Abstract:
Background: Pulmonary arterial hypertension (PAH) is a severe disease characterized by a progressive increase of pulmonary pressure and resistance leading to right heart failure. Pulmonary arterial hypertension is commonly diagnosed at a late stage of the disease and is associated with progressive clinical deterioration and premature death. The assessment of pulmonary artery pressure is important in clinical management and prognostic evaluation of patients with cardiovascular and pulmonary disease. Although PH can be detected invasively by right ventricular (RV) catheterization, accurate non-invasive assessment by echocardiography has many advantages. Reliable non-invasive evaluation of pulmonary pressure at present is still a problem as echocardiographic measurement of pulmonary hypertension relies on the presence of tricuspid regurgitation (TR). Objective: The purpose of this study was to determine whether right ventricular end diastolic diameter can predict the presence of pulmonary hypertension.

Methods: Eighty consecutive patients with echo detectable tricuspid regurgitation who underwent right heart catheterization for either diagnostic or therapeutic procedure were recruited. They were divided into two groups on the basis of pulmonary artery systolic pressure (PASP). Group I consists of 40 patients with PASP >35 mm Hg and Group II 40 patients having PASP < 35 mm Hg. Right ventricular end-diastolic diameter (RVD) was measured in the apical 4 chamber view. PASP was measured from right heart catheterization. Results: The RVD has strong correlation with catheter-derived PASP, at a cutoff value of >3 cm, predicted the presence of PAH with 78% sensitivity and 71% specificity. Conclusion: RVD is a good non-invasive predictor for PAH. RVD can predict the presence of PAH even in absence of TR and correlates well with PASP measured by RV catheterization.

Key words: Pulmonary arterial hypertension, Pulmonary artery systolic pressure, Right ventricular diameter.

Introduction:
Pulmonary arterial hypertension (PAH) is a disease of the pulmonary circulation where the pressure increases in the lungs causing increased resistance and afterload for the right ventricle (RV). Right ventricular response to pulmonary pressure-load involves hypertrophy and the wall tension decreases, at which stage the systolic functions are preserved. However, eventually, RV dilatation ensues leading to volume overload and tricuspid regurgitation (TR). Finally, whatever the cause is, pulmonary hypertension results in RV dysfunction and failure. Pulmonary artery pressure (PAP) is an important hemodynamic parameter that is used in the follow up of various cardiac and pulmonary disorders.

PAH is commonly diagnosed at a late stage of the disease and is associated with progressive clinical deterioration.
and premature death. Without treatment, the prognosis for patients with significant PAH is poor. The reported median life expectancy of idiopathic PAH is 2.8 years from the diagnosis. Recent meta-analysis of trials in the field of PAH has provided indications of a beneficial influence of PAH treatments on survival.\(^3\)

The diagnosis of PAH carries a poor prognosis unless medical or surgical therapy succeeds in decreasing pulmonary vascular resistance (PVR). PAH has a significant risk of major peri-operative cardiovascular complications e.g. cardiac arrest, pulmonary hypertensive crisis and death when undergoing sedation or anesthesia.\(^4\)

Elevated pulmonary artery pressures are associated with functional limitations and reduced long-term survival that is related to the severity of PAH, the patient’s functional class, and the underlying etiology of the PAH. The prognosis is worse in patients with HIV or collagen vascular disease, intermediate in those with idiopathic pulmonary hypertension, and best in those with congenital heart disease. Some medical therapies have been shown to improve functional class and survival in patients with PAH. Because of the morbidity and mortality associated with this condition, reliable methods for diagnosing PAH are needed. Current medical treatments and reproducible methods for serially assessing pulmonary artery pressure noninvasively are equally important.\(^5\)

PAP is measured invasively by means of the pulmonary artery catheter. The “gold standard” for the diagnosis of pulmonary hypertension is right-heart catheterization.\(^6\) This technique enables the direct determination of right atrial, right ventricular and pulmonary arterial pressure. The most frequent complications of cardiac catheter are events related to venous access, arrhythmias and hypotensive episodes related to vagal reactions or pulmonary vasoreactivity testing. The use of pulmonary artery catheters has declined in recent years due to the findings that the use of pulmonary artery catheter did not confer any benefit to management nor did it improve patient outcome.\(^7\) As this procedure is invasive, expensive, and potentially risky determining PAP noninvasively has been a current matter of research for years.\(^8\)

Echocardiography, on the other hand for a long time provided an alternative for the determination of PASP.\(^13\) Echocardiography is an inexpensive, easily available, reliable and reproducible method allowing serial measurements. It is the most commonly used noninvasive tool to determine PAP.\(^6\) In numerous studies, conventional Doppler has been used in estimating PAP.\(^8\)PAP is estimated noninvasively by the tricuspid regurgitation jet velocity, pulmonary acceleration time, right ventricular ejection time, pulmonary regurgitation and the isovolumic relaxation time in Doppler echocardiography.\(^9\)

