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ORIGINAL ARTICLE

Right Ventricular Functions Can Predict Left Ventricular Reverse Remodeling in Patients with Ischemic Cardiomyopathy after Revascularization.

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ABSTRACT

BACKGROUND: Left Ventricular reverse remodeling is a major indicator of functional improvement in patients with ischemic cardiomyopathy undergoing revascularization. We aimed to investigate the ability of right ventricular functions to predict left ventricular reverse remodeling (LVRR) in those patients.

METHODS Subjects presented with ICM (n=52) were included and underwent right ventricular (RV) functions assessment. By the end of study patients were divided into two groups depending on positive LVRR response defined as ≥15% decrease in LV end-systolic volume (LVESV). Group 1 (n=28) with positive LVRR and group 2 (n= 24) without.

RESULTS A significant difference between the two groups regarding right ventricular systolic tricuspid annular velocity (RV S'), RV myocardial performance index (RV MPI), RV free wall strain (RVFWS) and RV global longitudinal strain (RV GLS) was noticed. RV GLS was superior to RVFWS in prediction of LVRR (AUC difference of 0. 12, P= <0.001) and the later was superior to RV S' and RV MPI in the same regards.

CONCLUSION: We conclude that right ventricular function may predict LVRR outcome of revascularization, with the RV GLS being the most powerful predictor.

KEYWORDS
Right Ventricular Functions; Left Ventricular Reverse Remodeling; PCI.

INTRODUCTION

Evidences are accumulating to support the ability of right ventricular function measures to provide an insight into outcome of different cardiac diseases [1]. Beside their circulatory, humoral and neural connections, right ventricle (RV) and left ventricle (LV) are directly and inextricably linked through the interventricular septum, shared fibers and the common sac of pericardium [2]. A comprehensive study of the heart with a perspective that incorporate RV morphology and function is essential for uncovering its pathophysiologic mechanisms [3].

Cardiac remodeling is defined as all the cellular and interstitial alterations that drives the pathological changes in ventricular size and shape [4]. The main purpose of gradual LV dilatation occurring in the remodeling process is to delay the incidence of heart failure (HF) symptoms by preserving the stroke volume in spite of impaired left ventricular ejection fraction (LVEF) [5]. Intricately involved in this pathogenic process is the neuro hormonal changes that occurs through the activation of sympathetic and renin-angiotensin systems [6].

Reverse remodeling is a dynamic process in which failing ventricle tends towards normative geometry and function, and improved molecular and transcriptional abnormalities [7]. Left ventricular reverse remodeling (LVRR) is the main indicator of effective therapy and an important predictor of outcomes in patients with HF [4]. The current study was designed to explore the role of RV function, in patients with ICM and viable myocardium, as a predictor for LVRR after revascularization.

METHODS

The data supporting study findings are available from the corresponding author upon request.

Human subjects/informed consent statement: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and the Helsinki Declaration, with informed consent obtained from all patients for being included in the study**.**

Study population

This study was carried out in Cardiology Department, Zagazig University Hospitals, , from October 2017 –to- August 2019, after approval from institutional review board ,52 adult patients with ischemic cardiomyopathy (ICM) were included after an informed consent was obtained from all of them, and according to the guidelines of the Declaration of Helsinki enrolled patients were defined as severe left ventricular dysfunction with LVEF at or below 35%, in the presence of any of the following: a stenosis of a major coronary artery of ≥75% angiography, previous myocardial infarction (MI), and history of percutaneous coronary intervention (PCI), or coronary artery bypass graft surgery (CABG) [8], who had been proved to have viable myocardium based on Dobutamine stress echocardiography study. Patients with chronic obstructive pulmonary disease (COPD), chronic renal failure (CRF), advanced liver disease, restrictive cardiomyopathy (RCM), rheumatic heart disease (RHD), organic tricuspid valve disease, atrial fibrillation (AF), heart blocks (including right and left bundle branch blocks (BBB)), and/or poor echo window were excluded.

Patients were classified into 2 groups: Group 1 (responders) included 28 patients who developed a decrease in LVESV ≥15 % after PCI at six months follow up, and Group 2 (non-responders) included 24 cases who failed to develop a decrease in LVESV ≥15% after PCI at six months follow up [9]. The two groups were subjected to detailed history taking, clinical examination, laboratory investigations, and echocardiographic assessment, and were evaluated clinically monthly for six months, and echocardiography was repeated.

