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ORIGINAL ARTICLE

Right Ventricular Function is Associated With Quality of Life in Patients With Systemic Lupus Erythematosus Associated Pulmonary Arterial Hypertension

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Background Right ventricular (RV) function has been identified as an important determinant of outcome in patients with pulmonary hypertension. We aimed to investigate the relationship between echocardiographic-derived RV function and health-related quality of life (HRQOL) in patients with systemic lupus erythematosus associated pulmonary arterial hypertension (SLE-APAH), and to identify the best echocardiographic parameter for evaluating RV function in these patients.

Methods Sixty (60) consecutive patients with SLE-APAH (all female, mean age 33.6 ± 8.2 years) were recruited from May 2013 to November 2014. Echocardiograph, right heart catheterisation, SLE disease activity index (SLEDAI), and functional status and SF-36 generic questionnaire were assessed.

Results Echocardiograph-derived RV systolic function was significantly correlated with haemodynamics ($p < 0.05$), with tricuspid annular plane systolic excursion (TAPSE) showing the strongest correlation with pulmonary vascular resistance ($R^2 = 0.278$, $p < 0.001$) and cardiac index ($R^2 = 0.215$, $p < 0.001$). Patients with a TAPSE<17 mm had a shorter 6-minute-walk-distance (6MWD), lower mixed venous oxygen saturation, and higher plasma N-terminal pro-brain natriuretic peptide ($p < 0.05$). Patients with TAPSE <17 mm had lower physical component summary (PCS) and mental component summary (MCS) scores than those with TAPSE ≥17 mm (35.5 ± 13.2 vs. 55.0 ± 15.5; 46.3 ± 15.3 vs. 64.8 ± 18.8, respectively, all $p < 0.05$). On multiple regression analysis, a TAPSE <17 mm was independently related to lower PCS (β −15.797, 95% confidence interval [CI] −24.746 to −6.848, $p = 0.001$) and lower MCS (β −12.887, 95% CI −24.018 to −1.755, $p = 0.024$).

Conclusions TAPSE is a useful index for RV function assessment, and is associated with HRQOL in patients with SLE-APAH.

Keywords Right ventricle • Quality of life • Pulmonary artery hypertension • Systemic lupus erythematosus

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Introduction

Pulmonary artery hypertension (PAH) is a severe complication of systemic lupus erythematosus (SLE) characterised by progressive increases in pulmonary vascular load, leading to pulmonary vascular remodelling, right ventricular (RV) failure, exercise intolerance, and ultimately death [1–3]. Direct comparisons from the REVEAL registry showed that patients with connective tissue disease (CTD)-associated PAH had poorer survival as compared to patients with idiopathic PAH [4]. Among the CTDs group, however, patients with SLE-PAH had better outcomes than patients with other CTDs [5,6]. These differences suggest that PAH in SLE patients may have a different pathogenesis, however, that subset analysis on this group of patients has been lacking [7].

Previous studies have shown the natural history of PAH is heterogeneous, with more rapid clinical deterioration seen in patients with the greatest degree of RV dysfunction [8,9]. This underlines the importance of RV function assessment in patients with PAH. Echocardiography is not only a commonly used tool for diagnosing and assessing severity of PAH, but also the most convenient method to evaluate RV function in this disease [10–12]. Several echocardiographic parameters have been reported associating with poor prognosis in patients with PAH [13,14]. A comparative evaluation of RV function in patients with SLE-APAH, however, was lacking; and the optimal echocardiographic parameter to measure RV function in these patients remains to be established.

Health-related quality of life (HRQOL) which can provide sensitive indicators for monitoring disease progression and effectiveness of therapeutic interventions on patients' daily performance has become a matter of increasing interest in PAH [15,16], but few studies have focussed on patients with SLE-APAH. Moreover, the association of echocardiograph-derived RV function and HRQOL in patients with SLE-APAH has not been reported. This study aimed to assess the correlation of RV function with HRQOL, clinical and haemodynamic features and to identify the optimal echocardiographic index for evaluating RV function in patients with SLE-APAH.