By use of the maximum velocity of the tricuspid regurgitant jet PASP is determined and via the RV outflow tract flow acceleration time and pulmonary regurgitation, respectively the mean and diastolic PAP are estimated.\(^8,10\)-\(^13\)

In clinical practice, the most commonly used method involves incorporating peak TR velocity into modified Bernoulli equation to derive the trans-tricuspid gradient and adding the mean right atrial pressure to estimate PASP.\(^8,10,13\) The measurement relies entirely on the presence of adequate TR Doppler signal. But the disadvantages are: TR is not always present in every patient. The prevalence of TR increases with the severity of PAH, with TR most commonly seen where PASP >50mmHg. The prevalence may reach as high as 84–96%. In patients with mild to moderate PAH, the prevalence was lower at only 40–50 %. Jet direction, tachycardia and other sources of errors including respiratory variation may add further frustrations to the measurements.\(^8,10,13\)

The detection of PAH is particularly important in the acute situation because rapid diagnosis is often essential to improve patient outcome. The requirement of the presence of TR has made echocardiography nugatory in some situations.\(^14\)

This study examined the predictive value of a new index based on the right ventricular diameter (RVD) for the prediction of PH. The study was designed to demonstrate whether the RVD can predict the presence of PAH with high accuracy, without relying on TR.

**Materials and methods:**

This was a cross sectional analytical study, carried out during November 2009 to December 2010 at the Department of Cardiology of National Heart Foundation Hospital and Research Institute (NHFH&RI), Dhaka. Considering inclusion and exclusion criteria, consecutive 80 patients who had undergone right heart catheterization for suspected PAH were recruited irrespective of age and sex and divided into two groups. In group I 35 patients with TR-guided PASP >35 mm Hg were included and group II consisted of 35 patients with TR-guided PASP < 35 mm Hg. But patients with inadequate Doppler signal, suboptimal two-dimensional images, haemodynamically
unstable patients, congestive heart failure (NYHA class III and IV), RV outflow tract obstruction, arrhythmias and severe concomitant diseases (e.g. chronic liver disease, neoplastic disorder) were excluded. All patients underwent meticulous echocardiography and RVD was measured. Catheter-derived pulmonary pressure was measured by right heart catheterization.

**Transthoracic echocardiography (TTE):**
Comprehensive echocardiography was performed in each patient with standard echocardiography machine Vivid 7 (Vingmed- General Electric, Horten, Norway). All cases and controls were imaged in the left lateral decubitus position. Standard images were obtained using a 3.5 MHz transducer, at a depth of 16 cm in the parasternal long axis (PLAX) and short-axis (PSAX) and apical four chamber (A4C) views. For RVD, the internal medio-lateral dimension of the right ventricular end-diastolic diameter was measured along the minor axis in the apical four-chamber view, at a level of approximately one-third from the base of the RV.14

**Right heart catheterization**
All patients underwent right heart catheterization. A 7F Courmand catheter was inserted in the right femoral vein after administration of local anesthesia and vascular access. Under continuous pressure monitoring the catheter was positioned within the main pulmonary artery. Hemodynamic measurements were obtained at end expiration with patients in a supine position from pulmonary artery.

Demographic data including age and sex, history, physical examination of all patients were recorded. The data derived from TTE and right heart catheterization were also recorded in specified tabulated data collection sheet after proper informed consent of the patients. Data was analyzed using Statistical Package for the Social Sciences 16.0 (SPSS16.0). Results, unless stated otherwise are expressed as mean ± SD. Pearson product-moment correlation was calculated. Receiver operating characteristic curves were constructed using PASP = 35 mmHg as response variable. A confidence level of p < 0.05 was taken as significant.

**Results:**
RVD >3 cm was found 35 (77.8%) and 10 (28.6%) in group I and group II respectively. RVD <3 cm was found 10 (28.6%) in group I and 25 (71.4%) in group II. The mean RVD was 3.7±0.9 cm and 2.8±0.6 cm in group I and group II respectively. The mean difference of RVD was statistically significant (p<0.05) between two groups in unpaired t-test. (Figure I)

Significant positive correlation was found between PASP and RVD. The values of Pearson’s correlation coefficient was 0.698 which shows significant (p<0.05) correlations. Therefore, there was significant positive correlation between PASP and RVD. (Figure 2)
The ROC
(Regarding RVD area under the ROC curve = .821, standard error = .048, significance level = .001. When using RVD as a predictor for the presence of PH (PASP > 35 mmHg) at a cutoff of 3 cm provided a sensitivity and specificity of 78% and 71%, respectively. The positive (PPV) and negative (NPV) predictive values were 78% and 71%, respectively.)

