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Neutrophil percentage-to-albumin ratio and late gadolinium enhancement in clinically suspected myocarditis: a multicentre retrospective study

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Abstract

Background

Late gadolinium enhancement (LGE) on cardiac magnetic resonance (CMR) imaging identifies myocardial involvement in myocarditis and carries prognostic weight. The neutrophil percentage-to-albumin ratio (NPAR) combines neutrophil predominance with serum albumin, a negative acute-phase reactant. Whether NPAR is associated with LGE, and whether it adds information to its individual components and to routinely available clinical data, is unknown.

Methods

This retrospective observational study included 1,055 adults with clinically suspected myocarditis who underwent CMR at seven tertiary cardiovascular centres in Türkiye between October 2022 and September 2025. All studies were reviewed centrally by three cardiovascular radiologists blinded to clinical and laboratory data (Fleiss' $\kappa = 0.83$). Variables significant on univariable analysis ($p < 0.10$) were entered into multivariable logistic regression models, the shape of the association was examined using restricted cubic splines, and the incremental value of NPAR over the clinical and laboratory model was assessed using discrimination and reclassification metrics.

Results

LGE was present in 285 patients (27.0%). NPAR was higher in the LGE-positive group [1.65 (1.40–1.92) vs. 1.29 (1.02–1.55); $p < 0.001$]. In the multivariable model, NPAR remained independently associated with LGE positivity (adjusted odds ratio per 1 standard deviation 4.381, 95% confidence interval 3.248–5.907; $p < 0.001$), and the Nagelkerke R^2 rose from 0.157 to 0.387. Restricted cubic spline analysis showed a positive association across the observed range with evidence of non-linearity ($p = 0.013$). Adding NPAR increased the area under the curve of the model from 0.728 (0.687–0.768) to 0.839 (0.806–0.872) (difference 0.111; $p < 0.001$), with an integrated discrimination improvement of 0.194 (0.133–0.251) and a continuous net reclassification improvement of 0.843 (0.674–1.011), both $p < 0.001$. As a single marker, NPAR yielded an area under the curve of 0.750 (0.718–0.782) at a cut-off of 1.43, discriminating LGE better than either constituent (both $p < 0.0001$).

Conclusions

In clinically suspected myocarditis, NPAR was independently associated with CMR-defined LGE positivity, discriminated LGE better than either of its own components, and provided significant incremental discrimination and reclassification over a clinical and laboratory model. NPAR may serve as a low-cost adjunctive marker where access to CMR is constrained.

Background

Myocarditis is an inflammatory disease of the myocardium caused by infectious agents, immune activation or exposure to drugs and toxins, with a clinical spectrum ranging from asymptomatic troponin elevation to fulminant cardiogenic shock and sudden cardiac death [1–3]. Its recognition has increased substantially over the past decade, driven largely by the wider availability of cardiovascular magnetic resonance (CMR) imaging, which has shifted diagnosis away from endomyocardial biopsy toward non-invasive tissue characterisation in the majority of patients [4–6]. The 2025 European Society of Cardiology guidelines on myocarditis and pericarditis formalise this position, placing CMR at the centre of the diagnostic pathway for clinically suspected myocarditis [2].

Among CMR findings, late gadolinium enhancement (LGE) in a non-ischaemic distribution is the most established marker of myocardial involvement [7, 8]. Its importance is not only diagnostic. In a meta-analysis of eleven studies, the presence of LGE was associated with a substantially increased risk of adverse cardiac events in patients with acute myocarditis, and a comparable association has been reported in patients with clinically suspected disease [9, 10]. Adverse prognostic significance has been demonstrated even in patients with preserved left ventricular systolic function [11], and LGE characteristics carry incremental risk information beyond conventional functional parameters [12, 13]. Identifying which patients are likely to have LGE therefore has consequences for triage, surveillance and imaging prioritisation, particularly where CMR capacity is limited.

Access to CMR remains uneven, and in many settings the examination is performed days to weeks after presentation. Consequently, there is continuing interest in inexpensive, immediately available blood-based markers that reflect the systemic inflammatory response accompanying myocardial injury. Composite indices derived from the complete blood count have been examined across a range of cardiovascular conditions and in myocarditis specifically [14–16], and our group has previously reported an association between the pan-immune-inflammation value and CMR-defined LGE in hospitalised patients with myocarditis [17]. Two limitations recur in this literature. First, composite indices are rarely tested against the individual components from which they are constructed, leaving it unclear whether the composite adds information or merely repackages it. Second, statistical significance in a regression model is frequently reported without any assessment of whether the marker actually improves discrimination or reclassification when added to the information a clinician already has.

The neutrophil percentage-to-albumin ratio (NPAR) differs from these indices in that it combines a cellular inflammatory signal with serum albumin, a negative acute-phase reactant that falls in proportion to inflammatory activity, capillary leakage and overall illness burden. NPAR has been associated with adverse outcomes in ST-segment elevation myocardial infarction [18], critically ill patients with myocardial infarction [19], chronic heart failure [20], chronic kidney disease [21], diabetes and prediabetes [22], and hypertension [23]. Its behaviour in myocarditis, and specifically its relationship to CMR-defined myocardial involvement, has not been examined.

We therefore investigated whether NPAR, calculated from routinely available admission laboratory parameters, is independently associated with CMR-defined LGE positivity in patients with clinically suspected myocarditis. Because any composite index must justify itself against its own constituents, we further examined whether NPAR discriminates LGE positivity better than neutrophil percentage alone and serum albumin alone, characterised the shape of the association using restricted cubic splines, and quantified the incremental value of NPAR over a clinical and laboratory model using the integrated discrimination improvement and net reclassification improvement.

Methods

Study design and population

This retrospective, multicentre observational study included consecutive adults with clinically suspected myocarditis who underwent CMR at seven tertiary cardiovascular centres in Türkiye between October 2022 and September 2025. Clinically suspected myocarditis was defined according to the diagnostic criteria proposed by the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases [1], requiring at least one clinical presentation and at least one diagnostic criterion from different categories, in the absence of angiographically detectable coronary artery disease and of known pre-existing cardiovascular disease or extra-cardiac causes that could explain the syndrome.

Patients were excluded if CMR demonstrated an ischaemic LGE pattern or if obstructive coronary artery disease was known, if image quality was inadequate, if an alternative cardiomyopathy or specific alternative diagnosis was established, if admission laboratory or clinical data were missing, or if they were younger than 18 years. Patient selection is shown in Fig. 1.

Patients were recruited from seven tertiary cardiovascular centres. The number of patients contributed by each centre was as follows: Ankara Etlik City Hospital, 270 (25.6%); İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, 205 (19.4%); Ankara Bilkent City Hospital, 170 (16.1%); University of Health Sciences Gülhane Training and Research Hospital, 160 (15.2%); Başakşehir Çam and Sakura City Hospital, 150 (14.2%); Kocaeli University Faculty of Medicine, 52 (4.9%); and University of Health Sciences Bursa Yüksek İhtisas Training and Research Hospital, 48 (4.5%).

CMR protocol and LGE assessment

CMR protocol and LGE assessment
Late gadolinium enhancement images were acquired approximately 10 minutes after intravenous administration of a gadolinium-based contrast agent, using inversion-recovery or phase-sensitive inversion-recovery sequences in short-axis and standard long-axis planes. All CMR studies from the participating centres were transferred to a shared archive and reviewed centrally by three cardiovascular

radiologists (E.K.Ö., A.T.C. and B.A.), each with more than 10 years of dedicated cardiovascular imaging experience, who were blinded to clinical presentation, laboratory results and NPAR values.