Clinical assessment

All patients were assessed for common risk factors including hypertension, diabetes mellitus, smoking and/or dyslipidemia. Hypertension (previously diagnosed and/or treated by medication, diet and/or exercise) was defined as office systolic blood pressure (SBP) values of ≥140 mmHg, and /or diastolic blood pressure (DBP) values of ≥90 mmHg or more based on an average of ≥2 readings obtained on ≥2 occasions [10]. Diabetes mellitus was defined as a fasting plasma glucose ≥126 mg/dl, a casual plasma glucose≥200 mg/dl in the presence of symptoms, a 2-h plasma glucose during the 75-g oral glucose tolerance test (OGTT) ≥200mg/dl, and/or glycosylated hemoglobin (HbA1c) > 6.5% [11]. Patients were classified into non-smokers and current smokers (who smoke every day or some days during the past 30 days or quit less than 30 days before) [12]. Dyslipidemia is defined as elevated total cholesterol or low-density lipoprotein cholesterol (LDL-c) levels >116mg/dl, high-density lipoprotein (HDL) cholesterol <40 mg/dl in men and 50 mg/dl in women, or triglycerides >150 mg/dl [13]. clinical examination including resting blood pressure measurement, heart rate estimation, and full cardiac examination was done for all included patients.

Laboratory assessment

Complete blood count, kidney and liver function tests, glomerular filtration rate (e GFR) was calculated by MDRD 4- variable equation [GFR in mL/min per 1.73 m2 = 175 x serum creatinine -1.154 x age-0.203 x 1.212 (if patient is black) x 0.742 (if female)] [14].

Echocardiographic assessment

Transthoracic imaging of the heart was performed using a 2.5 MHz phased-array transducer and a transthoracic echocardiographic recorder system (Vivid E9 commercial ultrasound scanner with phased-array transducers (M5S-D and 4V-D). The chest lead electrocardiograms were simultaneously recorded. Examinations were done with the patient in left semi-lateral position; utilizing left parasternal long-axis, short-axis, apical four and five two-chamber views. Recordings and calculations of different parameters were performed according to the recommendations of the American Society of Echocardiography [15]. Dobutamine Stress Echocardiography (DSE) of LV and RV was done one day after proving viability and candidacy for revascularization. For DSE, Standard Dobutamine stress protocol was used starting at a Dobutamine infusion rate of 5µg /min/kg bodyweight, and thereafter increasing the dosage every 3 minutes to 10 and 20µg /kg/min [16]. The viability response is inferred from a segment with resting dysfunction that shows improvement, with contractile reserve in at least five dysfunctional segments as evidence for a viable myocardium that predicts more than 5% improvement in EF after revascularization [17]. 5.1. Assessment of left ventricular function and geometry: Ejection fraction was assessed according to the modified biplane method of Simpson in the parasternal long axis view, apical four and two chambers views for dynamic 2d imaging using the equation: LVEF= (LVEDV-LVESV)/LVEDV [18]. LV relative wall thickness was calculated according the formula: RWT=h/R, where h equals two times posterior wall thickness,

