ORIGINAL RESEARCH

Preoperative right ventricular strain as an early predictor of perioperative cardiac failure in patients undergoing mitral surgery: An exploratory study

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Abstract

Objectives: This study's primary purpose was to demonstrate the correlation of preoperative right ventricular free-wall longitudinal strain (RVFWLS) and pre-/postsurgical variation in strain (delta strain) with the clinical and echocardiographic diagnosis of right ventricular dysfunction. Its secondary purpose was to determine the correlation of RVFWLS and delta strain with length of stay (LOS) in the intensive care unit (ICU), ventilation days, trend of natriuretic peptide test. (NT-proBNP) and lactate in the first 48 h, incidence of acute renal failure, and 28-day mortality.

Design: Prospective observational study.

Setting: Cardio-thoracic and Vascular Anaesthesia Department and ICU of the University Hospital Integrated Trust of Verona.

Participants: Patients scheduled for mitral surgery.

Interventions: None.

Measurements and Main Results: All clinical and transoesophageal echocardiographic (TEE) parameters were collected at baseline, before surgery (T1) and at admission in the ICU postsurgery (T2). During the postoperative period, the clinical and echocardiographic diagnoses of right, left, or biventricular dysfunction were evaluated. TEE parameters were evaluated by a cardiologist offline. The patients were divided into two subgroups according to the development of any type of ventricular dysfunction. No statistically significant differences emerged between the two groups. According to a logistic regression model, a T1-RVFWLS value of −15%

appeared to predict biventricular dysfunction (sensitivity: 100%; specificity: 91.3%). No correlation between T1- or T2-RVFWLS and creatinine, hours of ventilation or ICU LOS was found.

Conclusions: Our study introduces a new parameter that could be used in perioperative evaluations to identify patients at risk of postoperative biventricular dysfunction.

K E Y W O R D S

bi-ventricular dysfunction, mitral surgery, perioperative cardiac failure, right ventricular dysfunction, right ventricular strain

1 | INTRODUCTION

The evaluation of right ventricular (RV) systolic function has important prognostic and therapeutic implications for many clinical procedures, especially heart surgery (e.g., valvular and bypass).[1–7] In fact, acute refractory RV failure is associated with a high in-hospital mortality rate that may reach 70%–75%.[1,2,8] Thus, early diagnosis is crucial to improve prevention and management.

Significant mitral valve regurgitation exerts detrimental effects on RV performance: volume overload, a rise in wedge pressure and the development of pulmonary hypertension with a subsequent increase in RV afterload may eventually cause RV dysfunction.[6] For the aforementioned reasons, in patients undergoing mitral valve surgery, RV reserve is low, and its functional impairment is frequent (25%–30%).[5,6]

Given this context, RV systolic function evaluation should be part of any routine examination. However, the geometric complexity of the RV shape, the presence of heavy apical trabeculations and the marked load dependence of several parameters make RV assessment with the standard echocardiographic exam difficult.[9,10]

Speckle tracking echocardiography (STE) allows for measuring myocardial active deformation (myocardial strain). "Speckles" are patterns generated by the interaction between myocardium and ultrasound. By analysing these patterns over time, it is possible to evaluate global and segmental myocardial active deformation.[11] The main advantage of STE is its relative angle independence, which allows for calculating myocardial deformation in any image plane. Furthermore, STE is not affected by tethering effects and can detect even small changes in myocardial reserve function.[11]

Several articles have shown STE's reliability in detecting RV dysfunction.[12,13] In perioperative settings, the assessment of RV function by STE could give additional useful information compared to conventional echocardiographic parameters. For these reasons, the primary purpose of our observational study was to evaluate the effectiveness of RV free-wall longitudinal strain (RVFWLS) as an early predictor of postoperative RV dysfunction in patients undergoing mitral valve surgery. We measured RVFWLS preoperatively and explored any relation or association to the development of right ventricular dysfunction in the first hours postop during patients' stays

in the intensive care unit (ICU). The secondary purposes of our study were to explore the relationships of RVFWLS with length of stay (LOS) in the ICU, ventilation days, NT-proBNP and lactate trends in the first 48 h, incidence of acute renal failure, and 28-day mortality, as well as the development of signs of biventricular or left ventricular failure.

