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Original Article

# Tricuspid regurgitation pressure gradient to diagnose pulmonary hypertension: a diagnostic accuracy study

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## *Abstract*

***Background*** Pulmonary hypertension carries significant morbidity and mortality in children. Early diagnosis and management may improve outcomes in children with pulmonary hypertension. Heart catheterization, a gold standard for diagnosing pulmonary hypertension, is an invasive procedure and not widely available. Echocardiography can be used as an alternative diagnostic tool for pulmonary hypertension.

***Objective*** To determine the diagnostic value of tricuspid regurgitation pressure gradient on echocardiography compared to heart catheterization to diagnose pulmonary hypertension in children.

***Methods*** This diagnostic test study was done with medical record data of children with acyanotic congenital heart disease who underwent cardiac catheterization and echocardiography procedures from January 2018 to December 2020 at Dr. Sardjito Hospital, Yogyakarta, Indonesia. Data were analyzed to obtain sensitivity, specificity, positive and negative predictive values, as well as positive and negative likelihood ratios.

***Results*** A total of 98 children with acyanotic congenital heart disease were included. The sensitivity and specificity of the tricuspid regurgitation pressure gradient to determine pulmonary artery pressure compared to heart catheterization were 64.4% and 54.5%, respectively. The positive likelihood ratio was 1.42. The pre-test and post-test probability of this study were 88.7% and 91.7%, respectively.

***Conclusion*** Tricuspid regurgitation pressure gradient measured using echocardiography has poor sensitivity and specificity to diagnose pulmonary hypertension. **[Paediatr Indones. 2022;62:367-72; DOI: https://doi.org/10.14238/pi62.6.2022.367-72** ].

***Keywords:*** *pulmonary hypertension; heart catheterization; tricuspid regurgitation; echocardiography*

Pulmonary hypertension (PH) is associated with significant mortality and morbidity, particularly in children with congenital heart disease (CHD). This progressive pulmonary vascular disease also increases the risk of mortality in children who undergo cardiac surgery for CHD.[1,2] Early diagnosis of pulmonary hypertension is needed in CHD patients because repair of the defect during late stage pulmonary hypertension has the poorest prognosis amongst other types of pulmonary hypertension.[3-5]

The gold standard of pulmonary artery pressure measurement is by cardiac catheterization. However, this procedure is invasive and has risks, related to the procedure itself, as well as the risk of allergy to the contrast material used.[6,7] Furthermore, cardiac catheterization is not widely available in all hospitals in Indonesia. Therefore, other diagnostic tools are needed and should be available in district hospitals in

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remote areas. An alternative, non-invasive diagnostic tool is transthoracic echocardiography. Among the echocardiographic criteria to detect the presence of pulmonary hypertension, tricuspid regurgitation pressure gradient may reflect the estimated systolic pulmonary arterial pressure (sPAP). To the best of our knowledge, this is among the first study in Indonesia to compare sPAP from echocardiography to that of cardiac catheterization, for the purpose of diagnosing pulmonary hypertension.

## Methods

This diagnostic test study with cross-sectional design was done with medical record data of children with acyanotic CHD who underwent cardiac catheterization and echocardiography procedures from January 2018 to December 2020 at Dr. Sardjito Hospital, Yogyakarta, Indonesia.

We included children aged less than 18 years with atrial septal defect (ASD), ventricle septal defect (VSD), and/or patent ductus arteriosus (PDA), as well as signs and symptoms of pulmonary hypertension, including tachypnea, tachycardia, lethargy, or failure to thrive. Subjects had undergone echocardiographic examinations and cardiac catheterization. We excluded patients with dysrhythmias, ventricular function abnormalities, rheumatic heart valve abnormalities, pulmonary disorders, Down syndrome, pulmonary stenosis, or complex CHD.

Pulmonary hypertension was defined by a tricuspid regurgitation pressure of more than 40 mmHg (velocity of 3.1m/sec), based on echocardiography as the index test. Alternatively, pulmonary hypertension was defined by sPAP >30 mmHg, using heart catheterization as the reference test.[2] Data were analyzed with *Statistical Package for the Social Science (SPSS) version 25* software. Continuous data are presented as mean and standard deviation (SD), or as median and interquartile range (IQR), for normally distributed and skewed data, respectively. Categorial variables were presented as count and percentages. Data normality was assessed by Kolmogorov-Smirnoff test. Statistical analysis results were considered significant for P values <0.05. The diagnostic test resulted in sensitivity, specificity, positive predictive value, negative predictive value, as well as positive and negative likelihood ratio, with 95% confidence intervals. This study was approved by the Ethics Committee of the Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada.

