

Appendix 1 Supplemental methods

Supplemental CMR image acquisition

The imaging protocol included (1) cine imaging, (2) T1 mapping, and (3) late gadolinium enhancement (LGE) imaging.

Cine imaging was performed with a single-shot balanced steady-state free-precession sequence. A stack of short-axis planes from the apex to the base and long-axis planes (two-, three-, and four-chamber views) was collected. The temporal resolution for strain imaging was maintained at 24–30 frames per cardiac cycle. The imaging parameters were as follows: field of view, 230 × 230 mm; voxels, 2 × 2 × 8 mm; repetition time, 3.0–3.2 ms; echo time, 1.5–1.6 ms; sense factor, 2; minimum inversion time, 105 ms; and flip angle, 45°.

LGE imaging was performed 10 minutes after injection of gadopentetate dimeglumine. LGE imaging was performed in the long-axis views and short-axis slices covering the entire left ventricular (LV) myocardium from the base to apex.

Native T1 mapping was obtained with a modified Look-Locker inversion recovery (MOLLI) sequence in three representative short-axis planes: basal, mid-ventricular, and apical. For extracellular volume (ECV) quantification, the same acquisition and plane was performed again 15 minutes after the administration of contrast. Hematocrit levels were measured within 1 week before the CMR examination to facilitate ECV calculation.

Supplemental cardiac image analysis

All CMR analyses, including cine images, T1 mapping, strain images, and LGE images, were performed with a dedicated post-processing workstation (cvi42 version 5.13, Circle Cardiovascular Imaging, Calgary, AB, Canada). Biventricular volume and function were obtained by tracing epicardial and endocardial contours automatically at end-diastolic and end-systolic phases based on LV short-axis cine images, followed by manual correction as necessary. The papillary muscle was contained in the left ventricular chamber. All volumes were indexed to body surface area.

Cardiac T1 mapping analysis were performed via the LV short axis MOLLI images with motion correction. The endocardial and epicardial contours were manually delineated on the precontrast and post-contrast T1-mapping images. A region of interest was placed in the LV cavity for blood pool T1 value quantification, with the papillary muscle being excluded. The ECV was calculated as follows:

$$ECV = (1 - \text{hematocrit}) \times \frac{\frac{1}{T1_{\text{myo-post}}} - \frac{1}{T1_{\text{myo-pre}}}}{\frac{1}{T1_{\text{blood-post}}} - \frac{1}{T1_{\text{blood-pre}}}} \quad [1]$$

Biventricular strain parameters were calculated from cine images with the cardiac MRI feature tracking module. The LV endocardial and epicardial contours were automatically traced at the LV end-diastolic phase and end-systolic phase. The drawn contours were verified in every phase and manually adjusted, while the endocardial trabeculae and papillary muscles were excluded. Peak LV global longitudinal strain (GLS) was derived from all three long-axis views (two-chamber, three-chamber, and four-chamber). Peak LV global circumferential strain and peak LV global radial strain were derived from short-axis slices. Peak RV GLS was acquired from a standard four-chamber long-axis slice. The endocardial and epicardial contours were delineated in the end-systolic and end-diastolic phase, while the endocardial trabeculae and papillary muscles were excluded. After software analysis, the RV GLS was obtained.

The presence of biventricular myocardial LGE was assessed visually by two experienced CMR readers (XH.T. and YL.Y.; both with 8 years of CMR experience), who were blinded to patients' clinical profiles and outcomes, with any controversial adjudicated by a second expert reader (H.L.; 20 years of experience). LGE positivity was considered present when hyperenhancement was consistently visualized in two orthogonal projections. RV was divided into 10 segments to count the number of segments affected by RV LGE. RV was segmented into distinct anatomical regions: outflow tract, free wall, angle, inferior regions at the basal and mid-RV cuts, and free-wall and inferior segments at the apex (37). Areas of LV LGE were defined as a myocardium with a signal intensity greater than 5 standard deviations above the mean signal intensity of the reference remote myocardium (38).

Table S1 Baseline CMR hepatic T1 tissue characteristics of patients with ARVC and healthy controls.