2 | METHODS

The study was conducted in the Cardio-thoracic and Vascular Anaesthesia and Intensive Care Unit of the University Hospital of Verona. All recorded patient data were included in the REINSURE-ARDS registry, a prospective registry of patients requiring ICU admission adopted by the emergency department and ICU of our institution. This registry was approved by our institutional review board (Prog. 1946CESC, Prot. 72485 12/11/2018, IRB amendment 26/02/2021). Patients' identities remained anonymous, and all participants or their legal representatives provided informed consent before inclusion in the registry and for the use of their clinical and biological data. The data of patients scheduled for elective isolated mitral surgery (both stenosis or regurgitation) or in combination with coronary bypass were collected, except for patients with right coronary artery (RCA) disease, assuming that right heart ischaemic conditions could affect per se RV function. Data collection was performed from September 2020 to July 2021.

A sample size of 41 patients was collected as indicated by the National Institute for Health and Care Research (NIHR) recommendations,[14] assuming an incidence of RV dysfunction of about 25% in patients undergoing mitral surgery.[5–7]

The inclusion criteria were isolated mitral surgery regardless of the mitral valve pathology (regurgitation or stenosis) or mitral valve surgery associated with left coronary artery bypass graft and age ≥18 years old. The exclusion criteria were adult congenital heart diseases, presence of moderate to severe aortic or tricuspid valvular disease, RCA disease, pregnancy, and absolute contraindications to transoesophageal echocardiography (TEE).

The dropout criteria were low-quality echocardiographic images due to the presence of areas with cones of shadows or poor

echocardiographic windows and the withdrawal of consent by the study participant.

2.1 | Data collection

All clinical and hemodynamic parameters were collected at baseline after the induction of anaesthesia before surgery (T1) and within 24 h after admission to the ICU after the intervention (T2). Echocardiographic parameters, especially of RVFWLS, were collected in T2 to explore a new parameter that results from the difference between preoperative and postoperative RVFWLS (i.e., delta strain) to identify even small statistically significant changes in RVFWLS that could help to predict the postoperative development of ventricular dysfunction. The haemodynamic state of the patient during the ICU stay was also recorded and summarized with the vasoactive-inotropic score.[15]

The demographic characteristics of the sample are summarized in Table 1. TEE parameters were measured at T1 and T2 according to our study protocol and evaluated offline by a cardiologist with specific skills in the STE method (Tables 2 and 3). General anaesthesia was administered to all patients according to the institutional protocol. After anaesthesia induction and orotracheal intubation, the TEE probe was inserted for image acquisition. Every image was acquired with a good electrocardiogram (ECG) trace and a frame rate of at least 70 ± 5 Hz, and at least five consecutive beats were recorded. The Epiq 7 Philips® TEE machine was used. The following images were recorded: middle oesophageal four-chamber view to see the left ventricle (LV) and RV; middle oesophageal long axis view to see the LV outflow tract (LVOT); transgastric views at the level of the mitral valve, papillary muscles and cardiac apex; middle oesophageal view inflow and outflow of the RV; transgastric view of the right basal ventricle to see the outflow of the RV; and five-chamber deep transgastric view.[16]

The RV dimensions were assessed in the middle oesophageal four-chamber view with the RV centered on the screen (RV longitudinal, basal, and mid diameters; RV end-diastolic and end-systolic area [EDA and ESA, respectively]).[9,17,18] Fractional area change (FAC) was

TABLE 1 Demographic, anamnestic, and operative variables of patients developing cardiac dysfunction and patients free from cardiac dysfunction.

	No dysfunction (n = 11)	Dysfunction (n = 27)	p Value
Sex (male)	6 (54.55%)	15 (55.56%)	0.82[#]
Smoking habit	4 (36.36%)	10 (37.04%)	0.97[##]
Obesity	2 (18.18%)	7 (25.93%)	>0.99[##]
Diabetes	0 (0.00%)	4 (14.81%)	0.56[##]
Dyslipidaemia	3 (27.27%)	13 (48.15%)	0.47[##]
Hypertension	9 (81.82%)	15 (55.56%)	0.08[#]
Age (years)	73.00 (61.00, 77.00)	69.00 (54.00, 77.00)	0.55**,**
ECC time (min)	102.00 (23.80)	134.00 (58.10)	0.07*,*
Aortic cross-clamp time (min)	81.00 (20.12)	100.00 (36.05)	0.30*,*

Note: Descriptive statistics: #, ## count (percentage); * mean (standard deviation); ** median (interquartile range). Between-group difference assessed by # χ^2 test; ## Fischer's exact test; * two-sample t test; ** Wilcoxon–Mann–Whitney test.
Abbreviations: ECC, extracorporeal circulation; n, number; %, percentage, dysfunction, any type of ventricular dysfunction (isolated right ventricular dysfunction, isolated left ventricular dysfunction, biventricular dysfunction).

