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Speckle-tracking echocardiographic evaluation of the right ventricle in patients with ischemic left ventricular dysfunction

Dorota Smolarek et al., Echocardiographic evaluation of the right ventricle

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Abstract

Background: The comprehensive assessment of right ventricular (RV) performance is of paramount importance because it is has been recognized as a strong prognostic factor in a variety of clinical settings. The aim herein was to evaluate the usefulness of RV longitudinal strain imaging by speckle-tracking echocardiography (STE) in daily clinical practice, especially in the context of RV systolic function and its changes after acute coronary syndrome (ACS).

Methods: This prospective study enrolled 63 patients with ischemic injury (left ventricular ejection fraction $[LVEF] \le 45\%$). Additionally, a subgroup was created: patients with ACS treated with successful percutaneous coronary intervention. The clinical and echocardiographic parameters, including STE, were analyzed.

Results: Significant correlations for both RV free-wall (RVFWSL) and four-chamber (RV4CSL) longitudinal strain evaluated by STE with New York Heart Association class, LVEF, E/E' ratio, as well as conventional parameters of RV function were found. RVFWSL

was able to detect subtle RV functional abnormalities, unreachable for traditional indices. RV recovery after ACS was not related to higher LVEF but better contractility of the interventricular septum (IVS) assessed by STE.

Conclusions: Right ventricular strain proved to be a useful two-dimensional echocardiographic method to detect impaired RV performance, which showed a significant relationship with clinical and other echocardiographic indices. The IVS played a vital role in RV recovery among ACS survivors.

Key words: right ventricle, speckle-tracking echocardiography, longitudinal strain, acute coronary syndrome, left ventricular fraction

Introduction

Nowadays, it is commonly acknowledged that right ventricular (RV) function has crucial diagnostic and prognostic importance in the management of many cardiovascular disease states including heart failure (HF) and ischemic heart disease [1–7].

Echocardiographic imaging of the RV remains a challenging task due to its complex anatomy and physiology [8, 9]. Therefore, additional tools that enable us to overcome certain imperfections of traditional techniques are needed for comprehensive and multiparametric RV function assessment. RV imaging using speckle-tracking echocardiography (STE) proved to be an important prognostic factor with high accuracy and reproducibility, which may be superior to the RV contraction indices routinely used and decisive for clinical practice [10– 14]. In accordance with previous studies, RV strain has proved to be a more sensitive imaging modality in detecting subtle myocardial dysfunction than traditional parameters [15–19].

Right ventricular involvement during acute coronary syndrome (ACS) has been reported as an incremental predictor of severe adverse events [12, 20–23]. The RV is more resistant to ischemia than the left ventricle (LV) due to its unique morphology and pathophysiology, with a high tendency to recover after the acute phase [24–29].

Thus, the aim of this study was to explore the usefulness of a non-conventional imaging tool, i.e., longitudinal strain imaging by STE, in daily clinical routine and its correlation with traditional echocardiographic parameters of RV performance. Furthermore,

we sought to evaluate RV systolic function and its changes after ACS treated with successful percutaneous coronary intervention (PCI).

Methods

Study population

Sixty-three patients with LV ischemic injury with left ventricular ejection fraction $(LVEF) \le 45\%$ (mean age 64.7 ± 9.7 years; 48 men) who were hospitalized in the Department of Cardiology between 2016 and 2018 were recruited to this study group. One subgroup was established. Cases consisted of patients with ACS treated with successful culprit-lesion PCI, who reached the follow-up visit (n = 34, mean age 63.6 ± 10.1 years; 27 men). Most of them suffered from anterior ST-segment elevation myocardial infarction (STEMI), and the fewest had inferior STEMI. Left anterior descending artery (LAD) PCI was performed most often.

The exclusion criteria included non-sinus rhythm, severe valvular heart disease, concomitant RV myocardial infarction, pericardial effusion affecting RV hemodynamics, and poor echocardiographic windows.

All subjects gave their written informed consent before participation. The study conforms to the principles outlined in the Declaration of Helsinki and was performed with the approval of the local Ethics Committee (KB-7/16).

