

Four chamber right ventricular longitudinal strain versus right free wall longitudinal strain. Prognostic value in patients with left heart disease

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Abstract

Background: *There is no consensus on which right ventricle (RV) strain parameter should be used in the clinical practice: four chamber RV longitudinal strain (4CH RV-LS) or free wall longitudinal strain (FWLS). The aim of this study was to analyze which RV strain parameter better predicts prognosis in patients with left heart disease.*

Methods: *One hundred and three outpatients with several degrees of functional tricuspid regurgitation severity secondary to left heart disease were prospectively included. 4CH RV-LS and FWLS were assessed using speckle tracking. Left ventricular (LV) systolic function was determined using LV ejection fraction and RV systolic function using tricuspid annular plane systolic excursion (TAPSE). Patients were followed up for 23.1 ± 12.4 months for an endpoint of cardiac hospitalization due to heart failure.*

Results: *The cutoff value related to RV dysfunction (TAPSE < 17 mm) was lower, in absolute value, for 4CH RV-LS (4CH RV-LS = -17.3%; FWLS = -19.5%). There were 33 adverse events during the follow-up. Patients with 4CH RV-LS > -17.3% (log rank [LR] = 22.033; $p < 0.001$); FWLS > -19.5% (LR = 12.2; $p < 0.001$), TAPSE < 17 mm (LR = 17.4; $p < 0.001$) and LV systolic dysfunction (LR = 13.3; $p < 0.001$) had lower event-free survival (Kaplan Meier). In Cox multivariate analysis, 4CH RV-LS > -17.3% (hazard ratio [HR] = 3.593; $p < 0.002$), TAPSE < 17 (HR = 2.093; $p < 0.055$) and LV systolic dysfunction (HR = 2.087; $p < 0.054$) had prognostic value, whereas FWLS did not reach significance.*

Conclusions: *Although both 4CH RV-LS and FWLS have prognostic value, 4CH RV-LS is a better predictor of episodes of heart failure in patients with left heart disease, providing additional information to that obtained by TAPSE. (Cardiol J 2016; 23, 2: 189–194)*

Key words: right ventricle, right ventricular function, strain, echocardiography, heart failure

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Introduction

Assessment of right ventricular (RV) function is of great importance for the management and prognosis of several heart diseases [1–3]. Its echocardiographic evaluation is limited mainly due to its complex anatomy and its high dependence on loading conditions.

Myocardial deformation techniques have been proposed as a different tool to evaluate RV function. Strain parameters provide a quantitative evaluation of global and regional deformation of the RV and speckle tracking assessment may grant certain advantages over Doppler tissue image such as angle-independence [4]. Due to the longitudinal alignment of deep muscle fibers of the RV from the base to the apex [5], longitudinal shortening is a major contribution of the RV function [6]; hence longitudinal strain can represent RV systolic function accurately. However, standardized data and consensus on which strain parameter is better related to RV function, whether four-chamber RV longitudinal strain (4CH RV-LS) or the single measurement of its free wall (FWLS), are lacking. The major difference is that 4CH RV-LS includes the interventricular septum which is an integral part of both ventricles. Some groups prefer FWLS, as they consider that the RV free wall contributes to the most important part in RV stroke volume, and to avoid overlapping with left ventricular (LV) global longitudinal strain [7], whereas others prefer 4CH RV-LS in order to assess the entire ventricle [3].

In this study, we sought to assess which RV strain parameter better correlates to prognosis in patients with left heart disease.

Methods

Patient characteristics

The study was carried out in a large tertiary care hospital. Out-patients with different types of left heart disease referred to our cardiac imaging unit were prospectively included.

In order to avoid potential selection bias choosing the patients in accordance with a given RV systolic function parameter, but at the same time trying to get a homogeneous representation of different degrees of RV dysfunction, we selected patients with different degrees of functional tricuspid regurgitation (TR), an indirect parameter of RV function. Thus, we included consecutive patients with different degree of TR severity associated to left heart disease.

Congenital heart disease, previous cardiac surgery, primary tricuspid disease and all types of pulmonary hypertension other than group 2 [8] were defined as exclusion criteria.

Patients' condition at the time of the study, including the presence of ankle swelling and the need for diuretic treatment was recorded. Patients were followed over 23.1 ± 12.4 months for an endpoint of cardiac hospitalization due to heart failure. Clinical events were obtained from medical records and direct interviews with patients. All work was in compliance with the declaration of Helsinki and performed with the approval of the local Ethics Committee.

