified based on Proportional Hazards Regression (COX) analysis. Time-to-event Receiver Operating Characteristic (ROC) curves were estimated to investigate the ability of variables to predict prognosis. The performance of PLR, TRV and combined indicator in the entire collective was compared to Mayo04 stage, Mayo12 stage and Euro15 stage by means of the area under the receiver operating characteristic curve (AUC). The Spearman correlation coefficient analysis was applied to evaluate the correlation between cardiac function and inflammatory indexes. OS was estimated using the Kaplan-Meier method, and differences in subgroups were assessed using the Log rank test for trend. All analyses were performed using SPSS.26 and R 4.4.2.

Results

General Characteristics of Patients

The baseline characteristics of the 83 patients [57 (68.7%) male and 26 (31.3%) female] in this study are listed in Table 1. The mean age of the patients was 61.42±10.7 years. Median OS was 22 (13–30) months with 41 (49.4%) patients alive at 14 months median follow-up (Figure 1). 68 (81.9%) patients had Lambda and 15 (18.1%) patients had Kappa as their AL subtype according to the isoform of the type of immunoglobulin light chain involved. The severity of cardiac involvement in all patients on admission was assessed. The cardiac function stages according to the NYHA classification system were grades II, III, and IV in 25 (30.1%), 44 (53%), and 14 (16.9%) patients, respectively. With respect to the Mayo04 staging system, 8 (9.7%), 28 (33.7%), and 47 (56.6%) patients were classified as stage I, II, and III, respectively. There were 4 (4.8%), 24 (28.9%), 32 (38.6%), and 23 (27.7%) patients with stages I, II, III, and IV, respectively, depending on the Mayo12 staging system. In addition, according to the Euro15 staging system, 8 (9.6%), 28 (33.7%), 23 (27.7%), and 24 (28.9%) patients were categorized as stage I, II, IIIa, and IIIb, respectively. On ECG, abnormal ST/T waves were present in 70 (84.3%) patients. In total, 42 (50.6%) patients had low voltage and 23 (27.7%) patients showed poor R-wave progression. Arrhythmias were present in 50 (60.2%) patients, of whom conduction block and atrial fibrillation were present in 36 (43.4%) and 16 (19.3%) patients, respectively. Due to the limitations of retrospective studies, echocardiographic data of 72 cases were available for our analysis. A substantial proportion of 18 (25.0%) patients demonstrated moderate to severe mitral/tricuspid valve regurgitation on echocardiography. In total, 7 (9.7%)

Table 1 Baseline Characteristics of the 83 Patients and a Comparison Between Survival and Death Group

	Total(n=83)	Survival Group(n=41)	Death Group(n=42)	P Value
Age, years	61.42±10.7	61.34±10.7	61.5±10.82	0.947
Cardial markers				
cTnT, pg/mL	87.65(24.53,156.93)	80.6(17.88,155.35)	88.2(26.48,188.65)	0.682
NTproBNP, pg/mL	5661(3238,10,683)	5474(2416,10,026)	7703(3588.75,11,995)	0.461
Echocardiography parameters				
LAD[a], mm	57(51,63)	57(53,62.75)	57(48.75,63.75)	0.844
LVEDD[a], mm	44(38,47.75)	45.5(37.5,47)	43(38,48.75)	0.835
IVST[a], mm	13(12,16)	14(12,15.65)	13(12,17)	0.964
LVPW[a], mm	13(11.4,15)	13.3(11.25,15)	13(11.4,16)	0.922
LVEF%[a]	54(43.5,63.25)	58(43.5,64)	52(44.25,57.5)	0.215
E/A[a]	1.59(0.92,2.79)	1.65(0.7,2.61)	1.42(1.15,2.9)	0.858
TRV[a], cm/s	270(213,299)	248(210,287.25)	280(236,330)	0.005
AFV[a], cm/s	94(73.75,105.25)	128.5(105.5,158.25)	122.5(105,134)	0.251
IVSMA[a], mm	5(4,7)	6(3.75,8)	5(4,6.5)	0.289
LVESD[a], mm	30(27,34)	30(28,33.25)	30(25.25,34)	0.473
LVMI[a], g/m^2	124.04(93.8,153.22)	117.11(98.10,139.34)	131.48(87.14,162.58)	0.732
RVD[a], mm	22(19,24.5)	21(19,23)	22(19,25)	0.461
RAD[a], mm	54(51,57)	54(50.5,57.5)	53(50.75,57)	0.547
MPAD[a], mm	24(23,28)	24.5(23,27.25)	24(23,28.75)	0.717
PAFV[a], cm/s	84(69,100)	85(73.5,103)	82(69,99)	0.532
PASP[a], mmHg	35(28,44)	34.5(24.25,40.75)	39(29,46)	0.106
Moderate to Severe Mitral valve regurgitationa[a]				0.586
No	54(75.0%)	28(77.8%)	26(72.2%)	
Yes	18(25.0%)	8(22.2%)	10(27.8%)	
Moderate to Severe Tricuspid valve regurgitation[a]				1.00
No	54(75.0%)	27(75.0%)	27(75.0%)	
Yes	18(25.0%)	9(25.0%)	9(25.0%)	
Moderate to Severe Aortic regurgitation[a]				0.691
No	65(90.3%)	33(91.7%)	32(88.9%)	
Yes	7(9.7%)	3(8.3%)	4(11.1%)	
Moderate to Severe Pulmonary valve regurgitation[a]				1.00
No	70(97.2%)	35(97.2%)	35(97.2%)	
Yes	2(2.8%)	1(2.8%)	1(2.8%)	
Pericardial effusion[a]				0.637
No	38(52.8%)	18(50%)	20(55.6%)	
Yes	34(47.2%)	18(50%)	16(44.4%)	
Serum indicators				
CRP, mg/L	4.5(1.63,9.4)	2.78(1.27,5.92)	5.96(3.14,14.72)	0.007
Hb, g/L	126(115,141)	126(116,145)	126(111.25,134.75)	0.533
PLT,10^9/L	185(146,266)	167(126,219)	241(154,286)	0.003
NE,10^9/L	4.72(3.47,7.91)	3.77(2.92,4.91)	5.87(4.36,14.69)	<0.001
LYM,10^9/L	1.56(1.15,2.18)	1.7(1.41,2.32)	1.41(1.03,1.88)	0.009
RBC,10^9/L	4.18(3.82,4.59)	4.18(3.71,4.56)	4.25(3.89,4.75)	0.494
MONO,10^9/L	0.39(0.28,0.5)	0.37(0.30,0.49)	0.41(0.28,0.51)	0.428
PLR	113.46(86.1,163)	95.98(71.85,109.76)	151.45(114.08,226.32)	<0.001
NLR	2.88(1.91,5.09)	2.07(1.45,3.28)	4.14(2.76,8.20)	<0.001
NMLR	3.18(2.14,5.75)	2.32(1.58,4.24)	4.42(2.98,8.71)	<0.001
SIRI	1.33(0.72,2.41)	0.9(0.52,1.64)	2.04(1.20,3.60)	<0.001
SII	571.22(308.29,1155.94)	369.65(233.15,510.87)	861.16(642.55,1840.11)	<0.001
ALT, U/L	18(12,31)	18(11.5,31.5)	17.5(13,31.25)	0.971
AST, U/L	23(17,31)	25(17,32)	23(17.75,29.25)	0.781

(*Continued*)

Table 1 (Continued).