Study design

This was an open-label, single-center study. The baseline examination including electrocardiography and echocardiography with detailed RV assessment was conducted during hospitalization, approximately 24 hours after PCI in the ACS subgroup, whereas the screening visit was carried out approximately after 3.5 months. All echocardiographic images were acquired by a single investigator using a portable ultrasound machine (VIVID Q, General Electric Healthcare, equipped with an M4S-RS probe). Data were digitized and stored on a computer. Strain measurements were performed off-line using an EchoPac workstation (Version 202, GE Healthcare) with a mode commonly used for LV strain assessment.

Standard transthoracic echocardiography and speckle-tracking measurements

Standardized comprehensive echocardiographic examinations were performed in accordance with the most up-to-date version of chamber quantification guidelines [30]. Images of the RV were obtained from dedicated RV-focused apical four-chamber views, on which longitudinal strain and traditional parameters, such as tricuspid annular plane systolic excursion (TAPSE), Doppler tissue imaging (DTI)-derived tricuspid lateral annular systolic velocity (S'-wave), right ventricular index of myocardial performance (RIMP), fractional area change (FAC), and myocardial acceleration during isovolumic contraction (IVA), were analyzed during breath-hold and at a frame rate between 40 and 80 fps for strain measurements, which was increased in cases of tachycardia. End of systole was identified by pulmonary valve closure detected on pulsed-wave Doppler tracing of the RV outflow tract, whereas end of diastole was defined as the peak of the R-wave in electrocardiogram. In the case of the presence of intraventricular conduction delay, end of diastole was detected manually as tricuspid valve closure from the continuous-wave Doppler profile of tricuspid regurgitation. The automatically generated region of interest (ROI) was manually adjusted in terms of width and orientation in order to include the entire RV myocardium, without the pericardium. The ROI consisted of both the IVS and RV free wall. Afterwards, detailed analysis of RV free-wall longitudinal strain (RVFWSL, 3 segments of RV free wall), RV fourchamber longitudinal strain (RV4CSL, 6 segments of both RV free wall and IVS), and RV septal longitudinal strain (RVSepSL, 3 segments of IVS) was conducted. RV4CSL was calculated in two ways: (a) the arithmetic mean of the segmental peak systolic strain values displayed by the software (RV4CSL 1) and (b) the systolic peak of the average strain curve created by the software (RV4CSL 2). According to the latest recommendations, RVFWSL > -20% (< 20% in absolute value) is likely abnormal, so we considered the value of -20% as a cut-off point [31].

Statistical analysis

Quantitative data are expressed as the mean and standard deviation. All data have been analyzed to identify any outliers or possible measurement errors. The assumption of normality was assessed with the Shapiro-Wilk test or with Q-Q plots. Differences between mean values in independent groups were examined by parametric Welch's t-test and complemented by nonparametric Mann-Whitney U test. For comparisons of mean levels of dependent variables, the parametric paired sample t-test was used. Pearson's correlation test was used to assess the relationship between different variables. In the case of dependence between qualitative data including factions, it was verified by an appropriate χ^2 test. A p-value of < 0.05 was considered statistically significant and the statistical analysis was performed using STATISTICA 13.1 software (Dell Inc. [2016], data analysis software system).

Results

Patients' characteristics

The clinical and echocardiographic characteristics of the study population are summarized in Table 1. A total of 63 participants fulfilled the enrolment criteria. In echocardiographic examination the mean LVEF was moderately reduced, LV filling pressures were elevated, and RV systolic indices (except for the mean value of pulsed-wave Doppler RIMP, which was slightly above the upper limit of the normal range, and RV4CLS which is strongly affected by LV function by definition) were normal.

Correlation analyses

As shown in Table 2, a statistically significant relationship between both RVFWSL and RV4CSL (greater than in the case of TAPSE and S'), and the level of dyspnea, as well as LV systolic and diastolic parameters, was observed.

Right ventricular strain assessed by STE (both RVFWSL and RV4CSL2) significantly correlated with traditional RV performance indices with the strongest relation observed for RVFWSL and pulsed-wave Doppler RIMP (r = 0.73; p < 0.001, Table 2).