RVD was classified into two groups of >3 cm and < 3 cm and analyzed by ROC. The validity of the RVD findings were correlated by calculating sensitivity, specificity, accuracy, positive and negative predictive values for prediction of PAH. Regarding RVD area under the ROC curve = .821, standard error = .048, 95% confidence interval = .726-.916, significance level = .001. When using RVD as a predictor for the presence of PAH (PASP > 35 mmHg) at a cutoff of 3 cm provided a sensitivity and specificity of 78% and 71%, respectively (accuracy of ROC = 82.1%). The positive (PPV) and negative (NPV) predictive values were 78% and 71%, respectively. (Figure 3)

The velocity of the TR jet measured with continuous-wave Doppler echocardiography correlates with PASP and is the mainstay of assessing the severity of PAH. However, to be useful, there must be a large enough regurgitant volume to produce a Doppler signal that allows accurate measurement of the peak TR velocity. In addition, to accurately measure PASP from TR velocities, it is necessary to know or estimate the mean right atrial pressure. Noninvasive assessment of right atrial pressure is challenging and often inaccurate. Because of these and other problems, traditional echocardiographic Doppler assessment of pulmonary artery pressures may be unfeasible or may lead to overestimation or underestimation of pulmonary pressures in up to 40% of individual patients. 5

A study comparing the measurement of pulmonary hypertension by three methods found noninvasive prediction of pulmonary artery pressure to be feasible in most patients. First, they used a systolic trans-tricuspid gradient to measure PAH. Here they showed that tricuspid pressure gradient provided reliable prediction of PASP. Secondly, acceleration time from pulmonary flow analysis was used to measure mean PAP. But found that pulmonary flow-based prediction of mean PAP was unsatisfactory but improved after correction of heart rate between 60 and 100 beats/min. There was a good correlation between corrected acceleration time and PAP. It is not useful in arrhythmia. Also right ventricular isovolumic relaxation time was used to measure PASP but its usefulness is limited by arrhythmias. Finally the author concluded that, among the three methods, tricuspid gradient measurement seems to be the most useful and practical. Heart rate correction may improve the accuracy of using acceleration time in predicting PAP; Doppler-determined right ventricular relaxation time seems to be of limited usefulness. 16

The absence of TR has made assessment of pulmonary pressure difficult, sometime eccentric jet of TR adds on with this. So there is still a need of reliable method to measure pulmonary pressure. The present study demonstrated that the RVD can predict the presence of PAH with high accuracy without relying on TR.

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It is known that RVD increases with PASP. 17 Increasing PASP increased the RV diameter and resulted in a positive correlation that could rule-in and rule out PAH when separate cutoffs were used. When using RVD as a predictor for the presence of PAH a cutoff of 3 cm provided a sensitivity and specificity of 78% and 71% respectively (accuracy of ROC 82.1%). The PPV and NPV were 78% and 71%, respectively. A previous study by McLean 14 found a cutoff of 3.6 cm provided sensitivity and specificity of 65% and 67% respectively. So, RVD is a relatively moderate predictor of PAH. Right heart catheter derived PASP has moderate positive correlation with RVD. Further study is needed for its significance.

**Fig.-3:** Receiver-operator characteristic curves of RVD.

**Discussion:**
PAH is a hemodynamic abnormality common to a variety of conditions that is characterized by increased RV afterload and work. The development and the level of PAH have been important criteria that determine the diagnostic, management, follow-up strategy and predict prognosis of various diseases. 15

Echocardiography with Doppler interrogation of the tricuspid and pulmonary valves has been recommended by the European Society of Cardiology as one of the first steps in evaluation of the patient with suspected PAH.
Conclusions:
RVD can be useful in cases where estimation of PAPs is limited either by inappropriate identification of the maximal TR signal or when additional echocardiographic parameters are needed to confirm the presence of pulmonary hypertension. In such situation RVD can be used as a new predictor of pulmonary hypertension when a separate cutoff RVD of 3 cm is taken in as it predicts PAH with good sensitivity, specificity and accuracy. So RVD is a useful noninvasive predictor of PAH. Certainly more studies are required not only to assess if the routine measurement of this parameter is sensitive but also to detect changes in RVD over time or with treatment of pulmonary hypertension.

Study limitations:
Inter and intra-observer variability, as well as, the differences in time between echocardiography and cardiac catheterization may constitute significant limitations in the study.

References: