Long-term Prognostic Value of Cardiac MRI Left Atrial Strain in ST-Segment Elevation Myocardial Infarction

Summary: 30 WORDS MAXIMUM

Left atrial strain derived by cardiac MRI was associated major adverse cardiac events after ST-segment elevation myocardial infarction, overriding outcome predictors such as left atrial volume and left ventricular function.

Key Results

- STEMI patients with impaired left atrial reservoir strain (21.8% or less) and conduit strain (10.5% or less) had significantly higher long-term risk of major adverse cardiac events than patients with reservoir strain larger than 21.8% and conduit strain larger than 10.5% (Log rank $P < .001$).
- Left atrial reservoir (hazard ratio, 0.84; $P < .001$) and conduit (hazard ratio, 0.81; $P < .001$) strains were independent predictors of major adverse cardiac events after STEMI, after adjusting for all included clinical and cardiac MRI outcome markers.
- The models including left atrial reservoir and conduit strains on top of traditional outcome markers had higher prognostic accuracy in predicting major adverse cardiac events than the model with only traditional outcome markers (Uno's C statistic, 0.75 versus 0.68; $P = .04$).

Abbreviations

GLS = global longitudinal strain,

LA = left atrial,

LAEF = LA ejection fraction,

LAV_{max} = maximal LA volume,

LV = left ventricular,

LVEF = LV ejection fraction,

MACE = major adverse cardiac event,

ROC = receiver operating characteristic,

STEMI = ST-segment elevation myocardial infarction.

Abstract 300 word maximum.

Background: Left atrial (LA) dysfunction is associated with morbidity and mortality. The relationship of LA strain to prognosis in patients with ST-segment elevation myocardial infarction (STEMI) is unknown.

Purpose: To evaluate LA strain as a long-term outcome predictor in STEMI in a prospective, multicenter cardiac MRI cohort.

Materials and Methods: STEMI patients who underwent primary percutaneous coronary intervention and cardiac MRI from seven sites (EARLY-MYO-CMR registry, clinical trial number NCT03768453) were included. The parent study took place between August 2013 and December 2018. LA longitudinal strain and strain rate parameters were derived from cine cardiac MRI using an in-house semi-automated method. Major adverse cardiac events (MACE) were defined as cardiovascular death, myocardial re-infarction, hospitalization for heart failure, and stroke. The association between LA performance and MACE was evaluated by using time-dependent receiver operating characteristic analysis, Kaplan-Meier analysis, and multivariable Cox regression analysis.

Results: A total of 321 (median age 59 years, range 27 to 75 years; 90% men) participants were included in this study. During median follow-up of 3.7 years, MACE occurred in 76 (23.7%) participants. Participants with impaired reservoir (21.8% or less) and conduit strain (10.5% or less) had a higher risk of MACE than those with reservoir strain larger than 21.8% and conduit strain larger than 10.5% ($P < .001$). Reservoir strain (hazard ratio (HR): 0.84, 95% confidence interval (CI): 0.77, 0.91; $P < .001$) and conduit strain (HR: 0.81, 95% CI: 0.73, 0.89; $P < .001$) were independent predictors of MACE after adjusting for known risk factors. Finally, LA reservoir and conduit strains provided incremental prognostic value over traditional outcome predictors (Uno's C statistic, 0.75 versus 0.68; $P = .04$).

Conclusion: Assessment of left atrial strain, as a measure of left atrial function, provided incremental prognostic information to established predictors in ST-segment elevation myocardial infarction.

Introduction

Left atrial (LA) size is a prognostic predictor in different cardiac diseases (1). Guidelines recommend assessment of maximal LA linear dimension, area, or volume (2), which are markers of past elevation of left ventricular (LV) filling pressure. These assessments are especially important for determining diastolic function (3), but they do not consider the complex LA and LV interactions with discrete reservoir, conduit, and booster bump phases that can impact cardiac performance (1). LA strain is a promising parameter for quantifying LA phasic function and is potentially a more sensitive indicator of real-time filling pressures than LA volume (4). Research interest in speckle tracking echocardiography-derived LA strain indices, which are not directly comparable with manually intensive volumetric analysis (5), is growing. However, there is lack of large-scale studies (6) and standardization among vendor systems, which are both needed before echocardiography-derived LA strain indices can be derived in clinical routine (7).

Capitalizing on the imaging quality of cine cardiac MRI, Kowallick et al performed feature tracking of LA wall contours using a third-party post-processing software and reported, versus control subjects, impaired LA reservoir and conduit function in hypertrophic cardiomyopathy and heart failure with preserved ejection fraction (8). A fast method has been developed to measure LA longitudinal phasic strains and strain rates on standard two- and four-chamber cine cardiac MRI. This method requires only annotations of three anatomical reference points per view (9), thereby obviating error-prone LA contour tracing around the LA appendage and pulmonary veins. Compared with standard cardiac MRI feature tracking, the fast method possessed good agreement, similar diagnostic discrimination for hypertrophic cardiomyopathy and heart failure compared to controls, superior reproducibility, and 55% reduction in evaluation time (9). The same method applied in the right atrium to measure

right atrial phasic strains and strain rates showed diagnostic and prognostic value in pulmonary arterial hypertension (10).

While echocardiography-assessed LA volume is a strong predictor of morbidity and mortality in patients after acute myocardial infarction (11,12), it remains unknown whether LA strain acts as a long-term prognostic factor in predicting these outcomes. Accordingly, current study aimed to: 1) evaluate the prognostic importance of LA strain indices quantified by means of the fast method in a large multicenter cohort of ST-segment elevation myocardial infarction (STEMI) patients during long-term follow-up; and 2) assess the incremental prognostic value of LA strain compared to traditional markers, such as LA volume and LV parameters, including longitudinal function.

Materials and Methods

Study Participants

Participants in this prospective study were identified from the image database of EARLY-MYO-CMR (EARLY assessment of MYOcardial tissue characteristics by CMR in STEMI) registry (13), which was a multicenter registry of patients with STEMI who underwent cardiac MRI at seven sites (ClinicalTrials.gov identifier NCT03768453). Participants were enrolled from August 2013 to December 2018. The registry was approved by an institutional review committee at each center. Patients were eligible for the registry if they had their first STEMI when they were at least 18 years old, underwent cardiac MRI within 1 week after symptom onset, and provided written consent. All subjects had sinus rhythm during cardiac MRI acquisition. Exclusion criteria are available in the Supplemental material. Part of the study population have been included in a prior study (13) comparing the efficacy of fibrinolytic therapy versus primary percutaneous coronary intervention in STEMI patients. The current study aimed to identify cardiac MRI-derived indices that are associated with

adverse clinical outcomes with long-term follow-ups. In addition, we included 40 normal controls as a comparative group, which were selected from a prior study (9).

Cardiac MRI Scan Acquisition

Cardiac MRI was performed on 1.5-T or 3-T scanners (Achieva TX, Philips Healthcare, Best, The Netherlands). Standard cine images were acquired with end-expiratory breath hold steady-state free precession sequences. Infarct size and microvascular obstruction were determined from late gadolinium enhancement images. Detailed MRI acquisition protocol can be found in the Supplemental material.

