Reduced fractional shortening of right ventricular outflow tract is associated with adverse outcomes in patients with left ventricular dysfunction

Masashi Yamaguchi¹, Toshihiro Tsuruda¹*, Yuki Watanabe², Hisamitsu Onitsuka¹, Kuniko Furukawa³, Takeshi Ideguchi¹, Junji Kawagoe¹, Tetsunori Ishikawa¹, Johji Kato⁴, Makoto Takenaga² and Kazuo Kitamura¹

Abstract

Background: Recent studies suggest the significance of right ventricular (RV) function in the outcome in patients with left ventricular dysfunction (LVSD); however, global assessment of RV remains to be determined by echocardiogram because of its complex geometry. This study aimed to validate RV outflow tract fractional shortening (RVOT-FS) in the evaluation of RV function and its prognostic value in patients with LVSD.

Methods: This study included eighty-one patients (62 ± 17 years, mean ± SD, male 79%) with reduced LV ejection fraction (LVEF) (≤40%). Two-dimensional echocardiogram of the parasternal short axis view was obtained at the level of the aortic root, and RVOT-FS was calculated as the ratio of end-diastole minus end-systole dimension to end-diastole dimension.

Results: RVOT-FS ranged from 0.04 to 0.8 (0.3 ± 0.2, mean ± SD), and correlated with LVEF (r = 0.33, p = 0.0028), RV fractional area change (r = 0.37, p = 0.0008) and brain natriuretic peptide level (r = -0.38, p = 0.0005). In Cox multivariate regression analysis, RVOT-FS [hazard ratio (HR) 0.028, 95% confidence interval (CI): 0.002-0.397; p = 0.008] and New York Heart Association functional class III-IV [HR 2.233, 95% CI: 1.048-4.761; p = 0.037] were independent factors to predict the events. During a median follow-up period of 319 days (1 to 1862 days), patients with RVOT-FS ≥ 0.2 showed a higher event-free rate than those < 0.2 by Kaplan-Meier analysis (log-rank test, p = 0.0016).

Conclusions: Our data suggest that RVOT-FS is a simple parameter reflecting the severity of both ventricular function in patients with LVSD. In addition, RVOT-FS might be useful to predict adverse outcomes in such a patient population.

Keywords: Heart failure, Right ventricle, Brain natriuretic peptide

Introduction

Left ventricular ejection fraction is well recognized in the adverse clinical outcomes of patients with chronic heart failure [1]; however, it loses statistical power when applied to patients with advanced heart failure [2]. In this setting, RV function determines exercise capacity and survival [2-4]. Although several echocardiographic parameters have been proposed [5], accurate global assessment of the RV is still challenging because of its complex anatomy; RV is not one chamber, but is composed of two distinct anatomic units, the RV sinus (from the tricuspid valve annulus to the proximal os infundibulum) and right ventricular outflow tract (RVOT) (from proximal os infundibulum to the pulmonary valve) [6]. Regional RVOT dysfunction is suggested to affect exercise tolerance after tetralogy of Fallot repair [7]. Thus, RVOT appears to have its own hemodynamic characteristics by reflecting the RV sinus and pulmonary artery [8]; however, few studies have addressed the impact of RVOT function on patients with left ventricular systolic dysfunction (LVSD). Based upon the unique nature of anatomy, we hypothesized that contractility of RVOT segment might be associated with the severity of heart failure and that it affects the prognosis of patients with LVSD. The aim of this study was to evaluate...
RVOT-fractional shortening (FS) with the clinical, laboratory and echocardiographic parameters. Second, we examined if the measurement of RVOT-FS is a useful parameter providing predictive value in these patients.

Methods

Patients
This study included 81 patients hospitalized at Miyazaki University Hospital between March 2007 and November 2011. Patients were selected based on the impaired LV systolic function (LV ejection fraction (EF) \( \leq 40\% \)) but not on clinical symptoms, and excluded if they had LVSD due to acute myocarditis and tachycardia-induced cardiomyopathy. Patients underwent coronary angiography, \(^{201}\)Tallium-\(^{123}\)I-\(\beta\)-methyl iodophenyl pentadecanoic acid scintigraphy, \(^{18}\)fluoro-deoxyglucose by positron emission tomography imaging, magnetic resonance imaging and endomyocardial biopsy to aid in the definition of the etiology of LVSD, such as ischemic heart disease, hypertensive heart disease, valvular heart disease and secondary cardiomyopathies (ex. sarcoidosis or other infiltrative cardiomyopathies). We notified the patients in writing and on the homepage, or gave written informed consent. This study was approved by the Human Investigation Review Committee of the University of Miyazaki (No.979) and conformed with the principles outlined in the Declaration of Helsinki (Cardiovasc Res 1997; 35: 2-4).

