

Strong Negative Correlation between Estimated Pulmonary Artery Systolic Pressure and Right Atrial Strain

Fuerte correlación negativa entre la presión sistólica pulmonar estimada y el strain auricular derecho

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ABSTRACT

Background: Echocardiography is used to assess pulmonary artery pressure, but the magnitude of tricuspid regurgitation is a limiting factor.

Objectives: The aim of this study was to evaluate the correlation between estimated pulmonary artery systolic pressure and right atrial strain.

Methods: A total of 40 patients with sinus rhythm and adequate tricuspid regurgitation were included. Tricuspid annular plane systolic excursion, the velocity of this excursion, right ventricular dimension and right atrial volume were determined. Peak right atrial basal strain and mid-lateral strain during the reservoir phase were averaged. Right atrial strain was compared in patients with estimated pulmonary artery systolic pressure <36 mmHg and ≥36 mmHg using Student's t test. Pearson's correlation coefficient was calculated between right atrial strain and estimated pulmonary artery systolic pressure using the bootstrapping method to evaluate the corresponding confidence interval.

Results: Mean age was 59±11 years and 45% were men. There were statistically significant differences in right atrial strain between patients with estimated pulmonary artery systolic pressure <36 mmHg and ≥36 mmHg (69.92±11.69 vs. 29.40±11.06; p=0.001; 95% CI: -53.93- -27.09). The correlation between estimated pulmonary artery systolic pressure and right atrial strain was -0.87 (p <0.01; 95% CI: -0.72- -0.93). The correlation coefficient was positive but weaker between estimated pulmonary artery systolic pressure, right atrial volume (r=0.67) and right ventricular dimension (r=0.59).

Conclusions: The results show a strong negative correlation between estimated pulmonary artery systolic pressure and right atrial strain which could be useful when tricuspid regurgitation is absent.

Key words: Echocardiography - Pulmonary hypertension/diagnostic imaging – Atrial function, Right

RESUMEN

Introducción: El ecocardiograma es utilizado para valorar la presión pulmonar. Pero la magnitud de la regurgitación tricuspídea (IT) es limitante.

Objetivo: El objetivo de este estudio fue evaluar la correlación entre la presión sistólica pulmonar (PSP) estimada y el strain auricular derecho (strain AD).

Material y métodos: Incluimos 40 pacientes con ritmo sinusal e IT adecuada. Se registró el desplazamiento sistólico del anillo tricuspídeo (TAPSE), la velocidad de dicho desplazamiento, el diámetro del ventrículo derecho (VD) y el volumen de la aurícula derecha (AD). Se promedió el strain máximo basal y medio lateral de la AD durante el período de reservorio. Se comparó el strain AD entre pacientes con una PSP estimada < 36 mm Hg y PSP ≥ 36 usando el test de t. Se calculó el índice de correlación de Pearson entre el strain AD y la PSP estimada. Para el intervalo de confianza se utilizó bootstrap.

Resultados: Edad promedio: 59±11. Hombres: 18 (45%). Hubo diferencias estadísticamente significativas en el strain AD entre pacientes con PSP estimada < 36 mm Hg y pacientes con PSP estimada ≥ 36 mm Hg (69,92±11,69 vs. 29,40±11,06; p: 0.001; IC 95%: -53,93- -27,09). El índice de correlación entre la PSP estimada y el strain AD fue -0,87 (p<0.01; IC 95%: -0.72- -0.93). El coeficiente de correlación fue positivo aunque débil entre la PSP y el volumen AD (r=0.67) y el diámetro del VD (r=0.59).

Conclusiones: Los resultados muestran una fuerte correlación negativa entre la PSP y el strain AD que podría ser útil ante la ausencia de IT.

Palabras clave: Ecocardiografía/métodos - Hipertensión pulmonar/diagnóstico por imagen - Aurícula derecha

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Abbreviations

| | | | |
|-----|---------------------------------|-----------|--|
| RA | Right atrium | PASP | Pulmonary artery systolic pressure |
| FR | Frame rate | TAPSE | Tricuspid annulus plane systolic excursion |
| PAH | Pulmonary arterial hypertension | RV | Right ventricle |
| HF | Heart failure | RA Strain | Right atrial strain |
| TR | Tricuspid regurgitation | | |

INTRODUCTION

Today, echocardiography plays a key role in the evaluation of heart valves and cardiac chambers' dimensions and function. The information provided by this test is useful for the diagnosis and influences decision-making for the treatment of several conditions.

