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ORIGINAL RESEARCH

HEART FAILURE AND CARDIOMYOPATHIES

Novel Pulse Waveform Index by Ambulatory Blood Pressure Monitoring and Cardiac Function

A Pilot Study

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ABSTRACT

BACKGROUND A simple ambulatory measure of cardiac function could be helpful for monitoring heart failure patients.

OBJECTIVES The purpose of this paper was to determine whether a novel pulse waveform analysis using data obtained by our developed multisensor-ambulatory blood pressure monitoring (ABPM) device, the 'Sf/Am' ratio, is associated with echocardiographic left ventricular ejection fraction (LVEF).

METHODS Multisensor-ABPM was conducted twice at baseline in 20 heart failure (HF) patients with HF-reduced LVEF or HF-preserved LVEF (median age 66 years, male 65%) and over a 6- to 12-month follow-up after patient-tailored treatment. We assessed the changes in the pulse waveform index Sf/Am and LVEF that occurred between the baseline and follow-up. The Sf/Am consists of the area of the ejection part in the square forward wave (Sf) and the amplitude of the measured wave (Am). We divided the patients into the recovered (n = 11) and not-recovered (n = 9) groups defined by a ≥10% increase in LVEF.

RESULTS Although the ambulatory BP levels and variabilities did not change in either group, the Sf/Am increased significantly in the recovered group (baseline 21.4 ± 4.5; follow-up, 25.6 ± 3.7, $P = 0.004$). The not-recovered group showed no difference between the baseline and follow-up. The follow-up/baseline Sf/Am ratio was significantly associated with the LVEF ratio ($r = 0.469$, $P = 0.037$). The Sf/Am was significantly correlated with the LVEF in overall measurements (n = 40, $r = 0.491$, $P = 0.001$).

CONCLUSIONS These results demonstrated that a novel noninvasive pulse waveform index, the Sf/Am measured by multisensor-ABPM is associated with LVEF. The Sf/Am may be useful for estimating cardiac function.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

Af = amplitude forward pulse wave

Am = amplitude measure pulse wave

ABPM = ambulatory blood pressure monitoring

BP = blood pressure

HF = heart failure

HFrecEF = heart failure with recovered ejection fraction

LVEF = left ventricular ejection fraction

SBP = systolic blood pressure

Sf = square forward pulse wave

Sr = square reflected pulse wave

The recovery of left ventricular function is one of the important goals of therapy for patients with heart failure (HF). Recent international guidelines have defined HF with a recovered ejection fraction (HFrecEF) and noted that HFrecEF is generally associated with a better clinical outcome.[1-3] Although international guidelines recommend examinations by echocardiography and catheterization for the evaluation of cardiac function,[1,2] these are highly specialized examinations in clinical practice, and there have been several studies of methods to estimate cardiac function using the blood pressure (BP) pulse wave instead.[4-11] Although the association between the BP pulse waveform index and cardiac function in patients with HF has been investigated, the majority of those investigations used an invasive method to evaluate the BP pulse waveform or were conducted in a laboratory setting.[7,10,12-14] There are few data about the association between the BP pulse waveform and cardiac function in HF patients in an ambulatory setting. The findings regarding changes in the BP pulse waveform index in patients with HFrecEF are also limited.

The improvement of cardiac systolic function leads to increased stroke volume, which results in increased average BP levels, BP variability (BPV), and pulse pressure as a hemodynamic change.[15-19] In practice, however, BP levels are well controlled by the adjustment of antihypertensive and cardioprotective medications. In the management of HF, it is difficult to detect the changes in cardiac function by using only occasional BP measurements, which may be due in part to BP assessments obtained in a limited clinical setting. Ambulatory BP monitoring (ABPM) is an informative tool that can obtain not only clinically reliable and accurate BP readings compared to office BP in an ambulatory setting; ABPM can also be used to evaluate various aspects of BP variability. Compared to office BP, ABPM is a superior predictor of cardiovascular outcomes and can detect masked hypertension and short-term 24-hour BP variability.[20-23]

We recently developed a cuff-oscillometric multisensor-ABPM device that can obtain the cuff volumetric pulse waveform from the diastolic phase of each BP measurement.[18,19,24,25] Using the pulse waveform obtained by the multisensor-ABPM device, we calculated a novel pulse waveform index, the Sf/Am ratio, which indicates cardiac systolic function. In the present study, we prospectively assessed the associations between a number of BP parameters and the pulse waveform index Sf/Am measured by the multisensor-ABPM device and the echocardiographic cardiac function in patients with or without recovered ejection function during the treatment of their HF.

