

Right ventricular free wall longitudinal strain in heart failure with preserved and mild reduced ejection fraction. Application and prognostic implications.

Daniel Grados-Saso¹, Juan Manuel Salvador-Casabón¹, Anyuli García-Gutiérrez², Ana María Martínez-Royo¹, Juan Ignacio Pérez-Calvo², Isaac Lacambra-Blasco¹

¹Department of Cardiology Hospital Clínico Universitario de Zaragoza, Aragón, ²Department of Internal Medicine Hospital Clínico Universitario de Zaragoza, Aragón, Spain

Grados-Saso D, Salvador-Casabón JM, García-Gutiérrez A, Martínez-Royo AM, Pérez-Calvo JI, Lacambra-Blasco I. **Right ventricular free wall longitudinal strain in heart failure with preserved and mild reduced ejection fraction. Application and prognostic implications.** Cardiology Lett. 2026;35(2):83–89

Abstract. *Aims:* Right ventricle (RV) plays an important role in heart failure with preserved and mild reduced ejection fraction. Quantification of right ventricular functional parameters by echocardiography is challenging. In this context an advanced quantification parameter such as right ventricular strain (a measure of myocardial deformation) represents a tool that can provide useful information in the assessment of RV function, with potential prognostic implications.

Methods: In a cohort of 71 prospectively included patients admitted for an episode of heart failure with preserved and mild reduced ejection fraction (LVEF >40%) right ventricular function was evaluated through right ventricular free wall longitudinal strain. Relationship with variables such as hospital readmission and cardiovascular mortality was studied.

Results: Worse right ventricular free wall longitudinal strain was associated to higher probability of cardiovascular mortality at six months. In multivariate analysis RV free wall strain remained a predictor of cardiovascular mortality at 6 months.

Conclusion: In patients with heart failure, impairment of right ventricular free wall strain is related to worse clinical outcome (increased cardiovascular mortality) regardless of other right ventricular functional parameters. Therefore, representing a non-invasive prognostic indicator in these patients, and could be useful in stratifying the risk of adverse events. Fig. 2, Tab. 6, Ref. 24, on-line full text (Free, PDF), www.cardiologyletters.sk

Key words: Heart failure – HFmrEF – HFpEF – Right ventricular free wall strain

The right ventricle (RV) plays an important role in the pathophysiology of heart failure with preserved and mild-reduced ejection fraction. Right ventricular dysfunction is associated with an increase in morbi-

dity and mortality in this population (1,2). The gold standard method for evaluation of the right ventricle is magnetic resonance imaging (3). However, a transthoracic echocardiogram is more commonly used in

clinical practice due to its greater accessibility. Quantification of right ventricular functional parameters by echocardiography is challenging due to the complex geometry of this heart chamber (4). Several methods are available to evaluate its function: tricuspid annular plane systolic excursion (TAPSE), fractional area change (FAC) and lateral tricuspid annular systolic velocity derived from tissue-Doppler (S') (5). These parameters, largely used for decades and of proven utility, present an important limitation: their values are dependent on the insonation angle and can be affected by changes in load as well as rotational and translational motions of the heart, especially present in the right ventricle (6).

Echocardiography provides an additional tool, such as the determination of RV strain, using techniques to study RV deformation that could be more sensitive to detect right ventricular dysfunction. Speckle-tracking programs are used to measure the three segments of the RV free wall. The lower limit of normality has been set at $<-20\%$, greater than 20 in absolute value (7,8).

In patients with heart failure (HF), an altered right ventricular function is common (9) and similarly to the left ventricle, there is most likely an association with the same fibrosis processes that affect the subendocardial layer in relation to the various prevalent comorbidities in HFpEF and HFmrEF. In addition, right ventricular dysfunction could contribute to the symptomatology

of heart failure, with worse symptomatic control, more admissions and worse clinical outcome (10,11).

We have aimed to evaluate right ventricular function by determining right ventricular free wall strain in addition to TAPSE, S' wave, and FAC in a cohort of patients admitted for an episode of heart failure with preserved and mild reduced ejection fraction (HFpEF and HFmrEF), evaluating their relation with variables such as hospital readmission and cardiovascular mortality.