LGE positivity was defined as visually detectable myocardial hyperenhancement in a non-ischaemic distribution pattern compatible with myocarditis-related myocardial injury, including subepicardial, mid-wall or patchy enhancement. Hyperenhancement in a typical ischaemic pattern corresponding to a coronary artery territory was not considered myocarditis-related LGE. Each study was read independently by all three readers and disagreements were resolved by joint review until consensus was reached. Interobserver agreement for LGE positivity before consensus was excellent (Fleiss' $\kappa = 0.83$; 95% CI 0.79–0.87). Total LGE burden was recorded as the percentage of involved myocardium using semi-automated signal thresholding with manual correction. The interval between the clinical diagnosis of suspected myocarditis and the CMR examination was recorded for each patient.

Laboratory assessment and calculation of NPAR

NPAR was calculated as neutrophil percentage (%) divided by serum albumin concentration expressed in g/L.

Because NPAR is derived from neutrophil percentage and serum albumin, its individual components were not entered simultaneously with NPAR in the same multivariable model, to avoid mathematical coupling and multicollinearity. The components were instead compared with NPAR in the receiver operating characteristic (ROC) analysis.

Use of artificial intelligence

A large language model (Claude, Anthropic) was used to assist with statistical scripting and manuscript preparation. All analyses and their interpretation were verified by the authors, who take full responsibility for the content of the work.

Statistical analysis

The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [24], and a completed STROBE checklist is provided as an additional file. Continuous variables are presented as mean ± standard deviation or median (interquartile range) according to distribution, and categorical variables as counts and percentages. Groups were compared using the Welch t test, the Mann–Whitney U test, the Pearson chi-square test or Fisher's exact test, as appropriate. Analyses were performed using available data; no imputation was undertaken, and the number of patients with available data is reported for each variable.

Univariable logistic regression analysis was performed for every variable that differed significantly between the two groups in the baseline comparison, with effect estimates reported per the unit stated

for each variable; peak cardiac troponin was natural-log transformed before entry. All variables associated with LGE positivity at $p < 0.10$ on univariable analysis were considered as candidates for the multivariable model.

Three groups of candidate variables were excluded a priori. CMR-derived parameters (CMR-derived left ventricular ejection fraction and stroke volume) were not entered, because the aim was to identify clinical, echocardiographic and laboratory predictors rather than predictors obtained from the same imaging modality used to define the outcome. Neutrophil percentage and serum albumin were not entered, because they are the mathematical components of NPAR; co-entry of neutrophil percentage produced a variance inflation factor of 11.6, and both components were instead compared with NPAR in the ROC analysis. Absolute neutrophil count was excluded for the same reason, being strongly correlated with NPAR (Spearman rho 0.66). The remaining candidates were entered simultaneously.

Model 1 therefore comprised body mass index, hypertension, chest pain, NYHA class > I, invasive coronary angiography, concomitant coronary stenosis, echocardiographic ejection fraction, white blood cell count, lymphocyte count, monocyte count, glucose, log-transformed peak troponin and C-reactive protein. Model 2 comprised Model 1 plus NPAR. Because a one-unit change in NPAR spans more than two standard deviations of its observed distribution, NPAR was standardised and is reported per 1 standard deviation. Because the interval from diagnosis to CMR differed between groups but was available for a subset of patients, it was added in a prespecified sensitivity model (Model 3). Multicollinearity was assessed using variance inflation factors and calibration using the Hosmer–Lemeshow test.

The shape of the association between NPAR and LGE positivity was examined using restricted cubic splines with four knots placed at the 5th, 35th, 65th and 95th percentiles of the NPAR distribution, adjusted for the Model 1 covariates and referenced to the cohort median. Non-linearity was tested by a likelihood ratio test comparing the spline model with a model in which NPAR was entered linearly.

The incremental value of NPAR beyond the clinical and laboratory model was quantified by the change in the area under the curve, compared using the DeLong method [25]; the integrated discrimination improvement (IDI); the continuous net reclassification improvement (NRI); and a categorical NRI using predicted-risk strata of < 10%, 10–30% and > 30%. Confidence intervals and p values for the IDI and NRI were obtained from 2,000 bootstrap resamples.

ROC curve analysis was additionally performed to compare the discriminatory performance of NPAR with that of its two components for LGE positivity. Areas under the curve with 95% confidence intervals were calculated, optimal cut-off values determined using the Youden index, and pairwise comparisons performed using the DeLong method. Serum albumin was entered with inverted sign so that higher values denote greater risk. A two-sided p value < 0.05 was considered statistically significant.

Results

A total of 1,055 patients with clinically suspected myocarditis who underwent CMR were included. LGE was detected in 285 patients (27.0%), whereas 770 patients (73.0%) had no evidence of LGE. Baseline characteristics according to LGE status are shown in Table 1.

Table 1
Baseline characteristics according to late gadolinium enhancement status

Characteristic	LGE negative (n = 770)	LGE positive (n = 285)	P value	n
Clinical characteristics				
Age, years	29.33 ± 10.67	30.17 ± 11.58	0.287	1053
Body mass index, kg/m²	25.23 ± 5.05	26.07 ± 4.35	0.016	833
Male sex, n (%)	440 (57.1)	165 (57.9)	0.825	1055
Diabetes mellitus, n (%)	21 (2.7)	10 (3.5)	0.505	1055
Hypertension, n (%)	45 (5.8)	30 (10.5)	0.009	1055
Hyperlipidemia, n (%)	20 (2.6)	11 (3.9)	0.281	1055
Chronic kidney disease, n (%)	9 (1.2)	2 (0.7)	0.737	1055
Cancer, n (%)	4 (0.5)	2 (0.7)	0.664	1055
Smoking, n (%)	213 (27.7)	64 (22.5)	0.088	1055
Dyspnea, n (%)	80 (10.4)	28 (9.8)	0.788	1055
Chest pain, n (%)	608 (79.0)	255 (89.5)	< 0.001	1055
Palpitations, n (%)	123 (16.0)	37 (13.0)	0.229	1055
Fever, n (%)	82 (10.6)	39 (13.7)	0.170	1055
Upper respiratory tract infection symptoms, n (%)	231 (30.0)	78 (27.4)	0.404	1055
NYHA class, n (%)			< 0.001	1055
Class I	734 (95.3)	249 (87.4)		
Class II	30 (3.9)	32 (11.2)		
Class III	6 (0.8)	4 (1.4)		
Echocardiographic findings				
Ejection fraction, %	58.19 ± 8.30	56.06 ± 11.36	0.006	1004
LVDD, mm	46.59 ± 4.82	47.48 ± 6.77	0.101	747
Left atrial diameter, mm	34.00 ± 4.93	34.32 ± 5.56	0.438	851
Pericardial involvement, n (%)	59 (7.7)	27 (9.5)	0.340	1055

Data are presented as mean ± standard deviation, median (interquartile range), or n (%). The n column gives the number of patients with available data; no imputation was performed.

Characteristic	LGE negative (n = 770)	LGE positive (n = 285)	P value	n
Clinical characteristics				
Coronary evaluation				
Coronary CT angiography, n (%)	275 (35.7)	96 (33.7)	0.540	1055
Invasive coronary angiography, n (%)	284 (36.9)	138 (48.4)	< 0.001	1055
Concomitant coronary stenosis, n (%)	14 (1.8)	14 (4.9)	0.005	1055
Cardiac magnetic resonance findings				
Time from diagnosis to CMR, days	11.0 (5.0–22.0)	27.0 (11.0–41.2)	< 0.001	817
CMR LV ejection fraction, %	60.18 ± 9.01	57.89 ± 9.89	0.002	775
CMR LV EDV, mL	119.0 (101.0–139.0)	123.0 (106.0–151.0)	0.098	508
CMR LV ESV, mL	47.0 (37.0–56.0)	51.5 (37.5–61.5)	0.061	503
CMR LV SV, mL	72.0 (61.0–85.0)	66.0 (51.5–84.0)	0.021	510
CMR RV ejection fraction, %	49.0 (45.0–56.0)	49.0 (45.0–54.2)	0.672	293
Total LGE, %	0.0 (0.0–0.0)	5.0 (2.0–7.0)	—	1055
Laboratory findings				
Hemoglobin, g/dL	14.33 ± 1.61	14.47 ± 1.64	0.273	943
White blood cell count, ×10³/μL	9.05 (7.20–11.50)	10.20 (7.95–12.80)	< 0.001	1055
Neutrophils, ×10³/μL	5.00 (3.60–6.10)	6.90 (5.10–8.70)	< 0.001	1055
Neutrophil percentage, %	55.32 ± 19.71	68.73 ± 15.23	< 0.001	1055
Lymphocytes, ×10³/μL	1.90 (1.30–2.45)	1.73 (1.10–2.33)	0.005	1055
Monocytes, ×10³/μL	0.70 (0.50–1.06)	0.98 (0.68–1.19)	< 0.001	1055
Platelets, ×10³/μL	226.0 (193.0–271.0)	234.0 (183.0–277.0)	0.990	1049
Glucose, mg/dL	98.66 ± 27.52	105.54 ± 37.20	0.007	882
Albumin, g/L	44.12 ± 3.71	42.04 ± 4.39	< 0.001	1050