	Total(n=83)	Survival Group(n=41)	Death Group(n=42)	P Value
ALB, g/L	36.4(32.7,41.4)	36.4(32.2,40.7)	36.3(32.7,41.43)	0.902
CREA, umol/L	85.3(72.8,130.3)	95.4(77.6,134.15)	78.3(61.75,117.95)	0.058
eGFR, mL/ min·1.73m²	75.78(52.99,96.01)	75.34(46.04,91.01)	79.21(54.63,99.42)	0.433
LDH, U/L	220(180,284)	206(175,243)	240(205,308.5)	0.029
iFLC/niFLC	8.4(3.96,29.38)	6.73(3.49,33.33)	8.82(5.22,23.65)	0.488
dFLC	179.4(59.9,394.3)	146.55(56.15,370.13)	191.4(69.98,408.68)	0.503
Gender				0.069
Male	57(68.7%)	32(78%)	25(59.5%)	
Female	26(31.3%)	9(22%)	17(40.5%)	
The type of light chain				0.364
Lambda	68(81.9%)	32(78%)	36(85.7%)	
Kappa	15(18.1%)	9(22%)	6(14.3%)	
Organs involved				
Kidney				0.903
No	46(55.4%)	23(56.1%)	23(54.8%)	
Yes	37(44.6%)	18(43.9%)	19(45.2%)	
Liver				0.738
No	73(88%)	37(90.2%)	36(85.7%)	
Yes	10(12%)	4(9.8%)	6(14.3%)	
Gastrointestinal tract				0.265
No	75(90.4%)	39(95.1%)	36(85.7%)	
Yes	8(9.6%)	2(4.9%)	6(14.3%)	
Lung				0.353
No	60(72.3%)	32(78%)	28(66.7%)	
Yes	23(27.7%)	9(22%)	14(33.3%)	
Never				0.364
No	68(81.9%)	32(78%)	36(85.7%)	
Yes	15(18.1%)	9(2%)	6(14.3%)	
Skin				0.748
No	64(77.1%)	31(75.6%)	33(78.6%)	
Yes	19(22.9%)	10(24.4%)	9(21.4%)	
Tongue				0.815
No	68(81.9%)	34(82.9%)	34(81.0%)	
Yes	15(18.1%)	7(17.1%)	8(19.0%)	
The number of involved				
Organs				0.543
1	14(16.9%)	7(17.1%)	7(16.7%)	
2	29(34.9%)	15(36.6%)	14(33.3%)	
3 or more	40(48.2%)	61(46.3%)	62(50%)	
Cardiac function				
Staging system				0.35
Mayo04 stage				
I	8(9.6%)	5(12.2%)	3(7.1%)	
II	28(33.7%)	16(39%)	12(28.6%)	
III	47(56.6%)	11(48.8%)	12(64.3%)	
Mayo12 stage				0.224
I	4(4.8%)	2(4.9%)	2(4.8%)	
II	24(28.9%)	15(36.6%)	9(21.4%)	
III	32(38.6%)	14(34.1%)	18(42.9%)	
IV	23(27.7%)	10(24.4%)	13(31%)	

(*Continued*)

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Table 1 (Continued).

	Total(n=83)	Survival Group(n=41)	Death Group(n=42)	P Value
Euro15 stage				0.457
I	8(9.6%)	5(12.2%)	3(7.1%)	
II	28(33.7%)	16(39%)	12(28.6%)	
IIIa	23(27.7%)	11(26.8%)	12(28.6%)	
IIIb	24(28.9%)	9(22%)	15(35.7%)	
NYHA class				0.006
II	25(30.1%)	17(41.4%)	8(19%)	
III	44(53%)	21(51.2%)	23(54.8%)	
IV	14(16.9%)	3(7.3%)	11(26.2%)	
Electrocardiogram				
Low voltage				0.743
No	41(49.4%)	21(51.2%)	20(47.6%)	
Yes	42(50.6%)	20(48.8%)	22(52.4%)	
Poor R wave progression				0.859
No	60(72.3%)	30(73.2%)	30(71.4%)	
Yes	23(27.7%)	11(26.8%)	12(28.6%)	
Atrial fibrillation				0.957
No	67(80.7%)	33(80.5%)	34(81%)	
Yes	16(19.3%)	8(19.5%)	8(19%)	
Conduction block				0.154
No	47(56.6%)	20(48.8%)	27(64.3%)	
Yes	36(43.4%)	21(51.2%)	15(35.7%)	
Arrhythmia				0.893
No	33(39.8%)	16(39%)	17(40.5%)	
Yes	50(60.2%)	25(61%)	25(59.5%)	
Abnormal ST/T wave				0.39
No	13(15.7%)	5(12.2%)	8(19%)	
Yes	70(84.3%)	36(87.8%)	34(81%)	

Notes: Data presented as mean ± standard deviation, median(interquartile range), or number (%). [a] Data available for 36 Survivors and 36 deceased.
Abbreviations: cTnT, Cardiac Troponin-T; NT-proBNP, N-terminal pro-B-type natriuretic peptide; LAD, Left Atrial Dimension; LVEDD, Left ventricular End-Diastolic Dimension; IVST, Interventricular Septal Thickness; LVPW, Left Ventricular Posterior Wall; LVEF, Left Ventricular Ejection Fraction; E/A, Early Diastolic Flow Velocity/ Atrial Contraction Flow Velocity; TRV, Tricuspid Regurgitation Velocity; AFV, Aortic Flow Velocity; IVSMA, Interventricular Septum Motion Amplitude; LVESD, Left Ventricular End-Systolic Diameter; LVMI, Left Ventricular Mass Index; RVD, Right Ventricular Diameter; RAD, Right Atrium Diameter; MPAD, Main Pulmonary Artery Diameter; PAFV, Pulmonary Artery Flow Velocity; PASP, Pulmonary Artery Systolic Pressure; CRP, C-Reactive Protein; RBC, Red Blood Cell; Hb, Hemoglobin; NE, Neutrophil; LYM, Lymphocyte; MONO, Monocyte; PLT, Platelet; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; ALB, Albumin; CREA, Creatinine; eGFR, estimated Glomerular Filtration Rate; LDH, Lactate Dehydrogenase; iFLC/niFLC, involved/non-involved free light chain; dFLC, Free Light Chain difference.

patients developed moderate to severe aortic regurgitation, whereas moderate to severe pulmonary valve regurgitation was present in 2 (2.8%) patients. In total, 38 (47.2%) patients exhibited pericardial effusion. In addition to the cardiac manifestations, the following symptoms of other organic involvement were found in 37 (44.6%) patients with kidney involvement, 23 (27.7%) with lung involvement, 15 (18.1%) with nervous system involvement, 10 (12%) with liver involvement, 8 (9.6%) with gastrointestinal tract involvement, 19 (22.9%) with skin involvement, and 15 (18.1%) with tongue involvement. The number of involved system damages with one, two, and three or more patients was 14 (16.9%), 29 (34.9%), and 40 (48.2%), respectively. Through the comparison of laboratory and imaging parameters between the survival group and death group, we found that the levels of PLR, NLR, NMLR, SIRI, SII, CRP, Neutrophil (NE), TRV, and Lactate Dehydrogenase (LDH) upon admission were significantly higher in deceased group. However, the LYM was remarkably lower in deceased cohort.