Parameter	ARVC patients (n=94)	Healthy controls (n=30)	P value
Hepatic native T1, ms	734.9±75.8	648.0±36.8	<0.001***
Hepatic post T1, ms	378.4±47.0	405.6±52.2	0.024*
Hepatic ECV, %	34.5±4.8	31.9±4.8	0.013*

Values are the mean ± SD. *, P<0.05; ***, P<0.001. CMR, cardiac magnetic resonance; ARVC, arrhythmogenic right ventricular cardiomyopathy; ECV, extracellular volume.

Table S2 Intra- and interobserver analyses of hepatic T1 tissue measurements.

Variable	Intraobserver reproducibility			Interobserver reproducibility		
	ICC	95% CI	Bias	ICC	95% CI	Bias
Hepatic native T1	0.921	0.812–0.968	–6.85	0.901	0.855–0.951	–5.20
Hepatic post T1	0.944	0.877–0.971	–3.40	0.931	0.826–0.978	0.85
Hepatic ECV	0.956	0.892–0.982	0.21	0.943	0.861–0.977	0.19

ICC, intraclass correlation coefficient; CI, confidence interval; ECV, extracellular volume.

Table S3 Linear regression analysis for the association of hepatic native T1 value and clinical and CMR features

Variable	Univariable		Multivariable	
	β	P value	β	P value
Age	−0.201	0.052		
Male	−0.309	0.002**	−0.409	0.001**
BSA	−0.134	0.199		
Systemic hypertension	−0.055	0.526		
Diabetes	0.074	0.477		
Family history of CAD	0.244	0.005**		
Family history of ARVC	0.115	0.269		
NYHA class III–IV	0.212	0.041*		
History of syncope	0.006	0.956		
NSVT	0.008	0.941		
24-h PVC count (≥ 1000)	0.241	0.019*		
Leads with T-wave inversion	0.258	0.012*		
Beta-blockers	−0.031	0.768		
ACE inhibitors	−0.008	0.937		
Antiarrhythmic drug	0.064	0.543		
Diuretic agent	0.249	0.016*		
ARVC risk score	0.246	0.046*	0.330	0.011*
Traditional CMR features				
LV EDVi	0.210	0.084		
LV ESVi	0.176	0.089		
LVEF	−0.161	0.121		
LV RWMA	0.169	0.103		
RV EDVi	0.249	0.015*		
RV ESVi	0.243	0.018*		
RVEF	−0.188	0.048*		
RV RWMA	0.103	0.322		
CMR-FT peak strain				
LV GLS	0.166	0.110		
LV GCS	0.014	0.893		
LV GRS	−0.033	0.750		

Table S3 (continued)

Variable	Univariable		Multivariable	
	β	P value	β	P value
RV GLS	0.130	0.212		
Cardiac tissue characterization				
LV LGE	0.033	0.750		
LV LGE extent	0.042	0.690		
LV fat infiltration	0.044	0.674		
RV LGE	0.030	0.777		
Number of RV LGE segments	0.120	0.249		
RV fat infiltration	0.107	0.304		
LV native T1	0.318	0.001**	0.231	0.045*
LV ECV	0.118	0.257		

β indicates standardized β coefficients. *, $P < 0.05$; **, $P < 0.01$. BSA, body surface area; CAD, coronary artery disease; ARVC, arrhythmogenic right ventricular cardiomyopathy; NYHA, New York Heart Association; NSVT, nonsustained ventricular tachycardia; PVC, premature ventricular complex; ACE, angiotensin-converting enzyme; LV, left ventricular; EDVi, end-diastolic volume index; ESVi, end-systolic volume index; LVEF, left ventricular ejection fraction; RWMA, regional wall motion abnormalities; RV, right ventricular; RVEF, right ventricular ejection fraction; CMR-FT, cardiac magnetic resonance feature tracking; GLS, global longitudinal strain; GCS, global circumferential strain; GRS, global radial strain; LGE, late gadolinium enhancement; ECV, extracellular volume.

Table S4 Test of the proportional hazards assumption with Schoenfeld residuals

Model	Variable	χ^2	df	P value
Model 1	ARVC risk score	0.672	1	0.41
	GLOBAL	0.672	1	0.41
Model 2	ARVC risk score	0.457	1	0.50
	RV GLS	0.162	1	0.69
	GLOBAL	0.479	2	0.79
Model 3	ARVC risk score	0.605	1	0.44
	RV GLS	0.130	1	0.72
	Hepatic native T1	1.457	1	0.23
	GLOBAL	2.108	3	0.55

The global test assessed the overall proportional hazards assumption for the model. All $P > 0.05$, indicating that the proportional hazards assumption was not violated. χ^2 , Chi-squared statistic; df, degrees of freedom; ARVC, arrhythmogenic right ventricular cardiomyopathy; RV, right ventricular; GLS, global longitudinal strain.