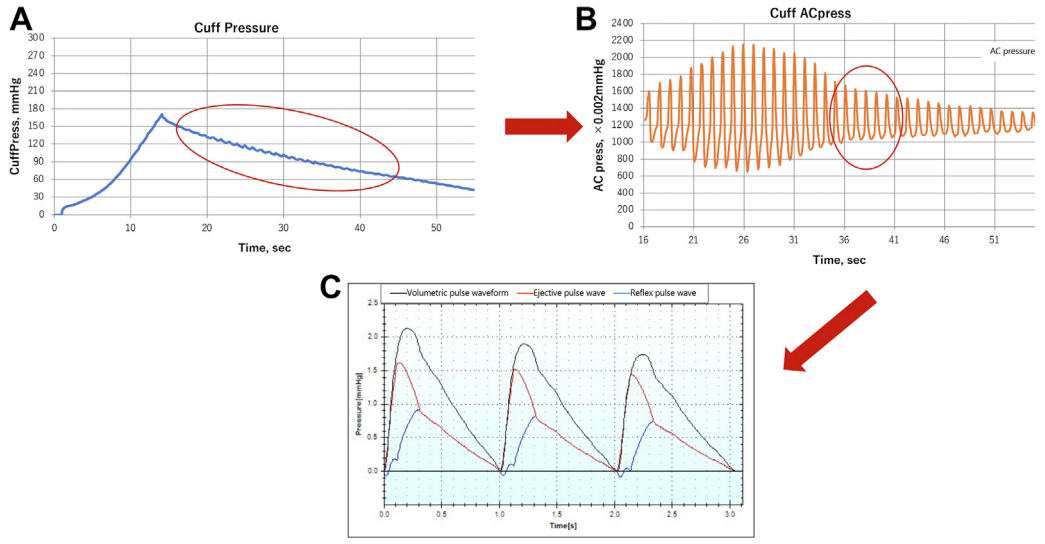
PATIENTS AND METHODS

STUDY DESIGN. This study was approved by the Institutional Review Board of the Jichi Medical University School of Medicine, and informed consent was obtained from all participants. We assessed the Sf/Am obtained by multisensor-ABPM measurements in 20 patients with HF after the patients' initial or adjusted treatments, and the multisensor-ABPM was applied again at a follow-up visit at 6 to 12 months after the completion of each patient's tailored treatment (Supplemental Figure 1). All examinations including multisensor-ABPM, echocardiography, and serum laboratory tests such as that for B-type natriuretic peptide (BNP) were conducted while the patients were in stable condition, ie, all patients could walk alone and were without oxygen administration. Patients were recruited in hospitalization or as outpatients. At baseline, most of the enrolled patients (18 of the total 20 patients) were hospitalized for an exacerbation of the HF, and ABPM was performed just prior to their discharge after the initial treatment. At follow-up, ABPM was performed after 6 to 12 months of outpatient drug adjustment.

We divided these patients into those whose left ventricular ejection fraction (LVEF) recovered with treatment ($n = 11$) and those whose LVEF did not recover ($n = 9$); a ≥10% increase in the LVEF was used as the cutoff.[26] We then compared the changes in the Sf/Am between the 2 groups. Echocardiography was conducted within 30 days before and after the multisensor-ABPM measurements and was performed by 2 trained sonographers using either of 2 ultrasound machines (iE33, Philips; Xario XG, Toshiba). Each patient's LVEF was calculated using 2-dimensional echocardiography findings from apical 2-chamber and 4-chamber views and the biplane methods of disks with reference to the guidelines issued by the American Society of Echocardiography and the European Association of Cardiovascular Imaging.[27] The LVEF was measured by one trained sonographer and confirmed by the other, blinded sonographer.

MULTISENSOR-ABPM. ABPM was measured automatically at 30-minute intervals for 24 hours using an oscillometric method by the multisensor-ABPM device (TM-2441, A&D Co).[25] Nighttime was defined as the period from the patient's bedtime to waking as assessed from the patient's diary. The ABPM measurements were performed according to the Japanese

FIGURE 1 **Multisensor-Ambulatory Blood Pressure Monitoring Device**



(A) Changes in cuff pulse pressure at the BP measurements (from occlusion of the brachial artery, ie, adding cuff pressure, to release, ie, release of the cuff pressure). (B) The extraction of the cuff-pressure changes due to brachial artery pulse oscillation. (C) Diastolic extraction pulse wave analysis (separation of the ejection pulse and reflex pulse). BP = blood pressure.

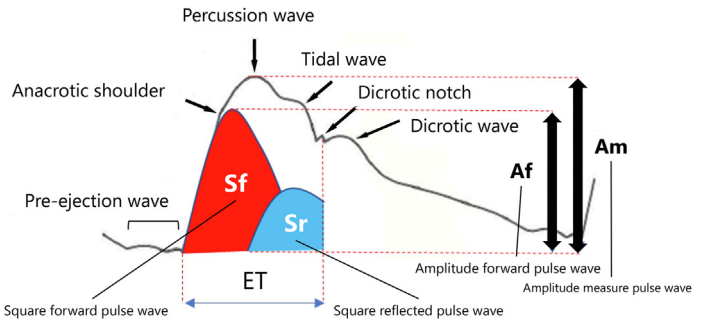
Circulation Society guidelines.[28] Regarding ambulatory BPV, we determined the SD, coefficient of variation, average real variability, and weighted SD for analysis.[22,29] The patients' physical activity was measured by a high-sensitive actigraph (accelerometer) incorporated in the multisensor-ABPM that detects the wearer's fine-scale physical movements in 3 directions. The 5-minute average values of physical activity (G) just before the BP measurements were used for the present analyses.[24,25]

PULSE-WAVEFORM ANALYSIS FOR THE CALCULATION OF SF/AM. We obtained the cuff volumetric pulse waveform from the diastolic phase of each BP measurement taken by the multisensor-ABPM device (**Figure 1**). Three stable pulse waves during the diastolic phase of each BP measurement were assessed for the pulse-waveform analysis, and their average values were calculated as the Sf/Am value. An inhibition of the blood flow causes a phase difference between the measured pulse wave (ie, the cuff volumetric pulse waveform) and the blood flow wave, and we therefore extracted the pulse waveform from the point of intravascular pressure that was less than or equal to the cuff pressure (ie, the cuff pressure after the point at which diastolic BP was measured) where the blood flow is not inhibited, taking into account the analysis error caused by the phase difference.

