Prognostic Relevance of Right Ventricular Remodeling after ST-Segment Elevation Myocardial Infarction in Patients Treated With Primary Percutaneous Coronary Intervention

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ST-segment elevation myocardial infarction (STEMI) often leads to changes in right ventricular (RV) function and size over time. The prognostic implications of RV remodeling after STEMI, however, are unknown. RV remodeling in patients who underwent STEMI with primary percutaneous coronary intervention (PCI) was defined by RV end-systolic area (RV ESA) change at 6 months after STEMI compared with baseline. The optimal threshold of RV ESA change (≥40%) to define RV remodeling was derived from spline curve analysis. Long-term outcomes were compared between patients with and without RV remodeling. A total of 2,280 patients were analyzed (mean age 60 ± 11 years, 76% were men). RV remodeling was present in 315 patients (14%). After a median follow-up of 76 months (interquartile range 51 to 106 months), 271 patients (12%) died (primary end point) and the composite end point of all-cause mortality and HF hospitalization (secondary end point) was observed in 292 patients (13%). After adjustment for various risk factors, including tricuspid annular plane systolic excursion (TAPSE), post-STEMI RV remodeling was independently associated with a higher risk of all-cause mortality (hazard ratio [HR] = 1.44, 95% confidence interval [CI] 1.02 to 2.02, p = 0.038) and the composite of all-cause mortality and HF hospitalization (HR = 1.41, 95% CI 1.02 to 1.96, p = 0.040). Finally, patients with RV remodeling had a significantly lower survival rate (Log-rank, p = 0.006) and event-free survival rate than those without RV remodeling during follow-up (log-rank, p = 0.006). RV post-infarct remodeling is associated with mortality and HF hospitalization, independent of RV systolic function. **(Am J Cardiol 2022;170:1−9)**

Abbreviations: STEMI, ST-segment elevation myocardial infarction; RV remodeling, right ventricular remodeling; HF hospitalization, Heart failure hospitalization

Right ventricular (RV) involvement in ST-segment elevation myocardial infarction (STEMI) develops in around 20% of patients after infarct,[1] reaching 50% in inferior STEMIs.[2] The right coronary artery (RCA) supplies most of the RV myocardium,[3] and proximal occlusion of this vessel affects the RV during an inferior STEMI.[4] Occlusion of the left anterior descending (LAD) coronary artery, however, can also impact on the RV with an anterior STEMI.[5] RV systolic dysfunction is commonly observed after STEMI, despite the use of primary percutaneous coronary intervention (PCI),[6,7] but usually recovers over time.[7,8] Despite gradual improvement of RV systolic function after infarct, RV involvement in STEMI is associated with worse long-term prognosis.[9,10] Although the evolution of RV function (when the blood supply of this chamber depends mostly on the culprit coronary vessel) has been well described, RV post-infarct remodeling has been less well defined. The prognostic implications of RV remodeling after STEMI have never been described before. Therefore, in the present study, we investigated the incidence of post-infarct RV remodeling and its impact on all-cause mortality and the composite of all-cause mortality and heart failure (HF) hospitalization using data from a large, contemporary registry of patients with STEMI who were treated with primary PCI and guideline-directed medical therapy.

Methods

Patients admitted with STEMI at the Leiden University Medical Center from September 2004 to December 2019 were included in an ongoing registry.[11] All patients

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underwent primary PCI and were treated with guideline-directed medical therapy according to a standardized institutional protocol, which is based on contemporary European Society of Cardiology guidelines.[12] Patients were followed up for the primary end point of all-cause mortality and the secondary end point of all-cause mortality and HF hospitalization. Survival data were collected from the departmental information system (EPD-Vision), which is linked to municipal registries; whereas data on HF hospitalization were acquired by review of medical records, which were archived in the previously mentioned departmental information system. HF hospitalization was defined as admission for worsening HF, which required intensification of intravenous diuretic therapy or device therapy implantation, specifically for HF. All data used in the present study were collected for routine clinical purposes and handled anonymously. The requirement of written informed consent was waived by the institutional review board on a patient level due to the retrospective design of the study.

According to the institutional protocol, all patients underwent transthoracic echocardiography within 48 h of admission, as well as at 3-, 6-, and 12-month follow-up visits. Patients underwent imaging in the left lateral decubitus position using a commercially available echocardiography system (Vivid 7, E9 and E95, GE Vingmed Ultrasound, Horten, Norway). M-mode and 2-dimensional (2D) images were obtained and saved in cine-loop format. Echocardiographic loops were digitally archived for offline analysis (EchoPac 202 and 203, GE Vingmed Ultrasound, Horten, Norway). The RV end-diastolic area (RV EDA) and end-systolic area (RV ESA) were measured on the RV-focused apical 4-chamber view by manual tracing of the RV endocardial border.[13] Tricuspid annular plane systolic excursion (TAPSE) was measured from the M-mode trace by positioning the cursor along the direction of the tricuspid lateral annulus.[13] Left ventricular (LV) ejection fraction (EF) was calculated by using the biplane Simpson method.[13]

RV remodeling was defined by an increase in RV ESA at 6 months after STEMI compared with baseline. The optimal threshold of RV ESA increases to define RV remodeling was derived from spline curve analysis, where the hazard ratio (HR) was greater than 1 (Figure 1). Based on the optimal threshold value of ≥40% RV ESA increase, the study population was dichotomized into those with and without RV post-infarct remodeling.

