Original articles

Doppler-derived acceleration rate of right ventricular early filling reliably predicts mean right atrial pressure at baseline and after loading manipulations in patients with chronic heart failure

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Key words:
Right atrial pressure; Doppler echocardiography; Chronic heart failure.

Background. **We investigated whether Doppler-derived variables of tricuspid flow could estimate mean right atrial pressure and monitor its changes after loading manipulations in patients with chronic heart failure.**

Methods. **Simultaneous mean right atrial pressure (Swan-Ganz catheterization) and tricuspid Doppler recordings were initially evaluated in 136 patients (23 with atrial fibrillation) with chronic heart failure and severe left ventricular systolic dysfunction, and then were repeated in 18 patients after unloading (sodium nitroprusside infusion) and in 13 patients after overloading (active leg elevation) manipulations.**

Results. **A significant correlation was observed between mean right atrial pressure and peak E velocity (r = 0.70), early deceleration time (r = -0.72) and acceleration time (r = -0.75). However, the best correlation found was between the acceleration rate of early flow and mean right atrial pressure, and it was identical in patients in sinus rhythm or with atrial fibrillation (r = 0.98). Moreover, after acute effective unloading or overloading manipulations, although all Doppler tricuspid variables changed significantly, the acceleration rate of early flow still emerged as the strongest independent predictor of mean right atrial pressure (r = 0.95 and 0.99, respectively).**

Conclusions. **Doppler-derived acceleration rate of early diastolic tricuspid flow is a powerful tool to predict mean right atrial pressure and to monitor its changes after loading manipulations.**

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Introduction

The estimation of right atrial pressure (RAP) is often needed for the diagnosis, management, and monitoring of various pathologic hemodynamic conditions and plays a significant role in patients with chronic heart failure (CHF). Right heart catheterization allows for an accurate measurement of RAP, but it is expensive and not without risks, particularly if prolonged monitoring is needed. Therefore, a noninvasive estimation of RAP would be a highly desirable alternative in clinical practice.

Several attempts have been made to obtain an accurate estimation of RAP by both two-dimensional and Doppler echocardiography[1-5]. However, despite the large number of studies, to date no model has been extensively adopted in clinical practice because of a number of clinical and methodological limitations[2,3,5].

In recent years, a close correlation has clearly been demonstrated between Doppler-derived transmitral flow recordings and left ventricular filling pressures[6-10]. More recently still, attention has focused on Doppler diastolic tricuspid flow as a means of predicting mean RAP[11-13]. It has been suggested that the acceleration rate of early right ventricular filling may represent an accurate and reliable tool for estimating mean RAP in patients with CHF[12]. However, in such patients RAP may change rapidly as a consequence of different loading manipulations. Whether the assessment of such dynamic

changes can be promptly detected by Doppler echocardiography has not yet been established.

Accordingly, this study was undertaken to: 1) gain further insights into the relation between tricuspid filling pattern and RAP in a large cohort of patients with CHF, and 2) determine if Doppler-derived variables of tricuspid flow could provide a simple noninvasive method of estimating mean RAP and an accurate bedside tool for monitoring RAP in CHF patients with severe left ventricular dysfunction, whether in sinus rhythm or with atrial fibrillation.

Methods

Study population. One hundred forty-five consecutive patients with CHF due to both ischemic and idiopathic dilated cardiomyopathy admitted to our Heart Failure Unit between September 1997 and June 1998 were evaluated for possible enrollment. All patients had severe left ventricular dysfunction, as defined by resting echocardiographic ejection fraction 35%, and were in New York Heart Association functional class II to IV. Nine patients were excluded because of inadequate recordings of Doppler tricuspid flow tracings (n = 6), presence of prosthetic tricuspid valve (n = 1), pericardial effusion (n = 1), and permanent electro-induced rhythm (n = 1). The remaining 136 patients (116 men and 20 women, mean age 56 – 10 years, range 37 to 74 years) were enrolled in the study. Patients were analyzed first all together and then in two separate subgroups: those in sinus rhythm (n = 113, 83%) and those with atrial fibrillation (n = 23, 17%). Informed consent was obtained from each patient before entry into the study. The Ethics Committee of our Institute approved the study protocol.

