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ORIGINAL ARTICLE
Heart Failure

Blood Oxygen, Sleep Disordered Breathing, and Respiratory Instability in Patients With Chronic Heart Failure

— PROST Subanalysis —

Tomoyuki Tobushi, MD; Toshiaki Kadokami, MD, PhD; Junya Takagawa, MD, PhD; Kaoru Dohi, MD, PhD; Shuji Joho, MD, PhD; Osamu Wada, MD, PhD; Shin-ichi Momomura, MD; Takashi Koyama, MD; Nobuhiko Haruki, MD PhD; Shin-ichi Ando, MD, PhD; Hidetsugu Asanoi, MD, PhD for the PROST Investigators

Background: Respiratory stability index (RSI), a semi-quantitative measure of respiratory instability, was found to reflect congestive and other clinical status of acutely decompensated heart failure in the PROST study. Given that the association between RSI and another important factors affecting respiration, such as peripheral oxygen saturation (SpO_2), and the influence of oxygen inhalation on this association were undetermined, and that the association between common sleep-disordered breathing (SDB) parameters and RSI was unknown, we performed a subanalysis using PROST data.

Methods and Results: Correlation analyses were performed to evaluate the relationships between RSI, SpO_2, and other SDB parameters (3% oxygen desaturation index [3%ODI], respiratory disturbance index [RDI]) using Spearman's rank correlation. RSI and overnight mean SpO_2 were not significantly correlated either after admission (n=38) or before discharge (n=36; r=0.27, P=0.10 and r=0.05, P=0.76, respectively). This correlation was also not affected by presence or absence of oxygen inhalation. 3%ODI, RDI and RSI were significantly and inversely correlated both after admission and before discharge.

Conclusions: RSI and blood oxygen level were not significantly correlated irrespective of oxygen inhalation, while the SDB parameters were significantly correlated, suggesting that RSI reflects lung congestion independently of blood oxygen concentration and, thus, can be a useful indicator of the non-invasive assessment of lung congestion.

Key Words: Apnea; Chronic heart failure; Respiratory instability; Sleep-disordered breathing; SpO_2

Heart failure (HF) has been rapidly increasing in the developed countries.[1] Efficient control of HF is an important issue, requiring establishment of a tool for convenient and reliable detection of the congestive state and of the other manifestations of HF in daily in-hospital clinical care or home care. HF patients are known to often have both obstructive and central sleep-disordered breathing (SDB).[2,3] Aside from central SDB, typically known as Cheyne-Stokes respiration (CSR), HF patients have been reported as having abnormal respiratory rhythms characterized by shallow and irregular breathing.[4–6] Such irregular breathing occurs not only during sleep, but also even when the patient is awake. Therefore, quantification of the irregular breathing and SDB may serve as an important marker of HF exacerbation and can be a useful tool in daily clinical practice. We previously proposed respiratory stability index (RSI) as a tool for quantifying irregular breathing.[7] In our previous study in HF patients, RSI increased with improvement in lung congestion, and had the potential to become a marker of congestion in HF.[8] In addition to lung congestion,[9–11] however, other factors known to contribute to respiratory stability include carbon dioxide concentration,[12] oxygen concentration,[13,14] sensitivity of chemoreceptors,[15] circulation time,[16,17] and upper

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Cardiovascular Medicine, Fukuokaken Saiseikai Futsukaichi Hospital, Fukuoka (T.T., T. Kadokami); Cardiology Division, Imizu Municipal Hospital, Toyama (J.T.); Department of Cardiology and Nephrology, Mie University Graduate School of Medicine, Mie (K.D); Second Department of Internal Medicine, Toyama University Hospital, Toyama (S.J.); Cardiovascular Medicine, Japan Community Health Care Organization Takaoka Fushiki Hospital, Toyama (O.W.); Cardiovascular Medicine, Jichi Medical University Saitama Medical Center, Saitama (S.M.); Cardiovascular Medicine, Matsumoto Kyoritsu Hospital, Nagano (T. Koyama); Department of Cardiology, Matsue Red Cross Hospital, Shimane (N.H.); Sleep Apnea Center, Kyushu University Hospital, Fukuoka (S.A.); and Department of Chronic Heart Failure Management, Global Center for Medical Engineering and Informatics, Osaka University, Osaka (H.A.), Japan