Echocardiography

Echocardiography was performed using an ATL Philips IE33 Ultrasound machine (Garnerville, NY, USA) with the determination of standard and Doppler parameters. Echocardiographic data on admission and at the out-patient clinic were stored (DICOM format), and reviewed digitally off-line on a desktop computer with ProSolv software (ProSolv Cardiovascular Analyzer 3.5; Indianapolis, IN, USA) by two experienced cardiologists. Size of the left atrium (LA), LV at end-diastole (LVDd) and end-systole (LVDs), and wall thickness of the intraventricular septum (IVSTd) and posterior wall (LVPWTd) at diastole were determined from the two-dimensional parasternal long-axis view on electrocardiogram. LVEF was calculated by the modified Simpson’s method in apical four- and two-chamber views. For evaluating the RV fractional area change (RVFAC), endocardial borders were outlined at end-diastole and end-systole, using an apical four-chamber view [9], and RVFAC (%) was calculated by (RV end-diastolic area – RV end-systolic area)/RV end-diastolic area x100. Tricuspid regurgitation-pressure gradient (TR-PG) was estimated by the peak continuous-wave Doppler velocity of the tricuspid regurgitation jet using the modified Bernoulli equation. The RVOT dimension was measured in end-diastole and end-systole at parasternal-short axis view at the level of the aortic root using two-dimensional echocardiogram, and RVOT-FS was calculated as (dimension at end-diastole – end-systole)/end-diastole (Figure 1). This was modified to the original study by Lindqvist et al. [8] who determined the RVOT dimension on M-mode. Each patient was asked to return for a follow-up echocardiogram or it was performed when they were re-admitted to the hospital.

Cine magnetic resonance imaging (cine MRI)

We validated the RVOT-FS assessed by echocardiogram with 1.5-Tesla MRI system (Signa HDxt, GE Healthcare UK Ltd., Buckinghamshire, United Kingdom). Nine subjects were in the supine position with breath holding in expiration and with a vector-cardiographic method for electrocardiographic gating. Transaxial slices using the rephrased gradient echo technique was planned to cover the heart from a level just below of diaphragm to bronchial bifurcation, with repetition time of 2.7-2.9 msec, echo time of 0.8-1.0 msec, a flip angle of 40 degree, and a slice thickness of 7-8 mm. An identical imaging plane before and after contrast injection was used to calculate RVOT-FS.}

![Figure 1 Two-dimensional view of right ventricular outflow tract at end-diastole and end-systole.](http://www.cardiovascularultrasound.com/content/11/1/19)
thickness of 10 mm. The diameters of RVOT at end-diastole and end-systole were measured on still frames with manual tracing by means of a track-ball cursor.

**Laboratory tests**
Plasma brain natriuretic peptide (BNP) concentration was measured by chemiluminescent immunoassay (ARCHITECT BNP-JP; Abott, Chiba, Japan). C-reactive protein in the serum was determined by the latex agglutination test with a measurement range of 0.01 to 32 mg/dL. Estimated glomerular filtration rate (eGFR) was calculated using the equation for the Modification of Diet in Renal Disease [10].

**Follow-up and end points**
Follow-up was performed by direct examination of medical records or by contact with cardiologists. All patients were followed up until October 2012 unless a major end point terminated the follow-up. In the present study, outcomes were included such as death from cardiovascular diseases (heart failure and lethal arrhythmia), requirement of cardiac transplantation, and unexpected hospitalization due to the worsening of heart failure [11].

**Statistical analysis**
Data analyses were performed using GraphPad Software Prism 5 (GraphPad Software, San Diego, CA, USA) for Bland-Altman plot and SPSS version 11.0 (SPSS Japan, Tokyo, Japan) for the rest of the analyses. We used Student’s t-test or Mann-Whitney test for two continuous parametric or nonparametric variables, and the Fisher’s exact test for qualitative data such as numbers and percentages. Unadjusted and adjusted associations of RVOT-FS with other clinical parameters were evaluated by Spearman rank-correlation coefficient and multivariate linear regression. There were close relationships between the following two variables [LVDd and LVDs (r = 0.886, p < 0.0001)] and [IVSTd and LVPWTd (r = 0.650, p < 0.0001)], and we removed LVDs and LVPWTd as variables in the analysis. A Cox proportional hazards model was used to determine any variables as significant factors to predict cardiovascular events in the study subjects. The covariates included in this model were age, sex, use of β-blocker, angiotensin converting enzyme inhibitor (ACE-I) /angiotensin II type 1 receptor antagonist (ARB), calcium channel blocker, diuretic and aldosterone antagonist, rhythm in electrocardiogram, echocardiographic parameters (LAD, IVSTd, LVDd, LVEF, RVFAC, RVOT-FS, TR-PG), BNP, eGFR, hemoglobin, total bilirubin, uric acid, C-reactive protein and New York Heart Association (NYHA) functional class. Results are presented as relative risk with 95% confident interval (CI). Kaplan-Meier analysis was constructed by receiver operating characteristics (ROC) analysis. In addition, Bland-Altman plots were used to evaluate agreement of measurements.

### Table 1 Patient’s characteristics

|                         | 62 ± 17 |
|-------------------------|---------|
| Age, years              | Male (79%) |
| NYHA functional class   | 17 (21%) |
| III-IV                  | I 31; II 33; III 15; IV 2 |
| Etiology                | 22 (27%) |
| IHD                     | 59 (73%) |
| Non-IHD                 | 4 (5%) |
| Valvular disease        | 37 (46%) |
| DCM                     | 5 (6%) |
| HCM                     | 7 (9%) |
| HHD                     | 6 (7%) |
| Other                   |         |
| Electrocardiogram       |         |
| Sinus rhythm            | 54 (67%) |
| Atrial fibrillation      | 19 (23%) |
| Pacing rhythm           | 8 (10%) |
| Medications             |         |
| Beta-blocker            | 62 (78%) |
| ACE-I/ARB               | 65 (80%) |
| Calcium channel blocker | 16 (20%) |
| Diuretic                | 61 (75%) |
| Aldosterone antagonist  | 47 (58%) |
| Laboratory test         |         |
| BNP (pg/mL)             | 765 ± 870 |
| Uric acid (mg/dL)       | 7.4 ± 2.6 |
| Hemoglobin (g/dL)       | 14.0 ± 2.1 |
| Total bilirubin (mg/dL) | 1.1 ± 0.8 |
| C-reactive protein (mg/dL) | 1.5 ± 2.9 |
| eGFR (mL/min/1.73 m²)   | 51 ± 20 |

**Echocardiographic examination**

|                         |         |
|-------------------------|---------|
| LAD (cm)                | 4.1 ± 0.8 |
| IVSTd (cm)              | 1.0 ± 0.3 |
| LVPWTd (cm)             | 1.1 ± 0.3 |
| LVDd (cm)               | 6.1 ± 1.0 |
| LVDs (cm)               | 5.4 ± 1.1 |
| LVEF (%)                | 30 ± 8 |
| RVFAC (%)               | 35 ± 14 |
| TR-PG (mmHg)            | 25 ± 12 |

Values are expressed as absolute numbers (%) or the mean ± SD.

NYHA New York Heart Association, IHD ischemic heart disease, DCM dilated cardiomyopathy, HCM hypertrophic cardiomyopathy, HHD hypertensive heart disease, Others include 2 sarcoidosis, 1 LV noncompaction, 1 restrictive cardiomyopathy and 2 unknown origin, ACE-I angiotensin converting enzyme inhibitor, ARB angiotensin II type 1 receptor antagonist, BNP brain natriuretic peptide, eGFR estimated glomerular filtration rate, LAD left atrial dimension (diastole), IVSTd intraventricular septal wall thickness (diastole), LVPWTd left ventricular posterior wall thickness (diastole), LVEF left ventricular ejection fraction, RVFAC right ventricular fractional area change, TR-PG tricuspid regurgitation-pressure gradient.
to compare the agreement of the two methods (echocardiography vs. cine MRI). The plot was displayed as the average of the two values and the difference between the two measurements. Results are shown as absolute numbers (%) or the mean ± standard deviation (SD). Statistical significance was accepted when p < 0.05.

**Results**

**Patients’ characteristics**

Table 1 summarizes clinical characteristics and echocardiographic variables of the 81 patients enrolled in this study. Etiology of LVSD was heterogeneous, and 23% of them exhibited atrial fibrillation, and mean value of LVEF was 30%.

**Spectrum of RVOT-FS**

RVOT diameter was 3.1 cm at end-diastole (range, 1.9-5.3 cm) and 2.1 cm at end-systole (range, 0.4-4.5 cm), and the mean value of RVOT-FS was 0.3 (range, 0.04-0.8). Table 2 summarizes that RVOT-FS was associated with NYHA functional class III-IV (r = -0.27), LAD (r = -0.45), LVDd (r = -0.29), LVDs (r = -0.32), LVEF (r = 0.33), RVFAC (r = 0.37), BNP (r = -0.38), uric acid (r = -0.28), total bilirubin (r = -0.30), or C-reactive protein (r = -0.29), but not with age, IVSTd, LVPWTd, TR-PG or eGFR. Figure 2 shows that plasma BNP level increased (A), whereas RVOT-FS decreased (B), according to NYHA functional class. As shown in Table 3, RVOT-FS was independently associated with BNP and LVDd.

**Clinical characteristics of patients with or without cardiovascular event**

During a median follow-up period of 319 days (1 to 1862 days), all-cause events occurred in 38 patients (cardiac death, 13; requirement of cardiac transplantation, 2; unexpected hospitalization due to the worsening of heart failure, 23). Table 4 summarizes that patients who had an event were older, with higher BNP and total bilirubin level, and a greater prevalence of diuretic use. On the other hand, they showed a lower concentration of eGFR. On the echocardiogram, LAD was significantly increased, whereas RVOT-FS and IVSTd were decreased in the event group. LVEF, RVFAC or TR-PG did not change between the two groups.

**Univariate and multivariate Cox regression analyses**

Table 5 summarizes the univariate and multivariate Cox regression analyses using forward step-wise variable selection. In univariate regression analysis, RVOT-FS, NYHA functional class III-IV, IVSTd, diuretic use, BNP and total bilirubin were extracted as significant factors.
Table 3 Multivariate regression analysis for RVOT-FS

| Dependent variable | Independent variable | Regression co-efficient | p value |
|--------------------|----------------------|-------------------------|---------|
| RVOT-FS            | BNP                  | -0.415                  | 0.001   |
|                    | LVDD                 | -0.324                  | 0.005   |

Age, NYHA functional class, LAD, IVSTd, LVDD, LVEF, RVFAC, TR-PG, total bilirubin, uric acid, BNP, C-reactive protein and eGFR were included as independent variables.

Table 4 Clinical characteristics and echocardiographic variables of patients with or without cardiovascular event

| Parameters                        | Cardiovascular event |
|-----------------------------------|----------------------|
|                                   | (-) (n = 43)         | (+) (n = 38)         | p value |
| Age (year)                        | 58 ± 17              | 66 ± 15              | 0.037   |
| Male (1, male; 2, female)         | 36.0 ± 17            | 28.0 ± 12            | 0.289   |
| NYHA functional class III-IV      | 6.0 ± 2.8            | 12.0 ± 6.6           | 0.067   |
| IHD (1, no; 2, yes)               | 10.0 ± 5.8           | 10.0 ± 5.0           | 0.800   |
| Rhythm (AF / pacing)              | 10.0 ± 5.8           | 17.0 ± 9.0           | 0.059   |
| BNP (pg/mL)                       | 580 ± 805            | 965 ± 903            | 0.005   |
| Total bilirubin (mg/dL)           | 0.93 ± 0.53          | 1.34 ± 0.98          | 0.018   |
| Uric acid (mg/dL)                 | 7.08 ± 1.89          | 7.76 ± 3.18          | 0.235   |
| eGFR (mL/min/1.73 m²)             | 55.8 ± 18.9          | 44.9 ± 19.8          | 0.015   |
| Hemoglobin (g/dL)                 | 14.3 ± 2.3           | 13.5 ± 1.9           | 0.081   |
| C-reactive protein (mg/dL)        | 1.4 ± 3.0            | 1.5 ± 2.9            | 0.039   |
| LAD (cm)                          | 3.89 ± 0.66          | 4.43 ± 0.91          | 0.003   |
| IVSTd (cm)                        | 1.08 ± 0.35          | 0.87 ± 0.24          | 0.004   |
| LVWThd (cm)                       | 1.11 ± 0.27          | 1.01 ± 0.21          | 0.070   |
| LVDD (cm)                         | 6.06 ± 0.79          | 6.22 ± 1.25          | 0.465   |
| LVDs (cm)                         | 5.28 ± 0.85          | 5.50 ± 1.28          | 0.356   |
| LVEF (%)                          | 31.4 ± 7.6           | 28.5 ± 7.8           | 0.093   |
| RVOT-FS                           | 0.38 ± 0.20          | 0.27 ± 0.17          | 0.008   |
| RVFAC (%)                         | 38.1 ± 14            | 32.1 ± 14            | 0.086   |
| TR-PG (mmHg)                      | 25.1 ± 14            | 25.9 ± 9.9           | 0.978   |
| Beta-blocker (1, no; 2, yes)      | 25.0 ± 9.9           | 29.0 ± 12.3          | 0.102   |
| ACE-I/ARB (1, no; 2, yes)         | 28.0 ± 12.3          | 30.0 ± 21.9          | 0.219   |
| Calcium channel blocker (1, no; 2, yes) | 11.0 ± 6.0 | 6.0 ± 4.13          | 0.041   |
| Diuretic use (1, no; 2, yes)      | 24.0 ± 12.3          | 36.0 ± 19.9          | <0.001  |
| Aldosterone antagonist (1, no; 2, yes) | 21.0 ± 12.3       | 25.0 ± 17.2          | 0.177   |