Study protocol. Patients underwent simultaneous baseline Doppler echocardiography and Swan-Ganz right-sided heart catheterization. After completion of baseline measurements the effect of unloading or overloading manipulations on mean RAP and tricuspid diastolic flow pattern was studied. For this purpose, simultaneous hemodynamic and Doppler recordings were repeated during a 0.5-2 μg/kg/min sodium nitroprusside infusion (18 patients) or after a 2 min active leg elevation (13 patients).

Simultaneous hemodynamic and Doppler echocardiographic examination. A 7F Swan-Ganz balloon-tipped catheter was introduced through a femoral or internal jugular vein and positioned under fluoroscopy in a pulmonary artery for right-sided heart catheterization. Two-dimensional and Doppler echocardiographic studies were performed using a Hewlett-Packard 1500 imaging system (77765A) with a 2.5 MHz probe. Examinations were performed with the patient lying in the supine position. Left ventricular volumes were calculated from orthogonal apical views, using the biplane area-length method[6]. Ejection fraction was derived from the standard equation. Tricuspid regurgitation was diagnosed by color Doppler flow mapping and graded as mild, moderate or severe according to previously reported criteria[14]. Diastolic tricuspid flow velocity was recorded by pulsed wave Doppler from the apical 4-chamber view as previously described[12]. After a 10 min rest for stabilization, simultaneous mean hemodynamic RAP and the Doppler tricuspid flow velocity signal were recorded for at least 1 min both on videotape and on paper at a chart speed of 100 mm/s, and the following Doppler parameters were measured: peak flow velocity in early diastole (E), acceleration rate, acceleration time, and deceleration time of early diastolic flow (all study patients), peak flow velocity during atrial contraction (A) and peak E/A velocity ratio (sinus rhythm patients). The acceleration rate of early diastolic tricuspid flow was measured as the slope of the segment between the onset of rapid right ventricular filling and peak E wave. Deceleration time was calculated as the time between peak E wave and the upper deceleration slope extrapolated to the zero baseline. Acceleration time was calculated as the time between the onset of tricuspid flow and peak E wave. All measurements represented an average of at least 5 (sinus rhythm patients) to 8 (atrial fibrillation patients) consecutive cardiac cycles to avoid respiration variability[13].

Reproducibility of noninvasive estimation of right atrial pressure. Intraobserver and interobserver reproducibility of Doppler echocardiographic measurements was assessed in 40 consecutive patients. Measurements were repeated by the same observer after an interval of at least 1 week and by a second independent observer. The variability of estimated mean RAP was then evaluated by calculating the mean – SD difference between two sets of observations. In addition, mean percent error was estimated as the absolute difference between the mean of each set of observations divided by their average.

Statistical analysis. Results are expressed as mean – SD. Correlations between Doppler parameters and mean RAP were performed with linear regression analysis. Stepwise regression analysis was also used to evaluate the predictive power of independent variables. Mean RAP estimated by the noninvasive equations was compared with actual mean RAP by using linear regression analysis and calculating the mean relative difference between paired measurements and their SD[15]. First global and then separate analysis was performed for patients in sinus rhythm and with atrial fibrillation. ANOVA was used for the analysis of the variability of Doppler parameters between baseline and unloading or overloading conditions. A value of $p < 0.05$ was considered statistically significant.

Results

Clinical, Doppler echocardiographic and hemodynamic data at baseline are presented in table I. All patients had moderate to severe left ventricular dilation, with severe systolic dysfunction as defined by resting ejection fraction 35%, and no significant differences were found between patients in sinus rhythm and with atrial fibrillation. Moderate dilation of the right atrium and mild right ventricular dilation were also found in the total population, with a more significant enlargement of the right atrium in patients with atrial fibrillation ($p < 0.01$). Moderate to severe tricuspid regurgitation was detected in 50% of patients (severe regurgitation 12%); both moderate and severe regurgitation were more frequent in patients with atrial fibrillation. Mean values of RAP and heart rate in the total population were 6 – 5 mmHg (range 0 to 20 mmHg) and 78 – 16 b/min respectively, with higher values in patients with atrial fibrillation, although this was not statistically significant.