and R is the LV end-diastolic dimension. RWT= (2 * PWT/LVEDD), while normal values are (from 0.32 to 0.42) [19]. The Systolic Sphericity Index (SI) was assessed in apical four chamber view, in end- systole, as the short to long axis ratio with long axis (L) length measured from LV apex to the mid- point of the mitral valve and short axis (S) length measured as the axis perpendicular to the mid- point of long axis. Normal values for SI systolic = 0.45 ± 0.06. [20]. LV diastolic function was assessed using E-wave deceleration time, mitral valve E/A ratio, E/e' ratio and filling pattern. E- wave deceleration time was calculated at apical four-chamber view with pulsed Doppler sample volume placed between mitral leaflet tips and measured as the time interval from peak E-wave to the zero- velocity baseline. Mitral valve E/A ratio was calculated as the ratio between E and A- wave velocity. The E/ e' ratio was assessed by tissue Doppler interrogation of the mitral valve from apical four-chamber view, for assessment of e' Septal wave velocity and calculation of E/e'. Restrictive filling pattern was defined as E/A ratio ≥ 2 with Average E/e′ > 14 [21]. 5.2. Assessment of right ventricular function: The RV long and short axis dimensions were measured in end-diastole, in apical four-chamber view [22]. Right ventricular fractional area change (RV FAC) was assessed as the difference between end- diastolic and end- systolic volumes measured manually by tracing the right ventricular endocardium in four chamber view without including the trabeculae in the wall. Normal values= (49 ± 7), with values < 35 are considered abnormal [22]. Tricuspid annular plane systolic excursion was assessed using M-mode echocardiography, by placing the M-mode cursor through the lateral portion of the tricuspid valve annulus in the apical four-chamber view with 23 mm ± 3.5 mm considered as normal values with values below 17mm considered abnormal [22]. Systolic pressure (RVSP) was determined from peak tricuspid regurgitation (TR) jet velocity, using the simplified Bernoulli equation combining this value with an estimate of the RA pressure from the degree of inspiratory collapse of the inferior vena cava [22]. Tissue Doppler velocity of the tricuspid annulus (S`) was assessed using pulsed wave tissue Doppler, with the sample volume aligned along the lateral tricuspid annulus, in apical four-chamber view. Normal values were 14.1 ± 2.3cm, with values < 10cm are considered abnormal [22]. RV myocardial performance index (Tie index, RVMPI) was derived by Doppler tissue imaging at the lateral tricuspid annulus from the formula: RV Tie Index= (isovolumic contraction time + isovolumic relaxation time)/ (ejection time) with normal values defined as 0.38 ± 0.08, and values > 0.54 are considered abnormal [22]. RV global and free wall longitudinal strain was assessed at the optimal four-chamber view, obtained through offline analysis of grayscale conventional trans-thoracic images acquired during breath-hold with ECG recording. Three consecutive heart cycles were recorded and averaged with frame rate was set between 60 and 80 frames, the endocardial border was traced manually in the end-diastolic frame, and the software subsequently traced the borders in the other frames automatically. The vectors of the velocities of the endocardial points were then displayed and overlaid onto the B-mode images [23]. The RV free wall and ventricular septum were both divided into three segments. Right ventricular global longitudinal strain (RVGLS) was defined as the measurement obtained from the average of the values from all six segments, while right ventricular free wall strain (RVFWS) as the average value from three RV free wall segments. Normal values for RVGLS are −25.8±3.0 and for RVFWS are −30.5±3.9 [23]. 5.3. Quantitative assessment of mitral regurgitation: The proximal iso-velocity surface area (PISA) method was used at apical four-chamber view, with reducing the Nyquist limit to 20 –40 cm/s. The radius of PISA was measured at mid-systole using the first aliasing. Continuous wave Doppler was used to measure MR maximum velocity and time velocity integral (TVI). Effective regurgitate orifice area (EROA) was measured using the formula: EROA= Flow/Peak velocity = (2πr2 X Aliasing velocity)/Peak velocity. While regurgitate volume (R Vol) was obtained using the standard formulas: R Vol= EROAX TVI. Mild regurgitation was defined by (EROA < 20 mm2 or an R Vol < 30mL) and moderate regurgitation by (EROA of 20– 39 mm2 or an R Vol of 30–59 mL) [24].

Percutaneous coronary intervention procedure

Percutaneous coronary intervention was performed within one week after DSE. The PCI and stent implantation were performed in a standard manner and through trans femoral approach. A successful procedure was defined as less than 10% stenosis after stent implantation, with normal TIMI flow grade 3 (visually assessed by angiography) without side branch loss, flow- limiting dissection, distal embolization or angiographic thrombus, and with no major cardiovascular complications including in-hospital MI, stroke, emergency CABG, or death [25].

STATISTICAL ANALYSIS

Standard descriptive statistics were used for the analysis. Mean and standard deviation were used to describe continuous normally distributed parameters, while count and percentages were used for categorical parameters. The SPSS Statistics

24.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for data analysis and the level of significance was fixed at P=0.05.