The Associations of Inflammation Indexes and Echocardiographic Parameters with Survival

The univariate Cox regression analysis revealed PLR, NLR, NMLR, SIRI, CRP, NE, LYM, LDH, TRV, NYHA classification, Mayo04 stage, Mayo12 stage, and Euro15 stage are risk factors for prognosis in patients with AL-CA

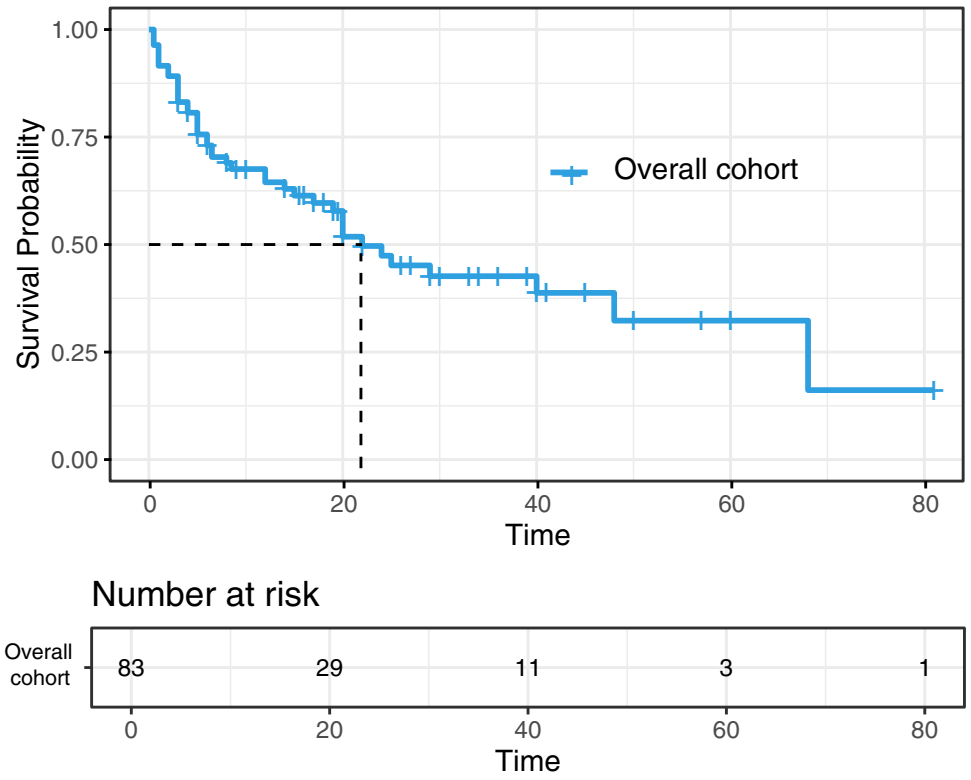

Figure 1 Kaplan-Meier survival curves of overall patients.

(Table 2). Significant variables on univariate COX regression analysis and relevant variables were subjected to multivariate COX regression analysis to identify independent predictors of OS. To avoid covariance problems, we tested for covariance among the relevant variables (Supplementary Table 1). The covariance diagnosis revealed a strenuous covariance between NLR, NMLR, and SIRI. Therefore, separate multivariable models were used to avoid statistical

Table 2 Results of Univariate Analyses of Various Prognostic Factors

	HR	95.0% CI	P value
TRV	1.012	(1.006,1.018)	<0.001
CRP	1.019	(1.004,1.034)	0.013
PLR	1.007	(1.004,1.009)	<0.001
NLR	1.057	(1.026,1.089)	<0.001
NMLR	1.057	(1.025,1.089)	<0.001
SIRI	1.253	(1.131,1.387)	<0.001
SII	1.000	(1.000,1.000)	<0.001
LYM	0.403	(0.234,0.692)	0.001
NE	1.071	(1.026,1.118)	0.002
LDH	1.005	(1.001,1.009)	0.01
NYHA class	1.875	(1.21,2.906)	0.005
Mayo04 stage	1.861	(1.092,3.172)	0.022
Euro15 stage	1.515	(1.094,2.099)	0.013
Mayo12 stage	1.427	(1.002,2.031)	0.049

Abbreviations: TRV, Tricuspid Regurgitation Velocity; CRP, C-Reactive Protein; PLT, Platelet; LYM, Lymphocyte; NE, Neutrophil; LDH, Lactate Dehydrogenase; 95% CI, 95% confidence interval.

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coupling of variables. Three separate models were created for the NLR, NMLR, and SIRI. The results demonstrated that PLR, LYM, TRV, and LVEF were independent prognostic factors (Table 3). Time-to-event ROC curve analyses illustrated that PLR, TRV, and the combined metric (PLR+TRV) were relatively stronger and more stable predictive indicators of short-term outcomes than other indicators (Figure 2A–C), and the combined metric (PLR+TRV) showed robust predictive performance within the third month (AUC=0.9). Notably, their predictive potential for long-term outcome was relatively weak (Supplementary Figure 1A–D). To determine whether PLR and TRV could provide predictive incremental value to the current clinical prognostic assessment systems for AL-CA cohorts (Mayo04 stage system, Mayo12 stage system, and Euro15 stage system), we applied the likelihood ratio $\chi 2$ test. The results indicated that PLR, TRV, and combined indicators (PLR+TRV) added predictive value to the Mayo04 stage (Figure 3A), Mayo12 stage (Figure 3B), and Euro15 stage (Figure 3C) models, respectively. Additionally, the combination of the two indicators had a substantially higher incremental predictive value for the traditional model.

The Correlation Between the Inflammation Indexes and the Severity of Cardiac Damage

To explore the correlation between inflammatory indexes and cardiac dysfunction, we applied Spearman correlation analysis to further clarify the relationship between cardiac function and inflammatory indexes in the AL-CA cohorts. The results indicated that inflammation indexes (PLR, NLR, NMLR, SIRI, and SII) were significantly positively correlated with NYHA cardiac function grading (Table 4). OS was also significantly shorter in patients with NYHA class III/IV than in those with NYHA class II (P=0.015) (Figure 4A). In the Mayo04 staging system, inflammation indexes (SIRI, PLR, NLR, NMLR, and SII) increased as the grade of the Mayo04 staging system increasing (Table 4). Compared with Mayo04 stage I/II, patients with Mayo04 stage III disease had significantly poorer OS (p=0.047) (Figure 4B). Analogously, inflammation indexes (NLR, NMLR, SIRI, and SII) increased with increasing Mayo12 stage increasing (Table 4). Patients with Mayo12 stage III/IV had relatively poorer OS in comparison with Mayo12 stage I/II, although the difference remained unremarkable (P=0.11) (Figure 4C). In addition, a statistically significant positive correlation was also observed between the inflammation indexes