Cardiac MRI Scan Assessment

MRI was used to quantify infarct size, microvascular obstruction, LV volumes, LV ejection fraction (EF), LA volumes, and LAEF by one cardiologist (H.G. with >8 years of experience in MRI). LV global longitudinal strain (GLS) was derived in long-axis cine cardiac MRI views with validated software (QStrain, Version 2.0, Medis BV, Leiden, The Netherlands) by one reader blinded to all patient characteristics and other MRI measurements (X.D.Z. with >6 years of experience in MRI feature tracking). As LV GLS is negative, we took its absolute value for a simple interpretation.

The fast semi-automated LA longitudinal strain analysis was performed on four- and two-chamber cine cardiac MRI images by one reader blinded to patient characteristics, follow-up information, and other clinical parameters (S.L. with >5 years of experience in MRI imaging), and results were reviewed by a second observer (R.S.T., a cardiologist with >20 years of experience in MRI). In each view, the distance (L) between each atrioventricular junction and a user-defined point at the mid posterior LA wall was automatically tracked throughout the cardiac cycle (**Fig 1a-b**) (14-17). LA longitudinal strain

(ε) at any time point (t) in the cardiac cycle was calculated based on the Lagrange strain formula (9), as follows: $\varepsilon(t) = (L(t) - L_0) \times 100/L_0$, where $L(t)$ and L_0 are the distance L at time t and the time of minimal LA volume, respectively. Phasic LA longitudinal strain and strain rate parameters – reservoir strain ε_s and strain rate SR_s, conduit strain ε_e and strain rate SR_e, and booster strain ε_a and strain rate SR_a – were derived (**Fig 1c-d**) (9). More details about MRI assessment are available in the Supplemental material.

Clinical Outcomes and Follow-up

Clinical follow-up was performed annually for up to 5 years by one cardiologist (J.H. with >4 years of experience), and verified by an adjudication committee, both blinded to cardiac MRI data The primary outcome measurement was major adverse cardiac events (MACE) defined as a composite of cardiovascular death, myocardial re-infarction, hospitalization for heart failure, and stroke. If more than one primary outcome occurred in the same participant, the first event was considered for the analysis.

Statistical Analysis

Continuous variables were expressed as means ± standard deviations or medians (interquartile range). Categorical variables were displayed as numbers (percentages) (More details in Supplemental material).

Using time-dependent receiver operating characteristic (ROC) analysis on patient predicted risk of MACE, statistically optimal cut-offs for classifying participants as high or low risk for MACE were determined based on Youden's J-statistic. Event-free survival curves were obtained by Kaplan-Meier analysis and compared by log-rank test.

The assessment of risk predictors of MACE using a Cox regression model incorporated both statistical and clinical considerations. An initial assessment was strictly

statistical using a backward-conditional variable selection procedure ($P < .05$) on candidate baseline and standard cardiac MRI parameters (Model 1) that exhibited statistically significant association with MACE at the $P < .05$ level in univariate analysis. Two additional multivariable analyses were performed to establish LA reservoir strain (Model 2: Model 1 + reservoir strain + other clinically relevant parameters) and conduit strain (Model 3: Model 1 + conduit strain + other clinically relevant parameters) as independent predictors of MACE. The incremental values of reservoir strain and conduit strain to traditional risk factors for adverse outcomes were assessed using Uno's C statistics with the significance levels.

Statistical analyses were performed using SPSS (Version 17.0, Chicago, IL, USA) and SAS (Version 9.4, Cary, NC, USA) software. A P value of $\leq .05$ was considered indicative of a statistically significant difference.

Results

Study Population

EARLY-MYO-CMR enrolled 536 participants, of whom 354 underwent primary percutaneous coronary intervention less than 12 hours after symptom onset, underwent cardiac MRI within a week of symptom onset (median 4 days, interquartile range, 3-6 days), and had at least one year of follow-up. After further excluding participants with incomplete follow-up information ($n = 21$) and inadequate cine cardiac MRI scan quality ($n = 12$), a total of 321 participants (median age 59 years, range 27 to 75 years; 90% men) were included in the present analysis (**Fig 2**).

During a median follow-up of 44 months (interquartile range, 32-58 months), MACE occurred in 76 of 321 (23.7%) participants: nine cardiovascular deaths, 42 hospitalizations for heart failure, 20 myocardial re-infarctions, and five strokes. These participants had a

significantly higher prevalence of hypertension, diabetes mellitus, Killip class of greater than 2, thrombolysis in myocardial infarction flow grade of less than 3 after percutaneous coronary intervention, anterior infarction, higher heart rate, higher high-sensitivity cardiac Troponin T, and higher thrombolysis in myocardial infarction risk score compared with participants without MACE (**Table 1a**).

Compared with healthy subjects, patients with STEMI had similar maximal LA volume (LAV_{max}) index (35 ± 10 vs. 36 ± 8 ml/m^2, P = .82) but significantly impaired LA strains and strain rates (all P < .001) (**Supplementary Table 1**).

Standard Cardiac MRI Parameters Predictive of MACE

Participants with MACE had lower LVEF and LV GLS, larger LV end-diastolic and end-systolic volume index and mass index, larger microvascular obstruction and infarct size as a percentage of LV mass, larger LA volume index (diastasis and minimal) and lower phasic LAEF (all P < .05) compared with those without events (**Table 1b**).

Variable Selection for Models

Among the LA strain and strain rate indices for predicting MACE, LA reservoir and conduit strains exhibited the highest integrated areas under the ROC curve (**Supplementary Fig 1**) and were therefore inputs as candidate predictors in subsequent multivariable analyses. Variables selected by backward-conditional algorithm as a parsimonious subset of independent predictors of MACE risk among baseline and standard cardiac MRI variables were infarct size and total LAEF (Model 1). LA reservoir strain and conduit strain were introduced separately into the multivariable analysis that included infarct size and total LAEF (Models 2 and 3). Moreover, age, diabetes, hypertension, Killip class of greater than or equal

to 2, LVEF, LV mass index, LV GLS and LAV_{max} index (all shown to be important in several STEMI studies [12, 18-21]) were also taken into account in Models 2 and 3.

Association of LA Strains with Clinical Measurements

LA reservoir strain was moderately correlated with LVEF (r = 0.45, P < .001), LV GLS (r = 0.49, P < .001), and infarct size (r = -0.34, P < .001). LA conduit strain was correlated with LVEF (r = 0.38, P < .001), LV GLS (r = 0.49, P < .001), and infarct size (r = -0.31, P < .001), while LA booster strain was only associated with LVEF (r = 0.31, P < .001). Moderate to strong correlations were exhibited between LA strain measurements and the corresponding LA phasic volumetric measurements (**Table 2**). **Figure 3** shows LA reservoir strain ε_s values plotted against tertiles of LV GLS and LAV_{max} index. For any given value of LAV_{max} index, ε_s was progressively reduced as the LV GLS became deteriorated; and for any given value of LV GLS, ε_s was decreased with increasing LAV_{max} index.