Mailing address: Shin-ichi Ando, MD, PhD, Sleep Apnea Center, Kyushu University Hospital, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan. E-mail: shinando@sleep.med.kyushu-u.ac.jp

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airway narrowing,[18] as well as sympathetic nervous activity regulating these factors.[19,20] It is unknown whether not only lung congestion, but also any of these factors were related to the RSI changes observed at HF exacerbation. With a focus on any association between blood oxygen or oxygen inhalation, SDB, and RSI, we conducted a subanalysis using PROST study data to determine (1) the influence of oxygen level (peripheral capillary oxygen saturation, SpO_2) on RSI; (2) the influence of oxygen inhalation on any relationship between RSI and SpO_2; and (3) an association between other SDB parameters and RSI.

Methods

Patients

All patients included for analysis in the PROST study (UMIN 000019905) were examined in the present study. The study design and results of the PROST study have been reported elsewhere.[8] In summary, PROST was a multicenter, prospective, observational study to examine the usefulness of RSI assessment during the recovery process from deterioration of chronic HF performed in 9 centers in Japan. Included were patients with New York Heart Association functional class III or IV who were admitted to hospital for acute decompensated HF. All patients were aged ≥20 years and had had no respiratory assist equipment such as positive pressure ventilation or oxygen inhalation before the index admission. Key exclusion criteria were acute coronary syndrome in the last 3 months, chronic obstructive pulmonary disease, central nervous disorders, hemodialysis, and symptomatic malignancies. Enrollment began in November 2015 and ended in April 2016, with follow-up completed in June 2016. The present study is a pre-specified subanalysis using data obtained from the PROST study.

Target Sample Size

In the PROST study, patients were enrolled from 9 centers in Japan. We started enrollment from the end of November. We assumed that during the winter period (December–April), for each center, on average 2 patients would be admitted for worsening HF, and the enrollment rate was 50%. As a result, we set the target sample size at 40, and we enrolled 44 patients.

Assessment of HF

The Central Adjudication Committee, composed of 3 cardiologists, determined, in a blinded manner, clinical HF status at hospitalization (exacerbation) and at discharge (recovery) for each patient.

Assessment of SDB

All night respiratory events were recorded using a portable respiratory polygraphy (PG) device (SAS-3200, Nihon Kohden, Tokyo, Japan) on 2 occasions: soon after admission (deterioration phase) and before discharge (post-recovery phase). The PG was set in place before bedtime at night and removed on waking. An airflow sensor was placed at the oronasal area, and an SpO_2 sensor was placed on a fingertip. Nasal pressure signals were digitized and sampled at 32 Hz and SpO_2 at 2 Hz. These data were analyzed off-line using a personal computer. SpO_2 was continuously measured, and mean and minimum SpO_2 were calculated. Respiratory disturbance index (RDI) was identified as follows: apnea was defined as a drop in the peak thermal sensor excursion >90% of baseline and lasting ≥10 s, and hypopnea was defined as a >50% reduction in oronasal airflow lasting ≥10 s together with a >3% drop in oxygen saturation. RDI was calculated as the sum of apnea and hypopnea episodes per hour of sleep.

RSI Measurement

The overnight airflow signals obtained by PG were full-wave rectified and detrended. The data then underwent spectral analysis (maximum entropy method) for determination of variability in the airflow component. RSI was defined as follows:[7]

RSI=1/(SD of respiratory component)

The program used to calculate RSI, created by one of the authors, underwent validation by an academic research organization (ARO) of Kyushu University Hospital.

Endpoints

The primary endpoint of this pre-specified subanalysis was the association of oxygen level (peripheral capillary oxygen saturation, SpO_2) and RSI. Secondary endpoints were influence of oxygen inhalation on any relationship between RSI and SpO_2, as well as on the association between other SDB parameters (3% oxygen desaturation index [3%ODI] and RDI) and the RSI. To determine whether oxygen inhalation affected the correlation between RSI and SpO_2, patients were classified into 2 groups, with and without oxygen inhalation at the first recording after admission, and the correlation between RSI and mean SpO_2 before and after treatment of HF was compared.

Statistical Analysis

Spearman's rank correlation coefficients were calculated to determine correlations. Correlation with RSI was examined for SpO_2, minimum SpO_2, % of time with SpO_2<90% and other SDB parameters such as 3%ODI and RDI. Differences in correlation according to oxygen inhalation status were evaluated using the linear mixed-effects models including an interaction term between each parameter and oxygen inhalation status. Influence of time point for the correlations between RSI and each parameter were also evaluated on similar models. We conducted univariate and multivariate linear regression analysis to clarify the effects on RSI. Statistical significance was defined as $P<0.05$. Statistical analysis was performed using SAS version 9.3 (SAS Institute, Cary, CA, USA).