Methods

A prospective cohort study was designed made up of patients admitted to hospital for clinical heart failure. Patients were consecutively included in the study. A complete doppler echocardiogram was performed. Measurements of the various parameters were performed following the recommendations of the quantification consensus guide of the European and American Echocardiography Societies. To determine right ventricular free wall strain (RVFWS), a 4-chamber view centered on right chambers was obtained and the image was optimized to obtain the maximum resolution with the greatest visualization of the entire RV free wall. (Figure 1)

Inclusion criteria were the following: patients admitted to hospital with an episode of heart failure, with preserved and mild reduced ejection fraction (measured

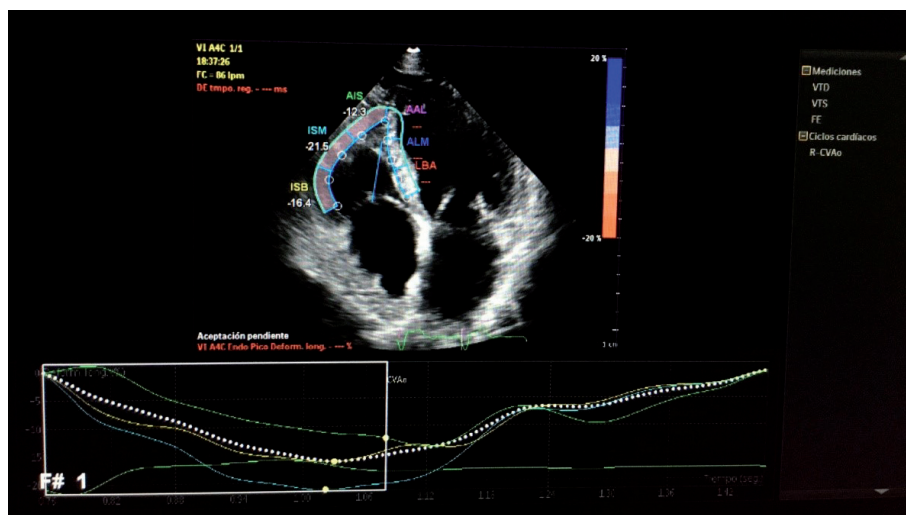


Figure 1 Determination of the right ventricular free wall strain through two dimensional speckle-tracking echocardiogram

by the bi-plane Simpson method at > 40%). Exclusion criteria were: significant heart valve disease (mitral, tricuspid or aortic regurgitation equal to or greater than grade III/IV), severe mitral or aortic stenosis; intervened valvular heart disease. The study was approved by the hospital ethical committee of clinical research. Patients were followed for six months. Readmissions for HF and deaths (from cardiovascular and non-cardiovascular causes) were recorded.

Statistical analysis

Continuous variables were described by mean and standard deviation (SD). The association between factors was assessed by statistical hypothesis testing using proportion comparison. In order to evaluate the contribution of RV free wall strain to mortality while controlling possible confounding factors, multivariate logistic regression models were performed. The effects were considered significant if $p < 0.05$. The two-tailed p values and the power of all statistical tests were taken into account when drawing conclusions.

Results

The total study population was initially 91 patients, of which 5 were excluded for presenting significant valvular disease (3 with moderate to severe or severe mitral regurgitation and 2 with severe aortic stenosis) and 11 were excluded owing to poor echocardiographic window, 4 unable to follow up, or refusal to sign informed consent. Thus, 71 patients were included in the analysis.

Clinical characteristics

Baseline clinical characteristics are summarized in **Table 1**.

The average body mass index (BMI) was 30.23 (4.8 SD) in women and 29.49 (5.38 SD) in men. The medical treatment received by patients is shown in **Table 2**.

The main echocardiographic variables are listed in **Table 3**.

Most of the patients showed RV longitudinal dysfunction revealed by longitudinal strain: the percentage of patients with decreased RV strain (less than 20% in absolute value) was 63%.