Data are presented as mean ± standard deviation, median (interquartile range), or n (%). The n column gives the number of patients with available data; no imputation was performed.

Characteristic	LGE negative (n = 770)	LGE positive (n = 285)	P value	n
Clinical characteristics				
Admission creatinine, mg/dL	0.82 (0.70–0.93)	0.83 (0.72–0.94)	0.484	1001
AST, U/L	29.0 (20.0–50.0)	30.0 (20.0–45.2)	0.857	1035
ALT, U/L	25.0 (18.0–41.2)	24.0 (17.0–37.0)	0.077	1036
LDH, U/L	253.0 (209.0–321.0)	236.0 (203.0–297.0)	0.194	668
Peak cardiac troponin, ng/L	126.5 (59.0–405.8)	514.0 (79.7–1042.0)	< 0.001	1053
C-reactive protein, mg/L	11.46 (2.02–52.65)	25.00 (6.00–71.46)	< 0.001	1055
Erythrocyte sedimentation rate, mm/h	13.0 (5.8–25.2)	10.0 (4.0–17.5)	0.035	243
Procalcitonin, ng/mL	0.17 (0.05–0.34)	0.18 (0.06–0.25)	0.197	729
Total cholesterol, mg/dL	151.0 (125.0–178.0)	152.0 (124.0–176.0)	0.761	740
Triglycerides, mg/dL	105.0 (76.0–152.5)	107.0 (78.0–153.0)	0.644	736
LDL cholesterol, mg/dL	90.0 (68.0–110.0)	88.0 (68.1–111.0)	0.951	769
HDL cholesterol, mg/dL	37.0 (30.0–45.0)	38.0 (30.0–46.0)	0.697	752
NPAR	1.29 (1.02–1.54)	1.63 (1.41–1.90)	< 0.001	1050
Data are presented as mean ± standard deviation, median (interquartile range), or n (%). The n column gives the number of patients with available data; no imputation was performed.				

Patients with LGE positivity had a higher body mass index and a higher prevalence of hypertension and chest pain, and had less favourable NYHA functional class. On echocardiography, LGE-positive patients had a lower left ventricular ejection fraction. Invasive coronary angiography had been performed more frequently in the LGE-positive group, and concomitant coronary stenosis was more common. CMR-derived left ventricular ejection fraction and stroke volume were lower in patients with LGE positivity, and the interval from diagnosis to CMR was longer [27.0 (11.0–41.2) vs. 11.0 (5.0–22.0) days; $p < 0.001$].

LGE-positive patients had higher white blood cell, neutrophil and monocyte counts and a higher neutrophil percentage, together with lower lymphocyte counts and lower serum albumin levels. Glucose, peak cardiac troponin, C-reactive protein and erythrocyte sedimentation rate were also higher, as was NPAR [1.65 (1.40–1.92) vs. 1.29 (1.02–1.55); $p < 0.001$].

Univariable analysis

Every variable that differed significantly between the groups at baseline was examined by univariable logistic regression (Table 2). Twenty-one variables were associated with LGE positivity at $p < 0.10$. NPAR showed the strongest association (odds ratio per 1 unit 8.918, 95% CI 6.007–13.238; odds ratio per 1 standard deviation 2.847, 95% CI 2.357–3.439; $p < 0.001$).

Table 2
Univariable logistic regression analysis for predictors of LGE positivity

Variable	OR (95% CI)	P value	n
Body mass index, per 1 kg/m²	1.039 (1.005–1.074)	0.025	833
Hypertension	1.895 (1.169–3.074)	0.010	1055
Chest pain	2.265 (1.494–3.434)	< 0.001	1055
NYHA class > I	2.948 (1.817–4.782)	< 0.001	1055
Invasive coronary angiography	1.606 (1.221–2.114)	< 0.001	1055
Concomitant coronary stenosis	2.790 (1.313–5.928)	0.008	1055
Ejection fraction, per 1%	0.978 (0.964–0.992)	0.002	1004
CMR LV ejection fraction, per 1%	0.975 (0.960–0.990)	0.002	775
CMR LV stroke volume, per 1 mL	0.991 (0.980–1.001)	0.082	510
Time from diagnosis to CMR, per 1 day	1.009 (1.004–1.013)	< 0.001	817
White blood cell count, per 1×10³/μL	1.074 (1.032–1.118)	< 0.001	1055
Neutrophils, per 1×10³/μL	1.464 (1.369–1.565)	< 0.001	1055
Neutrophil percentage, per 1%	1.043 (1.034–1.052)	< 0.001	1055
Lymphocytes, per 1×10³/μL	0.817 (0.706–0.946)	0.007	1055
Monocytes, per 1×10³/μL	3.307 (2.344–4.666)	< 0.001	1055
Albumin, per 1 g/L	0.876 (0.845–0.908)	< 0.001	1050
Glucose, per 1 mg/dL	1.007 (1.002–1.012)	0.006	882
Log peak troponin, per 1 log unit	1.313 (1.196–1.440)	< 0.001	1053
C-reactive protein, per 10 mg/L	1.044 (1.018–1.070)	< 0.001	1055
Erythrocyte sedimentation rate, per 1 mm/h	0.992 (0.977–1.008)	0.324	243
NPAR, per 1 unit	8.918 (6.007–13.238)	< 0.001	1050
NPAR, per 1 SD (0.478 units)	2.847 (2.357–3.439)	< 0.001	1050

Univariable logistic regression was performed for every variable that differed significantly between the groups in Table 1. Effect estimates are expressed per the unit stated for each variable. Peak cardiac troponin was natural-log transformed before entry.

Multivariable analysis

In the clinical and laboratory model without NPAR (Model 1; n = 769, 205 events), NYHA class > I, monocyte count and log-transformed peak troponin were independently associated with LGE positivity, and the model explained a modest proportion of the variance (Nagelkerke R^2 0.157). After the addition of NPAR (Model 2; n = 767, 204 events), NPAR was strongly and independently associated with the outcome (adjusted odds ratio per 1 standard deviation 4.381, 95% CI 3.248–5.907; $p < 0.001$), and the Nagelkerke R^2 rose to 0.387. NYHA class > I, monocyte count, lymphocyte count and concomitant coronary stenosis also remained independently associated with LGE positivity. All variance inflation factors were below 1.5 and calibration was adequate (Hosmer–Lemeshow $p = 0.445$). In the sensitivity model additionally adjusting for the interval from diagnosis to CMR (Model 3), the association between NPAR and LGE positivity was preserved. Multivariable models are presented in Table 3.