TABLE 2 Clinical characteristics of subjects subgrouped based on the presence or absence of any cardiac dysfunction before surgery.

T1: Presurgical evaluation	No dysfunction (n = 11)	Dysfunction (n = 27)	p Value
TAPSE (cm)	1.36 (0.16)	1.37 (0.35)	0.96*
S' TDI (cm/sec)	10.12 (2.10)	10.59 (2.77)	0.62*
PAPs (mmHg)	33.5 (26.00, 46.00)	29.00 (27.00, 32.00)	0.91**
RV FAC (%)	28.98 (10.05)	32.37 (8.27)	0.30*
RV EDA (cm^2)	18.30 (14.20, 19.30)	18.3 (15.00, 21.85)	0.57**
RV ESA (cm^2)	11 (8.80, 13.20)	11.30 (10.15, 14.56)	0.76**
LV EDV (mL)	102.00 (66.40, 146.00)	108.00 (93.00, 130.00)	0.75**
LV ESV (mL)	60.00 (35.70, 70.00)	52.65 (42.00, 57.90)	0.41**
LV EF (%)	45.98 (7.92)	51.47 (8.85)	0.08*
RV basal diameter (cm)	3.62 (3.27, 4.03)	4.00 (3.80, 4.18)	0.23**
RV mid diameter (cm)	3.20 (3.00, 3.65)	3.34 (3.19, 3.60)	0.64**
RV long. diameter (cm)	5.82 (1.59)	6.75 (0.95)	0.04*
RVOT VTI (cm)	13.38 (3.14)	11.91 (5.28)	0.43*
LVOT VTI (cm)	15.90 (5.79)	15.74 (4.52)	0.94*

Note: Descriptive statistics: * mean (standard deviation); ** median (interquartile range). Between-groups difference assessed by * two-sample t test; ** Wilcoxon–Mann–Whitney test.
Abbreviations: LV EDV, left ventricular end-diastolic volume; LV EF, left ventricular ejection fraction; LV ESV, left ventricular end-systolic volume; LVOT VTI, left ventricular outflow tract velocity time integral; n, number; PAPs, systolic pulmonary artery pressure; RV EDA, right ventricular end-diastolic area; RV ESA, right ventricular end-systolic area; RV FAC, right ventricular fractional area change; RV long. diameter, right ventricular longitudinal diameter; RVOT VTI, right ventricular outflow tract velocity time integral; S' TDI, systolic tissue Doppler imaging at the level of tricuspid annulus; T1, time after induction of anaesthesia before surgery; TAPSE, tricuspid annular plane systolic excursion.

TABLE 3 Clinical characteristics of subjects subgrouped based on the presence or absence of any cardiac dysfunction after surgery.

T2: Postsurgical evaluation	No dysfunction (n = 11)	Dysfunction (n = 27)	p Value
TAPSE (cm)	1.06 (0.34)	1.08 (0.19)	0.85*
S' TDI (cm/sec)	9.44 (3.67)	8.83 (2.26)	0.92*
PAPs (mmHg)	24 (20, 33)	24 (22, 27)	0.92**
RV FAC (%)	28.98 (10.54)	30.35 (11.59)	0.66*
RV EDA (cm²)	16.08 (14.55, 21.7)	16.45 (12.30, 21.10)	0.69**
RV ESA (cm²)	11.55 (9.00, 15.70)	11.75 (8.34, 16.60)	0.74**
LV EDV (mL)	72 (66.20, 95.00)	77.5 (55.00, 112.00)	0.94**
LV ESV (mL)	36.00 (26.00, 47.30)	45.00 (32.00, 49.00)	0.62**
LV EF (%)	46.12 (11.49)	45.45 (10.70)	0.35*
RV basal diameter (cm)	3.53 (3.15, 3.78)	3.26 (3.05, 3.57)	0.43**
RV mid diameter (cm)	3.33 (2.78, 3.85)	3.32 (3.00, 3.40)	0.41**
RV long. diameter (cm)	6.45 (1.03)	5.94 (1.72)	0.33*
RVOT VTI (cm)	14.2 (4.67)	17.17 (8.88)	0.44*
LVOT VTI (cm)	17.11 (5.93)	19.60 (8.52)	0.47*
Vasoactive-inotropic score	3 (2.5,3.75)	2 (1,4.5)	0.72**