Events

Within 6 months of inclusion in the study, 14% of patients had died of cardiovascular causes (heart failure or myocardial infarction, sudden death). Among the causes of death, 77% died from cardiovascular causes (72% of patients from heart failure, 5% from sudden

Table 1 Clinical characteristics

Clinical history	Percentage (number of patients)
Men	55%
Women	45%
Mean age years (SD)	77,58 (10,75)
Kidney failure	38,03% (27)
Dyslipidemia	50% (35)
Type 2 diabetes	42.25% (30)
Smoking	7.14%(5)
COPD	19.72% (14)
Atrial fibrillation	54.93% (39)
HBP	92,96% (66)
Ischemic heart disease	35% (25)

HBP – high blood pressure; COPD – chronic obstructive pulmonary disease; SD – standard deviation

Table 2 Medical treatment

Medical treatment	Percentage
ACE inhibitor	29%
ARBs	32%
MRA	19%
Beta blocker	60%
Furosemide	62%
Digoxin	19%
Thiazide	15%

ACE – angiotensin-converting enzyme; ARB – angiotensin receptor blockers; MRA – mineralocorticoid receptor antagonists

Table 3 Main echocardiographic variables

Parameter	
Proximal RVOT diameter (mm)	29,24 (SD 5.47)
Distal RVOT diameter (mm)	23.34 (SD 4.24)
TAPSE (mm)	19.03 (SD 3.36)
FAC (%)	52,6%
Tei Index	0.51 (SD 0.13)
RVFWLS (%)	15.29% (SD 4.41)
PASP (mmHg)	48.20 (SD 16.48)
LVEF	55,1% (SD 8,64)
HFmrEF (40-50%)/HFpEF (>50%)	35/65

Echocardiographic variables. Distal RVOT – Distal right ventricular outflow tract; FAC – Fractional area change; RVFWLS – right ventricular free-wall longitudinal strain; HFmrEF – mild reduced LVEF / HFpEF – preserved LVEF; % – percentage

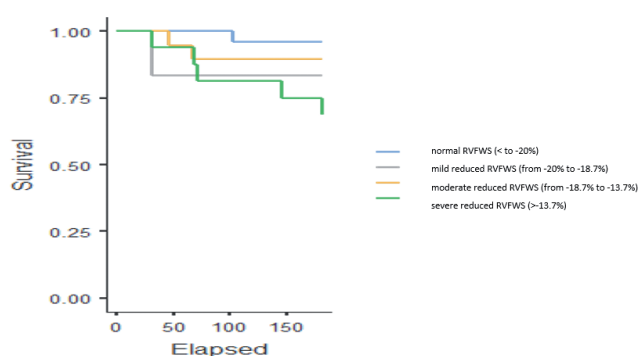


Figure 2 Cardiovascular mortality and RVFWS

death), 5% from kidney failure and 18% from neoplasia. A worse right ventricular free wall longitudinal strain was related to higher cardiovascular mortality (18,9 vs 13,96 (OR 0.86 (0.74;0.90, p 0.025) (Table 4). Neither

TAPSE nor FAC nor S wave were associated with a higher probability of readmission or mortality.

In a multivariate analysis that included age, BMI, E/e' ratio, ejection fraction (established risk factors of mortality in heart failure with preserved and mild reduced LVEF) the altered RV free wall strain remained a predictor of cardiovascular mortality at 6 months (Table 5).

Survival analysis

A Kaplan-Meier analysis was performed to estimate the survival function in our patients.

Statistically significant differences in survival were observed in patients with severely altered values compared to those with normal RVFWS values < -20% (Figure 2).

To assess the influence of the degree of depression of the deformation parameters on survival, RVFWS was

Table 4 Cardiovascular mortality at 6 months

	(total) N=71	No N=61	yes N=10	OR	p
RVFWLS	18.70 (13.73;20.73)	18.90 (14.00;20.90)	13.96 (10.83;18.82)	0.86 (0.74;0.90)	0.025
TAPSE	18.05 (17.07;21.00)	18.05 (17.23;21.00)	18.25 (16.90;22.00)	1.00 (0.81;1.22)	0.972
S	11.00 (10.00;12.00)	11.00 (10.00;12.00)	10.00 (9.00;11.00)	0.84 (0.58;1.20)	0.337
FAC	0.52 (0.46;0.62)	0.52 (0.45;0.61)	0.67 (0.51;0.73)	1.00 (0.97;1.04)	0.867

TAPSE – tricuspid annular plane systolic excursion; FAC – fractional area change; S – tricuspid TDI S wave; RVFWLS – right ventricular strain

