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Stress phase bandwidth as a predictor of left ventricular reverse remodeling in patients with new-onset acute decompensated heart failure with reduced ejection fraction

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Abstract

Background Stress phase bandwidth (SPBW), assessed using single-photon emission computed tomography (SPECT), is considered to be a useful indicator of left ventricular dyssynchrony. However, few reports have examined whether it can be used as an indicator for improvement of left ventricular ejection fraction (LVEF) in new-onset heart failure with reduced ejection fraction (HFrEF).

Methods and results A total of 64 patients (mean age 56 years, 39 male) who were admitted to our hospital with new-onset non-ischemic HFrEF (median LVEF 24.7%) from January 2018 to December 2022 in the SAKURA-HF registry and underwent SPECT were enrolled. The relationship between SPBW in the acute phase and LVEF improvement in the chronic phase was retrospectively investigated in the present study. LVEF improved significantly in the 36 patients (from 27.1 to 62.8%, $p<0.001$). Guideline-directed medical therapy in both groups was comparable. SPBW was significantly lower in the group with improved LVEF (median 55.5° vs. 79.0°, $p=0.010$). Logistic regression analysis revealed that SPBW was an independent predictor for LVEF improvement. Moreover, an SPBW of 71.0° was suggested as a possible cut-off value.

Conclusions SPBW may predict the improvement of LVEF in new-onset non-ischemic HFrEF, suggesting its potential utility in heart failure management.

Keywords HFrEF, HFrecEF, SPECT, Bandwidth, LV dyssynchrony, LV reverse remodeling

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Introduction

In recent years, the number of heart failure (HF) patients has been increasing along with the aging of society [1, 2]. Decompensated HF results in left ventricular (LV) enlargement and a reduction of LV contractility. It is often clinically experienced that the treatment of HF can reverse remodeling of the LV and improve cardiac function. The potential for reverse LV remodeling is particularly crucial in patients with new-onset HF with reduced LV ejection fraction (HFrEF), as the long-term prognosis can be improved by device therapy [3], and it would necessitate a change in the treatment strategy for HF therapy. While some imaging modalities, indices, and biomarkers have been implicated in LV remodeling, certainly remains elusive [4, 5].

Myocardial perfusion single-photon emission computed tomography (SPECT) is a highly reliable imaging technique supported by extensive evidence for anticipating cardiac events [6]. The stress phase bandwidth (SPBW), which is assessed using SPECT, is regarded as a valuable marker of LV dyssynchrony [7, 8]. The utilization of a LV dyssynchrony index, obtained through phase analysis using electrocardiogram (ECG)-gated SPECT, proves valuable in evaluating the severity and forecasting the prognosis of individuals with cardiac ailments [9–11]. Furthermore, this method exhibits outstanding diagnostic precision in identifying multivessel disease among patients with coronary artery disease (CAD) [12]. In a previous study, we reported that SPBW, an indicator of LV mechanical dyssynchrony, was a significant prognostic predictor independent of ischemic volume assessed by SPECT in patients with known or suspected CAD [13–19]. Nonetheless, there are limited studies investigating the potential utility of SPBW as an indicator of LV reverse remodeling in non-ischemic HFrEF patients. Therefore, we conducted a single-center prognostic study using our registry database to investigate the utility of SPBW as a prognostic modality of LV reverse remodeling in newly diagnosed HFrEF patients.

Methods

Study population

This is a retrospective sub-analysis from the SAKURA-HF registry (UMIN 000043852), which included consecutive patients with acute decompensated heart failure (ADHF) admitted to Nihon University Itabashi Hospital, Tokyo, Japan, who agreed to be followed for the collection of outcome data [20]. The diagnosis of ADHF was based on the Framingham criteria. All patients provided written informed consent. To evaluate potential prognostic factors, demographic, laboratory, and echocardiographic data were obtained at admission and after 6 months of HF treatment. HFrEF was defined as HF with LVEF of less than 40%.

We enrolled consecutive new-onset HFrEF patients between January 2018 and December 2022. A total of 354 patients were screened, but we excluded 138 who did not undergo SPECT, 64 who had ischemia heart disease, 3 who died during hospitalization, 22 whose prognosis could not be determined, 51 with non-sinus rhythm, 4 with left bundle branch block (LBBB), and 8 with pacemakers or implantable cardioverter defibrillators. As a result, we analyzed data from 64 patients (Fig. 1).

The study complied with the principles of the Declaration of Helsinki. The use of patient information was approved by the institutional review board of Nihon University Itabashi Hospital (RK-180612-2).

Echocardiography

Experienced sonographers conducted echocardiography upon admission and after 6 months of HF treatment, adhering to the guidelines set by the American Society of Echocardiography [21]. The LV end-diastolic diameter (LVDd), interventricular septum thickness (IVST), posterior wall thickness (PWT), and left atrial diameter (LAD) were measured using the parasternal long-axis view, and the LVEF was determined using the Teichholz method [22]. The LV mass index was calculated from LVDd, IVST, PWT, and body surface area (BSA) as follows: [0.8 × [1.04 × {(LVDd + IVST + PWT) ^3 - LVDd^3}] + 0.6] / BSA. LV diastolic function was assessed by calculating the ratio of early transmitral flow velocity to mitral annular velocity (E/e'), utilizing transmitral Doppler flow and tissue Doppler imaging. The long-axis diameter of the inferior vena cava (IVC) was measured from the subcostal view.

ECG-gated SPECT MPI and LV functional analysis

The rest ^{201}Tl and stress ^{99m}Tc-tetrofosmin ECG-gated SPECT myocardial perfusion imaging (MPI) was performed to rule out ischemic heart disease during ADHF admission. The SPECT procedure followed a previously documented protocol [9–13]. All patients received an intravenous (i.v.) injection of ^{201}Tl (111 MBq), and a 16-frame gated SPECT MPI was initiated 10 min after injection during rest. Subsequently, ^{99m}Tc-tetrofosmin (740 MBq) was administered via i.v. injection under stress induced by adenosine triphosphate (ATP). To prevent worsening of heart failure due to exercise, stress was applied using ATP instead of exercise. A 16-frame gated SPECT MPI acquisition was initiated 30 to 60 min after adenosine stress, with scans conducted first in the supine position and then in the prone position. No attenuation or scatter correction was applied. Continuous monitoring of a 12-lead ECG was carried out throughout the stress tests, with heart rate and blood pressure recorded at baseline and every minute for at least three minutes post-stress test.