Results

Patients

Of a total of 44 patients who provided informed consent in the PROST study, 2 patients withdrew consent before the end of initial PG and 1 patient underwent only initial PG. Baseline patient data for the remaining 41 patients after exclusion of these 3 patients are summarized in **Table 1** according to oxygen inhalation status. After-admission PG data were obtained from 38 patients, and before-discharge PG data were obtained from 36 patients. Those patients with apparent outliers from the PG data or with missing data as determined by the central review committee, were excluded from the 44 patients.

Oxygen inhalation was performed in 13 of the 39 patients after admission. Of these 13 patients, 12 patients had PG before discharge without oxygen inhalation. The flow rate

Table 1. Baseline Patient Characteristics

Variable	Without oxygen (n=29)	With oxygen (n=12)	Total (n=41)
Age (years)	74.9±12.3	65.7±8.8	72.2±12.1
Sex (Male)	17 (58.6)	8 (66.7)	25 (61.0)
Underlying heart disease			
DCM	6 (20.7)	0 (0.0)	6 (14.6)
IHD	10 (34.5)	5 (41.7)	15 (36.6)
VHD	3 (10.3)	2 (16.7)	5 (12.2)
Hypertensive heart disease	8 (27.6)	3 (25.0)	11 (26.8)
Others	2 (6.9)	2 (16.7)	4 (9.8)
Complications			
AF	16 (55.2)	7 (58.3)	23 (56.1)
DM	5 (17.2)	8 (66.7)	13 (31.7)
Hypertension	14 (48.3)	10 (83.3)	24 (58.5)
CKD	11 (37.9)	3 (25.0)	14 (34.1)
Functional capacity			
NYHA			
I	0 (0.0)	0 (0.0)	0 (0.0)
II	1 (3.4)	1 (8.3)	2 (4.9)
III	22 (75.9)	9 (75.0)	31 (75.6)
IV	6 (20.7)	2 (16.7)	8 (19.5)
Specific activity scale (Mets)	2.4±1.1	2.3±1.1	2.3±1.1
HR (beats/min)	84.1±23.5	102.2±44.2	89.4±31.5
Pulse rate (beats/min)	79.9±15.6	89.8±23.7	82.8±18.6
Systolic BP (mmHg)	120.3±19.0	126.8±29.6	122.2±22.4
Diastolic BP (mmHg)	71.0±13.6	81.5±21.6	74.0±16.8
Rales			
–	14 (48.3)	7 (58.3)	21 (51.2)
+	15 (51.7)	4 (33.3)	19 (46.3)
++	0 (0.0)	1 (8.3)	1 (2.4)
CTR (%)	63.8±9.1	61.3±4.1	63.1±7.9
LVDd (mm)	54.9±8.5	55.8±9.0	55.1±8.5
LVDs (mm)	42.7±11.2	44.0±9.3	43.0±10.6
LVEF (%)	44.6±17.9	42.9±11.3	44.2±16.3
LAD (%)	46.5±10.4	45.1±6.4	46.1±9.4
BNP (pg/mL)	808.69±544.18	1,375.32±2,887.18	974.53±1,602.43
Creatinine (mg/dL)	1.4±0.7	1.0±0.4	1.3±0.6
Medications			
Diuretic	20 (69.0)	6 (50.0)	26 (63.4)
ACEI/ARB	16 (55.2)	6 (50.0)	22 (53.7)
β-blocker	14 (48.3)	5 (41.7)	19 (46.3)
Inotropic drug	5 (17.2)	0 (0.0)	5 (12.2)
Aldosterone antagonist	15 (51.7)	6 (50.0)	21 (51.2)

Data given as mean±SD or n (%). ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; BNP, brain natriuretic peptide; BP, blood pressure; CKD, chronic kidney disease; CTR, cardiothoracic ratio; DCM, dilated cardiomyopathy; DM, diabetes mellitus; HR, heart rate; IHD, ischemic heart disease; LAD, left atrial diameter; LVDd, left ventricular end-diastolic diameter; LVDs, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association class; VDH, valvular heart disease.

of oxygen in the patients who had oxygen inhalation was 1 L/min in 1 patient, 2 L/min in 10 patients and 3 L/min in 1 patient. No patient used NIPPV at the time of PG in this study. In contrast, no oxygen inhalation was performed in 26 of 39 patients after admission, of whom 24 patients underwent PG before discharge (**Figure 1**). Respiratory indices according to oxygen inhalation status are shown in **Table 2**.