Many patients with systemic diseases, lung diseases or suspected elevated pulmonary artery pressure due to different causes are referred to the echocardiography laboratory to estimate pulmonary artery systolic pressure (PASP) and confirm the diagnosis of pulmonary arterial hypertension (PAH) or to monitor this condition.

According to guidelines, PASP can be assessed from peak tricuspid regurgitation (TR) jet velocity using the Bernoulli equation, adding right atrial (RA) pressure calculated from the inferior vena cava (IVC) diameter and its respiratory changes. (1)

These estimations are not always easy to obtain either due to absence or insignificant TR or inadequate alignment of the Doppler beam in the presence of TR eccentric jets, in most cases underestimating PASP calculation. Measurement of IVC diameter also represents a challenge because of anatomic variations between patients and the low correlation with RA pressure assessed by cardiac catheterization reported by some studies. (2) Thus, the estimation of pulmonary artery pressure may not be accurate.

The new echocardiographic techniques allow quantification of atrial myocardial strain and velocity during the different phases of the atrial cycle: the reservoir or expansion phase during ventricular systole, the conduit phase during passive ventricular filling and the booster-pump phase during active RA contraction (Figure 1).

Over the past years, many studies have demonstrated that RA size and function evaluated by strain reflect RV function and are strongly associated with clinical events in patients with PAH and heart failure (HF). (3-7)

The aim of this study was to assess the ability of the new echocardiographic techniques to detect PAH when conventional methods fail. Thus, patients with adequate TR to estimate PASP, as established by the American Society of Echocardiography (ASE) guidelines, were included in the study, and their values were compared with RA strain obtained by speckle-tracking echocardiography.

METHODS

We conducted a prospective registry of 122 patients between

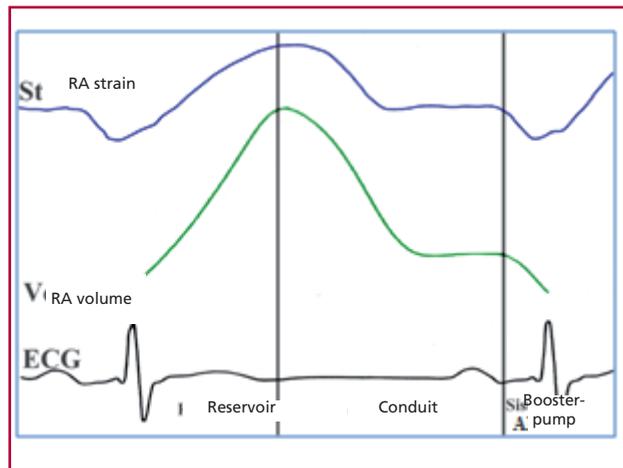
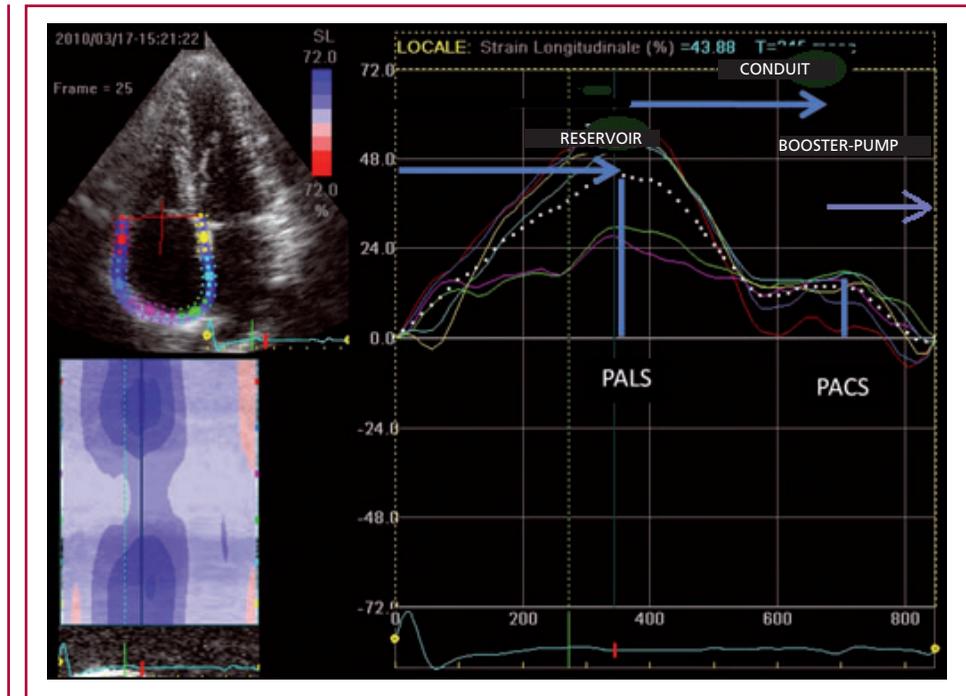