LA Strains and MACE Risk

Participants with MACE exhibited impaired LA phasic strains and strain rates (all P < .001) (**Table 1b**). Optimal cut-off values were 21.8% and 10.5% for reservoir strain and conduit strain, respectively, on time-dependent ROC analysis. Participants with reservoir strain of less than 21.8% or conduit strain of less than 10.5% displayed higher risks of MACE on Kaplan-Meier analysis (both log rank P < .001) (**Fig 4**).

Predictors of MACE by Multivariable Analysis

In backward-conditional multivariable Cox regression analyses on baseline and standard cardiac MRI indices, infarct size and total LAEF were identified as independent predictors for the occurrence of MACE (Model 1, **Table 3**). We then aimed to determine whether LA strains were associated with MACE once adjusted for infarct size, total LAEF, and other

clinically important variables (**Table 4**). In the final multivariable analyses, the variables associated with MACE were infarct size (hazard ratio (HR): 1.03, 95% confidence interval (CI): 1.01, 1.06; $P = .01$), LA reservoir strain (HR: 0.84, 95% CI: 0.77, 0.91; $P < .001$), and LA conduit strain (HR: 0.81, 95% CI: 0.73, 0.89; $P < .001$) (Models 2 and 3, **Table 4**). For every percent increase in LA reservoir strain, the risk of MACE decreases by a factor of 0.84 (or 16%) (Model 2); similarly, every percent increase in LA conduit strain is associated with decreased risk of MACE by a factor of 0.81 (or 19%) (Model 3), holding other risk factors constant.

Incremental Value of LA Strains for Predicting Adverse Events

LA reservoir strain provided incremental value to traditional cardiac MRI risk factors including LVEF, LV mass index, LV GLS, infarct size, and LAV_{max} (Uno's C statistic, 0.75 versus 0.68; $P = .04$). Similarly, when LA conduit strain was added separately to the traditional risk factors, the predictive power significantly increased as reflected by higher Uno's C statistic (0.75 versus 0.68; $P = .04$). The integrated area under the ROC curve for traditional risk factors was 0.76, which increased to 0.77 and 0.79 with the respective additions of reservoir strain and conduit strain. Results of time-dependent ROC analysis for each LA and LV functional parameters against MACE are shown in **Fig 5**. LA reservoir and conduit strains showed the highest integrated areas under the ROC curve in predicting MACE compared with other LA and LV parameters (noninferior to LV GLS and significantly better than other parameters). ROC curves for reservoir strain, conduit strain, total LAEF, passive LAEF, LAV_{max}, and LV GLS demonstrating their predictive abilities of MACE after 36 months follow-up are presented in **Fig 6**. Areas under the ROC curve for reservoir and conduit strains were higher than for other indices (all $P < .05$).

Discussion

The long-term prognostic value of left atrial (LA) function in patients with ST-segment elevation myocardial infarction (STEMI) who underwent primary percutaneous coronary intervention remains unclear. Our study evaluated the prognostic utility of LA strain indices in a large cardiac MRI cohort of STEMI patients during median follow-up of 3.7 years. First, patients after STEMI had significantly reduced LA strains and strain rates (all $P < .001$) compared with age- and sex-matched healthy subjects. Second, STEMI patients with LA reservoir strain less than 21.8% or conduit strain less than 10.5% had significantly higher long-term risk of major adverse cardiac events (MACE) than those with reservoir strain larger than 21.8% and conduit strain larger than 10.5% (Log rank $P < .001$). Third, LA reservoir (hazard ratio (HR), 0.84; $P < .001$) and conduit (HR, 0.81; $P < .001$) strains were independent predictors of MACE risk after STEMI, after adjusting for established clinical and cardiac MRI markers of cardiovascular risk. Finally, the addition of LA reservoir strain and conduit strain to traditional outcome markers provided higher prognostic accuracy in predicting MACE (Uno's C statistics increased from 0.68 to 0.75; $P = .04$).

Echocardiographic LA volume is a predictor of adverse outcome after acute myocardial infarction (11,12). Beyond LA size, LA mechanical function may improve risk stratification. Antoni et al (22) studied the prognostic importance of speckle tracking echocardiographic LA strain in STEMI, and found LA reservoir strain to be an independent predictor of mortality, nonfatal re-infarction and hospitalization for heart failure. However, LA strain measurement by speckle tracking is challenging due to low signal-to-noise ratio and the thin atrial wall. In our study we focused on the use of routine clinical cine cardiac MRI scans for fast and reliable quantification of LA dynamics with shorter measurement time and increased reproducibility.

In a multicenter prospective study that included more than 1200 acute myocardial infarction patients studied by cardiac MRI within 10 days after infarction, Schuster et al (23)

reported that MRI feature tracking-derived LA reservoir strain was independently predictive of MACE at 1-year follow-up, after accounting for established prognostic markers including LVEF, GLS, microvascular obstruction, and infarct size. In line with this and other studies (22), our study provided evidence that LA reservoir and conduit strains are strong independent predictors of clinical outcome at long-term follow-up. Hence, our findings highlight the capability and effectiveness of LA strain indices in long-term risk stratification of STEMI patients.

The finding that LA phasic function provided added prognostic values over LAV_{max} and LV GLS in our study can be explained as follows. First, LA function is more predictive of hemodynamic changes. Bergstra et al (24) found a large proportion of their enrolled patients with STEMI without physical signs of heart failure had elevated left-sided cardiac filling pressures revealed by early invasive hemodynamic measurements. LAV_{max} does not appear to be affected by acute ischemia or acute changes in LV filling (25), whereas LA strain has been found to correlate with LV filling pressure (26), an early prognostic indicator in STEMI (27). Second, atrial fibrillation is the most common arrhythmia following myocardial infarct and is associated with adverse cardiovascular outcomes (28). Prior studies demonstrated that LA strains and function are predictive of new-onset atrial fibrillation in patients after myocardial infarct and other cardiac diseases (1). These may explain, notwithstanding the association of LA phasic strain to LV GLS and LAV_{max}, the better prognostic performance of LA strains in our study.

Both infarct size and microvascular obstruction on delayed enhancement cardiac MRI are strongly associated with death and heart failure hospitalization after STEMI (19,29) and exhibit significant correlation with LA strains. LA reservoir strain and conduit strain remained as independent risk factors for MACE, indicating that LA strains provide additional

prognostic information in STEMI beyond infarct extent assessed by contrast-enhanced imaging markers.

Our study had limitations. Cardiac MRI data were acquired during the first 3 to 7 days after STEMI once participants were stabilized rather than at a single exact time point, which might be more accurate. The cut-off of abnormal reservoir (21.8%) and conduit (10.5%) strains obtained from time-dependent ROC analysis of the 321 participants may not represent the ground truth, which should ideally be derived from large normal populations. The heart rate differed between groups with and without MACE, however, the heart rate had no significant effect on LA strain measurements (Supplemental material).

