Right Ventricular Longitudinal Strain in the Clinical Routine: State-of-the-Art Review

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Introduction

The right ventricle (RV) plays a crucial role in determining patient functional status and outcome in nearly all cardiovascular conditions(1). Although the importance of RV function has been neglected for decades, accumulating evidence has proven its dramatic clinical relevance and has fuelled a growing interest in understanding the RV in health and disease. This work has led to acceptance that quantification of RV function should be part of any routine cardiac imaging workup either by transthoracic echocardiography (TTE) or cardiac magnetic resonance (CMR), just as it is for the left ventricle (LV). Nonetheless, the many anatomic and functional peculiarities of the RV compared to the LV, are compounded by increasingly recognized disparities in the adaptative remodelling of the two ventricles. These differences preclude any extrapolation of our knowledge about the LV pathophysiology to its right-sided counterpart and pose significant challenges to the non-invasive imaging assessment of RV function (2). The thinner and highly trabeculated RV wall is more challenging to image and manually delineate than the LV wall, and the conventional indices of RV function are affected by significant limitations due their dependency on load, angle of insonation or geometric assumptions (3).

In recent years, RV longitudinal strain (RVLS) by two-dimensional speckle-tracking echocardiography (2D STE) imaging emerged as a superior metric of RV systolic performance. RVLS is able to detect subclinical impairment of RV function and to better predict patient outcome in pressure or volume overload conditions, including pulmonary hypertension (PHT), severe tricuspid regurgitation or COVID-19 infection (4-6). However, despite 2D STE has become widely available, RVLS is still largely underused (7).

The purpose of this article is to provide a state-of-the-art review focusing on the fundamental aspects of RVLS, including a brief overview of the RV anatomy and functional adaptation to disease, a description of the RVLS methodology with practical recommendations and normative values, as well as the clinical and prognostic relevance of RVLS in various cardiovascular disorders. Ultimately, the scope of this review is to familiarize readers of the *Eur Heart J Cardiovasc Imaging* with the advantages and challenges of RVLS analysis with respect to conventional parameters, as an essential requisite for anyone interested to improve the accuracy and reproducibility of RV quantification in their practice.

RV structure and normal function

The RV is a thin-walled, crescent-shaped structure, consisting of an inlet portion (TV, chordae, papillary muscles), a trabeculated apex and an outlet (infundibulum) which supports the pulmonary valve. It is characterized by coarse trabeculations and two major muscular bands (moderator band, supraventricular crest) connecting the RV free wall to the septum. In contrast to the LV, the free wall of the RV has only two distinct layers. The thinner outer layer has predominantly circumferential fibres (25%), while the fibres of the dominant inner layer run in longitudinal direction(8).

The major mechanisms contributing to RV pump function are different from those of the LV and include: (1) contraction of the longitudinal fibres, which shortens the RV long-axis by drawing the tricuspid annulus toward the apex; (2) inward motion of the RV free wall by the shortening of circumferential fibres (transversal shortening or “bellows effect”); (3) interventricular septal motion; and (4) circumferential shortening of the RV outflow tract (3). Under normal conditions and likely due to the predominance of longitudinal fibres, longitudinal

shortening accounts for approximately 75% of RV contraction. In pressure overload states, RV contraction is less dependent on longitudinal shortening and the relative contribution of the "bellows" function becomes more relevant (9, 10). The RV is a volume pump, adapted to a vascular bed which has approximately only 1/6th of the systemic impedance. Consequently, the RV mass is only around 1/6th of that of the LV and in the adult, the RV free wall is only 3-5 mm thick (1, 11). As the RV and LV stroke volumes (SV) are the same, and the RV end-diastolic volume is 10-15% larger than the LV end-diastolic volume, the normal RVEF is lower than the LV ejection fraction (LVEF). Because of the higher surface-to-volume ratio of the RV compared to LV, a smaller inward motion is required to eject the same SV(8). The LV contributes significantly to RV ejection due to the systolic ventricular interaction via the interventricular septum: 20–40% of RV SV and systolic pressure result from LV contraction. Likewise, 4-10% of LV systolic pressure results from RV contraction (12). The RV contracts in a peristaltic fashion with a time delay between the inlet and outlet part of 20-50 ms (11). Flow studies show less vortex formation in the RV compared to the LV, but rather a helical flow towards the outflow, facilitated by the trabeculated apex (13).

Similar to the LV, RV function can be described by invasive pressure-volume-loops which allow the assessment of stroke work, and – during a preload change – end-systolic and end-diastolic elastance as measures of contractility and passive chamber stiffness, respectively. Non-invasive imaging describes surrogates of RV deformation (such as RVLS), which are in any case load dependent. Therefore, RVLS has to be interpreted considering pre- and afterload, as well as chamber shape. RVLS is often assessed at the free wall only and normally found to be approximately 30% in longitudinal direction (see Reference Values of RVLS) and 15% in the

circumferential direction. This deformation pattern of the RV is in contrast to the LV's, which shows lower longitudinal (around 20%) and higher circumferential strain (around 25%)(14, 15).