Continuous variables are presented as mean ± standard deviation when normally distributed (assessed by the Shapiro-Wilk test and distribution histograms) and as median (and interquartile range [IQR]), when not normally distributed. Categoric variables are presented as frequencies and percentages. Differences in continuous variables across the RV remodeling groups were evaluated using independent samples *t* tests (and Mann-Whitney *U* tests when indicated), whereas differences in categoric variables were compared using chi-square tests (and Fisher's exact tests when indicated). Changes in RV and right atrial (RA) dimensions and function between baseline and 6 months after STEMI were evaluated by linear mixed models with random intercepts. Survival analysis, including estimation of mean survival time and event-free survival time, was performed with the Kaplan-Meier method

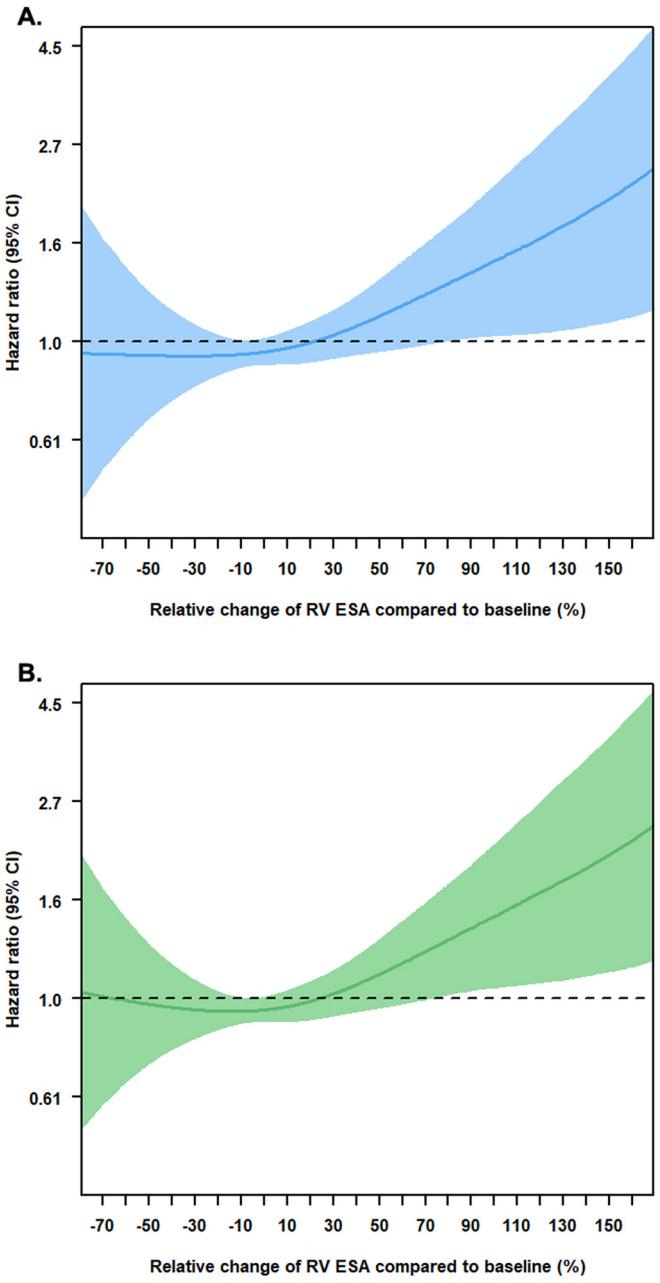

Figure 1. Spline curves for all-cause mortality (A) and the composite of all-cause mortality and HF hospitalization (B) across a range of relative change in RV ESA, plotted as a hazard ratio with overlaid 95% confidence intervals. HF, heart failure; RV ESA, right ventricular end-systolic area.

and differences across the functional RV remodeling groups were compared using log-rank tests. Univariable and multivariable Cox proportional hazard regression analyses were used to determine the relation between individual variables and the study end points. All continuous variables were assessed per 1 unit change in each variable. Multivariable analysis included variables, which showed a significant association (p value <0.05) on univariable analysis. All statistical tests were 2-sided, and a p value of <0.05 was considered to be statistically significant. Statistical analysis was performed using SPSS for Windows

