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Remnant Cholesterol Inflammatory Index Predicts Major Adverse Cardiovascular Events in Patients with Heart Failure with Preserved Ejection Fraction

Siliang Peng [1,†], Qiucheng Tao [2,†], Mengchao Jin [1], Jiapeng Chu [1], Jiayu Yin [1] and Hui Li [1,*]

[1] Department of Cardiology, The Second Affiliated Hospital of Soochow University, 215004 Suzhou, China
[2] Department of Radiology, Zhongda Hospital, Southeast University, 210009 Nanjing, China
* Correspondence: lihuifry@suda.edu.cn
† These authors contributed equally to this work.

Abstract

Background: Heart failure with preserved ejection fraction (HFpEF) is linked to cardiometabolic dysregulation and systemic inflammation. The remnant cholesterol inflammatory index (RCII) integrates remnant cholesterol and high-sensitivity C-reactive protein (hs-CRP), but its prognostic relevance in HFpEF is unknown. Methods: This single-center retrospective cohort study included 324 adults hospitalized with HFpEF between March 2022 and May 2026. RCII was calculated as remnant cholesterol (mg/dL) × hs-CRP (mg/L)/10 and log-transformed. The primary endpoint was the first occurrence of all-cause death or HF rehospitalization, termed major adverse cardiovascular events (MACEs) in this study. Associations were assessed by multivariable Cox regression and restricted cubic splines. Incremental value was quantified using net reclassification improvement (NRI) and integrated discrimination improvement (IDI). Results: Over a median follow-up of 24.1 months, 84 patients (25.9%) experienced MACE. Each 1-standard deviation increase in ln(RCII) was associated with the endpoint after adjustment for the measured covariates (adjusted HR, 1.80; 95% CI, 1.38–2.35; $p < 0.001$), and the highest tertile carried an approximately fourfold higher risk than the lowest (HR, 3.87; 95% CI, 2.02–7.39). The association was graded, without evidence of nonlinearity. Time-dependent AUCs for RCII were 0.655, 0.656, and 0.603 at 12, 24, and 30 months. Adding ln(RCII) raised the C-index of the clinical model from 0.707 to 0.736 ($p = 0.040$), with improved NRI but no statistically significant IDI improvement. Estimates were similar across 13 exploratory sensitivity analyses, but RCII correlated strongly with hs-CRP ($\rho = 0.918$) and their prognostic information overlapped substantially. Conclusions: Higher RCII was associated with MACE in HFpEF after adjustment for the measured covariates and provided modest incremental discrimination beyond the clinical model. Superiority over hs-CRP was not demonstrated, and external validation is required.

Keywords: heart failure with preserved ejection fraction; remnant cholesterol inflammatory index; inflammation; major adverse cardiovascular events; risk stratification

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1. Introduction

Heart failure (HF) remains a leading cause of mortality and disability worldwide. Heart failure with preserved ejection fraction (HFpEF) accounts for approximately half of all HF cases, and its prevalence continues to increase with population aging and the

growing burden of cardiometabolic comorbidities [1,2]. Current European Society of Cardiology (ESC) guidelines define HFpEF by symptoms and/or signs of HF, a left ventricular ejection fraction (LVEF) ≥ 50%, and objective evidence of cardiac structural or functional abnormalities consistent with elevated filling pressures [3,4]. Unlike heart failure with reduced ejection fraction (HFrEF), HFpEF is considered to arise from a distinct pathophysiological pathway in which obesity, hypertension, and chronic kidney disease promote systemic inflammation, coronary microvascular endothelial dysfunction, reduced nitric oxide bioavailability, and impaired cyclic guanosine monophosphate–protein kinase G signaling, ultimately contributing to myocardial hypertrophy, fibrosis, and diastolic stiffness [5]. HFpEF is also clinically heterogeneous, and phenotype-related factors such as obesity may influence natriuretic peptide concentrations and biomarker performance [6–8].

Remnant cholesterol (RC) represents the cholesterol content of triglyceride-rich lipoprotein remnants and can be readily estimated from routinely measured lipid parameters. RC has been identified as a causal risk factor for ischemic heart disease independent of low-density lipoprotein cholesterol (LDL-C) [9] and is increasingly recognized as a component of residual cardiovascular risk [10,11]. Genetic and epidemiological evidence further suggests that elevated RC contributes to both low-grade systemic inflammation and ischemic heart disease, whereas elevated LDL-C is associated primarily with ischemic heart disease [12]. This close biological relationship between remnant lipoproteins and inflammation is also supported by current consensus evidence [13]. The remnant cholesterol inflammatory index (RCII) combines RC and high-sensitivity C-reactive protein (hs-CRP) into a single composite measure. In this study, RCII was calculated as RC (mg/dL) × hs-CRP (mg/L)/10. Previous studies using the product of RC and CRP have reported associations with adverse outcomes in acute decompensated HF, coronary artery disease with T2DM, and population-based cohorts [14–16]. The stroke study by Yu et al. [17] instead used an RC/CRP ratio, which is mathematically distinct and cannot be considered a differently scaled version of the index used here. In addition, a close relationship between RC and inflammatory biomarkers has been demonstrated in patients undergoing percutaneous coronary intervention (PCI) [18], supporting the concept of a coupled lipid–inflammatory risk axis [19]. However, the prognostic relevance of RCII in patients with HFpEF has not been specifically investigated.

Accordingly, this study aimed to evaluate the association between RCII and major adverse cardiovascular events (MACEs), defined here as all-cause death or HF rehospitalization, in hospitalized patients with HFpEF and to determine whether RCII provides incremental discrimination and reclassification beyond established clinical risk markers.

2. Materials and Methods

2.1. Study Design and Population

This single-center retrospective cohort study screened 421 adults aged ≥18 years hospitalized with HFpEF as the principal diagnosis at the Second Affiliated Hospital of Soochow University between March 2022 and May 2026. These patients had already undergone screening for completeness of RCII and the prespecified adjustment variables. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. HFpEF was diagnosed in accordance with the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic HF and the 2023 Focused Update [3,4]. Eligible patients were required to have symptoms and/or signs of HF, LVEF ≥ 50%, and at least one echocardiographic abnormality: $E/e' > 9$, LAVI > 34 mL/m^2, LVMI ≥ 115 g/m^2 in men or ≥95 g/m^2 in women, or relative wall thickness >0.42. NT-proBNP was required to exceed 125 pg/mL in sinus rhythm or 365 pg/mL in atrial fibrillation, based on rhythm information available at clinical diagnosis. Patients

were excluded for any of the following, which correspond to the four exclusion categories shown in Figure 1: (1) acute myocardial infarction as the principal cause of presentation, decompensation requiring invasive mechanical ventilation, or severe valvular heart disease ($n = 48$); (2) active infection, autoimmune or other systemic inflammatory disease, or active malignancy ($n = 10$); (3) severe hepatic or renal dysfunction, defined as Child–Pugh class C cirrhosis, estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2, or maintenance dialysis ($n = 21$); and (4) absence of any post-discharge outcome information ($n = 18$). The patient-selection process is shown in Figure 1.