RV adaptation to disease

The relative increase of RV afterload in pathologic states can be much higher than relative increments of LV afterload, which explains the more pronounced decrease in functional parameters and eventual failure in an acute setting (lung emboli). Chronic pressure overload leads to an adaptive concentric hypertrophy of the RV wall (including trabeculae and muscular bands) which reduces wall stress. When this means of compensation becomes exhausted, the RV develops eccentric hypertrophy with progressive dilatation and dysfunction. Pressure overload is often better tolerated in congenital heart disease (e.g. congenital pulmonary valve stenosis, Eisenmenger syndrome) compared to acquired pathology (e.g. PHT)(16), possibly reflecting the different time-course of these entities. RV function in hypertrophy is characterised by a reduced longitudinal deformation and an increase of the circumferential component (14). Intraventricular dyssynchrony can lead to heterogeneous increase in wall stress and further deterioration of RV function(17). RV free wall shortening in PH may even extend after PV closure. The resulting diastolic leftward shift of the septum impairs LV filling and reduces SV(18). Hypertrophy and myocardial fibrosis also impair diastolic function of the RV(19).

RV volume overload causes eccentric hypertrophy, i.e. an increase in RV mass with preserved wall thickness. The increased wall stress of a larger ventricle, however, will eventually lead to the vicious cycle described above. Nevertheless, volume overload is often better and longer tolerated than pressure overload(20). A diastolic leftward shift of the septum may lead to simultaneous diastolic dysfunction of the LV. Studies investigating regional RV function in volume overload due to ASD report normal basal and elevated apical values of RVLS (21).

Strain in several pathologies remains reduced even years after repair, potentially as result of incomplete reverse remodelling or irreversible myocardial damage (21). In particular, avoidance of the latter is seen as an argument for early interventions in order achieve a normalization of RV function and better outcome(14).

Finally, RV myocardium may be directly affected by ischemia, cardiomyopathy and other pathology. The severity of RV dysfunction depends on the location and extent of the underlying changes and may be modulated by an additional volume or pressure load of the ventricle.

Assessment of RVLS

Strain is a dimensionless metric of myocardial function, describing the deformation of the myocardium that occurs during the cardiac cycle. RVLS is calculated as the percentage of systolic shortening of the RV wall from base to apex and expressed as negative values, despite the absolute values of RVLS (i.e. RVLS magnitude – Table 1) may be more practical for communication in clinical settings (i.e. larger magnitude suggesting better function).

2D STE is the current standard method for assessing RVLS in clinical practice, being less angle-dependent, more feasible and reproducible than tissue Doppler strain. Feasibility of RVLS by 2D STE relies heavily on the characteristics of the RV image acquisition by 2DE (22). In 2018, the EACVI/ASE/Industry Task Force has published recommendations for the standardization of RVLS image acquisition and analysis by 2D STE for both clinical and scientific purposes (23). **Figure 1** graphically summarizes the recommended protocol for image acquisition and analysis to measure RVLS in clinical practice.

According to the EACVI/ASE/Industry Task Force recommendations, RVLS quantification by 2D STE should be performed on the RV-focused apical 4-chamber view (**Figure 1, Video 1**), which is the same view that should be used to measure also RV size and function by conventional echocardiography (24). This is because the RV free wall is generally better visualized and measurements of RVLS are more reproducible when the RV-focused apical 4-chamber view is used compared to the conventional 4-chamber view centred on the LV **(Figure 2, Video 2)** (23). Also, RVLS values obtained from RV-focused view are larger in magnitude than those obtained from the conventional apical 4-chamber view (**Figure 3**) (25) and the current reference values of RVLS have been obtained on RV-focused view (see next section).

With the patient in a steep lateral position and the transducer at the LV apex (**Figure 1, Step 1**), the RV-focused apical 4-chamber view for RVLS analysis can be obtained by moving the transducer to a more lateral position and by tilting it towards the liver (**Figure 1, Step 3**) in order to position the LV apex at the centre of the scanning sector. The correct RV-focused apical 4-chamber view should display only the interatrial septum **(Video 1)** and not the LV outflow tract (seen if the plane position is too anterior, **Video 3**), nor the coronary sinus (plane position too posterior, **Video 4**) (**Figure 2**). Fine adjustments in probe orientation will enable to display the largest RV width, the apex and the entire free wall, which should be clearly visible throughout the cardiac cycle to allow optimal STE tracking (**Video 1**). Image depth, sector angle and gain should be adjusted to achieve an optimal quality image with a temporal resolution of 50-80 fps (**Figure 1, Step 5**). Respiratory manoeuvres are often needed to optimise spatial resolution and 3 consecutive cycles should be acquired during patient breath hold. RV end-systole should be identified based on the pulmonary valve closure click (PVC) on the RV outflow tract Doppler

tracing, which should be acquired immediately in sequence to minimize variations in cardiac cycle (**Figure 1, Step 6**).