Table 3 Results of Multivariate Analyses of Various Prognostic Factors

	Model 1		Model 2		Model 3	
	HR (95% CI)	**P Value**	**HR (95% CI)**	**P Value**	**HR (95% CI)**	**P Value**
CRP	0.923(0.851,1.001)	0.052	0.917(0.846,0.994)	0.035	0.92(0.847,0.9 98)	0.044
PLR	1.017(1.004,1.03)	0.01	1.015(1.003,1.028)	0.015	1.015(1.002,1.027)	0.022
SII	1.001(1,1.001)	0.199	1(0.998,1.002)	0.763	1.001(0.999,1.002)	0.414
SIRI	0.765(0.422,1.386)	0.377	——	——	——	——
NLR	——	——	1.049(0.579,1.903)	0.874	——	——
NMLR	——	——	——	——	0.938(0.596,1.476)	0.783
NE	1.131(0.895,1.43)	0.302	1.07(0.861,1.33)	0.539	1.082(0.875,1.337)	0.468
MONO	3.135(0.002,5676.687)	0.765	0.531(0.001,514.875)	0.857	0.79(0.001,676.379)	0.946
LYM	0.017(0.002,0.183)	0.001	0.032(0.002,0.43)	0.009	0.024(0.002,0.284)	0.003
TRV	1.031(1.012,1.051)	0.002	1.029(1.011,1.048)	0.002	1.03(1.011,1.049)	0.002
IVST	0.675(0.463,0.984)	0.041	0.719(0.5,1.033)	0.074	0.709(0.497,1.012)	0.058
RVD	0.916(0.703,1.193)	0.513	0.948(0.738,1.217)	0.673	0.945(0.735,1.215)	0.657
LVEF	0.866(0.764,0.982)	0.024	0.878(0.778,0.991)	0.035	0.875(0.774,0.988)	0.032
Euro15 stage	0.23(0.034,1.539)	0.13	0.197(0.028,1.408)	0.106	22.654(0.575,892.805)	0.096
Mayo12 stage	0.295(0.065,1.341)	0.114	0.352(0.076,1.638)	0.183	0.216(0.033,1.425)	0.111
Mayo04 stage	22.067(0.533,913.79)	0.103	24.211(0.598,979.802)	0.091	0.319(0.067,1.518)	0.151
NYHA class	2.392(0.654,8.749)	0.187	2.509(0.688,9.15)	0.164	2.471(0.684,8.927)	0.167
LDH	0.99(0.979,1.001)	0.067	0.991(0.98,1.001)	0.088	0.991(0.98,1.001)	0.091

Notes: Data presented as median (interquartile range) or mean±Standard Deviation.

Abbreviations: TRV, Tricuspid Regurgitation Velocity; NE, Neutrophil; LYM, Lymphocyte; MONO, Monocyte; CRP, C-Reactive Protein; IVST, Interventricular Septal Thickness; LVEF, Left Ventricular Ejection Fraction; RVD, Right Ventricular Diameter; LDH, Lactate Dehydrogenase; 95% CI, 95% confidence interval.

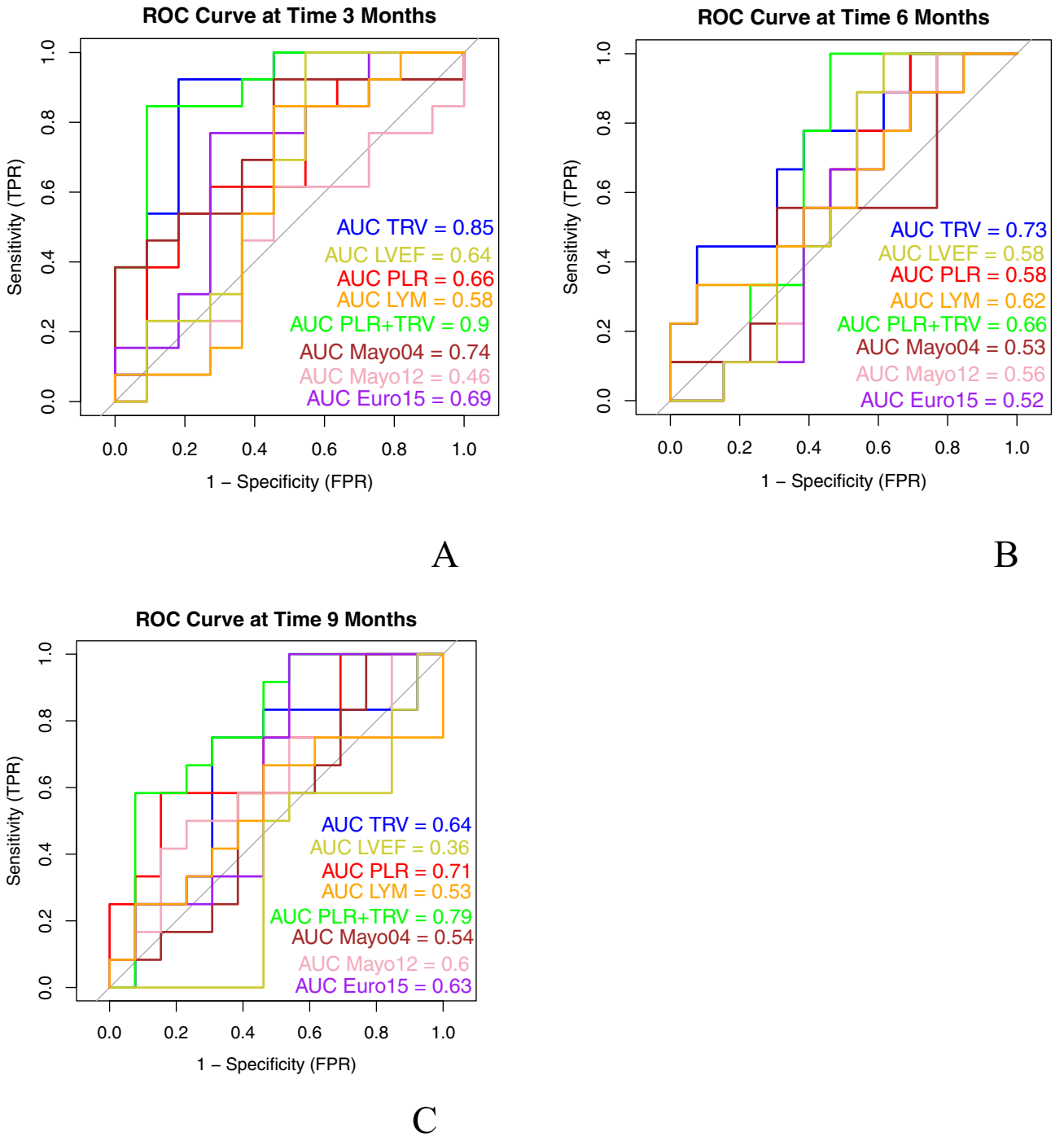

Figure 2 Time-to-event ROC analysis of relevant predictors. (**A**) The comparison of relevant predictors for 3-month time points; (**B**) The comparison of relevant predictors for 6-month time points; (**C**) The comparison of relevant predictors for 9-month time points.