Figure 1 demonstrates a very strong positive association between RV4CSL 1 and RV4CSL 2 (r = 0.99; p < 0.001). According to this finding, we used only one of them (RV4CSL 2) for further analyses.

The detection of subtle RV dysfunction

The assessment of RV strain in comparison with conventional RV systolic indices was performed. Half of the patients with reduced RVFWSL had normal S' value, and 36% of them had TAPSE value within the normal range (Fig. 2).

Clinical and echocardiographic assessment of the ACS subgroup

The comparative analysis of changes in clinical and echocardiographic parameters between the time of hospitalization and the follow-up visit was conducted in the ACS subgroup.

As given in Table 3, the degree of symptoms evaluated by means of New York Heart Association (NYHA) and Canadian Cardiovascular Society (CCS) classifications was significantly lower at the follow-up visit in the ACS subgroup (1.2 vs. 1.4; p = 0.02 and 0.03 vs. 3.8; p < 0.001, respectively). Initially, LVEF was moderately reduced (39.3%) and significantly improved afterwards (48.8%; p < 0.001), as well as RVSepSL (-10.6 vs. -15.1%; p < 0.001). Mean values of RV systolic function indices were initially within normal limits and improved further after 3.5 months, except for FAC, which also increased but without reaching statistical significance (p = 0.06, Table 3).

The correlation between LVEF changes and RV systolic performance indices changes was assessed in the ACS subgroup (Table 4). No significant relationships were observed, except for the S' value (0.36; p = 0.03). On the other hand, statistically significant correlation between most of RV systolic parameters changes and RVSepSL changes was demonstrated (Table 4). The strongest association (apart from RV4CSL, which comprises RVSepSL, and a high correlation is therefore obvious) was reported in the case of RVFWSL (0.62; p < 0.001).

Discussion

Echocardiographic evaluation of RV performance is a technically demanding task due to its unique anatomy and physiology. RV strain by STE is a useful tool that enables us to overcome the challenges encountered with conventional parameters.

According to Iacoviello et al. [31], both RV strain parameters – RVFWSL and RV4CSL – were significantly related to LVEF, E/e' ratio, and NYHA class. Moreover, they were significantly correlated with each other and the remaining indices of RV systolic function [31]. The findings of the cited study were similar to ours, which suggests that RV strain may be particularly useful in our clinical practice providing additional clinical implications. In the current study, the significance of RV strain was extensively investigated, and RVFWSL correlated with systolic and diastolic parameters of LV function and

conventional RV function parameters. The association between RV and LV systolic and diastolic function is well known and supports the concept of ventricular interdependence with a particular role of IVS contractility.

Nevertheless, there is a lack of uniformity in using RV strain parameters because some studies are based on RVFWSL whereas others use RV4CSL [17, 32, 33]. In accordance with the most up-to-date consensus document, it is recommended that RVFWSL be reported as a default parameter [34].

We compared two techniques of RV4CSL analysis — the arithmetic mean of the segmental peak systolic strain values displayed by the software, hence manually calculated by the operator from non-simultaneous segmental values (RV4CSL 1), and the systolic peak of the average strain curve created by the software (RV4CSL 2). We obtained very strong correlation between these two methods, which suggests that they can be used interchangeably. Muraru et al. [35] found no significant differences between the corresponding two techniques of RVFWSL measurement. Nevertheless, it is recommended that 6-segment ROI be used and that RVFWSL be computed by averaging the peak segmental values of 3 segments, because it is more feasible and reproducible [34, 35].

The findings of the present study indicate that RV strain measurements may have an advantage over traditional echocardiographic parameters in detecting subtle myocardial dysfunction, which agrees with scientific reports [14, 16, 36, 37]. Although the gold standard for non-invasive assessment of RV size and function is cardiac magnetic resonance imaging, it is time consuming, costly, and often not feasible. Thus, RV strain as the most sensitive two-dimensional echocardiographic marker of RV contractility, which is relatively easily obtainable and non-demanding, may play a vital role in the comprehensive evaluation of unique RV function in our daily clinical practice.

Right ventricular involvement in the course of ACS is a significant risk marker associated with increased morbidity and mortality [22, 23, 38, 39]. Different mechanisms may lead to RV impairment in ACS, such as RV myocardial stunning, which tends to be reversible, unalterable necrosis observed in RV infarction and RV dysfunction resulting from ventricular interdependence in the course of depressed LV global function [24, 40]. The latter is especially pronounced in anterior myocardial infarction, in which the degree of LV myocardial injury is extensive. Fortunately, in most cases of ACS without RV infarction, the RV regains its function within several weeks due to reabsorption of edema [41]. Moreover, the RV is relatively resistant to ischemia through other mechanisms: 1) coronary blood flow at rest is lower in the RV, and an appreciable perfusion throughout the entire cardiac cycle is feasible contrary to the LV; 2) resting oxygen consumption and extraction are also lower, leading to higher oxygen extraction reserve; (3) large system of collaterals from the left coronary circulation; and (4) possible retrograde perfusion directly from the RV cavity via the Thebesian veins [27, 28]. The above considerations are in agreement with the findings of the present study, where the improvement of the majority of RV function indices, along with LVEF and RVSepSL, was observed in ACS patients treated with successful PCI of the culprit lesion after a follow-up period.

In the next step we tried to investigate the reason for RV recovery in the course of ACS. No significant associations between LVEF changes and RV systolic parameter changes were observed, except for the S' value (weak correlation). On the other hand, a statistically significant relationship between changes of most RV systolic parameters and RVSepSL changes was demonstrated. The strongest association was reported for RVFWSL. These data emphasize the special role of IVS motion in RV functional recovery after ACS. A study by Popescu et al. [25] on 500 patients with myocardial infarction showed similar results. They repeatedly assessed RV function at acute and chronic phases of infarction and observed a significant increase of TAPSE at discharge. Similarly to our findings, they demonstrated that RV recovery was best related not to LVEF but to IVS contractility assessed by wall motion score index [25]. To the best of our knowledge, the present study is the first to evaluate the role of IVS motion in RV performance after ACS using STE.

Limitations of the study

This study has several limitations. Firstly, it is limited by the relatively modest size of the cohort. Nevertheless, we detected statistically significant changes of RV function in the ACS subgroup. The echocardiography was performed approximately 24 hours after PCI, when partial RV functional recovery was already possible, but this does not alter the conclusions of the study regarding RV performance improvement over time. Moreover, there is a lack of definite normal reference values of RV strain [30, 35, 36, 42, 43]. We used GE equipment for strain measurements, and this should be taken into account when comparing our results with other studies because strain values derived from vendor-specific two-dimensional speckle-tracking software are not interchangeable [44]. Finally, there is a lack of

uniformity in references to strain changes. We used the absolute value of the number to describe strain alteration, so the increase in strain meant that the value became more negative, which was in accordance with the currently applicable consensus document regarding twodimensional STE [45].

Conclusions

RV longitudinal strain by STE proved to be a useful two-dimensional echocardiographic method to detect impaired RV function, which showed correlations with multiple clinical and echocardiographic parameters. It was the contractility of IVS assessed by STE, rather than LVEF, that played a vital role in RV recovery among ACS survivors.

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Conflict of interest: None declared

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Figure 1. Analysis of correlation between RV4CSL 1 and RV4CSL 2; RV4CSL 1 — right ventricular four-chamber longitudinal strain as the arithmetic mean of the segmental peak systolic strain values displayed by the software, RV4CSL 2 — right ventricular four-chamber longitudinal strain as the mean strain from the averaged strain curve of all segments.



Figure 2. Right ventricle (RV) dysfunction assessed by RVFWSL in patients with normal tricuspid annular plane systolic excursion (TAPSE) and S'; RVFWSL — right ventricular free-wall longitudinal strain, S' — Doppler tissue imaging-derived tricuspid lateral annular systolic velocity.