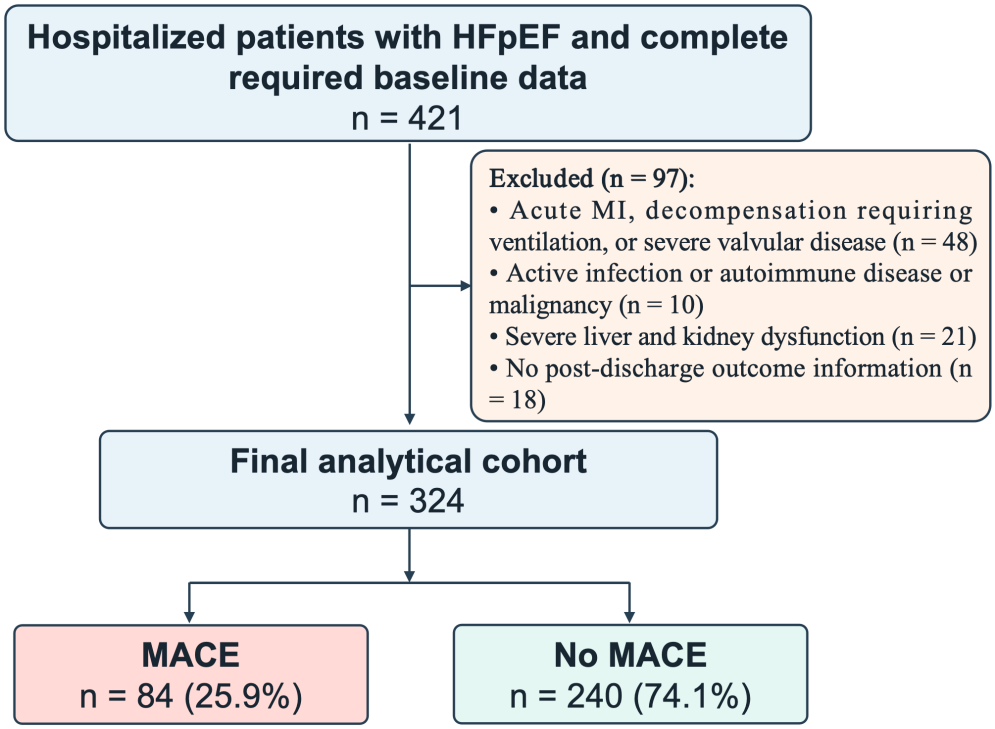


Figure 1. Flow diagram of patient selection. HFpEF, heart failure with preserved ejection fraction; MACE, major adverse cardiovascular event; MI, myocardial infarction.

The study protocol was approved by the Ethics Committee of the Second Affiliated Hospital of Soochow University (approval number: JD-HG-2026-068), and the study was conducted in accordance with the Declaration of Helsinki. The need for written informed consent was waived by the Ethics Committee of the Second Affiliated Hospital of Soochow University due to the retrospective nature of the study.

2.2. Clinical Data Collection

Two investigators independently reviewed the electronic health records and cross-checked the extracted data; discrepancies were resolved by consensus with a third investigator. Variables included demographic characteristics, medical history, laboratory measurements, echocardiographic findings, and medication use. Medication use referred to prescriptions at discharge from the index hospitalization. Available HFpEF-related characteristics included hypertension, diabetes mellitus, BMI, renal function, and echocardiographic indices of diastolic function and remodeling. Atrial fibrillation status, NYHA functional class, and coronary artery disease history were unavailable in the analytical dataset. Baseline parameters included age, sex, body mass index (BMI), systolic and diastolic blood pressure, and resting heart rate. Fasting venous blood samples obtained within 24 h of admission were used to measure total cholesterol, LDL-C, high-density lipoprotein cholesterol (HDL-C), triglycerides, hs-CRP, and other biochemical parameters. RC was

calculated as total cholesterol minus LDL-C minus HDL-C in mmol/L and converted to mg/dL by multiplying by 38.67. RCII was calculated as RC (mg/dL) × hs-CRP (mg/L)/10. hs-CRP was measured using a Mindray analyzer. Values below the reporting limit were analyzed as 0.5 mg/L; all other values were retained as recorded. All calculated RC and RCII values were positive, allowing direct natural-log transformation without an offset.

2.3. Follow-Up and Endpoint Definitions

Follow-up commenced at discharge from the index hospitalization and continued until the occurrence of the primary endpoint or the census date, whichever came first. No in-hospital deaths occurred among the 421 screened patients. Events during the index hospitalization were not counted toward the primary endpoint. Admission biomarkers were evaluated as predictors of post-discharge outcomes among patients who survived to discharge and had available post-discharge outcome information. Follow-up was conducted through outpatient visits, telephone contact, and review of electronic medical records. The primary endpoint was the first occurrence of all-cause death or HF rehospitalization, termed MACE in this study. Each patient contributed only the first qualifying event. Deaths following an initial HF rehospitalization were unavailable in the analytical dataset. HF-related events were adjudicated in accordance with ESC guidance [3,4]. Events occurring outside the study hospital were identified through telephone follow-up with patients or family members and verified against available medical records whenever possible. Two experienced cardiologists independently reviewed suspected events, and disagreements were resolved by a senior cardiologist.

2.4. Statistical Analysis

All analyses were performed in R 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria); tests were two-sided, and $p < 0.05$ was considered significant. Continuous variables were assessed using the Shapiro–Wilk test and summarized as mean ± SD or median (Q1, Q3). Two-group comparisons used the independent-samples *t*-test or Mann–Whitney U test, whereas comparisons across RCII tertiles used one-way ANOVA or the Kruskal–Wallis test. Categorical variables were expressed as *n* (%) and compared using χ^2 or Fisher's exact tests. Complete-case analyses were performed without imputation. Cox regression evaluated ln(RCII) per 1-SD increase (1.26) and RCII tertiles in separate models, with the lowest tertile as reference. Prespecified covariates—age, sex, BMI, diabetes, hypertension, eGFR, ln(NT-proBNP), E/e′, and LVMI—were entered simultaneously without univariable screening or stepwise selection. Left ventricular end-diastolic dimension and septal thickness were omitted because of overlap with LVMI. Discharge medications were excluded from the primary model. Proportional hazards were assessed using scaled Schoenfeld residuals, with stratified sensitivity analyses for nonproportional variables. Restricted cubic splines used knots at the 5th, 35th, 65th, and 95th percentiles and the cohort median as reference [20]. Discrimination was assessed using Harrell's C-index and inverse-probability-of-censoring-weighted (IPCW) cumulative/dynamic AUCs at 12, 24, and 30 months [21], with 95% CIs from 500 bootstrap resamples. The 36-month horizon was omitted because only eight patients remained at risk. Conventional ROC analysis and the Youden-derived cut-off were exploratory, supporting illustrative Kaplan–Meier comparisons using the log-rank test. Between-marker AUC differences were not formally tested. Incremental value was assessed using the ΔC-index and continuous NRI and IDI at 24 months [22]. Absolute risks were calculated from Cox linear predictors and Breslow-estimated baseline cumulative hazards. NRI and IDI were determined using IPCW based on the Kaplan–Meier censoring distribution; patients censored before 24 months were not classified as non-events. For NRI/IDI and C-index comparisons among clinical models

incorporating ln(RCII), ln(hs-CRP), or ln(RC) and ln(hs-CRP) separately, Wald 95% CIs and p values used standard errors from 1000 paired patient-level bootstrap resamples, refitting models, and re-estimating censoring weights where applicable. The clinical and RCII models underwent internal validation using 1000 patient-level bootstrap resamples. Model coefficients and baseline hazards were re-estimated in each resample, and fitted models were evaluated in both the resample and original cohort without further refitting. Mean training-minus-test differences were subtracted from apparent C-indices, Cox calibration slopes, and 24-month IPCW calibration slopes and Brier scores. The 24-month calibration slope was estimated by IPCW logistic regression of event status on the logit of predicted risk. Subgroup analyses using multiplicative interaction terms and 13 sensitivity analyses were exploratory. Medication-related analyses included subgroups defined by discharge statin and diuretic use and separate additional adjustments for statin use plus TG and for β-blocker use. An exploratory univariable Fine–Gray model evaluated ln(RCII) per 1-SD increase for first HF rehospitalization, treating preceding death as a competing event. Wald 95% CIs and p values used bootstrap standard errors of the log subdistribution hazard ratio from 1000 patient-level resamples, with model coefficients and censoring weights re-estimated in each resample.