(PLR, NLR, NMLR, SIRI, and SII) and the Euro15 stage (Table 4). Patients with Euro15 stage IIIa/IIIb also exhibited worse survival than those with Euro15 stage I/II, although the difference was not statistically significant (P=0.078) (Figure 4D).

The Relationship of Inflammation Indexes and the Type of AL

We further investigated the association between inflammation indexes and the AL subtype (Table 5). We found that the NLR (P<0.001), NMLR (P=0.002), SIRI (P=0.029), and SII (P<0.001) were significantly higher. Additionally, NYHA

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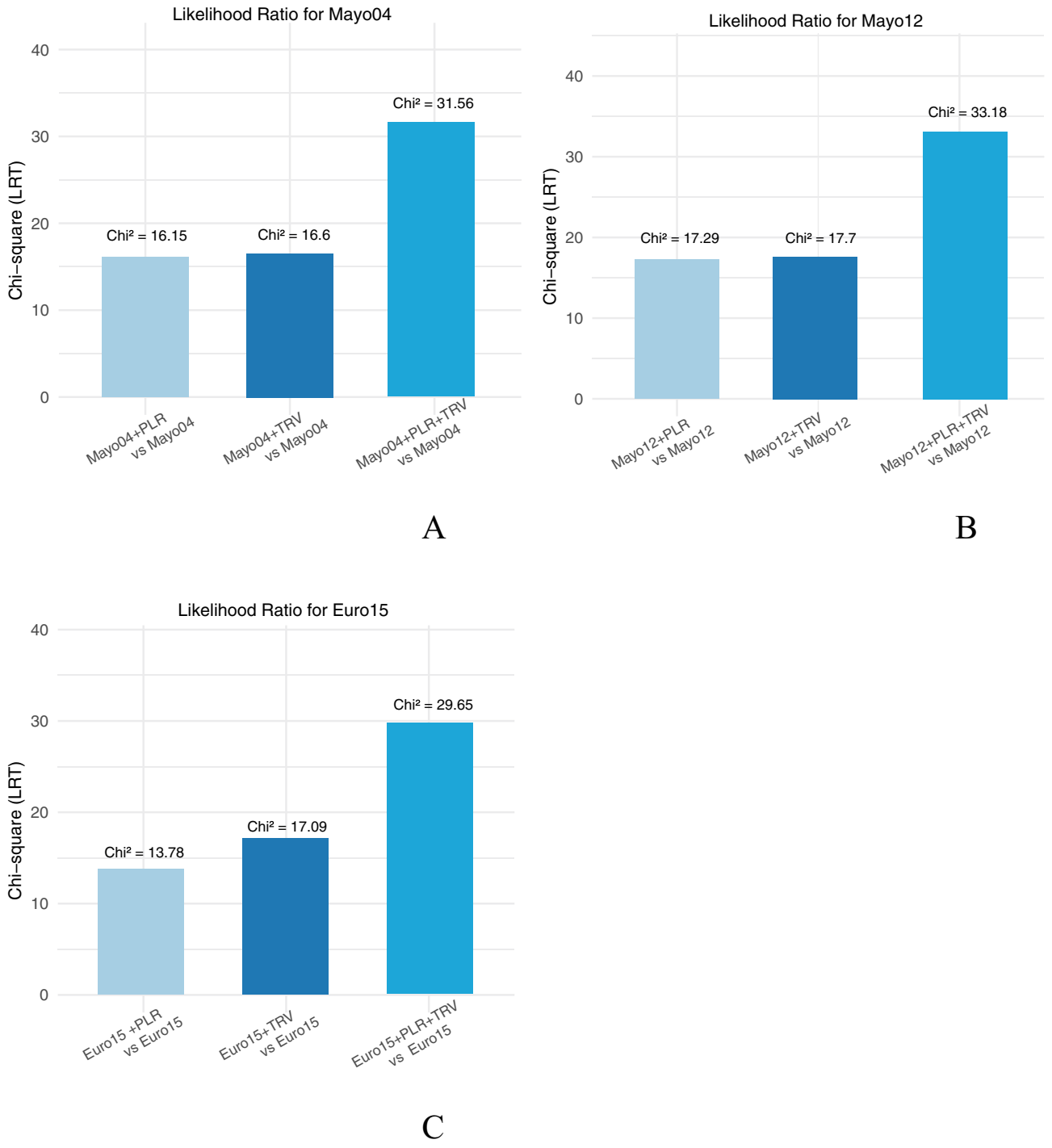

Figure 3 The incremental prognostic value of relevant predictors over traditional models presented as a likelihood ratio $\chi 2$ test. (**A**) The incremental prognostic value of relevant predictors over Mayo04 stage; (**B**) The incremental prognostic value of relevant predictors over Mayo12 stage; (**C**) The incremental prognostic value of relevant predictors over Euro15 stage.

class, Mayo04/12 stage, and Euro15 stage were relatively worse in the Lambda AL-CA group. We also observed that patients with Lambda AL-CA had inferior OS compared to those with Kappa AL-CA (20 vs 68 months; P=0.054), although the difference was not apparent (Figure 4E).

Table 4 The Correlation Analysis Between Inflammatory Index and Cardiac Function Classification

	R or P Value	NYHA Class	Mayo04 Stage	Mayo12 Stage	Euro15 Stage
LYM	R	−0.304**	−0.154	−0.133	−0.284**
	P value	0.005	0.165	0.232	0.009
NE	R	0.208	0.19	0.212	0.225*
	P value	0.059	0.085	0.055	0.041
MONO	R	0.206	0.187	0.109	0.213
	P value	0.062	0.09	0.327	0.053
PLR	R	0.302**	0.220*	0.184	0.275*
	P value	0.006	0.045	0.096	0.012
NLR	R	0.291**	0.229*	0.248*	0.311**
	P value	0.008	0.037	0.024	0.004
NMLR	R	0.300**	0.251*	0.249*	0.322**
	P value	0.006	0.022	0.023	0.003
SIRI	R	0.341**	0.270*	0.220*	0.351**
	P value	0.002	0.013	0.046	0.001
SII	R	0.265*	0.268*	0.270*	0.288**
	P value	0.015	0.014	0.014	0.008
CRP	R	0.202	0.129	0.192	0.148
	P value	0.089	0.279	0.106	0.214

Notes: * $p < 0.05$;** $p < 0.01$; R(correlation coefficient);
Abbreviations: NE, Neutrophil; LYM, Lymphocyte; MONO, Monocyte; CRP, C-Reactive Protein.

Discussion

In this retrospective study, we innovatively investigated the prognostic value of inflammatory indexes in patients with AL-CA. Based on the results of our analysis, elevated inflammation indexes PLR, NMLR, NLR, and SIRI were identified as risk factors for the prognosis of patients with AL-CA. In particular, the inflammation index PLR, TRV and combined indicator (PLR+TRV) had good predictive value for the short-term outcomes of patients in our study.