RESULTS

The two groups were homogenous in terms of demographic data, history, risk factors other than diabetes mellitus, NYHA functional class, mean blood pressure, EGFR, hemoglobin level, medications received for heart failure, and the target vessel for revascularization (no significant correlation between the re vascularized vessel and reverse remodeling) (Table 1). left ventricular functions by echocardiography showed no statistically significant difference between the study groups in terms of LVESV, LVEDV, LVRWT, LVSI, MR frequency and severity, restrictive filling or E wave deceleration time, while that of right ventricle showed a high significance (RV S' wave, RVFWLS and RVGLS (P values 0.05, <0.001 and <0.001 respectively) in group 1, and group 2 had significantly higher RVMPI (P=0.05). There was no statistically significant difference between the two groups, in terms of RV long axis diameter, RV short axis diameter, RV FAC, TAPSE and PASP (Table 2). RV S', RVGLS and RVFWS correlated positively to the change in left ventricular end-systolic volume (r=0. 35, P=<0. 05; r=0. 855, P<0.001; r=0. 424, P<0.01 respectively.) (Figure 1). Receiver operating curve (ROC) analysis of the predictive performance of the RV function parameters for LV reverse remodeling after revascularization, RVFWS, RVGLS and RV S` were proved to be good predictors of positive reverse remodeling. Logistic regression analysis showed RV global longitudinal strain to be the most significant independent variable (P =<0.05) (figure 2, tables 3 and 4)

Table 1: Characteristics of patients.

	Group 1- Responders (n = 28)	Group 2- non-responders (n = 24)	P value
Demographic data/ risk factors			
Age, years	53.3 (±6.8)	58.1 (±6.4)	> 0.05
Male sex, n (%)	23 (79.2%)	19 (82.1%)	> 0.05
Smoking, n (%)	17 (60.7%)	13 (54.0%)	> 0.05
Hypertension, n (%)	16 (57.1%)	11 (45.8%)	> 0.05
Diabetes, n (%)	11 (39.3%)	16 (60.7%)	< 0.05 *
BMI (kg/m^2)	25.7 (±2.9)	24.7 (±2.5)	> 0.05
Clinical/ laboratory data			
Mean BP	82.7 (±3.9)	80.2 (±5.9)	> 0.05
NYHA III/IV	8 (28.6%)	13 (54.2%)	> 0.05
Hb	12.1 (±0.86)	12.2 (±0.82)	> 0.05
eGFR	73.2 (±10.5)	67.9 (±13.1)	> 0.05
Medications			
Beta Blockers	23 (82.1%)	17 (70.8%)	> 0.05
ACEIs/ARBs	22 (78.6%)	17 (70.8%)	> 0.05
MRA	26 (92.9%)	20 (83.3%)	> 0.05
Diuretics	19 (79.2%)	16 (57.1%)	> 0.05
Re-vascularized territory			
LAD Territory	16 (57.1%)	9 (37.5%)	> 0.05
LCX Territory	12 (42.9%)	14 (58.3%)	> 0.05
RCA Territory	9 (32.1%)	11 (45.8%)	> 0.05

* Value of P <0.05 indicates statistically significant difference between the study groups.
The data are expressed as mean ± standard deviation or number (%).
ACEIs/ARBs indicates angiotensin convertase enzyme inhibitors/angiotensin receptor antagonists; BMI, body mass index; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; HTN, hypertension; LAD, left anterior descending artery; LCX, left circumflex artery; Mean BP, mean blood pressure; MRA, mineralocorticoid antagonists and RCA, right coronary artery.

Table 2: Echocardiographic findings:

	Group 1- Responders (n = 28)	Group 2- non-responders (n = 24)	P value
No MR	10 (35.7%)	6 (25.0%)	> 0.05
Mild MR	11 (39.3%)	8 (33.3%)	> 0.05

	Group 1- Responders (n = 28)	Group 2- non-responders (n = 24)	P value
Moderate MR	7 (25%)	10 (41.7%)	> 0.05
Restrictive Filling	9 (32.1%)	12 (50.0%)	> 0.05
LVESV	128.6 (±9.3)	128.1 (±9.1)	> 0.05
LV RWT	0.207 (±0.02)	0.202 (±0.01)	> 0.05
Systolic LV Sphericity Index	0.53 (±0.06)	0.56 (±0.01)	> 0.05
E/e'	10.86 (±2.5)	12.13 (±3.1)	> 0.05
E Wave DT	139.4 (±19.7)	130.1 (±18.7)	> 0.05
PASP	60.3 (±10.8)	65.2 (±7.4)	> 0.05
RV short axis D	42.9 (±4.3)	45.2 (±4.1)	> 0.05
RV long axis D	69.1 (±5.1)	71.6 (±6.2)	> 0.05
TAPSE	15.5 (±2.1)	14.7 (±1.6)	> 0.05
RV FAC	35.8 (±5.0)	35.0 (±5.6)	> 0.05
RV S'	9.1 (±1.1)	8.2 (±1.5)	< 0.05*
RV MPI	0.52 (±0.041)	0.55 (±0.039)	< 0.05*
RV GLS	18.8 (±1.58)	15.7± (1.59)	< 0.001**
RVFWS	19.4 (±2.4)	17.1 (±1.7)	< 0.001**