3. Results

3.1. Baseline Characteristics

A total of 324 patients with HFpEF were included. During a median follow-up of 24.1 months, 84 patients (25.9%) experienced MACEs. Of these first events, 68 (81.0%) were HF rehospitalizations, and 16 (19.0%) were all-cause deaths. Among patients experiencing each component as the first event, median times from discharge were 11.9 months (7.3, 22.0) and 17.2 months (12.9, 26.6), respectively. The median age was 71.0 (58.0, 79.0) years, 200 patients (61.7%) were male, and the median RCII was 7.45 (1.98, 18.17). All 324 patients had LVEF ≥ 50% and NT-proBNP > 125 pg/mL; 185 (57.1%) had NT-proBNP > 365 pg/mL. E/e′ > 9, LAVI > 34 mL/m^2, elevated sex-specific LVMI, and relative wall thickness >0.42 were present in 312 (96.3%), 297 (91.7%), 90 (27.8%), and 142 (43.8%) patients, respectively. All patients met at least one of these echocardiographic thresholds. These counts describe the overall cohort; rhythm-stratified verification was not possible.

Baseline characteristics according to the RCII tertile are shown in Table 1. Triglycerides, total cholesterol, remnant cholesterol, and hs-CRP increased across RCII tertiles (all $p < 0.02$; Table 1 and Supplementary Table S1). Age, sex, BMI, blood pressure, diabetes mellitus, hypertension, NT-proBNP, eGFR, E/e′, and LVMI showed no statistically significant differences across RCII tertiles (Table 1). Left atrial volume index, left atrial diameter, and pulmonary artery diameter showed small but statistically significant differences in the opposite direction to RCII (Supplementary Table S1). Discharge β-blocker use differed across RCII tertiles (67.6%, 55.6%, and 75.9%; $p = 0.006$), without a monotonic trend (p for trend = 0.196). The proportion of patients who experienced MACE rose steeply across tertiles, from 11.1% in tertile 1 to 22.2% in tertile 2 and 44.4% in tertile 3 ($p < 0.001$).

Table 1. Baseline characteristics of the study population stratified by the tertile of the remnant cholesterol inflammatory index.

Variable	Total (n = 324)	Tertile 1 (n = 108)	Tertile 2 (n = 108)	Tertile 3 (n = 108)	p Value
Age, years	71.00 (58.00, 79.00)	71.50 (58.00, 80.00)	71.50 (60.00, 79.25)	70.00 (58.00, 76.25)	0.444
Male, n (%)	200 (61.7)	71 (65.7)	67 (62.0)	62 (57.4)	0.451
Body mass index, kg/m^2	24.91 (23.31, 27.23)	24.72 (23.29, 27.15)	24.84 (23.33, 27.34)	25.02 (23.41, 27.07)	0.931

Table 1. *Cont.*

Variable	Total (n = 324)	Tertile 1 (n = 108)	Tertile 2 (n = 108)	Tertile 3 (n = 108)	p Value
Systolic blood pressure, mmHg	132.17 ± 19.35	131.10 ± 19.37	132.47 ± 18.93	132.94 ± 19.87	0.770
Diastolic blood pressure, mmHg	74.05 ± 13.06	73.94 ± 11.84	72.81 ± 14.47	75.39 ± 12.72	0.349
Heart rate, beats/min	75.00 (67.00, 84.00)	75.50 (67.75, 85.00)	73.00 (63.75, 80.25)	76.00 (68.75, 86.50)	0.129
Smoking, n (%)	39 (12.0)	10 (9.3)	14 (13.0)	15 (13.9)	0.542
Diabetes mellitus, n (%)	109 (33.6)	32 (29.6)	37 (34.3)	40 (37.0)	0.508
Hypertension, n (%)	228 (70.4)	74 (68.5)	74 (68.5)	80 (74.1)	0.587
Laboratory measurements					
NT-proBNP, pg/mL	601.24 (190.82, 2102.91)	877.90 (199.47, 2111.58)	422.45 (203.44, 1950.59)	546.58 (176.36, 2102.91)	0.233
Hemoglobin, g/L	130.00 (120.00, 143.00)	129.00 (118.75, 141.00)	130.00 (118.75, 146.25)	131.50 (121.75, 142.25)	0.443
Fasting glucose, mmol/L	5.80 (5.14, 7.04)	5.91 (5.16, 7.13)	5.52 (5.02, 6.78)	5.94 (5.22, 7.06)	0.292
Triglycerides, mmol/L	1.33 (0.93, 1.81)	1.15 (0.83, 1.65)	1.21 (0.84, 1.77)	1.62 (1.18, 2.03)	<0.001
Total cholesterol, mmol/L	3.83 (3.18, 4.92)	3.65 (2.93, 4.57)	3.77 (3.21, 4.71)	4.16 (3.42, 5.18)	0.016
LDL cholesterol, mmol/L	2.06 (1.46, 2.92)	2.00 (1.42, 2.91)	2.05 (1.39, 2.79)	2.12 (1.58, 3.24)	0.133
HDL cholesterol, mmol/L	1.08 (0.93, 1.31)	1.07 (0.93, 1.32)	1.10 (0.96, 1.33)	1.07 (0.92, 1.26)	0.430
Remnant cholesterol, mg/dL	22.62 (17.40, 30.55)	18.56 (14.89, 26.10)	21.46 (16.24, 28.33)	27.65 (21.46, 34.03)	<0.001
hs-CRP, mg/L	3.30 (0.94, 8.27)	0.68 (0.50, 1.01)	3.50 (2.29, 5.20)	9.81 (6.96, 10.00)	<0.001
RCII	7.45 (1.98, 18.17)	1.50 (1.00, 1.97)	7.45 (5.61, 10.37)	22.69 (18.17, 31.35)	<0.001
eGFR, mL/min/1.73 m^2	117.08 (98.44, 120.00)	120.00 (102.47, 120.00)	116.98 (96.32, 120.00)	114.63 (95.45, 120.00)	0.136
Echocardiography					
LVEF, %	65.00 (62.00, 69.00)	65.00 (62.00, 68.25)	65.00 (61.75, 69.25)	65.00 (62.00, 69.00)	0.698
E/e′	14.73 ± 3.24	14.65 ± 3.51	14.82 ± 3.45	14.74 ± 2.74	0.924
LAVI, mL/m^2	42.34 ± 5.98	43.49 ± 6.10	42.04 ± 5.95	41.49 ± 5.77	0.039
LVMI, g/m^2	88.53 (75.66, 108.21)	91.22 (79.49, 108.98)	86.68 (72.19, 105.61)	88.47 (75.43, 108.65)	0.340
Relative wall thickness	0.42 (0.38, 0.46)	0.43 (0.38, 0.47)	0.41 (0.36, 0.45)	0.41 (0.37, 0.47)	0.191
Left atrial diameter, mm	38.00 (35.00, 42.00)	40.00 (35.00, 44.00)	38.00 (34.75, 42.00)	38.00 (34.75, 41.00)	0.061
LVEDD, mm	45.00 (43.00, 49.00)	45.00 (43.00, 49.00)	45.50 (43.00, 48.25)	46.00 (43.00, 49.00)	0.999
IVS thickness, mm	10.00 (10.00, 12.00)	10.00 (10.00, 13.00)	10.00 (9.00, 12.00)	10.00 (10.00, 12.00)	0.564
LVPW thickness, mm	9.00 (9.00, 10.00)	10.00 (9.00, 10.00)	9.00 (8.00, 10.00)	9.00 (9.00, 10.00)	0.125
Pulmonary artery diameter, mm	20.00 (20.00, 22.00)	20.00 (20.00, 23.00)	20.00 (20.00, 22.00)	20.00 (20.00, 21.00)	0.013
Discharge medications, n (%)					
Statins	191 (59.0)	61 (56.5)	66 (61.1)	64 (59.3)	0.785
Diuretics	147 (45.4)	55 (50.9)	46 (42.6)	46 (42.6)	0.365
ACE inhibitors or ARBs	165 (50.9)	60 (55.6)	53 (49.1)	52 (48.1)	0.495
β-blockers	215 (66.4)	73 (67.6)	60 (55.6)	82 (75.9)	0.006