## Results

We included 98 CHD patients with clinical manifestations of pulmonary hypertension and median age of 24.5 (Q1 8; Q3 92) months, of whom 46 (46.9%) were males. The most common congenital heart defect was PDA in 32 patients (32.6%) (**Table 1**). Most pulmonary hypertension complaints were difficulty in gaining weight (54.1%), shortness of breath (42.9%), and fatigue (46.9%). The least complaint was a history of bluish/cyanotic state (13.3%). However, there were ten subjects (10.2%) who did not have any complaints regardless of their pulmonary hypertensive state, because they were referral cases from another health care providers, so their complaints of pulmonary hypertensive state was unidentified.

The tricuspid regurgitation pressure gradient sensitivity was 64.4% and specificity was 54.5% in diagnosing PH (**Table 2**). The value of diagnostic accuracy by echocardiography for pulmonary hypertension compared to catheterization was 63.3%. With the pre-test probability of 88.7%, echocardiography to assess the tricuspid regurgitation pressure gradient reached a post-test probability of 91.7% (**Figure 1**).

## Discussion

We compared two tools for diagnosing pulmonary hypertension, cardiac catheterization as the gold standard and transthoracic echocardiography of the tricuspid regurgitation pressure gradient as the index test. The diagnostic value of the index test was inadequate, with low sensitivity and specificity.

In general, complaints of patients with pulmonary hypertension are similar to those with heart failure, but patients with heart failure do not necessarily have pulmonary hypertension.[2,8] The prevalence of children with pulmonary hypertension in our hospital was 88.7%, with obvious signs and symptoms of

**Table 1**. Characteristics of subjects

| Characteristics | (N = 98) |
|---|---|
| Median age(Q1; Q3), months | 24.5 (8; 92) |
| Male sex, n (%) | 46 (46.9) |
| Median weight (Q1; Q3), kg | 8.45 (6.2; 16.2) |
| Median height (Q1; Q3), cm | 79.9 (66.8; 104.5) |
| Mean heart rate per minute, (SD) | 120.04 (21.44) |
| Median respiration rate (Q1; Q3), per minute | 28 (24; 32) |
| Clinical manifestations, n (%) | 88 (89.8) |
| Tachypnea | 42 (42.9) |
| Failure to thrive | 53 (54.1) |
| Interrupted feeding | 36 (36.7) |
| Fatigue | 46 (46.9) |
| Cough | 33 (33.7) |
| Excessive sweating | 26 (26.5) |
| Cyanosis | 13 (13.3) |
| Type of defect, n (%) | |
| Isolated | |
| ASD | 17 (17.3) |
| VSD | 31 (31.6) |
| PDA | 32 (32.6) |
| Non-isolated | |
| ASD, VSD | 1 (1.0) |
| PDA, ASD | 7 (7.1) |
| PDA, AVSD | 1 (1.0) |
| PDA, VSD | 8 (8.2) |
| Median defect size (Q1; Q3), mm | 6 (3.7; 11.5) |
| PH based on catheterization, n (%) | 87 (88.8) |
| Mean sPAP (SD), mmHg | 58.47 (17.6) |
| Median Dpap (Q1; Q3), mmHg | 29 (21; 38) |
| Median mPAP (Q1; Q3), mmHg | 41 (33; 53) |
| PH based on echocardiography, n (%) | 61 (62.2) |
| Gradation of tricuspid regurgitation, n (%) | |
| Trivial | 21 (24.4) |
| Mild | 42 (48.8) |
| Moderate | 9 (10.5) |
| Severe | 10 (11.6) |

ASD=atrial septal defect, VSD=ventricle septal defect, PDA=patent ductus arteriosus, PH=pulmonary hypertension, sPAP=systolic pulmonary arterial pressure, Dpap=diastolic pulmonary arterial pressure, mPAP=mean pulmonary artery pressure.

**Table 2**. Diagnostic value of echocardiography to assess pressure gradient

| Echocardiography | Cath | | Sensitivity (Sn) | Specificity (Sp) | Diagnostic accuracy | Positive predictive value | Negative predictive value | Positive likelihood ratio (LR+) | Negative likelihood ratio (LR-) |
|---|---|---|---|---|---|---|---|---|---|
| | PH (+) | PH (-) | | | | | | | |
| PH (+) | 56 | 5 | 64.4% | 54.5% | 63.3% | 91.8% | 16.2% | 1.42 | 0.65 |
| PH (-) | 31 | 6 | | | | | | | |