Echocardiography

A complete transthoracic echocardiogram was performed using a Vivid E9 device (GE Medical Systems, Horten, Norway) according to the standard protocol [9, 10]. All the studies were performed by two experienced echocardiographers (AG, JLM). Left atrial size was measured at its antero-posterior diameter from the long axis parasternal view in the end-systolic period and by its volume indexed volume from an apical 4-chamber view. LV ejection fraction (LVEF) was measured using apical biplane Simpson's method. LV dysfunction was defined as LVEF < 52% for men and LVEF < 54% for women according to the current recommendations [10]. The severity of TR was assessed using an integrated method including the estimation color area of the regurgitant jet in the right atrium, the vena contracta width (severe if the width of the vena contracta ≥ 7 mm), the proximal isovelocity surface area (PISA) method with Nyquist limit shift of 28 cm/s (mild if the radius of PISA was ≤ 5 mm, severe if the radius of PISA was ≥ 9 mm) and with the signal intensity and shape of the continuous wave Doppler of TR jet, according to the established practice guidelines [11]. TR was finally graded using a 4-point scale (normal, mild, moderate and severe). The systolic pulmonary artery pressure (SPAP) was estimated using TR peak velocity and right atrial pressure, which was estimated by the inferior vena cava diameter from long-axis subxiphoid view and its response to inspiration.

Two-dimensional speckle-tracking echocardiographic analysis was performed from a 4-chamber modified apical view focused on the RV. Three consecutive heart cycles were recorded and averaged. Images were optimized for strain analysis to improve frame rate to 50–90 frame/s. The analysis was performed offline by using Echo-PAC software (GE Medical System, Horton, Norway). To calculate 4CH

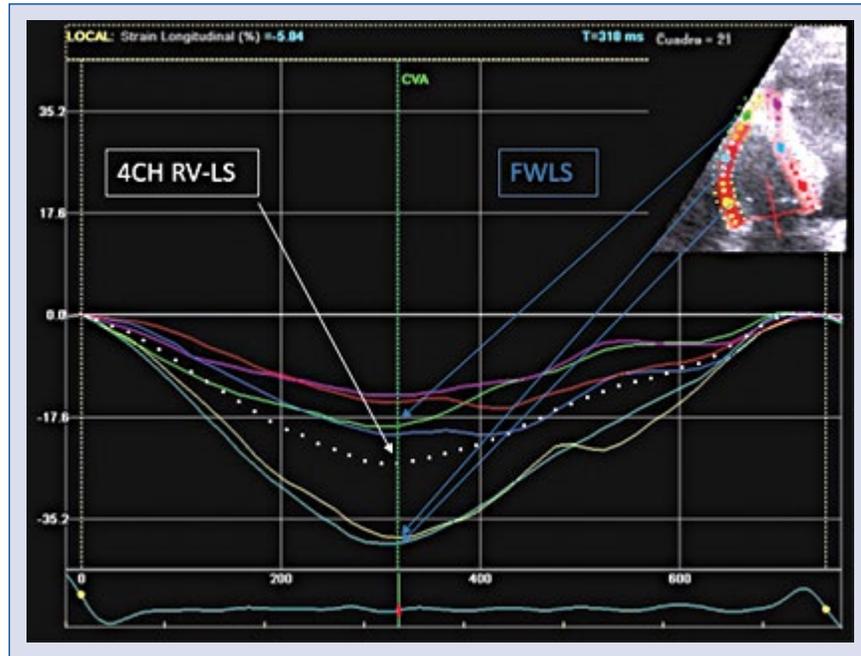


Figure 1. Right ventricular myocardial deformation study. Four chamber right ventricular longitudinal strain (4CH RV-LS) is obtained calculating the average peak strain values of the 6 analyzed segments. In the graphs, the dotted lines represent its value. Free wall longitudinal strain (FWLS) is obtained from the average of basal (yellow), medium (blue) and apical (green) values of right ventricle free wall.

