INTRODUCTION

Doppler echocardiography (DE) is a non-invasive screening test for pulmonary artery hypertension (PH). In the absence of pulmonary outflow obstruction, DE provides an estimate of the right ventricular systolic pressure (RVSP), which is equivalent to the systolic pulmonary arterial pressures (sPAP). The right ventricular systolic pressure, and thus the pulmonary arterial pressure, can be estimated from the tricuspid regurgitant (TR) jet velocity by using modified Bernoulli equation: RVSP = 4V^2 + RA pressure. In this equation, 'V' represents maximum TR jet velocity and RA denotes right atrial pressure. Tricuspid regurgitation is mandatory for this calculation which is fortunately found in 70% of normal subjects. Right atrial pressure (RAP) cannot be calculated with DE. However, it can be estimated by looking at inferior vena cava (IVC) diameter and its collapse with inspiration on two-dimensional echocardiography. Echocardiography can also provide information about the cause and consequences of PH, including right and left ventricular dimensions and function, heart valve abnormalities, right ventricular ejection and left ventricular filling characteristics, and presence of a pericardial effusion which may have prognostic value.

To the best of authors’ knowledge, no such study has been done in Pakistan. The objective of this study was to evaluate the correlation between RVSP and sPAP in our settings and to study the impact of RAP on this correlation in terms of correlation coefficient, error and diagnostic accuracy.
METHODOLOGY

This cross-sectional analytical study was conducted after approval from Hospital Review Board, at the Cardiology Department, Tahir Heart Institute, Chenab Nagar, Pakistan. Relevant data were collected from the Hospital database. All patients who underwent RHC from June 1, 2013 to December 31, 2014 were included. Patients with right ventricular outflow tract obstruction, non-availability of RVSP on DE and time interval greater than 30 days between RHC and DE were excluded.

Echocardiographic examinations were performed on commercially available ultrasound systems (Toshiba Nemio XG) using 2.5 MHz transducer. Images were obtained in left lateral decubitus for parasternal and apical views. Right ventricular systolic pressure was calculated from peak systolic TR velocity obtained with continuous-wave Doppler (CW) using modified Bernoulli equation: RVSP = 4V² + RAP. RAP was taken as continuous-wave Doppler (CW) using modified Bernoulli calculated from peak systolic TR velocity obtained with apical views. Right ventricular systolic pressure was obtained in left lateral decubitus for parasternal and apical views.

Statistical Package for Social Sciences (SPSS) version 20 was used for statistical analysis. Continuous variables were expressed in means ± standard deviations or, in situations where distributions were skewed as median and interquartile range. Interquartile range was expressed in brackets from median of quartile 1 to median of quartile 3. Nominal data were expressed in frequencies with percentages. Variable “Error” was calculated by subtracting sPAP from RVSP and converting negative values into same but positive integer (e.g. -7 converted to +7). Another variable “Adjusted Error” was calculated similarly but using adjusted RVSP instead of RVSP. Kruskal-Wallis test was used to compare medians of “Error” between different operators. Significance level was set at p ≤ 0.05. Pearson correlation coefficient and Bland-Altman method were used to correlate DE derived RVSP, and RHC derived sPAP. Using receiver operating characteristic (ROC) curve, the best cut-off value of RVSP was identified in predicting PH. Same statistical procedures were repeated with adjusted RVSP to obtain value of correlation coefficient, adjusted error and diagnostic accuracy.

RESULTS

Fifty-one (51) patients completed the study protocol. Males were 30 (58.8%) and females were 21 (42.2%). The mean age of the study population was 45.22 ±15.25 years. Mean time interval between DE and RHC was 8.57 ±8.21 days. The majority of the patients had rheumatic heart disease (43%) and atrial septal defect (33%). Out of 51 patients, 32 had PH.

Table I describes various parameters to correlate DE derived RVSP, and RHC derived sPAP. Median RVSP was 55 mmHg (45 to 70) while RHC derived median sPAP was 48 mmHg (36 to 70). Median error committed by the operators in estimating sPAP was 13 mmHg (7 to 20). Doppler derived RVSP was over-estimated in 23 (45%), under-estimated in 11 (22%) and found within ±10 mmHg limits in 17 (33%) patients. Pearson correlation coefficient (r) between these two variables was 0.72 (moderate correlation in statistical terms) with p < 0.001. Bland-Altman analysis showed bias of +4.43 mmHg and 95% limits of agreement (LOA) ranging from -34.61 to +43.47. This wide range of LOA in clinical context is indicative of inaccuracy. Median error committed by different operators varied from 9 to 23 (45%). Out of 51 patients, 32 had PH.

Table I: Correlation between RVSP and sPAP.

<table>
<thead>
<tr>
<th>Echo operator</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>Total</th>
</tr>
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<tr>
<td>n</td>
<td>17</td>
<td>11</td>
<td>13</td>
<td>10</td>
<td>51</td>
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<tr>
<td>RVSP - Median (IQR)</td>
<td>60 (50 to 70)</td>
<td>70 (50 to 100)</td>
<td>55 (45 to 80)</td>
<td>55 (45 to 80)</td>
<td>55 (45 to 70)</td>
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<tr>
<td>Adjusted RVSP - Median (IQR)</td>
<td>60 (46.5 to 67.5)</td>
<td>68 (42 to 99)</td>
<td>51 (41 to 83)</td>
<td>50.5 (38.25 to 64.75)</td>
<td>54 (43 to 71)</td>
</tr>
<tr>
<td>sPAP - Median (IQR)</td>
<td>55 (39.5 to 70)</td>
<td>53 (40 to 117)</td>
<td>38 (32 to 80)</td>
<td>36.5 (31.5 to 59.5)</td>
<td>48 (36 to 70)</td>
</tr>
<tr>
<td>Error - Median (IQR)</td>
<td>9 (5.5 to 15.5)</td>
<td>15 (10 to 31)</td>
<td>15 (8 to 30)</td>
<td>12.5 (6.25 to 21.25)</td>
<td>13 (7 to 20)</td>
</tr>
<tr>
<td>Adjusted error - Median (IQR)</td>
<td>8 (2.5 to 20.5)</td>
<td>10 (4 to 23)</td>
<td>13 (3.5 to 31.5)</td>
<td>8 (2 to 18)</td>
<td>9 (4 to 20)</td>
</tr>
</tbody>
</table>

Kruskal-Wallis test (comparing median of Error) p = 0.37

Bias Mean ±1.73 ±5.23 +9.8 +4.43
95% LOA -21.51 to +30.81 -52 to +49.05 -45.86 to +56.32 -14.67 to +34.28 -34.61 to +43.47
r (adjusted RVSP vs. sPAP) 0.52 (p=0.03) 0.81 (p=0.002) 0.67 (p=0.01) 0.86 (p=0.001) 0.75 (p=0.001)
r (RVSP vs. sPAP) 0.58 (p=0.01) 0.79 (p=0.004) 0.81 (p=0.02) 0.88 (p=0.001) 0.72 (p=0.001)

| IQR = Interquartile range (quartile 1 to quartile 3); LOA = Bland-Altman 95% limits of agreement; r = Pearson correlation coefficient |
15mmHg. However, using Kruskal-Wallis test, this variation was not found statistically significant (p = 0.37).

Using ROC curve, the best cut-off value of RVSP was > 52 mmHg with diagnostic accuracy of 75% (sensitivity 81%, specificity 69%) in predicting PH. Area under curve (AUC) was 0.81 (p < 0.001, 95% CI 0.68 to 0.93, Figure 1). Same ROC curve analysis with adjusted RVSP showed the best cut-off value of adjusted RVSP > 48 mmHg with diagnostic accuracy of 79% (sensitivity 84%, specificity 74%) in predicting PH (Table II). Impact of RAP on this correlation was assessed in terms of r, adjusted error and diagnostic accuracy. Median adjusted error reduced slightly (error = 13, adjusted error = 9 mmHg). Minimal improvement in r (0.72 to 0.75) and diagnostic accuracy (75% to 79%) were noted.

**DISCUSSION**

Correlation between DE derived RVSP and RHC derived sPAP was first described by Yock and Popp in 1984. They described good correlation (r = 0.93). This is followed by some studies of sample size ranging from 34 to 127 patients with good correlation. However, results of some other small studies questioned the reliability of DE in estimating pulmonary artery pressures. Good correlation does not necessarily mean that one test is an accurate substitute for another. Most of the above mentioned studies used r and Bland-Altman method to describe correlation between RVSP and sPAP. It was found that each method has its own merits and demerits. Another variable Error was calculated to find error per case in estimating sPAP on DE. Bland-Altman calculated bias by taking the mean of difference between two variables (testing variables). Mean value will be closer to zero as negative values (under-estimated) will cancel positive values (over-estimated). So Bias can tell us about over or under-estimation but won't identify true magnitude of error in study population. In this study, operator A showed good correlation with narrow 95% LOA range (approximately 50) as compared to operator B, where 95% LOA range was equal to 101. This better correlation by operator A was also supported by decreased median Error (operator A = 9, operator B = 15). However, the value of r was better for operator B (Table I) suggesting that r alone is not enough to describe such correlation. By assessing this correlation through these three methods simultaneously, the authors able to describe it as moderately positive (r = 0.72) and inaccurate correlation (95% LOA range = 77, median error = 13 mmHg) with frequent over-estimation of RVSP on DE. Expertise of different operators may influence the accuracy. So we compared the medians of error by different operators but did not find any significant difference.

Estimation of RAP is essential in calculation of RVSP through modified Bernoulli equation. As stated earlier, in this retrospective study, RAP was taken as 10 mmHg in all patients. American Society of Echocardiography 2010 guidelines recommend that RAP ranges from 0 to 5 mmHg if IVC diameter in supine position is < 21 mm and it collapses > 50% with inspiration (normal group). When IVC diameter is > 20 mm and it collapses < 50% then RAP is usually greater than 15 mmHg. Normal
diameter (≤ 20 mm) with subnormal collapse (≤ 50%) or above normal diameter with normal collapse constitutes intermediate group where RAP range is 5 to 10 mmHg. Guidelines recommend midrange values (i.e. 3 for normal and 8 for intermediate group). Some studies have evaluated the validity of the IVC parameters for the accuracy of the estimation of RAP. Most, but not all, studies have demonstrated good correlations between the IVC collapsibility index ([IVC max-IVC min] / IVC max) and RAP (0.57 < r ≤ 0.76). In this study, this default value (10 mmHg) of RAP was replaced with RHC derived RAP and then adjusted RVSP calculated. Hence, adjusted RVSP is calculated by both DE and RHC findings and cannot be attributed to DE alone. The objective was not to discourage the estimation of RAP, but to assess the impact of RAP on correlation between RVSP and sPAP. Only minimal improvement was found (Table I). This suggests that had RAP be estimated with 100% accuracy on DE, even then DE would have remained inaccurate in estimating sPAP.

Greiner et al. conducted a retrospective study on large sample of unselected patients. Their results validate the reliability of DE in estimating sPAP. They have highlighted the causes of over- and under-estimation of DE derived RVSP. Over-estimation was mainly due to maximum TR velocity boundary artifacts. They suggested that maximum velocity should be measured at the best spectral-wave boundary, avoiding Doppler artifacts (fringes). Incomplete spectral-wave envelope was second common reason. They suggested that only signals extended for at least half of the systole should be measured, and incomplete or absent TR may be avoided by increasing blood pool volume with a strategy as simple as drinking a cup of water before examination. Fisher et al. conducted a prospective study where time interval between DE and RHC was just one hour. Their results are in line with our results, apart from the fact that under-estimation was as common as over-estimation.

This study has few limitations which should be kept in mind while interpreting its results. It was a retrospective collected data and images of DE recordings were not available so the authors could not really look into the causes of over- or under-estimation. Maximum time interval between DE and RHC was set at 30 days. Pulmonary pressures in patients with PH are known to fluctuate significantly over the course of several hours. Mean time interval in this study was 8.57 ±8.21 days. The study population consisted of selected patients with suspicion of PH on DE. Hence, evaluation of diagnostic accuracy may be questioned. Sample size was small.

CONCLUSION

Doppler echocardiography is not very accurate in estimating pulmonary artery pressures. Over-estimation was more common than under-estimation. Correct estimation of right atrial pressures may improve the correlation between DE derived RVSP, and RHC derived sPAP. However, this contribution is only minimal.

REFERENCES


