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Different Combinations of Right Ventricular Longitudinal Velocity and Displacement Can Be Applied Effectively for Diagnosis of Right Heart Failure in Chinese Patients

Dechun Su, MD, PhD,[1] Wanxiang Zheng, MD,[2] Yan Liu, MD, PhD,[1] Tao Cong, MD, PhD,[1] Yinghui Sun, MD,[1] Zhijuan Shang, MD,[1] Ke Wang, MD, PhD[1]

[1]Department of Cardiology, The First Affiliated Hospital of Dalian Medical University, Dalian, Liaoning; [2]Department of Cardiology, The First Affiliated Hospital of Third Military Medical University, Chongqing, China

ABSTRACT

Background: The noninvasive evaluation of right ventricular function (RVF) in cardiovascular and pulmonary diseases remains a challenge. Internationally recommended echocardiographic parameters for the evaluation of RVF may not be applicable to China, because of the limited examination time per patient, the varying skill levels of ultrasonographers, inadequate allocation of professional specialties, and outdated instruments and equipment.

Methods: Sixty-two patients admitted for right heart failure and 52 healthy volunteers were included in the analysis. The tricuspid annular plane systolic excursion (TAPSE), peak systolic velocity in the tricuspid annulus of the right ventricular free wall (S′), myocardial performance index, right ventricular fractional area change, and Doppler peak strains in the base and mid cavity were evaluated and compared between groups.

Results: Compared with the control group, all RVF parameters in the right heart failure group showed significant deterioration ($P < .001$). However, only TAPSE and S′ were finally included in the discriminant equation. The diagnostic cutoff values derived from the receiver operating characteristic curve were <13.74 mm and <9.5 cm/s, respectively. The highest specificity in the diagnosis of right heart failure (100%) was achieved using S′ <9.5 cm/s, either alone or in combination with TAPSE <13.74 mm. The highest diagnostic sensitivity (90.32%) was achieved using either TAPSE <13.74 mm or S′ <9.5 cm/s alone.

Conclusion: TAPSE and S′ are more suitable than other parameters for the diagnosis of right heart failure in Chinese patients. Different combinations of TAPSE and S′ can be applied effectively for the diagnosis of right heart failure.

INTRODUCTION

The right ventricle plays an important role in many cardiovascular diseases, such as tetralogy of Fallot [Davlouros 2002], primary cardiomyopathy [Juilliere 1997], myocarditis [Mendes 1994], idiopathic pulmonary arterial hypertension [van Wolferen 2007], and myocardial infarction [Zehender 1993]. These diseases have a high incidence in patients with right heart failure and contribute to rates of disability and mortality, which are major health care issues. Right ventricular function (RVF) is an important predictive factor for exercise capacity and survival in advanced heart failure [Di Salvo 1995]. Determination of RVF is extremely valuable for the early diagnosis of cardiovascular and pulmonary diseases, and for the establishment of rational treatment plans.

However, the selection of an evaluation method that is noninvasive, low-cost, accurate, and easy to perform is still an unresolved issue. Cardiac catheterization, radionuclide ventriculography, and magnetic resonance imaging (MRI) are time-consuming, expensive, and/or invasive. For the noninvasive evaluation of the right ventricle, echocardiography has certain advantages. However, because of various factors, no single ultrasound parameter has been proven able to reflect RVF perfectly.

China has a large population, and the number of hospitalized patients is considerable; therefore, the echocardiography examination time for each patient usually has to be limited to within 20 minutes. In addition, there are some undesirable conditions in China, such as the varying skill levels of ultrasonographers, inadequate allocation of professional specialties, and outdated instruments and equipment [Wang 2011]. Therefore, internationally recommended indexes for the evaluation of RVF may not necessarily be applicable to China.

We selected the methodologies that were easy to apply in China, such as Doppler tissue imaging (DTI), M-mode echocardiography, peak systolic velocity in the tricuspid annulus of the right ventricular free wall (S′) measured by two-dimensional echocardiography, strain of the middle and basal segments of the right ventricular free wall, tricuspid annular plane systolic excursion (TAPSE), and right ventricular fractional area change (RVFAC). We aimed to investigate the diagnostic value of these parameters for right heart failure in clinical practice, in order to identify rapid and practical diagnostic indexes for right heart failure that are suitable for Chinese patients and applicable in China.

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Correspondence: Ke Wang, Department of Cardiology, The First Affiliated Hospital of Dalian Medical University, 222 Zhongshan Road, Dalian 116011, Liaoning, China; +86 13941152136 (e-mail: kewangdoc@126.com).

MATERIALS AND METHODS

Study Subjects

Sixty-two patients who were admitted to the Department of Cardiology of the First Affiliated Hospital of Dalian Medical University between April 2010 and March 2011 were included in the right heart failure group. Right heart failure was defined and diagnosed according to the 2008 ESC [Dickstein 2008] and the 2009 CCS guidelines [Howlett 2009] on heart failure. We included in our study patients with moderate or severe heart failure (17 functional class II, 25 functional class III, and 20 functional class IV). The inclusion criteria were diagnosis of a basic cardiopulmonary disease that could cause right heart failure, and showing symptoms and signs of right heart failure [Haddad 2008; Lang 2005]. The exclusion criteria were moderate to severe (or worse) tricuspid valve insufficiency, more than moderate pericardial effusion, constrictive pericarditis, restrictive cardiomyopathy, and severe hepatic or renal dysfunction.

Age-matched healthy adults were selected for the control group. All subjects investigated gave their written informed consent to immediate echocardiography. The research protocol was approved by the local institutional review committee.

Instruments and Methods

The patients' general data were collected and recorded in detail, including age, sex, medical history, and basic diseases. The echocardiography examination was performed using a Vivid 7 digital color Doppler ultrasound (GE Vingmed Ultrasound AS, Horten, Norway) for the following analyses. Commonly used parameters in two-dimensional echocardiography were measured as recommended [Lang 2006], including RVFAC and DTI of the tricuspid annulus movement, obtained from the apical 4-chamber view. A 1.5-mm sample volume was placed sequentially at the septum and free wall of the annular sites. Analysis was performed for the systolic (S′) and the early (E′) and late (A′) diastolic peak velocities. The DTI isovolumic relaxation time (IVRT) was obtained, measured from the cessation of the S-wave to the onset of the E′-wave. The myocardial performance index (MPI) was calculated as the sum of the isovolumic contraction time (IVCT) and the IVRT divided by the ejection time (ET), i.e., (IVCT + IVRT)/ET (Figure 1). In the standard apical four-chamber view and the M-mode ultrasound, the sample collection points were placed on the tricuspid annular sidewall at the junction between the tricuspid annulus and the right ventricular free wall. The maximum distance of the tricuspid annulus from the end-diastolic period to the end-systolic period (TAPSE) was measured for each cardiac cycle. Under the strain mode and in the apical four-chamber view, the right ventricular free wall was evenly divided into three segments: the basal segment (BS), middle segment (MS), and apical segment. The volume-sampling sites were set at the BS of the ventricular wall and the myocardium at the MS. The strain curves of these sampling points were recorded synchronously, and the peak systolic strain values were measured individually for each curve.

The images from each patient were collected separately by two ultrasonographers of the First Affiliated Hospital of Dalian Medical University. The examiners were trained for two weeks before the study on the indexes used in this study. Each parameter was measured over three cardiac cycles, or at least five cardiac cycles in the case of atrial fibrillation or an irregular ventricular rate. The final results were the means of the values obtained by the two examiners.

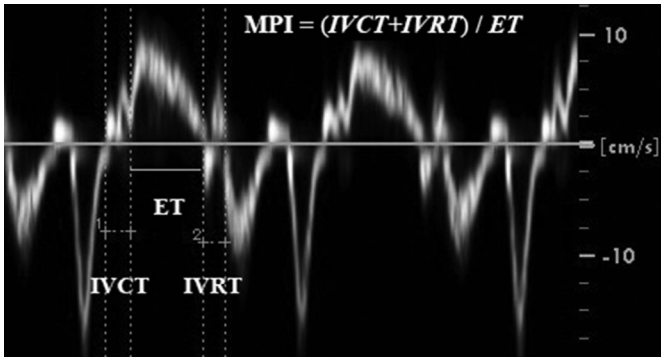

Figure 1. Tissue doppler-derived measurements of MPI obtained from the lateral tricuspid annulus. ET indicates ejection time; IVCT, isovolumic contraction time; IVRT, isovolumic relaxation time; MPI, myocardial performance index.

Statistical Analysis

Data are expressed as mean values ± standard deviation (SD) for parametric variables. Comparisons between groups were made using the unpaired t test, with $P < .05$ as the criterion of statistical significance. The receiver operating characteristic (ROC) curve was used to evaluate the values of all indexes in the diagnosis of right heart failure and to determine the optimum cutoff values. The six parameters, S′, TAPSE, RVFAC, BS strain, MS strain, and MPI, were used as independent variables. Whether they were dependent variables of right heart failure was determined by a stepwise

Table 1. Patients' Data

	RHF group (n = 62)	Control group (n = 52)	*P*
Age, y	60.8 ± 16.5	58.1 ± 15.5	.37
Sex, M/F	33/29	25/27	.58
Heart rate, bpm	78.3 ± 17.4	74.2 ± 8.3	.13
RVAW, mm	5.0 ± 0.4	4.2 ± 0.7	<.001
IVS, mm	9.6 ± 1.5	8.3 ± 1.5	<.001
RVEDd, cm	2.2 ± 0.5	1.7 ± 0.2	<.001
LVEDd, cm	5.8 ± 1.3	4.3 ± 0.5	<.001
LVEF, %	39 ± 15.6	59.7 ± 1.7	<.001

Data are expressed as mean ± standard deviation. RHF indicates right heart failure; RVAW, right ventricular anterior wall; IVS, interventricular septum; RVEDd, right ventricular end-diastolic diameter; LVEDd, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction.

method of discriminant analysis. The Fisher discriminant model was established, and back substitution was used to validate the diagnostic ability of the model. The interobserver agreement of the MPI was tested using Bland-Altman analysis for bias and precision [Bland 1986]. SPSS version 17.0 (SPSS, IBM, New York, USA) and Medcalc 11.3 (Medcalc Software, Ostend, Belgium) were used for computation.

RESULTS

Baseline Clinical Characteristics

The 62 patients enrolled in this study comprised 33 males and 29 females with an average age of 60.8 ± 16.5 years. There were 11 cases of coronary heart disease, 23 cases of dilated cardiomyopathy, 16 cases of valvular disease, 3 cases of right ventricular cardiomyopathy, 3 cases of chronic obstructive pulmonary disease, 3 cases of hyperthyroid heart disease, 2 cases of atrial septal defect, and 1 case of primary pulmonary hypertension. There were 52 patients in the control group, 25 males and 27 females, with an average age of 58.1 ± 15.5 years. Table 1 shows the baseline clinical characteristics of the patients and the results from the conventional two-dimensional ultrasound. The strain results for 10 right heart failure patients and 2 healthy individuals were not used because of unclear images, an irregular strain image curve, or incomplete display of the MS of the right ventricular free wall. Compared with the control group, all functional indexes of the right heart in the right heart failure group were significantly worse (Table 2).

Diagnostic Accuracy for Identifying Patients with Right Heart Failure

The diagnostic value of all the ultrasound indexes for right heart failure was evaluated using ROC curve analysis (Figure 2).

Table 2. Comparison of Functional Indicators between the Right Heart Failure Group and the Control Group

	n	RHF group	n	Control group	P
TAPSE, mm	62	10.9 ± 2.6	52	16.8 ± 2.8	<.001
S′, cm/s	62	7.9 ± 2.2	52	12.3 ± 1.8	<.001
MPI	60	0.6 ± 0.2	52	0.3 ± 0.1	<.001
RVEDA, cm^2	60	18.1 ± 5.8	52	11.9 ± 2.7	<.001
RVESA, cm^2	60	12.8 ± 4.8	52	6.7 ± 2.0	<.001
RVFAC, %	60	29.9 ± 10.1	52	44.2 ± 7.5	<.001
BS, %	52	20.2 ± 7.6	50	27.9 ± 6.1	<.001
MS, %	52	21.3 ± 8.3	50	32.8 ± 6.9	<.001

Data are expressed as means ± standard deviation. RHF indicates right heart failure; TAPSE, tricuspid annular plane systolic excursion; S′, the peak systolic velocity in the tricuspid annulus of the RV free wall; MPI, myocardial performance index; RVEDA, right ventricular end-diastolic area; RVESA, right ventricular end-systolic area; RVFAC, right ventricular fractional area change; BS, Doppler peak strain at the base; MS, Doppler peak strain at the mid cavity.

TAPSE, S′, MPI, RVFAC, and MS and BS strain all had diagnostic significance ($P < .001$); however, only TAPSE and S′ had areas under the ROC curves (AUC) above 0.9, being 0.939 and 0.934, respectively. The Youden index was 0.76 for TAPSE and 0.8 for S′, and the corresponding right heart failure diagnostic cutoff values were 13.74 mm and 9.5 cm/s, respectively. The AUCs for MPI, RVFAC, and MS and BS strain were 0.839, 0.865, 0.844, and 0.8, and the Youden indices were 0.56, 0.66, 0.59, and 0.55, respectively. The corresponding right heart failure diagnostic cutoff values were 0.58, 35.86%, 23.61%, and 23.46%, respectively. Stepwise discriminant analysis was used to screen the above indexes and establish discriminant equations. Since only TAPSE and S′ had independent diagnostic value, the other 4 indexes were excluded. The equations were as follows:

Right heart failure group: $Y = 1.166 \times \text{TAPSE} + 1.732 \times \text{Sm} - 14.144$

Control group: $Y = 1.779 \times \text{TAPSE} + 2.627 \times \text{Sm} - 31.808$

When the S′ and TAPSE data of the patients were reintroduced into the model, the diagnostic accuracy was 90.4%, the sensitivity was 87.1%, and the specificity was 94.2%.

Specific Diagnostic Value for Right Heart Failure Using TAPSE <13.74 mm and S′ <9.5 cm/s as Judgment Criteria

The distribution of specific data in the diagnosis of right heart failure, using TAPSE and S′ separately as determination criteria, is shown in Table 3. When S′ <9.5 cm/s was used alone or in combination with TAPSE <13.74 mm, the specificity of the right heart failure diagnosis was the highest,

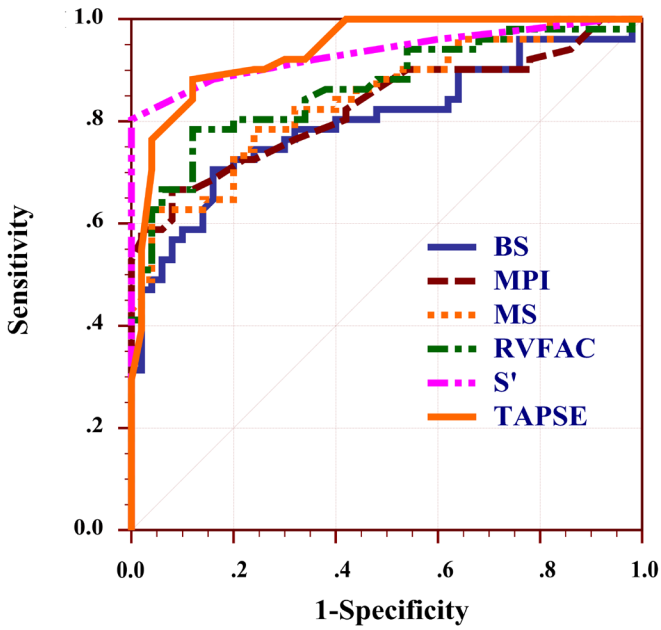

Figure 2. Receiver operating characteristic curves for Doppler peak strain at the base (BS), myocardial performance index (MPI), Doppler peak strain at the mid cavity (MS), right ventricular fractional area change (RVFAC), peak systolic velocity in the tricuspid annulus of the RV free wall (S'), and the tricuspid annular plane systolic excursion (TAPSE) for predicting heart failure.

Table 3. Using TAPSE and S' Cutoff Values as the Diagnostic Standard for Right Heart Failure

	Parameters	RHF, n T	RHF, n F	Sensitivity, %	Specificity, %	Misdiagnosis rate, %	Rate of missed diagnosis, %	PPV, %	NPV, %
TAPSE <13.74 mm	T	54	7	87.1	86.54	13.46	12.9	88.52	84.91
	F	8	45						
S′ <9.5 cm/s	T	51	0	82.26	100	0	17.74	100	82.54
	F	11	52						
TAPSE <13.74 mm & S′ <9.5 cm/s	T	49	0	79.03	100	0	20.97	100	80.0
	F	13	52						
TAPSE <13.74 mm or S′ <9.5 cm/s	T	56	7	90.32	86.54	13.46	9.68	88.89	88.24
	F	6	45						

T indicates right heart failure; F, no right heart failure; RHF, right heart failure; PPV, positive predictive value; NPV, negative predictive value; TAPSE, tricuspid annular plane systolic excursion; S′, systolic excursion velocity.

reaching 100%, and the misdiagnosis rate was 0%. When either TAPSE <13.74 mm or S′ <9.5 cm/s was used alone, the sensitivity of right heart failure diagnosis was the highest, reaching 90.32%, and the missed diagnosis rate was the lowest, being only 9.68% (Table 3).