Material and Methods

Between May 2013 and November 2014, we screened all adult patients with pulmonary hypertension (PH) who were referred to our hospital. Patients were screened for eligibility using the following inclusion and exclusion criteria. Inclusion criteria included: 1) fulfilment of the contemporary diagnostic criteria for PAH, including mean pulmonary arterial pressure (mPAP) $\geq$25 mmHg with a pulmonary capillary wedge pressure (PCWP) $\leq$15 mmHg and pulmonary vascular resistance (PVR) >3 Wood units by right heart catheterisation (RHC), and in the absence of other causes of pre-capillary PH (ie PH due to lung diseases, chronic thromboembolic pulmonary hypertension [CTEPH] or other miscellaneous causes of PAH) [17,18]; and 2) fulfillment of the diagnosis of SLE according to the revised American Rheumatism Association (ARA) criteria [19].

Exclusion criteria included: 1) overlapping syndromes or antiphospholipid syndrome; 2) significant valvular heart disease confirmed by echocardiograph (moderate to severe stenosis or insufficiency); 3) congenital heart disease; 4) impaired left ventricular (LV) systolic function defined as LV ejection fraction (LVEF) <50% from echocardiograph; 5) total lung capacity (TLC) <60% of predicted; and 6) moderate or severe pulmonary interstitial fibrosis on high resolution computed tomography (HRCT) scan.

All participants signed an informed consent prior to enrolment. The clinical study protocol, informed consent documents, and any other appropriate study related documents were reviewed and approved by the Ethics Committee of Peking Union Medical College Hospital (No. S-191).

Systemic lupus erythematosus activity was assessed using the SLE disease activity index (SLEDAI) [20], with SLEDAI <5 being considered as low SLE disease activity.

All subjects underwent echocardiography (Vivid I; GE Vingmed Ultrasound, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China) before RHC. All echocardiographic data were averaged for three beats. Left ventricular ejection fraction was assessed by biplane Simpson's rule. The ratio of peak early to late diastolic transmitral flow velocity (mitral E/A) was calculated by pulsed Doppler echocardiography. Peak early diastolic mitral annular velocity (e') at the lateral and septal basal regions was measured from the apical four-chamber view, so average e' velocity can be computed. The mitral E/e', ratio of peak early diastolic transmitral flow velocity to average peak early diastolic mitral annulus velocity was calculated as a Doppler parameter reflecting LV filling pressure [21]. Left ventricular eccentricity index, was defined as the ratio of the LV anterior-to-posterior dimension to the septal-to-lateral dimension at end-diastole from the mid-ventricular short-axis image [22,23]. Right ventricular end-diastolic area (RV EDA), right atrium (RA) EDA and RV fractional area change (RVFAC) were measured from the apical four-chamber view [10]. Tricuspid annular plane systolic excursion (TAPSE) was measured at the lateral tricuspid annulus by M-mode image [24]. The S' as peak systolic velocity of tricuspid annulus by pulsed-wave Doppler tissue imaging (DTI), was obtained from the apical approach in the view that achieves parallel alignment of Doppler beam with RV free wall longitudinal excursion [25]. The RV myocardial performance index (MPI) was measured as the ratio of the isovolumic time and the ejecting time by DTI [12]. The peak pulmonary artery systolic pressure (PASP) was calculated by adding the right atrial pressure (RAP) (estimated by the diameter and collapsibility of inferior vena cava [IVC]) to the systolic transtricuspid pressure gradient [12].

Haemodynamic assessments were obtained by RHC. An 8.5-F introducer sheet was placed in the right internal jugular vein or the left subclavian vein, and a 6-lumen 8-F Swan-Ganz catheter (Edwards Lifesciences World Trade, Irvine,

CA USA) was advanced into the pulmonary artery. Mean right atrial pressure (mRAP), mPAP, and PCWP were measured. Cardiac output (CO) was measured in triplicate with the thermodilution technique (Edwards Lifesciences World Trade). The cardiac index was calculated using CO indexed to body surface area. Peripheral vascular resistance was calculated using the standard haemodynamic formulas as follows: PVR = (mPAP-PCWP)/CO. Mixed-venous blood was obtained from the pulmonary arteries during RHC. Mixed-venous oxygen saturation (SvO_2) via blood gas analysis was assessed.