RSI and Mean SpO_2

RSI and overnight mean SpO_2 were not significantly correlated after admission (n=38) or before discharge in all patients (n=36; r=0.27, P=0.10; r=0.05, P=0.76, respectively). The extent of correlation between RSI and mean SpO_2 after admission did not significantly differ from that before discharge (P=0.55).

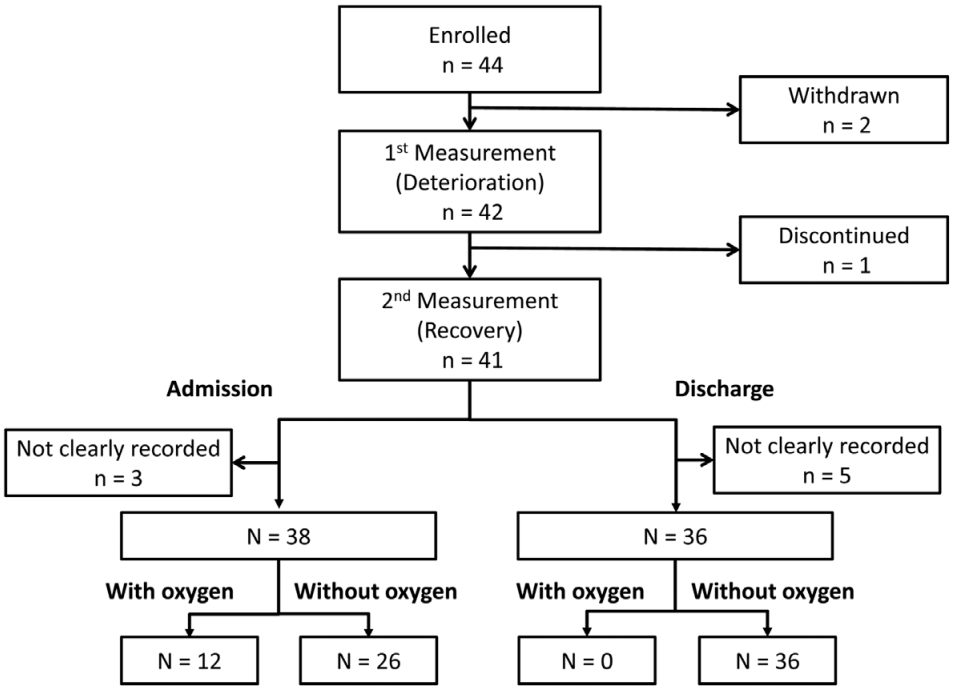

Figure 1. Patient selection process.

Table 2. Respiratory Indices vs. Oxygen Inhalation Status

Variable	After admission						Before discharge	
	n	All	n	With oxygen	n	Without oxygen	n	Without oxygen
SpO_2	38	95.0±2.5	12	97.3±2.0	26	94.0±2.0	36	95.7±1.9
RDI	38	17.2±18.6	12	13.6±16.2	26	18.8±19.7	36	13.6±16.2
3%ODI	38	18.2±17.6	12	11.3±13.0	26	21.4±18.8	36	13.3±14.5
Mean RSI	38	27.9±17.0	12	28.3±16.6	26	27.7±17.6	36	33.2±16.5

Data given as mean±SD. ODI, oxygen desaturation index; RDI, respiratory disturbance index; RSI, respiratory stability index; SpO_2, peripheral capillary oxygen saturation.

Effect of Oxygen Inhalation on RSI and Mean SpO_2

Of the patients with oxygen inhalation at PG after admission, RSI and mean SpO_2 were not significantly correlated after admission (n=12; r=0.17, P=0.60; **Figure 2A**). Also, of the patients without oxygen inhalation at PG after admission or before discharge, RSI and mean SpO_2 were not significantly correlated (after admission, r=0.37, P=0.06; before discharge, r=0.05, P=0.76; **Figure 2B**). In addition, on analysis of the influence of oxygen inhalation on the extent of correlation between mean SpO_2 and RSI, there was no significant interaction (P=0.80), meaning that the correlation between mean SpO_2 (%) and RSI was not influenced by oxygen inhalation.