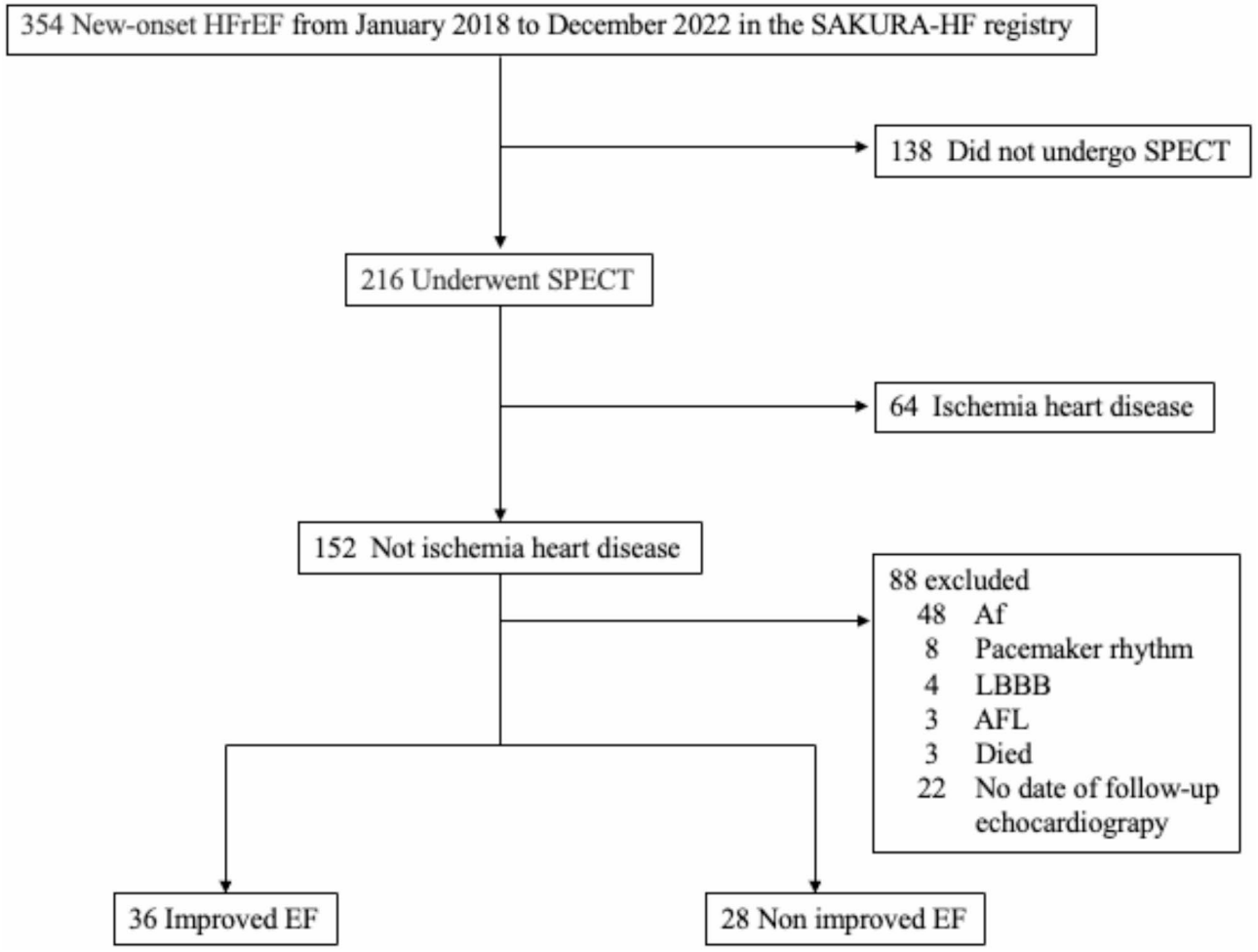

Fig. 1 Study flow diagram
HF, heart failure; HFrEF, heart failure with reduced ejection fraction; SPECT, single-photon emission computed tomography; Af, atrial fibrillation; LBBB, left bundle branch block; AFL, atrial flutter

Projection data spanning 360° were obtained using 64 × 64 matrices and a circular orbit. A triple-detector SPECT MPI system equipped with low-energy high-resolution collimators (GCA9300A; Canon Medical Systems Corp., Tokyo, Japan) was utilized. SPECT MPI scans were reconstructed from the data using a data processor (JETStream Workspace 3.0; Philips North America, Milpitas, CA, USA), incorporating a Butterworth filter for ^{201}Tl (order 5; cut-off frequency 0.42 cycles/cm), another for ^{99m}Tc (order 5; cut-off frequency 0.44 cycles/cm), and a ramp filter.

Quantitative analysis of 16-frame gated SPECT data was performed using QGS™ software (Cedars-Sinai Medical Center, Los Angeles, CA, USA) to determine the LVEF (%), left ventricular end-diastolic volume (LVEDV, mL), and left ventricular end-systolic volume (LVESV, mL) [15]. LV mechanical dyssynchrony was assessed using the phase histogram and phase map of the onset of myocardial contraction obtained through phase analysis with the Heart Risk View-F software (Nihon Medi-Physics, Tokyo, Japan) [16]. The histogram analysis yielded the standard deviation of the phase distribution (phase SD) and the 95% width of the histogram (phase bandwidth). A previous study using ^{99m}Tc-tetrofosmin (740 MBq) in patients with ischemic heart disease have reported that the bandwidth is intentionally higher at stress than at rest [17]. Therefore, the SPBW was used as the index in this study. The reason for the higher bandwidth at stress is thought to be that the reduction in blood flow in the affected area induces ventricular variability.

In this study, the normal upper limit of the phase bandwidth, assessed with ^{99m}Tc-tetrofosmin, was defined as 38° based on the mean plus 2 standard deviations (SDs) of the normal value. These normal values were derived from databases created by the working group of the Japanese Society of Nuclear Medicine [18]. The evaluation of LV mechanical dyssynchrony indices was carried out by two independent expert cardiologists who were not provided

with patient clinical information. If they disagreed, a third expert cardiologist or a radiologist was consulted.

Figure 2 shows representative phase histograms and phase map images in patients with no LV mechanical dyssynchrony (a) and severe LV mechanical dyssynchrony (b). The phase bandwidth and SD were 26.0° and 8.5 in patients without LV mechanical dyssynchrony, and 108.0° and 53.1, respectively, in patients with severe LV mechanical dyssynchrony.

Evaluations and study outcomes

We evaluated the relationship between SPBW during the acute phase and LV reverse remodeling in the chronic phase at 6 months after on-set HF, with LVEF improvement defined as recovery to 50% or greater after HF treatment.

Statistical analysis

Continuous variables were presented as the average value with the standard deviation or median with the interquartile range (IQR) as appropriate, and categorical variables were presented as the number and percentage of patients. Comparisons of continuous data were performed with Student's *t*-test or Wilcoxon's rank sum test. Categorical data were compared with the chi-squared test. Univariate and multivariate logistic regression analyses were performed to evaluate the association between SPBW in the acute phase and LVEF improvement in the chronic phase. In the multivariate logistic regression analysis, we constructed three multivariate models to adjust for etiologies of HF, including age, sex, hypertensive heart disease (HHD), and dilated cardiomyopathy (DCM), HF treatment, including age, sex, angiotensin receptor-neprilysin inhibitor (ARNi), and sodium-glucose cotransporter 2 inhibitor (SGLT2i), and Echocardiographic findings on admission, including age, sex, LV end-diastolic diameter, interventricular septum thickness, and posterior wall thickness. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. All statistical analyses were performed with the JMP Pro software program, ver. 16.1.0 (SAS Institute, Cary, USA). A p value < 0.05 was considered statistically significant.

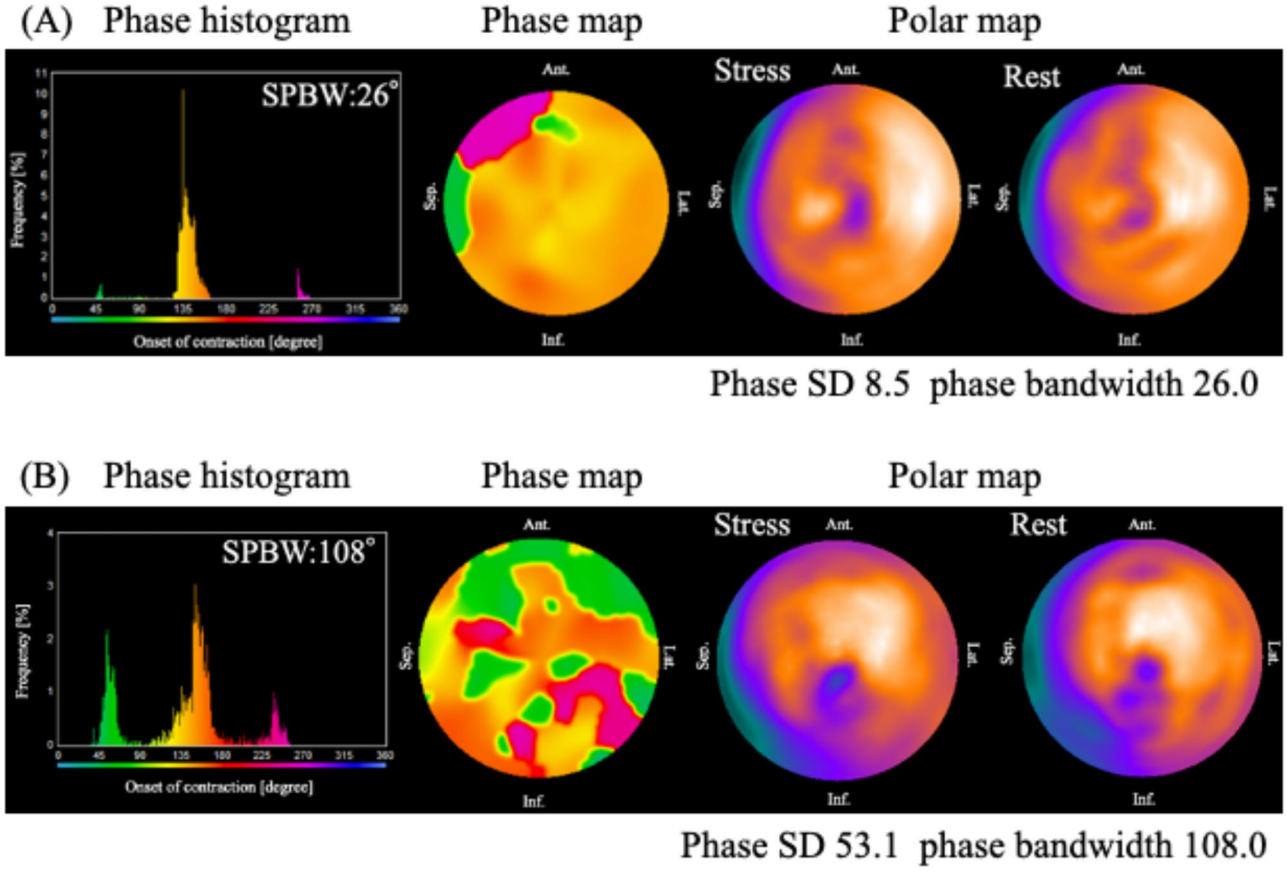

Fig. 2 Representative stress phase histograms, phase map, and polar map images of a patient without LV mechanical dyssynchrony (**A**) and a patient with severe LV mechanical dyssynchrony (**B**). Patient A had improved LVEF on echocardiography after 6 months of HF treatment. Patient B had not improved LVEF on echocardiography after 6 months of HF treatment

LV, left ventricular; LVEF, left ventricular ejection fraction; HF, heart failure; SPBW, stress phase bandwidth; SD, standard deviation

Results

Baseline characteristics

The baseline clinical characteristics of the study participants are shown in Table 1. A total of 64 patients (mean age: 56 years old, 39 males [60.9%]) who were admitted to Nihon University Itabashi Hospital with new-onset HFrEF (median LVEF at admission: 24.7 [21.1, 30.2] %) from January 2018 to December 2022 in the SAKURA-HF registry and underwent SPECT were analyzed.