Note: Descriptive statistics: * mean (standard deviation); ** median (interquartile range). Between-group differences assessed by * two-sample *t* test; ** Wilcoxon–Mann–Whitney test.

Abbreviations: LV EDV, left ventricular end-diastolic volume; LV EF, left ventricular ejection fraction; LV ESV, left ventricular end-systolic volume; LVOT VTI, left ventricular outflow tract velocity time integral; n, number; PAPs, systolic pulmonary artery pressure; S' TDI, systolic tissue Doppler imaging at the level of tricuspid annulus; T2, time range of 24 h after admission to the intensive care unit; TAPSE, tricuspid annular plane systolic excursion; RV EDA, right ventricular end-diastolic area; RV ESA, right ventricular end-systolic area; RV FAC, right ventricular fractional area change; RV long. diameter, right ventricular longitudinal diameter; RVOT VTI, right ventricular outflow tract velocity time integral.

calculated by subtracting the ESA from the EDA, dividing this value by the EDA and then multiplying the result by 100. Tricuspid annular plane systolic excursion (TAPSE) and S' tissue Doppler imaging (TDI) were recorded in the middle oesophageal four-chamber view or the deep transgastric RV inflow/outflow long-axis view, where the best alignment with the ultrasound beam and RV free-wall could be obtained.[1,17] The left ventricular ejection fraction (LVEF) was calculated using the modified Simpson's biplane method (on the middle oesophageal four-chamber and two-chamber views).[18,19] The study investigators

measured all TEE parameters on three different cardiac cycles, and the average (mean) value was recorded. Speckle tracking analysis software was used offline on the recorded middle oesophageal four-chamber views and analyzed over three cardiac cycles.[20]

The RV endocardial border (free-wall and septum) was traced at the end of the systole and manually adjusted to fully include the myocardium. RVFWLS was calculated as the average of the longitudinal strain of the three segments of the RV free-wall.[13] Since systolic contraction leads to shortening of the myocardium, the RVFWLS in 2D is reported as negative values. Negative strain values indicate tissue shortening and contraction; the greater the negative value, the better the myocardial systolic function. According to current scientific literature, the cut-off is <−20% for global RV longitudinal strain and <−23% for RVFWLS.[21–23]

During the postoperative ICU stay, the physician in charge (who was not directly involved in the study) recorded all patients' hemodynamic and respiratory parameters as standard practice and modified the patients' therapy according to clinical and echocardiographic findings. Some modifications were justified by the occurrence of right, left, or biventricular failure, which was reported on medical charts. These findings were considered for dividing the patients into subgroups and performing the subsequent statistical analysis. For example, RV failure could be diagnosed based on the significant enlargement of the RV together with a significant reduction in TAPSE or S' TDI or FAC and an increase in the severity of tricuspid regurgitation and pulmonary artery systolic pressure (PAPs), but also based on an increase in central venous pressure, peripheral oedema, or jugular turgor, among others.[24,25] On the other hand, LV dysfunction could be diagnosed either via clinical signs like hypotension, oligoanuria, pulmonary oedema, or significative reduction in ejection fraction (EF).[24] The echocardiographic evaluation, made by the physician in charge, could be performed by TEE or transthoracic echocardiography according to patients' echocardiographic windows following standard clinical practice and evaluation in the ICU. This clinical echocardiographic assessment was different from the T2-TEE evaluation.

Other recorded and analyzed parameters were LOS in the ICU, mechanical ventilation duration and mortality within 28 days.