Other SDB Parameters and RSI

The correlation between 3%ODI or RDI and RSI was examined. 3%ODI and RSI had a significant correlation both after admission and before discharge (after admission, r=−0.63, P<0.01; before discharge, r=−0.45, P<0.01; **Figure 3**). Also, RDI and RSI had a significant correlation after admission and before discharge (r=−0.56, P<0.01; r=−0.45, P<0.01, respectively; **Figure 4**). In addition, the correlation between 3%ODI and RSI or between RDI and RSI after admission did not differ to those before discharge (P=0.54 and P=0.42, respectively).

Indicators of RSI

We conducted univariate linear regression analysis for association with RSI (**Table 3**). We found that only gender tended to be related to RSI (P=0.006). Other factors (age, atrial fibrillation [AF], serum Na concentration, ejection fraction [EF], angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker, β-blocker, diuresis, inotropic agent) did not have a significant association with RSI. When we conducted multivariate linear regression analysis, however, using gender, age, AF and EF, only age and EF had a significant association with RSI (P=0.0034 and 0.036, respectively).

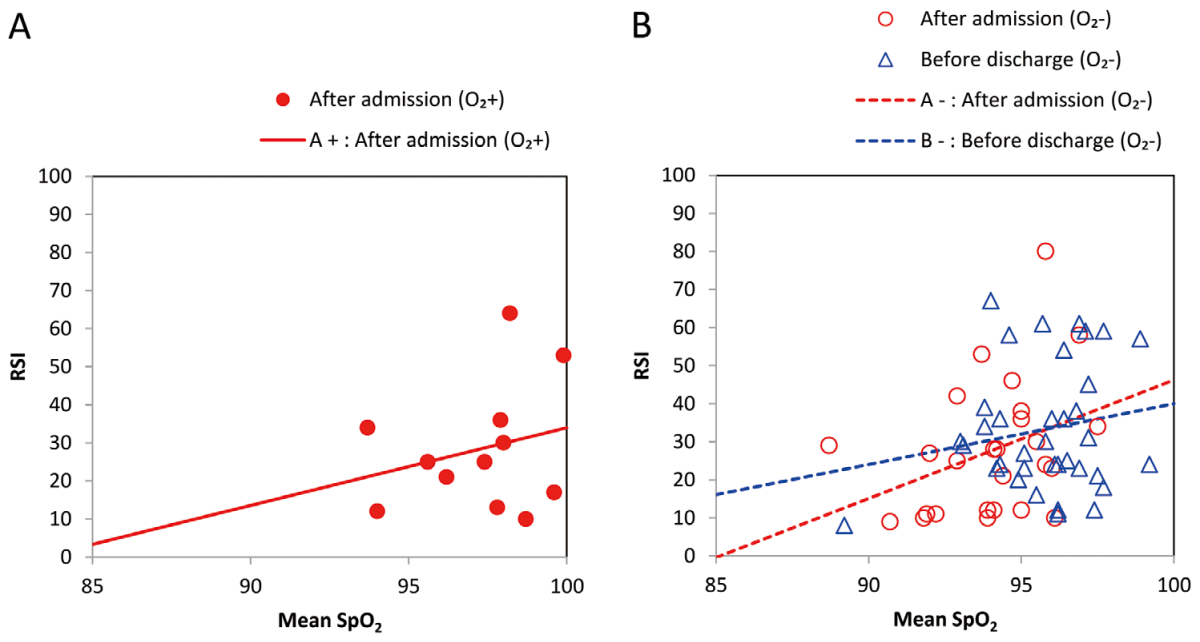

Figure 2. Respiratory stability index (RSI) vs. mean peripheral capillary oxygen saturation (SpO_2) in patients (**A**) with oxygen inhalation after admission (r=0.17, P=0.60; red solid line A+, regression line); and (**B**) without oxygen inhalation after admission (red open circles; r=0.37, P=0.06; red dash line A–, regression line) and before discharge (blue open triangles; r=0.05, P=0.76; blue dash line B–, regression line).

