

## Mean pulmonary pressure estimation by echocardiography: three equations comparison

*Estimación de la presión pulmonar media por ecocardiografía: comparación de tres ecuaciones*

Francisco Sánchez-Lezama,\* Carlos Harrison-Gómez,\*\* Adalberto Arceo-Navarro,\*\*\* Víctor Manuel Arredondo-Arzola,\*\*\*\* Rómulo Armenta-Flores,\*\*\*\*\* Luis Gerardo Domínguez-Carrillo\*\*\*\*\*

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Pulmonary artery pressure, echocardiography, equations.

### Palabras clave:

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\* Cardiologist. Chief of Echocardiography from Hospital Angeles Leon.

\*\* Cardiologist. Division of Cardiology from Hospital Angeles Leon.

\*\*\* Interventional Cardiologist. Division of Cardiology from Hospital Angeles Leon.

\*\*\*\* Cardiologist. Division of Cardiology from General Hospital of Zone No. 21 of IMSS, Leon, Guanajuato, Mexico.

\*\*\*\*\* Cardiovascular Surgeon. Division of Surgery from Hospital Aranda De La Parra, Leon, Guanajuato, Mexico.

\*\*\*\*\* Rehabilitation Medicine Specialist. Faculty of Medicine from Leon, Guanajuato University, Mexico.

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### ABSTRACT

**Background:** Mean pulmonary arterial pressure (PAP) estimation is possible by echocardiography through the pulmonary acceleration time measurement using mathematical equations; also, using the systolic pulmonary arterial pressure calculated from the tricuspid gradient assessed by continuous Doppler is a good method, having a 0.7 correlation with the catheter hemodynamic studies. **Objective:** To compare three different equations and define its usefulness on mean pulmonary arterial pressure estimation. **Material and methods:** From 4,000 echocardiograms performed, a sample of 187 studies were obtained; we used three different equations to calculate mean PAP, a cutoff of  $\geq 25$  mmHg was used as high PAP. **Results:** 187 patients aged  $54.5 \pm 22.6$  years; corresponding to 87 men (46.5%) and 100 women (53.5%). Equation 1, with 50 cases (26.7%) with PAH were detected; 69 cases (36.8%) with equation 2; and only 23 patients (12.3%) with equation 3. **Conclusions:** Equations 1 and 2 are useful as screening, while equation 3 has higher degree of discrimination.

### RESUMEN

**Introducción:** La estimación de la presión arterial media pulmonar es posible por ecocardiografía a través de la medición del tiempo de aceleración pulmonar utilizando ecuaciones matemáticas; así mismo, a partir del cálculo de la presión arterial sistólica utilizando el gradiente tricuspídeo medido por Doppler continuo, ya que presenta una correlación media de 0.7 al compararla con el estudio hemodinámico con catéter. **Objetivo:** Comparar la aplicación de 3 diferentes ecuaciones para estimar la presión arterial pulmonar media. **Material y métodos:** En una muestra de 187 estudios ecocardiográficos de un total de 4,000 efectuados, se realizaron los cálculos con cada una de las ecuaciones establecidas, tomando como punto de corte la PAP media  $\geq 25$  mmHg. **Resultados:** 187 pacientes con edad X y DE de  $54.5 \pm 22.6$  y variación de 18 a 94 años, correspondiendo a 87 hombres (46.5%) y 100 mujeres (53.5%); con la ecuación 1 se detectaron 50 casos (26.7%) con hipertensión arterial pulmonar, 69 casos (36.8%) con la ecuación 2, y solamente 23 casos (12.3%) con la ecuación 3. **Conclusiones:** las ecuaciones 1 y 2 resultan útiles como tamizaje, teniendo la ecuación 3 mayor grado de discriminación.

### INTRODUCTION

It is estimated that, all over the world, 25 million people have pulmonary hypertension (PH);<sup>1</sup> this is considered an unusual disease that injures lungs and the heart; it is characterized by pulmonary arteries pressure elevation which, if inadequately treated has high mortality; early recognition of PH providing opportune treatment significantly improves life quality of

the patients and is able to increase their life expectancy.