2.2 | Statistical analysis

The primary aim of the statistical analysis was to explore the relationship between T1-RVFWLS and variation in RVFWLS after surgery, called "delta strain," and the development of right ventricular heart failure (HF) signs. Delta strain was calculated as the difference between the RVFWLS values at T1 and T2. For this reason, the primary endpoint consisted of identifying a correlation of T1-RVFWLS and delta strain with a clinical and/or echocardiographic diagnosis of RV dysfunction. The study's secondary purpose was to investigate the relationship of RVFWLS and delta strain with LOS in the ICU, ventilation days, pro-BNP and lactate trends in the first 48 h, incidence of acute renal failure, 28-day mortality, and the development of signs of biventricular failure or left ventricular failure.

All collected variables were summarized as mean and standard deviation (SD) when normally distributed and median and inter-quartile range in case of skewness. Categorical variables were expressed as counts and percentages. Descriptive statistics were reported separately for the group of patients free from ventricular dysfunction and the pooled group in which at least one of the conditions (right, left, or biventricular dysfunction) was present. The differences between the two groups were evaluated by t test for continuous variables, the Wilcoxon–Mann–Whitney test for non-parametric variables and the χ^2 test for categorical variables. For small cell numbers ($n < 5$), the Fisher exact test was used.

In addition, T1- and T2-RVFWLS values were reported for each of the four conditions: no dysfunction, RV dysfunction, LV dysfunction, and biventricular dysfunction.

To address whether the RVFWLS variation predicted the onset of right, left, or biventricular dysfunction, three different logistic regression models were developed in which dysfunctions were the dependent variables and delta strain was the independent variable. Further, the T1-RVFWLS value was also entered as a possible predictor. To establish its role in estimating the possibility of dysfunction, the T1-RVFWLS value was introduced in an additional logistic model.

In cases where the delta strain or T1-RVFWLS value was statistically linked to the occurrence of a dysfunctional scenario (right, left, or biventricular), an ROC curve was constructed to identify a hypothetical cut-off value. The cut-off was identified by calculating the Youden index, the value that maximizes sensitivity and specificity.

The study had exploratory and hypothesis-generating objectives. Therefore, no formal power analysis was conducted. All statistical tests were two-tailed. Statistical significance was set at an alpha level of 5%. Statistical analysis was performed using STATA 17 software (www.stata.com).

3 | RESULTS

A total of 41 patients were enrolled in the study. Due to the dropout criteria for low-quality echocardiographic images, 38 subjects were included in the final analysis. The sample comprised 21 men (55%) and 17 women (45%). The mean population age was 68.1 years (SD: 10.9; Table 1). Twenty-seven patients (71.1%) had some grade of isolated ventricular cardiac dysfunction. More precisely, 15 subjects (39.5%) experienced isolated RV dysfunction, while four (10.5%) had isolated LV dysfunction. Biventricular dysfunction was detected in eight (21%) patients. The median vasoactive-inotropic score was 3 for the overall sample. In our sample, the main indication for surgery was severe mitral regurgitation: 23 patients (~60%) underwent mitral valve repair, and 15 (~40%) underwent mitral valve replacement. The mean aortic cross-clamp time was 94 min (SD: 32) and the mean extracorporeal circulation time was 121 min (SD: 38). The main demographic and clinical characteristics of the patients are summa-rized in Table 1. The patients were divided into two subgroups according to whether they had developed any type of ventricular

TABLE 4 Comparison of T1- and T2-right ventricular free-wall longitudinal strain values and delta strain values between patients with and without ventricular dysfunction.

	No dysfunction		Dysfunction		
	Mean	SD	Mean	SD	*p* Value
T1-RVFWLS (%)	−17.5	2.4	−16	3.3	0.22
T2-RVFWLS (%)	−12.3	2.4	−12.6	5.6	0.90
Delta strain (%)	4.8	3.8	2.5	4.2	0.20

Note: Between-group difference assessed by the two-sample *t* test.
Abbreviations: Delta strain, mean of absolute value of the difference between T1- and T2-right ventricular free-wall longitudinal strain; RVFWLS, right ventricular free-wall longitudinal strain; SD, standard deviation; T1, time after induction of anaesthesia before surgery; T2, time range of 24 h after admission to the intensive care unit.

dysfunction (both from the clinical perspective and the conventional echocardiographic evaluation). No statistically significant differences emerged between the two groups except for RV longitudinal diameter (Tables 3 and 4).

Similarly, no significant differences emerged between T1- and T2-RVFWLS and delta strain values when patients with and without cardiac dysfunction were compared (Table 4). We found a slightly longer extracorporeal circulation time and aortic cross-clamp time in patients who developed any cardiac dysfunction (134 vs. 102 min and 83 vs. 81 min, respectively), but the difference was not statistically significant.