Table 3
Multivariable logistic regression models for predictors of LGE positivity

Variable	Model 1 aOR (95% CI)	P	Model 2 aOR (95% CI)	P	Model 3 aOR (95% CI)	P
Body mass index (per 1 kg/m²)	1.023 (0.986–1.061)	0.228	1.023 (0.982–1.064)	0.278	1.032 (0.991–1.075)	0.131
Hypertension	1.253 (0.667–2.350)	0.483	1.100 (0.546–2.217)	0.790	1.049 (0.516–2.135)	0.894
Chest pain	1.084 (0.612–1.922)	0.781	0.919 (0.479–1.763)	0.799	1.082 (0.552–2.123)	0.818
NYHA class > I	2.287 (1.223–4.275)	0.010	2.131 (1.016–4.470)	0.045	1.910 (0.901–4.049)	0.091
Invasive coronary angiography	1.121 (0.774–1.622)	0.546	0.995 (0.651–1.521)	0.981	0.874 (0.561–1.362)	0.551
Concomitant coronary stenosis	2.318 (0.947–5.674)	0.066	2.991 (1.039–8.616)	0.042	2.597 (0.900–7.492)	0.078
Ejection fraction (per 1%)	0.992 (0.973–1.012)	0.430	0.990 (0.968–1.012)	0.365	0.989 (0.967–1.012)	0.343
White blood cell count (per 1×10³/μL)	0.941 (0.886–1.000)	0.050	0.966 (0.894–1.045)	0.390	0.963 (0.888–1.044)	0.362
Lymphocytes (per 1×10³/μL)	1.064 (0.877–1.291)	0.532	1.297 (1.024–1.643)	0.031	1.432 (1.110–1.846)	0.006
Monocytes (per 1×10³/μL)	4.612 (2.779–7.654)	< 0.001	8.264 (4.569–14.947)	< 0.001	9.244 (4.892–17.465)	< 0.001

Model 1 comprises all variables associated with LGE positivity at $p < 0.10$ on univariable analysis, except CMR-derived parameters and the components of NPAR (see Methods). Model 2: Model 1 plus NPAR. Model 3: Model 2 plus the interval from diagnosis to CMR.

Model fit: Model 1 — n = 769, events = 205, Cox & Snell $R^2 = 0.108$, Nagelkerke $R^2 = 0.157$. Model 2 — n = 767, events = 204, Cox & Snell $R^2 = 0.265$, Nagelkerke $R^2 = 0.387$. Model 3 — n = 688, events = 203, Cox & Snell $R^2 = 0.291$, Nagelkerke $R^2 = 0.414$.

NPAR is expressed per 1 standard deviation (0.478 units); the per-unit estimate is given in Table 2. All variance inflation factors in Model 2 were below 1.5, and calibration was adequate (Hosmer–Lemeshow chi² = 7.88, p = 0.445).

Variable	Model 1 aOR (95% CI)	P	Model 2 aOR (95% CI)	P	Model 3 aOR (95% CI)	P
Glucose (per 1 mg/dL)	1.003 (0.998–1.009)	0.181	1.000 (0.994–1.006)	0.950	1.000 (0.994–1.006)	0.962
Log peak troponin (per 1 log unit)	1.146 (1.020–1.287)	0.022	1.098 (0.962–1.253)	0.165	1.088 (0.948–1.247)	0.229
C-reactive protein (per 10 mg/L)	1.015 (0.980–1.052)	0.409	0.995 (0.953–1.038)	0.807	0.996 (0.953–1.041)	0.855
NPAR (per 1 SD)	—	—	4.381 (3.248–5.907)	< 0.001	4.537 (3.317–6.206)	< 0.001
Time from diagnosis to CMR (per 1 day)	—	—	—	—	1.006 (1.001–1.011)	0.031
Model 1 comprises all variables associated with LGE positivity at p < 0.10 on univariable analysis, except CMR-derived parameters and the components of NPAR (see Methods). Model 2: Model 1 plus NPAR. Model 3: Model 2 plus the interval from diagnosis to CMR.						
Model fit: Model 1 — n = 769, events = 205, Cox & Snell R^2 = 0.108, Nagelkerke R^2 = 0.157. Model 2 — n = 767, events = 204, Cox & Snell R^2 = 0.265, Nagelkerke R^2 = 0.387. Model 3 — n = 688, events = 203, Cox & Snell R^2 = 0.291, Nagelkerke R^2 = 0.414.						
NPAR is expressed per 1 standard deviation (0.478 units); the per-unit estimate is given in Table 2. All variance inflation factors in Model 2 were below 1.5, and calibration was adequate (Hosmer–Lemeshow chi² = 7.88, p = 0.445).						

Shape of the association

Restricted cubic spline analysis, adjusted for the Model 1 covariates, showed a monotonically increasing adjusted odds of LGE positivity across the observed range of NPAR, with a significant overall association (p < 0.001) and evidence of departure from linearity (p for non-linearity = 0.013). The slope was steepest across the lower and middle part of the distribution and flattened above approximately 1.8, indicating that most of the discriminatory information lies within the range in which the majority of patients fall rather than at extreme values (Fig. 3).

Incremental value of NPAR

Adding NPAR to the clinical and laboratory model increased the area under the curve from 0.728 (95% CI 0.687–0.768) to 0.839 (95% CI 0.806–0.872), a difference of 0.111 (95% CI 0.077–0.146; p < 0.001 by the DeLong method). The integrated discrimination improvement was 0.194 (95% CI 0.133–0.251; p < 0.001) and the continuous net reclassification improvement was 0.843 (95% CI 0.674–1.011; p < 0.001).

Using predicted-risk strata of < 10%, 10–30% and > 30%, the categorical net reclassification improvement was 0.494 (95% CI 0.313–0.585; p < 0.001), with 40.7% of patients with LGE correctly reclassified upward and 21.6% of patients without LGE correctly reclassified downward. These results are summarised in Table 4.

Table 4
Incremental value of NPAR over the clinical and laboratory model

Metric	Estimate (95% CI)		P value
Area under the curve, Model 1	0.728 (0.687–0.768)		
Area under the curve, Model 2	0.839 (0.806–0.872)		
Difference in area under the curve	0.111 (0.077–0.146)	DeLong test	< 0.001
Integrated discrimination improvement	0.194 (0.133–0.251)		< 0.001
Continuous net reclassification improvement	0.843 (0.674–1.011)		< 0.001
Categorical net reclassification improvement	0.494 (0.313–0.585)	< 10%, 10–30%, > 30%	< 0.001
Correctly reclassified upward, LGE positive	40.7%		
Correctly reclassified downward, LGE negative	21.6%		

Model 1 comprises the clinical and laboratory variables listed in Table 3; Model 2 is Model 1 plus NPAR. Analyses were performed in the 767 patients with complete data for all model covariates (204 events). Confidence intervals and p values for the reclassification metrics were obtained from 2,000 bootstrap resamples.

NPAR compared with its components

As a single marker, NPAR yielded an area under the curve of 0.750 (95% CI 0.718–0.782) for LGE positivity, with an optimal cut-off of 1.43 providing 73.6% sensitivity and 65.1% specificity. NPAR discriminated LGE positivity better than either of its constituents: neutrophil percentage (AUC 0.715, 95% CI 0.681–0.748; difference 0.0354, 95% CI 0.0211–0.0497; p < 0.0001) and serum albumin (AUC 0.636, 95% CI 0.597–0.675; difference 0.1140, 95% CI 0.0739–0.1540; p < 0.0001). ROC parameters and pairwise comparisons are given in Table 5 and comparative curves in Fig. 2.

Table 5 ROC analysis of NPAR and its components for predicting LGE positivity

A. ROC analysis (n = 1050)

Index	AUC	95% CI	Cut-off	Sensitivity	Specificity	P value
NPAR	0.750	0.718–0.782	1.43	73.6%	65.1%	< 0.001
Neutrophil percentage	0.715	0.681–0.748	66.11	58.5%	73.6%	< 0.001
Albumin (inverted)	0.636	0.597–0.675	40.80	38.7%	83.8%	< 0.001

B. Pairwise DeLong comparisons

Comparison	Difference between AUCs	95% CI	P value
NPAR vs Neutrophil percentage	0.0354	0.0211–0.0497	< 0.0001
NPAR vs Albumin	0.1140	0.0739–0.1540	< 0.0001

Optimal cut-off values were determined using the Youden index. Serum albumin was entered with inverted sign so that higher values indicate greater risk; the cut-off is reported on the original scale.