Table 1
Baseline patient characteristics

	Overall population (n=2280)	RV remodelers (n=315)	Non-RV remodelers (n=1965)	p-value
Age (years)	60±11	61±11	60±11	0.980
Male	1742 (76%)	237 (75%)	1505 (77%)	0.600
BMI (kg/m^2)	27±3.9	27±3.9	26±3.9	0.148
BSA (m^2)	1.99±0.21	1.99±0.21	1.99±0.21	0.618
Current smoker	1052 (46%)	135 (43%)	917 (47%)	0.238
Ex-smoker	282 (12%)	30 (10%)	252 (13%)	0.101
Hypertension	805 (35%)	123 (39%)	682 (35%)	0.111
Hyperlipidemia	462 (20%)	72 (23%)	390 (20%)	0.198
Family history of CAD	978 (43%)	127 (41%)	851 (44%)	0.362
DM	205 (9%)	44 (14%)	161 (8%)	0.001
Previous MI	147 (6%)	30 (10%)	117 (6%)	0.017
Killip class ≥ 2	99 (4%)	17 (5%)	82 (4%)	0.322
Peak TnI (ng/ml)	3.4 (1.4; 7.1)	4.1 (1.5; 8.7)	3.3 (1.3; 6.9)	0.011
eGFR (ml/min/1.73m^2)	86±18	86±18	86±18	0.777
Culprit vessel				
LMCA/LAD	1021 (45%)	176 (56%)	845 (43%)	<0.001
LCx	359 (16%)	47 (15%)	312 (16%)	0.665
RCA	883 (39%)	89 (28%)	794 (40%)	<0.001
Multivessel disease	1203 (53%)	159 (51%)	1044 (53%)	0.376
Discharge heart rate (bpm)	70±12	72±12	69±12	<0.001
Discharge SBP (mmHg)	115±16	115±17	115±16	0.659
Discharge DBP (mmHg)	70±11	70±11	69±11	0.263
DAPT	2209 (97%)	301 (96%)	1908 (97%)	0.237
ACEi/ARB	2217 (97%)	305 (97%)	1912 (97%)	0.824
Statin	2265 (99%)	312 (99%)	1953 (99%)	0.867
Beta-blocker	2154 (95%)	299 (95%)	1855 (95%)	0.575
LVEF (%)	49±9.8	47±11	49±9.6	<0.001
E/e' at baseline	11.8±4.8	12.1±5.9	11.8±4.6	0.256
RA area (cm^2)	14±3.9	12±3.7	14±3.9	<0.001
TAPSE (mm)	20±3.8	19±3.7	20±3.8	0.053
RV EDA (cm^2)	17±4.8	14±4.4	17±4.7	<0.001
RV ESA (cm^2)	9.0±3.5	7.0±2.3	9.5±3.5	<0.001

Values are mean ± SD = n (%), or median (IQR).

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BMI = body mass index; BSA = body surface area; CAD = coronary artery disease; DAPT = dual-antiplatelet therapy; DBP = diastolic blood pressure; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; LAD = left anterior descending coronary artery; LCx = left circumflex artery; LMCA = left main coronary artery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; RA = right atrium; RCA = right coronary artery; RV = right ventricular; RV EDA = RV end-diastolic area; RV ESA = RV end-systolic area; SBP = systolic blood pressure; TAPSE = tricuspid annular plane systolic excursion; TnI = troponin I.

version 25.0 (IBM Corporation, Armonk, New York) and R version 4.0.0 (R Foundation for Statistical Computing, Vienna, Austria) using following packages: ggplot2 package v3.3.2, survival package v3.1-12, and splines2 package v0.3.1.

Results

A total of 2,280 patients (mean age 60 ± 11, 76% were men) with STEMI and complete echocardiographic data at baseline and 6 months of follow-up were included in the present study. RV remodeling, defined as an increase in RV ESA of ≥40%, occurred in 315 patients (14%), whereas 1,965 patients (86%) did not experience RV remodeling at 6 months after STEMI. Baseline characteristics of the study population are summarized in Table 1. The left main coronary artery (LMCA) or LAD were more frequent culprit vessels in patients with RV remodeling than patients without RV remodeling (56% vs 43%, p <0.001). In contrast, the RCA was less likely to be the culprit vessel in patients with RV remodeling compared with patients without RV remodeling (28% vs 40%, p <0.001). The prevalence of diabetes mellitus (14% vs 8%, p = 0.001) and previous MI (10% vs 6%, p = 0.017) was significantly higher in patients with RV remodeling. Myocardial damage, as assessed by troponin I, was higher (4.1 vs 3.3 ng/ml, p = 0.011); and LV systolic function, as assessed by LVEF, was more impaired (47 ± 11% vs 49 ± 9.6%, p <0.001) in patients with RV remodeling than patients without RV remodeling. LV diastolic function, as assessed by E/e' ratio at baseline, was comparable between RV remodelers and non-RV remodelers (12.1 ± 5.9 vs 11.8 ± 4.6, p = 0.256), whereas it was more impaired in RV remodelers than non-RV remodelers at 6 months after STEMI (14.2 ± 8.2 vs 12.0 ± 6.0, p <0.001). The prevalence of LV post-infarct remodeling was significantly higher in patients with RV remodeling (35% vs 28%, p = 0.015).

At baseline, patients with RV remodeling had smaller RV EDA (14 ± 4.4 cm^2 vs 17 ± 4.7 cm^2, p <0.001) (Figure 2A, Table 1), RV ESA (7.0 ± 2.3 cm^2 vs 9.5 ± 3.5

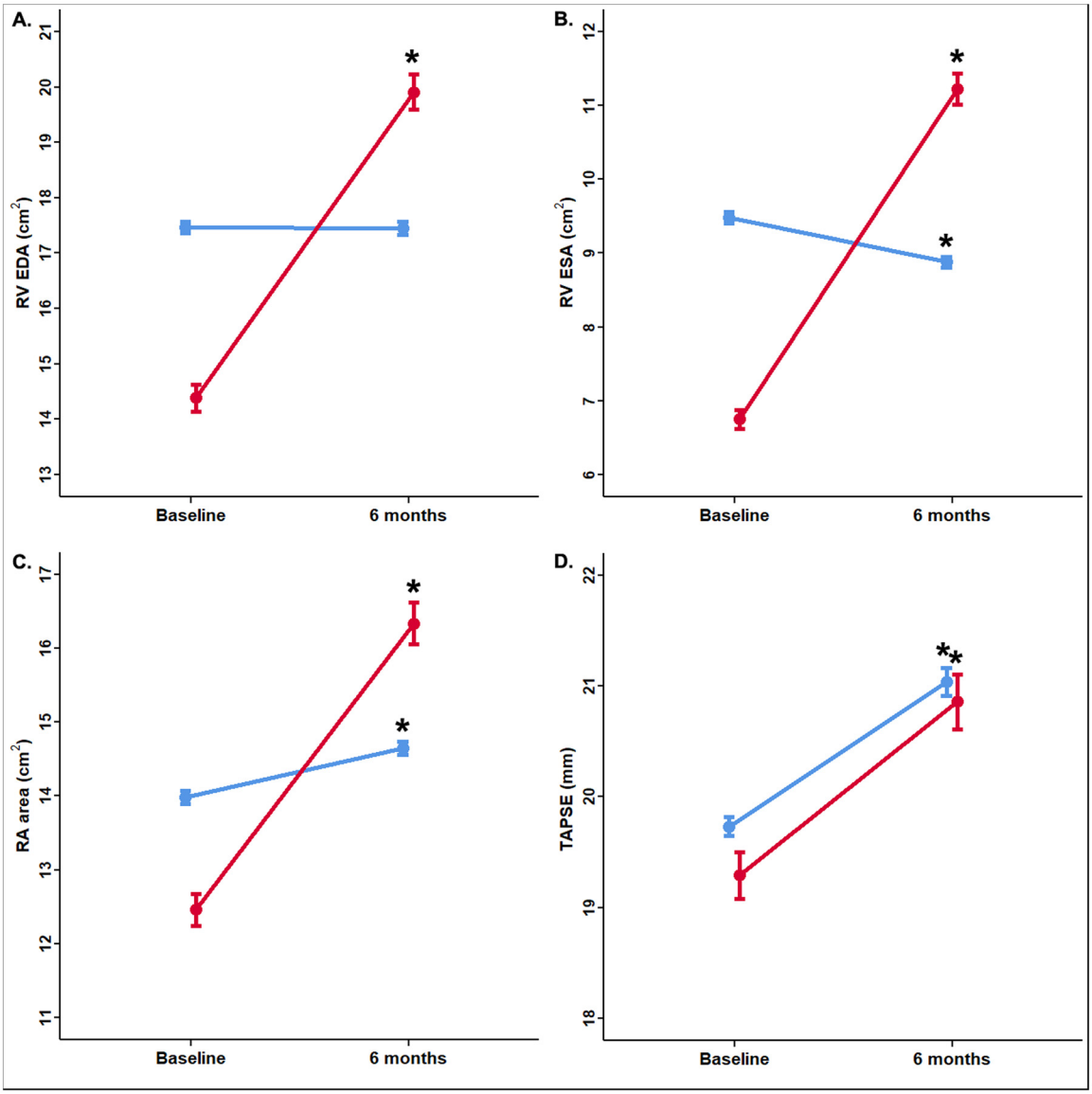

Figure 2. Changes from baseline to 6 months in RV EDA (A), RV ESA (B), RA area (C) and TAPSE (D) in patients with RV remodeling (red line) and without RV remodeling (blue line). *p <0.001 compared with baseline. Data are presented as mean ± SE. RA, right atrial; RV, right ventricular; RV EDA, RV end-diastolic area; RV ESA, RV end-systolic area; TAPSE, tricuspid annular plane systolic excursion; SE, standard error of the mean.

cm^2, p <0.001) (Figure 2B, Table 1), and RA areas (12 ± 3.7 vs 14 ± 3.9, p <0.001) (Figure 2C, Table 1) than patients without RV remodeling; whereas there was no significant difference between patients with and without RV remodeling in terms of RV function, as assessed by TAPSE (19 ± 3.7 mm vs 20 ± 3.8 mm, p = 0.053) (Figure 2D, Table 1). From baseline to 6 months of follow-up, RV EDA significantly increased in patients with RV remodeling (14 vs 20 cm^2, p <0.001), whereas RV EDA was unchanged in patients without RV remodeling (17 vs 17 cm^2, p = 0.837) (Figure 2A). RV ESA was significantly increased in patients with RV remodeling (7 vs 11 cm^2, p <0.001) and significantly reduced in patients without RV remodeling (9.5 vs 9 cm^2, p <0.001) (Figure 2B). The RA area was significantly increased in both RV remodelers (12 vs 16 cm^2, p <0.001) and non-RV remodelers (14 vs 15 cm^2, p <0.001) (Figure 2C). RV function, as assessed by TAPSE, significantly improved in both groups (19 vs 21 mm, p <0.001 for RV remodeling and 20 vs 21 mm, p <0.001 for no RV remodeling) 6 months after STEM (Figure 2D).