Health related QOL was evaluated by the Mandarin version of the SF-36 as our previous report, [26] which proved to be reliable and valid in the previous surveys in China [27,28]. All patients enrolled in the study were requested to complete the SF-36 questionnaires which include eight domains of health: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE) and mental health (MH). Scores for the SF-36 were summarised into a physical component summary (PCS) score and a mental component summary (MCS) score and ranged from 0 (worst) to 100 (best). Because Chinese normative data was not available, we used the previously reported SF-36 scale scores of Chinese women from a population-based survey of five cities in China [28].

Functional status was assessed by World Health Organization (WHO) functional class (an adaptation of the New York Heart Association functional classification). Exercise capacity was evaluated by 6-minute walking distance (6MWD).

Statistical Analysis

Continuous variables were expressed as the mean ± standard deviation (SD) or median (interquartile range) and categorical variables as frequency (percentage). Linear regression analysis was used to determine the relationships between echocardiograph-derived RV function and haemodynamics and HRQOL. As TAPSE showing the strongest correlation with haemodynamics among echocardiographic-derived RV measures, our subjects were divided into two groups according to the recommended abnormality threshold of TAPSE by American Society of Echocardiography (ASE) guideline [29]: patients with a TAPSE <17 mm and those with a TAPSE ≥17 mm. The mean group values were compared using two-tailed t test or Mann-Whitney U test, and proportions using Chi-square test or Fisher's exact test.

Univariate linear regression analysis was performed to identify the factors associating with PCS and MCS. On the basis of potential clinical and haemodynamic relevance, the following clinical and echocardiographic candidate variables were tested: age, duration of SLE, SLEDAI≥ 5, body mass index (BMI), mean blood pressure (BP), heart rate, plasma N-terminal pro-brain natriuretic peptide (NT-proBNP), 6MWD, LV eccentricity index, RV basal diameter, RV EDA, RA EDA, TAPSE <17 mm, RVFAC, S′, RV MPI, PASP, and presence of pericardial effusion (PE).

Of all four echocardiographic-derived RV systolic function, including TAPSE, RVFAC, S′, and RV MPI, TAPSE exhibited the highest regression coefficient with PCS and MCS scores, thus, TAPSE < 17 mm as the only indicator of echocardiographic-derived RV systolic function entered the multivariate model. Other candidate variables that associated with PCS or MCS on univariate analysis ($p < 0.10$) were all included in the corresponding stepwise multivariate model with entry and retention in the model set at a significance level of 0.05.

Regression coefficients (β) and 95% confidence intervals (CI) were generated for each variable. A two-tailed p value of <0.05 was considered as statistically significant. Statistical analysis was performed using SPSS software (SPSS version 22.0, IBM Inc., Armonk, NY, USA).

Results

A total of 60 female SLE-APAH participants with a mean age of 33.6 years were enrolled (Table 1). At the time of enrolment, the median duration of SLE was 4 years. There were 35 patients (58.3%) with low disease activity (SLEDAI 0-4).

Table 1 Clinical and haemodynamic parameters for enrolled subjects.

Variable	Total (n = 60)
Age, years	33.6 ± 8.2
Duration of SLE, median (IQR), years	5 (2, 11)
Raynaud's phenomenon, n (%)	38 (63.3)
Kidney involvement, n (%)	8 (13.3)
SLEDAI < 5, n (%)	35 (58.3)
BMI, kg/m^2	20.5 ± 2.9
SBP, mmHg	113 ± 15
DBP, mmHg	75 ± 10
Heart rate, beats/min	82 ± 14
NT-proBNP, median (IQR), ng/ml	911.0 (217.0, 2306.0)
WHO Class III~ IV, n (%)	25 (41.7)
6MWD, m	439 ± 115
mRAP, mmHg	4.8 ± 4.5
mPAP, mmHg	43.6 ± 9.9
PVR, Wood Units	9.6 ± 4.1
Cardiac index, L/min/m^2	2.5 ± 0.6
SvO_2, %	70.9 ± 8.9

Data are reported as mean ± standard deviation unless otherwise specified.