Values are expressed as absolute number or the mean ± SD. Each variable was analyzed by 1) unpaired t-test, 2) Fisher’s exact test and 3) Mann-Whitney test.

Table 5 Univariate and multivariate Cox regression analyses

| Variables            | Univariate analysis | Multivariate analysis |
|----------------------|---------------------|-----------------------|
|                      | HR                  | 95% CI                | HR                  | 95% CI                |
| RVOT-FS              | 0.110               | 0.014-0.886           | 0.038               | 0.028                 | 0.002-0.397           | 0.008               |
| NYHA functional class III-IV | 2.828 | 1.380-5.793           | 0.004               | 2.233                 | 1.048-4.761           | 0.037               |
| IVSTd                | 0.112               | 0.030-0.415           | 0.001               | Diuretic use          | 6.872                 | 1.654-28.548        | 0.008               |
| BNP                  | 1.000               | 1.000-1.001           | 0.018               | Total bilirubin       | 1.675                 | 1.217-2.306         | 0.002               |

Univariate and multivariate Cox regression analyses were constructed with forward step-wise variable selection. HR hazard ratio, CI confidence interval. Covariates included age (year), sex (male, 1; female, 2; NYHA functional class III-IV (0, I-II; 1, III-IV); sinus rhythm in electrocardiogram (no, 0; yes, 1); BNP (pg/mL), eGFR (mL/min/1.73 m²), total bilirubin (mg/dL), uric acid (mg/dL) and C-reactive protein (mg/dL). echocardiographic parameters such as LAD (cm), IVSTd (cm), LVDD (cm), LVFAC (%), RVOT-FS, TR-PG (mmHg); use (no, 0; yes, 1) of beta-blocker, ACE-I/ARB, calcium channel blocker, diuretic and aldosterone antagonist.

for predicting cardiovascular events. In multivariate Cox regression analysis, RVOT-FS and NYHA functional class III-IV remained independent factors. Based on the ROC analysis with sensitivity of 86% and specificity of 47% (Figure 3A), we divided the patients into RVOT-FS > 0.2 or < 0.2. As shown in Figure 3B, RVOT-FS > 0.2 had a higher prevalence of event-free periods, compared with < 0.2 (log-rank test p = 0.0016).

Reproducibility, and validation of RVOT-FS with cine MRI
Reproducibility of the RVOT-FS measurement was evaluated by calculating the intra- and inter-observer variability in 20 patients. The intra- and inter-observer coefficient variables were 2.5 and 14.7, respectively. We also carried out cine MRI for nine subjects to examine the validity of RVOT-FS assessed by echocardiogram. The Bland-Altman plots demonstrated no evidence of substantial fixed or proportional bias in the two methods (Figure 4).

Discussion
Assessment of RV function is important to understand the pathophysiology of heart failure; however, it is still challenging to find a simple and comprehensive parameter by echocardiogram. In this study, we demonstrated that RVOT-FS reflects the severity of both left- and right-sided ventricular function. In addition, our data suggested that RVOT-FS might be a useful parameter to predict cardiovascular events in patients with LVSD.

RV originates from a different embryological source to LV [12]. RVOT is defined as a region between the sub-pulmonary infundibulum and pulmonary valve, and is distinct from the rest of RV in origin and anatomy [5,6,8]. The measurement of RVOT has not been standardized in healthy subjects; however, the mean diastolic dimension is distinct from the rest of RV in origin and anatomy [5,6,8].
reported to be 2.8 cm [5] and RVOT-FS is 0.61 [8] to 0.98 [13]. In this study, patients with LVSD exhibited a relatively enlarged diastolic dimension of RVOT along with its reduced contractility. The pathophysiological and clinical relevance of RVOT-FS measurement was not completely elucidated in this study; however, several potential mechanisms can be suggested. Original study by Lindqvist et al. [8] showed that RVOT-FS correlated with several RV functional parameters, and our data support that RVOT-FS positively correlated with RVFAC. There are few reports to demonstrate the RVOT-FS with clinical, laboratory and echocardiographic variables, and our data indicate the unique characteristics of this value. Positive correlation with total bilirubin concentration is likely to reflect the increased central venous pressure by the impaired RV hemodynamics [14], and inverse correlation with serum concentrations of uric acid [15] and C-reactive protein [16], in part by indirectly reflecting the chronic systemic inflammation, oxidative stress and diuretic use. It is of note that RVOT-FS was also associated with chamber size of LA and LV, and LVEF. We found that RVOT-FS is associated with LV end-diastolic dimension and BNP independently, suggesting that the magnitude of RVOT-FS reflects the structural and functional capacity of LV as well as RV [17,18]. The continuity of superficial muscle fibers encircle RV and LV represents the traction of both ventricular free walls, and makes up the anatomic basis for mechanical ventricular-ventricular interaction [19,20]. LV hemodynamic behavior was reported to be indirectly assessed by the motion of aortic root [21], and our data implicate that LV overload influences the motion of RVOT. In other point of view, we speculate that the regional contractility of RVOT may affect the LV stroke volume if LV function have failed, because the RVOT segment contributes to up to 15% of total RV stroke volume [6], but need further investigation. In line with previous reports [14,22-25], cardiovascular events occurred in patients who were older, with the increased LA size, BNP and total bilirubin concentration, and frequent diuretic use. Interestingly, the prevalence of events was greater in patients with decreased RVOT-FS than LVEF, TR-PG or RVFAC. A number of factors contribute to the outcome in patients with advanced heart failure. In this study, diuretic use, BNP and total bilirubin, LV wall thickness as well as RVOT-FS and NYHA functional class was extracted as the predictors of follow-up patients by Univariate Cox regression analysis. LV overload is initially compensated by the adequate increase of wall thickness, and our data support that the reduced LV wall thickness exhibited poor outcome, and our data suggest that the reduced LV wall thickness exhibited poor outcome, and it appears to be a consequence of maladaptive LV remodeling resulting from myocyte cell loss [26]. Multivariate Cox regression analysis demonstrated that RVOT-FS as well as the severity of heart failure was an independent prognostic value, and we showed that RVOT-FS <0.2 exhibited poorer prognosis. However, the specificity of cut-off value chosen by ROC curve was low, and this might have been due to the wide distribution of RVOT-FS in patients with NYHA.

Figure 3 A, Receiver operating characteristics (ROC) analysis and B, Kaplan-Meier analysis to evaluate the cardiovascular event-free rate according to the RVOT-FS in LVSD patients. AUC, area under the curve.

Figure 4 Bland-Altman plots of RVOT-FS measurement between echocardiography and cine MRI to determine the substantial variability of fixed or proportional bias. The 95% limits of agreement are shown as two dotted lines.
functional class I or II. In the follow-up echocardiogram, we observed that deterioration of RVOT-FS with a minimal change in LVEF resulted in a poor outcome (data not shown). Drighil et al. [13] reported that RVOT-FS improved more rapidly than other RV functional parameters such as RVFAC or tricuspid annular plane systolic excursion after mitral valve commissurotomy. Thus, sequential assessment of RVOT-FS by echocardiogram might lead to a more accurate diagnosis and would help to determine the medical approach. Furthermore, it would be interesting whether the intervention of any specific pharmacotherapy and medical device to improve the cardiovascular mortality/morbidity are associated with the contractility of RVOT.

Study limitation
This is a retrospective observation study with a small number of heterogeneous pathologies in patients with LVSD. We did not assess the other RV systolic parameters, such as peak systolic tricuspid annular velocity, integral of the systolic wave, and tricuspid annular plane systolic excursion [27]. In addition, we understand that an oblique section of echocardiographic imaging at the level of RVOT leads to underestimation of the value. Moreover, this study included 23% patients with atrial fibrillation, and single measurement of RVOT-FS potentially hampers the accurate value. We validated the value with cine MRI, but we agree that the reproducibility was sub-optimal [28], and it is necessary to improve it by newer technologies [20].

Conclusion
The present study suggests that RVOT-FS is a parameter to assess the severity of both ventricular functions in LVSD patients. In addition, our findings implicate a measurement of RVOT-FS might provide a predictive value in such a patient population.