Pre-test probability (A+C) /(A+B+C+D) = 88.7%; LR+ = sensitivity/(1-specificity); LR- = (1-sensitivity)/specificity); Pre-test odds = prevalence : (1- prevalence) = 0.887/0.113 = 7.8; Post-test odds = pre-test odds x LR + = 7.8 x 1.42 = 11.1; Post-test probability = post-test odds: (1 + post-test odds) x 100% = 91.7

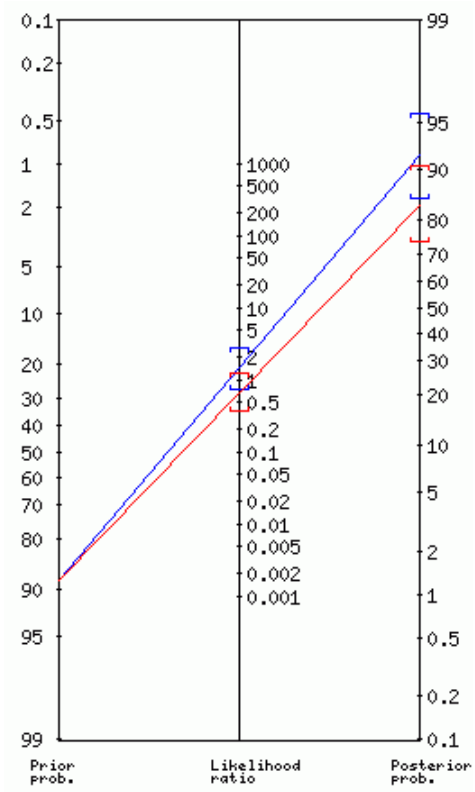


**Figure 1**. Diagram of likelihood ratio

pulmonary hypertension. The high prevalence was probably due to our hospital status as a pediatric cardiac referral center. The majority of patients presented with delayed diagnoses of congenital heart disease.[1]

There was a difference of only three points between pre-test and post-test probability, indicating that the results of this study were not meaningful. In addition, the likelihood ratio obtained (1.42) was below 10, which suggests that subjects had lower probability of pulmonary hypertension. The greater the likelihood ratio, the more likely a person is to suffer from a disease (the possibility of a correct diagnosis is greater).

We found that the sensitivity of measuring tricuspid regurgitation pressure gradient with echocardiography for diagnosing pulmonary hypertension was 64.4%. This sensitivity is low for a diagnostic tool. To diagnose a disease, it is expected that the index test should have a high sensitivity, such that it can exclude the diagnosis when its result is negative. Sensitivity and specificity in our study were also lower when compared to the results of meta-analyses.[9,10] Several factors may have compromised the diagnostic value of our study, including measurement of tricuspid regurgitation, including the degree of difficulty obtaining the appropriate envelope to accurately measure the pressure gradient or velocity in the computation of tricuspid regurgitation.[11,12] In addition, the tricuspid regurgitation velocity may be influenced by other parameters such as demographic characteristics, mechanical factors, remodeling of the right heart cavity, and other factors (possibly reflecting the presence of atrial fibrillation or occult organic tricuspid valve disease).[13] It may be better to not only measure tricuspid regurgitation pressure gradient, but also other indicators in the echocardiographic examination to diagnose pulmonary hypertension, including right ventricular diameter, systolic pressure in the right ventricle, diastolic and mean pressure in the pulmonary artery, and left ventricle eccentricity index .[9]

In this study, transthoracic echocardiography and cardiac catheterization were performed by pediatric

cardiologists, with good Kappa values.[3] The Kappa value of 0.89 in our study was within the reference study target range.[1,3] As such, echocardiography and cardiac catheterization findings should closely approximate the actual condition of the patient and uniform technique.

The weakness of diagnostic test studies is that they depend heavily on condition prevalence in which the study takes place. Since this study was conducted at a referral tertiary hospital, our results cannot be generalized to other hospitals in Indonesia, especially hospitals with limited resources. Therefore, comparative studies are needed to determine the diagnostic value of this tool in identifying pulmonary hypertension. Because of peripheral hospitals do not have cardiac catheterization facilities, patients with clinical pulmonary hypertension can instead be examined for tricuspid pressure gradient regurgitation by echocardiography at a peripheral hospital, and then referred for cardiac catheterization as the gold standard tool for diagnosing pulmonary hypertension at a cardiac center hospital. Further study is needed to examine the diagnostic value of signs and symptoms of pulmonary hypertension compared to cardiac catheterization prior to creating diagnostic criteria or a scoring system in diagnosing pulmonary hypertension in children.

In conclusion, measurement of tricuspid regurgitation pressure gradient using transthoracic echocardiography is a non-invasive test to diagnose pulmonary hypertension, with sensitivity and specificity of 64.4% and 54.4%, respectively.

## Conflict of interest

None declared.

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