Current perspective

The usefulness of pulsed tissue Doppler for the clinical assessment of right ventricular function

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Key words:
Diastole; Right ventricle; Systole.

Standard Doppler echocardiographic evaluation of the right ventricular (RV) function has several limitations because of a difficult technical approach. The purpose of the present review was to investigate, even in the light of such problems, the usefulness of pulsed tissue Doppler (TD) during the assessment of RV transverse and longitudinal function on the basis of the regional velocities and time intervals.

TD-derived (systolic and diastolic) velocities of the RV free wall and of the lateral tricuspid annulus have been used to establish reference values in healthy subjects and in different cardiac diseases. Some studies have shown the usefulness of myocardial systolic velocities for the detection of RV systolic failure at rest and of right coronary artery stenosis during stress. The myocardial early diastolic velocities, combined to Doppler standard tricuspid inflow measurements, represent reliable indexes of right chamber hemodynamics, the ratio between the Doppler tricuspid E velocity and the TD-derived early diastolic velocity of the lateral tricuspid annulus being positively related to the mean right atrial pressure after heart transplantation. Even the assessment of RV regional time intervals may have clinical implications. In particular, the relaxation time of the lateral tricuspid annulus, very short or even absent in healthy subjects, increases progressively with the pulmonary systolic artery pressure and its length is strongly influenced also by the increasing RV wall thickness in septal hypertrophic cardiomyopathy and in hypertensive left ventricular hypertrophy. The interaction between the two ventricles is identified by assessing the TD velocities of the RV tricuspid annulus which are often associated with the corresponding velocities of the mitral annulus in different pathologies. On the grounds of these studies, the clinical use of pulsed TD merits consideration. Longitudinal follow-up of TD RV patterns will be useful to evaluate the progression from early RV wall dysfunction until the development of global RV failure and the possible beneficial effect of cardiac drugs on RV function as determined by TD evaluation.

(Ital Heart J 2002; 3 (4): 241-247)

Received December 3, 2001; revision received February 6, 2002; accepted February 21, 2002.

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Introduction

In contrast to early investigations[1-3], it is now recognized that the right ventricle is not a passive conduit but functions as a pump. While left ventricular (LV) function may be accurately assessed at standard Doppler echocardiography[4-6], the evaluation of the right ventricular (RV) structure and function has several limitations due to a difficult approach, mainly related to the fact that this chamber is located behind the sternum and to its geometric configuration (the main RV components, that is the inlet tract, the trabecular part and the outlet tract are positioned in different planes).

This precludes accurate volume and wall motion determination using currently available echocardiographic imaging techniques[7]. Furthermore, it has to be taken into account that the RV stroke volume is dependent on the interaction of the free wall, the interventricular septum and the outflow tract, each of which markedly differs in geometric and contractile properties. Even the evaluation of RV hemodynamic function on the basis of both conventional diastolic and systolic indexes is problematic because values are not comparable to those obtained for the left ventricle. Finally, even the characteristics of the pulmonary artery resistances have to be carefully taken into consideration since under abnormal conditions the highly compliant pulmonary vascular bed may become a high pressure system. All these aspects present important clinical implications in different diseases involving the right ventricle such as coronary artery disease, chronic obstructive lung disease, congenital heart disease, arrhythmogenic dysplasia, and even in LV pathologies which influence this chamber because of anatomical and/or functional interactions[8,9]. On these grounds, the present review highlights the potential applications of pulsed tissue Doppler (TD) in the clinical setting.

Standard Doppler echocardiographic approach to the right ventricle

Several attempts have been performed to measure RV volumes, and thus the RV ejection fraction, by using different geometric models and applying the area-length method or modified Simpson rule[7,10]. Despite the good correlation with angiographic RV volumes and ejection fraction, these techniques are very complex and not easy to perform in a clinical setting. In the 1980s, Kaul et al.[11], taking into account that the RV shortening occurs mainly along its longitudinal axis, proposed the measure of the tricuspid annular plane systolic excursion (TAPSE) as an accurate index of RV systolic function. This determination may be performed at two-dimensional or M-mode techniques. The TAPSE highlighted strong correlations with the RV ejection fraction measured at both radionuclide ventriculography and RV catheterization[11]. It appears largely reduced in several pathologies involving the right ventricle such as RV myocardial infarction[12] and heart failure[13,14], and even in LV acute infarction of the inferior wall[12]. The main limitation of the assessment of the TAPSE is that it allows for the estimate of only the RV systolic function whereas it is recognized that the atrioventricular plane displacement is related to both the systolic and diastolic performance[15]. Further information about RV systolic function is provided by the RV Doppler outflow tract profile where velocities and systolic time intervals (RV pre-ejection time, ejection time, acceleration time and their ratios) can be easily measured and are also very sensitive to changes in pulmonary artery pressure[16]. In case of an increase in the systolic pulmonary artery pressure, the Doppler RV ejection curve is characterized by a prolonged RV pre-ejection period, an early systolic peak velocity and an acceleration time < 60 ms, while the peak velocity of a tricuspid regurgitation may be used to quantify the degree of systolic pulmonary artery pressure[17-19]. With regard to the necessity of obtaining information about RV diastolic function, the detection of pulmonary regurgitation allows the quantification of the RV end-diastolic and mean pulmonary artery pressures[18,19] while the Doppler-derived tricuspid inflow pattern is useful for the determination of the homologous velocities and time intervals currently obtained by LV mitral inflow[20]. It also has to be mentioned that RV volume overload produces RV dilation and paradoxical motion of the interventricular septum mainly due to a reversal of the end-diastolic pressure gradient between the two ventricles[21], whereas RV pressure overload is often associated with hypertrophy of the RV free wall, whose identification necessitates multiple-view echocardiography[22].

Tissue Doppler approach to the right ventricle

Color or pulsed TD extends Doppler applications beyond the analysis of cardiac blood flows to the evaluation of myocardial wall function[23-25]. In particular, pulsed TD allows for serial quantitative assessment of systolic and diastolic motion of the LV and RV walls, by measuring the regional velocities and time intervals. Pulsed TD of the right ventricle may be performed by placing, in the apical 4-chamber view, the sample volume at the level of the myocardial walls (in particular, the RV anterior wall and the septal wall) or at the level of the lateral tricuspid annulus which provides information about the global longitudinal RV motion. The schema of the typical RV pulsed TD profile, characterized by a systolic myocardial (S_m) velocity above the baseline and two diastolic – early (E_m) and atrial (E_m) – velocities under the baseline, is depicted in figure 1. The myocardial systolic indexes include the peak velocity of S_m (m/s), the pre-contraction time (from the onset of the ECG Q wave to the beginning of S_m veloc-

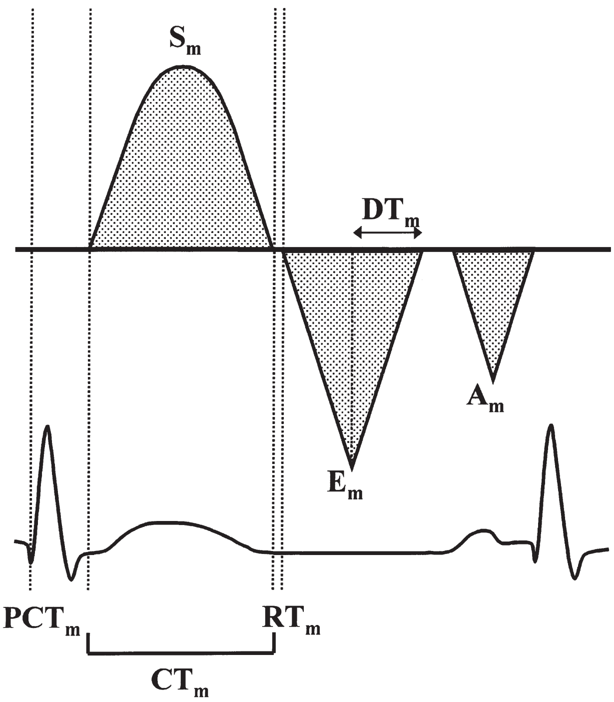

Figure 1. *Schema of the right ventricular tissue Doppler normal pattern, characterized by a myocardial systolic (S_m) velocity and two diastolic velocities – early (E_m) and atrial (A_m). The right ventricular myocardial relaxation time (RT_m) is much shorter than at the level of the left ventricular walls. CT_m = myocardial contraction time; DT_m = myocardial deceleration time; PCT_m = myocardial pre-contraction time.*

ity) and the contraction time (from the onset to the end of S_m) (both in ms). The myocardial diastolic indexes are represented by the peak velocities of E_m and A_m (m/s), the E_m/A_m ratio, the E_m deceleration time (ms), and the relaxation time (RT_m, in ms) (taken as the time interval occurring between the end of S_m and the onset of E_m) which is much shorter than at the level of the LV walls. The major advantage of pulsed TD compared to the analysis of RV longitudinal shortening (TAPSE) is that it allows very easy and fast assessment of the atrioventricular plane displacement and also permits an estimation of both the RV systolic and diastolic functions.