Recently, accumulating evidences have illustrated that inflammatory indexes are simple and easily accessible indicators that reflect the systemic immune and inflammatory status of the human body. Several inflammation indexes, such as NLR, PLR, SII, and SIRI, have been demonstrated to be efficacious predictors of outcomes in various malignant tumors,[14] and inflammatory diseases.[22] The elevated PLR has also been recognized as an auxiliary biomarker for severity and survival prognosis in patients with HF.[23,24] Similarly, patients with AL-CA are characterized by HF.[25] Our study, for the first time, revealed that inflammation index PLR was an independent risk factor for the prognosis of patients with AL-CA. This discovery reinforced the important predictive value of the inflammatory index not only in patients with non-amyloidotic HF, but also in patients with AL-CA characterized by HF, and provides a new insight into the further comprehension of the inflammatory mechanisms of this disorder and their implications for patient outcomes. Preceding researches have reported that inflammation, as an adaptive response involved in the homeostatic balance of the organism, can be triggered by a host of factors, including infection, tissue injury, tissue stress, and malfunctioning.[26] Hayashi et al observed that the myocardial injury induced by amyloid fibrils acting as damage-associated molecular patterns (DAMPs) can activate tissue macrophages and dendritic cells through the Toll-like receptors (TLRs), which leads to the production of inflammatory mediators.[27] Jordan et al also found numerous immunological response-related cytokines and chemokines, such as chemokine ligand (CXCL)-1/2/3, Interleukin (IL)-1β/6/8/11, and colony-stimulating factor (CSF)-2/3, were upregulated in response to amyloid fibrils in AL-CA by RNA sequence and Gene Ontology (GO) analysis.[28] These cytokines play a potential role in neutrophil/granulocyte/monocyte/platelet proliferation, survival, mobilization, and inflammation activation.[28] Monoclonal ALs may also be directly toxic to other cell types, including mesangial and endothelial cells. They affect multiple organ systems by inducing the production reactive oxygen species (ROS) and the activation p38 Mitogen-Activated Protein Kinase (MAPK) pathway, resulting in a systemic inflammatory response.[29] On

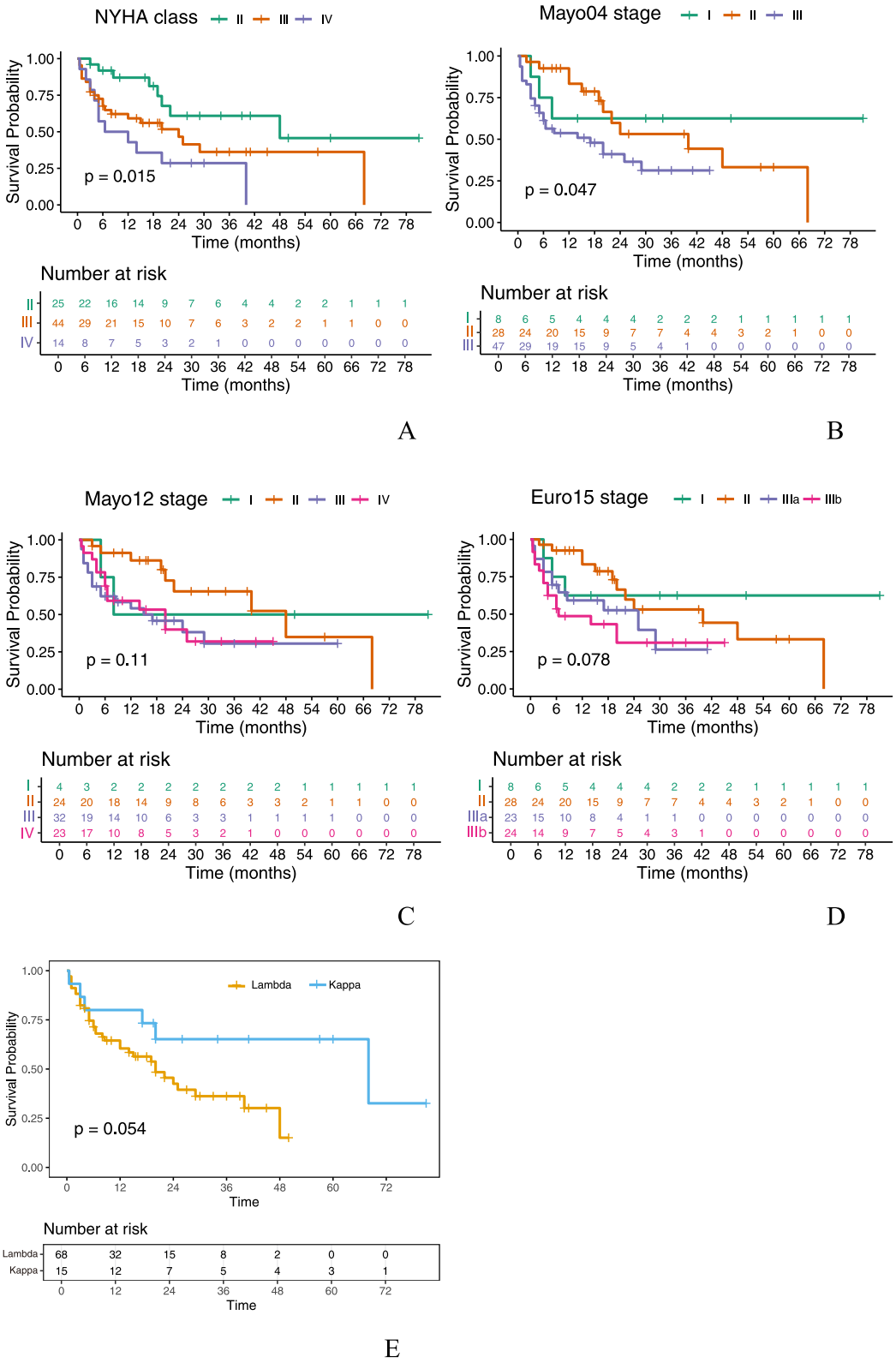

Figure 4 Kaplan-Meier survival curves of the patients. (**A**) OS by the NYHA class; (**B**) OS by the Mayo04 stage; (**C**) OS by the Mayo12 stage; (**D**)OS by the Euro15 stage; (**E**) OS by the type of light chain.