Abbreviations: IQR, interquartile range; SLE, systemic lupus erythematosus; SLEDAI, systemic lupus erythematosus disease activity index; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; NT-proBNP, plasma N-terminal pro-brain natriuretic peptide; WHO, World Health Organization; 6MWD, six-minute walking distance; mRAP, mean right atrium pressure; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; SvO_2, mixed venous oxygen saturation.

Haemodynamics indicated an increased mPAP and PVR (Table 1). The echocardiographic parameters of all participants are summarised in Table 2. Scores for the eight subscales of the SF-36 were significantly lower in patients with SLE-APAH than Chinese women [28] (Figure 1), ranging from a low of 20.4 ± 31.4 for RP to a high of 70.8 ± 15.9 for MH, with the average PCS and MCS scores of 46.4 and 56.9 respectively.

Echocardiographic measures including RVFAC, TAPSE, RV EDA, and LV eccentricity index were correlated with haemodynamics, while TAPSE showed the strongest correlation with PVR and cardiac index among all the RV parameters (Table 3). There was no relationship between echocardiographically estimated PASP and cardiac index, although PASP correlated with invasively derived mPAP and PVR. There were no correlations between RV wall thickness or RV diastolic function and haemodynamic variables.

Table 2 Echocardiographic parameters for all subjects.

Parameters	Total (n = 60)
LVEDV, ml	71.7 ± 24.7
LVEF (Biplane), %	62.7 ± 11.8
Mitral E/A, median (IQR)	1.11 (0.87, 1.50)
Mitral e′, cm/s, median (IQR)	8.0 (5.5, 10.5)
Mitral E/e′, median (IQR)	6.6 (5.1, 9.2)
LV eccentricity index	1.23 ± 0.27
RV basal diameter, mm	44 ± 9
RV EDA, cm^2	23.3 ± 5.8
RA EDA, cm^2	15.0 ± 3.5
PASP, mmHg	54.2 ± 7.8
RVFAC†, %	21.5 ± 10.0
TAPSE, mm	16.5 ± 3.5
S′, cm/s	8.9 ± 2.3
RV MPI	0.52 ± 0.13
RV E/A, median (IQR)	0.88 (0.71, 1.16)
RV E/e′	5.1 ± 2.2
RVW, mm	5.3 ± 1.5
IVC, mm	14.513.5
IVC collapsibility <50%, no. (%)	10 (16.7)
PE, no. (%)	13 (21.7)

Data are reported as mean ± standard deviation unless otherwise specified.

Abbreviations: LV, left ventricular; EDV, end-diastolic volume; EF, ejection fraction; Mitral E/A, ratio of peak early to late diastolic transmitral flow velocity; Mitral e′, average peak early diastolic mitral annular velocity; Mitral E/e′, ratio of peak early diastolic transmitral flow velocity to average peak early diastolic mitral annular velocity; RA, right atrium; RV, right ventricle; EDA, end-diastolic area; PASP, pulmonary artery systolic pressure; FAC, fractional area change; TAPSE, tricuspid annular plane systolic excursion; S′, peak systolic velocity at the tricuspid valve; MPI, myocardial performance index; RV E/A, ratio of peak early to late diastolic transtricuspid flow velocity; RV E/e′, ratio of peak diastolic transtricuspid flow velocity to peak early diastolic tricuspid annular velocity; RVW, right ventricular free wall thickness; IVC, inferior vena cava; PE, pericardial effusion; RVFAC, right ventricular fractional area change.

†RVFAC was not obtained in three patients, because of incomplete image acquisition.

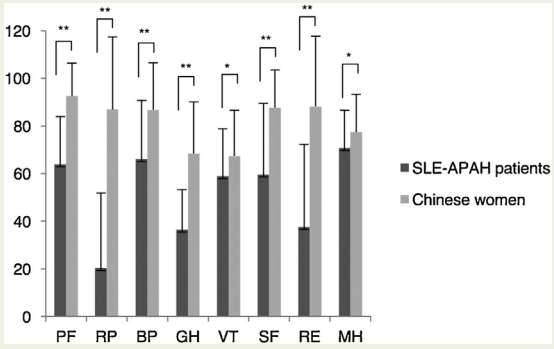

Figure 1 SF-36 scores obtained in each domain between the study subjects and Chinese women.
Grey bars represent SF-36 scores of Chinese women from the previous report [28]. Black bars represent patients with SLE-APAH.
Each bar indicates mean ± standard deviation.
*p < 0.05, **p < 0.001.
Abbreviations: PF, physical functioning; RH, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health; SLE-APAH, systemic lupus erythematosus associated pulmonary arterial hypertension