Discussion

In this multicentre cohort of patients with clinically suspected myocarditis who underwent CMR, NPAR was independently associated with LGE positivity after adjustment for every clinical, echocardiographic and laboratory variable that differed between the groups. Three findings extend beyond a conventional association analysis. First, NPAR outperformed each of its own two constituents in discriminating LGE positivity, indicating that the combination of neutrophil predominance with a negative acute-phase reactant carries information that neither component conveys alone. Second, the association was graded across the observed range of NPAR rather than driven by extreme values, with a significant departure from linearity. Third, and most relevant to clinical use, adding NPAR to a model already containing thirteen clinical and laboratory variables raised the area under the curve by 0.111 and produced an integrated discrimination improvement of 0.194 and a continuous net reclassification improvement of 0.843, all highly significant. NPAR therefore adds measurable information to what a clinician already has at the bedside, rather than merely reaching statistical significance in a regression model.

Our findings extend the growing interest in blood-count-derived inflammatory indices in myocarditis. A previous study from our group showed that the pan-immune-inflammation value was independently associated with CMR-defined LGE in hospitalised patients with myocarditis [17]. The present study builds on that observation in a substantially larger, multicentre cohort and addresses a question that composite-index studies frequently leave open: whether the composite adds anything to its parts. The DeLong comparisons answer this directly for NPAR relative to neutrophil percentage and serum albumin. Reclassification metrics are reported far less often than odds ratios in the biomarker literature, yet they address the question that matters clinically: whether knowing the marker changes the estimated probability of disease in the right direction. Using pragmatic risk strata of < 10%, 10–30% and > 30%, NPAR moved 40.7% of patients with LGE into a higher risk category and 21.6% of patients without LGE into a lower one. The magnitude of the integrated discrimination improvement should nonetheless be

interpreted with the usual caution: these metrics were derived and evaluated in the same cohort, without external validation, and are known to be optimistic under such circumstances.

More recently, the systemic inflammation response index was reported to be associated with both the presence and the extent of LGE in a single-centre cohort of 170 patients with acute myocarditis, with a higher reported discriminatory performance than that observed for NPAR here [26]. That cohort was drawn from a single centre over a shorter period, was restricted to patients imaged within four weeks of symptom onset, and had a different case mix, all of which limit direct numerical comparison. Our findings extend the observation to a substantially larger multicentre population and to a different index, and additionally address a question that the earlier work did not: whether a composite marker outperforms the individual components from which it is built.

The association between NPAR and LGE is biologically plausible, although it should be interpreted cautiously. Neutrophil predominance reflects activation of the innate immune response, which participates in the early inflammatory phase of myocardial injury. The albumin component is unlikely to act merely as a nutritional marker: hypoalbuminaemia in acute illness is driven by transcriptional downregulation, redistribution across a leaky capillary barrier and accelerated catabolism, all of which are inflammation-dependent processes [27]. A higher NPAR therefore captures a combined state of cellular inflammatory activation and depleted albumin reserve, which may explain why it discriminates better than either signal in isolation. Inflammation-mediated myocardial injury and subsequent extracellular matrix remodelling are central to the evolution of myocarditis [28]. NPAR does not measure myocardial inflammation directly; it is best understood as an accessible systemic correlate of the inflammatory milieu associated with CMR-detected myocardial involvement, and the relationship remains associative rather than causal.

Alternative explanations warrant consideration. NPAR may simply track overall illness severity rather than myocardial involvement specifically; higher NPAR values could reflect a more intense systemic inflammatory response that is itself associated with a greater likelihood of undergoing and completing a diagnostic pathway that ends in a positive CMR. Several observations argue against this being the whole explanation. The association persisted after adjustment for C-reactive protein and peak troponin, both of which capture severity of the inflammatory and myocardial injury response, and after adjustment for the interval from diagnosis to CMR. NPAR also discriminated LGE better than neutrophil percentage and albumin individually, which would not be expected if the signal were driven solely by generic illness severity. Nevertheless, residual confounding cannot be excluded in a retrospective design.

The spline analysis adds a further nuance. The adjusted odds of LGE positivity rose steeply across the lower and middle part of the NPAR distribution and flattened above approximately 1.8, so that further increases at the upper end of the range conveyed comparatively little additional information. This pattern argues against the use of a single high threshold to define a high-risk group, and supports the interpretation of NPAR as a graded marker of inflammatory burden across the range in which most

patients fall. It also means that the dichotomised cut-off of 1.43, while convenient, discards information; the continuous form of the marker should be preferred where a model-based estimate is feasible.

An additional observation deserves comment. The interval between clinical diagnosis and CMR was longer in LGE-positive patients, and this interval was itself independently associated with LGE positivity. Two non-exclusive explanations are plausible: patients with a more severe or protracted clinical course may have undergone imaging later, and myocardial injury may become more readily detectable as oedema resolves and replacement fibrosis consolidates [29]. Importantly, the association between NPAR and LGE positivity persisted after adjustment for this interval, indicating that the relationship is not an artefact of differential imaging timing. Nevertheless, the finding underscores that LGE in clinically suspected myocarditis is a time-dependent phenotype and that studies of blood-based markers should account for the imaging interval.

Our cohort was young, with a mean age of approximately 30 years, which is consistent with the demographic profile of acute myocarditis reported in contemporary registries [5, 30] and reflects the predominance of young adults among patients referred for CMR with clinically suspected disease.

The optimal NPAR cut-off in our cohort was 1.43. Direct comparison with published thresholds requires caution, because the NPAR literature is divided between studies expressing serum albumin in g/L and those expressing it in g/dL, producing threshold values that differ approximately tenfold for the same underlying ratio. Wang et al., for example, defined risk groups using thresholds of 18.0 and 21.2 with albumin in g/dL [20], whereas our cut-off of 1.43 is expressed with albumin in g/L and corresponds to approximately 14.3 on that scale. Explicit reporting of the albumin unit is necessary if thresholds are to be compared or validated across cohorts, and we would encourage this in future work.

Clinically, NPAR may help refine early risk assessment in patients with clinically suspected myocarditis. It is calculated from a complete blood count and a serum albumin measurement, requires no additional cost or processing, and is available at first contact. Where CMR access is constrained or delayed, NPAR may help prioritise patients for earlier imaging and closer surveillance. However, its discriminatory performance was moderate, with approximately 74% sensitivity and 65% specificity at the optimal cut-off of the marker used alone, and NPAR should not be regarded as a substitute for CMR or for comprehensive clinical assessment.

Limitations

Several limitations should be acknowledged. First, the retrospective design may introduce selection bias and residual confounding despite multivariable adjustment. Second, although the multicentre design increases generalisability, inter-centre differences in referral patterns, laboratory platforms, treatment strategies and CMR acquisition protocols may have influenced the findings, and patient-level centre identifiers were not available, so a centre-adjusted analysis could not be performed. Third, the diagnosis was based on clinically suspected myocarditis rather than systematic endomyocardial biopsy, and etiologic classification was not available for all patients; the observed LGE rate of 27.0% is lower than

that reported in biopsy-confirmed or hospitalised cohorts and reflects the broader clinical spectrum captured by our inclusion criteria [31, 32]. Fourth, CMR assessment was based on LGE alone; T2-weighted imaging and T1/T2 mapping were not uniformly available across centres and across the study period, so the 2018 Lake Louise Criteria could not be applied [7]. Fifth, NPAR was measured at initial presentation, and serial changes in inflammatory indices were not assessed. Sixth, the timing of CMR relative to symptom onset varied and may have affected LGE detection, although adjustment for this interval did not alter the principal finding. Seventh, the reclassification metrics were derived and assessed in the same cohort; without external validation these estimates are likely to be optimistic, and the incremental value of NPAR requires confirmation in an independent population. Finally, this study focused on CMR-defined myocardial involvement rather than long-term clinical outcomes. Prospective studies with standardised CMR protocols including parametric mapping, serial biomarker measurements and follow-up for arrhythmia, heart failure and mortality are needed to determine whether NPAR provides incremental prognostic value.