After 6 months of HF treatment, LVEF improved significantly in the 36 patients (from 27.1 [22.5, 33.8] % to 62.8 [59.4, 65.7] %, $p < 0.001$). There were no significant differences in the demographic and laboratory data between the two groups. Guideline-directed medical therapy in both groups was almost comparable, but the improved EF group had a significantly higher rate of ARNi and SGLT2i administration rate at discharge than the non-improved EF group (47.2% vs. 17.9%, $p = 0.029$, 63.9% vs. 25.0%, $p = 0.005$).

Echocardiographic data at admission and after 6 months of HF treatment

The echocardiographic data is shown in Table 2. The LVEF, LV mass index, LAD, E wave velocity, E/e' ratio and maximum IVC diameter at admission did not differ between the two groups. At 6 months after HF treatment, the LVDd, LV mass index and LAD in the improved EF group were significantly smaller than those in the non-improved EF group. The mean duration from baseline to follow-up echocardiography was 218 ± 67 days.

LV functional analysis data with ECG-gated SPECT MPI of ADHF patients

The LV functional analysis with ECG-gated SPECT MPI for each group is shown in Table 3. EDV and LVEF in

Table 1 Clinical characteristics of patients stratified into two groups according to LVEF improvement

Variables	Overall ($n = 64$)	Improved EF ($n = 36$)	Non-improved EF ($n = 28$)	p value
Demographic variables at admission				
Age, year	56 ± 15	55 ± 15	58 ± 15	0.53
Male, n, (%)	39 (60.9)	22 (61.1)	17 (60.7)	1.00
Body mass index, kg/m^2	25.6 ± 4.7	26.0 ± 4.9	25.0 ± 4.5	0.39
Systolic blood pressure, mmHg	146 ± 32	151 ± 38	140 ± 19	0.18
NYHA class ≥ III, n, (%)	51 (79.7)	30 (83.3)	21 (75.0)	0.61
Laboratory variables at admission				
Hemoglobin, g/dl	13.4 ± 2.7	13.5 ± 2.6	13.4 ± 2.9	0.97
eGFR, ml/min/1.73 m^2	53.9 ± 21.5	53.8 ± 20.8	54.0 ± 22.7	0.97
CRP, mg/dl	1.2 ± 3.0	1.5 ± 3.9	0.7 ± 0.9	0.28
HbA1c, %	6.2 ± 0.7	6.3 ± 0.7	6.0 ± 0.8	0.19
Albumin, g/dl	3.7 ± 0.6	3.6 ± 0.6	3.8 ± 0.7	0.19
NT-proBNP, pg/ml	4408 (2405, 9940)	5460 (2682, 14747)	4201 (2322, 5901)	0.28
Etiology				
HHD, n, (%)	28 (43.8)	23 (63.9)	5 (17.9)	**0.001**
Valvular, n, (%)	8 (12.5)	6 (16.7)	2 (7.1)	0.45
DCM, n, (%)	18 (28.1)	5 (13.9)	13 (46.4)	**0.010**
Sarcoidosis, n, (%)	1 (1.6)	0 (0)	1 (3.6)	0.90
Carditis, n, (%)	3 (4.7)	2 (5.6)	1 (3.6)	1.00
CTRCD, n, (%)	3 (4.7)	0 (0)	3 (10.7)	0.16
Others, n, (%)	6 (9.4)	3 (8.3)	3 (10.7)	1.00
Heart failure medication at discharge				
RASi, n, (%)	56 (87.5)	34 (94.4)	22 (78.6)	0.13
ACEi, n, (%)	23 (35.9)	13 (36.1)	10 (35.7)	1.00
ARB, n, (%)	12 (18.8)	5 (13.9)	7 (25.0)	0.42
ARNi, n, (%)	22 (34.4)	17 (47.2)	5 (17.9)	**0.029**
Beta-blocker, n, (%)	59 (92.2)	34 (94.4)	25 (89.3)	0.77
MRA, n, (%)	50 (78.1)	29 (80.6)	21 (75.0)	0.82
SGLT2i, n, (%)	30 (46.9)	23 (63.9)	7 (25.0)	**0.005**

Data are expressed as mean ± SD or median (interquartile range)

Significant p values are written in bold

LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; eGFR, estimated glomerular filtration rate; CRP, C reactive protein; HbA1c, Hemoglobin A1c; NT-proBNP, N-terminal pro-brain natriuretic peptide; HHD, hypertensive heart disease; DCM, dilated cardiomyopathy; CTRCD, cancer therapeutics-related cardiac dysfunction; RASi, renin-angiotensin system inhibitor; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; MRA, mineralocorticoid receptor antagonist; SGLT2i, sodium-glucose cotransporter 2 inhibitor

Table 2 Echocardiographic data of patients stratified into two groups according to LVEF improvement