It is noteworthy that in patients with cardiac dysfunction, the T2-RVFWLS value was very similar to that of patients without dysfunction, while the T1-RVFWLS value was higher (less negative). Consequently, the delta strain was smaller.

This T1-RVFWLS difference, when investigated by logistic regression models, appeared to play a significant role in patients with biventricular dysfunction. In fact, as indicated in Table 5, for a one-point increase in T1-RVFWLS, the odds of biventricular dysfunction increased to more than double (OR: 2.17; 95% CI: 1.22–3.84). This result reached statistical significance. However, this trend was not observed in patients with isolated RV or LV dysfunction.

Finally, when the T1-RVFWLS value was analyzed through an ROC curve (Figure 1), an AUC of 95.9% emerged. The ROC curve can be considered a "post hoc" analysis that we performed after seeing that the T1-RVFWLS was a predictor of biventricular dysfunction. Moreover, the cut-point analysis (Table 6) showed that an RVFWLS value greater than or equal to −15.00% was always associated with the onset of biventricular dysfunction. Furthermore, this cut-point value could maximize the specificity and sensitivity of the T1-RVFWLS value in predicting biventricular dysfunction (sensitivity: 100%; specificity: 91.30%).

Finally, no statistical difference was found in the secondary endpoint analysis of the correlation of RVFWLS and delta strain with the LOS in the ICU, ventilation days, lactate trend pro-BNP values in the first 48 h, incidence of acute renal failure and 28-day mortality (Table 7).

TABLE 5 Logistic regression analysis of the role of T1-right ventricular free-wall longitudinal strain and delta strain in determining the odds of right, left, or biventricular dysfunction.

	OR	95% CI	p Value
RV dysfunction			
T1-RVFWLS	0.96	0.79–1.16	0.66
Delta strain	1.00	0.81–1.24	0.99
LV dysfunction			
T1-RVFWLS	1.18	0.92–1.52	0.20
Delta strain	1.02	0.79–1.31	0.88
Biventricular dysfunction			
T1-RVFWLS	2.17	1.22–3.84	0.008
Delta strain	1.06	0.62–1.82	0.83
Overall dysfunction			
T1-strain	1.11	0.82–1.49	0.51
Delta strain	0.87	0.70–1.10	0.26

Abbreviations: CI, confidence interval; delta strain, mean of absolute value of the difference between T1- and T2-right ventricular free-wall strain; LV, left ventricle; OR, odds ratio; Overall dysfunction, the development of any type of ventricular dysfunction (isolated LV, isolated RV or biventricular dysfunction); RV, right ventricle; RVFWLS, right ventricle free-wall longitudinal strain; T1, time after induction of anaesthesia before surgery.
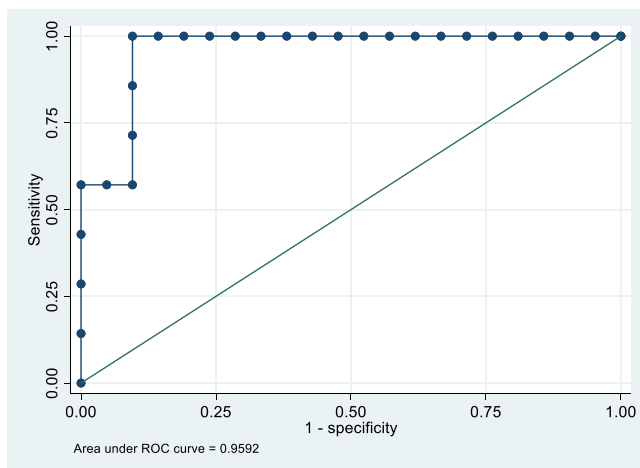
FIGURE 1 ROC analysis of the role of T1-right ventricle free-wall longitudinal strain in classifying patients with biventricular dysfunction. AUC: 95.9% (95% CI: 0.89%–100%). T1, time after induction of anaesthesia before surgery.

TABLE 6 Cut-point analysis of T1-right ventricular free-wall longitudinal strain values in classifying patients with or without biventricular dysfunction.