RV-LS, the endocardial edge of the RV was manually traced in the 4-chamber view. The region of interest, composed from 6 segments, was automatically positioned to track frame by frame the RV throughout the cardiac cycle. The endocardial contour and width were manually adjusted when necessary to provide optimal tracking [12]. 4CH RV-LS was calculated as the mean of peak systolic values observed in the 6 segments, while FWLS was calculated as the mean of basal, mid and apical RV free-wall values (Fig. 1). Tricuspid annular plane systolic excursion (TAPSE) was estimated by M-mode [mm], measured between end-diastole and peak-systole. RV dysfunction was defined as TAPSE < 17 mm according to the current recommendations [10].

Statistical analysis

Continuous variables are shown using mean and standard deviation; discrete variables using absolute and relative frequency. Chi-square test was used among discrete variables for statistical analysis. Fisher's test was used in cases where frequency was below 5. Assumption normality was performed by histogram and by Kolmogorov-Smirnov test. Student's t-test was used for comparison of continuous variables, or Mann-Whitney test when conditions of normal distribution were

not met. For variables correlation contrast, Pearson correlation test was used, or Spearman's test when conditions of normal distribution were not met. The optimal cutoff value related to RV dysfunction defined by TAPSE < 17 mm was determined by the receiver-operating characteristic curve analysis. In two models of linear regression, 4CH RV-LS and FWLS were set as dependent variables, with LVEF, and TAPSE as co-variables, with a backwards strategy. Kaplan-Meier survival plots were calculated from baseline to time of adverse event and compared using the log-rank test. Cox proportional-hazards regression model was used to assess the risk of combined endpoint associated with 4CH RV-LS, FWLS, LVEF and TAPSE. Statistical analysis was performed using SPSS system version 16 and Stata 13. All p values reported are from 2-sided tests, and p values < 0.05 were considered statistically significant.

Results

Patient characteristics

A total 103 patients (67 females, mean age 72.9 ± 14 years old) with different left heart diseases were included in this study. Sixteen percent with severe TR, 30% with moderate TR, 29% with mild

Table 1. Clinical and echocardiographic characteristics.

Age [years]	72.9 ± 14.4
Women	65%
Atrial fibrillation	41%
Hypertensive cardiomyopathy	25%
Ischemic cardiomyopathy	17%
Myocardial infarction	11%
Dilated cardiomyopathy	8% (n = 8)
Moderate to severe left heart valvulopathy	34% (n = 35)
Aortic valve*: stenosis/ /regurgitation	12%/9%
Mitral valve*: stenosis/ /regurgitation	10%/19%
LA dimension [mm]	45.2 ± 10.2
Indexed LA volume [cc/m ²]	38 ± 13
LVEF [%]	64.3 ± 13.9
LV systolic dysfunction	18%
SPAP [mm Hg]	49.6 ± 19.0
TRS (severe, moderate, mild, none)	16%/30%/29%/25%
TAPSE [mm]	20.1 ± 4.9
RV systolic dysfunction	31% (n = 32)
4CH RV-LS	-19.35 ± 5.6
FWLS	-21.85 ± 7.3
RA pressure [mm Hg]	9.4 ± 5.8
Previous HF	38%
Ankle swelling	29%
Diuretic treatment	41%

Functional class ≥ 2 61.2% *Moderate or severe impairment; LA — left atrium; LVEF — left ventricular ejection fraction; LV — left ventricle; SPAP — systolic pulmonary artery pressure; TRS — tricuspid regurgitation severity; TAPSE — tricuspid annular plane systolic excursion; RV — right ventricle; 4CH RV-LS — four chamber right ventricular longitudinal strain; FWLS — free wall longitudinal strain; RA — right atrium; HF — heart failure

TR and 25% without TR. LV systolic dysfunction was present in 18% of the total of the population and RV systolic dysfunction in 31%. Sixty-one percent of patients were in functional class ≥ 2, 38% had completed prior admission for heart failure and 41% needed diuretic therapy chronically. The clinical and echocardiographic data of the population are summarized in Table 1.

Right ventricular strain and biventricular function

4CH RV-LS and FWLS showed significant correlations with TAPSE ($r = -0.520$, $p < 0.005$ and $r = -0.471$, $p < 0.001$, respectively). The best cutoff value related to RV dysfunction (TAPSE <

< 17 mm) was lower for of 4CH RV-LS (-17.3%; area under the curve [AUC] = 0.775, $p < 0.01$) than for FWLS (-19.5%; AUC = 0.754, $p < 0.001$).

Linear regression analysis showed FWLS depended exclusively on TAPSE (coefficient of determination 0.186; correlation with TAPSE = -0.613; 95% confidence interval [CI]: -0.865-0.360), while 4CH RV-LS depended on LVEF and TAPSE (coefficient of determination 0.327; correlation with LVEF = -0.104; 95% CI: -0.174 to -0.033; correlation with TAPSE = -0.492; 95% CI: 0.694-0.290).

Right ventricular strain and outcome

During a follow-up of 23.1 ± 12.4 months, there were 33 adverse events. In Kaplan-Meier analysis, patients 4CH RV-LS > -17.3% (log rank [LR] = 22.033; $p < 0.001$), TAPSE < 17 mm (LR = 17.4; $p < 0.001$), FWLS > -19.5% (LR = 12.2; $p < 0.001$) and LV systolic dysfunction (LR = 13.3; $p < 0.001$) had lower event-free survival (Fig. 2).

After univariate analysis by Cox-proportional hazard regression analysis, TAPSE, LVEF, 4CH RV-LS and FWLS were associated with adverse outcomes (hazard ratio [HR] for a 4CH RV-LS > -17.3% = 5.19; $p < 0.001$; HR for a FWLS > -19.5% = 3.38; $p < 0.001$). In Cox multivariate analysis, with TAPSE < 17 mm, 4CH RV-LS > -17.3%, FWLS > -22.7% and low LVEF; only 4CH RV-LS > -17.3% (HR = 3.593; $p < 0.002$), TAPSE < 17 (HR = 2.093; $p < 0.055$) and LV systolic dysfunction (HR = 2.087; $p < 0.054$) had prognostic value whereas FWLS did not reach significance. The inclusion of the TR severity and the SPAP in the model did not change the results.

Discussion

In the present study, the authors assessed the prognostic value of 4CH RV-LS and FWLS in patients with left heart disease. The main finding is that although both parameters are prognostic markers, 4CH RV-LS shows a stronger association with episodes of heart failure than FWLS, providing additional prognostic information to that obtained with TAPSE and LVEF.

The fact that 4CH RV-LS has greater prognostic value than FWLS points to the importance of the septum in global RV function. In our study, both strain parameters correlate similarly with RV systolic function estimated by TAPSE, however, 4CH RV-LS has a stronger correlation with LVEF than FWLS suggesting that 4CH RV-LS is not only related with the RV function but also reflects the influence of LV function on it. This parameter could

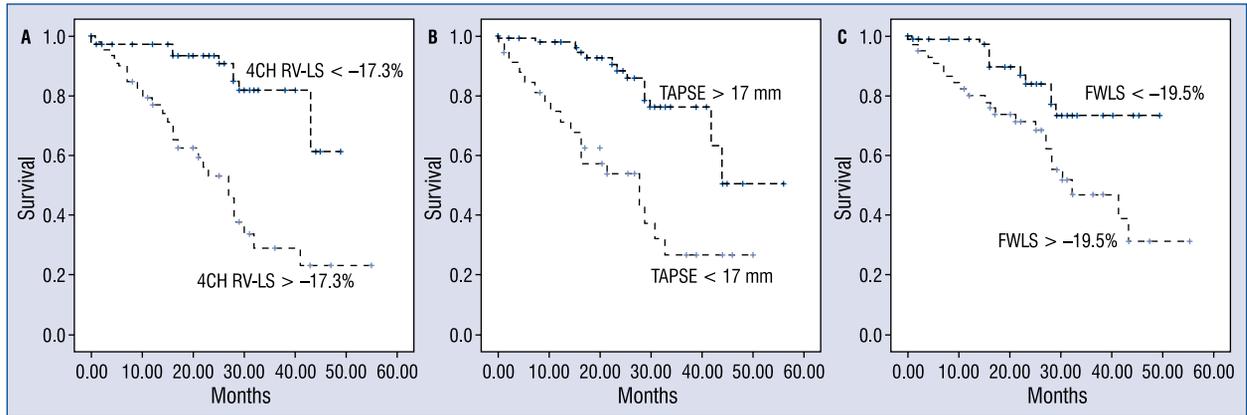


Figure 2. Kaplan-Meier analysis according to four chamber right ventricular longitudinal strain (**A.** 4CH RV-LS; $> -17.3\%$) and free wall longitudinal strain (**C.** FWLS; $> -19.5\%$); **B.** Tricuspid annular plane systolic excursion (TAPSE).

therefore be considered a marker of biventricular function, a fact that could partly explain its better prognostic significance. Our finding is consistent with a general agreement that the malfunction of one chamber may influence the function of the neighboring chamber [13].