Variables	Overall (*n* = 64)	Improved EF (*n* = 36)	Non-improved EF (*n* = 28)	*p* value
At admission				
LVDd, mm	61.4 (55.6, 66.9)	59.2 (54.2, 63.0)	63.9 (59.7, 68.6)	**0.007**
IVST, mm	10.0 (8.3, 11.6)	10.6 (8.9, 11.9)	8.8 (7.8, 10.4)	**0.020**
PWT, mm	10.5 (8.7, 11.9)	11.1 (9.3, 12.7)	9.4 (7.5, 11.2)	**0.006**
LV mass index, g/m^2	152.2 (131.0, 187.1)	147.3 (121.4, 191.2)	156.4 (133.0, 183.3)	0.93
LVEF, %	24.7 (21.1, 30.2)	27.1 (22.5, 33.8)	23.5 (18.5, 29.1)	0.06
LAD, mm	43.5 (40.1, 46.1)	43.7 (40.0, 47.2)	43.1 (40.1, 45.9)	0.66
E wave velocity, m/s	86.7 (64.8, 96.7)	87.8 (64.0, 101.8)	82.1 (65.7, 93.8)	0.19
E/e' ratio	18.5 ± 7.0	18.6 ± 6.1	18.4 ± 8.0	0.91
Maximum IVC diameter, mm	16.5 (13.6, 20.1)	16.1 (13.5, 19.7)	17.7 (13.8, 22.2)	0.33
After 6 months of HF treatment.				
LVDd, mm	51.3 (45.7, 57.4)	46.5 (42.6, 52.0)	56.9 (51.7, 62.9)	**< 0.001**
IVST, mm	10.6 (8.8, 11.6)	10.7 (8.9,12.0)	10.2 (8.7, 11.0)	0.18
PWT, mm	10.4 (8.8, 11.3)	10.6 (9.2, 11.4)	10.0 (8.8, 10.8)	0.22
LV mass index, g/m^2	121.5 (99.1, 140.0)	102.7 (86.2, 126.9)	135.2 (121.9, 159.3)	**< 0.001**
LVEF, %	53.9 (38.3, 63.8)	62.8 (59.4, 65.7)	36.2 (27.3, 40.6)	**< 0.001**
LAD, mm	36.9 (32.8, 41.1)	35.6 (31.8, 38.6)	38.9 (34.3, 42.9)	**0.024**
E wave velocity, m/s	52.4 (45.5, 63.7)	53.7 (48.7, 67.1)	51.5 (43.0, 61.2)	0.22
E/e' ratio	11.8 ± 7.4	10.4 ± 4.9	13.6 ± 9.5	0.09
Maximum IVC diameter, mm	13.5 (11.7, 15.0)	13.4 (11.3, 14.4)	13.6 (12.0, 15.7)	0.28

Data are expressed as mean ± SD or median (interquartile range)

Significant *p* values are written in bold

LVEF, left ventricular ejection fraction; LVDd, left ventricular end-diastolic diameter; IVST, interventricular septum thickness; PWT, posterior wall thickness; LV, left ventricular; LAD, left atrial diameter; IVC, inferior vena cava; HF, heart failure

Table 3 LV functional analysis data with ECG-gated SPECT MPI at admission of patients stratified into two groups according to LVEF improvement

Variables	Overall (*n* = 64)	Improved EF (*n* = 36)	Non-improved EF (*n* = 28)	*p* value
Rest phase SD, °	38.9 (26.7, 46.1)	38.7 (28.4, 43.6)	39.4 (22.9, 48.6)	0.76
Rest phase bandwidth, °	108.5 (80.0, 137.3)	104.5 (84.5, 131.3)	117.0 (75.8, 140.0)	0.70
Rest LVEDV, ml	203.0 ± 71.3	186.9 ± 60.8	223.6 ± 79.3	**0.040**
Rest LVEF, %	32.8 ± 10.9	33.3 ± 11.2	32.0 ± 10.5	0.64
Stress phase SD, °	19.6 (12.5, 30.5)	16.4 (11.8, 24.6)	27.5 (15.0, 35.7)	**0.010**
Stress phase bandwidth, °	61.5 (44.8, 91.5)	55.5 (43.8, 71.0)	79.0 (49.8, 103.3)	**0.010**
Stress LVEDV, ml	200.9 ± 64.7	184.4 ± 56.7	222.1 ± 69.0	**0.020**
Stress LVEF, %	29.6 ± 9.3	31.0 ± 9.8	27.7 ± 8.4	0.17

Data are expressed as mean ± SD or median (interquartile range)

Significant *p* values are written in bold

LV, left ventricular; ECG, electrocardiogram; SPECT, single photon emission computed tomography; MPI, myocardial perfusion imaging; LVEF, left ventricular ejection fraction; SD, standard deviation; LVEDV, left ventricular end-diastolic volume

both rest and stress phase were comparable between the two groups. SPBW was significantly lower in the group with improved EF (55.5 [43.8, 71.0] ° vs. 79.0 [49.8, 103.3] °, $p = 0.010$). A receiver operating characteristic curve analysis assessed the predictive value of the SPBW in the acute phase and found that an SPBW value of 71.0° had a sensitivity of 78% and a specificity of 61% for predicting LVEF improvement (C-statistic = 0.69) (Fig. 3). Baseline characteristics stratified by the SPBW cutoff value of 71.0° showed significant differences in LVDd, and E wave velocity (Table 4). The prevalence of HHD tended to be lower in patients with SPBW ≥ 71.0° compared to those with SPBW < 71.0° (29.6% vs. 54.1%, $p = 0.091$). Similarly, LVDd was significantly greater in the SPBW ≥ 71.0° group (63.4 mm vs. 59.0 mm, $p = 0.030$), while LVEF was lower (22.9% vs. 26.6%, $p = 0.032$) and E wave velocity was also lower (73.0 m/s vs. 87.4 m/s, $p = 0.020$). In addition, the positive predictive value (PPV) and negative predictive value (NPV) for SPBW ≥ 71.0° were 62.2% and 68.0%, respectively.

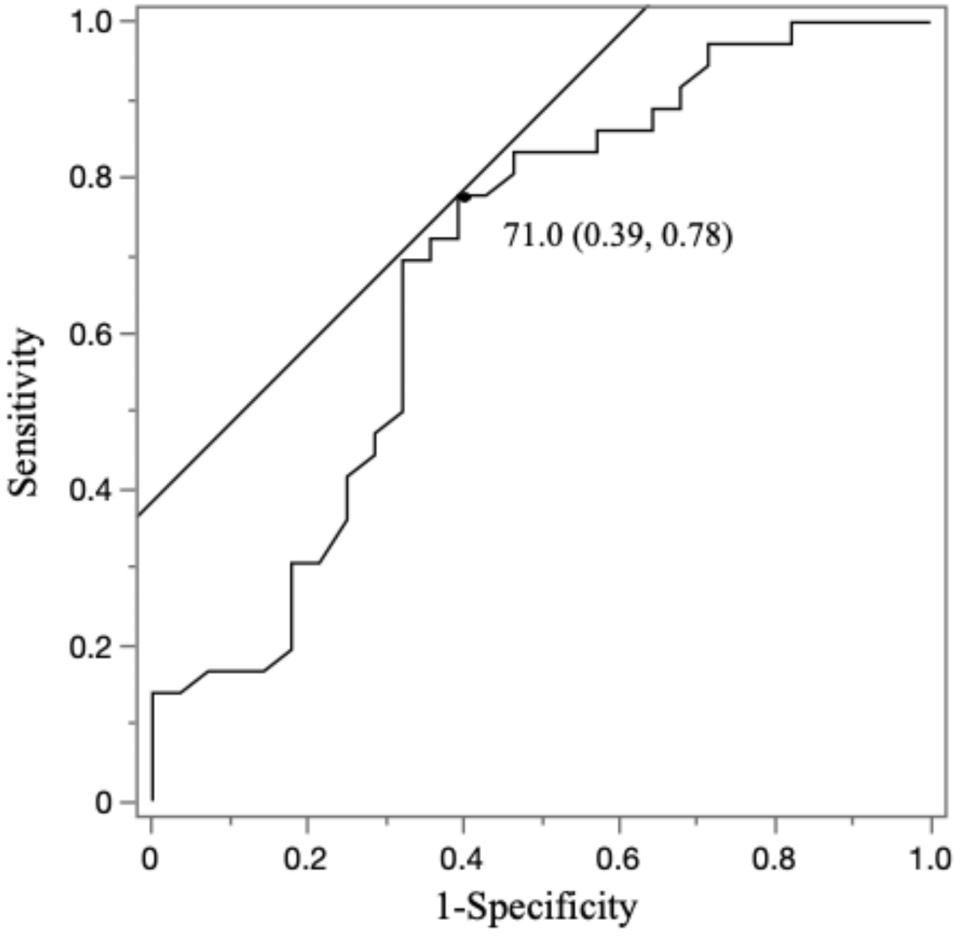

Fig. 3 ROC curve analysis for SPBW showed a favorable predictive value (C-statistic = 0.69) for improved LVEF. The optimal cutoff value was determined to be 71.0 degrees, resulting in a sensitivity of 78% and specificity of 61%
ROC curve, receiver operating characteristic curve; SPBW, stress phase bandwidth; C-statistic, concordant statistic; LVEF, left ventricular ejection fraction

Univariate and multivariate analyses to identify factors associated with LVEF improvement

Logistic regression analysis revealed the SPBW was an independent predictor for LVEF improvement. Univariate logistic regression showed that LVEF improvement was significantly associated with HHD ($p < 0.001$), DCM ($p = 0.006$), ARNi ($p = 0.018$) and SGLT2i administration ($p = 0.003$), LVDd ($p = 0.008$), IVST ($p = 0.024$), PWT ($p = 0.007$), and LVEF ($p = 0.042$) on echocardiography at admission, rest LVEDV ($p = 0.049$), stress phase SD ($p = 0.010$), SPBW ($p = 0.005$), stress LVEDV on ECG-gated SPECT MPI ($p = 0.027$) (Table 5). Multivariate analysis demonstrated that SPBW remained an independent predictor for LVEF improvement, even after adjusting for the etiologies of HF [Model 1 (HHD and DCM): OR 0.97 (0.95–0.99), $p = 0.016$], HF treatment [Model 2 (ARNi and SGLT2i): OR 0.96 (0.93–0.98), $p = 0.003$], and echocardiographic findings on admission [Model 3 (IVST and PWT): OR 0.97 (0.95–0.99), $p = 0.013$; Model 4 (LVDd): OR 0.98 (0.95-1.00), $p = 0.047$] (Table 6).

Discussion

This study is the first to demonstrate the utility of SPBW, an index of LV mechanical dyssynchrony assessed by ECG-gated SPECT MPI, in predicting LVEF improvement in patients with new-onset and non-ischemic HFrEF. The main findings of this study are summarized as follows: in patients with new-onset and non-ischemic HFrEF, those with a lower SPBW at admission exhibited significantly greater improvement in LVEF and LV enlargement on echocardiography at 6 months after ADHF treatment. In addition to well-established predictive indices of LVEF improvement, such as female sex, diabetes mellitus, left atrial volume, and others [23–25], SPBW has also been identified as a valuable predictor.

A previous study has documented that in patients with non-ischemic cardiomyopathy (NICM), EF 35–50%, and QRS < 150 ms, increased SPBW was an independent predictor of all-cause mortality [10]. SPBW serves as a visualization of dyssynchrony, reflecting cardiac reserve capacity. Previous studies have demonstrated that SPBW is wider in obese or diabetic patients without a history of

Table 4 Clinical differences between patients stratified into two groups by SPBW

Variables	SPBW < 71 (*n* = 37)	SPBW ≥ 71 (*n* = 27)	*p* value
Age, years	53.5 ± 14.4	60.3 ± 14.7	0.07
Male, n (%)	20 (54.1)	19 (70.4)	0.29
BMI, kg/m^2	26.2 ± 4.7	24.8 ± 4.7	0.26
sBP, mmHg	147.6 ± 36.3	144.1 ± 24.1	0.67
NYHA ≥ III, n (%)	30 (81.1)	21 (77.8)	0.99
NT-proBNP, pg/ml	4402 (1947, 9566)	4413 (2698, 14875)	0.36
HHD, n (%)	20 (54.1)	8 (29.6)	0.09
DCM, n (%)	8 (21.6)	10 (37.0)	0.28
RASi, n (%)	31 (83.8)	25 (92.6)	0.50
Beta-blockers, n (%)	32 (86.5)	27 (100)	0.13
MRA, n (%)	28 (75.7)	22 (81.5)	0.80
SGLT2i, n (%)	19 (51.4)	11 (40.7)	0.56
LVDd, mm	59.0 (54.8, 63.4)	63.4 (60.0, 68.3)	**0.030**
IVST, mm	10.3 (8.6, 11.7)	9.0 (8.0, 11.1)	0.28
PWT, mm	10.9 (8.8, 12.6)	9.7 (8.0, 11.5)	0.17
LVMI, g/m^2	141.8 (129.3, 190.1)	166.4 (139.9, 185.5)	0.19
LVEF, %	26.6 (23.1, 32.0)	25.0 (19.4, 30.5)	**0.032**
LAD, mm	43.5 (41.3, 46.0)	43.4 (39.4, 46.5)	0.98
E wave velocity, m/s	87.4 (79.0, 103.8)	73.0 (54.2, 93.1)	**0.020**
E/e' ratio	18.1 ± 7.5	19.9 ± 6.4	0.60
Maximum IVC, mm	15.1 (12.7, 19.6)	17.5 (14.5, 22.3)	0.13