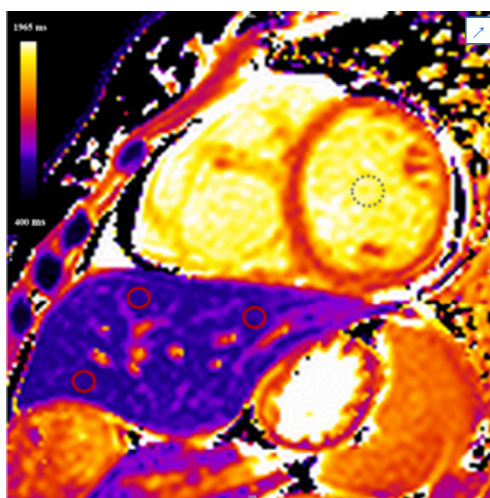


Figure S1 Standard cardiac Look-Locker inversion recovery sequence-derived T1 maps were used to determine hepatic T1 values. Hepatic T1 values were derived from standard cardiac T1 maps. Three regions of interest (red circle) were delineated within the hepatic parenchyma, while the lumen of hepatic vessels was excluded the average of these three regions of interests represents the hepatic T1 values. A region of interest (gray dotted circle) was placed in the LV cavity for blood pool T1 value quantification.

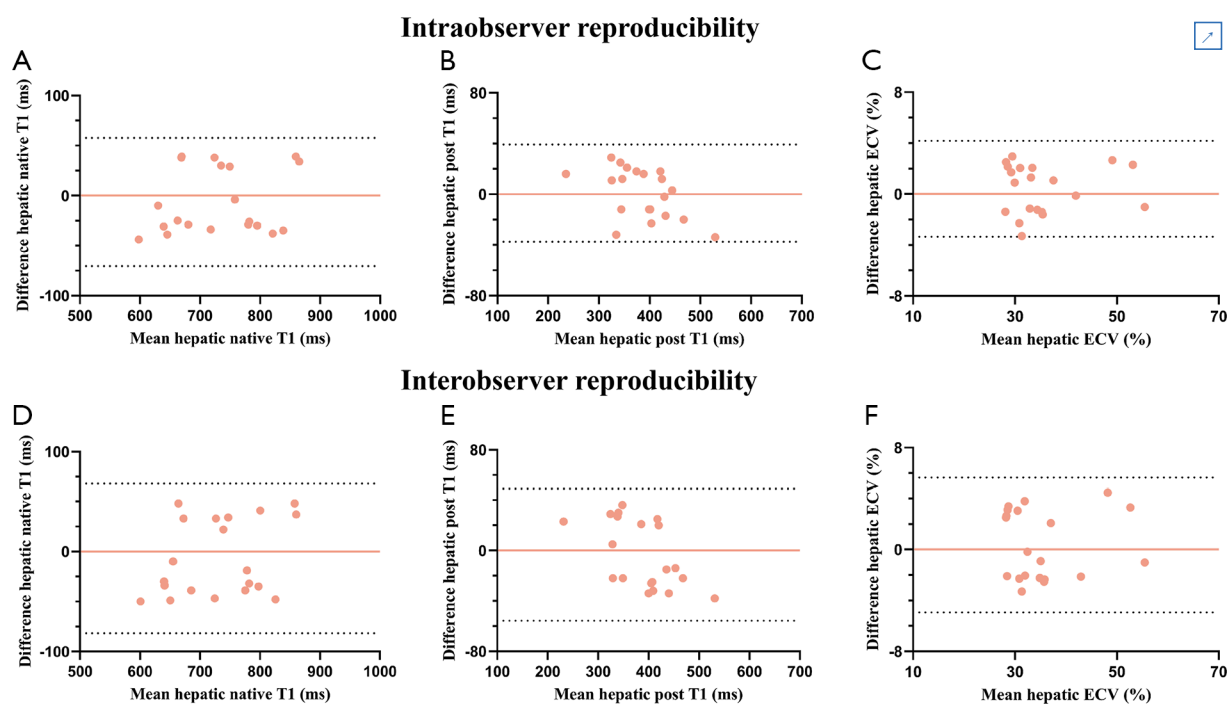


Figure S2 Bland-Altman plots for the intra- and interobserver reproducibility of hepatic T1 tissue. Bland-Altman plots represent the