* Value of P <0.05 indicates statistically significant difference between the study groups.
** Value of P <0.01 indicates highly significant difference between the study groups.
The data are expressed as mean ± standard deviation or number (%).
E Wave DT indicates E wave deceleration time; LVEDV, left ventricular end diastolic volume; LVESV, left ventricular end systolic volume; LV RWT, left ventricular relative wall thickness; MR, mitral regurgitation; PASP, pulmonary artery systolic pressure; RV FAC, right ventricular fractional area change; RVGLS, right ventricular global longitudinal strain; RV S', tricuspid annular tissue Doppler velocity; RVMPI, right ventricular myocardial performance index; RVFWS, right ventricular free wall strain and TAPSE, tricuspid annular plane systolic excursion.

Table (3): Characteristic performance of RV MPI, RV S', RV GLS and RVFWS with their best cut off to determine reverse remodeling

Parameter	Cut off	Sensitivity	Specificity	Area	95% CI	P
RV MPI	0.51	60.7 %	25 %	0.335	0.188 to 0.482	< 0.05*
RV GLS	-16.5	96.4 %	66.7 %	0.913	0.837 to 0.989	< 0.001**
RVFWS	-17.5	85.7 %	71.8 %	0.793	0.665 to 0.921	< 0.001**
RV S'	7.5	92.9 %	37.5 %	0.67	0.517 to 0.822	< 0.05*

* Value of P <0.05 indicates statistically significant difference between the study groups.
** Value of P <0.01 indicates highly significant difference between the study groups.
RVGLS indicates right ventricular global longitudinal strain; RV S', tricuspid annular tissue Doppler velocity; RVMPI, right ventricular myocardial performance index and RVFWS, right ventricular free wall strain.

Table (4): Logistic regression analysis

Variables	Coefficient	S.E.	Wald chi-square	Odds ratio (95 % CI)	P
RVMPI	-.274	0.154	3.178	0.760 (0.563 to 1.028)	> 0.05
RV GLS	1.480	0.530	7.800	4.392 (1.555 to 12.408)	< 0.05*
RVFWS	0.431	0.314	1.888	1.539 (0.832 to 2.848)	> 0.05
RV S'	0.695	0.515	1.819	2.003 (0.730 to 5.498)	> 0.05
RV S'	0.695	0.515	1.819	2.003 (0.730 to 5.498)	> 0.05

Df (degree of freedom) for all variables equals 1
* P value < 0.05 is significant.
RVGLS indicates right ventricular global longitudinal strain; RV S', tricuspid annular tissue Doppler velocity; RVMPI, right ventricular myocardial performance index and RVFWS, right ventricular free wall strain

	RV S'	RV GLS	RVFWS	RV MPI	Δ LVESV
RV S'	1.00	0.38**	0.278*	-0.25	0.35*
RV GLS	0.38**	1.00	0.39**	-0.203	0.855**
RVFWS	0.278*	0.39**	1.00	-0.147	0.424**
RV MPI	-0.25	-0.203	-0.147	1.00	-0.162
Δ LVESV	0.35*	0.855**	0.424**	-0.162	1.00

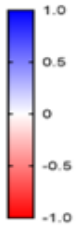

Figure 1. Correlation matrix of Pearson's coefficient for right ventricular functions in study groups
* Value of P <0.05 indicates statistically significant difference between the study groups.
** Value of P <0.01 indicates highly significant difference between the study groups.

Δ LVESV indicates left ventricular end systolic volume; RVGLS, right ventricular global longitudinal strain; RV S', tricuspid annular tissue Doppler velocity; RVMPI, right ventricular myocardial performance index and RVFWS, right ventricular free wall strain.