Free wall RVLS is the average strain value of the 3 segments of the RV free wall, but 6 segment RVLS can be obtained by including both the free wall and interventricular septum (15). Free wall RVLS is commonly recommended for clinical practice, yet there are conditions where RVLS including the septum might be of interest (see Clinical and prognostic value of RVLS).

Even if the aim is to measure only the RVLS at the free wall, the region of interest (ROI) should include both the RV free wall and septum. ROI width should be adjusted according to the thickness and position of free wall RV myocardium. Placing the ROI too externally (including the pericardium) or too low (below the tricuspid annulus) will lead to RVLS underestimation (**Figure 4, Videos 5--9**). Conversely, RVLS will be overestimated if the ROI width is too thin and encompasses mainly the endocardial layer. Software algorithms measuring the RVLS at the endocardium provide different values than software measuring the full wall or mid-myocardium (23). Tracking quality should always be verified visually on the cine loops showing the ROI superimposed on the RV myocardium and on the strain curve patterns (**Figure 1, Step 7**). Suboptimal tracking in some regions may be sometimes resolved by manually re-adjusting the ROI position.

There are several commercially available software packages that can be used to measure RVLS in clinical practice, either dedicated for RV, or designed for LV and adaptable to RV. These software packages share similarities and differences in terms of STE algorithm and analysis workflow. Tracking results showed little influence from vendor-specific image characteristics and seem to depend mainly on the STE software used (26). However, inter-vendor variability was reported to be acceptable for global RVLS (27). Conversely, regional RVLS showed an

unacceptable level of variability (up to 30–40%). Segmental RVLS is therefore not recommended for clinical use (23).

STE applied on three-dimensional (3D) data sets of RV is conceptually attractive, as it could allow the evaluation of the whole RV myocardium and the analysis of multidirectional and principal RV strain, without issues related to apical foreshortening. However, due to several issues (e.g. lower spatial and temporal resolution of transthoracic 3D versus 2D acquisitions, lack of standardization, no commercially available software dedicated for the quantification of multidirectional RV strain based on 3D STE derived RV mesh etc), the added value of RV 3D strain is currently under investigation (28, 29).

Reference values of RVLS

Reference ranges of RVLS obtained from the dedicated RV-focused view using 2DSTE in healthy subjects are summarized in **Table 1**. Small studies (<120 enrolled subjects), as well those using the standard apical 4-chamber view for RVLS analysis have not been included. Absolute values of free wall RVLS were higher than those of 6-segment RVLS across the studies, with the lowest level of normality (LLN) for free wall RVLS ranging from −13.3 to −22.7% (15, 30-33). Although no significant differences in RVLS were found in one study comparing three frequently used commercial ultrasound systems (34), RVLS measurements may be affected by the 2DSTE software algorithm used for RVLS analysis. A useful rule of thumb is that free wall RVLS higher than −20% (lower than 20% in absolute value) is likely abnormal, as suggested by 2015 EACVI/ASE chamber quantification guidelines (24) and the recent multinational WASE study (33).

Women have higher absolute RVLS values than men (2±4 % strain units) and dedicated sex-specific limits of normality should be ideally used in the single patient (15, 31, 33). LLN of free wall RVLS are higher with approximately 1 strain unit (%) in women than men (15, 31, 33). The largest WASE study to date including a multi-ethnic population did not show significant differences in RVLS between ethnic groups (33).

Absolute RVLS values decrease with age in healthy adults, but these differences are small and probably not clinically relevant (15, 31, 33). A meta-analysis comprising 10 studies in healthy children reported significantly higher absolute RVLS reference values than in adults: LLN of free wall RVLS −27% (35). Accordingly, for clinical purposes it seems reasonable to use the same LLN in all age groups, except in children (15).

Regional differences of normal RVLS values

While RVLS was significantly higher in the free wall than in the septum in all prior studies, the data on RVLS values among the RV free wall segments are conflicting. A significant base-to-apex segmental strain gradient was observed in the RV free wall in children (35) and in one adult study (34). Other studies with adult population found all segments of RV free wall having similar RVLS values (36). Conversely, basal segments were reported as having either the highest (37) or the lowest values (38) among the 3 RV free wall segments. Furthermore, two studies (15, 30) found that the mid-segments of the RV free wall showed larger RVLS magnitudes than apical and basal RV segments. Sanz-de la Garza et al. (38) reported that the segmental differences in RVLS across RV free wall segments present at rest disappeared during exercise. Based on these data, and the inter-vendor variability of segmental RVLS (39), it is not possible to propose any reference ranges of segmental RVLS for clinical use.