intraobserver (A-C) and interobserver (D-F) reproducibility for hepatic T1 tissue assessed in 20 randomly patients with ARVC. These parameters demonstrated strong inter- and intra-observer agreement. ECV, extracellular volume; ARVC, arrhythmogenic right ventricular cardiomyopathy.

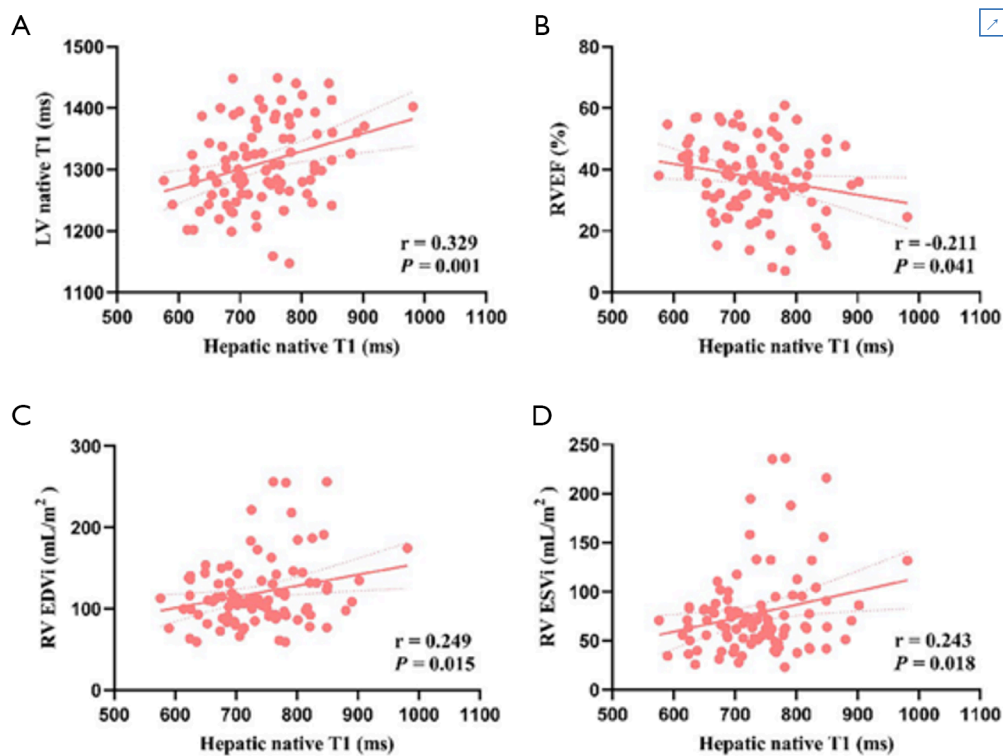


Figure S3 The correlation between hepatic native T1 and cardiac parameters in patients with ARVC. Scatter plots show that the hepatic native T1 were significantly associated with LV native T1 (A), RVEF (B), RV EDVi (C), and RV ESVi (D) in patients with ARVC. LV, left ventricular; RV, right ventricular; RVEF, right ventricular ejection fraction; EDVi, end-diastolic volume index; ESVi, end-systolic volume index.