After a median follow-up of 76 (IQR 51 to 106) months, 271 patients (12%) died (primary end point). The mortality rate was significantly higher (16%) in patients with RV remodeling than patients without RV remodeling (11%) (p = 0.030). Cumulative event rates for all-cause mortality at 120 months were 23% and 17% for patients with and without RV remodeling, respectively. The RV remodeling group had a significantly lower survival rate than the nonremodeling group (log-rank p = 0.006) (Figure 3A). After stratification according to RV remodeling subgroups, (1) non-RV remodeling (relative change in RV ESA ≤0%), (2) small-to-moderate RV remodeling (relative change in RV ESA 1% to 40%), and (3) large RV remodeling (relative change in RV ESA ≥40%), large RV remodelers

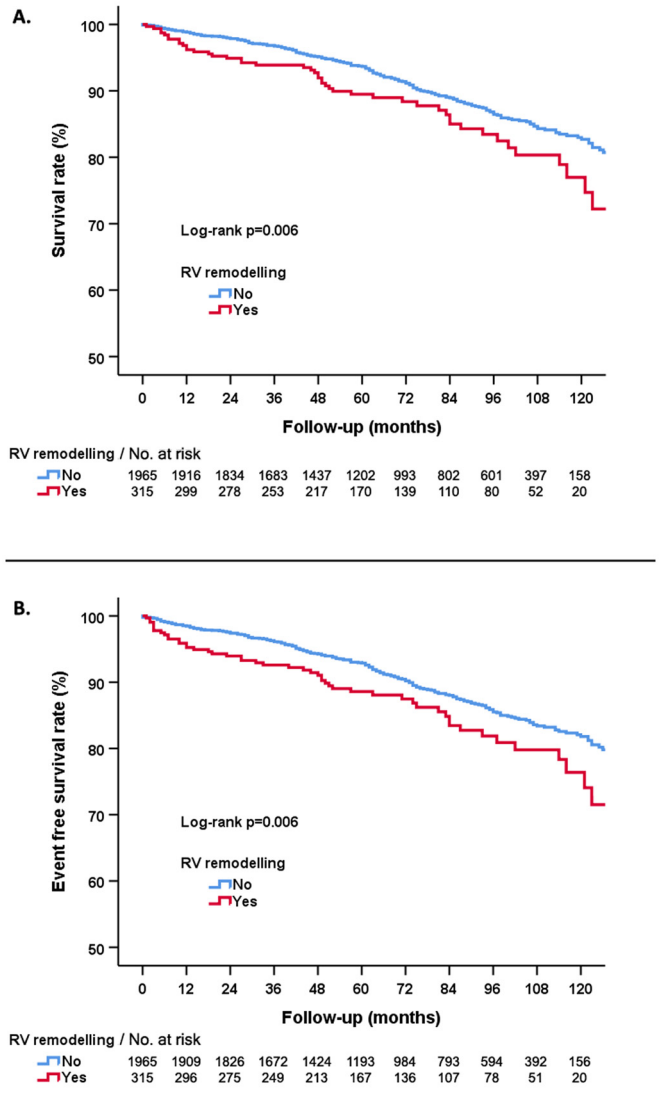

Figure 3. Kaplan-Meier curves for all-cause mortality (A) and the composite of all-cause mortality and HF hospitalization (B), stratified according to RV remodeling groups. HF, heart failure; RV, right ventricular.

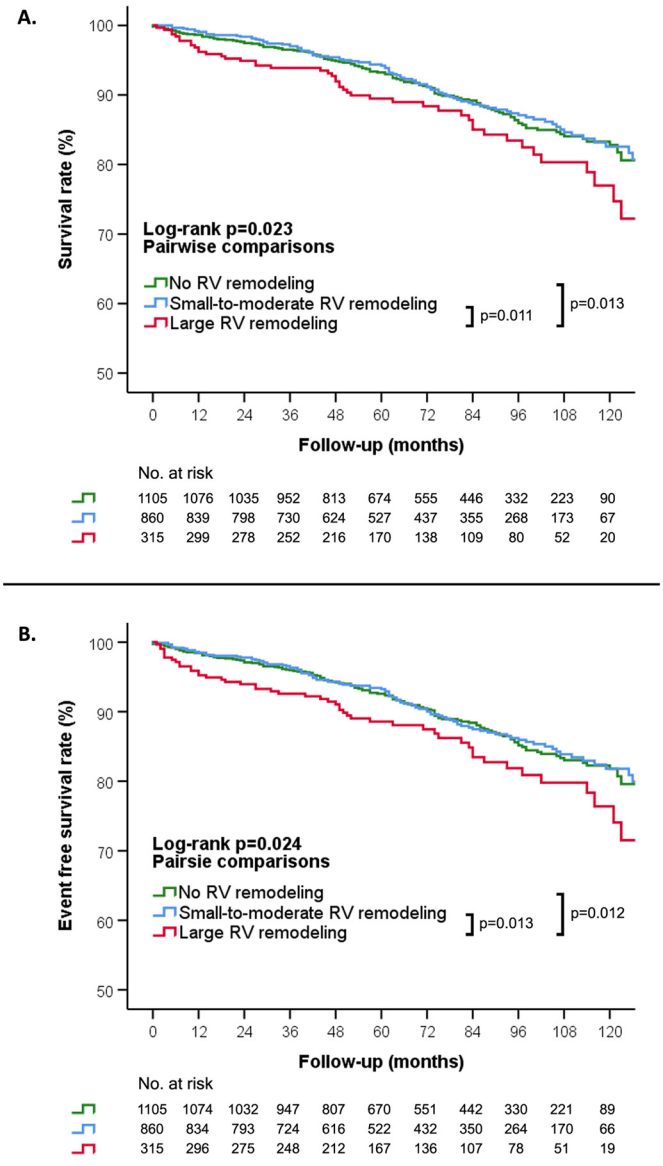

Figure 4. Kaplan-Meier curves for all-cause mortality (A) and the composite of all-cause mortality and HF hospitalization (B), stratified according to RV remodeling subgroups, namely: (1) no RV remodeling (relative change in RV ESA ≤0%), (2) small-to-moderate RV remodeling (relative change in RV ESA 1% to 40%), and (3) large RV remodeling (relative change in RV ESA ≥40%). ESA, end-systolic area; HF, heart failure; RV, right ventricular.

experienced a significantly lower survival rate than the other subgroups (log-rank p = 0.011 and p = 0.013 for large RV remodelers vs small-to-moderate RV remodelers and non-RV remodelers, respectively) (Figure 4A). The association between RV remodeling and all-cause mortality was investigated by univariable and multivariable Cox regression models (Table 2). RV remodeling was significantly associated with a higher risk of all-cause mortality in univariable analysis (HR = 1.54, 95% confidence interval [CI] 1.13 to 2.09, p = 0.007) and independently associated on multivariable analysis (HR = 1.44, 95% CI 1.02 to 2.02, p = 0.038) (Table 2).

After a median follow-up of 75 (IQR 50 to 106) months, the composite of all-cause mortality and HF hospitalization (secondary end point) was observed in 292 patients (13%) and was greater (17%) in those with RV remodeling than those without (12%) (p = 0.034). The cumulative event rate for the composite of all-cause mortality and HF hospitalization at 120 months was 24% and 18% for patients with and without RV remodeling, respectively. RV remodelers had a significantly lower event-free survival rate than non-remodelers (log-rank p = 0.006) (Figure 3B). Subgroup analysis according to the magnitude of RV remodeling demonstrated that large RV remodelers had a significantly lower event-free survival than other groups (log-rank p = 0.013 and p = 0.012 for large RV remodelers vs small-to-moderate RV remodelers and non-RV remodelers, respectively) (Figure 4B). RV remodeling was significantly associated with a higher risk of experiencing the composite end point of all-cause mortality and HF hospitalization in both univariable and multivariable Cox regression

Table 2
Univariable and multivariable Cox regression analyses for all-cause mortality

	Univariable analysis			Multivariable analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
Age (years)	1.09	1.08-1.10	<0.001	1.07	1.05-1.09	<0.001
Male	0.85	0.65-1.11	0.238			
BSA (m^2)	0.27	0.15-0.48	<0.001	0.94	0.47-1.87	0.849
Current smoker	0.85	0.67-1.08	0.179			
Ex-smoker	1.25	0.88-1.78	0.213			
Hypertension	1.29	1.01-1.65	0.041	0.92	0.70-1.22	0.557
Hyperlipidemia	1.00	0.74-1.35	0.990			
Family history of CAD	0.60	0.47-0.78	<0.001	0.92	0.69-1.22	0.549
DM	2.28	1.67-3.13	<0.001	1.61	1.13-2.30	0.008
Previous MI	2.46	1.76-3.45	<0.001	1.67	1.15-2.44	0.007
Killip class ≥ 2	2.54	1.69-3.81	<0.001	1.21	0.76-1.93	0.424
Peak TnI (ng/ml)	1.04	1.02-1.06	<0.001	1.03	1.01-1.05	0.012
eGFR (ml/min/1.73m^2)	0.97	0.97-0.98	<0.001	1.00	0.99-1.01	0.419
LMCA/LAD culprit vessel	0.95	0.74-1.20	0.645			
Multivessel disease	1.66	1.29-2.12	<0.001	1.06	0.80-1.41	0.679
Discharge heart rate (bpm)	1.02	1.01-1.03	<0.001	1.01	1.00-1.03	0.018
Discharge SBP (mmHg)	1.00	0.99-1.01	0.533			
Discharge DBP (mmHg)	0.98	0.97-0.99	0.003	0.99	0.98-1.00	0.065
DAPT	0.59	0.35-0.99	0.045	0.75	0.41-1.38	0.357
ACEi/ARB	0.37	0.22-0.63	<0.001	1.14	0.57-2.29	0.703
Statin	0.62	0.15-2.49	0.500			
Beta-blocker	0.85	0.52-1.39	0.524			
E/e'	1.07	1.04-1.09	<0.001	1.01	0.99-1.04	0.286
RA area (cm^2) at 6 months	0.99	0.96-1.03	0.695			
TAPSE (mm) at 6 months	0.91	0.88-0.94	<0.001	0.96	0.92-0.99	0.015
RV remodeling	1.54	1.13-2.09	0.007	1.44	1.02-2.02	0.038

