Valuation of equations derived from the pulmonary flow and tricuspid regurgitation. Utility in the pulmonary vasoreactivity test.

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Abstract

Background: Mean Pulmonary artery pressure (MPAP) is an indispensable hemodynamic variable for the diagnosis, classification and prognosis of Pulmonary Hypertension (PH). Its quantification is performed invasively by right heart catheterization (RHC) and non-invasively by Doppler echocardiography. Masuyama proposed its measurement by the transvalvular diastolic pulmonary gradient derived from the initial maximum velocity of pulmonary regurgitation (ΔPRi2) corresponding closely to the invasive measurement. Objectives: to compare 3 known echocardiographic methods to estimate MPAP and demonstrate the usefulness of the Chemla’s method in the Pulmonary Vascular Reactivity Test (PVRT).

Methods: prospective, observational, double-blind study divided into two stages. A) 30 patients underwent diagnostic Doppler echocardiography in our center. Tricuspid regurgitation (TR) and pulmonary acceleration time (PAT) were measured to derive the equations: (1) 0.61xSPAP + 1.95 (Chemla) (2) Gradient mean pressure TR (ΔPmTR) + RAP (right atrial pressure) (Aduen). (3) 79-0.45xPAT or 90-0.60xTAP depending on the value of PAT. B) 10 patients enrolled to PVRT comparing the echocardiographic measurement (Chemla) with RHC.

Results: in the first part of the study was found a high correlation between the 3 equations: Chemla-Aduen, R=0.91; Chemla-Kitabatake, R=0.87; Aduen-Kitabatake, R=0.91. In the second part comparing the MPAP-Chemla and RHC we obtained high correlation: in time 0, 30 min and recovery: (R=0.87, 0.99,0.98, respectively). Both parts of the study showed limits concordance satisfactory with mean value of the difference between the methods close to 1 in the t30 and tR of the PVRT.

Conclusion: the methods dependent on the measurement of the TR are effective and reliably for estimating MPAP. The Chemla’s method is useful in the PVRT.

Key words: doppler echocardiography; pulmonary acceleration time; right heart catheterization; pulmonary hypertension

Abbreviations and acronyms

TRV : Peak tricuspid regurgitant velocity
RVOT : Right ventricular outflow tract
PVR : Pulmonary vascular resistance
MPAP : Mean pulmonary artery pressure
PH : Pulmonary Hypertension
PAT : Pulmonary acceleration time
RHC : Right heart catheterization
RAP : Right atrial pressure
PVRT : Pulmonary vascular reactivity test

Introduction

PH is a disease diagnosed by MPAP measurement, ideally from the earliest stage. Sustained elevation of the afterload is imposed by the different mechanisms of muscle wall hypertrophy, thickening and endothelial fibrosis, proliferation of adventitia with fibrinoid necrosis, pro-inflammatory and thrombogenic status, conditioning ischemia and apoptosis of the pulmonary blood vessels independent of the etiology of the disease.[1-3] The elevation of MPAP is estimated with more confidence invasively, however, different authors have channeled efforts to offer its non-invasive measurement successfully starting from different Doppler echocardiographic equations. The determination of PRi2 evaluable in 80% of cases has been a reference method for a long time. [4] Years ago, Kitabatake et al [5], suggested estimating MPAP through the calculation of PAT, complemented with the study of pulmonary flow morphology. Chemla et al, [6] proposed a method derived from the maximum velocity of TR and quantification of systolic pulmonary arterial
pressure (SPAP) with the modified Bernoulli equation obtaining values close to those obtained invasively. Another equation derived from TR is based on the estimation of the mean pressure gradient (ΔmTR) and the RAP, stated by Aduen et al. [7]. There aren’t studies that report the usefulness of these methods in PVRT.

**Methods**

Prospective, double-blind, observational study that was divided into two stages. The first part enrolled 30 patients with an indication of diagnostic Doppler echocardiography performed in our Unit of echocardiographic studies during the period between January 14 and February 14, 2019. No distinction was made by age group, sex, comorbidities, nor omitted the medication. There weren’t exclusion criteria. The clinical, hemodynamic and demographic characteristics are shown in Table 1.

<table>
<thead>
<tr>
<th>SEX (M/F)</th>
<th>17/13</th>
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</thead>
<tbody>
<tr>
<td>AGE mean (RANGE) years</td>
<td>58 (17-84)</td>
</tr>
<tr>
<td>Ejection fraction mean (RANGE) (%)</td>
<td>57 (8-78)</td>
</tr>
<tr>
<td>Pulmonary arterial pressure systolic mean (RANGE) mmHg</td>
<td>31 (18-72)</td>
</tr>
<tr>
<td>RVD mean (RANGE) mm</td>
<td>28 (19-46)</td>
</tr>
<tr>
<td>PAT</td>
<td>125 (80-147)</td>
</tr>
<tr>
<td>TRV mean (RANGE) m/s</td>
<td>2.42 (1.74-3.78)</td>
</tr>
<tr>
<td>ΔmTR mean (RANGE) mmHg</td>
<td>16.35 (8.21-32)</td>
</tr>
<tr>
<td>RAP media (RANGO) mm</td>
<td>7 (5-20)</td>
</tr>
</tbody>
</table>

**DIAGNOSTICS:**

| SAH | 11 |
| Mixed Cardiopathy SAH+ ischemia | 5 |
| Hypertensive dilated Heart Disease | 2 |
| Chronic ischemia Cardiopathy | 1 |
| Chest pain in study | 2 |
| Palpitaciones in study | 2 |
| Bacterial Endocarditis | 1 |
| Dilatation of Aorta ascending | 1 |
| COPD | 2 |
| Pericardial effusion | 1 |
| Chronic ischemia Cardiopathy OCAD:Vessel 1 | 1 |
| Healthy patient | 1 |

**RAP =** right atrium pressure; **RVD =** right ventrículo diameter; **ΔmTR =** mean gradient of tricuspid regurgitation; **WU =** Woods Units; **PAT =** pulmonary acceleration time; **TRV =** peak tricuspid regurgitant velocity; **SAH =** systemic arterial hypertension; **OCAD =** obstructive coronary artery disease; **COPD =** chronic obstructive pulmonary disease

**Table 1. Clinical, hemodynamic and demographic characteristics of the patients (Group 1)**

In the second part of the study, 11 patients referred from the pneumonology, Child Cardiology and Cardiology of the same center with presumptive diagnosis of HP, of different etiology, degree of severity and echocardiographic criteria to perform the pulmonary vascular reactivity test. These patients were studied from July to December 2009. Exclusion criteria: patients with hemodynamic instability, chronic or acute hypoxemia, coagulation disorders. One patient was withdrawn from the study due to the impossibility of performing measurements with the catheter and in 2 patients only the initial measurements were made due to the significant pulmonary hemodynamic improvement that they presented with the treatment, with respect to the reference echocardiogram. The clinical, hemodynamic and demographic characteristics are shown in Table 2.
COPD=Chronic Obstructive Pulmonary disease PAH=Pulmonary arterial Hypertension PH= Pulmonary hypertension PVRcat=Pulmonary vascular resistance by catheterization;PVRecho= pulmonary vascular resistance by echocardiographic RVD= right ventricular diameter; WU=Wood Units

Calculation obtained by the equation proposed by Abbas: PVR echo= TRV/TVIrvot x 10 + 0.16

Table 2. Clinical, hemodynamic and demographic characteristics of patients (group 2).

All patients signed informed consent. The study was approved by the Hospital’s Bioethics and Medical Ethics Committee.

Echocardiography: Doppler and two-dimensional measurements were performed with Philips Sonos 7500 S3 and Philips iE33 SE1 equipment according to the guidelines of the American Society of Echocardiography [8,9]. The PAT (m/s) was obtained with a pulse wave signal from the antegrade pulmonary flow proximal to the pulmonary valve in the view of the parasternal short axis at the level of large vessels. The Doppler sample volume was placed just before the valve was closed. The acceleration time of the right ventricular outflow tract (RVOT) was measured from the beginning to the maximum flow velocity [10]. The derived equation to obtain the MPAP calculation will depend on its value. If PAT> 120, MPAP = 79-(0.45xPAT) [11]. PAT≤120, MPAP = 90-(0.60xPAT). [12] The TRV (m/s) was obtained with continuous Doppler placed in the tricuspid regurgitant flow at the valvular level. The view 4 cameras were also evaluated with the intention of obtaining the maximum possible velocity. With this and the RAP, using the Bernoulli modified equation, the values of systolic pulmonary arterial pressure (SPAP), [11, 13] were obtained, then to calculate the MPAP with the equation proposed by Chemla [7] = 0.61xSPAP + 1.95. The PmTR was evaluated with continuous Doppler by tracking tricuspid regurgitant flow. The mean pressure difference is measured from the time-velocity integral (TVI) [10]. The formula proposed by Aduen is MPAP = ΔPmTR + RAP. The EF (ejection fraction) was determined by Simpson’s method in the 4-chamber view. In both parts of the work, the measurements were performed 3 times and averaged.

Right cardiac catheterization: In the Hemodynamics Unit, patients from the second group (10) were placed Swan Ganz catheter, 6 or 7 french (F) to obtain measurements of pulmonary pressures and flows. The Seldinger technique was used to approach the internal jugular vein (VYI) or subclavian [14]. Cardiac output (CO) was determined by the thermodilution technique and PVR with the equation: PVR: MPAP-PCP/CO. MPAP measurements; SPAP and diastolic pulmonary arterial pressure (PDAP) were performed automatically by the team. PCP was obtained by minting the ball. [14, 16]

Statistical analysis: MedCalc statistic software 2019, version 18.11.3 / 14.0 of SPSS was used. Linear regression analysis of the MPAP was performed between the invasive and non-invasive method (Chemla’s method et al). Also between the methods of Chemla, Aduen and Kitabatake. Pearson’s correlation coefficient was determined in all cases, and a regression equation was derived. The calculated values were then studied using the Bland-Altman analysis to determine the limits of concordance, SD and average of the differences between the methods in both parts of the study. The images were reassessed to quantify the reliability of the intraobserver and interobserver.