In conclusion, left atrial (LA) strain parameters, which are readily obtainable from post-processing of standard four- and two-chamber cine cardiac MRI scans, provided important prognostic information for predicting adverse outcomes in patients after ST-segment elevation myocardial infarction (STEMI). In comparison to traditional outcome markers such as LA size and left ventricular global longitudinal strain, LA strain had an incremental prognostic value in STEMI, and therefore should be considered a useful adjunct to established imaging markers.

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TABLE 1a: Baseline and Angiographic Characteristics of Participants With and Without MACE

	All Participants (*n* = 321)	No MACE (*n* = 245)	MACE (*n* = 76)	*P* value
Age, years	59 (54-64)	58 (53-64)	59 (54-65)	.39
Men, *n* (%)	290 (90)	223 (91)	67 (88)	.46
Body surface area, m^2	1.9 ± 0.2	1.9 ± 0.1	1.9 ± 0.2	.69
Body mass index, kg/m^2	25 ± 3	25 ± 3	25 ± 3	.57
Cardiac risk factors, *n* (%)				
Hypertension	186 (58)	134 (55)	52 (68)	.03
Diabetes	99 (31)	68 (28)	31 (41)	.03
Smoker	221 (69)	167 (68)	54 (71)	.64
Hyperlipidemia	196 (61)	153 (62)	43 (57)	.36
Heart rate, beats/min	78 ± 14	77 ± 14	82 ± 15	.01
Killip class, *n* (%)				.04
1	301 (93)	234 (95)	67 (88)	
2	17 (5)	9 (4)	8 (11)	
3	2 (1)	2 (1)	0 (0)	
4	1 (1)	0 (0)	1 (1)	
Time to reperfusion, hours	4.6 (3.5-5.7)	4.8 (3.6-5.7)	4.5 (3.4-5.6)	.46
Anterior infarction, *n* (%)	140 (44)	94 (38)	46 (61)	.001
Multivessel disease, *n* (%)	180 (56)	135 (55)	44 (58)	.69
hs-cTnT, ng/l	27 (6-58)	24 (7-50)	38 (6-102)	.01
SCr, µmol/l	72 (63-82)	72 (63-82)	70 (61-84)	.73
eGRF, $ml/min/1.73m^2$	101 (87-116)	101 (87-118)	104 (85-115)	.78
TIMI flow before PCI				.78
0	155 (48)	118 (48)	37 (49)	
1	14 (4)	11 (4)	3 (4)	
2	41 (13)	29 (12)	12 (16)	
3	111 (35)	87 (36)	24 (31)	
TIMI flow after PCI				.04
0	2 (1)	0 (0)	2 (3)	
1	6 (2)	5 (2)	1 (1)	
2	31 (9)	21 (9)	10 (13)	
3	282 (88)	219 (89)	63 (83)	
TIMI risk score	2.8 ± 1.8	2.6 ± 1.7	3.1 ± 2.0	.048

Note.—Data are presented as mean ± standard deviation, n (%), or median (25^{th} to 75^{th} percentile). eGFR = estimated glomerular filtration rate, MACE = major adverse cardiac events, hs-cTnT = high-

sensitivity cardiac troponin T, PCI = percutaneous coronary intervention, SCr = serum creatinine, TIMI = thrombolysis in myocardial infarction.

TABLE 1b: Cardiac MRI Characteristics of Participants With and Without MACE

	All Participants (*n* = 321)	No MACE (*n* = 245)	MACE (*n* = 76)	*P* value
LVEF, %	52 ± 11	54 ± 10	47 ± 12	< .001
LV end-diastolic volume index, ml/m^2	67 ± 14	66 ± 13	70 ± 17	.03
LV end-systolic volume index, ml/m^2	32 ± 13	31 ± 11	38 ± 16	< .001
LV mass index, g/m^2	68 ± 22	66 ± 20	75 ± 26	.002
Microvascular obstruction, *n* (%)	228 (71)	172 (70)	56 (74)	.63
Microvascular obstruction, % of LV mass	0.9 (0.0-3.0)	0.8 (0.0-2.7)	1.6 (0.1-5.2)	.01
Infarct size, % of LV mass	23 (17-31)	22 (16-29)	31 (21-41)	< .001
LV GLS, %	14 ± 4	15 ± 4	12 ± 4	< .001
LA volume index, ml/m^2				
Maximal	35 ± 10	35 ± 9	37 ± 12	.17
Diastasis	28 ± 9	27 ± 8	30 ± 11	.02
Minimal	18 ± 7	17 ± 6	21 ± 10	.004
LAEF, %				
Total	50 ± 9	51 ± 8	45 ± 11	< .001
Passive	22 ± 7	23 ± 7	19 ± 7	< .001
Active	35 ± 9	36 ± 8	32 ± 10	.003
LA longitudinal strain, %				
Reservoir strain	23 ± 6	25 ± 5	19 ± 6	< .001
Conduit strain	11 ± 4	12 ± 4	8 ± 3	< .001
Booster strain	12 ± 4	13 ± 4	11 ± 4	< .001
LA longitudinal strain rate, 1/s				
Reservoir strain rate	1.3 ± 0.4	1.3 ± 0.3	1.1 ± 0.4	< .001
Conduit strain rate	-1.2 ± 0.5	-1.3 ± 0.5	-1.0 ± 0.3	< .001
Booster strain rate	-1.6 ± 0.6	-1.7 ± 0.6	-1.4 ± 0.6	< .001

Note.—Data are presented as mean ± standard deviation, n (%), or median (25^{th} to 75^{th} percentile). GLS = global longitudinal strain, LA = left atrial, LAEF = left atrial ejection fraction, LV = left ventricular, LVEF = left ventricular ejection fraction, MACE = major adverse cardiac events.

TABLE 2: Associations of LA Strains with Clinical Parameters

	LA reservoir strain		LA conduit strain		LA booster strain	
	r	*P* value	*r*	*P* value	*r*	*P* value
LVEF	0.45	< .001	0.38	< .001	0.31	< .001
LV mass index	-0.18	.001	-0.14	.01	-0.14	.01
LV end-diastolic volume index	-0.17	.002	-0.09	.10	-0.17	.002
LV GLS	0.49	< .001	0.49	< .001	0.28	< .001
Infarct size, % of LV mass	-0.34†	< .001	-0.31†	< .001	-0.24†	< .001
Microvascular obstruction, % of LV mass	-0.28†	< .001	-0.15†	.01	-0.29†	< .001
LAV_{max} index	-0.37	< .001	-0.17	.002	-0.40	< .001
LAV_{min} index	-0.62	< .001	-0.37	< .001	-0.58	< .001
Total LAEF	0.80	< .001	0.57	< .001	0.67	< .001
Passive LAEF	0.64	< .001	0.75	< .001	0.25	< .001
Active LAEF	0.62	< .001	0.24	< .001	0.71	< .001

Note.—GLS = global longitudinal strain, LA = left atrial, LAEF = left atrial ejection fraction, LAV_{max} = maximal left atrial volume, LAV_{min} = minimal left atrial volume, LV = left ventricular, LVEF = left ventricular ejection fraction, *r* = Pearson's correlation (except for infarct size and microvascular obstruction).

†By Spearman correlation analysis.