Data are expressed as mean ± SD or median (interquartile range)

Significant *p* values are written in bold

BMI, body mass index; sBP, systolic blood pressure; NYHA, New York Heart Association; NT-proBNP, N-terminal pro-brain natriuretic peptide; HHD, hypertensive heart disease; DCM, dialated cardiomyopathy; RASi, renin-angiotensin system inhibitor, MRA, mineralocorticoid receptor antagonist; SGLT2i, sodium-glucose cotransporter 2 inhibitor; LVDd, left ventricular end-diastolic diameter; IVST, interventricular septum thickness; PWT, posterior wall thickness; LVMI, left ventricular mass index; LVEF, left ventricular ejection fraction; IVC, inferior vena cava diameter

or suspected ischemic heart disease and normal cardiac function than in non-obese or non-diabetic patients [16, 18, 19]. Even in chronic kidney disease (CKD) patients or dialysis patients with normal cardiac function, the incidence of subsequent events is significantly lower when the bandwidth is narrower [26, 27]. Therefore, SPBW is recognized as a marker for the early assessment of myocardial damage. Our study further revealed that HFrEF with pronounced myocardial damage and reduced cardiac reserve is characterized by a wider SPBW.

An important finding of this study is that the use of SPBW can predict LV reverse remodeling in patients with new-onset and non-ischemic HFrEF. HFrEF is a global concern and growing public health issue [1, 2]. Improvement in LVEF is associated with improved health status and lower risk of future clinical events, making LVEF improvement an important therapeutic target for medical interventions in HFrEF patients [28–33]. Our results regarding the role of SPBW could influence the management of patients with new-onset and non-ischemic HFrEF. For example, we believe that patients with high SPBW should be treated more rigorously from the time of admission. Advanced HF treatments, such as cardiac resynchronization therapy, should be considered in cases with high SPBW, in addition to HF drug therapy. In contrast, a low SPBW may help avoid unnecessary implantable cardioverter-defibrillator (ICD) implantation. Guidelines recommend the use of a WCD for 3 months after HF onset in NICM patients with EF ≤ 35% and no history of fatal arrhythmia. This allows for LVEF improvement assessment with therapy to determine ICD need for primary prevention of sudden cardiac death at 3 months [34, 35]. LVEF may continue to improve beyond 3 months after HF therapy initiation, so ICD indication should be reconsidered, potentially avoiding ICD in some patients [36]. The evaluation of ICD therapy in the management of HF requires a careful and nuanced approach to patient selection, particularly in the elderly population. It is important to consider the utility of multiple prognostic scores to identify patients who may derive limited benefit from ICD therapy and who could be effectively managed with guideline-directed medical therapy (GDMT) alone. A previous study revealed that the MADIT-II score provided superior predictive value for one-year and long-term all-cause mortality in patients aged 75 years and older [37]. The higher sensitivity and specificity of the MADIT-II score make it a valuable tool for identifying patients who may not require ICD implantation, consistent with the goal of minimizing the risk of inappropriate shocks and other complications associated with device therapy. These findings support a more personalized approach to the management of elderly HF

Table 5 Univariate logistic regression analyses of factors associated with LVEF improvement

Variables	Univariate analysis		
	Odds ratio	**95% CI**	***p* value**
Demographic variables at admission			
Age	0.99	0.96–1.02	0.52
Male	1.02	0.37–2.80	0.97
Body mass index	1.05	0.94–1.17	0.39
Systolic blood pressure	1.01	1.00-1.03	0.19
NYHA class ≥ III	1.67	0.49–5.87	0.41
Laboratory variables at admission			
Hemoglobin	1.00	0.83–1.21	0.96
eGFR	1.00	0.98–1.02	0.97
HbA1c	1.64	0.80–3.60	0.19
NT-proBNP	1.13	0.77–1.70	0.54
Etiology			
HHD	8.14	2.65–29.11	**< 0.001**
Valvular	2.60	0.54–18.81	0.27
DCM	0.19	0.05–0.59	**0.006**
Carditis	1.59	0.14–35.25	0.71
Heart failure medication at discharge			
RASi	4.64	0.97–33.64	0.07
ACEi	1.02	0.36–2.89	0.97
ARB	0.48	0.13–1.72	0.26
ARNi	4.12	1.35–14.44	**0.018**
Beta-blocker	2.04	0.32–16.37	0.45
MRA	1.38	0.41–4.62	0.60
SGLT2i	5.31	1.85–16.74	**0.003**
Echocardiographic variables at admission			
LVDd	0.90	0.83–0.97	**0.008**
IVST	1.33	1.05–1.74	**0.024**
PWT	1.41	1.11–1.84	**0.007**
LV mass index	1.00	0.99–1.01	0.85
LVEF	1.08	1.00-1.17	**0.042**
LAD	0.99	0.90–1.08	0.79
E wave velocity	1.02	1.00-1.04	0.10
E/e' ratio	1.00	0.93–1.08	0.91
Maximum IVC diameter	0.94	0.84–1.04	0.25
SPECT MPI variables at admission			
Rest phase SD	0.99	0.96–1.02	0.51
Rest phase bandwidth	1.00	0.98–1.01	0.64
Rest LVEDV	0.99	0.98-1.00	**0.049**
Rest LVEF	1.01	0.97–1.06	0.63
Stress phase SD	0.94	0.89–0.98	**0.010**
Stress phase bandwidth	0.97	0.95–0.99	**0.005**
Stress LVEDV	0.99	0.98-1.00	**0.027**
Stress LVEF	1.04	0.99–1.10	0.17