Table 1. *Cont.*

Variable	Total (n = 324)	Tertile 1 (n = 108)	Tertile 2 (n = 108)	Tertile 3 (n = 108)	p Value
Mineralocorticoid receptor antagonists	44 (13.6)	21 (19.4)	11 (10.2)	12 (11.1)	0.091
MACE during follow-up, n (%)	84 (25.9)	12 (11.1)	24 (22.2)	48 (44.4)	<0.001

Data are presented as mean ± SD, median (first quartile, third quartile), or n (%). Comparisons across tertiles used one-way ANOVA, the Kruskal–Wallis test, or the χ^2/Fisher's exact test, as appropriate. RCII tertiles were <3.15, 3.15–14.05, and >14.05. ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; E/e′, ratio of early mitral inflow velocity to early diastolic mitral annular velocity; HDL, high-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; IVS, interventricular septum; LAVI, left atrial volume index; LDL, low-density lipoprotein; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; LVPW, left ventricular posterior wall; MACE, major adverse cardiovascular event; NT-proBNP, N-terminal pro-B-type natriuretic peptide; RCII, remnant cholesterol inflammatory index; SD, standard deviation.

Baseline characteristics according to MACE status are presented in Supplementary Table S2. Patients who developed MACE were more often female and more frequently had diabetes mellitus and hypertension (all $p < 0.03$). They also had higher hs-CRP, remnant cholesterol, and NT-proBNP concentrations; lower eGFR; and greater E/e′, LVMI, and interventricular septal thickness (all $p \leq 0.035$). RCII was approximately threefold higher in the MACE group than in the no-MACE group [17.19 (7.66, 26.16) vs. 5.73 (1.63, 14.02); $p < 0.001$]. Conventional lipid measures did not differ significantly between groups.

3.2. Collinearity Between RCII and Its Components

RCII correlated strongly with hs-CRP (Spearman $\rho = 0.918$) and moderately with RC ($\rho = 0.431$), but only weakly with conventional lipid measures ($\rho \leq 0.29$) and minimally with NT-proBNP, E/e′, LVMI, age, or BMI (all $\rho < 0.07$) (Supplementary Table S3A). Because $\ln(\text{RCII}) = \ln(\text{RC}) + \ln(\text{hs-CRP}) - \ln(10)$, simultaneous inclusion of all three log-transformed terms produces perfect collinearity. Accordingly, ln(RC) and ln(hs-CRP) were not included as covariates in models containing ln(RCII) (Supplementary Table S3B). The high correlation with hs-CRP indicates that RCII is numerically dominated by its inflammatory component, and this is considered further in the Discussion section.

3.3. Association Between RCII and MACE in Patients with HFpEF

In univariable Cox analysis, each 1-SD increase in ln(RCII) was associated with a 74% higher risk of MACE (HR, 1.74; 95% CI, 1.37–2.23; $p < 0.001$). The association remained significant after full adjustment (HR, 1.80; 95% CI, 1.38–2.35; $p < 0.001$; Table 2). Compared with the lowest tertile, the highest RCII tertile was associated with an approximately fourfold higher adjusted risk (HR, 3.87; 95% CI, 2.02–7.39; $p < 0.001$), with a significant trend across tertiles (p for trend <0.001). Diabetes, ln(NT-proBNP), E/e′, and LVMI also remained independently associated with MACE. The proportional hazards assumption was satisfied for RCII ($p = 0.42$) but showed modest violations for sex and LVMI; stratification by these variables yielded a similar estimate (HR, 1.78; 95% CI, 1.35–2.35; $p < 0.001$; Supplementary Table S4). In exploratory univariable Fine–Gray analysis accounting for death as a competing event, higher RCII was associated with first HF rehospitalization (subdistribution HR per 1-SD increase in ln(RCII), 1.64; 95% CI, 1.26–2.13; $p < 0.001$).

Table 2. Univariable and multivariable Cox proportional hazards regression analysis for major adverse cardiovascular events.