Diagnosis of PH is essentially hemodynamic; according to the last world consensus it is defined as resting mean pulmonary arterial pressure (mPAP)  $\geq 25$  mmHg.<sup>2</sup> Echocardiogram is an excellent screening method for the initial evaluation of the patient in whom PH is suspected, because there are several equations that may be used to calculate PAP; it may be

estimated through de pulmonary acceleration time using mathematic equations.<sup>3,4</sup> On the other hand, tricuspid regurgitation is a very common finding in patients with PH, and it is seen in 80% of cases with systolic PAP > 35 mmHg and in 96% of patients with systolic PAP > 50 mmHg.<sup>5</sup> In order to assess the systolic PAP the Bernoulli equations is used, starting with the peak systolic pressure gradient from the right ventricle to the right atrium measured by continuous Doppler (with a correlation of 0.7<sup>6</sup> in comparison with catheter measurement), once this is obtained, it is possible to calculate mean PAP.<sup>7</sup> Since three equations have been reported for this aim,<sup>3,4,7</sup> we used them in a randomized sample, comparing the results to evaluate its correlation and usefulness using echocardiogram-Doppler technology.

## METHODS

**Sample characteristics:** From 4,000 echocardiograms performed in patients older than 18 years, no matter the gender, a simple randomized sampling was made; using the equation  $N = (2^2 \times P \times Q)/d^2$ , the sample was calculated on  $N = 160$ ; however 187 cases were included in the study, representing 4.67% of the total 4,000 echocardiograms performed; adequate acoustic window was the unique condition considered.

**Equipment:** Philips iE33 or Sonus 5500 echocardiography equipments were used; conventional measurements were performed including M mode, bidimensional, pulsed wave Doppler, continuous wave Doppler, color Doppler; tissue Doppler was made when it was considered necessary to assess mitral annulus velocity.

**Measurements:** Mean pulmonary arterial pressure was calculated using three different equations: two of them using the pulmonary acceleration time, defined as the time interval from de beginning of flow through the pulmonary valve to the maximum peak velocity. These equations were expressed as E1, E2, corresponding:

Equation 1<sup>3</sup> (E1): mean PAP = 80 - (pulmonary acceleration time/2).

Equation 2<sup>4</sup> (E2): mean PAP = 79 - (0.45 × pulmonary acceleration time).

Another method used to calculate the mean pulmonary arterial pressure included the calculation of the pulmonary systolic pressure, which was determined primarily calculating the systolic pressure gradient peak from the right ventricle to the right atrium assessed through the simplified Bernoulli<sup>7</sup> equation ( $4 \times \text{squared } V$ ), where  $V$  = peak systolic velocity of tricuspid regurgitation (TR) measured using continuous Doppler and then the right atrium pressure was added (5, 10 or 15 mmHg according to the collapse of the inferior venous cava during inspiration) and, in this way, the right ventricle systolic pressure was calculated, which, in the absence of right ventricle outlet obstruction is similar to the pulmonary systolic pressure. So that the following was named as Equation 3:

E3:<sup>7</sup> mean PAP = 0.61 × systolic PAP + 2 mmHg.

Mean PAP cutoff point was considered as  $\geq 25$  mmHg.

## STATISTICAL ANALYSIS

$\chi^2$  was used because of three qualitative variables were compared, with level of confidence of 95%, for  $\alpha = 0.05$ , and two grades of freedom; 5.99 was the critical value. Kappa coefficient was used to evaluate the agreement or discrepancy among equations, and variance analysis was also used in order to compare differences among the PH estimations reported for each equation.

## RESULTS

One hundred eighty seven patients were studied with mean age and SD of  $54.5 \pm 22.6$  years and range of 18 to 94 years; of these 87 were men (46.5%) and 100 were women (53.5%); there was no significant statistically difference between the gender. Applying E1, 50 patients (26.7%) were detected with mPAP  $\geq 25$  mmHg; using E2, 69 patients (36.8%); and with E3, only 23 cases (12.3%). Comparing the equations using  $\chi^2$ , E3 provides a value of 30.224, greatly upper than the critical value of 5.99 which corresponds to  $p < 0.05$ , and it indicates that significant statistically difference exists when this equation is applied and is com-