Variables	Mean ± SD or N (%)	
CLINICAL		
Age [years]	64.7 ± 9.7	
Male sex	48 (76.2%)	
Body mass index [kg/m ²]	26.8 ± 4.8	
SBP [mmHg]	121.6 ± 17.0	
NYHA III or IV	10 (15.9%)	
CCS III or IV	40 (63.5%)	
Arterial hypertension	31 (49.2%)	
Diabetes	13 (20.6%)	
Active athletes	0 (0%)	
ECHOCARDIOGRAPHIC		ABNORMALITY THRESHOLD
LVEF [%]	35.8 ± 8.4	Male < 52, Female < 54
E/e'	17.0 ± 5.9	> 14
TAPSE [cm]	1.9 ± 0.4	< 1.7
S' [cm/s]	11.2 ± 2.6	< 9.5
Tissue Doppler RIMP	0.53 ± 0.12	> 0.54
Pulsed Doppler RIMP	0.44 ± 0.15	> 0.43
FAC [%]	41.1 ± 8.6	< 35
$IVA [m/s^2]$	2.7 ± 0.9	< 2.2
RVFWSL [%]	-21.7 ± 6.0	> -20
RV4CSL 2 [%]	-16.2 ± 4.7	Not officially established
RVSepSL [%]	-9.5 ± 4.1	Not officially established
Frames per second	68.1 ± 10.3	Advisable for STE: 40–80

Table 1. Clinical and echocardiographic characteristics of the entire population (n = 63).

SD — standard deviation; NYHA — New York Heart Association; CCS — Canadian Cardiovascular Society grading scale; SBP — systolic blood pressure; LVEF — left ventricular ejection fraction; TAPSE — tricuspid annular plane systolic excursion; S' — Doppler tissue imaging (DTI)-derived tricuspid lateral annular systolic velocity; RIMP — right ventricular index of myocardial performance; FAC — fractional area change; IVA — myocardial acceleration during isovolumic contraction; RVFWSL — right ventricular free-wall longitudinal strain; RV4CSL 2 — right ventricular four-chamber longitudinal strain as the mean strain from the averaged strain curve of all segments; RVSepSL — right ventricular septal longitudinal strain; STE — speckle-tracking echocardiography

Table 2. Correlation analyses between right ventricular function indices and selected clinical and echocardiographic parameters in the study group (n = 63).

Variable	RVFWSL (p)	RV4CSL 2 (p)	TAPSE (p)	S' (p)
NYHA	0.52 (< 0.001)	0.52 (< 0.001)	-0.36 (0.003)	-0.31 (0.012)
LVEF	-0.67 (< 0.001)	-0.68 (< 0.001)	0.50 (< 0.001)	0.39 (0.001)
E/e'	0.54 (< 0.001)	0.53 (< 0.001)	-0.33 (0.008)	-0.31 (0.015)
LAA	0.46 (0.001)	0.43 (< 0.001)	-0.21 (0.098)	-0.37 (0.003)
TAPSE	-0.67 (< 0.001)	-0.66 (< 0.001)		

S'	-0.58 (< 0.001)	-0.54 (< 0.001)
Tissue Doppler RIMP	0.62 (< 0.001)	0.64 (< 0.001)
Pulsed Doppler RIMP	0.73 (< 0.001)	0.70 (< 0.001)
FAC	-0.62 (< 0.001)	-0.61 (< 0.001)
IVA	-0.58 (< 0.001)	-0.54 (< 0.001)

NYHA — New York Heart Association; LVEF — left ventricular ejection fraction; LAA — left atrial area; TAPSE — tricuspid annular plane systolic excursion; S' — Doppler tissue imaging (DTI)-derived tricuspid lateral annular systolic velocity; RIMP — right ventricular index of myocardial performance; FAC — fractional area change; IVA — myocardial acceleration during isovolumic contraction; RVFWSL — right ventricular freewall longitudinal strain; RV4CSL 2 — right ventricular four-chamber longitudinal strain as the mean strain from the averaged strain curve of all segments

Table 3. Comparison of clinical and echocardiographic data in the ACS subgroup at baseline and follow-up.