Conclusions

NPAR was independently associated with LGE positivity in patients with clinically suspected myocarditis, discriminated CMR-defined myocardial involvement better than either of its own components, and provided significant incremental discrimination and reclassification when added to a model containing the clinical and laboratory variables available at presentation. These findings support NPAR as a low-cost adjunctive marker for identifying patients with a higher likelihood of myocardial involvement. Further prospective studies are warranted to validate its clinical utility and to determine whether it improves risk stratification when combined with established clinical, laboratory and CMR parameters.

Abbreviations

ALT
alanine aminotransferase
AST
aspartate aminotransferase
AUC
area under the curve
CI
confidence interval
CMR
cardiac magnetic resonance
CRP
C-reactive protein
EDV
end-diastolic volume
ESV

end-systolic volume
HDL
high-density lipoprotein
IDI
integrated discrimination improvement
LDH
lactate dehydrogenase
LDL
low-density lipoprotein
LGE
late gadolinium enhancement
LV
left ventricle
LVDD
left ventricular end-diastolic diameter
NPAR
neutrophil percentage-to-albumin ratio
NRI
net reclassification improvement
NYHA
New York Heart Association
OR
odds ratio
ROC
receiver operating characteristic
RV
right ventricle
SD
standard deviation
STROBE
Strengthening the Reporting of Observational Studies in Epidemiology
SV
stroke volume

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ankara Etlik City Hospital No. 2 Scientific Research Evaluation and Ethics Committee (approval number AEŞH-BADEK2-2025-666; approval date 2 December 2025). The approval covered all participating centres, and

no additional local ethics approval was required. The requirement for informed consent was waived by the same ethics committee owing to the retrospective design of the study. All patient data were anonymised before analysis.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

Conceptualization, M.T.Ö., A.G. and V.O.T.; methodology, M.T.Ö., S.K. and B.Ö.; software, M.T.Ö.; validation, S.A., K.K. and K.K.; formal analysis, M.T.Ö., E.B.T. and B.Ö.; investigation, İ.H.U., S.U., M.Ö., E.U., A.Ç., B.N.G., G.Ç., M.K.C., H.A., D.O., Ç.T., M.S.K. and E.G.G.; resources, A.G., K.K., S.A., K.K., F.L. and V.O.T.; data curation, M.T.Ö., İ.H.U., S.U. and Ç.T.; CMR image analysis and interpretation, E.K.Ö. and A.T.C.; writing—original draft preparation, M.T.Ö.; writing—review and editing, A.G., S.K., E.B.T., B.Ö., U.Ç.Y. and V.O.T.; visualization, M.T.Ö.; supervision, V.O.T. and B.Ö.; project administration, M.T.Ö. All authors have read and agreed to the published version of the manuscript

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Authors' information

Not applicable.

Availability of data and materials

The datasets generated and analysed during the current study are not publicly available because they contain information that could compromise the privacy of research participants, but are available from the corresponding author on reasonable request.

References

1. Caforio ALP, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Eur Heart J. 2013;34(33):2636–48.
2. Schulz-Menger J, Collini V, Gröschel J, Adler Y, Brucato A, Christian V, et al. 2025 ESC Guidelines for the management of myocarditis and pericarditis. Eur Heart J. 2025;46:3952–4041.
3. Brociek E, Tymińska A, Giordani AS, Caforio ALP, Wojnicz R, Grabowski M, et al. Myocarditis: etiology, pathogenesis, and their implications in clinical practice. Biology. 2023;12(6):874.
4. Tschöpe C, Ammirati E, Bozkurt B, Caforio ALP, Cooper LT, Felix SB, et al. Myocarditis and inflammatory cardiomyopathy: current evidence and future directions. Nat Rev Cardiol. 2021;18(3):169–93.
5. Ammirati E, Frigerio M, Adler ED, Basso C, Birnie DH, Brambatti M, et al. Management of acute myocarditis and chronic inflammatory cardiomyopathy: an expert consensus document. Circ Heart Fail. 2020;13(11):e007405.
6. Ammirati E, Moslehi JJ. Diagnosis and treatment of acute myocarditis: a review. JAMA. 2023;329(13):1098–113.
7. Ferreira VM, Schulz-Menger J, Holmvang G, Kramer CM, Carbone I, Sechtem U, et al. Cardiovascular magnetic resonance in nonischemic myocardial inflammation: expert recommendations. J Am Coll Cardiol. 2018;72(24):3158–76.
8. Friedrich MG, Sechtem U, Schulz-Menger J, Holmvang G, Alakija P, Cooper LT, et al. Cardiovascular magnetic resonance in myocarditis: a JACC white paper. J Am Coll Cardiol. 2009;53(17):1475–87.
9. Georgiopoulos G, Figliozzi S, Sanguineti F, Aquaro GD, di Bella G, Stamatelopoulos K, et al. Prognostic impact of late gadolinium enhancement by cardiovascular magnetic resonance in myocarditis: a systematic review and meta-analysis. Circ Cardiovasc Imaging. 2021;14(1):e011492.
10. Yang F, Wang J, Li W, Xu Y, Wan K, Zeng R, et al. The prognostic value of late gadolinium enhancement in myocarditis and clinically suspected myocarditis: systematic review and meta-analysis. Eur Radiol. 2020;30(5):2616–26.
11. Aquaro GD, Perfetti M, Camastra G, Monti L, Dellegrottaglie S, Moro C, et al. Cardiac MR with late gadolinium enhancement in acute myocarditis with preserved systolic function: ITAMY study. J Am Coll Cardiol. 2017;70(16):1977–87.
12. Gräni C, Eichhorn C, Bière L, Murthy VL, Agarwal V, Kaneko K, et al. Prognostic value of cardiac magnetic resonance tissue characterization in risk stratifying patients with suspected myocarditis. J Am Coll Cardiol. 2017;70(16):1964–76.
13. Aquaro GD, Ghebru Habtemicael Y, Camastra G, Monti L, Dellegrottaglie S, Moro C, et al. Prognostic value of repeating cardiac magnetic resonance in patients with acute myocarditis. J Am Coll Cardiol. 2019;74(20):2439–48.

14. Xia Y, Xia C, Wu L, Li Z, Li H, Zhang J. Systemic immune inflammation index (SII), system inflammation response index (SIRI) and risk of all-cause mortality and cardiovascular mortality: a 20-year follow-up cohort study of 42,875 US adults. J Clin Med. 2023;12(3):1128.
15. Kangel D, Ozyılmaz İ, Ozkok S, Özcanoğlu HD, Güzelbağ AN, Çevlik B, et al. New systemic inflammatory indices as predictors of fulminant myocarditis in children. Diagnostics. 2025;15(8):961.
16. Wang S, Xu H, Guo Z, Tian Y, Guo X, Chu H, et al. Association of inflammatory index with the severity of disease in patients with acute myocarditis: a retrospective observational study. Front Endocrinol. 2025;16:1597427.
17. Kalkan S, Özkök S, Demirtaş İ, Türkmen ÖF, Tekin AF, Gürsoy MO, et al. Pan-immune-inflammation value: a new predictor of cardiac scar in hospitalized myocarditis patients. Biomark Med. 2025;19(15):647–56.
18. Cui H, Ding X, Li W, Chen H, Li H. The neutrophil percentage to albumin ratio as a new predictor of in-hospital mortality in patients with ST-segment elevation myocardial infarction. Med Sci Monit. 2019;25:7845–52.
19. Lin Y, Lin Y, Yue J, Zou Q. The neutrophil percentage-to-albumin ratio is associated with all-cause mortality in critically ill patients with acute myocardial infarction. BMC Cardiovasc Disord. 2022;22(1):115.
20. Wang X, Zhang Y, Wang Y, Liu J, Xu X, Liu J, et al. The neutrophil percentage-to-albumin ratio is associated with all-cause mortality in patients with chronic heart failure. BMC Cardiovasc Disord. 2023;23(1):568.
21. Liu M, Gou Y, Yang P. Neutrophil percentage-to-albumin ratio is associated with all cause and cardiovascular disease mortality in chronic kidney disease based on NHANES 2001–2018. Sci Rep. 2025;15(1):26546.
22. Li Y, Wei W, Liu K. Neutrophil percentage to albumin ratio predicts all-cause and cardiovascular mortality in patients with diabetes or prediabetes from NHANES 1999–2018. Sci Rep. 2025;15(1):22863.
23. Yang Y, Ding R, Li T, Li R, Song Y, Yuan Y, et al. Elevated neutrophil-percentage-to-albumin ratio predicts increased all-cause and cardiovascular mortality in hypertensive patients: evidence from NHANES 1999–2018. Maturitas. 2025;192:108169.
24. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007;370(9596):1453–7.
25. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics. 1988;44(3):837–45.
26. Altınsoy M, Kurtuluş Öztürk E, Turan Şerifler N, Kayhan Altuner T, Başyiğit F. Systemic inflammation response index is associated with the presence and extent of late gadolinium enhancement in acute myocarditis. J Clin Med. 2026;15(12):4505.

27. Soeters PB, Wolfe RR, Shenkin A. Hypoalbuminemia: pathogenesis and clinical significance. JPEN J Parenter Enter Nutr. 2019;43(2):181–93.
28. Frangogiannis NG. The inflammatory response in myocardial injury, repair, and remodelling. Nat Rev Cardiol. 2014;11(5):255–65.
29. von Knobelsdorff-Brenkenhoff F, Schüler J, Dogangüzel S, Dieringer MA, Rudolph A, Greiser A, et al. Detection and monitoring of acute myocarditis applying quantitative cardiovascular magnetic resonance. Circ Cardiovasc Imaging. 2017;10(2):e005242.
30. Ammirati E, Cipriani M, Moro C, Raineri C, Pini D, Sormani P, et al. Clinical presentation and outcome in a contemporary cohort of patients with acute myocarditis: multicenter Lombardy registry. Circulation. 2018;138(11):1088–99.
31. Ismail TF, Hua A, Plein S, D'Cruz DP, Fernando MMA, Friedrich MG, et al. The role of cardiovascular magnetic resonance in the evaluation of acute myocarditis and inflammatory cardiomyopathies in clinical practice: a comprehensive review. Eur Heart J Cardiovasc Imaging. 2022;23(4):450–64.
32. Bernhard B, Marxer ME, Zurkirchen JC, Schütze J, Wahl A, Elchinova E, et al. Prognostic implications of clinical and imaging diagnostic criteria for myocarditis. J Am Coll Cardiol. 2024;84(15):1373–87.

Figures

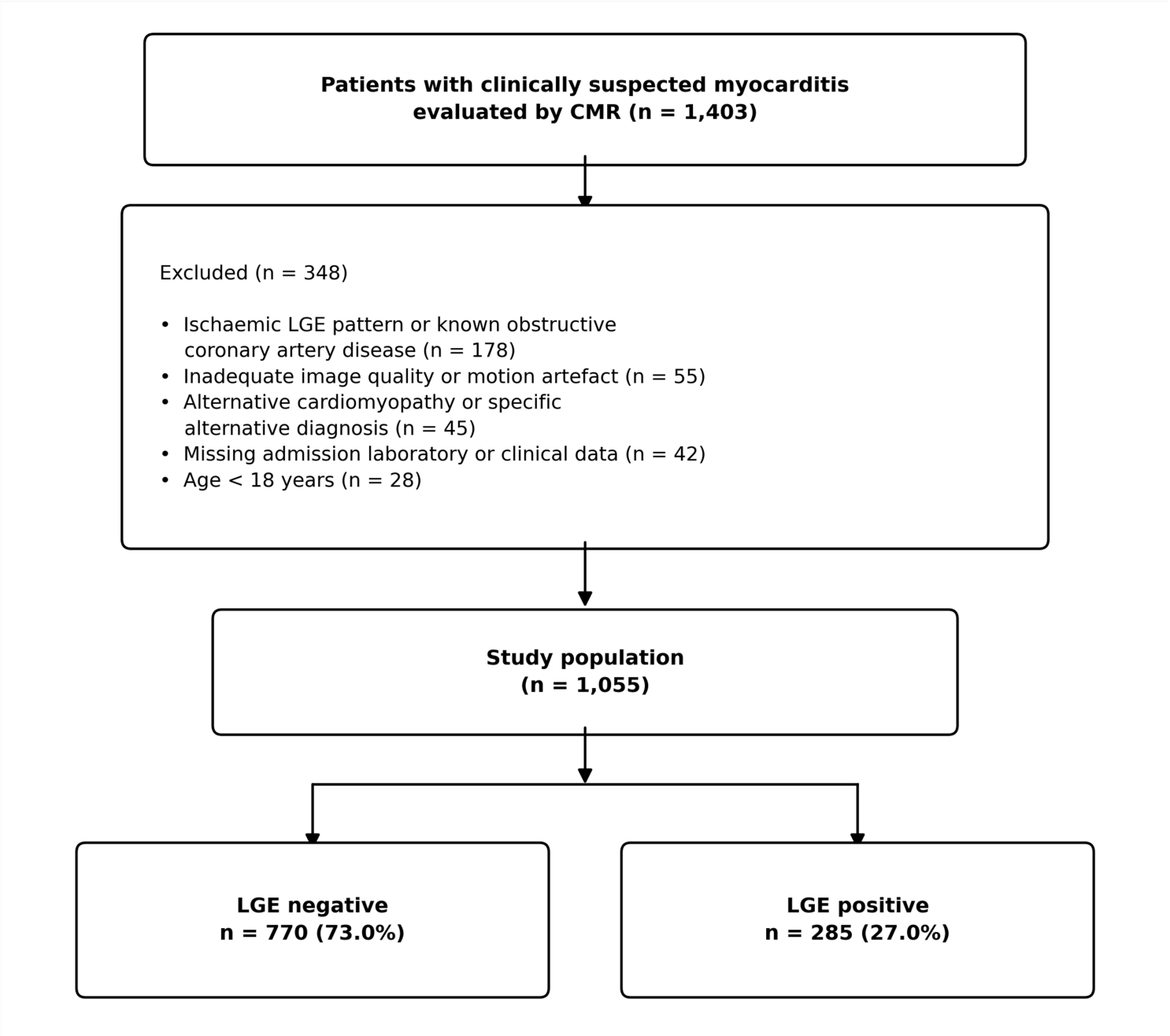


Figure 1

Flowchart of patient selection and grouping according to late gadolinium enhancement status. CMR cardiac magnetic resonance, LGE late gadolinium enhancement