Patients with a TAPSE < 17 mm had a shorter 6MWD, lower mixed venous oxygen saturation (SvO_2%), higher plasma NT-proBNP, lower systolic BP and higher heart rates. Patients with a TAPSE < 17 mm also demonstrated an increased right heart dimension (Table 4).

By univariate linear regression analysis, echocardiographic-derived RV parameters, including TAPSE, RVFAC, S′ and LV eccentricity index were correlated with PCS, while TAPSE and S′ were also correlated with MCS ($p < 0.05$). In contrast, age, duration of SLE, heart rate, NT-proBNP, RV basal diameter, RV EDA, RA EDA, PASP, and presence of PE were not associated with PCS or MCS.

Patients with a TAPSE <17 mm had a significantly lower score in almost each domain of the SF-36 as compared to patients with a TAPSE ≥17 mm (Figure 2). A lower TAPSE (<17 mm) exhibited the strongest correlation with PCS and MCS scores among all echocardiographically-derived RV measures, as well as its association with haemodynamics (Tables 3, 5 and 6).

After adjusting for clinical profile, exercise capacity, and echocardiograph-derived RV indices, only a TAPSE of <17 mm was associated with both PCS and MCS scores ($p < 0.05$) (Tables 5 and 6). As echocardiographically-derived RV systolic function, including RVFAC and S′, also correlated with PCS or MCS scores in univariate analysis, the prognostic value of RVFAC and S′ on PCS and MCS was also tested using multiple stepwise linear regression, however, neither of them was independently related to PCS or MCS.

Table 3 Correlation of RV parameters with haemodynamics.

	mPAP		PVR		cardiac index	
	R^2	P-value	R^2	P-value	R^2	P-value
RV basal diameter, mm	0.057	0.075	0.069	0.050	0.054	0.086
RV EDA, cm^2	0.169	0.002	0.182	0.001	0.158	0.002
LV eccentricity index	0.100	0.016	0.277	<0.001	0.207	<0.001
RVFAC, %	0.194	0.001	0.256	<0.001	0.185	0.001
S′, cm/s	0.016	0.346	0.074	0.042	0.039	0.145
TAPSE, mm	0.085	0.026	0.278	<0.001	0.215	<0.001
RV E/A	0.001	0.784	0.004	0.657	0.039	0.151
RV E/e′	0.061	0.072	0.045	0.124	0.060	0.074
RV MPI	0.001	0.845	0.035	0.166	0.050	0.096
PASP, mmHg	0.239	<0.001	0.274	<0.001	0.073	0.057

Abbreviations: PASP, peak pulmonary artery systolic pressure; RV, right ventricular; MPI, myocardial performance index; RV E/A, ratio of peak early to late diastolic transtricuspid flow velocity; RV E/e′, ratio of peak early diastolic transtricuspid flow velocity; TAPSE, tricuspid annular plane systolic excursion; RVFAC, right ventricular fractional area change; LV, left ventricular; RV EDA, right ventricular end-diastolic area; RV, right ventricular; S′, peak systolic velocity at the tricuspid valve.

Table 4 Clinical, haemodynamic, and echocardiograph-derived RV parameters according to value of TAPSE.