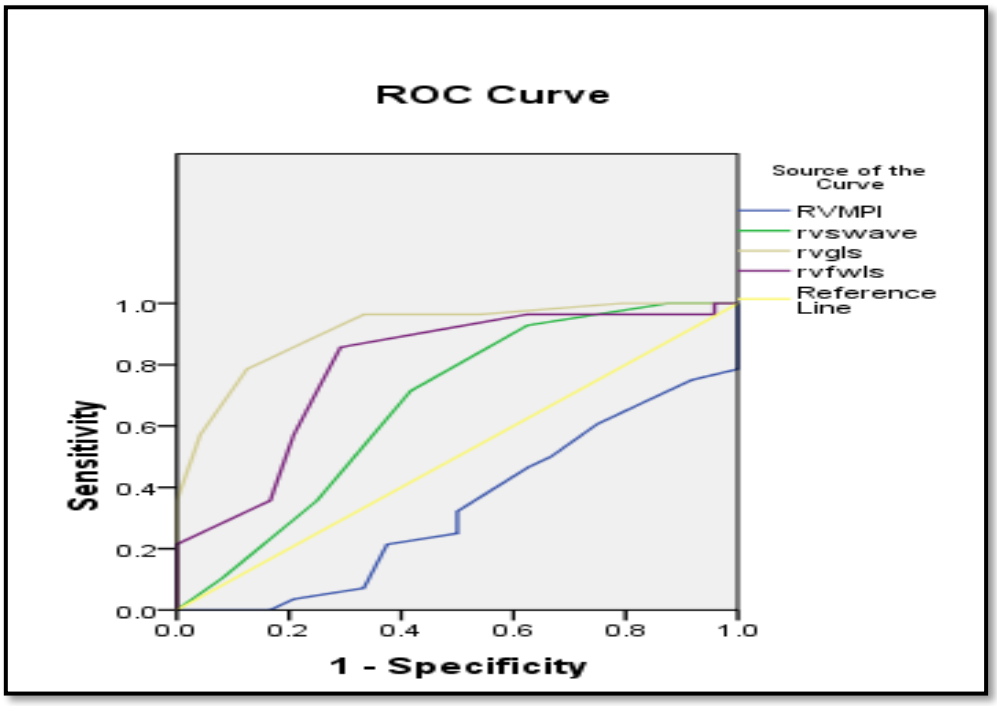

Figure (2): ROC analysis of Left Ventricular Remodeling predictive value of RV MPI, RV S', RV GLS and RVFWS

DISCUSSION

Evidence demonstrated that right ventricular remodeling occurs in early stages of virtually every LV disease. In ischemic cardiomyopathy, several mechanisms could be responsible for RV dysfunction including direct mechanical and indirect circulatory, hemodynamic and neuro hormonal mechanisms, as well as common pathological process. Unfavorable LV remodeling response in the presence of RV dysfunction could have many reasons. RV damage may be a sensitive indicator of the extent and degree of heart failure [26, 27].

Right ventricular functions, particularly RV strain, have been a topic for extensive study for prognostication of heart failure of different types and etiologies. Many studies have uncovered the LVRR predictive value of right ventricular functions in cardiac resynchronization therapy (CRT) patients; nevertheless, to the best of our