pared with equations 1 and 2; there was also significant statistically difference between E1 and E2 values since  $p < 0.05$ . Kappa coefficient showed  $K = 0.1$  between E1 and E2; equally, K value between E2 and E3 was  $= 0.1$ , both comparisons showed that more measurements differ than expected because of random. On the other hand, observations indicate that as the difference between pre-ejection period and acceleration time increases, the values of mean PAP (mPAP) are lower. Using E3, in which adding the right atrium pressure (inferred by inferior cava vein diameter) to right ventricular pressure is required, the results show, as it was expected, a linear projection; in other words, an increase in mean pulmonary pressure of 3 mmHg was detected for each 5 points of increase in estimation of right atrium pressure. Comparing equations, it was found that E2 reported estimations of mean pulmonary pressure  $15.48 \pm 6.68$  mmHg greater than those calculated using E3. Likewise E2 reported estimations of mean pulmonary pressure  $3.5 \pm 1.4$  mmHg greater than those calculated using E1.

## DISCUSSION

Diagnosis of PH is a sequential process that begins with a clinical suspicion and requires confirmation. Furthermore, assessment of stage and severity of the disease by clinical, echocardiographic, hemodynamic, biomarkers and exercise capacity parameters is of most importance, because the treatment choice depends on them.

Value of Doppler echocardiography in the study of PAH can be summarized in: a) proper anatomical heart evaluation; b) pulmonary circulation evaluation and functional assessment of the right chambers of the heart; and c) pulmonary pressure semi-quantitative estimation.

Respect to equations applied, this study indicates that E3 equation has, theoretically, a high specificity for detecting PH if compared with the gold standard (right heart catheterization), because the number of false positives (healthy individuals inappropriately classified as with pulmonary hypertension) would be very low. On the other side, equations 1 and 2 have a higher sensitivity but possibly with an important number of false positives. According to the

obtained Kappa coefficient, it is different to use the E1 or E2 equations, both may well serve as screening tests; then, the E3 can be considered (if the measurements can be performed) more useful in that patient in whom PH is clinically suspected, because it has (theoretically) a stronger discriminative power. According to the results of our study, the E2 overestimates the number of patients with PH, which causes an increase of three folds the number of patients with apparent PH when E2 is compared with E3; also, E1 equation overestimates the number of patients with PH, disclosing two folds more patients than when E3 is used. This is important in situations of marking boundaries between normal and pathological condition. However, it should be reminded that equation 3 is based on the systolic pulmonary pressure value obtained by the systolic tricuspid gradient and, to prove mean pulmonary pressure  $\geq 25$  mmHg, systolic pressure should be  $\geq 38$  mmHg (speed of 2.9 m/s) if the right atrium pressure<sup>8</sup> is considered at 5 mmHg. This establishes: higher systolic pulmonary arterial pressure, higher mean pulmonary arterial pressure.

It should be noted that the Mahan equation (E2) has been usually used to estimate the mean PAP, then the equation is applied by the echocardiography equipment that makes this calculation automatically. In this work, when the mPAP values obtained by this method are compared with the estimated values obtained by the tricuspid regurgitation gradient method (E3), a poor correlation is observed, due to that Mahan equation (E2) overestimates in three folds (at least in this study) the number of patients likely to have PAH.

Important to note is that it is possible to find systolic pressures between 30 and 38 mmHg in which mean pressure is  $\geq 25$  mmHg (due to increased vascular resistance); in those cases, if the mean average pressure obtained by the E1 or E2 proves high values ( $\geq 25$  mmHg), a close patient monitoring might seem justified because the possible increased risk of pulmonary hypertension development (due that E1 and E2 are more sensitive but less specific than E3), or if high clinical suspicion exists, proceed to perform a right heart catheterization in order to confirm the diagnosis. This applies to cases in which estimated right atrial pressure is inaccurate.