Pulsed TD has been evaluated in healthy adults in studies which assessed the TD-derived RV transverse and longitudinal velocities, establishing normal reference values for adults at the level of the RV free wall[26,27] and of the lateral tricuspid annulus[28]. Of interest, the regional diastolic E_m and E_m/A_m ratio show a downward trend with aging. In our experience[29-32], we also evaluated the RV myocardial systolic and diastolic time intervals. Experimental studies have reported that in normal conditions, the right ventricle, unlike the left ventricle, starts its diastolic filling without an isovolumic relaxation period[33] since it works against a lower vascular impedance. Accordingly and as mentioned above, we observed that the TD-derived RV RT_m (measured at the level of the free RV wall or of the lateral tricuspid annulus) is very short or even absent in healthy subjects[28-32].

The assessment of right ventricular regional velocities by pulsed tissue Doppler in diseases

The possible usefulness of pulsed TD for the detection of the RV myocardial dysfunction occurring in several pathologies directly or indirectly involving the right ventricle has been investigated.

Heart failure. Meluzin et al.[34] demonstrated that the evaluation of the tricuspid annular peak systolic velocity provides a simple and non-invasive means for the assessment of the global RV systolic longitudinal function in patients with congestive heart failure. The authors observed a significantly lower peak systolic tricuspid velocity in patients affected by heart failure, being closely related to the RV ejection fraction as measured at first-pass radionuclide ventriculography. Of interest, a systolic annular peak velocity < 11.5 cm/s predicted RV systolic dysfunction (a RV ejection fraction < 45%) with a sensitivity of 90% and a specificity of 85%. The proposed approach offers a parameter which may be quickly determined, renders the analysis of the tricuspid annular motion more attractive, and extends its application in the clinical setting.

Heart transplantation. Sundereswaran et al.[35] have reported other possible applications of TD. These authors measured the RV filling pressure after heart transplantation and compared pulsed TD RV measurements to those obtained at right-sided cardiac catheterization. In a series of 38 transplanted patients, the authors combined the Doppler tricuspid E velocity with the E_m of the lateral tricuspid annulus and observed that the E/E_m ratio was positively and strongly related to the mean right atrial pressure ($r = 0.79$, $p < 0.001$). This study has a main clinical implication since the mean right atrial pressure is a recognized predictor of acute transplant rejection.

Coronary artery disease. Pulsed TD has also been used for the detection of coronary artery disease involving the right ventricle. Using pulsed TD (RV free walls close to the tricuspid annulus), Rambaldi et al.[36] assessed the feasibility and diagnostic accuracy of right coronary artery narrowing during dobutamine stress echocardiography. A progressive blunted increase and/or a decrease in the S_m velocity (< 25% of the increase) between 10 μg/kg/min and peak stress was predictive of a significant right coronary artery narrowing (≥ 50%), with a sensitivity of 82%, a specificity of 78% and an overall accuracy of 79%. In the setting of acute myocardial infarction, Alam et al.[37] found a significant reduction in the S_m peak velocity of the lateral tricuspid annulus in inferior myocardial infarction, compared to both normal subjects as well as to patients with anterior myocardial infarction. Moreover, by dividing patients with inferior myocardial infarction according to the presence or absence of RV involvement (on the basis of ECG signs), it was shown that patients with RV infarction had lower S_m and E_m peak velocities than those observed in patients without ECG evidence of RV infarction.

The importance of assessing the right ventricular regional time intervals by pulsed tissue Doppler

Our groups at the "Federico II" University and Monaldi Hospital of Naples have investigated, using pulsed TD, the RV function in different pathologies directly or indirectly involving the right ventricle and, in particular, have identified early changes in the RV diastolic time intervals.

Pulmonary arterial hypertension. In one of these studies, we used pulsed TD of the lateral tricuspid annulus in the setting of chronic obstructive lung disease with or without pulmonary arterial hypertension[29] and compared the standard Doppler echocardiographic measurements of two groups of patients to those of healthy controls. The standard Doppler tricuspid E/A ratio and the TD-derived RV E_m/A_m ratio were impaired in both groups of patients with chronic obstructive lung disease (with a normal or elevated pulmonary artery pressure) while the TAPSE was modified only in the presence of pulmonary hypertension. However, only the TD RV annular RT_m was able to distinguish the three groups, its values progressively increasing from those observed in normal subjects to those found in patients with lung disease but normal pulmonary artery pressure to those with lung disease and pulmonary hypertension (all $p < 0.01$). In the overall population (also including controls with at least minimal tricuspid regurgitation), the length of the RV lateral tricuspid annular RT_m was positively related to the degree of pulmonary artery systolic pressure (Fig. 2), even after adjusting for clinical and echocardiographic confounders. Thus, the pulsed TD tricuspid annular pattern identifies patients with different levels of RV dysfunction due to chronic obstructive lung disease and pulmonary hypertension. Although the degree of pulmonary artery systolic pressure may be accurately determined by measuring the tricuspid regurgitation jet at standard continuous wave Doppler[17], the method proposed in this study represents a useful alternative in the subset of patients in whom lung hyperinflation may sometimes be responsible for suboptimal visualization of the Doppler signal in the right chambers.

Hypertrophic cardiomyopathy. In another study including 30 patients with hypertrophic cardiomyopathy involving the ventricular septum[30], we evaluated the RV myocardial function and its interaction with the left ventricle by analyzing the TD parameters of both the posterior septum and the RV free lateral wall. Except for the A peak velocity, the other Doppler tricuspid inflow measurements were significantly impaired in hypertrophic cardiomyopathy, in the absence of TAPSE changes. TD RV analysis showed a longer RV RT_m in hypertrophic cardiomyopathy than in controls ($p < 0.00001$), without any significant differences in the other regional diastolic and systolic measurements. In the overall population, the Doppler measurements of the RV and LV inflows were not significantly associated while the majority of TD-derived systolic and diastolic measurements were positively associated with the homologous TD septal indexes. In addition, a significant inverse relation was found between the septal wall thickness and the regional relaxation index (RV RT_m - LV RT_m/RV $RT_m \times 100$) (Fig. 3). This study highlighted the ability of pulsed TD to detect RV regional dysfunction in septal hypertrophic cardiomyopathy and provides evidence of the ventricular interaction occurring under these circumstances. The ventricular interdependence has been clearly demonstrated in physiologic and pathologic conditions both in animals and humans[8,9].

Systemic arterial hypertension. Pulsed TD may be useful for the evaluation of RV dysfunction even in pathologies not directly involving the right ventricle such as systemic arterial hypertension[31]. In our hypertensive population, TD showed a reduction in the E_m/A_m ratio and a lengthening of the RT_m at the RV lateral tricuspid annulus in comparison with controls (both $p < 0.00001$). Figure 4 depicts the RV tricuspid annular pattern in a hypertensive patient in whom the E_m/A_m ratio was < 1 and the RT_m was prolonged. In the overall population, after adjusting for clinical and echocardiographic confounders by separate multivariate models, the length of the TD RV RT_m was positively related to the magnitude of the RV anterior wall thickness while the RV E_m/A_m ratio was positively related to the homologous index of the LV lateral mitral