	T1-RVFWLS	Sensitivity (%)	Specificity (%)	Correctly classified (%)
≥	−22.08	100.00	0.00	25.81
≥	−21.08	100.00	4.35	29.03
≥	−21	100.00	8.70	32.26
≥	−20.1	100.00	13.04	35.48
≥	−19.26	100.00	17.39	38.71
≥	−19.2	100.00	21.74	41.94
≥	−18.49	100.00	26.09	45.16
≥	−18.4	100.00	30.43	48.39
≥	−18.3	100.00	34.78	51.61
≥	−18.15	100.00	43.48	58.06
≥	−17.7	100.00	47.83	61.29
≥	−17.11	100.00	52.17	64.52
≥	−16.85	100.00	56.52	67.74
≥	−16.8	100.00	60.87	70.97
≥	−16.7	100.00	65.22	74.19
≥	−16.5	100.00	69.57	77.42
≥	−16.24	100.00	73.91	80.65
≥	−15.7	100.00	78.26	83.87
≥	−15.4	100.00	82.61	87.10
≥	−15.1	100.00	86.96	90.32
≥	−15	100.00	91.30	93.55
≥	−14.98	87.50	91.30	90.32
≥	−13.4	75.00	91.30	87.10
≥	−13	62.50	91.30	83.87
≥	−11.84	50.00	91.30	80.65
≥	−11.73	50.00	95.65	83.87
≥	−11	50.00	100.00	87.10
≥	−10.58	37.50	100.00	83.87
≥	−8.3	25.00	100.00	80.65
≥	−7.7	12.50	100.00	77.42
>	−7.7	0.00	100.00	74.19

Abbreviations: RVFWLS, right ventricular free-wall longitudinal strain; T1, time after induction of anesthesia before surgery.

4 | DISCUSSION

Patients with mitral valve disease who require surgery can develop both clinical and echocardiographic signs of HF after surgical valve repair or replacement.[5,7,26] LV contractile dysfunction, a consequence of ventricular dilatation that develops as an adaptation to the volume overload caused by mitral valve regurgitation, is responsible for several of the haemodynamic impairments found in these patients.[27,28] Moreover, a reduction in cardiac output and the consequent tissue hypoperfusion sequelae, such as poor nephron perfusion and reduced glomerular filtration rate, are commonly detected.

TABLE 7 Secondary endpoint data of the overall sample.

	Mean ± SD
pO$_2$ (mmHg)	98.97 ± 29.73
MAP (mmHg)	75.9 ± 4.99
Creatinine (μmol/L)	86.7 ± 25.66
Troponine (ng/mL)	807.58 ± 802.51
Lactate (mmol/L)	3.21 ± 3.30
SAPS II score	35 ± 9.35
Vasoactive-inotropic score	3.00[a]
Mechanical ventilation time (h)	17 ± 40.1
Length of ICU stay (days)	2.15 ± 2.88
Mortality	0

Abbreviations: ECC, extracorporeal circulation; ICU, intensive care unit; MAP, mean arterial pressure; pO$_2$, oxygen partial pressure in blood gas analysis; SAPS II score, amplified acute physiology score.
[a]Median.

Furthermore, mitral valve disease has a negative impact on pulmonary circulation and consequently, on the RV.[29] Pulmonary hypertension, due to venous congestion and the backward transmission of elevated left atrial pressure consequent to mitral valve disease, causes progressive structural changes in the distal arterioles and endothelial injury. These factors are responsible for the development of tricuspid regurgitation and RV hypertrophic remodeling and enlargement.[2,30,31]

In our study, the reduction in RV function was detected in the postoperative period through the observation of clinical signs and echocardiographic parameters. RVFWLS became less negative because of ventricular impairment caused by surgery. Other morpho-functional parameters used to assess ventricular function (e.g., TAPSE and S' TDI) also showed a similar change. To detect even small statistically significant changes in RVFWLS that could help to predict the postoperative development of ventricular dysfunction (isolated RV failure, isolated LV failure or biventricular failure), the new concept of "delta strain," which is the difference between T1- and T2-RVFWLS, was introduced. However, no statistical association was found between T1-RVFWLS or T2-RVFWLS or delta strain and the clinical development of HF in the postoperative period. Surprisingly, the T2-RVFWLS values of patients developing clinical signs of ventricular dysfunction after surgery were similar to those of patients who did not develop any signs of dysfunction. Paradoxically, the delta strain of patients developing ventricular dysfunction was smaller than that of patients who were free from ventricular dysfunction signs. We expected the opposite: a greater drop in RV function in patients developing HF signs. This means that T2-RVFWLS and delta strain, which describe the trend of RVFWLS after surgery, are not useful parameters to predict HF development. A possible explanation for these findings is that T2-RVFWLS is affected by surgery as well as TAPSE.[32,33] Another explanation could be that negative inotropic effects of analgosedation were still influencing RV