Pulse waves are composed of forward and backward traveling waves, corresponding to components originating from cardiac ejection (the ejection wave component) and peripheral resistance (the reflected wave component), respectively.[30,31] Several attempts have been made to separate ejection-wave and reflected-wave components.[30-33] With reference to those studies, we also attempted to separate ejection-wave and reflected-wave components in the present study by using the volumetric pulse waveform acquired during the BP measurements.[32] We extracted the pulsation component in the cuff pressure data collected by the multisensor-ABPM as the cuff volumetric pulse waveform by using a newly developed pulse wave recognition algorithm. The details of the methods used for the pulse-waveform analysis are provided in the Supplemental Figures 2 to 4 and the Supplemental Appendix.

Figure 2 shows the component of the pulse waveform obtained by the multisensor-ABPM, with which we calculated the novel pulse waveform index Sf/Am. The area of the ejection part is the square forward pulse wave (Sf), and the amplitude measured by the pulse waveform (Am) is a parameter representing artery properties and cuff compliance. The brachial cuff volume pulse wave is generated when blood is ejected from the cardiac outflow through the blood vessels and then

FIGURE 2 Methods for Obtaining the Cuff Volumetric Pulse Waveform by BP Measurements Using the Multisensor-ABPM Device



Sf: the ejection area in which the brachial cuff volume pulse wave is separated into the ejection and reflection parts, ie, the parameters that are used to evaluate the cardiac ejection fraction. Am: the actual measured amplitude of the brachial cuff volume pulse wave, a parameter defined by the central arterial compliance, peripheral arterial properties, and cuff compliance (wearing-state cuff sensitivity) at that time. Ejection time (ET): the time from the pulse wave's rise point to the cut scar. Af = amplitude forward pulse wave; Am = amplitude measure pulse wave; Sf = square forward pulse wave; Sr = square reflected pulse wave.

oscillates with the cuff volume, and it is interpreted as a parameter expressing the cardiac ejection. At the same time, the pulse wave includes the effects of central arterial compliance, the nature of the obliterating artery, and cuff compliance. This pulse waveform is divided into the ejection wave and the reflex wave.

Regarding the Sf, only the cardiac ejection area was isolated from the early volume pulse wave, and its area was parameterized. The value of Am was interpreted as a parameter that includes the cuff compliance along with the ejection area and the reflection area characterized as the peripheral arteries' compliance. The Sf was then divided by the Am, ie, Sf/Am, to eliminate the effect of arterial and cuff compliance from the area of the ejection wave, and we thus hypothesize that the Sf/Am value indicates cardiac systolic function.

STATISTICAL ANALYSES. The resulting data are presented as the mean ± SD for the continuous variables or as percentages for the categorical variables.

TABLE 1 The Baseline Characteristics of the Patients With Heart Failure

	All Patients (N = 20)	Recovered LVEF (n = 11)	Not Recovered LVEF (n = 9)	*P* Value
Age, y	63.3 ± 14.1	55.1 ± 13.2	73.2 ± 6.9	0.002
Male	13 (65.0)	9 (81.8)	4 (44.4)	0.081
BMI, kg/m^2	27.0 ± 7.3	28.2 ± 9.1	25.6 ± 4.4	0.446
NYHA CHF class III/IV	6 (30.0)	3 (27.3)	3 (33.3)	0.769
Coronary artery disease	3 (15.0)	1 (9.1)	2 (22.2)	0.413
Atrial fibrillation	5 (25.0)	2 (18.2)	3 (33.3)	0.436
Prehistory of stroke	1 (5.0)	1 (9.1)	0 (0)	0.353
Diabetes	5 (25.0)	3 (27.3)	2 (22.2)	0.795
Dyslipidemia	13 (65.0)	7 (63.6)	6 (66.7)	0.888
Medications				
ACE-I	5 (25.0)	4 (36.4)	1 (11.1)	0.194
ARB	10 (50.0)	5 (45.5)	5 (55.6)	0.653
Calcium-channel blocker	7 (35.0)	4 (36.4)	3 (33.3)	0.888
β-blocker	16 (80.0)	9 (81.8)	7 (77.8)	0.822
α-blocker	1 (5.0)	0 (0)	1 (11.1)	0.257
Thiazide diuretics	3 (15.0)	1 (9.1)	2 (22.2)	0.413
MRA	7 (35.0)	4 (36.4)	3 (33.3)	0.888
Loop diuretics	20 (100.0)	11 (100.0)	9 (100.0)	-
No. of medications[a]	3.5 ± 1.0	3.5 ± 0.8	3.4 ± 1.2	0.983
Antiplatelet therapy	5 (25.0)	2 (18.2)	3 (33.3)	0.436
Office BP				
SBP	119.2 ± 18.6	115.2 ± 22.5	124.0 ± 11.8	0.304
DBP	75.1 ± 17.2	77.9 ± 22.0	71.7 ± 8.4	0.442
PR	78.6 ± 17.8	86.3 ± 16.4	69.2 ± 15.5	0.027
LVEF, %	34.8 ± 11.5	29.8 ± 7.2	40.8 ± 13.3	0.046
LVMI	137.2 ± 34.4	128.1 ± 22.3	148.4 ± 44.1	0.234
BNP in stable condition (log-transformed BNP), pg/mL	149.0 ± 117.8 (2.0 ± 0.4)	156.7 ± 145.6 (2.0 ± 0.5)	139.4 ± 79.4 (2.1 ± 0.3)	0.688

Values are mean ± SD or n (%). Demographic variables and clinical and behavioral characteristics were assessed by t-test (for continuous data) and chi-square-test (for categorical data). [a]The number of antihypertensive medications was defined as the number of classes of medications as follows: ACE-I, ARB, calcium-channel blocker, β-blocker, α-blocker, thiazide diuretics, MRA, and loop diuretics.

ACE-I = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; BMI = body mass index; BNP = B-type natriuretic peptide; BP = blood pressure; CHF = congestive heart failure; DBP = diastolic BP; LVEF = left ventricular ejection fraction; LVMI = left ventricular mass index; MRA = mineralocorticoid receptor antagonist; PR = pulse rate; SBP = systolic blood pressure.

TABLE 2 Ambulatory Blood Pressure Parameters of the 20 Patients With HF, at Baseline and Follow-Up

	Baseline				Follow-Up			
	All Patients	Recovered LVEF (n = 11)	Not Recovered LVEF (n = 9)	*P* Value	Recovered LVEF (n = 11)	*P* Value[a]	Not Recovered LVEF (n = 9)	*P* Value[a]
24-h SBP	113.8 ± 17.0	115.5 ± 22.1	111.6 ± 8.3	0.623	113.7 ± 21.7	0.606	116.1 ± 14.4	0.341
DBP	74.6 ± 13.8	79.4 ± 16.4	68.8 ± 6.8	0.087	74.9 ± 13.0	0.040	71.6 ± 8.9	0.400
PR	71.5 ± 11.0	74.2 ± 10.9	68.2 ± 10.9	0.235	67.9 ± 6.3	0.130	66.6 ± 10.0	0.644
PP	39.2 ± 9.2	36.1 ± 8.1	42.8 ± 9.7	0.117	38.8 ± 10.6	0.339	44.5 ± 11.6	0.545
Daytime SBP	115.4 ± 17.2	116.5 ± 22.8	114.1 ± 7.4	0.764	117.4 ± 22.1	0.749	118.7 ± 11.9	0.306
DBP	75.3 ± 13.9	79.7 ± 16.4	69.9 ± 11.1	0.118	77.2 ± 13.9	0.222	73.7 ± 10.2	0.317
PR	72.5 ± 13.9	74.9 ± 11.2	69.6 ± 11.1	0.303	70.0 ± 6.4	0.233	68.6 ± 12.1	0.811
PP	40.1 ± 9.3	36.7 ± 8.6	44.2 ± 8.9	0.075	40.3 ± 11.7	0.207	45.1 ± 8.3	0.702
Nighttime SBP	109.7 ± 17.8	112.6 ± 21.6	106.1 ± 11.8	0.401	105.9 ± 20.8	0.272	112.1 ± 19.6	0.273
DBP	73.2 ± 14.4	78.8 ± 16.9	66.5 ± 6.5	0.054	69.6 ± 12.5	0.031	68.3 ± 7.9	0.511
PR	70.4 ± 13.3	74.6 ± 14.2	65.4 ± 10.6	0.115	62.8 ± 7.1	0.041	63.9 ± 8.9	0.635
PP	36.4 ± 10.7	33.8 ± 9.7	39.6 ± 11.5	0.250	36.4 ± 9.5	0.527	43.8 ± 16.3	0.246
Ambulatory BP variability								
24-h SBP SD	18.3 ± 6.7	17.3 ± 6.9	19.6 ± 6.6	0.459	20.2 ± 8.1	0.136	19.5 ± 4.3	0.973
CV	16.1 ± 5.8	14.7 ± 4.9	17.8 ± 6.7	0.277	18.2 ± 7.6	0.115	16.9 ± 3.6	0.658
ARV	18.9 ± 10.0	17.4 ± 9.0	20.7 ± 11.5	0.500	21.5 ± 9.5	0.089	25.5 ± 16.4	0.396
Daytime SBP SD	27.3 ± 15.4	26.9 ± 16.8	27.8 ± 14.5	0.910	27.0 ± 12.2	0.989	32.7 ± 19.6	0.287
CV	23.2 ± 11.7	22.1 ± 11.4	24.4 ± 12.7	0.677	23.7 ± 12.0	0.720	27.0 ± 14.8	0.385
ARV	20.2 ± 10.6	18.9 ± 9.6	21.9 ± 12.2	0.562	23.6 ± 12.1	0.144	30.1 ± 21.1	0.189
Nighttime SBP SD	18.5 ± 13.9	15.9 ± 14.4	21.5 ± 13.5	0.379	17.0 ± 9.3	0.814	25.3 ± 20.1	0.534
CV	16.4 ± 11.7	13.6 ± 12.0	19.7 ± 11.1	0.255	17.3 ± 12.1	0.466	21.4 ± 13.8	0.697
ARV	16.0 ± 10.4	13.5 ± 8.3	19.0 ± 12.5	0.250	16.7 ± 6.6	0.287	18.3 ± 14.5	0.925
Weighted-SD at 24-h SBP	24.6 ± 13.6	23.8 ± 14.8	25.5 ± 12.9	0.788	23.9 ± 10.6	0.985	29.5 ± 18.5	0.382

Values are mean ± SD. Normally distributed continuous data from 2 unrelated samples were compared using Student's *t*-test and continuous data repeated measures from 2 related samples were compared using paired *t*-tests. [a]*P* values in the comparison between baseline and follow-up by paired t-test.

ARV = average real variability; BP = blood pressure; CV = coefficient of variation; DBP = diastolic blood pressure; PP = pulse pressure; PR = pulse rate; SBP = systolic blood pressure.

Normally distributed, continuous, and categorical data from 2 unrelated samples were compared using the Student's *t*-test and the chi-square test. Continuous and categorical data's repeated measures from 2 related samples were compared using a paired *t*-test and Wilcoxon's signed-rank test. The correlations between the Sf/Am and LVEF data were assessed using Pearson's correlation. To assess the relationships of changes in the Sf/Am and the LVEF from baseline to follow-up, we used the ratio of baseline and follow-up values of the Sf/Am and LVEF. All analyses were performed using SPSS, version 28.0 (SPSS). Two-sided probability values <0.05 were considered significant in all tests.

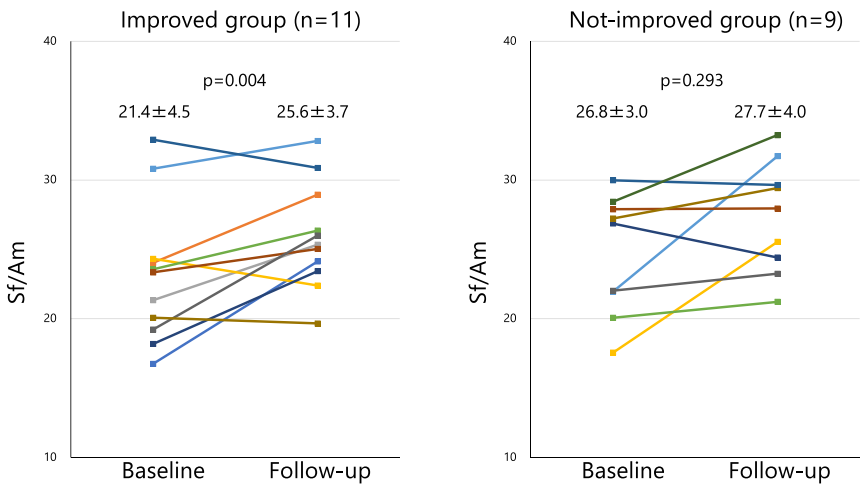
RESULTS

PATIENT CHARACTERISTICS. The total series of 20 patients with HF (mean age, 63.3 ± 14.1 years; male, 65.0%; ischemic heart disease, 15.0%; atrial fibrillation, 25.0%) was divided into the recovered (n = 11) and not-recovered (n = 9) LVEF groups. Table 1 summarizes the patients' characteristics at baseline. The prevalence of the use of each class of medications was not significantly different between the baseline and the follow-up in either group (Supplemental Table 1). Regarding the changes of clinical characteristics from baseline to follow-up, in the recovered group, the LVEF increased significantly from 29.8% ± 7.2% at baseline to 44.9% ± 5.8% at follow-up ($P < 0.001$); the BNP level decreased from 156.7 ± 145.6 to 79.0 ± 127.3 (compare with the log-transformed value: 2.0 ± 0.5 and 1.4 ± 0.7, $P = 0.002$); and the number of antihypertensive medications did not change significantly from baseline to follow-up (3.4 ± 1.4 to 3.5 ± 1.4, $P = 0.756$).

The LVEF in the not-recovered group did not change significantly (40.8% ± 13.3% at baseline vs 39.7% ± 12.5% at follow-up, $P = 0.771$); the respective BNP values were 139.4 ± 79.4 and 349.2 ± 371.1 (compare with the log-transformed value: 2.1 ± 0.3 and 2.2 ± 0.7, $P = 0.559$); and the number of antihypertensive medications did not change significantly (3.4 ± 1.3 vs 3.8 ± 1.1, $P = 0.500$).