Table 5 Cardiovascular death at 6 months. Multivariate analysis

CVdeath6m		no	Yes	OR (univariate)	OR (multivariate)
RVFWLS	Mean (SD)	17.7 (4.3)	14.7 (4.6)	0.86 (0.73-1.00, p=0.040)	0.70 (0.43-0.92, p=0.045)
Age	Mean (SD)	77.0 (10.9)	81.2 (9.3)	1.04 (0.98-1.13, p=0.250)	0.92 (0.80-1.04, p=0.201)
BMI	Mean (SD)	29.5 (4.8)	32.5 (6.7)	1.11 (0.98-1.26, p=0.101)	1.07 (0.81-1.44, p=0.642)
E/e'	Mean (SD)	17.1 (7.3)	25.1 (9.1)	1.11 (1.03-1.22, p=0.015)	1.18 (0.85-1.62, p=0.249)
E/e' average	Mean (SD)	15.0 (6.0)	26.2 (13.7)	1.15 (1.04-1.34, p=0.025)	1.06 (0.84-1.53, p=0.672)
LVEF	Mean (SD)	54.3 (8.7)	59.5 (7.0)	1.08 (0.99-1.18, p=0.090)	1.04 (0.90-1.21, p=0.572)

BMI – body mass index; TAPSE – tricuspid annular plane systolic excursion; RVFWLS – right ventricular strain; E/e' – ratio between E wave pulsed doppler and tissular doppler; LVEF – left ventricular ejection fraction

Table 6 Cardiovascular mortality and RVFWS. Survival analysis

RVFWLS		v	SE	Z	p
no depression	mild depression	1,03	0,80	1,30	0,19
no depression	moderate depression	0,71	0,86	0,83	0,40
no depression	severe depression	2,79	1,18	2,37	0,01
mild depression	moderate depression	-0,52	0,95	-0,54	0,58
mild depression	severe depression	0,99	1,28	0,77	0,44
moderate depression	severe depression	1,86	1,31	1,41	0,15

RVFWLS – right ventricular free-wall longitudinal strain. No depression (> -20%), mild depression (-20.7 to -18.7%), moderate depression (-18.7 to -13.7%) and 4) severe depression (> -13.7%)

stratified by quartiles. Four groups were established based on the quartiles found (13.7%, 18.7% and 20%) according to the severity of RVFWS depression: no depression ($>-20\%$) mild depression (-20.7 to -18.7%) moderate depression (-18.7 to -13.7%) and 4) severe depression ($>-13.7\%$) (Table 6).

Discussion

The use of techniques for studying RV deformation by echocardiography (global longitudinal strain) can provide useful information in the assessment of RV function quickly and non-invasively. The technique was developed in a similar way to that used for the study of left ventricular function (12,13).

Right ventricular function can be affected in patients with heart failure by the same processes that cause left ventricular dysfunction (14). In patients with pulmonary hypertension, RV free wall strain is significantly lower than that of healthy control subjects (15) but the degree or duration of right ventricular pressure overload does not fully explain right ventricular dysfunction in HFpEF (16).

In the same way that different comorbidities such as HBP (high blood pressure), diabetes mellitus, obesity and coronary artery disease directly affect longitudinal systolic and diastolic function of the left ventricle as a consequence of fibrotic subendocardial change (17,18), they can also affect the subendocardial fibers of the right ventricle (19). Authors such as Kosmala and collaborators observed right ventricular dysfunction in diabetic patients with preserved ejection fraction, with no difference in TAPSE or S wave (20). Diabetes is one of the main causes of HFpEF, mainly because of a greater presence of ischemic heart disease, although multiple pathophysiological mechanisms have also been implicated. A metabolic toxic effect on cardiomyocytes has been postulated among other reasons. In our study, we observed a high prevalence of DM (46%) in our patients, as they correspond to the group of patients with preserved and mild reduced EF. Right ventricular longitudinal dysfunction has also been evidenced in patients with hypertension (21), supporting the theory of involvement of both ventricles (not only the LV, but also the RV) in relation to HBP and other comorbidities such as DM that would cause a global effect on myocardial cells.

There is most likely to be an association with the same fibrosis process that affects the subendocardial layer of the LV and also to a lesser extent with the pressure overload secondary to pulmonary hypertension. The arrangement of the myocardial fibers in the right ventricle is predominantly longitudinal. There is a predominant longitudinal subendocardial layer and a thinner circumferential subepicardial layer. Thus, the process of right ventricular contraction and relaxation occur fundamentally in the longitudinal direction, this component being the one that contributes the most to the right ventricular ejection volume, much more than that of the contraction movement of the circumferential fibers (22).