Table 5 Comparisons of Clinical Parameters and Inflammation Indexes Between Lambda and Kappa Subtype

	Total (n=83)	Lambda (n=68)	Kappa (n=15)	P value
Age, years	61.42±10.7	61.24 ± 10.78	62.27 ± 10.67	0.754
Serum indicators				
CRP, mg/L	4.5(1.63,9.4)	4.64(1.76,13.77)	2.04(1.15,6.1)	0.092
Hb, g/L	126(115,141)	126.5(115,143)	126(108,134)	0.335
PLT, 10^9/L	185(146,266)	184.5(147,265.5)	193(126,272)	0.785
LYM, 10^9/L	1.56(1.15,2.18)	1.53(1.07,1.94)	1.87(1.3,2.28)	0.082
NE, 10^9/L	4.18(3.82,4.59)	5.00(3.70,9.15)	3.68(2.83,5.18)	0.152
RBC, 10^9/L	4.72(3.47,7.91)	4.22(3.91,4.60)	3.98(3.52,4.56)	0.292
MONO, 10^9/L	0.39(0.28,0.5)	0.40(0.28,0.51)	0.36(0.2,0.48)	0.31
PLR	113.46(86.1,163)	118.69(91.9,176.76)	100.45(68,117.69)	0.091
NLR	2.88(1.91,5.09)	3.35(2.37,6.23)	1.46(1.2,2.4)	<0.001
NMLR	3.18(2.14,5.75)	3.65(2.59,6.69)	1.58(1.38,3.51)	0.002
SIRI	1.33(0.72,2.41)	1.42(0.86,2.95)	0.94(0.28,2.22)	0.029
SII	571.22(308.29,1155.94)	687.92(392.89,1295.04)	275.26(181.89,386.57)	<0.001
Gender				0.767
Male	57(68.7%)	46(67.6%)	11(73.3%)	
Female	26(31.3%)	22(32.4%)	4(26.7%)	
Cardiac function				
Staging system				
NYHA class				0.204
II	25(30.1%)	18(26.5%)	7(46.7%)	
III	44(53%)	38(55.9%)	6(40%)	
IV	14(16.9%)	12(17.6%)	2(13.3%)	
Mayo04 stage				0.376
I	8(9.6%)	6(8.8%)	2(13.3%)	
II	28(33.7%)	22(32.4%)	6(40%)	
III	47(56.6%)	40(58.8%)	7(46.7%)	
Mayo12 stage				0.261
I	4(4.8%)	3(4.4%)	1(6.7%)	
II	24(28.9%)	18(26.5%)	6(40%)	
III	32(38.6%)	27(39.7%)	5(33.3%)	
IV	23(27.7%)	20(29.4%)	3(20%)	
Euro15 stage				0.826
I	8(9.6%)	6(8.8%)	2(13.3%)	
II	28(33.7%)	22(32.4%)	6(40%)	
IIIa	23(27.7%)	20(29.4%)	3(20%)	
IIIb	24(28.9%)	20(29.4%)	4(26.7%)	

Notes: Data presented as median(interquartile range) or mean±Standard Deviation.

Abbreviations: cTnT, Cardiac Troponin-T; NT-proBNP, N-terminal pro-B-type natriuretic peptide; RBC, Red Blood Cell; NE, Neutrophil; LYM, Lymphocyte; MONO, Monocyte; CRP, C-Reactive Protein; Hb, Hemoglobin; PLT, Platelet; NYHA, New York Heart Association.

the other hand, multiple researches reported, regardless of the etiology of the HF, inflammation is recognized as an important driver in HF patients. Sympathetic activation in patients with HF has been linked to platelet activation,[30] and further modulates the relative distribution of leukocyte subpopulations through the release of epinephrine, leading to a concomitant elevation in neutrophil counts.[26] HF, as a persistent stress stimulus, also induces the activation of the hypothalamic-pituitary-adrenergic axis, which negatively interacts with lymphocytes and leads to lymphocytopenia.[31] Indeed, our study likewise revealed that decreased lymphocyte counts were associated with a poor prognosis. Additionally, elevated left ventricular filling pressure and myocardial hypoxia in patients with HF can also contribute to monocyte mobilization. Activated monocytes excrete massive inflammatory cytokines [eg, tumor necrosis factor

(TNF), IL-6], which not only promotes myocardial fibrosis but also further enhances self-activation, resulting in persistent inflammatory amplification and ultimately leading to elevated serum monocyte counts.[31] These findings further indicate that the inflammatory response exhibits an essential role in the progression of AL-CA with HF, involving adaptive changes in a wide range of blood cell subsets, including neutrophils, monocytes, and lymphocytes, whose numerical dynamics can be quantified by inflammatory indexes such as the NLR, NMLR, and PLR.

In addition to the inflammatory indexes calculated based on blood cell counts, our study also found that other hematological markers associated with inflammation were significantly higher in patients with a more dismal prognosis. C-reactive protein (CRP), a classical acute-phase response protein, increases rapidly after the occurrence of tissue injury or inflammatory response, and its expression level is remarkably correlated with the intensity of the inflammatory response and the severity of tissue injury.[32] Our investigation revealed that elevated CRP levels were associated with adverse outcomes in patients with AL-CA using univariate analysis, but their prognostic predictive value was not significant after further adjustment for confounders. Nevertheless, a study by Usman et al revealed that CRP was an independent predictor of mortality risk in 236 patients with AL-CA.[32] This result illustrated the crucial role of CRP in mirroring the inflammatory status and prognostic assessment of AL-CA patients. The reason for these discrepancies may be the differences in the enrolled population due to the relatively larger sample size of the latter study.

Echocardiography has been widely employed as a noninvasive and well-established safety technique for prognostic evaluation of AL-CA. Relevant parameters, such as decreased left ventricle basal strain,[33] SVI (stroke volume index),[34] left ventricular ejection time (LVET),[35] myocardial contraction fraction,[34] cardiac index (CI),[34] 3D peak atrial longitudinal strain (3D-PALS),[36] left to right ventricular area ratio,[37] right ventricular global longitudinal strain (GLS)[38,] and Left Atrial Enlargement,[39] increased left atrioventricular coupling index (LACI)[40,] greater wall thickness[41] have been considered to be closely associated with AL-CA patient outcomes. In particular, elevated pulmonary artery systolic pressure (PASP), pulmonary artery wedge pressure (PAWP)/CI ratio,[42] and lowered Tricuspid Annular Plane Systolic Excursion (TAPSE)/PASP[43] have also been associated with AL-CA prognosis in recent studies. Echocardiography-determined TRV is considered a valid estimate for pulmonary artery pressure (PAP).[44] Our findings demonstrate for the first time that TRV elevation correlates significantly with worse outcomes in patients with AL-CA, a category of restrictive cardiomyopathy.[45] This implies that PAP alterations may have a potential prognostic value in AL-CA. Earlier studies have also pointed out that elevated PAP is a prevalent complication in patients with cardiac amyloidosis and has been regarded as a pivotal indicator for identifying patients at high mortality risk.[46,47] Historically, Eder et al also indicated that deposition of amyloidosis proteins in AL-CA causes restrictive cardiomyopathy.[48] Increased PAP is likely to be correlated with hemodynamic disturbances attributed to diastolic dysfunction secondary to intrinsic myocardial stiffness.[49] Furthermore, the deposition of amyloid in the pulmonary vessels may be another mechanism of elevated PAP.[50] Amyloid deposition in the blood vessel walls can result in endothelial dysfunction. Abnormal endothelial cells express lower levels of vasodilatory substances as well as increased levels of vasoconstrictive substances and promote the onset of vasoconstriction, smooth muscle cells, and endothelial cell proliferation.[51] The above mentioned findings and mechanisms further support the perception that TRV is elevated in AL-CA patients with a poor prognosis. However, we failed to observe any prognostic predictive value of PASP for the outcome of patients with AL-CA. The reasons for such results may be as follows: the level of PASP is not only affected by TRV, but also related to Right Atrial Pressure (RAP).[52] Further exploration of the relationship between RAP and prognosis in patients with AL-CA is warranted.