knowledge, its value in ICM patients undergoing revascularization has not been addressed [28, 29].
In the current study we report three main findings. First, the study groups have a significant difference in right ventricular functions namely RVS', RVFWS, RVGLS and RVMPI. Secondly, RVGLS, RVFWS and RVS' show acceptable predictive power for LVRR in ICM patients after revascularization. Finally, RV global longitudinal strain is the most significant independent variable related to LVRR.
Regarding RV strain measurements, there is no clear consensus among imaging specialists as to whether global or free wall measurements should be obtained as a standard. RV strain analysis by speckle tracking has been recently studied in relation to outcome in patients with different types and etiologies of HF. Motoki et al. demonstrated the prognostic significance of RVGLS over RVFWS in patients with CHF [30].
We have demonstrated that right ventricular global longitudinal strain of less than -16.5% is an independent predictor of successful reverse remodeling of the left ventricle. RVGLS represents the global RV systolic function, as contributed by RV free wall as well as the LV contribution through the inter-ventricular septum. Interventricular septum is considered to be the central pillar of the heart since its spiral myofibers connect the two ventricles in an intricate interweaving manner to form a common and a highly interdependent functional unit, despite the marked disparity in mass, geometry and hemodynamics, between the two ventricles. The septal contribution of RV pressure generation is well recognized [31] and it might be attenuated patients with HFrEF.
In a study on patients treated with CRT, Sade et al. showed that RV free wall longitudinal strain is the most powerful predictor of both reverse remodeling and long-term survival after CRT [32]. The investigators in that study did not include RVGLS as a possible target for investigation. In a prospective study on 266 patients with HFrEF, Houard et al. showed that RVGLS was superior to RVFWS in providing strong prognostic value to predict overall mortality. However, in another recent study, RVFWS was the only parameter (using multivariable regression analysis) remained independently associated with outcomes in patients with HFrEF and it was speculated that RVGLS might be affected by LV dysfunction as the septum is an integral part of LV [33].
RVMPI was significantly higher in group 2 than group 1 and strongly negatively correlated with the occurrence of LV reverse remodeling. Several studies have evaluated the prognostic value of RVMPI, in different cardiac pathologies, and showed it to have a more powerful prognostic value than other conventional echocardiographic parameters of RV [34].
Despite TAPSE has been shown to be a predictor for LV reverse remodeling after CRT [35], it showed no statistical difference between the study groups. Also, multivariable analysis has not shown RV S` wave to be a significant predictor for LV reverse remodeling. In one hand, we think that the sample size might not be sufficient to demonstrate a real difference in TAPSE and RV S` between the two groups. In the other hand, TAPSE and RV S` are recognized to only represent the basal RV free wall longitudinal contraction not the entire RV and hence, a meaningful relationship to LVRR is not guaranteed. Moreover, the accuracy of their measurement is limited by being angle-dependent [22].
Speckle tracking echocardiography (STE) have the advantage of being angle independent and having improved signal-to-noise ratio [22]. Moreover, STE can discriminate between normal active myocardial deformation, and passively displaced dysfunctional segments, by the act of tethering and global cardiac motion [36].
The study population shows difference in prevalence of diabetes mellitus between groups which may raise concerns about the generalizability of results. Diabetes alters cellular metabolism, homeostasis and apoptotic pathways. Moreover, the glycation of extracellular matrix proteins adds to the pathophysiology of remodeling/ reverse remodeling processes. However, we found that diabetes is not significantly correlating to the changes in LVESV. Kahr et al. showed that DM predicts poor reverse remodeling response after CRT [37]. Ischemic cardiomyopathy patients who are candidates for CRT usually are not eligible for anymore revascularization. We trust the underlying pathophysiology of reverse remodeling after revascularization is distinct from that after CRT with more metabolic and respiratory elements in the former, and more electromechanical elements in the later [8, 37].
Another concern is that, theoretically, the area and size of the re-vascularized territory may impact the reverse remodeling of LV. We could find no significant difference between the two groups regarding revascularization target vessel. Also, no correlation was found between the different targets for revascularization; left anterior descending artery (LAD), left circumflex artery (LCX), right coronary artery (RCA); and the reverse remodeling. This could be explained partially by the great disparity in the ability of patients with

significant coronary stenosis to acquire a well-developed collateral circulation [38]. Moreover, in looking for the interventricular septum as most important contributor for the ventricular interdependence and the central pillar of the heart, its blood supply is always shared between the LAD and either the RCA or the LCX, according to the dominance [39].

The current study assessed the longitudinal strain of RV only. Due to the thin wall and the complex geometry of the RV, beside the challenge of adequate imaging of the retrosternal positioned chamber, 2D Speckle tracking was not attempted in any study for evaluating the radial and the circumferential RV strains. Other imaging modalities such as 3D echocardiography and CMR could be used in future studies to assess the prognostic value of these measures. Another limitation is the small sample size and relatively short term follow up. We believe that a longer time of follow up may give better insight into the prognostic value of different RV functions.

Clinical Implications

By demonstrating a strong, and independent predictive power of RVGLS, our data suggests that, patients with ICM who are candidates for revascularization, assessment of RV function by conventional measurements, complemented with strain analysis could help identifying patients who are more or less probable to show a favorable reverse remodeling response after revascularization.

CONCLUSION

RV function is a prognostic marker in patients with ICM, who are candidates for revascularization. It predicts LV reverse remodeling after PCI.

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