Interesting observations emerge from the survival analysis. Patients with significant depression of right ventricular strain (RVFWS $>-13.7\%$) had statistically higher mortality rate than those with normal RVFWS (RVFWS $>-20\%$).

The alteration in RV deformation parameters could represent a greater decline in ventricular function and would therefore reflect a more advanced stage of the disease.

Our results through longitudinal strain revealed right ventricular dysfunction in HFpEF and HFmrEF with a worse clinical outcome. However, other functional parameters such as TAPSE and FAC were not as altered nor were they related to higher HF readmission or cardiovascular mortality. Maintaining normal TAPSE in HFpEF patients is not synonymous with normal RV function. TAPSE is a regional indicator that describes longitudinal function of the RV at lateral basal level and can be affected by load changes such as volumetric overload. Despite its wide utilization and proven prognostic value, it could be a less sensitive indicator of ventricular dysfunction than free wall strain. Fractional area change calculation is dependent on a good image quality and correct acquisition of the RV centric plane with meticulous endocardial border delineation (that is more trabeculated than the LV). It is also time consuming and cannot always be obtained reliably.

There is less data available on the Tei Index in RV functional assessment in this patient population. Tei index has been widely used for the study of left ventricular dysfunction, as it is an easy to apply tool for ventricular dysfunction (23). Its main disadvantage is the angle dependence and that it does not differentiate systolic from

diastolic dysfunction. As it requires several measurements for its calculation, it can constitute a potential source of error if one or more erroneous measurements are linked together, a weakness common in a large number of echocardiographic formulas.

When image quality is adequate and endocardial border detection is correct, RV free wall longitudinal strain is quantified semi-automatically with less chance of error than other parameters that require more measurements.

Our study has some limitations. One is that the RV function was evaluated by transthoracic echocardiography. Other more accurate and objective methods such as magnetic resonance imaging (gold standard) would have increased the reliability of the study in assessing right ventricular function. The availability of echocardiography is greater in clinical practice and its use much more widespread. Progressive improvement of the technology applied to echocardiography allows the assessment of increasingly accurate and reproducible measurements, even more so with the incorporation of semi-automatic methods as in the case of strain. The characteristics of patients in our sample (advanced age) may not be applicable to the younger population: however, heart failure with preserved ejection fraction affects increasingly elderly patients and no clinically relevant differences in strain have been established in the literature depending on age (24).

Conclusions

In patients with heart failure with preserved and mild reduced ejection fraction, impairment of right ventricular free wall strain is common and is related to worse clinical outcome (increased cardiovascular mortality at six months) regardless of other right ventricular functional parameters and left ventricular ejection fraction, therefore representing a sensitive non-invasive prognostic indicator in these patients, which could be useful in stratifying the risk of adverse events.

Conflict of interest: The authors declare that they have no conflict of interest related to this article.

Acknowledgments: Our thanks to the echocardiography laboratory at the University Clinical Hospital of Zaragoza.