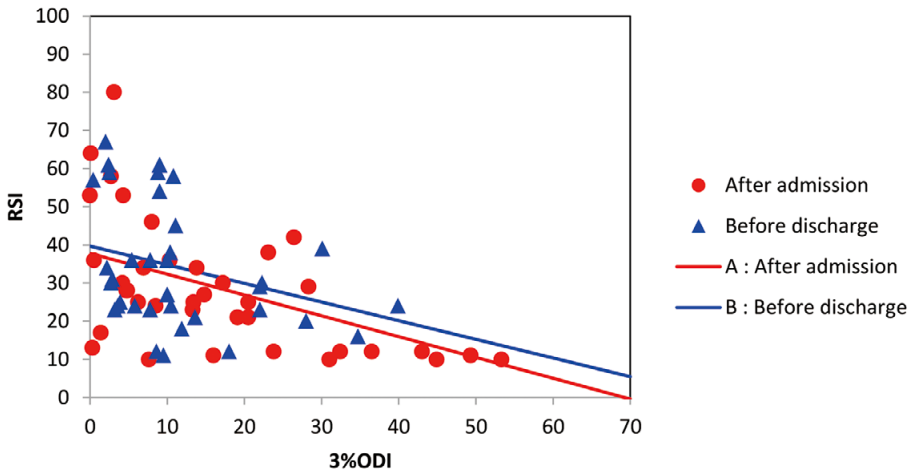

Figure 3. Respiratory stability index (RSI) vs. 3% oxygen desaturation index (3%ODI) after admission (red circles; r=–0.63, P<0.01; red solid line A, regression line) and before discharge (blue triangles; r=–0.45, P<0.01; blue solid line B, regression line).

RSI and Minimum SpO_2 and % of Time at SpO_2<90%

Correlation between RSI and minimum SpO_2 and % of time spent at SpO_2<90% were examined (**Table 4**). There were no correlation between RSI and minimum SpO_2 (P=0.15 after admission, P=0.31 before discharge). There was a significant correlation, however, between RSI and % of time spent at SpO_2<90% in all patients (r=−0.33, P<0.05), and in patients without oxygen inhalation after admission (r=−0.41, P<0.05), but the correlation disappeared before discharge (P=0.33).

Discussion

The PROST study was a multicenter study to examine whether a marker of RSI in HF patients could be used as a surrogate marker of lung congestion and so on.[8] In the

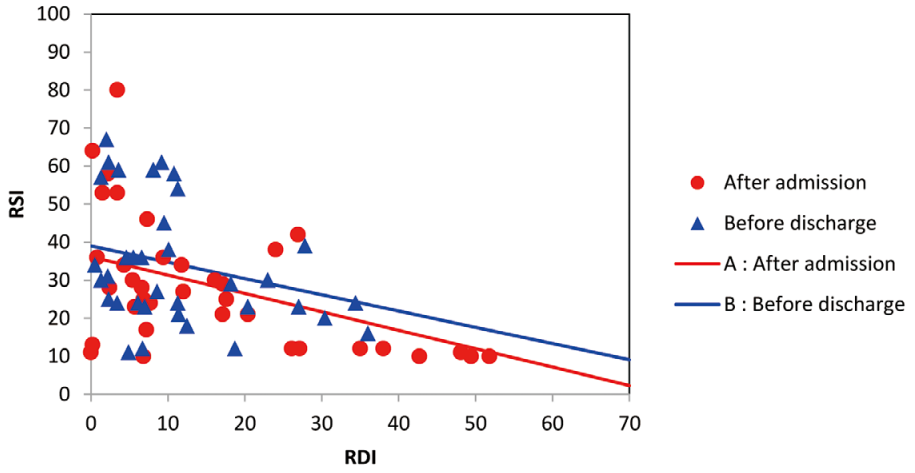

Figure 4. Respiratory stability index (RSI) vs. respiratory disturbance index (RDI) after admission (red circles; r=−0.56, P<0.01; red solid line A, regression line) and before discharge (blue triangles; r=−0.45, P<0.01; blue solid line B, regression line).

Table 3. Indicators of RSI

Variable	Univariate analysis		Multivariate analysis	
	Regression coefficient	P-value	Regression coefficient	P-value
Sex (male)	−15.20	0.006	−11.72	0.056
Age (years)	−0.31	0.18	−0.78	0.0034
AF	−6.81	0.23	−7.68	0.17
LVEF (%)	0.30	0.15	0.45	0.036
ACEI/ARB	−0.12	0.98		
β-blocker	8.73	0.12		
Diuresis	16.22	0.19		
Inotropic agents	−7.69	0.24		
Serum Na (mEq/L)	0.22	0.75		

Abbreviations as in Tables 1,2.