Variable	TAPSE ≥17 mm (n = 36)	TAPSE <17 mm (n = 24)	P-value
Age, years	33.1 ± 7.8	34.3 ± 8.9	0.573
Duration of SLE, median (IQR), years	3.5 (1.1, 11.8)	4.5 (3.0, 10.4)	0.472
SLEDAI ≥ 5, no. (%)	11 (0.6)	14 (58.3)	0.033
BMI, kg/m^2	21.2 ± 2.6	19.5 ± 2.9	0.022
SBP, mmHg	116 ± 15	108 ± 13	0.033
DBP, mmHg	76 ± 10	73 ± 11	0.229
HR, beats/min	79 ± 13	87 ± 15	0.035
NT-proBNP, median (IQR), ng/ml	503.0 (132.5, 2,005.0)	1279.0 (505.0, 2,749.0)	0.048
WHO Class III∼ IV, no. (%)	12 (33.3)	13 (54.2)	0.109
6MWD, m	476.5 ± 82.4	377.9 ± 135.3	0.003
mRAP, mmHg	4.0 ± 3.6	6.4 ± 5.5	0.085
mPAP, mmHg	41.7 ± 9.4	46.5 ± 10.0	0.063
PVR, Wood Units	8.0 ± 3.0	12.1 ± 4.3	<0.001
Cardiac index, $L/min/m^2$	2.8 ± 0.5	2.2 ± 0.5	<0.001
SvO_2, %	74.2 ± 6.9	65.3 ± 9.2	<0.001
LV eccentricity index	1.2 ± 0.2	1.4 ± 0.3	0.002
RV EDA, cm^2	22.4 ± 5.9	28.3 ± 7.9	0.002
RA EDA, cm^2	14.2 ± 3.8	20.0 ± 8.0	0.001
RVFAC, %	26.1 ± 11.7	18.1 ± 11.6	0.014
S′, cm/s	10.7 ± 2.1	9.1 ± 1.7	0.004
RV MPI	0.47 ± 0.09	0.60 ± 0.16	<0.001
RV E/A	0.83 (0.69, 1.0)	0.90 (0.77, 1.31)	0.101
RV E/e′	4.7 ± 1.9	5.6 ± 2.6	0.124
RVW, mm	5.5 ± 1.5	5.1 ± 1.5	0.330
IVC collapsibility <50%	3 (8.3)	7 (29.2)	0.073
PE (%)	8 (22.2)	5 (20.8)	0.898

Abbreviations: PE, pericardial effusion; IVC, inferior vena cava; RV, right ventricular; MPI, myocardial performance index; RVFAC, right ventricular fractional area change; RV EDA, right ventricular end-diastolic area; RA, right atrial; LV, left ventricular; S′, peak systolic velocity at the tricuspid valve; RV E/A, ratio of peak early to late diastolic transtricuspid flow velocity; RV E/e′, ratio of peak early diastolic transtricuspid flow velocity to peak early diastolic tricuspid annular velocity; RVW, right ventricular free wall thickness; SvO_2, mixed venous oxygen saturation; PVR, pulmonary vascular resistance; mPAP, mean pulmonary arterial pressure; mRAP, mean right atrium pressure; 6MWD, 6-minute walk distance; plasma N-terminal pro-brain natriuretic peptide; HR, heart rate; DPB, diastolic blood pressure; SBP, systolic blood pressure; BMI, body mass index; SLE, systemic lupus erythematosus; SLEDAI, systemic lupus erythematosus disease activity index; IQR, interquartile range.