Clinical and prognostic value of RVLS

RVLS offers incremental functional information and prognostic value over the conventional echocardiographic indices of RV systolic function in various cardiovascular disease (**Figure 5, Table S1**).

Heart failure

RV function has a major influence on outcome in both acute and chronic heart failure (40, 41). It is therefore recommended to assess RV function in patients with heart failure(24) to optimise treatment or to ultimately schedule patients for left ventricular assist device (LVAD) or heart transplantation. RVLS is useful for assessment of RV function in heart failure. Recent studies showed that RVLS correlated well with RV SV, providing a better estimation of RV systolic performance than TAPSE and S' in patients referred for heart transplantation(42), and correlated with the extent of RV myocardial fibrosis and functional capacity(43). These findings were confirmed in a larger study, reporting RVLS as a better predictor of episodes of heart failure in patients with left heart disease, providing additional information to that obtained by TAPSE(44). Similar results have been found in end-stage dilated cardiomyopathy caused by LMNA mutations(45). The progression of RV dysfunction by RVLS was a significant marker of adverse heart failure outcome in 101 patients with LMNA disease.

LVAD implantation is increasingly used to treat heart failure. RV dysfunction is often a limitation to this treatment and is associated with high morbidity and mortality. Decreased RVLS was associated with an increased risk for RV failure among patients undergoing LVAD implantation and was incremental to the Michigan risk score as a predictor of RV failure(46). RV

strain from subcostal view was feasible also in critically ill patients, including those with VVECMO, and could be useful as prognostic marker(47).

Cardiomyopathies

RVLS is useful to assess RV function in several cardiomyopathies (**Figure 6, Video 10**). The most relevant cardiomyopathy is RV arrhythmogenic cardiomyopathy (ARVC), which predominantly affects the RV. Emerging awareness of LV involvement has resulted in a change to the more general term arrhythmogenic cardiomyopathy (ACM). Nevertheless, it is of great importance to assess the RV in these patients, since the RV most often shows abnormalities in an early stage, when risk stratification for ventricular arrhythmias is most important(48). Several papers in the last 15 years have shown added value of RVLS in ACM patients(49). Kjaergaard et al found usefulness of RVLS in 30 ACM patients (50) and Sarvari et al (51) confirmed these findings in a larger cohort and added the usefulness of RVLS to detect asymptomatic mutation carriers at risk of ventricular arrhythmias. Furthermore, RVLS increased risk stratification when used together with ECG changes in ACM patients with early disease (48). RVLS was also a risk marker in a prospective cohort of 117 ACM mutation carriers with no events at baseline who were followed for 4.2 years (52). These reported studies have used 3- or 6-segment approaches; the 3 RV free wall segments are RV-specific, while the 6 segments model include the interventricular septum, which is rarely affected in ACM. Nonetheless, the 6-segment model is important for measurement of RV mechanical dispersion (the standard deviation of the time intervals from R wave on ECG to the 6 segmental peak strain values, **Figure 7B**), which reflects RV contraction heterogeneity, a robust marker for ventricular arrhythmias in ACM (48, 52), which has been externally validated (53). Other approaches to assess the RVLS in ACM have

been proposed by Mast et al (54), using the strain pattern from RV free wall as diagnostic markers of early disease and also for risk stratification of ventricular arrhythmias (**Figures 7-8**)(53). Furthermore, RVLS has been used to assess RV function and risk of ventricular arrhythmias in athletes' heart. Lie et al found that athletes with ventricular arrhythmias had impaired RV function by RVLS and had more myocardial fibrosis compared to healthy athletes (55). Athletes with life-threatening arrhythmic events had additional LV contraction abnormalities. These phenotypes mimicked ACM and may potentially be induced by high doses of exercise in susceptible individuals.

PH and systemic sclerosis

As changes in haemodynamic and RV function parameters are not necessarily correlated in PHT (56), RV evaluation is of critical importance in patients with PHT. In part because of this dissociation of haemodynamics and RV function, and in part because of the limitations of measuring PHT by echocardiography, patients who are apparently stable may demonstrate a reduction of RV function (57). Normalization of RV size and function is therefore an important treatment goal in PHT (58). Thus, an adequate echocardiogram in PHT should include assessment of not only RV pressure, but also RV hypertrophy, RV volume and RV function. The problem is that all of these parameters present challenges in quantitation with conventional echocardiography, and as a consequence, RA and RV size, and RV function are often assessed subjectively (59). Conventional quantitative markers, such as TAPSE, are associated with outcome and disease progression (60), yet may be misleading because of translational motion of the RV free wall (61). In contrast, RVLS is a sensitive parameter over small variations in PASP, with less variability than conventional markers (62). Free wall RVLS is associated with functional capacity, natriuretic peptides, RV failure and survival, even after adjustment for age and sex (6). Wright et al (63)

confirmed the strong and independent association of free wall RVLS with outcome throughout follow-up, with better predictive value than TAPSE (**Figure 9**). After accounting for follow-up time and baseline function, only changes in free wall RVLS, IVC size and RA area were associated with outcome (63).

PHT has a particularly adverse profile in patients with systemic sclerosis (64). A specific pattern for RV involvement in scleroderma (SSc) patients has been proposed by Mukherjee (65). This involves lower fractional area change (FAC; 49% vs 55%; p=0.002) albeit within the normal range, and preserved RVLS (-20.4% versus -17.7%; p=0.005), because greater basal RVLS (-32.2% vs -23.3%; p=0.0001) compensates for worse mid RVLS (-12.4% vs -20.9%; p<0.0001) and apical RVLS (-8.5% vs -17.1%; p<0.0001). The regional difference in the base compared with the apex was significantly greater for SSc than for controls (p<0.0001 for interaction). These differences were unchanged after adjusting for RVSP. TAPSE was not different between SSc and control subjects (p=0.307).

Other work shows that the abnormal RV response in SSc is related to pulmonary fibrosis and PHT (66). Those with both of these abnormalities have the most impaired free wall RVLS (-16.8±3.1%) followed by those with pulmonary fibrosis only (-21.5±3.6%) and neither fibrosis nor PHT (-24.0±4.4%). All three SSc groups showed impaired free wall RVLS compared with controls (-28.0±4.2%). Importantly, multivariable regression analysis demonstrated that pulmonary fibrosis and LVEF were independently associated with impaired free wall RVLS in SSc patients.

However, this suggestion of a specific SSc “signature” is controversial. In a study of CMR feature-tracking of 38 SSc patients, the 19 patients with SSc-PHT had lower free wall RVLS than SSc without PHT, and the latter were no different from controls. Free wall RVLS correlated with mPAP (R = 0.68, p<0.001), and free wall RVLS had an AUC of 0.86 for prediction of PHT (67).

Valvular Heart Disease

Data on the use of RVLS for the assessment of RV function in left-sided heart disease is scarce. The increasing use of TAVR in higher-risk patients, however, has triggered research investigating the value of RVLS for patient management and prognosis.

In a study with 340 patients with asymptomatic AS, the combined end-point of HF hospitalisation and death was only related to LV global longitudinal strain, but not to RVLS (68). However, in 128 patients with low-flow, low-gradient aortic stenosis with low LVEF, free wall RVLS was independently associated with mortality, and both RVFWS at rest and with stress (worse than -13% and -14%, respectively) had an incremental prognostic value over LV global longitudinal strain (69). In patients with severe aortic stenosis, RVLS is frequently found to be reduced (70) and does not necessarily improve after TAVR (71). Other studies reported improved free wall RVLS after TAVR but not in patients undergoing surgery (72), or in patients with normal flow, but not in those with low flow (70). Post-interventional low cardiac output syndrome after TAVR impairs short term outcome and was repeatedly found to be related to reduced free wall RVLS before TAVR (73). Likewise, free wall RVLS is associated with post-interventional mortality (71, 74).

Mitral regurgitation (MR) leads to increased pulmonary venous and arterial pressure which increases RV afterload and reduces RV function. This reduced RV function has prognostic value in patients undergoing valvular surgery. A significant reduction of PASP, TR severity and improvement of RV function as measured by free wall RVLS has been described after transapical MV replacement (75). This may be explained by unloading of the RV, as Hyllen found a significant postoperative increase in free wall RVLS only in patients whose preoperative

PASP was above 50 mmHg (76). The intervention itself can also lead to a transient reduction of RVLS, more in patients with open sternotomy and less after a minimally invasive treatment (77). Particularly in patients with ischemic MR, however, the RV frequently continues to deteriorate after MV surgery despite concomitant TR surgery and a regression in LV size (78). Pre-operative RV dysfunction appears to have independent prognostic value. In addition, improvement of LV function is limited in the setting of low baseline free wall RVLS (worse than -15%), while patients with better RV function improved (79). Others found that only the resolution of RVLS at one month after intervention predicted subsequent myocardial recovery, and that patients with such "RV reserve" had a lower risk of hospitalization for heart failure (80).

Tricuspid regurgitation (TR) and reduced RV function impair outcome after MV repair, but surgery does not necessarily improve the situation (78). RVLS has been intensively studied in the past years to find better parameters for patient management. In a study in 267 TAVR, Hirasawa confirmed that the severity of TR was related to reduced RV function, and that free wall RVLS by echo was more predictive than RVEF by CT (81). Reduced RV function may also facilitate the development of TR; in 175 patients with lone atrial fibrillation, those who had low free wall RVLS were most likely to develop TR during follow-up (82).

RVLS is also shown to be a risk factor for long term survival, independent from TR severity. In a study of 896 patients, a cut-off of -23% for free wall RVLS could distinguish two groups with better and worse survival within 2.8 years, better than TAPSE or FAC (5). Measured before isolated surgery for severe TR in a cohort of 155 patients, Kim found a free wall RVLS worse than - 24% to be associated with a higher risk of postoperative mortality or hospitalization (**Figure 10**)(83).

Congenital Heart Disease

Assessment of RV function in patients with congenital disease is particularly challenging, as strain values depend on pre- and afterload as well as RV size, which can all vary to a large extent in these pathologies (see **RV adaptation to disease**).

An atrial septal defect (ASD) causes initially a volume load before the increasing resistance of the pulmonary circulation leads to higher afterload for the RV. Van de Bruaene showed higher RVLS values before and lower RV strain values after ASD closure, as compared to 20 age-matched controls (21). In patients with an open ASD, RVLS correlated with the shunt fraction (and thus with volume load), the lower RVLS after ASD closure can be explained by the persistent larger volumes of the RV.

In patients with pulmonary regurgitation after repair of ToF have demonstrated an inverse relation between the degree of pulmonary regurgitation and RVLS (84). RVLS is predictive for the improvement in exercise capacity after pulmonary valve repair (85), and combined echocardiography and CMR study in patients with repaired ToF showed reduced RV and LV strain, suggesting also an impairment of LV function despite normal LVEF (86). Besides that, RV mechanical dyssynchrony may contribute more to the reduced exercise tolerance than volume overload due to significant pulmonary regurgitation in ToF patients (87).

A systemic RV shows reduced longitudinal and increased circumferential function as an adaptive mechanism to the abnormally increased afterload (see **RV adaptation to disease**) (14). In a study in 129 patients with TGA and congenitally-corrected TGA, Diller found RVLS to be predictive for outcome (symptomatic worsening, relevant arrhythmia or death) independent of RVEF on CMR imaging, history of clinically relevant arrhythmia, or functional class (88).

RVLS by cardiovascular magnetic resonance feature tracking (CMR-FT)

RVLS can be obtained by cardiovascular magnetic resonance feature-tracking (CMR-FT) imaging, but to date has not been widely applied in clinical settings for disease discrimination and risk stratification. This is likely due to the lack of standardization of acquisition and analysis of RVLS and reported moderate inter-modality agreement with echocardiography, as well as a poor agreement between CMR-FT techniques (89). RVLS values obtained by CMR-FT are not interchangeable with 2D STE-derived RVLS, being lower in magnitude. This is likely related to the lower temporal resolution of CMR cine images (approximately 30 frames/cardiac cycle), the differences in strain definition and tracking algorithms (i.e. the dominant feature with CMR-FT is the endocardial contour, while most evidence with 2D STE has been obtained with algorithms tracking the full wall thickness), temporal averaging and image plane orientation (90, 91). Moreover, the test-retest reproducibility of RVLS by CMR-FT was reported to be lower than RVEF by CMR and RVLS by 2D STE (90).

Despite these issues, the potential clinical value of CMR-FT RVLS has been demonstrated in several studies. Hu and colleagues observed that RVLS was an independent predictor of RV dysfunction (odds ratio: 1.246, 95% CI: 1.037–1.496) and that this index was lower in type 2 diabetes mellitus compared to controls, even if RVEF was within normal limits (92). CMR-FT RVLS has a potential role to help in differentiating patients with various arrhythmic conditions, such as ARVC, Brugada syndrome and RV outflow tract tachycardia (93). Prati found that the analysis of RVLS and mechanical dispersion by CMR-FT allowed a correct identification of most ARVC patients having no or only minor CMR criteria for ARVC diagnosis according to the 2010 Task Force criteria (94). RVLS by 3D CMR-FT has been suggested as a promising method to more accurately quantify RV deformation by CMR and was

recently found to be associated with significant prognostic value in patients with dilated cardiomyopathy (95).

Conclusions

Myocardial deformation imaging is a very attractive clinical tool for the assessment of RV systolic performance, providing incremental diagnostic and prognostic information over the traditional indices of RV function. Among various imaging modalities, echocardiography is currently the method of choice for clinical assessment of RVLS. The methodology of 2D STE to obtain RVLS has been recently standardised and demonstrated to be feasible, accurate and robust for clinical use. Inter-technique and inter-vendor comparability and reliability of RVLS are improving. RVLS is advantageous because it is more sensitive to subtle changes in myocardial function than TAPSE, S', FAC or RVEF, representing a sensitive tool for the long-term follow-up of patients. Proper interpretation of measurements requires a deep understanding of RV mechanics and pathologic tissue characteristics in different cardiovascular conditions, as well as the influence of loading conditions, image properties and tracking algorithms on RVLS measurements.

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Figure Legends.

Figure 1. Recommended protocol for image acquisition and analysis to measure RVLS in clinical practice

Figure 2. Examples of different RV 4-chamber views from the apical window. The recommended view for assessing RVLS is the RV-focused 4-chamber view (top right)

Figure 3. Using RV-focused apical 4-chamber view for RVLS analysis (right) results in higher strain magnitudes than using the standard 4-chamber view (left)

Figure 4. Potential pitfalls in the delineation of the region of interest (ROI) for RVLS analysis, in comparison with the correct method shown in the central image

Figure 5. Additive value of RVLS to conventional parameters of RV systolic function in different clinical settings

Figure 6. RVLS analysis in biventricular Takotsubo cardiomyopathy with regional dyskinesia of the apical segments (shown as positive segmental strain curves during systole)

Figure 7. RV deformation pattern recognition of the basal segment and RV mechanical dispersion performed on an RV-focused 4-chamber view in ACM. (A) Based on predefined criteria, a division into 3 different deformation patterns is identified (6). Type I is normal deformation; type II is characterized by delayed onset of shortening, reduced systolic peak strain, and minor post-systolic shortening; type III is characterized by little or no systolic peak strain, predominantly systolic stretching, and major post-systolic shortening. (B) For RV mechanical dispersion (RVMD), a 6-segment model of the RV was used, including both the lateral wall and the interventricular septum. It was calculated as the SD of the segmental time intervals from onset Q/R on the surface ECG to peak negative strain and expressed in ms. Horizontal arrows in B indicate the time interval until

peak shortening for each segment. EMI = electromechanical interval (time to onset of shortening); PVC = pulmonic valve closure.

Figure 8. Risk stratification for ventricular arrhythmias by pattern recognition in ACM. Adapted with permission from Kirkels FP et al. (48).

Figure 9. Comparison of outcomes in pulmonary hypertension (PHT) according to quartiles of free wall RVLS, pulmonary arterial systolic pressure and TAPSE (reproduced with permission from (63).

Figure 10. Impaired RV longitudinal deformation in a patient with massive functional tricuspid regurgitation (free wall RVLS = -12.7%). A, Large PISA radius at color Doppler imaging, measuring 16 mm at 28 cm/s Nyquist limit; B, Intense, triangular CW Doppler profile; C, Systolic reverse flow in hepatic vein by color Doppler; D, Systolic reverse flow in hepatic vein by PW Doppler; E, RV longitudinal strain quantification showing impaired RV myocardial function

Video Legends

Video 1. Right ventricular focused apical 4-chamber view

Video 2. Conventional apical 4-chamber view

Video 3. Incorrect right ventricular focused apical 4-chamber view - too anterior.

Video 4. Incorrect right ventricular focused apical 4-chamber view - too posterior.

Video 5. Incorrect delineation of the region of interest (ROI) – lower ends are placed too high

Video 6. Incorrect delineation of the region of interest (ROI) – lower ends are placed too low

Video 7. Incorrect delineation of the region of interest (ROI) – apical lateral region is outside the imaging sector

Video 8. Incorrect delineation of the region of interest (ROI) – too external including the pericardium

Video 9. Correct delineation of the region of interest (ROI)

Video 10. Biventricular Takotsubo cardiomyopathy with RV and LV apical dyskinesia

Table 1. Reference ranges for RVLS by 2D speckle-tracking echocardiography.

*as reported in the original publication or calculated as 2 standard deviations of the mean; LLN – lowest level of normality; NR – not reported.

					Free wall 3-segment RVLS, %		6-segment RVLS, %	
Study (year of publication)	**Sample size**	**Women (%)**	**Ultrasound system(s)**	**Software**	**Average**	**LLN**	**Average**	**LLN**
Fine et al. (2013)(34)	186	61	Philips iE33, GE Vivid 7, Siemens Sequoia C512	Syngo VVI	-21.7±4.2	-13.3	-20.4±3.2	-14.0
Chia et al. (2014)(37)	136	47	GE Vivid 7	EchoPac	-27.3±3.3	-20.7	-22.4±2.4	-17.6
Morris et al. (2016)(32)	238	50	GE Vivid 7	EchoPac	-28.5±4.8	-18.9	-24.5±3.8	-16.9
Muraru et al. (2016)(15)	250	55	GE Vivid E9	EchoPac	-30.5±3.9	-22.7	-25.8±3.0	-19.8
McGhie et al. (2017)(96)	147	50	Philips iE33 or EPIQ7	TomTec	-25.4±5.0	-15.4	NR	NR
Park et al. (2018)(31)	493	53	GE	EchoPac	-26.4±4.2	-18.0	-21.5±3.2	-15.1
Addetia et al. (2021)(33)	1913	49	Philips, Siemens, GE	TomTec	-28.3±4.3	-20.0	-25.4±3.8	-18.2

Supplementary Table S1. Other recent studies addressing the added clinical value of right ventricular longitudinal strain in various clinical settings.