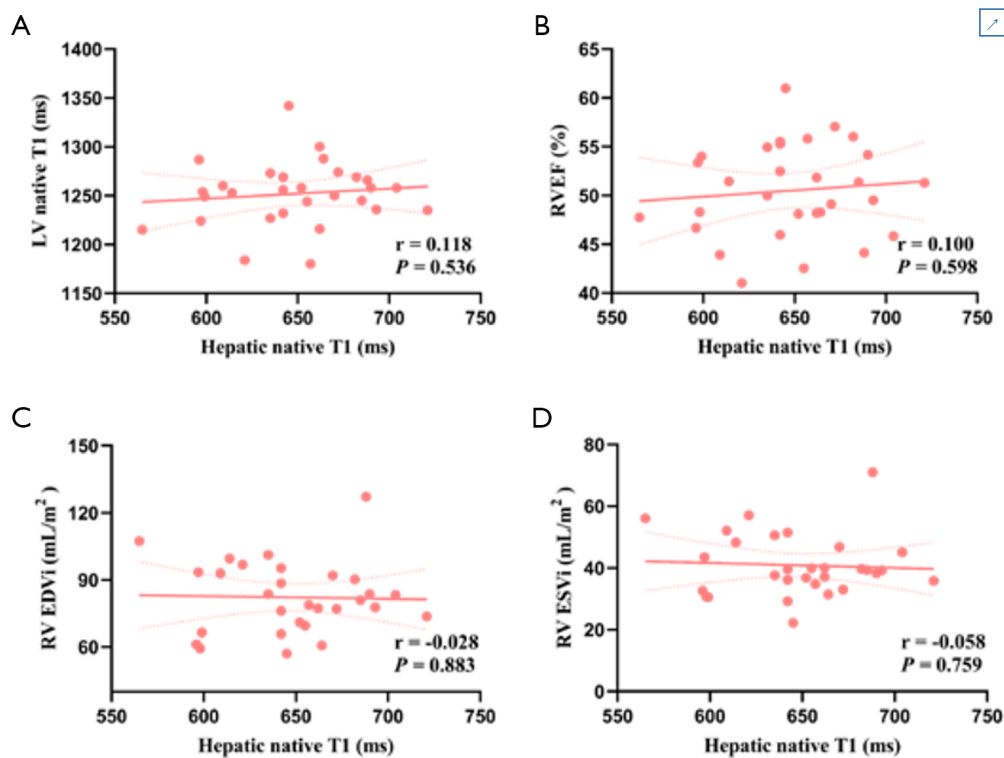


Figure S4 The correlation between hepatic native T1 and cardiac parameters in healthy controls. Scatter plots show that the hepatic native T1 were not significantly associated with LV native T1 (A), RVEF (B), RV EDVi (C), or RV ESVi (D) in healthy controls. LV, left ventricular; RV, right ventricular; RVEF, right ventricular ejection fraction; EDVi, end-diastolic volume index; ESVi, end-systolic volume index.