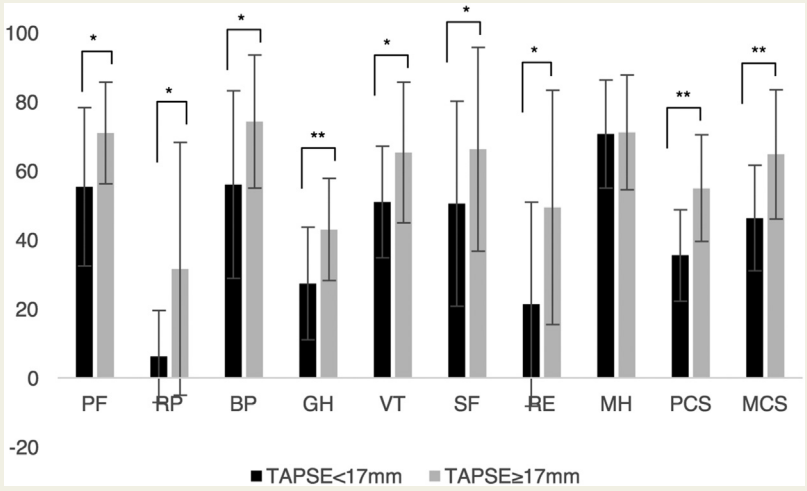

Figure 2 SF-36 scores between SLE-APAH patients from different TAPSE groups.
Black and grey bars represent SF-36 scores of SLE-APAH patients with a TAPSE <17 mm and a TAPSE of ≥17 mm respectively.
Each bar indicates mean ± standard deviation.
*$p < 0.05$, **$p < 0.001$.
Abbreviations: PCS, physical component summary; MCS, mental component summary; SLE-APAH, systemic lupus erythematosus associated pulmonary arterial hypertension; TAPSE, tricuspid annular plane systolic excursion; PF, physical functioning; RH, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health

Discussion

Our study provides new insights into the RV function and its relationship with HRQOL in patients with SLE-APAH. The present study revealed that RV systolic function was correlated with haemodynamics in patients with SLE-APAH. Moreover, among all echocardiograph-derived RV parameters, TAPSE showed the strongest correlation with haemodynamics. A lower TAPSE was related with a worse HRQOL in patients with SLE-APAH.

A previous report showed that echocardiography provided a more accurate and relevant definition of RV function than a standard RHC in patients with PH [30]. Indeed, we found echocardiograph-derived RV function not only correlated with functional status and haemodynamic indices, but also associated with HRQOL in patients with SLE-APAH,

Table 5 Relationship between clinical and echocardiograph-derived RV measures and PCS: results of univariate and multivariate analyses.

Variable	Unadjusted β (95% CI)	P-value	Adjusted β (95% CI)*	P-value
BMI, kg/m^2	2.408 (0.934 ~ 3.883)	0.002		
SLEDAI ≥ 5	−11.663 (−20.336 ~ −2.989)	0.009		
BP mean, mmHg	0.609 (0.209 ~ 1.009)	0.003		
6MWD, m	0.082 (0.042 ~ 0.121)	<0.001	0.058 (0.019 ~ 0.097)	0.005
LV eccentricity index	−26.059 (−45.100 ~ −7.019)	0.008		
TAPSE <17 mm	−18.187 (−26.115 ~ −10.260)	<0.001	−15.797 (−24.746 ~ −6.848)	0.001
S′, cm/s	3.049 (0.902 ~ 5.196)	0.006		
RVFAC	39.992 (2.616 ~ 77.367)	0.036		
RV MPI	30.918 (−64.195 ~ 2.359)	0.068		

Abbreviations: PCS, physical component summary; CI, confidence interval; BP, blood pressure; RV MPI, right ventricular myocardial performance index; RVFAC, right ventricular fractional area change; S′, peak systolic velocity at the tricuspid valve; TAPSE, tricuspid annular plane systolic excursion; LV, left ventricular; 6MWD, 6-minute walk distance; BP, blood pressure, SLEDAI, systemic lupus erythematosus disease activity index; BMI, body mass index.
*The multivariable models included BMI, SLEDAI ≥ 5, BP mean, 6MWD, LV eccentricity index, and TAPSE <17 mm.

Table 6 Relationship between clinical and echocardiograph-derived RV measures and MCS: results of univariate and multivariate analyses.

Variable	Unadjusted β (95% CI)	p value	Adjusted β (95% CI)*	p value
BMI, kg/m^2	2.500 (0.838 ~ 4.161)	0.004		
SLEDAI ≥ 5	−7.278 (−17.343 ~ 2.787)	0.153		
BP mean, mmHg	0.097 (−0.300 ~ 0.655)	0.459		
6MWD, m	0.053 (0.005 ~ 0.101)	0.031		
LV eccentricity index	5.777 (−16.865 ~ 28.418)	0.611		
TAPSE <17 mm	−17.616 (−26.828 ~ −8.405)	<0.001	−12.887 (−24.018 ~ −1.755)	0.024
S′, cm/s	3.353 (0.938 ~ 5.769)	0.007		
RVFAC	−0.975 (−44.213 ~ 42.263)	0.964		
RV MPI	−27.536 (−64.991 ~ 9.920)	0.147		

MCS, mental component summary.