Table 4. Correlations Between RSI and Other SpO_2 Parameters

Correlation between RSI and	Phase	O_2 inhalation	n		Coefficient	P-value
			Minimum SpO_2 (%)			
Minimum SpO_2	After admission	All	38	84.0±8.7	0.24	0.15
		O_2(+)	12	88.8±7.4	0.39	0.21
		O_2(−)	26	81.8±8.5	0.23	0.27
	Before discharge	All O_2(−)	36	85.8±7.5	0.18	0.31
			% of time spent at SpO_2<90% (%)			
% of time spent at SpO_2<90%	After admission	All	38	9.1±14.7	−0.33	0.041
		O_2(+)	12	2.5±6.7	−0.34	0.28
		O_2(−)	26	12.1±16.5	−0.41	0.04
	Before discharge	All O_2(−)	36	3.9±10.8	−0.17	0.33

Data given as mean±SD. O_2(+), with oxygen inhalation; O_2(−), without oxygen inhalation. Other abbreviations as in Table 2.

PROST study, nocturnal PG was performed following admission due to HF deterioration and at the end of hospital treatment, with measurement of RSI, a tool newly developed by the authors and calculated as the reciprocal of the variability of the respiratory cycle. RSI was compared between the 2 time points, and significantly increased with apparent improvement in HF, indicating the usefulness of RSI as a surrogate marker of HF. The present subanalysis assessed the correlation between RSI and blood oxygen concentration, oxygen inhalation, and other SDB parameters, among the factors other than lung congestion that can contribute to respiratory stability. There was no correlation, however, between oxygen concentration and RSI, and this was not affected by the presence or absence of oxygen inhalation. Thus, neither blood oxygen concentration nor oxygen inhalation affected respiratory instability as measured by RSI. Thus, we may conclude that RSI can be taken as a marker that almost solely reflects the level of pulmonary congestion.

Peripheral chemoreceptors are known to monitor arterial oxygen partial pressure, and their hypoxic chemoreceptor-mediated stimulation increases the ascending impulse and thus causes increase in the respiratory rate and in sympathetic nervous activity, causing heart rate increase.[21] According to the present subanalysis, however, respiratory control via lung congestion-related pulmonary receptor stimulation, C-fiber receptor stimulation,[22] and pulmonary stretch receptor stimulation,[23,24] appears to more strongly affect the regularity of respiration rather than chemoreceptor-mediated stimulation through hypoxia.

RSI and SpO_2 after admission were weakly (although not significantly) correlated (r=0.27, P=0.10). Before discharge, however, RSI and SpO_2 were not correlated at all. This indicates a possibility that patients with lower SpO_2 had more severe HF with more intense congestion in the acute phase, resulting in the shown weak association between RSI and SpO_2.

We found % of time spent at SpO_2<90% was significantly associated with RSI. Longer time spent at SpO_2<90% might have a stronger association than minimum SPO_2, probably because longer desaturation must mean higher congestion, and it would have a greater effect on the whole night analysis of respiratory stability than a short duration desaturation.

In the linear regression analysis between RSI and the various factors that might affect RSI, aged patients with low EF had low RSI, namely low respiratory stability. In aged patients, the respiratory feedback system tends to be impaired, and low-EF patients would have low cardiac output, both of which are known to reduce respiratory stability. As for the influence of gender, given that the current study consisted of a small number of patients, further study is needed to obtain a definitive answer on the influence of gender on RSI.

A high prevalence of obstructive and central SDB is known in HF patients. We observed significant correlation between RDI or 3%ODI and RSI. Respiratory instability during sleep in patients with HF is considered to consist of obstructive and/or central type SDB and rapid and shallow type unstable respiration, caused mainly by pulmonary receptor stimulation. The frequency of the former oscillation resides at a low and narrow range from 0.01 Hz to 0.1 Hz, whereas that of the latter oscillation, mainly due to pulmonary congestion, scatters at a higher and wide frequency range from 0.1 Hz to 0.5 Hz, and comprises the major part of RSI.[8] Given that central SDB is considered to relate mainly to cardiac output status and that obstructive SDB may not be strongly related to HF status but is more strongly related to obesity or anatomical problems, it is possible that RSI is independent of or only slightly related to the degree of SDB. Therefore, the present finding that there was a significant correlation between 3%ODI and RDI with RSI means that RSI could reflect overall respiratory instability in patients with HF, although it mainly reflects the instability caused by pulmonary congestion. Further analyses utilizing the combinations of SDB parameters and RSI and optimization of their rate of combinations may enable more accurate monitoring of the severity of congestion in HF.

Estimated Effect of Respiratory Disorder Pattern on RSI

Because our analysis was based on the data from simple PG, we cannot assess the difference in the actual influence of CSR and obstructive sleep apnea (OSA) separately on the various frequency components of the data. We consider, however, that given that CSR in patients with very low cardiac output generally is very regular and periodic, and that each respiration itself is very regular, this would result in the production of 2 distinct narrow peaks in the power spectrum at lower (0.008–0.039 Hz) and higher frequency (0.08–0.5 Hz) in the area used in the calculation of RSI. In this kind of case, given that the lower frequency peak would be very tall and narrow, this power would be adopted for the calculation, resulting in a wider distribution of standard deviation of frequency (low RSI). In contrast, the breathing in OSA is usually irregular, and this would result in a broader distribution of the power in the low frequency area. As a result, this low-frequency power would not be adopted because the peak is <50% of the higher frequency peak power (from the definition of the RSI calculation), meaning that the standard deviation of frequency distribution would be lower (higher RSI). In the presence of pulmonary congestion, however, respiration would be rapid and shallow, and this would result in a broader distribution of power in the higher respiratory frequency range in CSR and OSA patients equally. In summary, the influence of CSR and OSA on RSI would be different, but the degree of influence would vary depending on the HF status of each patient.

Study Limitations

First, in patients with very low SpO_2 on admission, oxygen inhalation was given, resulting in normal SpO_2, and PG would have been performed after their condition had somewhat stabilized. This might have led to smaller intra-individual and inter-individual differences in SpO_2 between before and after treatment. Thus, the narrowed RSI-SpO_2 analysis range may have led to decreased precision of the analysis. From an ethical viewpoint, however, prolonged monitoring of patients with very low SpO_2 without treatment of the low oxygen status is unacceptable. One possible solution would be the analysis of very brief data recorded before the start of treatment. Further analysis with this technique may enable assessment of a broader SpO_2 range, thus producing more reliable results.

Second, blood carbon dioxide (CO_2) concentration, which also has a major effect on respiratory control, could not be measured in this study. Thus, it remains unknown whether CO_2 is correlated with RSI, or whether CO_2 affects any relationship between RSI and congestion or oxygen

saturation. These should be analyzed in future studies with the use of monitoring of CO_2.

Third, the threshold of the power in the frequency range used for calculation of RSI was decided semi-empirically. Given that the power of variability in the low frequency range, which may be related to SDB; and the power of respiratory variability in the high frequency range, which may be more related to lung congestion, were not evenly evaluated, absolute assessment of SDB influence was difficult. With improvement of the algorithm based on results from more patients in the future, the more theoretical analysis of different frequency ranges would become feasible.

Fourth, given that we assessed SDB based on PG, not on polysomnography, we could not classify SDB into central and obstructive types, and could not assess the influence of arousal. We consider that some patients must have had CSR and, given that it consists of low-frequency power, it must have affected RSI in a different way to OSA.

Fifth, the sample size with oxygen (n=12 at admission) and without oxygen (n=26 at admission) is small. We concluded that oxygen inhalation and RSI were not significantly correlated using the linear mixed-effects models, including an interaction term between each parameter and oxygen inhalation status (r=0.17, P=0.60). But we cannot completely rule out the possibility that the small sample size might have affected these results.

Sixth, we consider that the lag time from oxygenation to detection at the chemoreceptor might have an association with RSI, and the analysis would be important. Given, however, that there are various methods to measure the lag time from PG data and we did not validate any method for the current study, due to the length of time required for this, we did not analyze the lag time in the current study.

Conclusions

RSI, a marker of respiratory stability, was not significantly correlated with oxygen level in HF patients nor was it affected by oxygen inhalation, suggesting that RSI may be an index specifically reflecting lung congestion independently from blood oxygen concentration or oxygen inhalation. In contrast, markers of SDB, 3%ODI or RDI, and RSI were significantly and inversely correlated, suggesting a pathophysiological analogy of RSI and SDB in HF.

Conflicts of Interest

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