CHANGES IN AMBULATORY BLOOD PRESSURE. Table 2 summarizes the changes in ambulatory BP

FIGURE 3 Components of the Cuff Volumetric Pulse Waveform



The Sf/Am increased significantly in the recovered LVEF group (n = 11, Sf/Am at baseline and follow-up, 21.4 ± 4.5 and 25.6 ± 3.7, $P = 0.004$), but there was no similar increase in the not-recovered group (n = 9, Sf/Am at baseline and follow-up, 26.8 ± 3.0 and 27.7 ± 4.0, $P = 0.293$). Am = amplitude measure pulse wave; Sf = square forward pulse wave.

profiles at baseline and follow-up in both patient groups. In the recovered LVEF group, the 24-hour and nighttime diastolic BP values were decreased at follow-up compared to the baseline levels, and the nighttime pulse rate data were also decreased at follow-up vs the baseline. The 24-hour, daytime, and nighttime ambulatory SBP did not change significantly from baseline to follow-up in the recovered group. In contrast, in the not-recovered LVEF group, none of the parameters of ambulatory BP changed significantly from baseline to follow-up. In both the recovered and not-recovered groups, the ambulatory BPV parameters, SD, coefficient of variation, and average real variability of 24-hour, daytime, and nighttime SBP and weighted-SD of 24-hour SBP did not change significantly from baseline to follow-up after treatment.

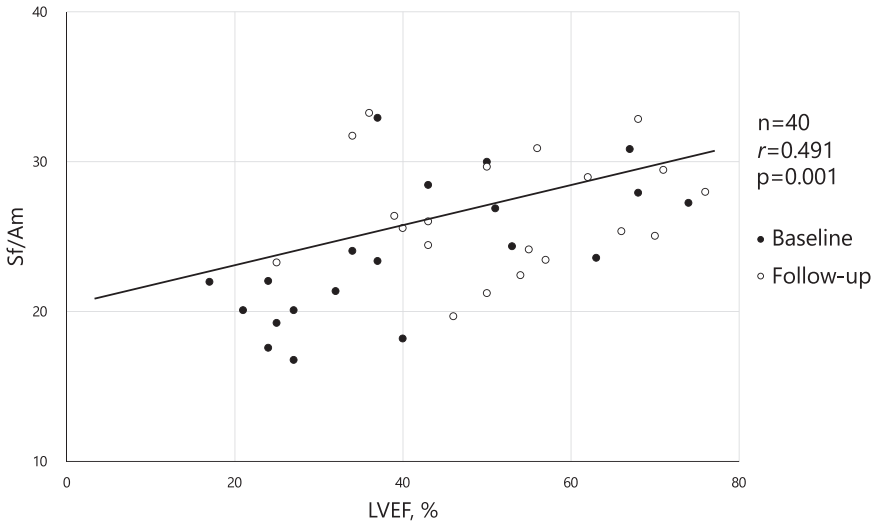
As shown by the data of the patients' physical activity obtained by the multisensor-ABPM, the average of the 24-hour physical activity was not significantly changed from baseline to follow-up in either LVEF group: the physical activity [G] values in the recovered group were 262.0 ± 96.5 at baseline and 299.7 ± 134.5 at follow-up ($P = 0.241$), and those in the not-recovered group were 364.8 ± 175.9 and 356.4 ± 155.6 ($P = 0.829$).

THE NOVEL PULSE WAVEFORM INDEX SF/AM AND CARDIAC FUNCTION. The values of Sf/Am at both baseline and follow-up were found to be normally distributed, as determined by the Shapiro-Wilk test ($P = 0.670$ at baseline and $P = 0.749$ at follow-up). The Sf/Am increased significantly in the recovered LVEF group (n = 11, Sf/Am at baseline and follow-up, 21.4 ± 4.5 and 25.6 ± 3.7, $P = 0.004$), but there was no similar increase in the not-recovered group (n = 9, Sf/Am at baseline and follow-up, 26.8 ± 3.0 and 27.7 ± 4.0, $P = 0.293$) (**Figure 3**). In the recovered group, the Sf/Am values also increased significantly for the daytime (awake, $P = 0.003$) and nighttime (sleeping, $P = 0.008$). In the not-recovered group, both the daytime and nighttime Sf/Am values did not change significantly from baseline to follow-up.

The pulse waveform index Sf/Am (average value of 24-hour) was significantly associated with the LVEF in the overall measurements, ie, the Sf/Am value evaluated by the 2 ABPM measurements at baseline and follow-up (n = 40, $r = 0.491$, $P = 0.001$) (**Figure 4**). The Sf/Am values for the daytime and nighttime also had significant relationships with the LVEF in overall measurements (daytime, n = 40, $r = 0.459$, $P = 0.003$; nighttime, n = 39, $r = 0.508$, $P = 0.001$) (Supplemental Figures 5 and 6). We also assessed the 24-hour average value of ejection time in the pulse waveform analysis (**Figure 2**); the ejection time was not significantly correlated with the LVEF (n = 40, $r = 0.263$, $P = 0.101$) (Supplemental Figure 7).

In the assessment of the changes in the Sf/Am and LVEF from baseline to follow-up, the ratio of the baseline and follow-up Sf/Am values was significantly

FIGURE 4 Scatterplot Illustrating the Relationship Between the Sf/Am and the Echocardiographic LVEF at Baseline and Follow-Up



There was a significant relationship between the Sf/Am and LVEF (n = 40, Pearson's correlation $r = 0.491$, $P = 0.001$). Am = amplitude measure pulse wave; Sf = square forward pulse wave; LVEF = left ventricular ejection fraction.

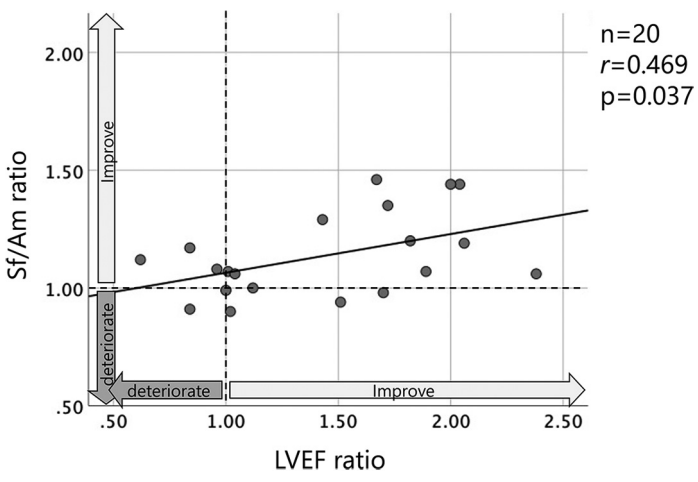
related to the ratio of baseline and follow-up LVEF values ($r = 0.469$, $P = 0.037$) (**Figure 5**). Moreover, according to the Sf/Am for the daytime or nighttime, the ratio of baseline and follow-up Sf/Am values in the daytime was significantly associated with the LVEF ratio ($r = 0.533$, $P = 0.015$) (Supplemental Figure 8). However, the ratio of before and after Sf/Am data for the nighttime was not related to the LVEF ratio ($r = 0.318$, $P = 0.185$) (Supplemental Figure 9).

DISCUSSION

The results of this study demonstrated that the pulse waveform measurement obtained noninvasively with a multisensor-ABPM device, ie, the Sf/Am, was associated with the LVEF before and after treatment in patients with HF (**Central Illustration**). To the best of our knowledge, this study is the first to assess the changes in ambulatory BP profiles and the pulse waveform index between before and after the improvement of the LVEF in patients with HFrecEF. An advantage of the novel pulse waveform index Sf/Am is that its use might estimate patients' cardiac function in ambulatory settings, thus enabling assessments of the changes in a patient's hemodynamic state and cardiac function during physical activities in the daytime and rest and sleep at nighttime. Our present findings suggest the possibility of a new hemodynamic assessment by ABPM that may be useful for the estimation of cardiac function.

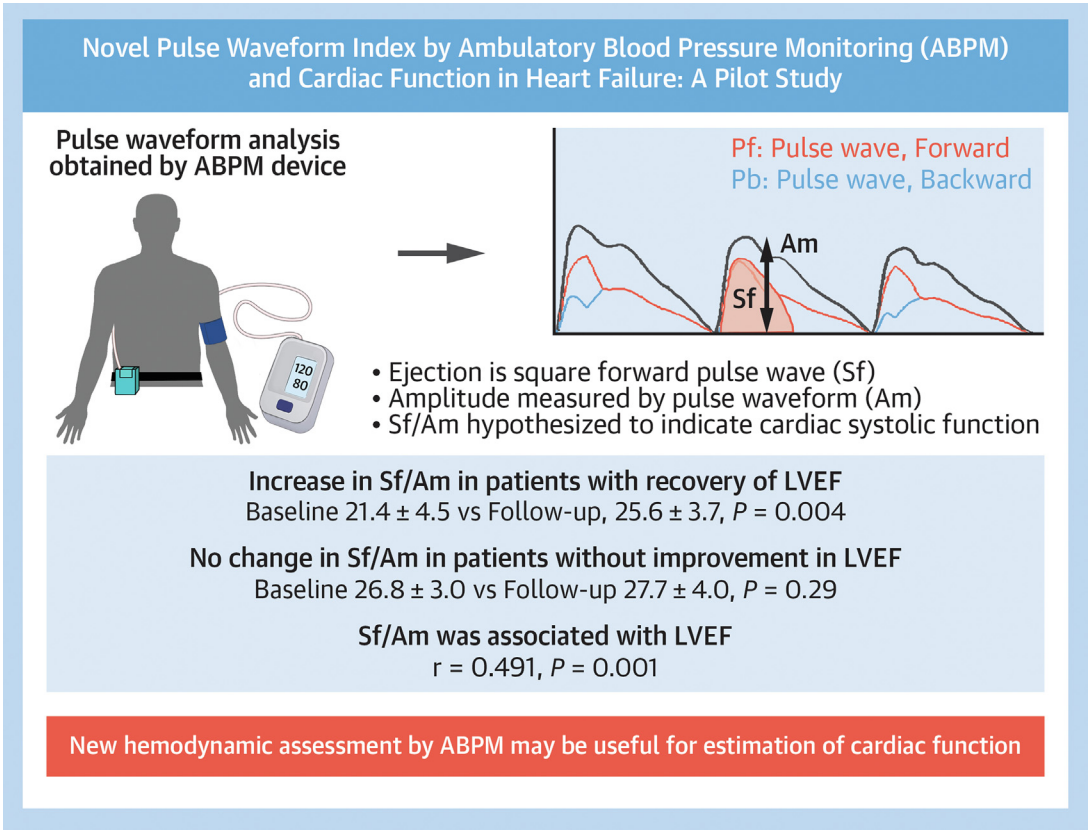
Several methods for estimating cardiac function from pulse waveforms in invasive arterial monitoring have been established, and this monitoring has been reported to be useful in operative or intensive care settings.[8,34,35] Few research groups have evaluated