function (T2-RVFWLS was evaluated just a few hours post-surgery).[34] Interestingly, in a logistic regression model, T1-RVFWLS predicted biventricular dysfunction. A hypothesis to explain this finding could be that T1-RVFWLS identifies a more compromised heart condition (both ventricles involved), which becomes manifest after cardiac surgery. This result could be supported by a greater RV enlargement. Indeed, we found a statistically significant difference between the two groups (patients free from ventricular dysfunction and patients developing it) in terms of longitudinal RV diameter. An increase in RV size is a sign of RV remodeling.[35]

Furthermore, in the T1 evaluation of LV EF, the group that developed cardiac dysfunction seemed to have a higher EF. We explained this finding with the presence of more severe mitral impairment and a more relevant overestimation of LV EF due to pathologic ventricular unloading backwards to the left atrium. The current study maintains the focus on the echocardiographic monitoring of parameters that could be predictive of contractile dysfunction in the perioperative period. Data from our study seem to indicate the potential utility of the T1-RVFWLS as an index of RV functional reserve in patients undergoing mitral valve surgery. The inclusion of this new parameter in the perioperative patient's evaluation would help to identify those patients at risk of postoperative biventricular cardiac failure early. In a review, Silverton et al.[36] show that Transthoracic echocardiography-based measures of RV global longitudinal strain, compared to a reference standard of cardiac magnetic resonance imaging (MRI), RVFWS, seem to have the best correlation with three-dimensional right ventricle ejection fraction (3D RVEF). An abnormal intraoperative RV longitudinal strain was found to be a good predictor of RV dysfunction when compared to a reference standard of 3D RVEF.[37] TTE-derived RVFWS was also associated with all-cause mortality 1 year after transcatheter aortic valve replacement[38,39] such that an abnormal preoperative RV strain with TTE was also associated with the development of RV failure.[40–47] One of the main limitations of this study lies in the fact that the results come from a limited sample, making it undersized; therefore, the results must be considered with great caution due to the imprecision and instability of the estimates and the impossibility of adjusting the effect size for the characteristics of the subjects. It follows that we cannot draw clinically relevant conclusions, which need to be demonstrated with studies of adequate size and power; nevertheless, we have observed in our sample a trend that, if confirmed in larger studies, could support the use of this method as a tool for cardiovascular risk stratification in the immediate perioperative context.

Another limitation of our study is the use of TEE, which has no standardized value for chamber quantification and ventricular function. Furthermore, chamber quantification may be less reliable for foreshortening problems. Finally, the fact that echocardiographic measurements were taken after the induction of general anaesthesia may have affected haemodynamics because of the negative inotropic effect of hypnotic and analgesic drugs. However, TEE is a valuable tool in cardiac anaesthesiology and intensive care, and particular attention was paid to image acquisition during this study. Another

problem is that a standardized cutoff for RV strain is not available yet, and several articles report different values of strain to identify normality.[13,21]

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

TRANSPARENCY STATEMENT

The lead author A. Gambaro affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA AVAILABILITY STATEMENT

Author elects to not share data.

ETHICS STATEMENT

The authors state that the work being submitted has been performed in accordance with Wiley's Best Practice Guidelines on Publishing Ethics in an ethical and responsible way, with no research misconduct, which includes, but is not limited to, data fabrication and falsification, plagiarism, image manipulation, unethical research, biased reporting, authorship abuse, redundant or duplicate publication, and undeclared conflicts of interest. All patient data recorded were included in the REINSURE-ARDS registry, a prospective registry of patients requiring intensive care unit (ICU) admission adopted in the emergency department and ICU of our institution. This registry was approved by our institutional review board (Prog. 1946CESC, Prot. 72485 12/11/2018, IRB amendment 26/02/2021). Patients' identities remained anonymous, and all participants or their legal representatives provided informed consent before their inclusion in the registry and for the use of their clinical and biological data.

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