Notably, the echocardiographic parameter LVEF serves as an important measure of left ventricular systolic function. The independent prognostic predictive value of LVEF for AL-CA was demonstrated in our study. Consistent with our results, Kristen et al also revealed that LVEF was strongly associated with poor prognosis in patients with AL-CA.[53] Nevertheless, the independent predictive potential of LVEF has been controversial in different studies. Other investigations have proposed that although reduced LVEF may identify high-risk AL-CA patients, LVEF may not have an independent prognostic predictive value in multivariate analyses.[32,54] This may be explained by the fact that myocardial involvement in patients with AL-CA is not only associated with systolic dysfunction but also with increased myocardial stiffness and diastolic dysfunction. The prognostic value of LVEF in AL-CA patients warrants further investigation.

In addition, we found that PLR, TRV, and joint indicator (PLR+TRV) added incremental prognostic value beyond traditional amyloidosis staging systems, especially joint indicators (Figure 3A–C), indicating that incorporating PLR and TRV into the

currently established amyloidosis staging systems may contribute to improving prognostic performance and optimizing risk stratification in the AL-CA population. It is an accessible, convenient, and safe approach to the initial assessment of a patient's condition, so that prompt and intensive treatment can be implemented to optimize the patient's prognosis.

The severity of cardiac involvement is the predominant determinant of prognosis in patients with AL-CA. Currently, diverse staging systems (NYHA classification, Mayo04 stage, Mayo12 stage, and Euro15 stage) are widely used to assess the severity of cardiac dysfunction. Whether accessible, low-cost hematologic parameters have additional predictive value in the appraisal of cardiac involvement severity in patients with AL-CA is also warranted. To further determine the correlation between inflammatory indexes and cardiac function, we employed Spearman correlation analysis to evaluate the relationship between inflammatory indexes and cardiac function stage. The results demonstrated that the levels of inflammatory indexes (NLR, NMLR, SII and SIRI) increased progressively with the severity of cardiac involvement, irrespective of NYHA classification, Mayo 04/12 stage or Euro15 stage. Comprehensively, we hypothesize that the inflammatory response may play a key role in the progression of AL-CA and is closely associated with the clinical deterioration of cardiac dysfunction. Dynamic monitoring of alterations in inflammatory indexes might serve as an accessible method for monitoring cardiac function in patients with AL-CA. Further multicenter studies with larger sample sizes are warranted to validate the finding.

Another notable finding was that the inflammation indexes were associated with the type of light chain, as shown in Table 4. Our results revealed that patients with Lambda AL-CA were more likely to have higher inflammation indexes (NLR, NMLR, SIRI, and SII) than those with Kappa AL-CA. Additionally, more advanced cardiac function classes in the Mayo04/12, Euro15, and NYHA classification systems were revealed in the Lambda AL-CA group, although the difference was not statistically significant. Additionally, the results showed that the patients with poorer cardiac function had higher inflammation indexes and shorter OS (Table 4 and Figure 4A–C), which further confirmed that the patients with Lambda chains presented relatively worse outcomes (20. vs 68 months, P=0.054) (Figure 4E). Consistent with our study, Czyżewska et al previously found that the presence of monoclonal Lambda chains in patients with AL-CA may be associated with more severe damage to cardiomyocytes, with higher NT-proBNP and TnI concentrations leading to poorer outcomes. In addition, escalation of Lambda monoclonal chain concentration is associated with shorter survival.[55] Another study by Kumar et al at the Mayo Clinic also suggested that monoclonal chain Lambda forming amyloid was an unfavorable prognostic factor and associated with more severe heart dysfunction in patients diagnosed with AL amyloidosis.[56] Whether different light chain types have distinct pathogeneses of amyloidosis deposition and cardiotoxicity in AL amyloidosis remains unclear, and more in-depth studies are needed to reveal the exact mechanism.

Limitations

However, our study has some limitations. This was a single-center retrospective study, with inherent biases in historical data collection and patient selection. Furthermore, owing to the relatively low prevalence of AL-CA, the limited sample size intrinsically affected the generalizability of our conclusions. Another limitation is that more than 10% of the patients in this study lacked echocardiographic data, and this absence may have led to selection bias despite our efforts to ensure the robustness and validity of our analysis through rigorous statistical methods. In the future, multicenter, large-sample-size studies incorporating more elaborate echocardiography data will be worthwhile to further validate our conclusions.

Conclusion

In summary, our study represents an innovative study revealing the clinical correlation of inflammation indexes with survival, cardiac function classification, and type of light chain in a cohort with AL-CA. The parameter PLR, TRV and combined indicator (PLR+TRV) offers good prognostic value for short-term outcome and provides incremental prognostic value based on traditional clinical staging model, which demonstrates that broadly available, cost-effective, and simple parameters can be considered for predicting the prognosis of AL-CA. Their potential value in the surveillance of disease efficacy also deserves further exploration.

Abbreviation

AL-CA, Light-chain myocardial amyloidosis; AL, Light chain; cTnT, Cardiac Troponin-T; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; LAD, Left Atrial Dimension; LVEDD, Left ventricular End-Diastolic Dimension; IVST, Interventricular Septal Thickness; LVPW, Left Ventricular Posterior Wall; LVEF, Left Ventricular Ejection Fraction; E/A, Early Diastolic Flow Velocity/ Atrial Contraction Flow Velocity; TRV, Tricuspid Regurgitation Velocity; AFV, Aortic Flow Velocity; IVSMA, Interventricular Septum Motion Amplitude; LVESD, Left Ventricular End-Systolic Diameter; LVMI, Left Ventricular Mass Index; RVD, Right Ventricular Diameter; RAD, Right Atrium Diameter; MPAD, Main Pulmonary Artery Diameter; PAFV, Pulmonary Artery Flow Velocity; PASP, Pulmonary Artery Systolic Pressure; RAP, Right Atrial Pressure; CRP, C-Reactive Protein; RBC, Red Blood Cell; Hb, Hemoglobin; NE, Neutrophil; LYM, Lymphocyte; MONO, Monocyte; PLT, Platelet; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; ALB, Albumin; CREA, Creatinine; eGFR, estimated Glomerular Filtration Rate; LDH, Lactate Dehydrogenase; iFLC/niFLC, involved/non-involved free light chain; dFLC, Free Light Chain difference; HF, heart failure; vWF, von Willebrand Factor; TNF, Tumor necrosis factor; IL, Interleukin; DAMPs, Damage-associated molecular patterns; TLRs, Toll-like receptors; CXCL, Chemokine ligand; CSF, Colony-stimulating factor; ROS, reactive oxygen species; MAPK, Mitogen-Activated Protein Kinase.

Ethics Approval and Informed Consent

This study was a retrospective study, and all patient information collection and processing were strictly confidential. All patients provided their informed consent prior to study commencement and gave consent to have their data published. Our procedures were carried out in accordance with the Declaration of Helsinki. The ethics committee of the Beijing Anzhen Hospital Affiliated to Capital Medical University approved the study (approval number: 2024261x).

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Disclosure

The authors report no conflicts of interest in this work.

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