FIGURE 5 Scatterplot Illustrating the Relationship Between the Changes in Sf/Am and the Echocardiographic LVEF From Baseline to Follow-Up



These changes in Sf/Am and LVEF are represented as a ratio between baseline and follow-up. The values had a significant relationship (n = 20, Pearson's correlation $r = 0.469$, $P = 0.037$). Am = amplitude measure pulse wave; Sf = square forward pulse wave; LVEF = left ventricular ejection fraction.

CENTRAL ILLUSTRATION **A Pilot Study of Novel Pulse Waveform Index by ABPM and Cardiac Function in Heart Failure**



Narita K, et al. JACC Adv. 2024;3(1):100737.

We developed a novel pulse waveform index "Sf/Am" obtained by cuff-oscillometric BP measurements, which was related to echocardiographic LVEF. Our study results suggest that a novel pulse waveform analysis obtained by noninvasive BP measurements may be able to estimate cardiac function. ABPM = ambulatory blood pressure monitoring; Am = amplitude measure pulse wave; BP = blood pressure; LVEF = left ventricular ejection fraction; Sf = square forward pulse wave.

cardiac function by noninvasive pulse wave measurements.[10] Pulse-waveform analyses for estimating aspects of cardiac function such as the cardiac output revealed by noninvasive methods have used the volume clamp method with a finger-cuff or radial artery applanation tonometry using a sensor placed on the radial artery. Both the volume clamp method and radial artery applanation tonometry acquire the estimated arterial waveform to estimate cardiac output.[5,12,36,37]

In our series of HF patients, the pulse waveform index Sf/Am was correlated with the changes in the LVEF despite the unchanged ambulatory BP parameters, including the 24-hour ambulatory BP and the BP variability between the baseline and follow-up. An improvement of cardiac function usually leads to an elevation of BP levels[38]; in practice, however, BP levels are well controlled by antihypertensive medications. It is thus difficult to detect changes in cardiac function by obtaining only occasional BP measurements. The multisensor-ABPM provides a large number of BP measurements compared to occasional office BP measurements. Given these limitations of BP measurements, the multisensor-ABPM appears to be able to provide a noninvasive and accurate estimation of cardiac

function. If the pulse-waveform analysis obtained by BP measurements is developed further, it may be possible to screen cardiac function noninvasively using BP measurements in routine medical care.

STUDY STRENGTHS AND LIMITATIONS. The strong point of this study is that the use of the Sf/Am makes it possible to estimate patients' cardiac function by using their BP measurements. Most examinations of cardiac function are performed in laboratories and other experimental settings, but the Sf/Am can be measured in ambulatory settings. However, there are several study limitations to address. 1) The number of patients was small (n = 20), which may have resulted in type 2 error. Furthermore, several confounding factors including demographic characteristics could not be adequately adjusted for due to the limited sample size in this study. 2) The correlations between the Sf/Am and LVEF were significant but not strongly correlated (r values were approximately 0.4-0.5). 3) The patient age was younger in the recovered group compared to the not-recovered group. There were also significant differences in patient characteristics at baseline. 4) Although the ABPM measurements were performed while the patients were in stable condition, ie, all patients could walk alone, most of the patients were still hospitalized at baseline. However, there were no significant differences in the amount of physical activity between before and after the ABPM measurements. 5) Although the echocardiographic LVEF was measured and confirmed by 2 sonographers, there was no confirmation by cardiologists, and there was a lack of data regarding inter- and intra-observer variability in the LVEF. 6) There were technical problems with accuracy in the pulse waveform collection when the BP measurements were obtained by the multisensor-ABPM. Pulse waves in the pressure interval below diastolic pressure, which is considered to have the smallest effect of external force on arterial vessels, are used for pulse-wave analyses; however, when artifacts (body movement, arrhythmia, etc.) occur within the relevant pressure interval, the analysis may be faulty.

CONCLUSIONS

While this study was conducted with a small number of patients, its results demonstrated that noninvasive pulse waveform measurements obtained using a multisensor-ABPM device, ie, the Sf/Am, exhibited a modest association with the LVEF before and after treatment in patients with HF. Our present findings suggest the possibility of a new hemodynamic assessment by ABPM that may be useful for estimations of cardiac function. A large-sample observational study is necessary to further clarify the relationship between the Sf/Am ratio and cardiac function in order to establish the usefulness of the new pulse waveform index obtained by BP measurements.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The novel pulse waveform index 'Sf/Am' calculated from the cuff volumetric pulse wave obtained by BP measurements was correlated with echocardiographic LVEF in patients with HF.

TRANSLATIONAL OUTLOOK: The pulse waveform index Sf/Am has potential for screening cardiac function noninvasively by using BP measurements in routine medical care.

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KEY WORDS **blood pressure, cardiac function, heart failure, pulse waveform analysis**

APPENDIX **For supplemental material, tables, and figures, please see the online version of this paper.**