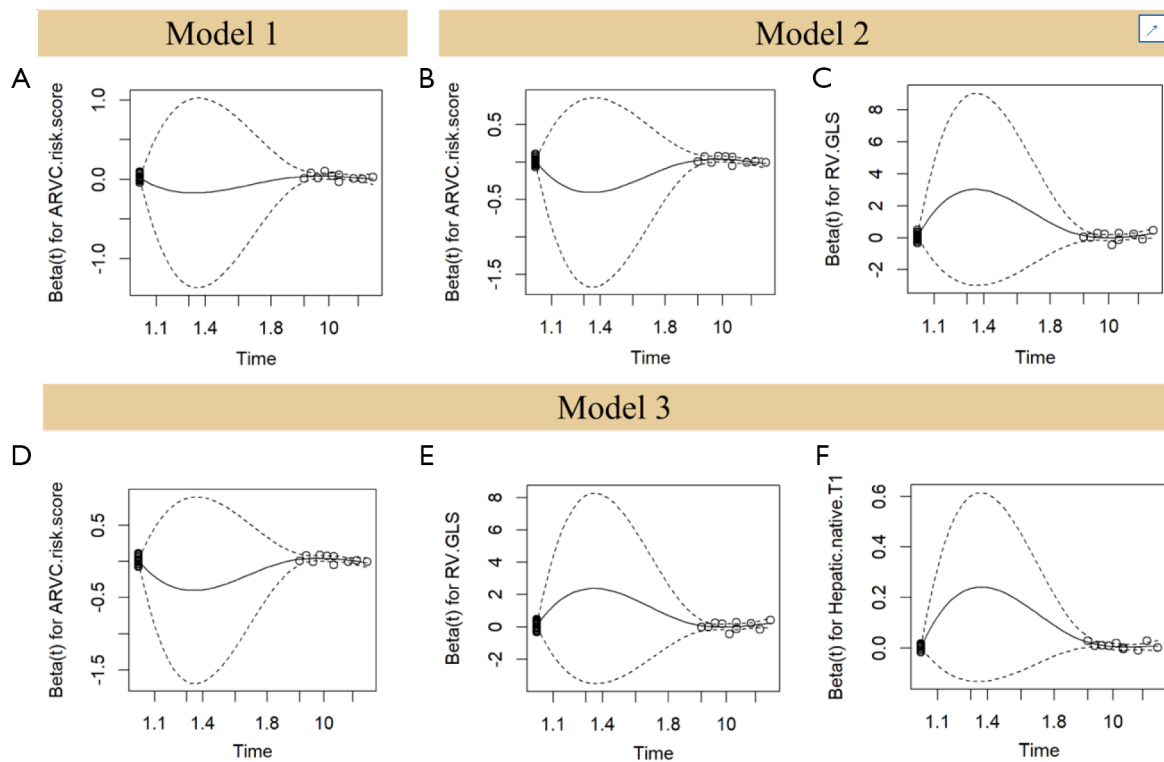
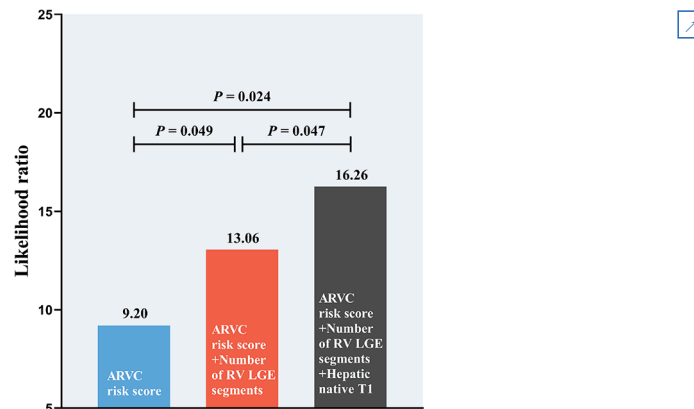


Figure S5 The smoothed scatter plots of residuals against time in three models (A-F). The smoothed scatter plots of residuals against time showed no systematic trends, confirming that the proportional hazards assumption was reasonable for our models. ARVC, arrhythmogenic right ventricular cardiomyopathy; RV, right ventricular; GLS, global longitudinal strain.



	Model 1: ARVC risk score		Model 2: Model 1 + Number of RV LGE segments		Model 3: Model 2 + Hepatic native T1	
	Fit	P value	Fit	P value	Fit	P value
Likelihood ratio	9.20		13.06	vs. Model 1: 0.049	16.26	vs. Model 1: 0.024 vs. Model 2: 0.047
C-statistics	0.680		0.724		0.738	
Continuous NRI			0.16 (0.03-0.37)	vs. Model 1: < 0.001	0.34 (0.01-0.48) 0.21 (0.04-0.43)	vs. Model 1: < 0.001 vs. Model 2: < 0.001
Covariates*						
ARVC risk score	1.02 (1.01-1.04)	0.004	1.02 (1.00-1.03)	0.020	1.02 (1.00-1.04)	0.007
Number of RV LGE segments			1.16 (1.01-1.35)	0.043	1.13 (0.97-1.31)	0.112
Hepatic native T1					1.01 (1.00-1.01)	0.012

Figure S6 Incremental value of hepatic native T1 relative to ARVC risk score and the number of RV LGE segments. Nested multivariable models for sustained ventricular arrhythmias. The addition of hepatic native T1 to model 2 (ARVC risk score and number of RV LGE segments) was associated with an additional significant increase in the likelihood test ($P=0.047$). *, for the covariates in the multivariable Cox regression analysis, HRs and 95% CIs are reported instead of fit statistics. ARVC, arrhythmogenic right ventricular cardiomyopathy; RV, right ventricular; LGE, late gadolinium enhancement; NRI, net reclassification improvement; CI, confidence interval; HR, hazard ratio.