Variable	Univariable HR (95% CI)	*p* Value	Multivariable HR (95% CI) [a]	*p* Value
ln(RCII), per 1-SD increment [b]	1.74 (1.37–2.23)	<0.001	1.80 (1.38–2.35)	<0.001
RCII tertile				
Tertile 1 (<3.15), reference	1.00	—	1.00	—
Tertile 2 (3.15–14.05)	2.05 (1.03–4.11)	0.042	1.92 (0.94–3.92)	0.074
Tertile 3 (>14.05)	3.71 (1.97–6.98)	<0.001	3.87 (2.02–7.39)	<0.001
P for trend	—	<0.001	—	<0.001
Other candidate variables [c]				
Age, per 1 year	1.012 (0.995–1.028)	0.174	1.010 (0.991–1.028)	0.309
Male sex	0.864 (0.560–1.334)	0.510	0.965 (0.606–1.536)	0.881
Body mass index, per 1 kg/m^2	0.996 (0.939–1.057)	0.902	1.001 (0.942–1.065)	0.966
Smoking	1.281 (0.615–2.668)	0.508	—	—
Systolic blood pressure, per 1 mmHg	1.005 (0.995–1.015)	0.311	—	—
Diastolic blood pressure, per 1 mmHg	1.003 (0.988–1.019)	0.674	—	—
Heart rate, per 1 beat/min	0.997 (0.982–1.011)	0.660	—	—
Diabetes mellitus	1.839 (1.194–2.833)	0.006	1.678 (1.050–2.682)	0.030
Hypertension	1.909 (1.107–3.294)	0.020	1.629 (0.907–2.924)	0.102
ln(NT-proBNP), per 1 unit	1.263 (1.086–1.470)	0.002	1.242 (1.065–1.448)	0.006
Hemoglobin, per 1 g/L	1.000 (0.990–1.010)	0.963	—	—
Fasting glucose, per 1 mmol/L	1.010 (0.935–1.091)	0.802	—	—
Triglycerides, per 1 mmol/L	1.073 (0.872–1.321)	0.505	—	—
Total cholesterol, per 1 mmol/L	0.970 (0.822–1.146)	0.723	—	—
LDL cholesterol, per 1 mmol/L	0.915 (0.744–1.126)	0.403	—	—
HDL cholesterol, per 1 mmol/L	0.831 (0.416–1.658)	0.599	—	—
Remnant cholesterol, per 1 mg/dL	1.011 (0.998–1.023)	0.103	—	—
ln(hs-CRP), per 1 unit	1.605 (1.279–2.013)	<0.001	—	—
eGFR, per 1 mL/min/1.73 m^2	0.990 (0.981–1.000)	0.039	0.991 (0.982–1.001)	0.083
LVEF, per 1%	0.978 (0.949–1.008)	0.148	—	—
E/e′, per 1 unit	1.100 (1.025–1.180)	0.008	1.119 (1.040–1.204)	0.003
LAVI, per 1 mL/m^2	0.995 (0.961–1.031)	0.800	—	—
LVMI, per 10 g/m^2	1.096 (1.041–1.153)	<0.001	1.100 (1.038–1.166)	0.001
Relative wall thickness, per 0.1 unit	0.940 (0.767–1.151)	0.549	—	—
Left atrial diameter, per 1 mm	0.991 (0.957–1.026)	0.600	—	—
LVEDD, per 1 mm	1.045 (1.011–1.081)	0.009	—	—
IVS thickness, per 1 mm	1.092 (1.004–1.187)	0.041	—	—
LVPW thickness, per 1 mm	1.058 (0.948–1.181)	0.315	—	—
Pulmonary artery diameter, per 1 mm	0.959 (0.888–1.036)	0.285	—	—
Statins	0.840 (0.545–1.294)	0.428	—	—
Diuretics	1.031 (0.672–1.584)	0.888	—	—
ACE inhibitors or ARBs	0.928 (0.604–1.425)	0.732	—	—
β-blockers	1.323 (0.819–2.138)	0.253	—	—
Mineralocorticoid receptor antagonists	0.853 (0.440–1.651)	0.636	—	—

[a] The fully adjusted model comprised nine pre-specified covariates: age, sex, body mass index, diabetes mellitus, hypertension, eGFR, ln(NT-proBNP), E/e′, and LVMI. An em dash (—) indicates that the variable was not entered into this model. Covariates were selected on the basis of established prognostic relevance in HFpEF rather than by univariable screening; LVEDD and IVS thickness were not entered because of substantial overlap with LVMI. RC, hs-CRP, and the lipid variables used to derive RC were not included as covariates in the primary RCII model. Simultaneous inclusion of ln(RCII), ln(RC), and ln(hs-CRP) would cause perfect collinearity (Supplementary Table S3); all variance inflation factors in the fully adjusted model were ≤1.15. [b] Continuous ln(RCII) and RCII tertiles were evaluated in separate adjusted models with the same covariates and were not entered simultaneously. The HR for continuous ln(RCII) is expressed per 1-SD increment (1 SD = 1.26 on the natural-log scale). Adjusted estimates for other covariates are from the model containing continuous ln(RCII). [c] HRs for other continuous variables correspond to the increments specified in the row labels, without SD standardization. For ln-transformed biomarkers, increments refer to the natural-log scale. These estimates are reported to three decimal places. CI, confidence interval; HFpEF, heart failure with preserved ejection fraction; HR, hazard ratio; SD, standard deviation; other abbreviations as in Table 1.

Restricted cubic spline analysis showed an overall association between RCII and MACE ($p < 0.001$), with no statistically significant evidence of nonlinearity (adjusted p for non-

linearity = 0.437; Figure 2). MACE-free survival differed across RCII tertiles (log-rank $\chi^2 = 20.29$; $p < 0.001$), with observed event rates of 11.1%, 22.2%, and 44.4% in tertiles 1, 2, and 3, respectively (Figure 3A). Using the exploratory ROC-derived cut-off of 16.84, patients with high RCII also had lower MACE-free survival (log-rank $\chi^2 = 28.36$; $p < 0.001$) and a higher adjusted risk of MACE (HR, 3.45; 95% CI, 2.18–5.46; Figure 3B).

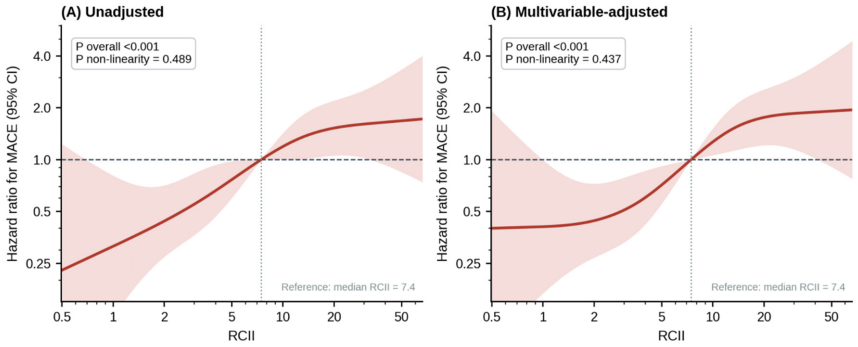


Figure 2. Restricted cubic spline analysis of the association between RCII and MACE. (**A**) Unadjusted model. (**B**) Multivariable-adjusted model. Solid curves represent hazard ratios, and shaded areas indicate 95% confidence intervals. The horizontal axis displays RCII on a logarithmic scale, with the cohort median as the reference. Wider confidence intervals at the extremes indicate greater uncertainty. MACE, major adverse cardiovascular event, defined in this study as all-cause death or HF rehospitalization; RCII, remnant cholesterol inflammatory index.

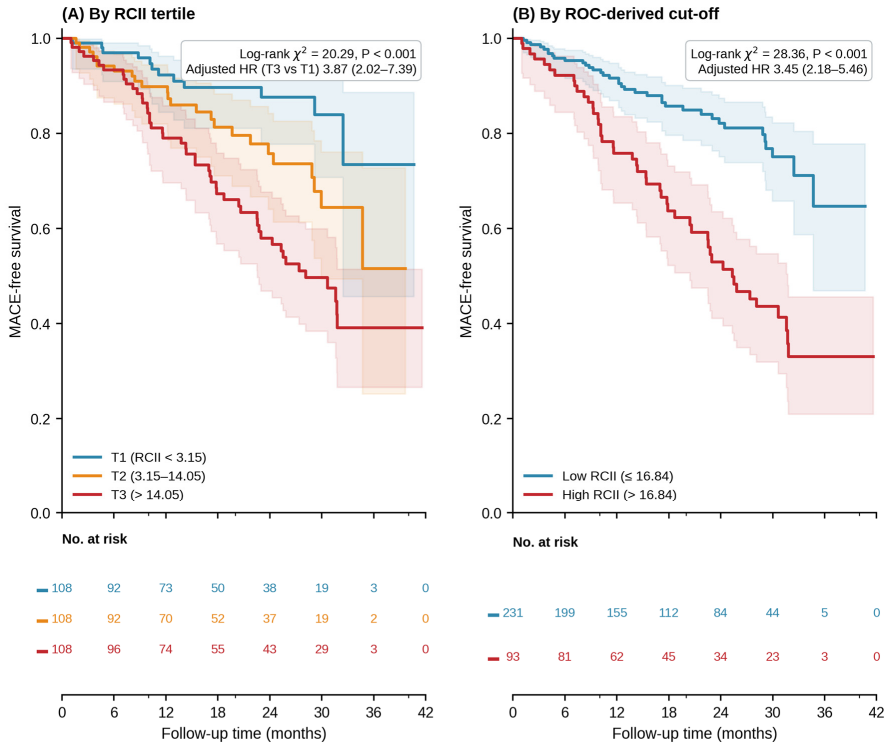


Figure 3. Kaplan–Meier curves for MACE-free survival according to RCII. Panel (**A**) shows survival across RCII tertiles: T1, <3.15; T2, 3.15–14.05; and T3, >14.05. Panel (**B**) presents an exploratory comparison using the cut-off of 16.84 derived from this cohort by conventional ROC analysis, which does not account for censoring or differences in follow-up duration. This cut-off is not a validated clinical decision threshold. Shaded areas represent 95% confidence intervals, and numbers at risk are displayed below each panel. Numbers at risk are reported immediately before each indicated time point. MACE, major adverse cardiovascular event; RCII, remnant cholesterol inflammatory index; ROC, receiver operating characteristic.

3.4. Discrimination, Risk Stratification, and Incremental Value

In exploratory conventional ROC analysis, RCII yielded an AUC of 0.719 (95% CI, 0.656–0.781), which was numerically higher than that of its individual components and of the other evaluated markers (Figure 4A). The exploratory cut-off of 16.84, selected using Youden's index, provided 57.1% sensitivity and 80.8% specificity in this cohort; it has not been validated for clinical decision-making. Time-dependent analysis showed moderate discrimination by RCII that was stable over the first two years and declined thereafter: AUCs were 0.655 (95% CI, 0.559–0.733) at 12 months, 0.656 (95% CI, 0.574–0.734) at 24 months, and 0.603 (95% CI, 0.503–0.703) at 30 months (Table 3 and Figure 4B). Corresponding values for the comparator markers were numerically lower or similar at every horizon, with substantially overlapping confidence intervals; no formal comparison of time-dependent AUCs between markers was performed. Only 8 patients remained at risk immediately before 36 months, and estimates at that horizon were uninformative for all six markers (95% CI widths >0.39) and are therefore not reported.

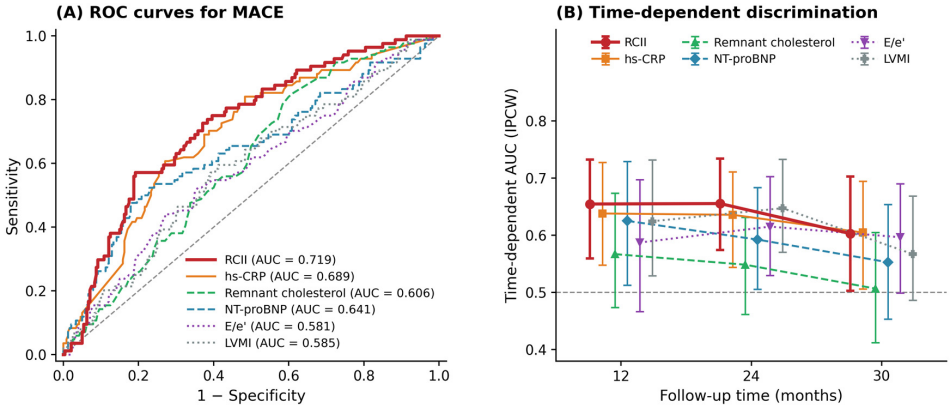


Figure 4. Discriminatory performance of RCII and comparator markers for MACE. Panel (**A**) shows exploratory conventional ROC curves over the overall follow-up period for RCII, hs-CRP, RC, NT-proBNP, E/e′, and LVMI. Panel (**B**) shows cumulative/dynamic time-dependent AUCs at 12, 24, and 30 months estimated with inverse-probability-of-censoring weighting; symbols denote point estimates, and error bars are 95% confidence intervals from 500 bootstrap resamples, with markers horizontally offset within each time point to avoid overplotting. AUC, area under the curve; hs-CRP, high-sensitivity C-reactive protein; LVMI, left ventricular mass index; MACE, major adverse cardiovascular event; NT-proBNP, N-terminal pro-B-type natriuretic peptide; RC, remnant cholesterol; RCII, remnant cholesterol inflammatory index; ROC, receiver operating characteristic.

Table 3. Time-dependent discrimination for major adverse cardiovascular events at 12, 24, and 30 months.

Marker	12-Month AUC (95% CI)	24-Month AUC (95% CI)	30-Month AUC (95% CI)
RCII	0.655 (0.559–0.733)	0.656 (0.574–0.734)	0.603 (0.503–0.703)
hs-CRP	0.638 (0.548–0.728)	0.636 (0.544–0.711)	0.605 (0.506–0.695)
Remnant cholesterol	0.567 (0.474–0.674)	0.549 (0.462–0.631)	0.507 (0.412–0.605)
NT-proBNP	0.625 (0.513–0.729)	0.593 (0.506–0.684)	0.553 (0.454–0.654)
E/e′	0.587 (0.467–0.697)	0.615 (0.530–0.703)	0.597 (0.499–0.690)
LVMI	0.625 (0.529–0.732)	0.647 (0.571–0.733)	0.567 (0.487–0.669)
Cases/controls at horizon, *n*	38/217	67/118	78/67

Unadjusted cumulative/dynamic AUCs were estimated using inverse-probability-of-censoring weighting, with 95% CIs from 500 bootstrap resamples. Cases experienced their first MACE by each horizon; controls remained event-free under observation beyond it. Between-marker AUCs were not formally compared. AUC, area under the receiver operating characteristic curve; CI, confidence interval; other abbreviations as in Table 1.

The clinical models incorporating ln(hs-CRP), ln(RCII), or ln(RC) and ln(hs-CRP) separately had C-indices of 0.728, 0.736, and 0.738, respectively. RCII did not significantly improve discrimination over hs-CRP (ΔC-index, 0.0088; 95% CI, −0.0074 to 0.0250; $p = 0.287$). The separate-component model also showed no significant improvement over RCII (ΔC-index, 0.0015; 95% CI, −0.0092 to 0.0122; $p = 0.779$; Supplementary Table S5).