Variable	Mean ± SD	t	р
NYHA-1/NYHA-2	$1.4 \pm 0.8/1.2 \pm 0.4$	2.54	0.02
CCS-1/CCS-2	$3.8 \pm 0.4/0.03 \pm 0.2$	48.64	< 0.001
LVEF-1/LVEF-2 [%]	$39.3 \pm 5.7/48.8 \pm 8.1$	-8.79	< 0.001
E/e'-1/ E/e'-2	$16.5 \pm 5.1/12.4 \pm 4.7$	4.79	< 0.001
TAPSE-1/TAPSE-2 [cm]	$2.0 \pm 0.3/2.3 \pm 0.3$	-4.87	< 0.001
S'-1/S'-2 [cm/s]	$12.3 \pm 2.3/13.2 \pm 2.1$	-2.58	0.02
TD RIMP-1/TD RIMP-2	$0.51 \pm 0.10/0.42 \pm 0.08$	6.11	< 0.001
PD RIMP-1/PD RIMP-2	$0.38 \pm 0.11 / 0.31 \pm 0.08$	3.68	0.001
FAC-1/FAC-2 [%]	$43.2 \pm 6.9/45.9 \pm 6.2$	-1.92	0.06
IVA-1/IVA-2 [m/s ²]	$3.0 \pm 0.9/3.3 \pm 0.9$	-2.11	0.04
RV4CSL 2-1/RV4CSL 2-2 [%]	$-18.0 \pm 3.7/-22.2 \pm 3.5$	6.98	< 0.001
RVFWSL-1/RVFWSL-2 [%]	$-24.0 \pm 4.4/-27.8 \pm 4.3$	5.07	< 0.001
RVSepSL-1/RVSepSL-2 [%]	$-10.6 \pm 3.8/-15.1 \pm 4.3$	6.57	< 0.001

-1 data at baseline; -2 data at follow-up; NYHA — New York Heart Association; CCS — Canadian Cardiovascular Society grading scale; LVEF — left ventricular ejection fraction; TAPSE — tricuspid annular plane systolic excursion; S' — Doppler tissue imaging (DTI)-derived tricuspid lateral annular systolic velocity; TD — Tissue Doppler; PD — Pulsed Doppler; RIMP — right ventricular index of myocardial performance; FAC — fractional area change; IVA — myocardial acceleration during isovolumic contraction; RV4CSL 2 — right ventricular four-chamber longitudinal strain as the mean strain from the averaged strain curve of all segments; RVFWSL — right ventricular free-wall longitudinal strain; RVSepSL — right ventricular septal longitudinal strain

Table 4. Correlations between changes in RV systolic function parameters and

LVEF/RVSepSL changes in the ACS subgroup.

Variable	LVEF change	RVSepSL change

TAPSE change (p)	0.13 (0.45)	-0.43 (0.01)
S' change (p)	0.36 (0.03)	-0.36 (0.04)
Tissue Doppler RIMP change (p)	-0.32 (0.07)	0.32 (0.07)
Pulsed Doppler RIMP change (p)	-0.21 (0.25)	0.54 (0.001)
FAC change (p)	0.16 (0.38)	-0.35 (0.05)
IVA change (p)	0.14 (0.43)	-0.06 (0.75)
RVFWSL change (p)	-0.08 (0.67)	0.62 (< 0.001)
RV4CSL 2 change (p)	0.15 (0.41)	0.85 (< 0.001)

ACS — acute coronary syndrome; LVEF — left ventricular ejection fraction; RVSepSL — right ventricular septal longitudinal strain; TAPSE — tricuspid annular plane systolic excursion; S' — Doppler tissue imaging (DTI)-derived tricuspid lateral annular systolic velocity; RIMP — right ventricular index of myocardial performance; FAC — fractional area change; IVA — myocardial acceleration during isovolumic contraction; RVFWSL — right ventricular free-wall longitudinal strain; RV4CSL 2 — right ventricular four-chamber longitudinal strain as the mean strain from the averaged strain curve of all segments