Results

The characteristics of the patients of the first group (30) are shown in Table 1. The average SPAP was 31 (18-72) and PAT of 125 (80-147). Once patients presented a diagnosis of systemic arterial hypertension (SAH) and 5 Mixed Heart Disease: ischemic and hypertensive. The linear correlation analysis between the 3 methods reported the following: Chemla-Aduen, R² = 0.91; Chemla-Kitabatake R² = 0.87; Kitabatake-Aduen R² = 0.91 (Figure 1).
The Bland Altman analysis showed satisfactory agreement limits between all the analyzed methods and the average value of the MPAP differences between the echocardiographic methods close to 1:Chemla-Kitabatake (mean 1.27, L: 5.72 / -8.26, Chemla- Aduen (mean 0.22, L: 5.71 / -6.16); Kitabatake-Aduen (mean 1.045; L: 9.57 / -7.49) (Figure 2).

In the second group analyzed (table 2) 8 of them presented equal or lesser PCP of 12 mmHg, the subgroups being varied within the classification of PH accepted by ESC: 1.4.4 Congenital heart disease: interatrial communication (2); 2.3. Valvulopathies: mitral valve type severe mitral regurgitation (2), valve disease aortic and mitral type double mild lesion (1); 3.1. Severe COPD + severe PH (3) and 3.5 pulmonary development diseases: Dilatation of the pulmonary artery trunk (1). In the second stage of the study the linear correlation analysis between RHC and the Chemla equation, reported high correlation in t0, t30 and tR (R² = 0.87, 0.99 and 0.98 respectively, 95% C.I.) (Figure 3).
Bland Altman’s analysis showed that the mean value of the difference between MPAP measured invasively and non-invasively in the PVRT was close to 1 in t30 and tR. 1. t0: mean-2.1, L: 15.25 / -11.05; t30: average-0.75, L: 2.70 / -2.61; tR: average-1, L: 4.02 / -6.02. Concordance limits (mean value ± 1.96 × SD) (Fig 4).

**Discussion**

The knowledge of pulmonary arterial pressure (PAP) is essential for the treatment of heart disease. Non-invasive measurements can be derived from Doppler interrogation of the right ventricular outflow tract (RVOT), tricuspid regurgitation (TR) and pulmonary regurgitation (RP) signals [17, 25]. For more than 20 years have been able to use echocardiographic equations to obtain the MPAP. Kitabatake et al [5] demonstrated estimation from the PAT obtained with pulsed Doppler in the RVOT and described different flow velocity patterns with the presence of systolic notch in severe cases of PH. Subsequent observations showed that heart rate (HR) outside the normal range reduces the effectiveness of this method. On the other hand, Dabestani et al [20] validated the flow velocity patterns of pulmonary artery and found that a PAT≤100 ms corresponded to high PAP (sensitivity 78%, specificity 100%). This method is less accurate than the estimates derived from TR, especially at high or low heart rates [10] in the present work we find high HR-related...
limitations for PAT

Regarding the equations derived from TR, the method of Chemla et al [6] reported the inconvenience of the impossibility or underestimation of the maximum velocity of TR and/or wrong measurement of RAP.[10] In this study we could include all patients, with a high correlation between the methods (Chemla-Aduen). On the other hand Aduen et al, reported in their work superiority in their method when finding an average difference of the MPAP values with respect to the RHC of -1.6, less than the SPAP traditionally obtained with TR (-3.6) and comparing it with the PR method (-13.9) [7]. In a recent retrospective study [25] where they compared the 3 methods analyzed in this study, among others, with invasively obtained measurements, they found superiority with the Aduen equation. Also when this author compared his method, the Chemla equation and the Syyed equation with the measurements obtained invasively, he found a discrete superiority in his method.[17] In this study we didn’t apply the equation derived from PR (Masuyama et al.),[1] because its registration was possible in less than 60% of the sample analyzed. In the second stage of our investigation, we found a very high correlation when comparing the MPAP values obtained by RHC and the Chemla equation in the 6 stages of the PVRT (we show in the study t0, T30 and tR). We show correspondence as indicated by this author: that PAP values> 30 mmHg correspond to PMAP> 20 mmHg, representing approximately 60% of the PSAP constantly. [3] No studies are currently available that report comparative invasive and non-invasive measurements of MPAP in the PVRT because the RHC is considered the gold standard for its implementation [9, 26]. Based on the encouraging results of this work, we recommend developing studies with a larger population of patients who estimate MPAP and other variables involved through echocardiography and RHC.

Conclusions

We have effective and reliable TR-derived equations to estimate MPAP in a large group of patients. The Chemla’s method is useful and accurate in the PVRT.

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References