TABLE 3: Univariate and Multivariable Cox Proportional Hazards Model for MACE Risk Using Baseline Characteristics and Cardiac MRI Indices

	Univariate analysis		Multivariable backward conditional selection (Model 1)	
	HR	*P* value	HR	*P* value
Hypertension	0.58 (0.36-0.94)	.03	-	
Diabetes	0.63 (0.40-1.00)	.049	-	
Heart rate, beats/min	1.02 (1.00-1.03)	.02	-	
Killip class ≥ 2	0.48 (0.24-0.95)	.04	-	
TIMI flow after PCI < 3	0.67 (0.37-1.21)	.18	Excluded	
TIMI risk score	1.17 (1.03-1.32)	.01	-	
Anterior infarction	0.46 (0.29-0.74)	.001	-	
hs-cTnT, ng/l	1.01 (1.01-1.02)	< .001	-	
LVEF, %	0.95 (0.93-0.97)	< .001	-	
LV end-diastolic volume index, ml/m^2	1.02 (1.01-1.04)	.001	-	
LV end-systolic volume index, ml/m^2	1.04 (1.02-1.05)	< .001	-	
LV mass index, g/m^2	1.01 (1.01-1.02)	.001	-	
Microvascular obstruction, % of LV mass	1.13 (1.07-1.20)	< .001	-	
Infarct size, % of LV mass	1.05 (1.04-1.07)	< .001	1.04 (1.02-1.06)	< .001
LV GLS, %	0.85 (0.80-0.91)	< .001	-	
LA volume index, ml/m^2				
Diastasis	1.04 (1.01-1.06)	.003	-	
Minimal	1.05 (1.03-1.08)	< .001	-	
LAEF, %				
Total	0.94 (0.92-0.96)	< .001	0.97 (0.94-0.99)	.01
Passive	0.93 (0.90-0.96)	< .001	-	
Active	0.96 (0.94-0.98)	< .001	-	

Note.—Numbers in parentheses are the 95% confidence interval. GLS = global longitudinal strain, HR = hazard ratio, hs-cTnT = high-sensitivity cardiac troponin T, LA = left atrial, LAEF = left atrial ejection fraction, LV = left ventricular, LVEF = left ventricular ejection fraction, PCI = percutaneous coronary intervention, TIMI = thrombolysis in myocardial infarction.

TABLE 4: Multivariable Cox Proportional Hazards Model for MACE Risk Using Selected Clinical Variables and LA Reservoir and Conduit Strains

Parameter	Multivariable analysis with LA reservoir strain (Model 2)		Multivariable analysis with LA conduit strain (Model 3)	
	HR	*P* value	HR	*P* value
Age, years	0.99 (0.96-1.02)	.60	0.98 (0.94-1.01)	.14
Hypertension	0.77 (0.46-1.27)	.30	0.88 (0.53-1.48)	.63
Diabetes	0.74 (0.46-1.19)	.21	0.81 (0.50-1.30)	.37
Killip class ≥ 2	1.40 (0.66-2.99)	.38	1.69 (0.79-3.62)	.18
LVEF, %	1.00 (0.96-1.03)	.79	1.00 (0.96-1.03)	.83
LV mass index, g/m^2	1.01 (1.00-1.02)	.11	1.01 (1.00-1.02)	.07
LV GLS, %	1.01 (0.92-1.12)	.81	1.04 (0.94-1.15)	.50
Infarct size, % of LV mass	1.03 (1.01-1.06)	.01	1.03 (1.01-1.06)	.01
LAV_{max} index, ml/m^2	0.99 (0.97-1.02)	.53	1.01 (0.98-1.03)	.64
Total LAEF, %	1.04 (1.00-1.08)	.08	0.99 (0.96-1.03)	.75
LA reservoir strain, %	0.84 (0.77-0.91)	< .001	…	…
LA conduit strain, %	…	…	0.81 (0.73-0.89)	< .001

Note.—Numbers in parentheses are the 95% confidence interval. GLS = global longitudinal strain, HR = hazard ratio, LA = left atrial, LAEF = left atrial ejection fraction, LAV_{max} = maximal left atrial volume, LV = left ventricular, LVEF = left ventricular ejection fraction.

Figure legends

Figure 1: Fast semi-automated left atrial longitudinal strain. **(a)** and (**b)**, LA tracking at in cine cardiac MRI **(a)** four- and **(b)** two-chamber views. Squares denote the anatomical reference points (atrioventricular junction and mid posterior LA wall) that were tracked automatically throughout the cardiac cycle. The strain of each wall was calculated as a percentage using the presented strain formula. **(c) and (d)** Strain (ε) and strain rate (*SR*) curves. **(c)** LA strain and strain rate in a 55-year-old male patient without an event and **(d)** LA strain in a 56-year-old male patient with an event. ε_s = reservoir strain, ε_e = conduit strain, ε_a = booster strain, SR_s = reservoir strain rate, SR_e = conduit strain rate, SR_a = booster strain rate.

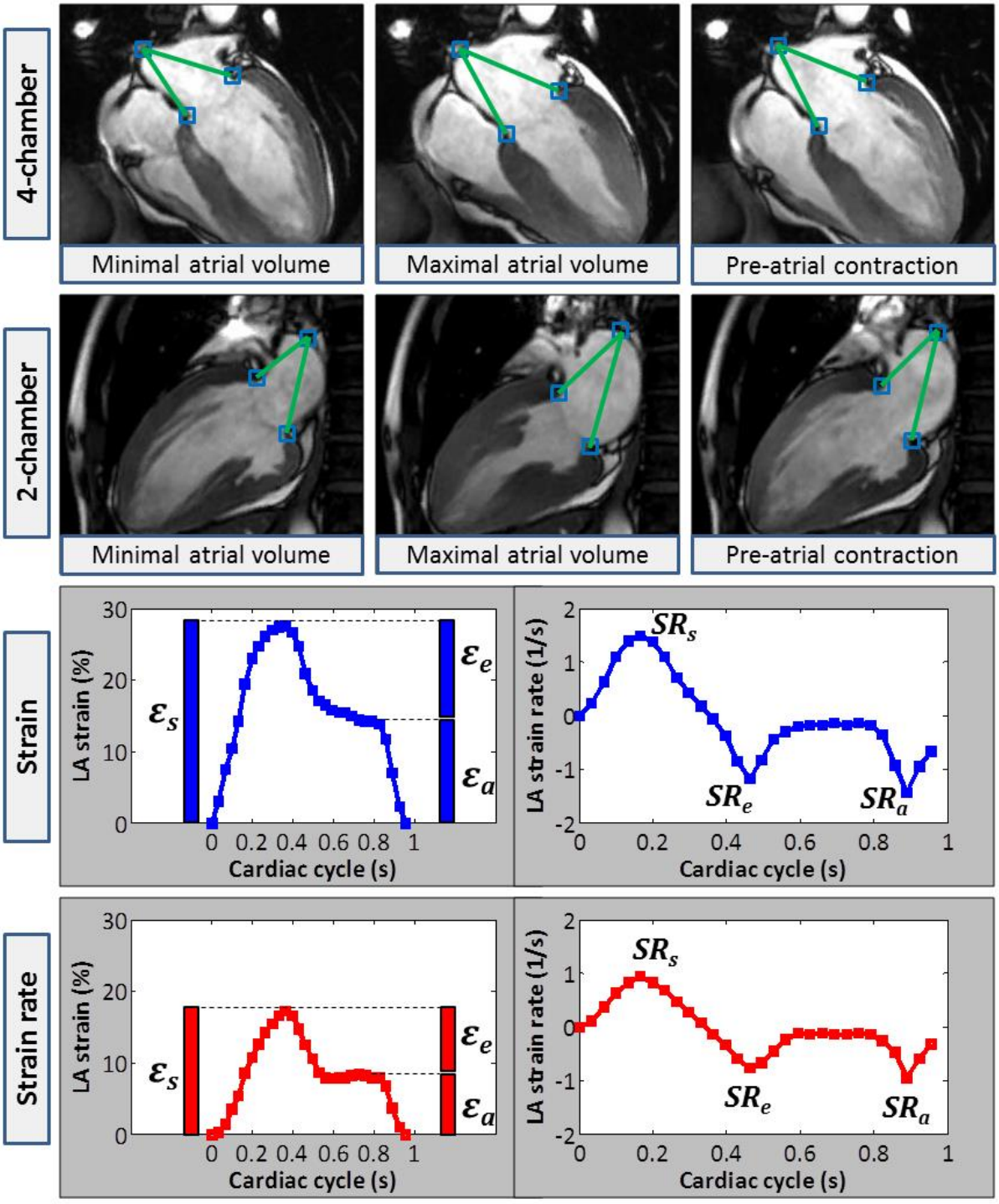
Figure 2: Study flowchart. LV = left ventricular. MACE = major adverse cardiac event.