Abbreviations: RV MPI, right ventricular myocardial performance index; RVFAC, right ventricular fractional area change; S′, peak systolic velocity at the tricuspid valve; TAPSE, tricuspid annular plane systolic excursion; LV, left ventricular; 6MWD, 6-minute walk distance; BP, blood pressure; BP, blood pressure, SLEDAI, systemic lupus erythematosus disease activity index.

*The multivariable models included BMI, 6MWD, and TAPSE <17 mm.

suggesting monitoring of RV function with noninvasive imaging modalities as being more acceptable and valuable to patients with SLE-APAH. Furthermore, Veerdonk et al. [31] studied the relationship between the effect of PH therapy on arterial load and RV function, and demonstrated that changes in PVR only moderately correlated with changes in RVEF, moreover, in 25% of patients with PVR improved, progressive RV dysfunction was seen and associated with poorer outcome. It suggested that therapy focussing on RV systolic function may be an important therapeutic target for PAH and echocardiograph is a useful indicator for evaluating treatment effect in SLE-APAH patients.

Recently, HRQOL, which can assess the patient's subjective perception of the impact of disease and treatment on their daily life, has become increasingly important in defining overall health status and has been used as a patient-reported outcome in a few PAH clinical trials [32,33]. Our study is the first, to our knowledge, to assess the relationship between echocardiograph-derived RV function and HRQOL in patients with SLE-APAH. Our study demonstrated that RV systolic function is of greater importance in determining HRQOL than clinical and functional measures in patients with SLE-APAH. Echocardiographic RV function assessment should be considered to be included in clinical practice and used as a secondary outcome in future clinical trials of SLE-APAH.

Recent studies have shown that TAPSE reflected RV systolic function and prognosis in patients with PAH, and that serial measuring of TAPSE played an important role in monitoring responses to PAH therapy [5,34]. In the present study, TAPSE was the only echocardiograph-derived RV parameter correlating to both physical and mental component summary scores in patients with SLE-APAH. Furthermore, TAPSE also correlated well with pulmonary haemodynamics and exercise capacity, consistent with a previous study in PAH [24]. Although we statistically showed TAPSE correlated with pulmonary haemodynamics and better than other echocardiograph-derived RV parameters, the correlation was modest at its best. The small sample size may limit the conclusiveness of our results and future studies with a larger number of patients with SLE-APAH, will be required to confirm our findings.

In addition, TAPSE is easily measured and highly reproducible with greater prognostic relevance compared to other echocardiographic indicators of RV function in patients with PH [24]. Recently, three-dimensional (3D) and 2D and 3D speckle-tracking (2D-STE, 3D-STE) echocardiography have been validated as promising tools for the evaluation of RV systolic function in patients with PAH [35,36]. These promising echocardiographic parameters had a significant correlation with RV failure haemodynamics, and were better than conventional parameters [36]. However, these techniques have several limitations. First, the STE strain software used was originally created for the assessment of LV systolic function and only later adapted for the RV [37]. However, RV geometry and spatial orientation are different from LV, including the RV chamber shape, which is more complex, and a thin RV wall that makes it difficult to limit the width of the region of interest to the myocardium, especially when the images are not excellent. Moreover, these techniques need post hoc offline analysis, expertise and cost much time, which makes it difficult to use in routine clinical practice.

Limitations

The small sample size and cross-sectional design may limit the conclusiveness of our results. Second, HRQOL could be affected by a lot of residual confounding factors (such as socioeconomic status and education) that we did not analyse, which might have caused biases. Further, large follow-up

studies are needed to assess the relationship between RV function and outcome and effect of therapy in patients with SLE-APAH.

Conclusion

Echocardiographic measurements as promising noninvasive indices of RV remodelling and function are correlated with quality of life, as well as clinical and haemodynamic features in patients with SLE-APAH. In particular, TAPSE is superior to other echocardiograph-derived RV indices in determining HRQOL of these patients. Thus, findings from the current study that TAPSE imparts important role in evaluating HRQOL in patients with SLE-APAH are particularly clinically relevant, and TAPSE, an easily obtained echocardiographic parameter, would be applicable to clinical practice.

Declaration of Conflicting Interests

The authors declare that there is no conflict of interest.

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