Recent publications have pointed to the prognostic value of RV strain in patients with heart failure [3, 14, 15], but mostly in patients with severe LV dysfunction. Our data is consistent with that of Motoki et al. [3], who found that in patients with heart failure and low LVEF ($25 \pm 6\%$), 4CH RV-LS is a more reliable predictor of events than FWLS. The cutoff point shown in this study in event prediction (4CH RV-LS $> -14.8\%$) is above ours (-17.3%). Besides differences between vendors, their patients had severe LV dysfunction, thus tending to worsen the value of RV longitudinal strain, as opposed to our population. Therefore, the 4CH RV-LS values used in patients with LV dysfunction are not fully extrapolated to other populations with normal LVEF. According to these data, 4CH RV-LS should be preferred over the FWLS when the objective is to assess the prognosis of patients with left heart disease. The FWLS could become a useful tool for the evaluation of isolated RV function, as in the study of right cardiomyopathy [16] or after interventionism as the impact of ventricular assistance devices [17].

Clinical practice guidelines for the assessment of the right heart [18] do not establish a strain cutoff point for RV systolic dysfunction evaluation. The latest recommendations for quantification of cardiac cavities [10] first suggested as abnormal a cutoff value for longitudinal RV FWLS strain of $> -20\%$, while recognizing that the values may

depend on the vendor and version of the used program. Meris et al. [12] established the cutoff value for 4CH RV-LS in -19% , Lee et al. [19] in -16.8% and Park et al. [14] in -15.4% ; for FWLS, Ternacle et al. [7] established the cutoff in -21% . In our sample of patients, using TAPSE as a reference [18, 20], the best value related to RV systolic dysfunction for 4CH RV-LS (-17.3%) was lower in absolute value than for FWLS (-19.5%).

We have to take into account that our sample was selected by its TR severity. It is difficult to assess the influence that the load conditions may have on the deformation and the strain results. The intrinsic RV function may be somewhere hidden in the dataset. Therefore, different load conditions and LV function probably impact on RV deformation and may partially explain the different values published in the literature.

Nevertheless, our data reflect that although both RV strain parameters reflect in somehow RV function, the cutoff values related to RV dysfunction should be lower in absolute value for 4CH RV-LS.

Limitations of the study

As a limitation of this study, it must be pointed out that data on RV ejection fraction as an indicator of the RV systolic function are missing. Although previous studies have validated the 4CH RV-LS with RV ejection fraction by cardiac magnetic resonance [14] and although the RV ejection fraction obtained by echocardiography also has limitations, its estimation would have offered interesting information to the study.

To avoid a selection bias we did not include patients through a direct measurement of RV func-

tion but by an indirect measure of the RV overload, as is the severity of the functional TR. However, the selection of patients by TR severity can be a confounding factor in assessing RV function [21]. The volume overload generated by TR can lead to an increase in the percentage of deformation, increasing our values. In any case, the higher predictive value of 4CH RV-LS over FWLS remains after including the TR severity in Cox-proportional hazard regression analysis.

A percentage of patients with coronary heart disease were included in the study and prior infarct on the right coronary artery could also reduce the RV strain, however, in our sample only 3 patients had inferior myocardial infarct and none of them extension to the RV.

The study was conducted at a single center with a relatively small sample size. The heterogeneity of the sample does not allow the analysis of absolute reference values for event prediction in each of the different etiologies.

Conclusions

The assessment of RV strain parameters is relevant for risk stratification of patients with left heart diseases. Our study shows 4CH RV-LS as a better predictor of heart failure episodes than the isolated determination of FWLS. Moreover, 4CH RV-LS provides additional prognostic information to that obtained by TAPSE and LVEF. These findings suggest that the use of 4CH RV-LS in clinical practice could improve the prognostic assessment of patients with left heart disease, although further studies evaluating the impact of medical decision based on the determination of the 4CH RV-LS on the prognosis of these patients are required.

Conflict of interest: None declared

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