Relation of Doppler echocardiographic variables and mean right atrial pressure. The correlations between Doppler-derived tricuspid flow velocity variables and mean RAP at baseline are reported in table II. No correlation was found between RAP and tricuspid peak A velocity, and there was a very weak correlation between RAP and E/A ratio ($r = 0.46$). There was a modest positive correlation between peak E velocity and RAP in the total population ($r = 0.70$); however, this correlation was greater in patients with atrial fibrillation ($r = 0.82$) than in those in sinus rhythm ($r = 0.68$). Similarly, we found a stronger negative correlation between deceleration time of early diastole and RAP in the atrial fibrillation group ($r = -0.83$) than in the sinus rhythm group ($r = -0.70$). Acceleration time of early tricuspid flow velocity also showed a good correlation with RAP in the two groups ($r = -0.75$). However, the best correlation found was between the acceleration rate of early tricuspid flow and RAP (total population, $r = 0.98$), and this correlation was identical in the two groups (Fig. 1). By stepwise regression analysis, the acceleration rate of early tricuspid flow emerged as the sole independent predictor of mean RAP in both groups ($r = 0.98$, $p < 0.0001$). The analysis led to the following equations: RAP = -1.263 + 0.01116*acceleration rate in patients in sinus rhythm, and RAP = -1.083 + 0.1083*acceleration rate in patients with atrial fibrillation. On Bland-Altman analysis, the mean relative difference between measured and estimated RAPs was close to 0 for the whole population,

Table II. Correlations between tricuspid Doppler variables and mean right atrial pressure.

	All patients (n=136)	Sinus rhythm (n=113)	Atrial fibrillation (n=23)
E (cm/s)	0.70*	0.68**	0.82**
A (cm/s)		0.21	
E/A ratio		0.46*	
DT (ms)	-0.72**	-0.70**	-0.83**
AcT (ms)	-0.75**	-0.75**	-0.75**
Ac (cm/s^2)	0.98**	0.98**	0.98**

* $p < 0.0005$; ** $p < 0.0001$. Abbreviations as in table I.

Table I. Baseline clinical, hemodynamic and echocardiographic characteristics in the total population and in patients in sinus rhythm or with atrial fibrillation.

	All patients (n=136)	Sinus rhythm (n=113)	Atrial fibrillation (n=23)
Age (years)	56 – 10	55 – 10	58 – 9
Coronary artery disease	98 (72%)	81 (72%)	17 (74%)
Heart rate (b/min)	78 – 16	77 – 14	83 – 19
Ejection fraction (%)	21 – 7	22 – 8	17 – 4
LVEDVI (ml/m^2)	128 – 40	126 – 40	131 – 41
RVEDD (mm)	45 – 8	44 – 9	47 – 7
Right atrial area (cm^2)	22 – 7	21 – 7	26 – 4*
TR moderate/severe	68 (50%)	53 (47%)	15 (65%)
RAP (mmHg)	6 – 5	5 – 4	7 – 5
Peak E velocity (cm/s)	46 – 17	46 – 17	49 – 16
Peak A velocity (cm/s)		41 – 14	
E/A ratio		1.22 – 0.6	
AcT (ms)	96 – 39	97 – 38	85 – 39
DT (ms)	189 – 60	187 – 59	191 – 60
Ac (cm/s^2)	617 – 404	582 – 371	763 – 480

Data presented are mean values – SD or number (%) of patients. A = peak flow velocity during atrial contraction; Ac = acceleration rate of early right ventricular filling; AcT = acceleration time of early right ventricular filling; DT = deceleration time of early right ventricular filling; E = peak flow velocity of early right ventricular filling; LVEDVI = left ventricular end-diastolic volume index; RAP = right atrial pressure; RVEDD = right ventricular end-diastolic diameter; TR = tricuspid regurgitation. * $p < 0.01$ sinus rhythm vs atrial fibrillation patients.