Significant *p* values are written in bold

LVEF, left ventricular ejection fraction; CI confidence interval; NYHA, New York Heart Association; eGFR, estimated glomerular filtration rate; HbA1c, Haemoglobin A1c; NT-proBNP, N-terminal pro-brain natriuretic peptide; HHD, hypertensive heart disease; DCM, diastolic cardiomyopathy; CTRCD, cancer therapeutics-related cardiac dysfunction; RASi, renin-angiotensin system inhibitor; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; MRA, mineralocorticoid receptor antagonist; SGLT2i, sodium-glucose cotransporter 2 inhibitor; LVDd, left ventricular end-diastolic diameter; IVST, interventricular septum thickness; PWT, posterior wall thickness; LV, left ventricular; LAD, left atrial dimension; IVC, inferior vena cava; SPECT, single photon emission computed tomography; MPI, myocardial perfusion imaging; SD, standard deviation; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume

Table 6 Multivariate logistic regression analyses for association between SPBW and LVEF improvement

	SPBW		
	Odds ratio	**95% CI**	***p* value**
Model 1	0.97	0.95–0.99	**0.016**
Model 2	0.96	0.93–0.98	**0.003**
Model 3	0.97	0.95–0.99	**0.013**
Model 4	0.98	0.95-1.00	**0.047**

Significant *p* values are written in bold

Model 1: Age, sex, HHD, DCM, SPBW

Model 2: Age, sex, ARNi, SGLT2i, SPBW

Model 3: Age, sex, IVST, PWT, SPBW

Model 4: Age, sex, LVDd, SPBW

CI, confidence interval; SPBW, stress phase bandwidth; LVEF, left ventricular ejection fraction; HHD, hypertensive heart disease; DCM, diastolic cardiomyopathy; ARNi, angiotensin receptor-neprilysin inhibitor; SGLT2i, sodium-glucose cotransporter 2 inhibitor; IVST, interventricular septum thickness; PWT, posterior wall thickness; LVDd, left ventricular end-diastolic diameter

patients, where the integration of prognostic scores can improve clinical decision making and patient outcomes. The use of these scores helps to stratify patients based on their risk profile, optimizing therapeutic strategies and potentially avoiding unnecessary interventions in those less likely to experience life-threatening arrhythmic events. Therefore, a normal bandwidth may be useful in predicting further improvement in cardiac function, potentially allowing timely avoidance of ICD implantation in patients with an LVEF ≤ 35% at 3 months. Such careful management based on SPBW assessment is likely to be beneficial in new-onset and non-ischemic HFrEF patients.

Chronic inflammatory response and nutritional status significantly influence long-term outcomes in patients with HFrEF. The C-reactive protein-to-albumin ratio (CAR) study highlighted the importance of the chronic inflammatory response in HFrEF patients. An elevated CAR, reflecting both increased inflammation and poor nutritional status, is associated with higher long-term mortality rates in HFrEF patients with ICDs [38]. Chronic inflammation, as evidenced by elevated C-reactive protein levels, may exacerbate HF by promoting further myocardial injury and LV remodeling. In addition, hypoalbuminemia, indicative of malnutrition and systemic inflammation, contributes to adverse outcomes by reducing the body's capacity to manage physiological stress and repair tissues. On the other hand, the prognostic nutritional index (PNI), derived from serum albumin levels and total lymphocyte count, serves as a robust predictor of long-term mortality in HFrEF patients. The study on PNI demonstrated that lower PNI values were significantly associated with increased mortality in this patient population [39]. Malnutrition, as reflected by low PNI, compromises the immune response and overall health, making patients more susceptible to complications and reducing their ability to recover from cardiac events. The findings suggest that assessing nutritional status using PNI may help identify patients at higher risk of adverse outcomes, allowing for early nutritional and therapeutic interventions. Both CAR and PNI are critical for risk stratification and tailored management in HFrEF. High CAR and low PNI are associated with increased mortality, highlighting the need for integrated approaches that address both inflammation and nutrition. Managing inflammation and improving nutritional status could improve patient outcomes by reducing mortality and improving quality of life. Thus, incorporating these markers into routine clinical practice may aid in the early identification of high-risk patients, allowing for more personalized and effective interventions.

This observational study has several limitations. First, the present study was a retrospective, single-center investigation with a relatively small sample size. Second, the study found no significant differences in baseline characteristics, such as some etiologies and the rate of SGLT2i administration, between patients with improved LVEF and those without. Differences in etiology did not have a significant statistical impact due to the small population size. While there was a significant difference in the SGLT2i administration rate between the two groups, when combined with SPBW in a multivariate analysis, the difference remained significant for SPBW. Additionally, SGLT2i should be administered regardless of SPBW values, as there is also a report suggesting that SGLT2i improves LVEF [40]. Third, there were multiple exclusion criteria and dropouts in this study. It was necessary to exclude patients with atrial fibrillation (Af), atrial flutter (AFL), pacemaker rhythm, or LBBB. In patients with Af or AFL, accurate recording of accumulation counts is challenging, and in patients with a pacemaker rhythm, SPBW tends to be wider than in others. Moreover, it has been demonstrated that assessing dyssynchrony in the bandwidth and considering PMI improves the prognosis for LBBB [41–43]. Furthermore, echocardiography performed at admission showed significant differences in LVEF between the two groups. However, the numerical difference was small, and the measurement of LVEF may vary to somewhat between technologists. LVEF measured by SPECT, which is a machine-based measurement with high accuracy and reproducibility, showed no difference between the two groups.

Conclusions

SPBW reflects the synchrony of LV contraction, with a lower SPBW indicating preserved cardiac reserve. Thus, out study demonstrated that SPBW may serve as an indicator for LV reverse remodeling in new-onset non-ischemic HFrEF patients, suggesting its potential utility in HF management. Further validation studies are expected to

perform to evaluate the clinical usefulness of the SPBW in managing HFrEF patients.

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Author contributions
YT and DK conceived and designed the study. YT, SM, HF, and KF acquired data. SY, TH, and YS interpreted clinical findings. YT and DK drafted the manuscript. KT and OY supervised the conceptualization and review process of the manuscript. All the authors have read and approved the final version of the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
All procedures were performed according to the ethical standards of the institutional research committee, as well as the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study and its protocols were approved on October 1, 2019, by the Nihon University Itabashi Hospital, Clinical Research Judging Committee (RK-191008-4).

Consent for publication
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Competing interests
The authors declare no competing interests.

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