References

1. Melenovsky V, Hwang SJ, Lin G, Redfield MM, Borlaug BA. Right heart dysfunction in heart failure with preserved ejection fraction. *Eur Heart J*. 2014;35:3452–3462.
2. Mohammed SF, Hussain I, AbouEzzeddine OF, Abou Ezzeddine OF, Takahama H, Kwon SH, et al. Right ventricular function in heart failure with preserved ejection fraction: a community-based study. *Circulation*. 2014;130:2310–2320.
3. Moreira H, Volpe GJ, Marin-Neto JA, Nwabuo CC, Ambale-Venkatesh B, Gali LG, et al. Right ventricular systolic dysfunction in Chagas disease defined by speckle-tracking echocardiography: a comparative study with cardiac magnetic resonance imaging. *JASE*. 2017;30:493–502.
4. Kaul S, TeiC, Hopkins JM, ShahPM. Assessment of right ventricular function using two-dimensional echocardiography. *Am Heart J*. 1984;107:526–531.
5. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al. Guidelines for the echocardiographic assessment of the right heart in adults: A report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr*. 2010;23:685–713.
6. Barón A. Deformación de la pared libre del ventrículo derecho: evaluación no volumétrica de la función. *Rev Colomb Cardiol*. 2012;19:223–224.
7. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults. *J Am Soc Echocardiogr*. 2015; 28:1–39.
8. Teske AJ, De Boeck BW, Olimulder M, Prakken NH, Doevendans AF, Cramer MJ. Echocardiographic assessment of regional right ventricular function: a head-to-head comparison between 2-dimensional and tissue Doppler derived strain analysis. *J Am Soc Echocardiogr*. 2008;21:275–283.
9. Morris DA, Gailani M, Vaz Pérez A, Blaschke F, Dietz R, Haverkamp W, et al. Right ventricular myocardial systolic and diastolic dysfunction in heart failure with normal left ventricular ejection fraction. *J Am Soc Echocardiogr*. 2011;24:886–897.
10. Damman K, Navis G, Smilde TD, Voors AA, van der Bij W, van Veldhuisen DJ, et al. Decreased cardiac output, venous congestion and the association with renal impairment in patients with cardiac dysfunction. *Eur J Heart Fail*. 2007;9:872–878.
11. Obokata M, Reddy YNV, Melenovsky V, Pislaru S, Borlaug BA. Deterioration in right ventricular structure and function over time in patients with heart failure and preserved ejection fraction. *Eur Heart J*. 2019;40:689–697.
12. Meris A, Faletra F, Conca C, Klersy C, Regoli F, Klimusina J, et al. Timing and magnitude of regional right ventricular function: a speckle-tracking derived strain study of normal subjects and patients with right ventricular dysfunction. *J Am Soc Echocardiogr*. 2010;23:823–831.
13. D'Andrea A, Caso P, Bossone E, Scarafilo R, Riegler L, Di Salvo G, et al. Right ventricular myocardial involvement in either physiological or pathological left ventricular hypertrophy: an

- ultrasound speckle-tracking two-dimensional strain analysis. *Eur J Echocardiogr.* 2010;11:492-500.
14. Cikes, M, Solomon S. An integrative approach for assessment of cardiac function in HF. *Eur Heart J.* 2016;37:1642-1650.
15. Fukuda Y, Tanaka H, Sugiyama D, Ryo K, Onishi T, Fukuya H, et al. Utility of right ventricular free wall speckle-tracking strain for evaluation of right ventricular performance in patients with pulmonary hypertension. *J Am Soc Echocardiogr.* 2011;24:1101-1108.
16. Bogaard HJ, Natarajan R, Henderson SC, Long CS, Kraskauskas D, Smithson L, et al. Chronic pulmonary artery pressure elevation is insufficient to explain right heart failure. *Circulation.* 2009;120:1951-1960.
17. Ng AC, Delgado V, Bertini M, van der Meer RW, Rijzewijk LJ, Shanks M, et al. Findings from left ventricular strain and strain rate imaging in asymptomatic patients with type 2 diabetes mellitus. *Am J Cardiol.* 2009;104:1398-1401.
18. Stanton T, Marwick TH. Assessment of subendocardial structure and function. *J Am Coll Cardiol Img.* 2010;3:867-875.
19. Broberg CS, Chugh SS, Conklin C, Sahn DJ, Jerosch-Herold M. Quantification of diffuse myocardial fibrosis and its association with myocardial dysfunction in congenital heart disease. *Circ Cardiovasc Imaging.* 2010;3:727-734.
20. Kosmala W, Colonna P, Przewlocka-Kosmala M, Mazurek W. Right ventricular dysfunction in asymptomatic diabetic patients. *Diabetes Care.* 2004;27:2736-2738.
21. Cicala S, Galderisi M, Caso P, Petrocelli A, D'Errico A, de Divitiis, O, et al. Right ventricular diastolic dysfunction in arterial systemic hypertension: analysis by pulsed tissue Doppler. *Eur J Echocardiogr.* 2002;3:135-142.
22. Leather HA, Ama' R, Missant C, Rex S, Rademakers FE, Wouters PF. Longitudinal but not circumferential deformation reflects global contractile function in the right ventricle with open pericardium. *Am J Physiol Heart Circ Physiol.* 2006;290:2369-2375.
23. Goroshi M, Chand D. Myocardial Performance Index (Tei Index): A simple tool to identify cardiac dysfunction in patients with diabetes mellitus. *Indian Heart J.* 2016;68:83-87.
24. Muraru D, Onciul S, Peluso D, Soriani N, Cucchini U, Aruta P, et al. Sex- and Method-Specific Reference Values for Right Ventricular Strain by 2-Dimensional Speckle-Tracking Echocardiography. *Circ Cardiovasc Imaging.* 2016;9:e003866.