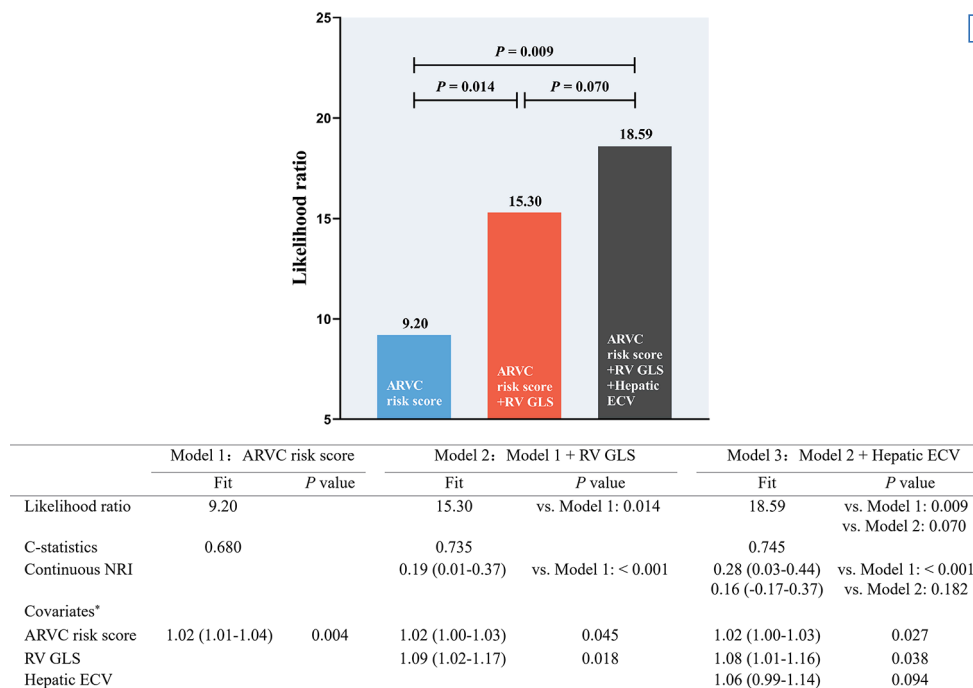


Figure S7 Incremental value of hepatic ECV relative to ARVC risk score and RV GLS. Nested multivariable models for sustained ventricular arrhythmias. The addition of hepatic ECV to model 2 (ARVC risk score and RV GLS) did not significantly improve the model fit according to the likelihood test ($P=0.070$). *, for the covariates in the multivariable Cox regression analysis, HRs and 95% CIs are reported instead of fit statistics. ARVC, arrhythmogenic right ventricular cardiomyopathy; RV, right ventricular; GLS, global longitudinal strain; ECV, **extracellular volume** NRI, net reclassification improvement; CI, confidence interval; HR, hazard ratio.