Adding RCII to the clinical model increased the Harrell C-index from 0.707 to 0.736 (ΔC-index, 0.029; 95% CI, 0.001–0.076; $p = 0.040$). The IPCW-adjusted continuous NRI at 24 months was 0.626 (95% CI, 0.317–0.935; $p < 0.001$), primarily reflecting its event component. The non-event component was not statistically significant (0.102; 95% CI, −0.078 to 0.282; $p = 0.268$). The IDI was 0.060 (95% CI, −0.002 to 0.123; $p = 0.059$) (Table 4). After bootstrap correction for optimism, the clinical model and the model incorporating ln(RCII) had C-indices of 0.671 and 0.705, respectively. The corresponding optimism-corrected Cox calibration slopes were 0.804 and 0.818, indicating some overfitting. At 24 months, optimism-corrected calibration slopes were 0.684 and 0.691, and Brier scores were 0.191 and 0.184, for the clinical and RCII models, respectively. These findings indicate persistent overfitting and only a small improvement in overall prediction error.

Table 4. Incremental predictive value and internal validation of RCII beyond the clinical model.

A. Apparent Performance		
Metric	**Estimate (95% CI)**	***p* Value**
Harrell C-index, clinical model	0.707 (0.660–0.774)	—
Harrell C-index, clinical model + ln(RCII)	0.736 (0.696–0.808)	—
ΔC-index	0.029 (0.001–0.076)	0.040
Continuous NRI at 24 months	0.626 (0.317–0.935)	<0.001
Event component	0.524 (0.327–0.722)	<0.001
Non-event component	0.102 (−0.078–0.282)	0.268
IDI at 24 months	0.060 (−0.002–0.123)	0.059
B. Optimism-corrected performance		
Metric	**Clinical model**	**Clinical model + RCII**
Harrell C-index	0.671	0.705
24-month calibration slope	0.684	0.691
24-month Brier score	0.191	0.184

The clinical model included the nine covariates listed in Table 2. Panel A reports apparent performance; panel B reports performance after optimism correction using 1000 patient-level bootstrap resamples. NRI, IDI, and 24-month calibration and Brier scores account for censoring using IPCW. CI, confidence interval; IDI, integrated discrimination improvement; IPCW, inverse-probability-of-censoring weighting; NRI, net reclassification improvement; RCII, remnant cholesterol inflammatory index. Other abbreviations are defined in Tables 1 and 2. An em dash indicates not applicable.

3.5. Subgroup and Sensitivity Analyses

Exploratory subgroup analyses detected no statistically significant interactions (all p for interaction ≥ 0.174; Table 5), but limited precision prevents interpreting these findings as evidence of identical associations across groups. The association remained significant after additional adjustment for discharge statin use and triglycerides. Additional adjustment for discharge β-blocker use yielded a similar association between ln(RCII) and MACE (HR per 1-SD increase, 1.78; 95% CI, 1.37–2.33; $p < 0.001$). Results were also consistent across all 13 sensitivity analyses (adjusted HR range, 1.77–2.08; Supplementary Table S4), including an analysis restricted to 0.5 < hs-CRP < 10 mg/L.

Table 5. Exploratory subgroup analyses of the association between the remnant cholesterol inflammatory index and major adverse cardiovascular events.

Subgroup	*n*	Events, *n* (%)	HR per 1-SD ln(RCII) (95% CI)	*p* Value	P for Interaction
Age					
<65 years	122	25 (20.5)	1.71 (1.03–2.84)	0.037	
≥65 years	202	59 (29.2)	1.81 (1.28–2.56)	<0.001	0.984
Sex					
Male	200	43 (21.5)	2.43 (1.58–3.73)	<0.001	
Female	124	41 (33.1)	1.51 (1.04–2.18)	0.029	0.174
Body mass index					
<25 kg/m^2	174	41 (23.6)	1.96 (1.33–2.88)	<0.001	
≥25 kg/m^2	150	43 (28.7)	1.84 (1.25–2.69)	0.002	0.989
Diabetes mellitus					
No	215	47 (21.9)	1.77 (1.24–2.52)	0.002	
Yes	109	37 (33.9)	2.18 (1.39–3.41)	<0.001	0.720
Hypertension					
No	96	16 (16.7)	1.73 (0.91–3.27)	0.093	
Yes	228	68 (29.8)	1.88 (1.38–2.55)	<0.001	0.870
Statin therapy					
No	133	36 (27.1)	2.08 (1.30–3.33)	0.002	
Yes	191	48 (25.1)	1.86 (1.29–2.69)	<0.001	0.837
Diuretic therapy					
No	177	45 (25.4)	1.98 (1.34–2.91)	<0.001	
Yes	147	39 (26.5)	1.58 (1.06–2.37)	0.025	0.645
eGFR					
<90 mL/min/1.73 m^2	58	21 (36.2)	1.73 (0.85–3.55)	0.133	
≥90 mL/min/1.73 m^2	266	63 (23.7)	1.86 (1.37–2.52)	<0.001	0.953
NT-proBNP					
<median	162	29 (17.9)	1.73 (1.09–2.73)	0.019	
≥median	162	55 (34.0)	1.85 (1.32–2.60)	<0.001	0.746
hs-CRP					
<2 mg/L	122	15 (12.3)	2.47 (0.73–8.40)	0.147	
≥2 mg/L	202	69 (34.2)	1.90 (1.18–3.04)	0.008	0.526

Subgroup analyses were exploratory. Limited event counts reduce the precision of interaction tests, and nonsignificant interaction *p* values do not establish equivalent associations across subgroups. The hs-CRP-stratified findings require particular caution because hs-CRP is a component of RCII. Abbreviations as in Tables 1 and 2.

4. Discussion

In this retrospective cohort of patients hospitalized with HFpEF, higher RCII was associated with MACE after adjustment for the measured covariates. Each 1-SD increase in ln(RCII) was associated with an 80% higher adjusted risk, and patients in the highest tertile had an approximately fourfold higher risk than those in the lowest tertile. Nonlinearity was not statistically detected, but this does not establish a strictly linear relationship, particularly at the sparsely observed extremes. RCII also provided incremental discrimination and reclassification beyond a clinical model incorporating NT-proBNP and echocardiographic measures of diastolic function and remodeling, although the improvement in discrimination over hs-CRP was not statistically significant and a clinically meaningful advantage remains unestablished.

To our knowledge, this is the first study to specifically evaluate RCII in patients with HFpEF. The observed association is broadly consistent in direction with reports using RCII calculated as a product in acute decompensated HF, patients with coronary artery disease and T2DM, and population-based cohorts [14–16]. An apparently contrasting finding was reported in a cohort of 2823 patients hospitalized with HF across the full LVEF spectrum,

in whom lower RC was associated with higher all-cause mortality [23]. This finding was interpreted as reverse epidemiology, whereby low cholesterol in advanced HF may reflect malnutrition, cachexia, or hepatic congestion. The discrepancy may be explained partly by differences in HF phenotype and by the distinction between RC alone and RCII. In the present cohort, RC alone showed a weaker association with MACE than RCII, whereas conventional lipid parameters were not associated with outcomes. These findings suggest that the prognostic meaning of RC-based measures may vary according to ventricular phenotype, inflammatory burden, and nutritional status and should therefore be validated within specific HF populations.