Figure 3: Chart shows bivariate association of left atrial (LA) strain with LA volume and left ventricular (LV) longitudinal strain. ε_s = LA reservoir strain; GLS = global longitudinal strain; LAV_{max} = maximal LA volume

Figure 4: Kaplan-Meier curves representing survival free of major adverse cardiac events (MACE). Participants with (**a**) left atrial (LA) reservoir strain (ε_s) of less than or equal to 21.8% and (**b**) LA conduit strain (ε_e) of less than or equal to 10.5% displayed significantly higher risk of MACE.

Figure 5: Time-dependent receiver operating characteristic analysis for left atrial (LA) and left ventricular (LV) functional parameters. LA reservoir and conduit strains had highest integrated area under the ROC curve (AUC). $^{*}P < .05$ and $^{\dagger}P < .001$ as compared with LA reservoir and conduit strains; *P* value obtained by significance test of Uno's C statistic.

Figure 6: Receiver operating characteristic (ROC) analysis for prediction of major adverse cardiac events after 3 years. The area under the ROC curve (AUC) values for left atrial (LA) reservoir and conduit strains were significantly higher than AUCs for other indices. LV = left ventricular. $^{*}P < .05$ and $^{\dagger}P < .001$ as compared with LA reservoir and conduit strains; *P* value obtained by significance test of Uno's C statistic.



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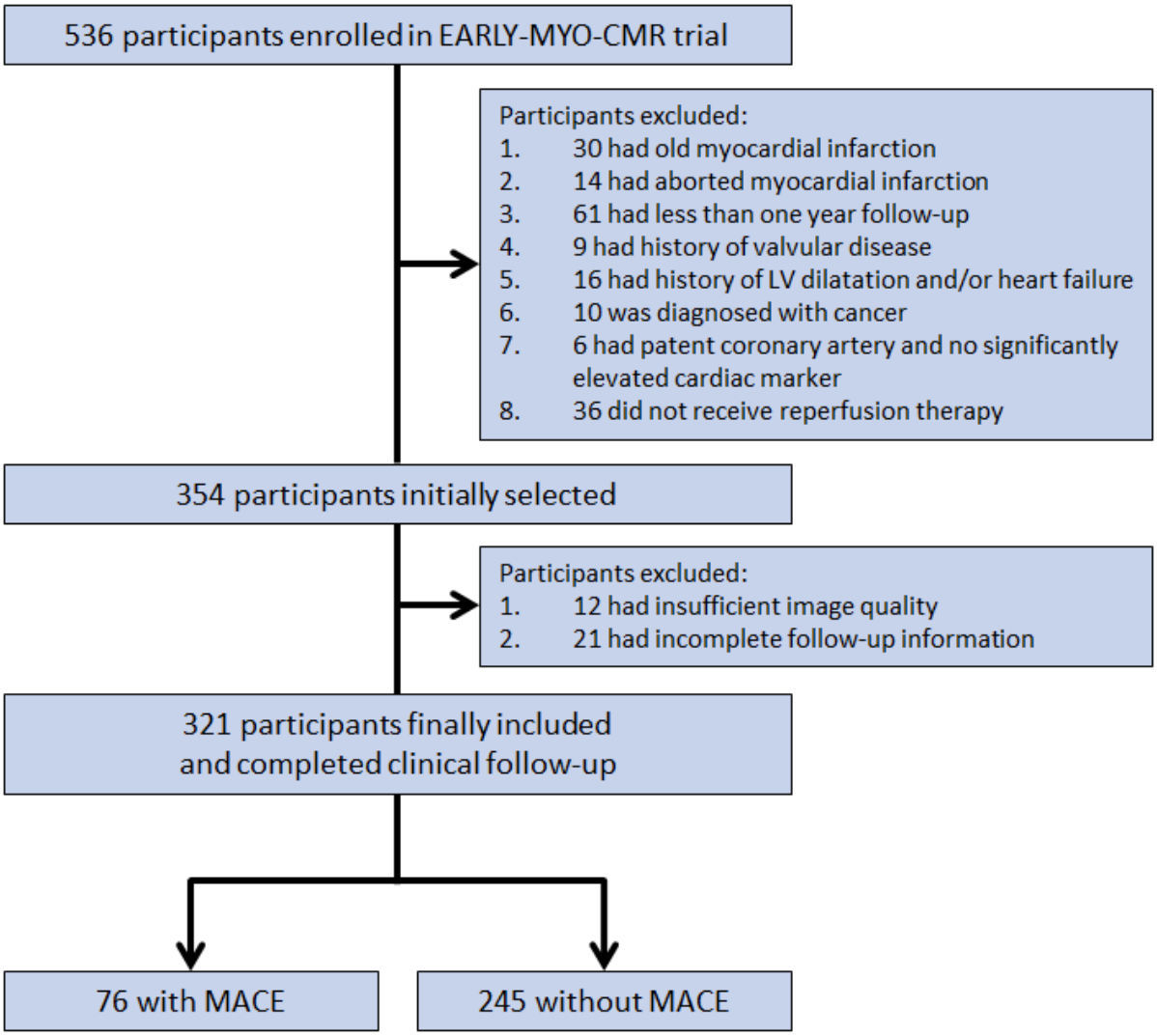