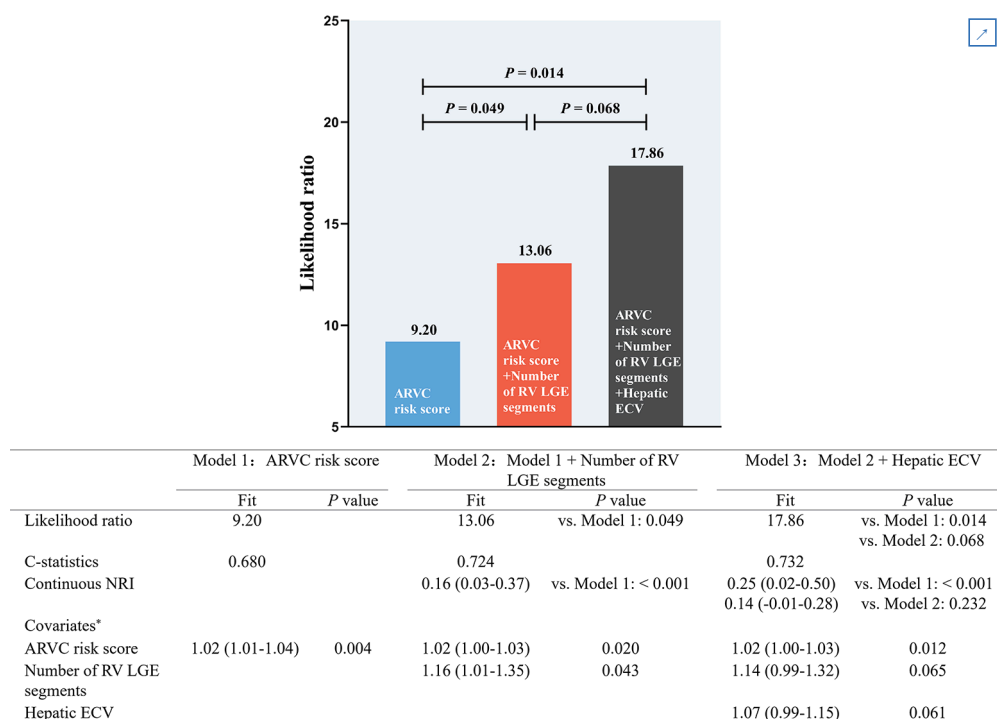


Figure S8 Incremental value of hepatic ECV relative to ARVC risk score and the number of RV LGE segments. Nested multivariable models for sustained ventricular arrhythmias. The addition of hepatic ECV to the model 2 (ARVC risk score and number of RV LGE segments) did not significantly improve the model fit according to the likelihood test ($P=0.068$). *, for the covariates in the multivariable Cox regression analysis, HRs and 95% CIs are reported instead of fit statistics. ARVC, arrhythmogenic right ventricular cardiomyopathy; RV, right ventricular; LGE, late gadolinium enhancement; ECV, **extracellular volume** NRI, net reclassification improvement; CI, confidence interval; HR, hazard ratio.

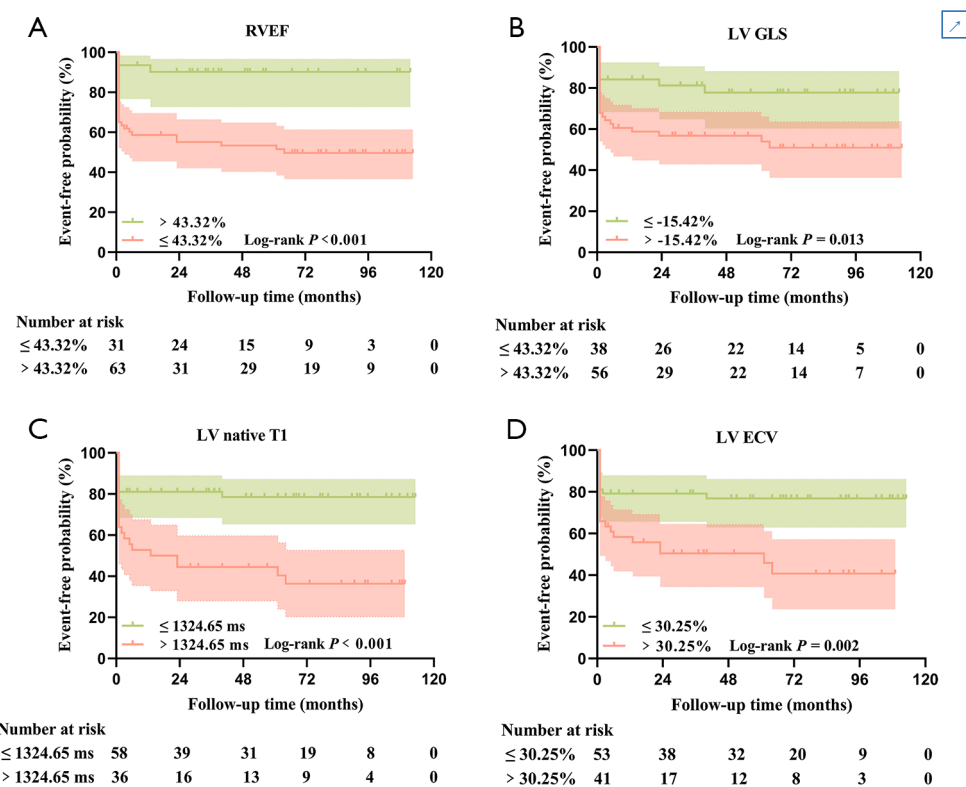


Figure S9 Survival analysis of RVEF, LV GLS, LV native T1, and LV ECV for sustained VA. A worse RVEF (A), impaired LV GLS (B), higher LV native T1 values (C), and elevated LV ECV (D) were associated with a higher probability of sustained VA. VA, ventricular arrhythmia; RVEF, right ventricular ejection fraction; LV, left ventricular; GLS, global longitudinal strain; ECV, extracellular volume.