Fig. 1. Atrial volume increases progressively until the end of ventricular systole (reservoir phase) followed by two consecutive emptying phases (conduit phase and booster-pump phase).

18 and 90 years of age undergoing echocardiography evaluation from February 2015 to March 2016. The information was stored in a database. Fourteen patients were excluded due to technical errors in image acquisition, low frame rate or suboptimal ultrasound window.

A total of 40 patients were analyzed. All the patients underwent echocardiographic evaluation with a GE Vivid E9 ultrasound machine, using standard technique. All the patients included were in sinus rhythm and presented adequate TR to estimate PASP. Conventional echocardiographic measurements were performed, and TAPSE, tricuspid annular systolic velocity by tissue Doppler imaging (TDI) and RV diameter above the tricuspid valve were recorded. Right atrial volume was estimated by the method of disk summation from the apical 4-chamber view according to ASE recommendations, and was corrected for body surface area (BSA). Pulmonary artery systolic pressure was calculated by adding the value obtained from peak TR jet velocity using the Bernoulli equation and the RA pressure estimated from the subcostal view of IVC diameter and its respiratory changes. Right atrial peak longitudinal strain was calculated by averaging the values of the RA basal and mid-lateral segment strain during the reservoir phase obtained from the apical 4-chamber view using speckle tracking echocardiography (Figure 2). Right atrial septal segment strain was not measured because this segment contains more fibrous tissue than muscle, and as it also shares the wall of the left atrium its strain would be influenced by that of the left atrium. Neither was the lateral apical segment considered due to its connection with the IVC. These measurements were stored in cine loop format and acquired at a frame rate (FR) >50 frames per second using the software provided by the device and adapting the width of the area of interest to atrial wall

Fig. 2. Right atrial strain. PALS: Peak atrial lateral strain. PACS: Peak atrial contraction strain.



thickness. All off-line analyses were performed by the same operator in at least two stored beats.

Right atrial strain in patients with an estimated PASP <36 mmHg was compared with that of patients with PASP \geq 36 mmHg using Student's *t* test.

Pearson's correlation coefficient was calculated to compare RA strain with the estimated PASP and the corresponding confidence interval was calculated using the bootstrapping method. A *p* value <0.01 was considered statistically significant.

RESULTS

Mean age was 59 ± 11 years and 18 patients (45%) were men. Ten patients (25%) were current smokers, 15 (37%) had hypertension, 1 was diabetic (2.5%) and 7 (17%) had dyslipidemia (Table 1).

There were statistically significant differences in RA strain between patients with an estimated PASP <36 mmHg and those with an estimated PASP \geq 36 mmHg (69.92 ± 11.69 vs. 29.40 ± 11.06 ; *p*=0.001; 95% CI: -53.93- -27.09). Right ventricular diameter measured above the tricuspid annulus and RA volume/BSA index were slightly greater in patients with PASP \geq 36 mmHg but this difference did not reach statistical significance (34.47 ± 3.98 vs. 42 ± 5.09 mm; *p*=0.03; 95% CI: 1.3-13.75; and 24.22 ± 8.04 vs. 40.8 ± 15.27 ml/m²; *p*=0.07; 95% CI: -21.19-35.35, respectively) (Table 2).

The correlation coefficient between estimated PASP and RA strain was -0.87 (*p* <0.01; 95% CI: -0.72- -0.93). (Figure 3) The correlation coefficient was positive, but weaker, between PASP, RA volume (*r*=0.67) and RV dimension (*r*=0.59).

There was no relationship between RA strain and tricuspid annular systolic velocity (*r*=0.27) or TAPSE (*r*=0.09).

Table 1. Demographic characteristics

| | Number of patients | % |
|-----------------|--------------------|------|
| Age | 59 ± 11 years | -- |
| Sex | 18 men | 45% |
| | 22 women | 55% |
| HT | 15 | 37% |
| Current smokers | 10 | 25% |
| Diabetics | 1 | 2.5% |
| Dyslipidemia | 7 | 17% |

HT: Hypertension

A second evaluation from the stored loops was performed in 50% of patients, but no significant differences were found.

The analysis of RA strain proved to be easy and reproducible when an adequate ultrasound window was available and a correct FR (>60 cycles per second) was used. The software used did not allow the analysis in the ultrasound machine and the need of using a workstation makes the procedure longer.

DISCUSSION

Echocardiography is useful to detect and manage PAH. The ability of conventional techniques in PAH has been validated in previous studies; however, these methods are not always feasible due to technical issues.

Fisher et al. reported differences of 10 mmHg or greater between PASP measured by echocardiography and the one obtained by cardiac catheterization in 48% of patients. (8) Also, Padeletti et al. observed a low correlation between PASP measured by echo-

| Variable | PASP <36 mmHg | PASP ≥36 mmHg | p | 95% CI |
|--|---------------|---------------|--------------|----------------|
| TAPSE (mm) | 23.64±4.02 | 22.4±3.13 | 22.4±3.13 | -- |
| Tricuspid annular systolic velocity (cm/s) | 13.43±2.80 | 10.10±2.74 | 10.10±2.74 | -- |
| Right ventricular diameter (mm) | 34.47±3.98 | 42±5.09 | 42±5.09 | 1.30 – 13.75 |
| RA vol/m2 (ml/m2) | 24.22±8.04 | 40.80±15.27 | 40.80±15.27 | -21.19 – 35.35 |
| E/e' ratio | 5.17±2.48 | 7.36±3.78 | 7.36±3.78 | -- |
| RA strain | 69.92 ± 11.69 | 29.4 ± 11.06 | 29.4 ± 11.06 | -49 - -27 |

PASP: Pulmonary artery systolic pressure. TAPSE: Tricuspid annular plane systolic excursion. RA: Right atrial.

Table 2. Differences in echocardiographic parameters between patients with normal PASP and high PASP.

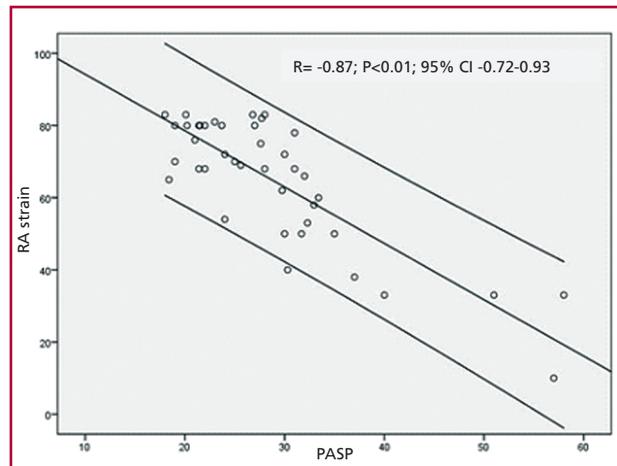


Fig. 3. Correlation coefficient between PASP assessed by echocardiography and RA strain.

cardiography and catheterization ($r=0.45$, $p=0.012$), particularly in patients with pulmonary vascular resistance (PVR) ≥ 1.5 Wood units. (4) These findings alert us about the accuracy of the values.

In view of these facts, and to understand the physiology of cardiac and RA mechanics, several groups, including us, started evaluating RA size and function using strain, in an attempt to determine its value as a diagnostic and prognostic method.

Elevated pulmonary artery pressure is transmitted backward to the right chambers. In early stages, RV systolic function remains preserved, but the hypertrophy and dilation developed to compensate pressure overload produces a certain degree of diastolic dysfunction. Normally, RA contraction accounts for up to 30% of RV cardiac output. (9) Reservoir and conduit phases, represented by the positive RA strain, decrease with age, while the booster-pump phase or negative strain increases in order to preserve RA ejective volume. (10) The same mechanism is observed in the setting of PAH, where positive strain decreases and atrial contraction accounts for almost 50% of RV cardiac output. (11)

As far as we know, two studies have reported reference values of RA strain in healthy volunteers, (10, 12) but our study is the first one to correlate RA strain and PASP measured by echocardiography in the gen-

eral population.