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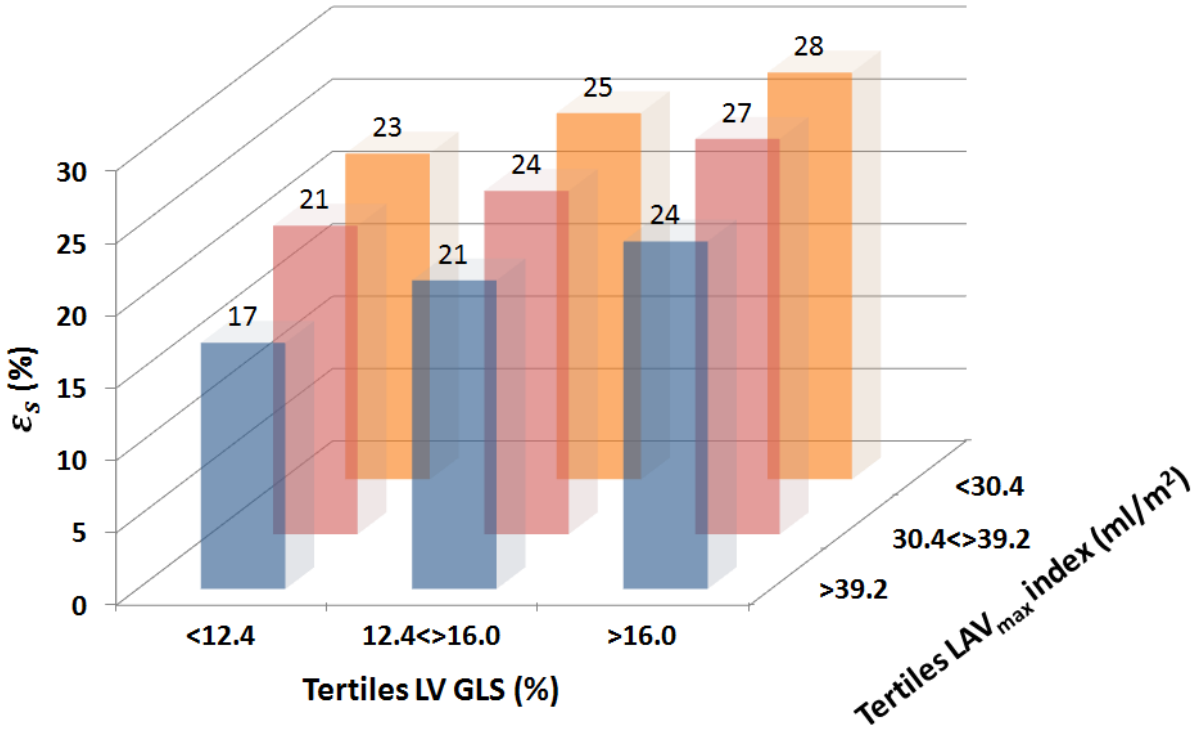

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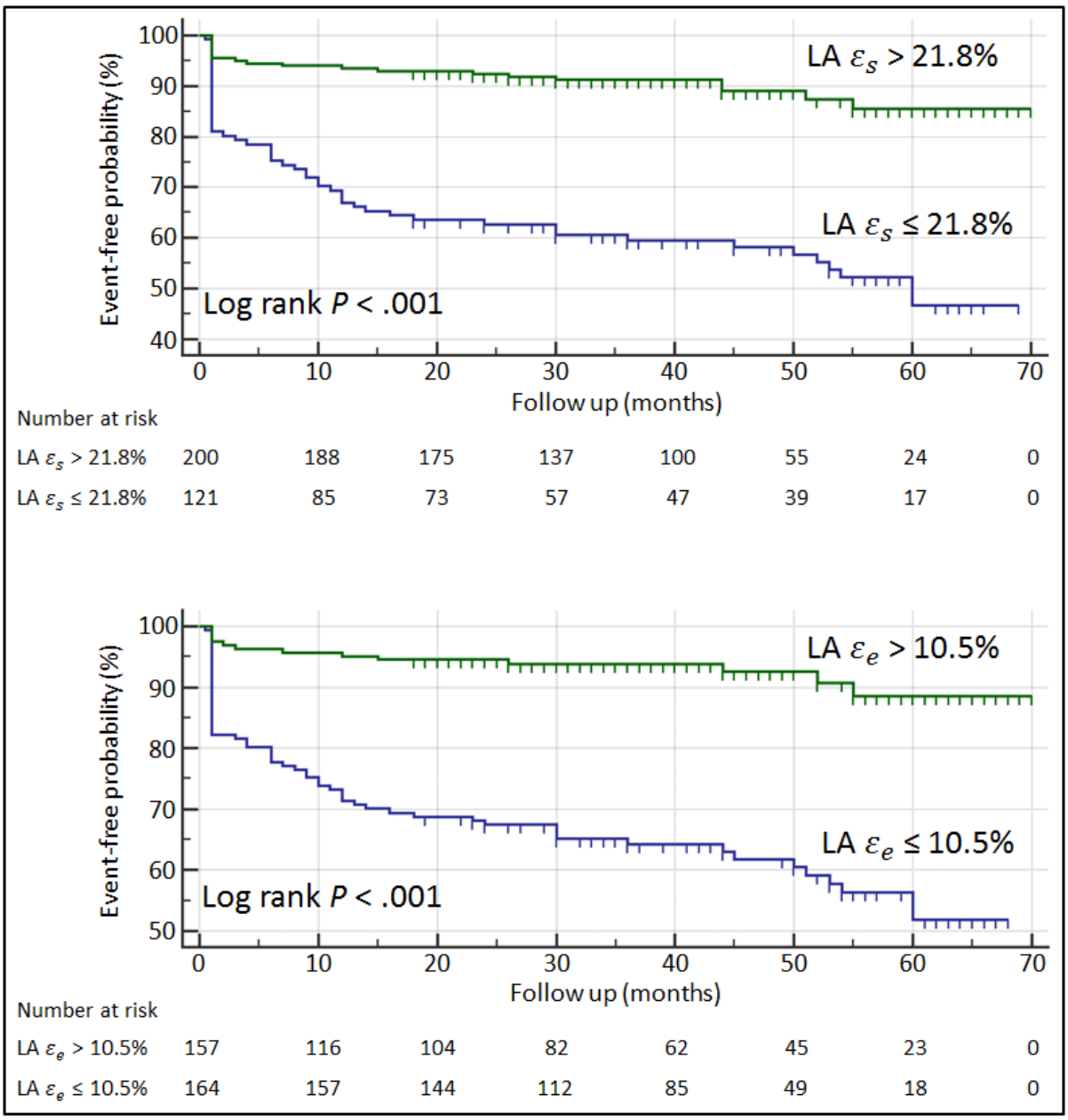