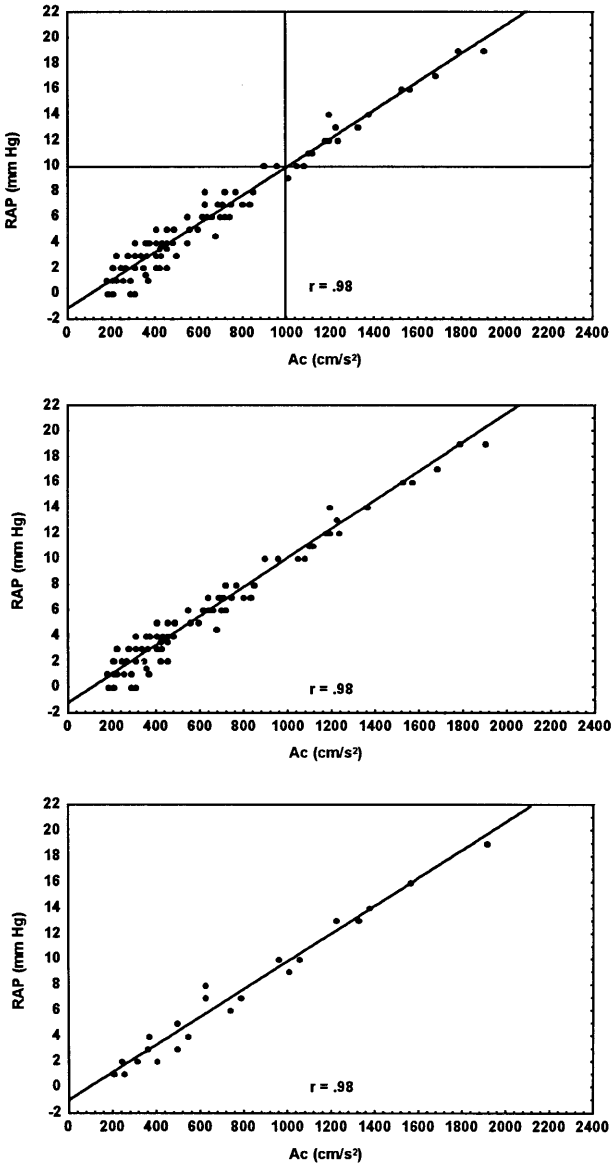

Figure 1. *Scatter plot of linear correlation between the acceleration rate (Ac) of early tricuspid flow and mean right atrial pressure (RAP) in the total population* (top), *and in the two subgroups of patients in sinus rhythm (n = 113)* (middle) *and with atrial fibrillation (n = 23)* (bottom). Vertical continuous line *marks the value of 992 cm/s² in Ac of early tricuspid flow that predicts a value of 10 mmHg in mean RAP* (horizontal continuous line), *above which RAP is commonly considered significantly above the norm.*

indicating the absence of any systematic error (Fig. 2). The value of 992 cm/s² in the acceleration rate of early tricuspid flow was the best cut-off point in predicting 10 mmHg in RAP (i.e. the limit above which RAP is commonly considered above the norm). Sensitivity and specificity of > 992 cm/s² in the acceleration rate of early tricuspid flow in predicting > 10 mmHg in mean RAP were 100 and 96% respectively (positive predictive power 93%, negative predictive power 99%) (Fig. 1, top). Moreover, since patients with severe tricuspid regurgitation have generally been excluded from previous studies, we separately analyzed the correlations between the acceleration rate of early tricuspid flow and mean RAP in a subset of 16 patients with severe tricuspid regurgitation, and found the same high (r = 0.98) correlation.

Doppler-derived tricuspid flow pattern modifications during different loading conditions. Changes in tricuspid flow pattern between baseline and after loading manipulations are presented in table III. After un-

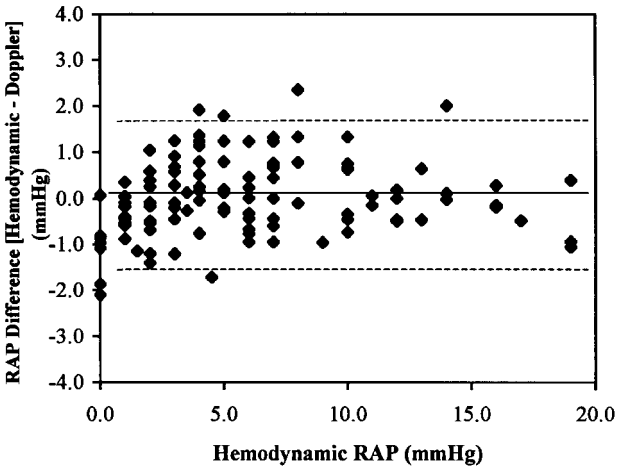

Figure 2. *Bland-Altman plots of differences* (y axis) *between measured (hemodynamic) and estimated (Doppler) mean right atrial pressure (RAP) vs their measured (hemodynamic) values* (x axis). *The relative mean difference between hemodynamic and Doppler RAP was very close to 0* (central horizontal line), *indicating the absence of any systematic underestimation or overestimation. The standard deviation of differences was 1.7 mmHg.*

Table III. Tricuspid flow Doppler variables at baseline and after loading manipulations.

	Overloading (n=13)		Unloading (n=18)	
	Baseline	Legs up	Baseline	NTP
E (cm/s)	36 – 11*	44 – 13	61 – 22*	42 –11
A (cm/s)	37 – 5*	42 – 8	33 – 11	45 – 22
E/A ratio	0.98 – 0.50**	1.17 – 0.48	2.2 – 1.2**	1.17 – 0.89
DT (ms)	216 – 51§	167 – 47	142 – 49**	217 – 51
AcT (ms)	126 – 45§§	67 – 22	67 – 22**	119 – 51
Ac (cm/s²)	315 – 101§	792 – 367	1000 – 373§§	419 – 248

Data presented are mean values – SD. NTP = nitroprusside. Other abbreviations as in table I. * $p < 0.05$; ** $p < 0.01$; § $p < 0.005$; §§ $p < 0.001$.

loading (18 patients treated with nitroprusside infusion), mean RAP decreased significantly from 10 – 4 to 3 – 3 mmHg. Consequently, a significant reduction in E/A velocity ratio ($p < 0.01$), peak E ($p < 0.05$) and acceleration rate ($p < 0.001$) of early diastolic flow together with a significant increase ($p < 0.01$) in acceleration time and deceleration time of early diastole were found (Fig. 3). The opposite pattern was observed after overloading conditions (13 patients underwent 2 min active leg elevation), in which mean RAP increased from 2 – 1 to 7 – 3 mmHg: the acceleration rate of early tricuspid flow significantly increased ($p < 0.05$), whereas deceleration time and acceleration time significantly decreased ($p < 0.05$). Linear regression analysis of Doppler data after both unloading and overloading manipulations confirmed a strong correlation between the acceleration rate of early tricuspid flow and mean RAP (Fig. 4). Despite significant variations in most of the Doppler-derived variables tested, at stepwise multivariate analysis the acceleration rate of early tricuspid flow remained the strongest and the sole independent predictor of mean RAP both after unloading ($r = 0.95$, $p < 0.0001$) and overloading ($r = 0.99$, $p < 0.0001$) manipulations.

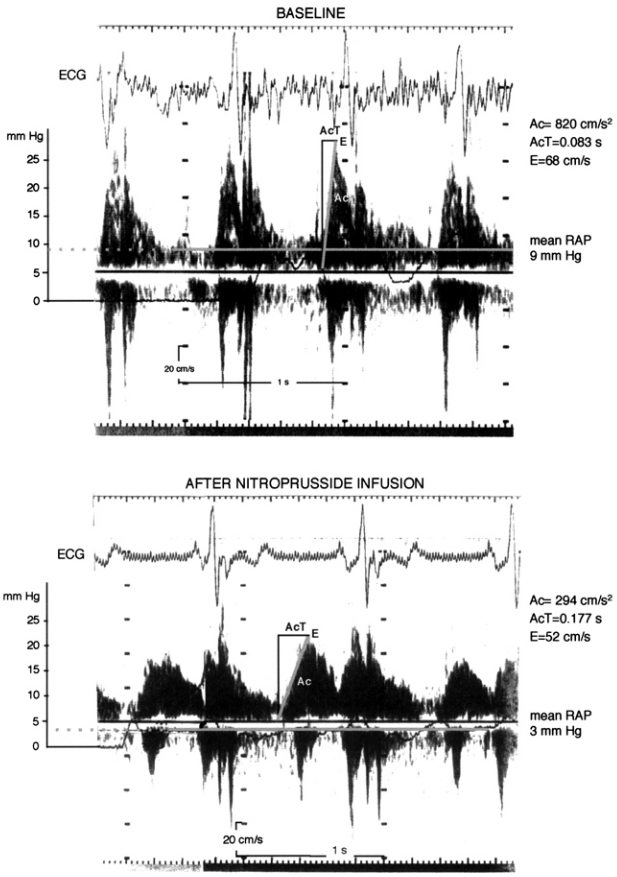

Figure 3. *Tricuspid flow velocity waves simultaneously recorded with RAP hemodynamic curve and electrocardiographic (ECG) trace at baseline* (top) *and after nitroprusside infusion* (bottom). *At baseline mean RAP was 9 mmHg and Ac of early tricuspid flow was 820 cm/s²; after nitroprusside infusion RAP dropped to 2 mmHg and Ac of early tricuspid flow dropped to 200 cm/s². AcT = acceleration time; E = peak flow velocity in early diastole. Other abbreviations as in figure 1.*