Our results are fairly similar to those published in patients with PAH and HF. In the previously mentioned study, Padeletti et al. observed a strong negative correlation between RA strain and PASP measured by cardiac catheterization ($r -0.81$, $p < 0.001$). This correlation persisted even after the administration of sodium nitroprusside. Based on these findings, the authors concluded that a peak atrial longitudinal strain (PALS) of 10.3% is a strong predictor of PASP ≥ 50 mmHg (area under the curve: 0.93, $p=0.005$; 100% sensitivity and 78% specificity). (4)

In the rest of the studies including mostly patients with PAH, RA strain was significantly lower compared with control patients, in agreement with our control group with PASP ≥ 36 mmHg. These studies also demonstrated a negative correlation with RA size (measured either by area or volume) and RA pressure (measured by cardiac catheterization), and a positive correlation with RV function (as RV shortening fraction measured by echocardiography or as cardiac index by catheterization) but not with pulmonary hemodynamics assessment. This difference with Padeletti et al.'s study may be probably related with the fact that the patients in their study presented low catheterization PASP, mean PAP and RV pressure values because they were in a heart transplantation program and had low cardiac output (3, 5-7, 13-15).

The studies evaluating survival and adverse events in PAH established RA size and pressure as predictors of outcomes in this population. (16, 17) Thus, strain could be another useful marker in this context due to its strong correlation with these parameters.

In recent years, two articles published in JACC have associated RA strain as a prognostic marker of PAH. One is the study by Sakata et al. who concluded that PALS $\leq 23\%$ has 100% sensitivity and 87% specificity to predict mortality (area under the curve 0.98; $p < 0.001$). (6)

The other belongs to Bhave et al. who reported that among patients who met the primary endpoint of prostacyclin initiation, lung transplantation, or death at 6 months, RA strain was significantly lower than among those who did not (20% vs. 33%, $p=0.002$). However, RA strain was not an independent predictive factor due to the small sample size. (7)

Finally, D'Andrea et al. conducted a study on 90

patients with systemic sclerosis (SSc) without PAH. In the SSc patients, right atrial lateral strain was significantly lower compared with the control group (38.5 ± 9.5 vs. $55.5 \pm 37\%$; $p < 0.0001$). In the univariate and multivariate analysis, RA lateral strain showed a negative correlation with RA area and PASP after peak exercise assessed by stress echocardiography ($r = -0.38$, $p < 0.01$; and $r = -0.58$, $p < 0.0005$, respectively). Of interest, RA lateral strain was significantly lower in the subgroup of SSc patients with pulmonary fibrosis measured by computed tomography scan (34.6 ± 9.4 vs. $46.5 \pm 8.6\%$, $p < 0.0001$). Thus, they established that RA lateral strain $< 25\%$ could identify patients with pulmonary fibrosis with 90% sensitivity and 74% specificity (area under the curve 0.83; 95% CI: 0.66-0.84, $p < 0.0001$). (14)

Consequently, RA strain could represent a parameter of early dysfunction to identify high-risk patients before PASP increases.

Unlike most studies which considered the average of the six atrial segments to analyze the results, we only used the basal and mid-lateral segments. In those studies analyzing the six segments, RA lateral wall strain was higher than that of the septal wall, and higher in the basal segments than in the apical segments. This explains why their values are slightly lower than ours in the control group, as we only considered the segments corresponding to the higher values.

All the publications, including the present study, reported that RA strain analysis is feasible in nearly 90% of cases and has acceptable intraobserver and interobserver variability, constituting an easy and reproducible technique despite the off-line analysis is more time-consuming.

Right atrial strain analysis could be useful for a significant number of patients with PAH that cannot be detected by traditional methods or for follow-up and stratification of patients with PAH, HF or systemic diseases.

The results published so far present statistically significant and consistent results along the lines of thought. However, we believe it necessary to establish a uniform standard method to measure RA strain to obtain more consistent results in order to achieve reference values to help identify patients at risk.

CONCLUSION

Right atrial strain is a parameter of diastolic function that is affected by pressure overload, even in its early stages. The results show a strong negative correlation between PASP and RA strain which could be useful in selected cases when TR is absent or difficult to quantify.

Conflicts of interest

None declared

(See authors' conflict of interest forms on the web/ Supplementary Material).

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