First Author, Journal, Year	Study population	Sample size (n)	Design	Strain parameters	Results	Cut-off values (%)
Van Kessel M et al, *Int J Cardiovasc Imaging*, 2016 (1)	PH Group 1,3,4,5 and TAPSE>16 mm	57	Retrospective	RVFWLS	RVFWLS was a significant predictor of all-cause mortality in patients with PH and RV dysfunction, but with normal TAPSE	-20
da Costa AA et al, *Int J Cardiovasc Imaging*, 2017(2)	PH Group 1	66	_	RVFWLS	RVFWLS had good correlation with RV ejection fraction measured with CMR and was the only independent echocardiographic predictor of hospitalization and death	-14%
Kemal HS et al. *Echocardiography*, 2017(3)	PH Group 1 and 4	92	Prospective	RVFWLS	RVFWLS correlated well with functional class, NT-proBNP, 6-minute walking distance and with all follow-up adverse events, death, and clinical right heart failure	-12.5
Iacoviello et al, *Echocardiography*, 2016(4)	Stable, HFrEF (LVEF< 45%) outpatients	332	-	RVFWLS RV4CLS	Both RV4CLS and RVFWLS (but not TAPSE, FAC and S-wave velocity) were associated with all-cause mortality during follow-up	RV4CLS= -14 RVFWLS= -20.6

Freed et al, *Circ Cardiovasc Imaging*, 2016(5)	HFpEF	308	Prospective	RVFWLS	RVFWLS was independently associated with composite outcome of cardiovascular hospitalization or death	_
Houard L et al. *J Am Coll Cardiol Cardiovasc Imaging 2019 (6)*	HFrEF	266	Retrospective	RVFWLS RV4CLS	RV4CLS and RVFWLS provide strong additional prognostic value to predict overall and CV mortality in HFrEF, with higher predictive value than CMR RVEF, CMR-FT RV strain, TAPSE, or FAC	-19%
Seo et al, *Eur Heart J Cardiovasc Imaging*, 2019(7)	Clinically stable outpatients with first diagnosis of dilated cardiomyopathy	143	Prospective	RVFWLS RV4CLS	RVFWLS, but not conventional echocardiographic indices of RV function, independently predicted MACE	-16.5
Chang WT et al, *J Am Soc Echocardiogr,* 2016 (8)	Chronic angina and proven coronary artery disease	208	Retrospective	RVFWLS	RVFWLS was an independent prognostic factor for both cardiovascular mortality and hemodynamically unstable ventricular arrhythmia	-18
Gorter TM et al, *Am J Cardiol,* 2016(9)	STEMI treated with primary percutaneous coronary intervention	258	Prospective	RVFWLS	RV dysfunction occurs in 1/3 of STEMI patients treatec with primary PCI. However, it is reversible in most patients	-20
Goedemans L et al. *J Am Soc Echocardiogr*, 2019(10)	STEMI and chronic obstructive pulmonary disease	117	Retrospective	RVFWLS	STEMI patients with relatively preserved LVEF, and COPD had significantly worse RVFWSL compared with patients without COPD. Moreover, RVFWSL > -20% was	-20

					independently associated with worse survival.	
Christiansen JR et al. *Eur Heart J Cardiovasc Imaging* 2016(11)	Adult survivors of childhood malignant lymphoma or acute lymphoblastic leukaemia	246	Prospective	RVFWLS	Impaired RV function was found in 30% of survivors, both in subgroups treated with anthracyclines and mediastinal radiotherapy. RV systolic dysfunction was more than 3 times more often in survivors with LV dysfunction	-21.2%
Mitroi C et al. *Int J Cardiol 2021* (12)	Brugada syndrome (BrS)	71	Prospective	RVFWLS RV4CLS	Patients with BrS had lower RV strain and greater RV mechanical dispersion compared with controls. Adding the RVOT contraction time to the calculation of RV mechanical dispersion (RVMDm) may help assess risk for arrhythmic events during follow-up	>42 ms
Baruch et al. *Eur Heart J Cardiovasc Imaging* 2021(13)	Hospitalized patients with COVID-19	80	Prospective	RVFWLS RV4CLS	Reduction in RV strain was associated with poorer lung ultrasound score and improved at the follow-up evaluation due to better RV hemodynamics	-

Abbreviations: CMR, cardiac magnetic resonance; COPD, chronic obstructive pulmonary disease; DSE, dobutamine stress echocardiography; HFpEF, heart failure and preserved left ventricular ejection fraction; HFrEF, heart failure and reduced left ventricular ejection fraction; LV, left ventricle/ventricular; LVEF; left ventricular ejection fraction; MACE, major adverse cardiac events; pts, patients; PAH, pulmonary artery hypertension; PCI, percutaneous coronary intervention; PH,

pulmonary hypertension; RV, right ventricular; RV4CLS, right ventricular 4-chamber longitudinal strain; RVFWLS, right ventricular free-wall longitudinal strain; RVOT, right ventricular outflow tract; RVMDm, modified right ventricular mechanical dispersion

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