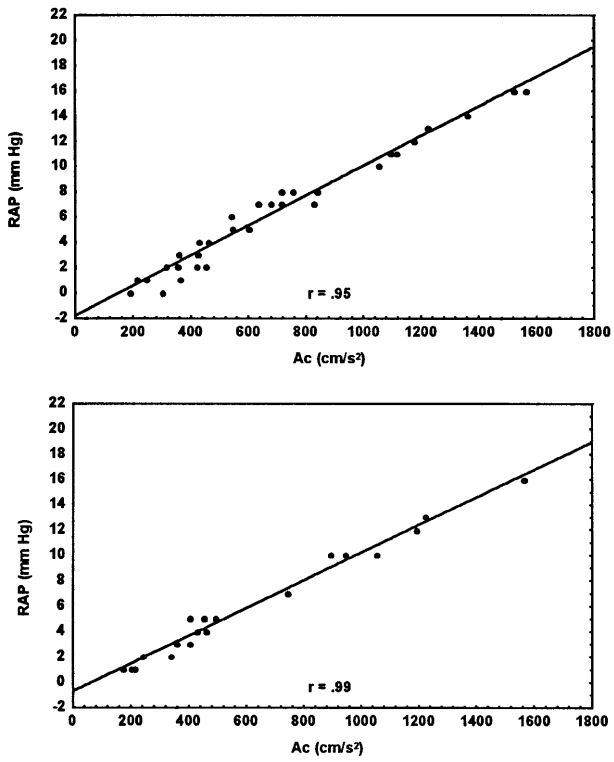

Figure 4. *Scatter plots of Ac of early tricuspid flow vs mean RAP both before and after unloading (18 patients)* (top), *and before and after overloading manipulations (13 patients)* (bottom). *Abbreviations as in figure 1.*

Reproducibility of noninvasive estimation of mean right atrial pressure by Doppler echocardiography. Interobserver and intraobserver variability was 1.5 and 1.8% for peak E velocity, 1 and 1.3% for peak A velocity, 3 and 2.8% for the acceleration rate of early tricuspid flow, 5 and 3% for acceleration time, 6 and 5% for deceleration time. Coefficients of interobserver and intraobserver variability were not statistically significant for any of the tricuspid flow variables measured.

Discussion

In the past decade several attempts have been made to noninvasively estimate RAP, and echocardiography has always been considered the most reliable tool. Morphologic parameters such as respiratory motion of the inferior vena cava, its respiratory diameters and percent collapse (caval index)[2-4], left hepatic vein diameter[5] or right atrial dimension (areas, volumes) were initially studied. More recently, functional data such as left hepatic or tricuspid flow variables have been considered[13]. Some of these indexes, however, offer only semiquantitative measures of RAP, and have failed to demonstrate any prognostic value. Others, although highly sensitive and specific, are useful only in selected groups of patients because of technical or clinical limitations pertaining to the mode of measurement. In addition, most

previous studies suffered from a number of limitations, such as non-simultaneous echocardiographic and hemodynamic recordings[3-5], or the lack of homogeneity of study populations due to the inclusion of both normal and CHF patients[8,11] or patients with extremely different pathologic conditions (mechanical ventilation, primary hypertension)[2-5,13].

On the basis of the well known close correlation between Doppler transmitral flow and left ventricular filling pressure, i.e. mean left atrial pressure[6-10], we hypothesized that the same correlation might be found in the right cavities and hence analyzed Doppler-derived parameters of right ventricular filling to verify the possibility of predicting mean RAP. In particular, we focused on the early filling as it is easy to record and is not influenced by heart rate[11,16]. Analyzing the Doppler tricuspid velocity profile and mean RAP (Swan-Ganz catheter) recorded simultaneously in patients with severe left ventricular systolic dysfunction, we found that the acceleration rate of early tricuspid flow is the most powerful and accurate predictor of mean RAP, both in patients in sinus rhythm and in those with atrial fibrillation, irrespective of whether the recordings are at baseline or after acute loading manipulations.

Relation between tricuspid flow recordings and mean right atrial pressure at baseline and after loading manipulations. It has previously been demonstrated that deceleration time of left ventricular early filling by Doppler echocardiography is inversely related to pulmonary wedge pressure (i.e. mean left atrial pressure), and the correlation appears to be linear (r = -0.90) between 8 and 35 mmHg[10,17]. We found a similar but weaker correlation between RAP and deceleration time of early tricuspid flow (r = -0.72), and we speculate that this is probably due to the lower pressures commonly found in the right circulation (0-20 mmHg in the present study). Interestingly, as observed in a preliminary study[12], we demonstrated a very close correlation between the acceleration rate of early right ventricular filling and mean RAP both in the total population (r = 0.98) and when patients in sinus rhythm or with atrial fibrillation were considered separately (r = 0.98). Moreover, when acute loading manipulations resulting in effective RAP changes were made, all Doppler tricuspid flow variables changed significantly but the acceleration rate of early tricuspid flow still emerged as the strongest predictor of mean RAP. The correlation between RAP and the acceleration rate of early tricuspid flow is unlikely to be affected by the degree of tricuspid regurgitation, as we found the same close relation even in patients with severe tricuspid insufficiency (r = 0.98).

As this parameter provides a quantitative estimate of RAP, it can easily allow for an accurate noninvasive prediction of systolic pulmonary artery pressure, by simply adding the RAP value to the right atrium-ventricular gradient derived by means of the widely accepted modified Bernoulli equation. In fact, in a recent preliminary report[18] in a group of patients with CHF and left ventricular systolic dysfunction, RAP by pulsed Doppler yielded an accurate quantitative estimation of a wide range (from 15 to 79 mmHg) of systolic pulmonary pressure values (r = 0.98).

Mechanisms. The close relation we found between the acceleration rate of early tricuspid flow and RAP has a pathophysiologic explanation. Similarly as for the left ventricular filling pattern, the major determinant of tricuspid flow velocities is the transvalvular pressure gradient. Unlike the left ventricle, however, the right ventricle is a crescent shaped chamber with a larger surface area with respect to the volume, has more compliant and thinner walls, and functions as a low-pressure conduit, unable to generate high intracavitary pressures. In this setting, during early ventricular filling the transvalvular pressure gradient depends mostly on RAP, and the systolic atrial contribution to the mean value of RAP can be considered irrelevant, particularly in the presence of dilated atria due to the poor contractility of thin and stretched walls. Since from hydrodynamic physics pressure *(P)* is equal to a force *(F)* acting on a surface *(S)* and *F* corresponds to the acceleration *(a)* impressed on a mass *(m)*, the equation $P = (m*a)/S$ demonstrates the close and direct relation between pressure and acceleration. The acceleration rate of early tricuspid flow represents the acceleration of blood mass produced by all the forces inside the right atrium on the tricuspid valve surface during rapid right ventricular filling: this could explain why it is closely related to mean RAP.

Study limitations. In this study few variables were used to evaluate RAP. In fact, we did not consider vena cava measurements, nor left hepatic vein dimensions or its Doppler velocity pattern. However, as previously mentioned, measurements of dimensions or of Doppler flow of the vena cava and of the hepatic vein are also difficult and poorly reproducible, particularly in patients with CHF and severe left ventricular dysfunction. As the aim of our study was to identify a simple, accurate and extensively applicable method of estimating RAP, we analyzed only the tricuspid flow velocity profile. The simultaneous recording of RAP and tricuspid Doppler flow strongly supports our results. It should be noted, however, that such a strong relationship does not necessarily apply to normal subjects or to patients in different conditions, e.g. right ventricular hypertrophy, pericardial effusion, massive ischemia; further studies are warranted in these populations.

Conclusions. Doppler-derived acceleration rate of early tricuspid flow provides a simple and noninvasive method of estimating and monitoring RAP in patients with CHF and severe left ventricular dysfunction, whether in sinus rhythm or with atrial fibrillation and irrespective of the degree of tricuspid regurgitation or type of loading condition, and may improve the noninvasive esti-

mation of systolic pulmonary artery pressure.

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