Interobserver Variability

An analysis of the interobserver variability was performed in 62 consecutive right heart failure patients and 52 consecutive control patients who were evaluated by two blinded operators. The mean difference in the control group was 0 at a 95% interval of agreement, with an absolute difference of -0.14 to 0.13. The mean difference in the right heart failure group was -0.03 at a 95% interval of agreement, with an absolute difference of -0.8 to 0.74 (Figures 3 and 4).

DISCUSSION

Ventricular contraction is achieved by the combined action of the circular myocardial fibers, longitudinal myocardial fibers, and ventricular septal motion. Compared to the left ventricle, the right ventricle has a greater proportion of longitudinal myocardial fibers, which play a more important role in blood pumping [Carlsson 2007]. The velocity and displacement of the longitudinal movement of the tricuspid annulus can reflect RVF in the long-axis direction and the overall contractile function of the right ventricle. Because the left ventricular contractile function usually affects the systolic motion of the tricuspid annulus at the interventricular septum, the tricuspid annulus movement at this location cannot simply reflect the RVF. In particular, the right heart failure of most patients included in this study developed from left heart failure (ie, dilated or ischemic cardiomyopathy). As a result, the contractile function of both the left and right ventricles decreased, and the decrease in the left ventricular contractile function usually affected the functional assessment of the right ventricle via its effects on the interventricular septum and pericardium [Dell'Italia 2012]. The septum may be a morphologically and functionally bilayer structure that is supplied by different coronary arteries [Boettler 2005]. Therefore, this study only adopted the systolic displacement and velocity of the tricuspid annulus at the right ventricular free wall as indexes for the evaluation of the overall contractile function of the right ventricle.

The right ventricle can be imaged clearly in the apical four-chamber view. Compared with other indexes for the assessment of cardiac function, TAPSE has numerous advantages, such as easy operation, no requirement for endocardium tracing, not being constrained by the geometric morphology, high reproducibility, no extra cost, and easy wide application. Therefore, it can be used for an immediate understanding of the state of cardiac function at the bedside [Rudski 2010]. The measurement of TAPSE is not affected by cardiac rhythm. A right ventricular TAPSE ≤14 mm and pulmonary arterial systolic pressure ≥40 mmHg are independent predictors for poor prognosis in patients with chronic heart failure [Ghio 2013]. Consistent with previous studies [Lamia 2007; Ueti 2002], this study also showed that TAPSE was closely associated with right ventricular contractile function, as evidenced by the fact that the TAPSE value in the right heart failure group was significantly lower than that in the healthy control group. Using TAPSE <13.74 mm as a determination criterion, the sensitivity and specificity for the diagnosis of right ventricular failure were both relatively high, and the missed diagnosis and misdiagnosis rates were both lower than 15%.

DTI does not depend on the geometric morphology of the ventricles and does not require tracing of the endocardium. In addition, this approach is not affected by the strength of the echo signals reflected by tissues and is not influenced by preload or afterload [Vogel 2002]. The peak systolic velocity of longitudinal motion in the tricuspid annulus (S′) can reflect the right ventricular longitudinal systolic function, which is easy to derive, has good reproducibility, and can be used widely [De Castro 2008; Turhan 2007]. The S′ value of the tricuspid annulus in the right heart failure group in this study was significantly lower than that in the normal control group.

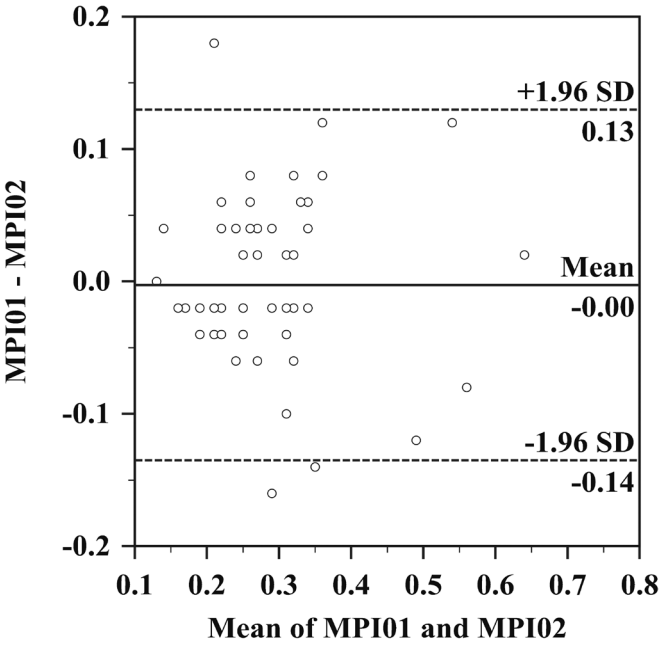

Figure 3. Bland-Altman plot for the myocardial performance index (MPI) at the basal tricuspid lateral annulus for the control group. The differences between the methods are displayed against the average of both measures. The lines represent the mean difference and 95% interval of agreement for the absolute values of the differences (n = 52).

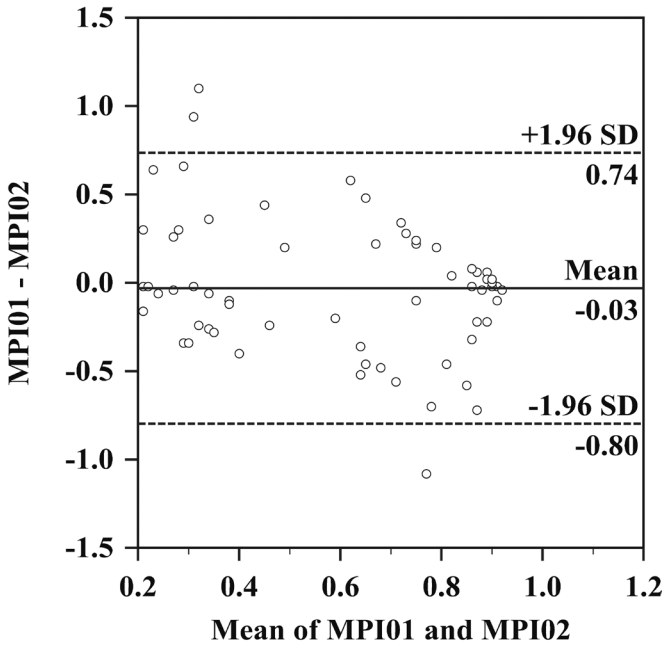

Figure 4. Bland-Altman plot for the myocardial performance index (MPI) at the basal tricuspid lateral annulus for the right heart failure group. The differences between the methods are displayed against the average of both measures. The lines represent the mean difference and 95% interval of agreement for the absolute values of the differences (n = 62).

With a value <9.5 cm/s as cutoff, the sensitivity of S′ for the diagnosis of right heart failure was over 80%, and the specificity reached 100%. Meluzin et al [Meluzin 2001] showed that S′ and right ventricular ejection fraction measured by radionuclide ventriculography had a high correlation, as evidenced by the result that the diagnostic sensitivity of S′ <11.5 cm/s for patients who had a right ventricular ejection fraction <45% was 90%, with a specificity of 85%. The sensitivity in this study was lower than that reported by Meluzin et al, while the specificity was higher, perhaps because of the lower cutoff value that we selected.

The MPI is a parameter reflecting the overall ventricular function. Compared with TAPSE and S′, the MPI can more sensitively reflect early changes in overall ventricular function [Tei 1995]. Although there was a difference in the MPI between the two groups in this study, the MPI was not included in the final discriminant equation. The interobserver reproducibility test showed that the reproducibility of the right heart failure group was worse than that of the control group. The start and end points of S′, E′, and A′ in patients with right heart failure are usually difficult to distinguish using DTI. Furthermore, when right heart failure is accompanied by atrial fibrillation and an irregular R-R interval, the MPI results will not be accurate; however, in this study, patients with atrial fibrillation accounted for 48.39%. All of the above factors could lead to low reproducibility and low accuracy for this index. Furthermore, additional issues also affect the above problems, such as the varied skill levels of the ultrasonographers, and the insufficient examination and analysis time for each patient due to the huge population of China.