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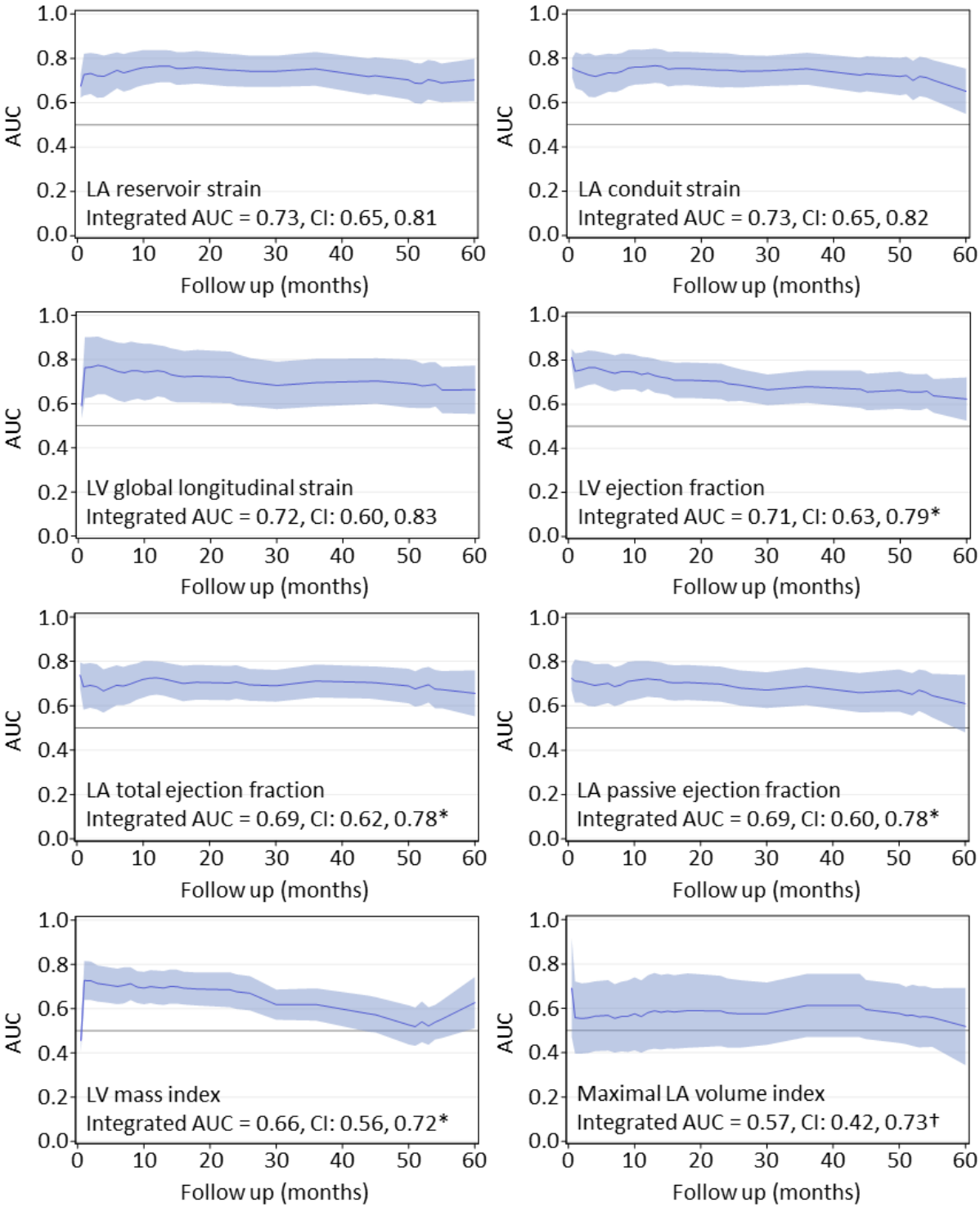

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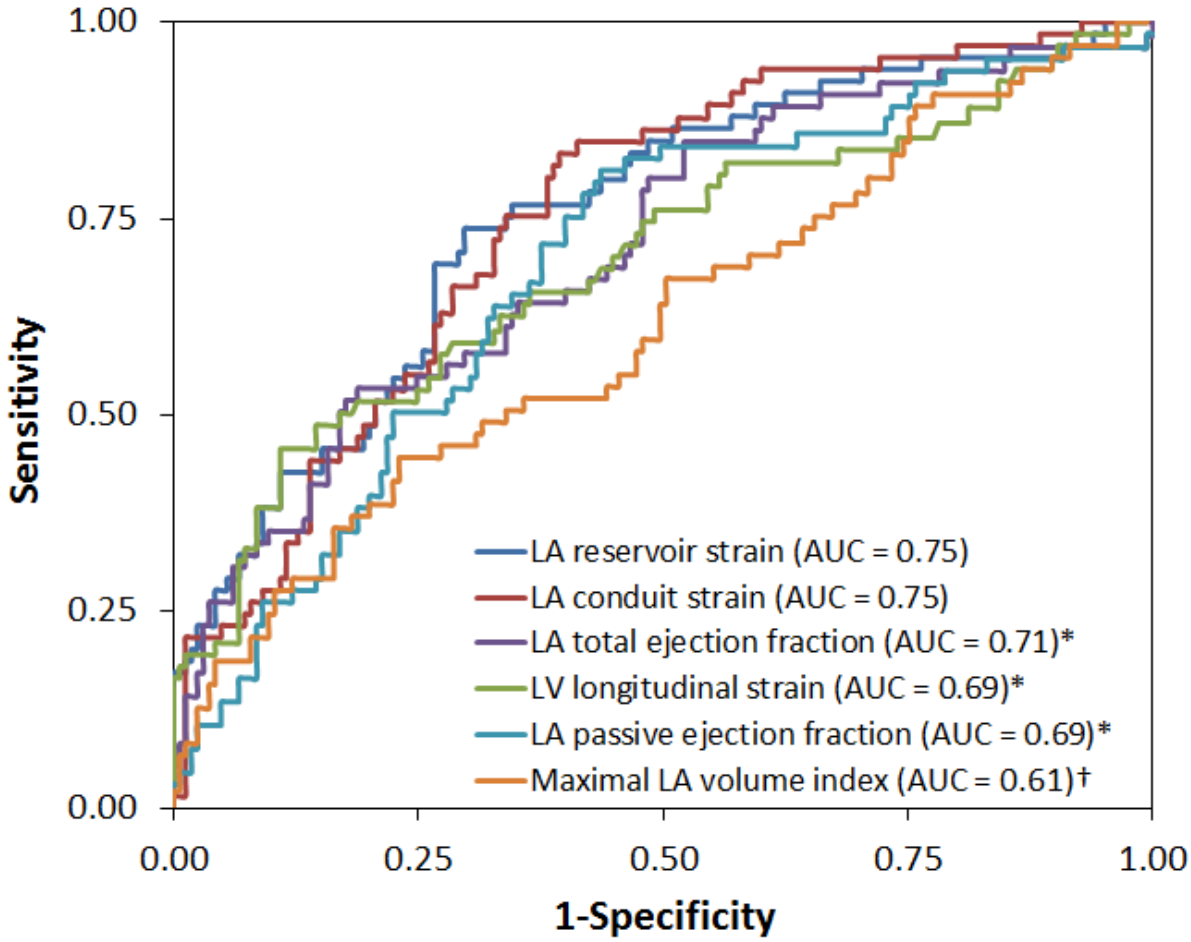

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