Abbreviations
RVOT: Right ventricular outflow tract; LVSD: Left ventricular systolic dysfunction; FS: Fractional shortening; EF: Ejection fraction; LA: Left atrium; LVDd: LV dimension at end-diastole; LVDs: LV dimension at end-systole; IVSTd: Wall thickness of the intraventricular septum; LVPWTd: Wall thickness of the posterior wall; TR-PG: Tricuspid regurgitation-pressure gradient; RVFAC: RV fractional area change; MRI: Magnetic resonance imaging; ACE-I: Angiotensin converting enzyme inhibitor; ARB: Angiotensin II type 1 receptor antagonist; BNP: Brain natriuretic peptide; eGFR: Estimated glomerular filtration rate; ACE-I: Angiotensin converting enzyme inhibitor; ARB: Angiotensin II type 1 receptor antagonist; NYHA: New York Heart Association; ROC: Receiver operating characteristics; SD: Standard deviation.

Competing interests
The authors have no competing interest.

Authors’ contributions
MY, TT and KI designed the study, investigated all patients and analyzed the data. MY and TT wrote the manuscript. MY, TT and KF performed echocardiogram and acquired the measurement. YW and MT performed cine MRI and analyzed the data. HO, T. Ideguchi, J. Kawagoe, and T. Ishikawa have interpreted the data and have been involved in drafting the manuscript. J. Kato performed the statistical analysis and made critical review of the manuscript. All authors have read and given final approval of the manuscript.

Author details
1Department of Internal Medicine, Circulatory and Body Fluid Regulation, Faculty of Medicine, University of Miyazaki, 5200 Khira Kiyotake, Miyazaki 889-1692, Japan. 2Internal Medicine, Fujimoto Central Hospital, 3584-1 Midarabashi Kitakawauchi, Miyazaki 880-0941, Japan. 3Clinical laboratory, Miyazaki University Hospital, 5200 Khira Kiyotake, Miyazaki 889-1692, Japan. 4Frontier Science Research Center, University of Miyazaki, 5200 Khira Kiyotake, Miyazaki 889-1692, Japan.

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References
1. Wang TJ, Evans JC, Benjamin EJ, Levy D, LeRoy EC, Vasan RS: Natural history of asymptomatic left ventricular systolic dysfunction in the community. Circulation 2003, 108(8):977–982.
2. Ghio S, Gavazzi A, Campana C, Inserra C, Klesyr C, Sebastiani R, Arbustini E, Recucasi F, Tavazzi L: Independent and additive prognostic value of right ventricular systolic function and pulmonary artery pressure in patients with chronic heart failure. J Am Coll Cardiol 2001, 37(1):183–188.
3. Meyer P, Filippatos GS, Ahmed M, Ikkandaian AE, Bttner V, Perry GJ, White M, Awan B, Mubl M, Dallalta L, et al: Effects of right ventricular ejection fraction on outcomes in chronic systolic heart failure. Circulation 2010, 121(2):252–258.
4. Di Salvo G, Mathier M, Semignan MJ, Dec GW: Preserved right ventricular ejection fraction predicts exercise capacity and survival in advanced heart failure. J Am Coll Cardiol 1995, 25(3):1143–1153.
5. Rudski LG, Lai WW, Alfalo J, Hua L, Handschumacher MD, Chandrasekaran K, Solomon LD, Louie EK, Schiller NB: 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(7):885–713.
6. Geva T, Powell AJ, Crawford EC, Chung T, Colan SD: Evaluation of regional differences in right ventricular systolic function by acoustic quantification echocardiography and cine magnetic resonance imaging. Circulation 1998, 98(4):339–345.
7. Wald RM, Haber I, Wald R, Valente AM, Powell AJ, Geva T: Effects of regional dysfunction and late gadolinium enhancement on global right ventricular function and exercise capacity in patients with repaired tetralogy of Fallot. Circulation 2009, 119(10):1370–1377.
8. Lindqvist P, Hemein M, Kazzam E: Right ventricular outflow-tract fractional shortening: an applicable measure of right ventricular systolic function. Eur J Echocardiogr 2003, 4(1):29–35.
9. Anavekar NS, Gerson D, Skalli H, Kwong RY, Yucel EK, Solomon SD: Two-dimensional assessment of right ventricular function: an echocardiographic-MRI correlative study. Echocardiography 2007, 24(5):452–456.
10. Matsuo S, Imai E, Hori M, Yasuda Y, Tomita K, Nitta K, Yamagata K, Tomino Y, Yokoyama H, Hishida A: Revised Equations for Estimated GFR from Serum Creatinine in Japan. Am J Kidney Dis 2000, 35(6):982–992.
11. Margolis JR, Gillum RF, Feinleib M, Brasch RC, Fabzitz RR: Community surveillance for coronary heart disease: the Framingham Cardiovascular Disease Survey. Methods and preliminary results. Am J Epidemiol 1974, 100(6):425–436.
12. Zeffran S, Kelly RC, Melichar SA, Buckingham ME, Brown NA: Right ventricular myocardium derives from the anterior heart field. Circ Res 2004, 95(5):261–268.
13. Drighil A, Bennis A, Mathewson JW, Lancelotti P, Rocha P: Immediate impact of successful percutaneous mitral valve commissurotomy on right ventricular function. Eur J Echocardiogr 2008, 9(4):S36–S41.
14. Shinagawa H, Inomata T, Koitabashi T, Nakano H, Takeuchi I, Naruke T, Ohsaka T, Nishii M, Takehana H, Izumi T: Prognostic significance of increased serum bilirubin levels coincident with cardiac decompensation in chronic heart failure. Circ J 2008, 72(3):364–369.
15. Wu AH, Ghali JK, Neuberg GW, O’Conor CM, Carson PE, Levy WC: Uric acid level and allopurinol use as risk markers of mortality and morbidity in systolic heart failure. Am Heart J 2010, 160(5):928–933.
16. Anand IS, Latini R, Florea VG, Kuskowski MA, Rector T, Masson S, Signorini S, Mocarelli P, Hester A, Glazer R, et al: C-reactive protein in heart failure: prognostic value and the effect of valsartan. Circulation 2005, 112(10):1428–1434.
17. Troisi F, Greco S, Brunetti ND, Di Biase M: Right heart dysfunction assessed with echography, B-type natriuretic peptide and cardiopulmonary test in patients with chronic heart failure. J Cardiovasc Med (Hagerstown) 2008, 9(7):672–676.

18. Vogelsang TW, Jensen RJ, Monrad AL, Russ K, Olesen UH, Hesse B, Kjaer A: Independent effects of both right and left ventricular function on plasma brain natriuretic peptide. Eur J Heart Fail 2007, 9(9):892–896.

19. Haddad F, Hunt SA, Rosenthal DN, Murphy DJ: Right ventricular function in cardiovascular disease, part I: anatomy, physiology, aging, and functional assessment of the right ventricle. Circulation 2008, 117(1):1436–1448.

20. Saremi F, Ho SY, Cabrera JA, Sánchez-Quintana D: Right ventricular outflow tract imaging with CT and MRI: Part 2, Function. AJR Am J Roentgenol 2013, 200(1):W51–61.

21. Pratt RC, Parisi AF, Harrington JJ, Sasahara AA: The influence of left ventricular stroke volume on aortic root motion: an echocardiographic study. Circulation 1976, 53(6):947–953.

22. Hughes CV, Wong M, Johnson G, Cohn JN: Influence of age on mechanisms and prognosis of heart failure. The V-HeFT VA Cooperative Studies Group. Circulation 1993, 87(6 Suppl):VI111–117.

23. Wang TJ, Larson MG, Levy D, Benjamin EJ, Leip EP, Omland T, Wolf PA, Vasan RS: Plasma natriuretic peptide levels and the risk of cardiovascular events and death. N Engl J Med 2004, 350(7):655–663.

24. Hamaguchi S, Kinugawa S, Tsuchihashi-Makaya M, Goto D, Yamada S, Yokoshiki H, Takeshita A, Tsutsui H: Loop diuretic use at discharge is associated with adverse outcomes in hospitalized patients with heart failure: a report from the Japanese cardiac registry of heart failure in cardiology (JCARE-CARD). Circ J 2012, 76(8):1920–1927.

25. Abhayaratna WP, Seward JB, Appleton CP, Douglas PS, Oh JK, Tajik AJ, Tsang TS: Left atrial size: physiologic determinants and clinical applications. J Am Coll Cardiol 2006, 47(12):2357–2363.

26. Dini FL, Capozza P, Donati F, Simioniuc A, Corciu A, Fontanive P, Pironi A, Di Bello V, Maralli M: Patterns of left ventricular remodeling in chronic heart failure: prevalence and prognostic implications. Am Heart J 2011, 161(6):1088–1095.

27. Darny T, Vallet C, Lairèz O, Deswarte G, Paulino A, Maisong P, Vermes E, Guereft P, Adnot S, Dubois-Randé JL, et al: Comparison of four right ventricular systolic echocardiographic parameters to predict adverse outcomes in chronic heart failure. Eur J Heart Fail 2009, 11(9):818–824.

28. Pinedo M, Villacorta E, Tapia C, Arnold R, López J, Revilla A, Gómez I, Fulquet E, San Román JA: Inter- and intra-observer variability in the echocardiographic evaluation of right ventricular function. Rev Esp Cardiol 2010, 63(7):802–809.

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