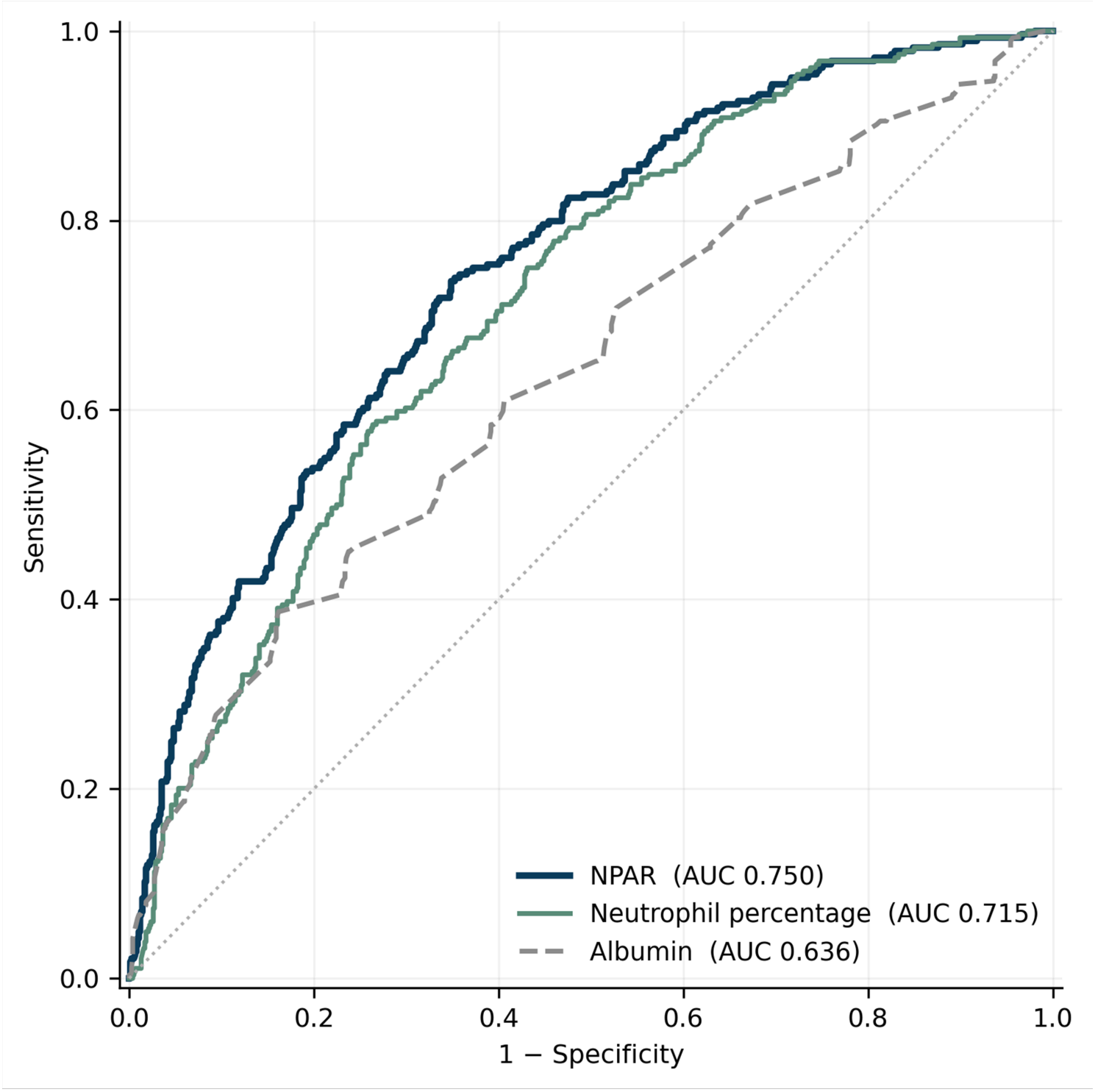


Figure 2

Receiver operating characteristic curves of NPAR and its individual components for predicting late gadolinium enhancement positivity (n = 1,050). AUC area under the curve, NPAR neutrophil percentage-to-albumin ratio

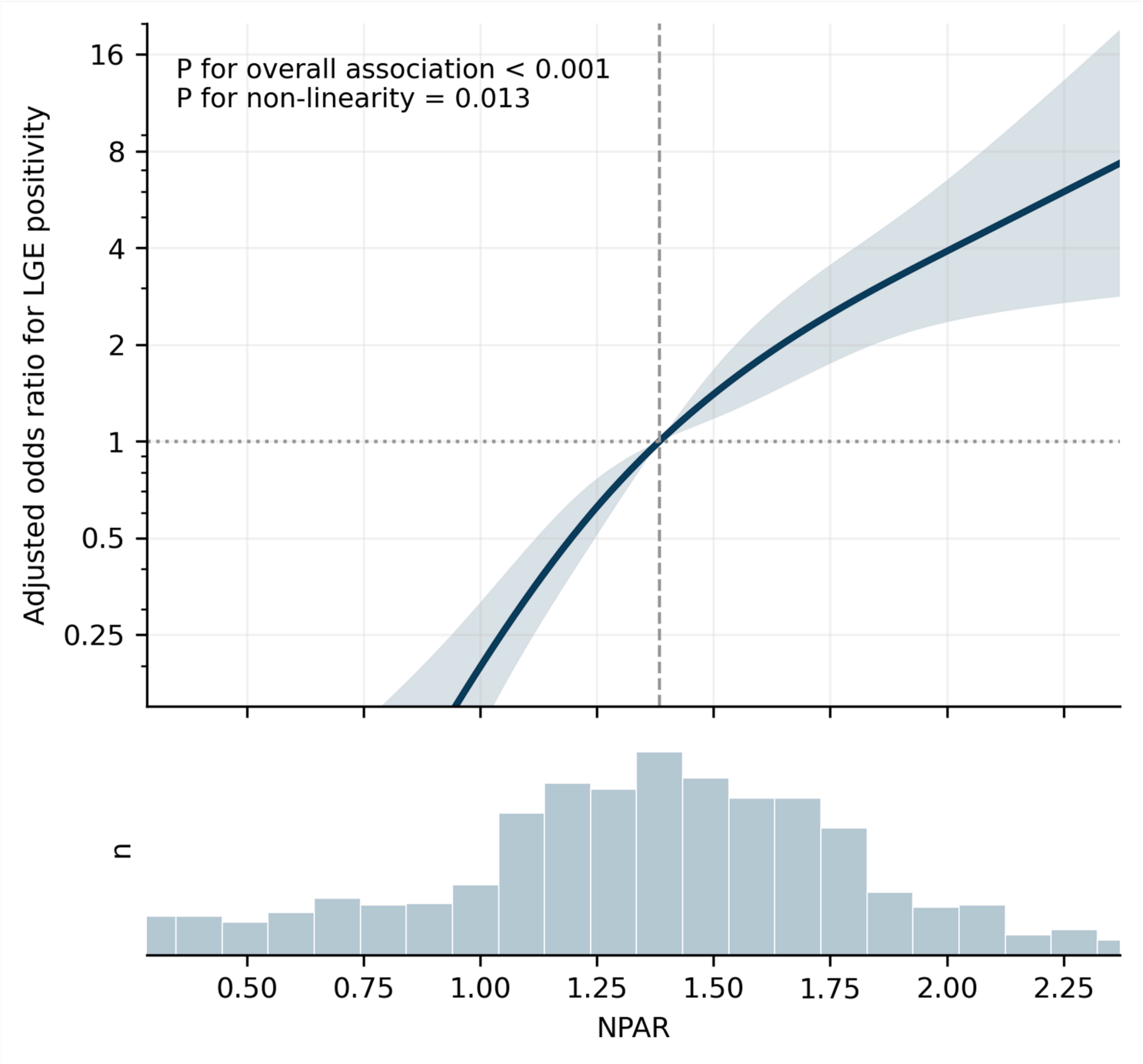


Figure 3

Restricted cubic spline curve of the adjusted association between NPAR and late gadolinium enhancement positivity (n = 767). Four knots were placed at the 5th, 35th, 65th and 95th percentiles of the NPAR distribution and the model was adjusted for the Model 1 covariates. The solid line shows the adjusted odds ratio referenced to the cohort median NPAR (dashed vertical line) and the shaded area the 95% confidence interval. The lower panel shows the distribution of NPAR. LGE late gadolinium enhancement, NPAR neutrophil percentage-to-albumin ratio