From a mechanistic perspective, the findings fit within the comorbidity-driven inflammatory paradigm of HFpEF outlined above [5], in which triglyceride-rich lipoprotein remnants entering the arterial and myocardial interstitium promote macrophage lipid uptake and local inflammatory signaling [13]. A plausible anatomical substrate for this coupling is epicardial adipose tissue, a visceral fat depot in direct contact with the myocardium that expands with the same cardiometabolic comorbidities that drive HFpEF and that secretes both remnant-lipoprotein-related lipids and pro-inflammatory cytokines directly into the coronary microcirculation and pericardial space; epicardial fat volume has been independently associated with more advanced diastolic dysfunction and adverse outcomes in HFpEF [24]. At the cytokine level, interleukin-6 is a plausible unifying signal: it is both a determinant of hepatic remnant-lipoprotein clearance and the principal upstream driver of hepatic CRP synthesis, and elevated interleukin-6 independently predicts incident HFpEF in the general population [25]. This shared upstream signal offers a mechanistic explanation for why RCII correlated so strongly with hs-CRP in the present cohort ($\rho = 0.918$) rather than behaving as a marker of two independent processes. RCII may therefore represent a convenient peripheral readout of a biologically interconnected lipid–inflammatory pathway rather than merely the sum of two unrelated risk factors [19].

Higher RC across RCII tertiles partly reflects its inclusion in the index, whereas accompanying TG differences may reflect the metabolic relationship between triglyceride-rich lipoproteins and their cholesterol-containing remnants [13]. These baseline differences do not themselves establish the prognostic superiority of RCII over conventional lipid measures. RCII correlated strongly with hs-CRP ($\rho = 0.918$), and paired comparisons did not demonstrate superior discrimination over hs-CRP or the separate-component model. Although RCII uses a single biomarker term, this simplicity does not establish a clinical advantage. The interaction between ln(RC) and ln(hs-CRP) was sub-multiplicative (HR, 0.69; 95% CI, 0.52–0.92; $p = 0.010$), but this statistical finding does not establish biological antagonism or overestimation of absolute risk. The added clinical value of RCII beyond hs-CRP therefore remains unestablished. These considerations should not be read as evidence against the biological relevance of inflammation in HFpEF. hs-CRP itself is a well-validated prognostic marker in this syndrome: a systematic review and meta-analysis reported that elevated CRP independently predicts both incident HFpEF and subsequent all-cause and cardiovascular mortality across multiple cohorts [26]. A study in dilated cardiomyopathy reported improved diagnostic discrimination when the delta neutrophil index was combined with CRP, while both markers were associated with mortality [27]. Dilated cardiomyopathy is distinct from HFpEF, and these findings provide context for evaluating combined inflammatory markers without establishing the incremental prognostic value of RCII in HFpEF.

RCII and NT-proBNP both remained associated with MACE in the adjusted model, although residual confounding limits the interpretation of these associations. NT-proBNP primarily reflects ventricular wall stress and hemodynamic burden, whereas RCII integrates lipid-related metabolic abnormalities and systemic inflammation. RCII may therefore

identify a metabolic–inflammatory risk dimension not fully represented by conventional HF biomarkers.

RCII is calculated from a standard lipid profile and hs-CRP and does not require additional imaging, specialized assays, or complex computation. If externally validated, it may complement existing risk-assessment tools and help identify patients who warrant closer follow-up and more intensive management of modifiable risk factors. Whether such management should specifically target the RCII value, however, is not established by an association study of this kind, and trial evidence from other populations urges caution in extrapolating from either component. Anti-inflammatory therapy directed at the interleukin-1β/interleukin-6 axis reduced recurrent cardiovascular events independently of LDL-cholesterol lowering in the CANTOS trial [28], supporting a causal role for the inflammatory component; by contrast, pharmacological triglyceride and remnant-cholesterol lowering with pemafibrate in the PROMINENT trial reduced remnant cholesterol by approximately one-quarter without reducing cardiovascular events [29], suggesting that the lipid component of RCII may be more a marker of risk than a modifiable target in its own right. This asymmetry—an inflammatory component with trial-level evidence of causality and a lipid component without it—is consistent with RCII's own correlation structure in the present cohort and reinforces that its principal value at this stage is prognostic rather than therapeutic. The exploratory cut-off of 16.84 should not guide clinical decisions. Despite modest improvements in discrimination, imperfect optimism-corrected calibration and uncertain gains in IDI and non-event reclassification limit claims of reliable individual risk prediction.

Several limitations should be acknowledged. First, the single-center retrospective design and limited events restrict generalizability and increase the risk of overfitting and imprecision. Selection based on complete baseline data and available follow-up may introduce bias, while excluding patients requiring invasive mechanical ventilation or with severe valvular disease further limits applicability. Bootstrap validation does not replace external validation; subgroup and sensitivity analyses remain exploratory. Second, unavailable research data on atrial fibrillation, coronary artery disease, NYHA class, SGLT2 inhibitor and sacubitril/valsartan use, admission prescriptions, and in-hospital treatment changes leave potential residual confounding. Missing atrial fibrillation data prevented retrospective verification of rhythm-specific diagnostic thresholds, while uniform NT-proBNP thresholds may underrepresent patients with obesity and low peptide concentrations. A single admission RCII measurement may reflect acute illness, congestion, or early treatment and cannot distinguish transient from persistent inflammation; its performance relative to measurements after stabilization was not evaluated. Third, HF rehospitalization accounted for most first events, with only 16 deaths as first events, limiting mortality-specific inference. The competing-risk analysis was exploratory and unadjusted. Fourth, causality cannot be established, and whether lowering RCII improves outcomes remains unknown. External validation specifically in HFpEF populations is required before clinical application.

5. Conclusions

In this retrospective cohort of patients hospitalized with HFpEF, higher RCII was associated with post-discharge MACE after adjustment for the measured covariates and provided modest incremental discrimination beyond the clinical model. Superiority over hs-CRP was not demonstrated. Residual confounding by unmeasured clinical and treatment factors cannot be excluded, and external validation is required before clinical application.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/jcdd13110607/s1. Table S1: Monotonic trend of baseline characteristics across tertiles of the remnant cholesterol inflammatory index; Table S2: Baseline characteristics of the study population stratified by the occurrence of major adverse cardiovascular events; Table S3: Correlation structure of the remnant cholesterol inflammatory index and variance inflation factors; Table S4: Sensitivity analyses for the association between the remnant cholesterol inflammatory index and major adverse cardiovascular events; Table S5: Head-to-head comparison of RCII with its individual components.

Author Contributions: S.P. and Q.T. contributed equally to this work. S.P.: Conceptualization, Methodology, Formal Analysis, Investigation, Data Curation, Visualization, Writing—Original Draft. Q.T.: Methodology, Validation, Formal Analysis, Visualization, Writing—Review and Editing. M.J., J.C., and J.Y.: Investigation, Data Curation, Follow-Up, Writing—Review and Editing. H.L.: Conceptualization, Supervision, Project Administration, Funding Acquisition, Writing—Review and Editing. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study protocol was approved by the Ethics Committee of the Second Affiliated Hospital of Soochow University (approval number: JD-HG-2026-068; approval date: 2 July 2026), and the study was conducted in accordance with the Declaration of Helsinki.

Informed Consent Statement: The need for written informed consent was waived by the Ethics Committee of the Second Affiliated Hospital of Soochow University due to the retrospective nature of the study.

Data Availability Statement: The data that support the findings of this study are not publicly available due to privacy reasons but are available from the corresponding author upon request (szhoulihui@163.com).

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

The following abbreviations are used in this manuscript:

HFpEF	Heart failure with preserved ejection fraction
RCII	Remnant cholesterol inflammatory index
MACEs	Major adverse cardiovascular events
NRI	Net reclassification
IDI	Integrated discrimination improvement

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