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BMI = body mass index; BSA = body surface area; CAD = coronary artery disease; CI = confidence interval; DAPT = dual-antiplatelet therapy; DBP = diastolic blood pressure; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; HR = hazard ratio; LAD = left anterior descending coronary artery; LCx = left circumflex artery; LMCA = left main coronary artery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; RA = right atrium; RCA = right coronary artery; RV = right ventricular; RV EDA = RV end-diastolic area; RV ESA = RV end-systolic area; SBP = systolic blood pressure; TAPSE = tricuspid annular plane systolic excursion; TnI = troponin I.

models (HR = 1.51, 95% CI 1.12 to 2.04, p = 0.007 and HR = 1.41, 95% CI 1.02 to 1.96, p = 0.040, respectively) (Table 3).

Discussion

The key findings from the present study of patients with STEMI are that: (1) the incidence of adverse RV remodeling, based on RV ESA at 6 months after infarct, is fairly low (14%) in the modern era of primary PCI; and (2) the presence of adverse RV post-infarct remodeling is independently associated with worse long-term outcomes.

A STEMI involving the LV inferior wall is often associated with post-infarct RV functional impairment.[4,14] Revascularization of the culprit vessel by means of primary PCI has dramatically improved RV function after infarct.[7,15,16] In a study consisting of 53 patients with inferior MI who were treated by primary PCI, RV function fully recovered in those patients in whom complete reperfusion of the vessel was achieved.[15] In the Survival And Ventricular Enlargement trial,[16] in which thrombolysis or primary PCI were utilized for emergent revascularization, RV function (measured by radionuclide ventriculography at 10 to 11 days after MI) was preserved in the majority of patients with an inferior MI. In a cohort of 940 patients with STEMI treated with primary PCI, RV systolic dysfunction (defined as a TAPSE ≤15 mm) was documented in 15% of patients, although RV function recovered in more than half of them by 6 months after STEMI.[7] The rapid and often complete recovery of RV function after STEMI has been attributed to the RV's unique resistance to ischemia, which is the result of a more favorable oxygen supply-demand relation than that of the LV. The RV has a lower mass than the LV and is subject to a lower afterload. Additionally, extensive collaterals are often present and perfusion occurs in both systole and diastole.[17]

Regardless of the recovery of RV systolic function after STEMI, RV adverse remodeling (defined as an increase in RV EDA by 20%) was still observed in 25% of individuals at 6 months after the index event in a study by Hoogslag et al.[7] By using computed tomography, Hirose and colleagues evaluated changes in RV volume over time in patients with STEMI who were treated with primary PCI or thrombolysis.[18] The RV end-diastolic and end-systolic volumes significantly increased from hospital discharge to 1 year after MI in patients with an anterior MI, whereas neither RV end-diastolic or end-systolic volumes increased significantly in those with inferior MIs. These findings suggest that post-MI RV remodeling is more likely to occur in the presence of an anterior infarct. Accordingly, in the present study, patients with adverse RV remodeling had a significantly higher prevalence of LMCA/LAD culprit vessels

Table 3
Univariable and multivariable Cox regression analyses for the composite of all-cause mortality and HF hospitalization

	Univariable analysis			Multivariable analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
Age (years)	1.08	1.07-1.09	<0.001	1.06	1.05-1.08	<0.001
Male	0.88	0.68-1.14	0.333			
BSA (m^2)	0.30	0.17-0.53	<0.001	1.01	0.52-1.97	0.974
Current smoker	0.84	0.66-1.06	0.131			
Ex-smoker	1.26	0.90-1.76	0.183			
Hypertension	1.24	0.98-1.57	0.073	0.90	0.69-1.18	0.447
Hyperlipidemia	1.00	0.75-1.34	0.987			
Family history of CAD	0.64	0.50-0.81	<0.001	0.93	0.70-1.22	0.592
DM	2.21	1.62-3.00	<0.001	1.59	1.13-2.24	0.008
Previous MI	2.59	1.88-3.58	<0.001	1.83	1.28-2.62	0.001
Killip class ≥ 2	2.37	1.58-3.55	<0.001	1.18	0.75-1.88	0.474
Peak TnI (ng/ml)	1.05	1.03-1.07	<0.001	1.04	1.02-1.06	<0.001
eGFR (ml/min/1.73m^2)	0.98	0.97-0.98	<0.001	1.00	0.99-1.01	0.881
LMCA/LAD culprit vessel	0.98	0.78-1.23	0.847			
Multivessel disease	1.64	1.30-2.09	<0.001	1.07	0.82-1.40	0.619
Discharge heart rate (bpm)	1.02	1.01-1.03	<0.001	1.01	1.00-1.03	0.010
Discharge SBP (mmHg)	1.00	0.99-1.00	0.386			
Discharge DBP (mmHg)	0.98	0.97-0.99	0.003	0.99	0.98-1.00	0.048
DAPT	0.58	0.35-0.95	0.031	0.72	0.40-1.30	0.275
ACEi/ARB	0.38	0.23-0.64	<0.001	1.02	0.53-1.96	0.961
Statin	0.41	0.13-1.28	0.125			
Beta-blocker	0.93	0.57-1.52	0.775			
E/e'	1.07	1.05-1.09	<0.001	1.02	1.00-1.04	0.098
RA area (cm^2) at 6 months	1.00	0.97-1.03	0.891			
TAPSE (mm) at 6 months	0.91	0.88-0.94	<0.001	0.96	0.92-0.99	0.009
RV remodeling	1.51	1.12-2.04	0.007	1.41	1.02-1.96	0.040