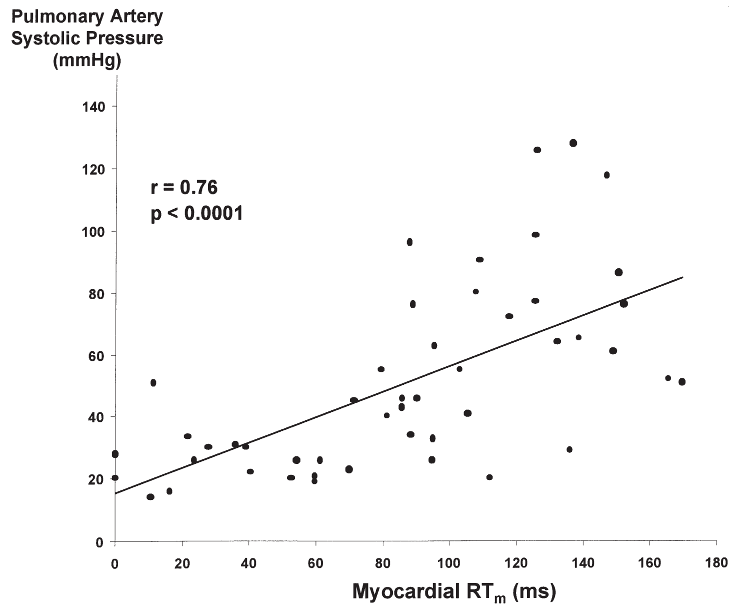

Figure 2. *Scatter plots and regression line between the myocardial relaxation time (RT_m) and the pulmonary artery systolic pressure. From Caso et al.[29], modified.*

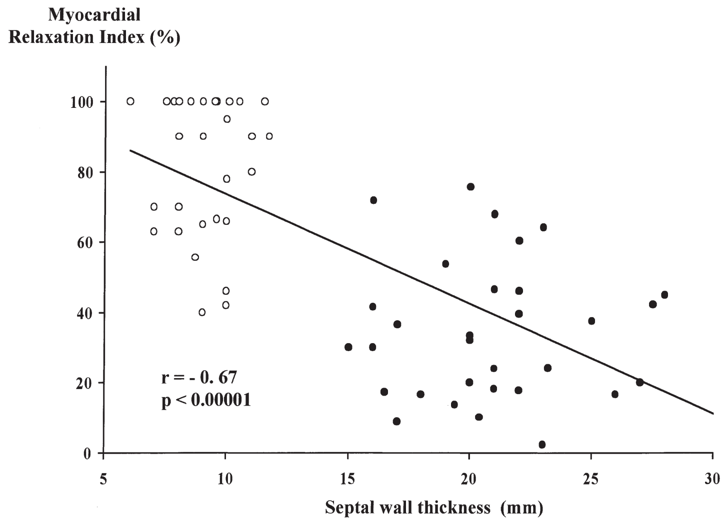

Figure 3. *Inverse relation between the interventricular septal wall thickness and the myocardial relaxation index in the overall population. From Severino et al.[30], modified.*

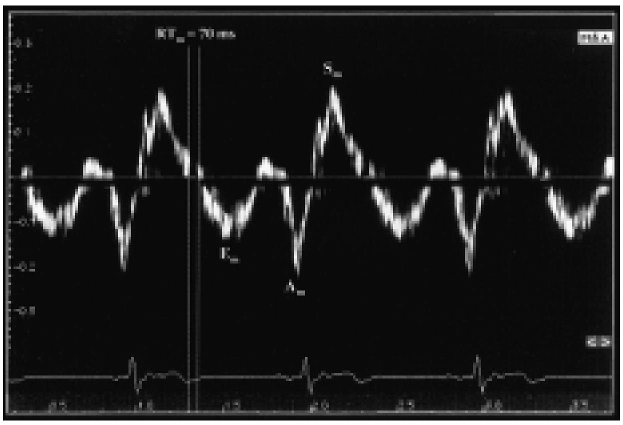

Figure 4. *Tissue Doppler pattern of the right ventricular lateral tricuspid annulus in a hypertensive patient. The right ventricular E_m/A_m ratio is < 1 and the RT_m is prolonged (70 ms). Abbreviations as in figure 1. From Cicala et al.[31], modified.*

annulus (both p < 0.00001). These findings indicate that systemic arterial hypertension is associated with longitudinal RV diastolic dysfunction. The prolonged active relaxation of hypertensive patients is independently associated with the degree of RV hypertrophy, while the impairment of passive wall properties appears mainly due to the ventricular interaction occurring in conditions of LV pressure overload. An additional comparison between the effects induced by hypertensive LV hypertrophy and those deriving from septal hypertrophic cardiomyopathy on RV function, showed how TD identifies much more evident impairment, in RV relaxation, of the lateral tricuspid annulus in hypertrophic cardiomyopathy[32]. Of interest, the degree of prolongation in the tricuspid annular RT_m was associated with the increase in both the septal and RV wall thicknesses in the overall population (Fig. 5).