With the echocardiographic findings it is possible to establish:

1. Improbable PH: when the speed of TR is  $\leq 2.8$  m/s, systolic PAP  $\leq 36$  mmHg without other suggestive echocardiographic signs of PH.
2. Possible PH: a) when the speed of TR is  $\leq 2.8$  m/s, systolic PAP  $\leq 36$  mmHg but with other suggestive echocardiographic signs of PH; b) TR speed between 2.9 and 3.4 m/s, systolic PAP between 37 and 50 mmHg with or without suggestive echocardiographic signs of PH, and c) undetermined TR speed (no signal), but with other echocardiographic suggestive signs of PH.
3. Probable PH: when the speed of TR is  $\geq 3.4$  m/s, PAP  $> 50$  mmHg with or without suggestive echocardiographic signs of PH.

Echocardiography is an essential element in the study of PH, to support the diagnosis and monitoring the disease. As an essential part of the diagnostic algorithm of this disease, it can help exclude PH secondary to congenital shunts, PH secondary to pulmonary venous hypertension, and obstructive pulmonary thromboembolism among others. It can also help predict prognosis of these patients, monitor the therapeutic effect of specific treatment and also detect preclinical disease states.

Doppler echocardiography does not replace the right heart catheterization, but its application can provide comparable data to invasive measurement. Overall, the correlation between systolic pulmonary pressure (SPP) estimated by echocardiography compared with catheterization measurement varies from 0.57 to 0.85 with an average of 0.74. However, the SPP observed on echocardiography can overestimate the hemodynamic value with a difference  $> 10$  mmHg up in 48% of cases. Moreover, we can obtain a flow of tricuspid regurgitation to estimate pulmonary pressure in approximately 80% of patients with documented systolic pulmonary pressure above 35 mmHg.

Echocardiography ability to estimate SPP varies with the underlying disease; as an example, in the report of Arcasoy et al,<sup>9</sup> from 374 patients with lung disease, only in 44% the echocardiograms where of good quality for SPP estimation. Moreover it should be reminded that SPP values change with

age and body weight; SPP  $> 40$  mmHg are found in 6% of individuals over 50 years and about 5% in people with body mass index  $> 30$ .

PH cannot be defined with complete precision by a cutoff value of the SPP obtained by Doppler method, so that controversy exists considering the estimated pulmonary pressure obtained by Doppler echocardiography.<sup>10,11</sup> However, this method is a fundamental step in the study of patients in whom PH is suspected, because the presence of mid systolic collapse and acceleration times less than 80 ms of pulmonary flow, reinforces the chances that the patient has significant PH. Instead, other echocardiographic variables must be considered, such as right chambers dilation (inferior cava vein, right atrium, right ventricle and pulmonary artery) and flattening or inversion of the interventricular septum into the left ventricle.

Finally, the PH is clinically defined as a group of diseases characterized by progressive increase in pulmonary vascular resistance, leading to right ventricular failure and premature death; besides, the prognosis is conditioned by: the pathophysiological interactions between progression (or regression) rate of obstructive pulmonary microcirculation changes and the overloaded<sup>12</sup> right ventricle (RV) responses; principal prognostic factors in this disease are expression (hemodynamic, clinical and biochemical) of the right ventricular function; increased afterload remains the main determinant of heart failure in patients with PH and chronic thromboembolic pulmonary hypertension (CTPH), because when it is removed following a lung transplant or after thrombo-endarterectomy there is a rapid RV function recovery.

We consider that the main limitation in this study is that we did not make a direct correlation with the gold standard test. However, mathematical calculations suggest that the use of E3, obtained by echocardiography, appears to be the one that provides greater certainty (when the acoustic window is adequate) in the non-invasive diagnostic approach study of patients with suspected PH.

## CONCLUSIONS

When the values of mean PAP obtained using equations E1 and E2 are compared with the

values obtained by the mathematical calculation of E3, a very little or no correlation is observed, mainly because equations E1 and E2 may overestimate the number of patients with PH in more than 50%.

Our group proposes to calculate the mean PAP with equations E2 and E3; if PAP is elevated with E2 and normal with E3, there must be a close clinical and echocardiographic follow up of the patient before a diagnosis of pulmonary hypertension is established.

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#### Correspondence to:

**Dr. Francisco Sanchez Lezama**  
Hospital Angeles Leon  
E-mail: [sanchezlezama@angelesleon.com](mailto:sanchezlezama@angelesleon.com)