The stepwise discriminant analysis and ROC results all indicated that S′ and TAPSE had much greater diagnostic values for right heart failure than the other parameters. Back substitution of all parameters for all included cases into the discriminant equation showed that the diagnostic accuracy was 90.7%, the sensitivity was 87.1%, and the specificity was 94.2%, indicating that the discriminant equation certainly has diagnostic value for Chinese patients with right heart failure. Thus, this diagnostic equation could be recommended in basic level hospitals in China. The application of the joint standard of TAPSE <13.74 mm and S′ <9.5 cm/s had the highest sensitivity in diagnosis and the lowest missed diagnosis rate; therefore, it could be used for the screening of right heart failure. When these two standards were used in combination, or S′ was used alone, the specificity reached 100% as the sensitivity decreased, and the misdiagnosis rate was zero; thus, this technique could be used to rule out heart failure and reduce the misdiagnosis rate. The combination of TAPSE and S′, which are simple measurements available in primary care units, increased the diagnostic accuracy in right heart failure.

RVFAC has a close correlation with the right ventricular ejection fraction measured by MRI [Anavekar 2007], and it can effectively predict mortality in cardiovascular diseases [Zornoff 2002]. However, the stepwise discriminant analysis showed that the diagnostic value of RVFAC for right heart failure was clearly not as high as that of S′ and TAPSE. This

might be because the right heart failure in many patients in this study developed from left heart failure; thus, the right ventricle might be compressed by the enlarged left ventricular cavities, affecting the accuracy of the RVEDA, RVESA, and RVFAC measurements. Another possible reason is technological limitations leading to a lower sensitivity for RVFAC compared to S′ and TAPSE, such as the inaccurate tracing of the endocardium due to the abundance of right ventricular trabecular muscle.

Myocardial strain more accurately reflects the characteristics of local myocardial movement. For a cutoff value of right ventricular systolic strain <20%, the sensitivity and specificity in the assessment of right ventricular dysfunction were 91% and 63%, respectively [Urheim 2005]. Right ventricular global longitudinal strain is a sensitive marker of right ventricular dysfunction and correlates with postoperative mortality [Ternacle 2013]. Animal studies showed that the apical position of the heart is relatively stable during the cardiac cycle [Rushmer 1953], and the magnitude of its movement is far smaller than the movement of the valve annulus. In addition, a portion of patients with right heart failure have an enlarged right ventricle; thus, it is difficult to acquire complete apical images simultaneously in the apical four-chamber view. Therefore, in this study, we selected only the basal and middle segments of the right ventricular free wall for strain analysis. We found that the BS and MS of the right ventricular wall in patients with right heart failure both had significantly lower strain values than those in the normal control group, and the reduction in MS strain was more significant. This indicated that patients with right heart failure symptoms and signs already showed abnormal changes in the mechanical movement of the right ventricle, and that these abnormal changes were even more apparent in the MS. In both the right heart failure and control groups, the strain in the MS was slightly higher than in the BS, suggesting that a larger deformation occurred in the MS of the right ventricle, possibly due to its greater activity. However, the BS and MS strain values were not included in the discriminant equation. We found that the reproducibility of strain was not ideal. It was difficult to obtain satisfactory images to identify each peak wave in the heart failure patients. Indicatively, 10 cases in the heart failure group did not have strain results because of unsatisfactory imaging. Consequently, the clinical application of this index is limited.

Limitations

The sample size was small. A large-scale trial is required for further confirmation. Second, patients were screened strictly based on their symptoms and signs, but the right ventricular contractile function was not evaluated using "gold standard" methods, such as MRI or cardiac catheterization; this may have decreased the reliability of the experimental results. Third, this study included patients with significant clinical symptoms and severe disease and the conclusions may not apply to patients with a mild condition. Fourth, this study did not use three-dimensional ultrasound. However, this technique does not correspond to current clinical conditions and cannot be promoted in China because of its high requirements in terms of instruments and ultrasound operators.

CONCLUSION

1. TAPSE and S′ of the tricuspid annulus are simple and reliable indexes for the diagnosis of right heart failure and the assessment of right ventricular contractile function; in particular, they are suitable for conditions in China; 2. The optimized combination and the discriminant equation of TAPSE and S′ of the tricuspid annulus can quantitatively reflect RVF. The parallel use of these two indexes can increase the sensitivity and decrease the missed diagnosis rate, thus being suitable for screening for right heart failure. When these two methods are used in combination, the specificity is high, and the misdiagnosis rate is low, suggesting that this methodology can be applied in clinical diagnosis to rule out right heart failure.

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