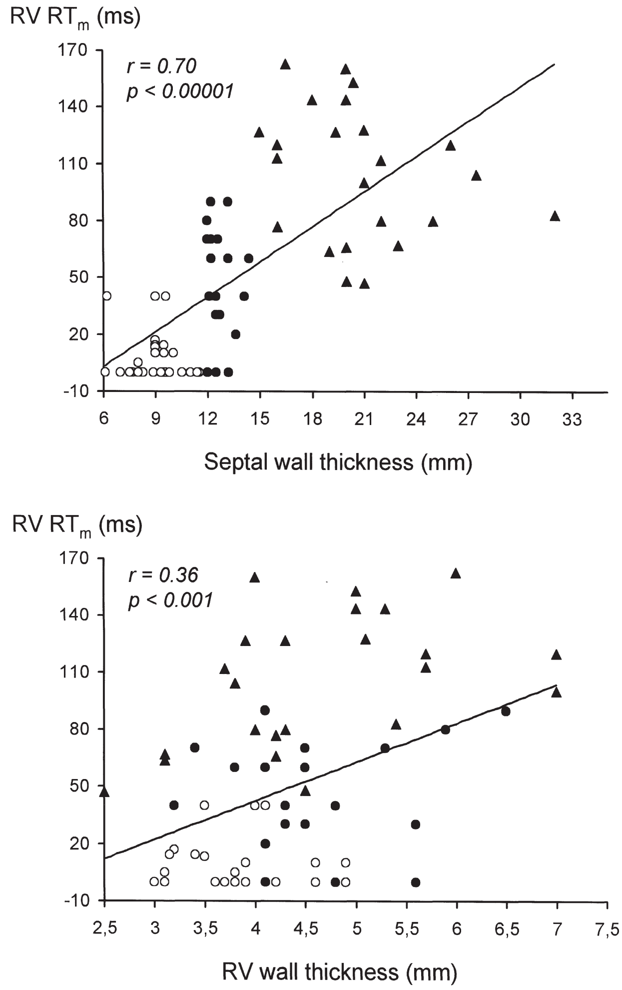

Figure 5. *Scatter plots and regression line of the right ventricular (RV) myocardial relaxation time (RT_m) with both the septal wall thickness* (upper panel) *and RV anterior wall thickness* (lower panel) *in the overall population.* Open circles: *controls;* filled circles: *hypertensives with left ventricular hypertrophy;* triangles: *patients with hypertrophic cardiomyopathy. From Galderisi et al.[32], with permission.*

Limitations of the pulsed tissue Doppler right ventricular approach

While these studies, applying pulsed TD for the investigation of RV function, appear very encouraging, it is fair to state that even the TD evaluation of RV tricuspid annular motion has a potential limitation. Mainly, this technique does not take the base-to-apex movement of the entire heart into account and could consequently produce controversial findings the inaccuracy of which is proportional to the angle occurring between the transducer and the annular point of the same tricuspid motion[38]. With regard to this aspect, a good point in favor of TD is, however, that the function of the right ventricle is mainly dependent on its contraction and relaxation along the long axis[1].

Summary and clinical implications

Despite this limitation, all the above-mentioned studies show the usefulness of pulsed TD for the analysis of the changes in RV function occurring in several pathologic conditions and for a better understanding of the mechanisms underlying RV dysfunction in diseases directly or indirectly involving this chamber. To date, the increasing interest in this tool as a means of assessing the right ventricle is widely justified in view of the demonstrated impact of the RV function on survival in patients with advanced heart failure[39,40]. On these grounds, the applications of pulsed TD in the clinical setting merit consideration. In fact, the myocardial systolic velocities are useful for the detection of RV systolic failure at rest and of right coronary artery stenosis during stress while the myocardial early diastolic velocities, combined to Doppler standard tricuspid inflow measurements, represent reliable indexes of the right atrial pressure even after heart transplantation. On the other hand, the myocardial diastolic time intervals, in particular the myocardial relaxation time, are very sensitive to variations in the loading conditions and to RV wall hypertrophy. Future studies should be addressed towards the longitudinal follow-up of TD RV patterns, to the determination of the progression from early RV wall dysfunction until the evidence of RV global failure and to the evaluation of the possible beneficial effect of cardiac medications on TD-derived RV measurements.

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