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BMI = body mass index; BSA = body surface area; CAD = coronary artery disease; CI = confidence interval; DAPT = dual-antiplatelet therapy; DBP = diastolic blood pressure; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; HR = hazard ratio; LAD = left anterior descending coronary artery; LCx = left circumflex artery; LMCA = left main coronary artery; LVEF = left ventricular ejection fraction; MI = myocardial infarction; RA = right atrium; RCA = right coronary artery; RV = right ventricular; RV EDA = RV end-diastolic area; RV ESA = RV end-systolic area; SBP = systolic blood pressure; TAPSE = tricuspid annular plane systolic excursion; TnI = troponin I.

and/or anterior MI (56% vs 43%, p <0.001) than those without.

In the present study, patients who underwent STEMI with primary PCI and who were treated with guideline-directed medical therapy were included. Regardless of the near-universal prescription of β-blockers (95% of patients) and angiotensin-converting enzyme inhibitors (ACEi)/angiotensin-receptor blockers (ARB) (97% of patients), RV remodeling developed in 315 patients (14%) and the presence of RV remodeling was significantly associated with worse outcome. This may identify an opportunity for RV-directed treatment to attenuate the detrimental effects of adverse RV remodeling after infarct.

The evidence underpinning the beneficial effects of anti-remodeling drugs on the RV is mostly derived from preclinical animal studies and small human studies and originate outside of the post-infarct context.[19,20] Boogaard et al studied the effect of adrenergic receptor blockade with carvedilol in an animal model of pulmonary hypertension, demonstrating RV reverse remodeling and improved RV systolic function.[19] The effects of carvedilol on RV remodeling were also investigated in a study of patients with chronic stable HF with systemic RVs by Giardini et al.[20] After 12 months of treatment with carvedilol, RV end-diastolic and end-systolic volumes were significantly reduced on CMR. The benefit of ACEi/ARB treatment in patients with RV failure is often ascribed to the LV effects, and it is largely unknown if such drugs have an independent effect on RV function and structure. A meta-analysis investigating the effect of ACEi/ARB therapy in patients with RV dysfunction demonstrated no significant impact of these drugs on RV end-diastolic and end-systolic volumes.[21]

RV remodeling may cause displacement of the interventricular septum, which in turn decreases LV compliance and impairs LV filling due to ventricular interdependence. Decreased LV filling leads to a reduction of overall cardiac output.[22] RV volume reduction could therefore be a therapeutic target in those patients who undergo post-infarct remodeling of this chamber. This may not only alleviate symptoms but also positively affect cardiac output and systemic organ perfusion. A pilot study by Nonin et al[23] in patients with HFrEF showed a greater response to a selective vasopressin type 2 receptor antagonist in terms of 24-hour urine output in patients who had undergone adverse RV remodeling. In addition, selective vasopressin type 2 receptor antagonist responders experienced a better prognosis. Interestingly, the impact of adverse RV remodeling and responsiveness to tolvaptan was independent of LVEF and LV end-diastolic diameter.

Adverse RV remodeling is frequently accompanied by secondary tricuspid regurgitation, which can cause a reduction in effective forward RV stroke volume. In recent years,

transcatheter tricuspid valve repair has emerged as a treatment option for secondary tricuspid regurgitation.[24] Patients with moderate-to-severe secondary tricuspid regurgitation who underwent transcatheter tricuspid valve edge-to-edge repair have demonstrated reverse RV remodeling (a reduction in RV EDA and RV ESA) at 6 months after the procedure.[25,26] Those patients who underwent transcatheter tricuspid valve repair and showed evidence of RV reverse remodeling also experienced a higher event-free survival (composite of death, repeat intervention, and HF hospitalization).

The present study is subject to the limitations of its retrospective and single-center nature. Echocardiographic measurements were not performed by a core laboratory, and end points were adjudicated locally. TAPSE is known to have a number of limitations, such as being unable to do imaging on the complex 3-dimensional (3D) structure of the RV, as well as its angle- and load-dependency. 3D-echocardiography and CMR RV data were not systematically collected even though these techniques suffer much less from the limitations imposed by 2D function parameters (e.g., TAPSE). RV size and function are sensitive to afterload (which varies over time), but we were unable to correct for the effect of pulmonary arterial pressure because these data were not available for all patients. The incidence of HF hospitalization may have been underestimated due to the fact that only admissions from our institution were captured in the registry. Lastly, we did not have access to data distinguishing cardiac from noncardiac causes of mortality.

In conclusion, RV remodeling, defined by an increase in RV ESA at 6 months after infarct, has prognostic value, which is independent from RV function. Identification of patients with adverse RV remodeling after STEMI may allow the institution of targeted strategies in this high-risk patient population.

Disclosures

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