Echocardiographically-Derived Septal Positional Angle (EDSPA) as a Measure of Elevated Right Ventricular Systolic Pressure

Jennifer Huang[1], Zach Hutchinson[2], Grant Burch[1], Brendan Kelly[1], and Erin Madriago[2]

[1]Oregon Health and Science University
[2]Oregon Health & Science University

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Abstract

Background: Pulmonary hypertension is a significant yet rare disease that can have many long-term consequences, including death. Cardiac catheterization is the gold standard for measuring pulmonary artery mean pressures (PAMP), but is invasive and risks potentially serious complications. This study aimed to create a semi-quantitative, non-invasive measure of PAMP using septal positioning. Methods: This study was a retrospective study of patients with and without pulmonary hypertension who had a transthoracic echocardiogram and cardiac catheterization. Patients undergoing atrial septal defect closure represented controls. Two blinded readers calculated the "Echocardiographically-Derived Septal Positional Angle (EDSPA)" which was compared to corresponding catheterization data including mean pulmonary artery pressures. Results: A total of 159 children were included, of which 151 had useable echocardiographic data. 40 children were identified as having pulmonary hypertension while 111 children had an atrial septal defect. Patient age ranged from a minimum of 54 days and maximum of 19 years [mean 7.1 years (SD=5.30)]. Inter-observer variability between two readers [Pearson correlation coefficient of 0.939 ($p < 0.001$)] and intra-observer variability were low [intraclass correlation coefficient (ICC) of 0.95 and 0.96 for each observer respectively]. An EDSPA of [?]39° predicted a PAMP>20 mmHg (as measured by cardiac catheterization) with a 76% sensitivity and 76% specificity (AUC 0.846). Conclusions: EDSPA is a useful, non-invasive, and reproducible echocardiographic measure of PAMP that is easy to perform. With a sensitivity and specificity near 80%, it has significant utility in screening for pulmonary hypertension and determining which patients should undergo further invasive diagnostic testing.

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Department of Pediatrics, Oregon Health and Science University, Portland, OR, USA.

Jennifer Huang, MD

707 SW Gaines St.

CDRC-P

Portland, OR 97239

huangje@ohsu.edu

T: (503) 494-6524

F: (503) 494-2824

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Results: A total of 159 children were included, of which 150 had useable echocardiographic data. 39 children were identified as having pulmonary hypertension while 111 children had an atrial septal defect. Patient age ranged from a minimum of 54 days and maximum of 19 years [mean 7.1 years (SD=5.30)]. Inter-observer variability between two readers [Pearson correlation coefficient of 0.939 (p <0.001)] and intra-observer variability were low [intraclass correlation coefficient (ICC) of 0.95 and 0.96 for each observer respectively]. An EDSPA of [?]39° predicted a PAMP>20 mmHg (as measured by cardiac catheterization) with a 76% sensitivity and 76% specificity (AUC 0.846).

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Key Words

Pediatric cardiology, pulmonary hypertension, echocardiography, cardiac catheterization

Introduction

Pulmonary hypertension is a rare disease that can have many long term consequences including significant disability and death[1]. Traditionally, echocardiography has been used to identify patients with this disease because of its non-invasive nature. Various indirect parameters demonstrated with echocardiography can indirectly help quantify right ventricular systolic pressure (tricuspid regurgitant velocity, ventricular septal defect velocity) or mean pulmonary artery pressure (patent ductus arteriosus velocity, early pulmonary regurgitation velocity); however for many patients, these jets are insufficient or absent for quantification. In particular, the tricuspid valve regurgitant velocity cannot be obtained in 30-54% of pediatric echocardiograms performed for assessment of pulmonary hypertension[2-6]. Qualitative assessment of the position of the interventricular septum has been used to gauge whether a right ventricle is "sub-systemic, half-systemic, or supra-systemic"[7-10]. In patients with normal right ventricular systolic pressures (RVSP), the septum bows towards the right ventricle and the left ventricle is rounded in short axis during systole (Figure 1B); whereas, in those with elevated RVSP, the septum is flattened and can even bow into the left ventricle in suprasystemic RVSP conditions. While used frequently, this qualitative assessment may yield significant inter-reader and intra-reader variability[11]. Another recently published echocardiographic measure, the eccentricity index, which is the ratio of the LV dimension parallel to the septum to the LV dimension perpendicular to the septum is limited by dependence upon a normal left ventricular geometry, precise placement of a perpendicular line through the septum, and precision in timing the measurement within the cardiac cycle[12]. Catheter-based measurements are the gold-standard for assessment of RVSP because of their direct measurements, however these procedures are invasive and have known and potentially catastrophic complications[13].

Given that septal position is frequently the only available method for non-invasive assessment for elevated right ventricular pressures in many children, a quantitative assessment of that curvature could be useful to assist in the diagnosis and medical management of patients with pulmonary hypertension. Some quantifications of septal position like the left ventricular end-diastolic eccentricity index[12]and the septal flattening angle[14] have been compared with other echocardiographic measures of right ventricular systolic pressure such as the tricuspid regurgitant jet velocity. The only other quantifications of septal position to compare with gold-standard catheterization direct-pressure measurements is the normalized septal curvature[9] and the eccentricity index[12].

The aim of this study was to create a novel semi-quantitative measurement of septal positioning that was easy to perform, reproducible, and accurate in identifying significant pulmonary hypertension.

Materials and Methods

This study was designed as a retrospective study of patients with and without pulmonary hypertension who had a transthoracic echocardiogram and cardiac catheterization less than 90 days apart. Subjects were identified for the study based on a survey of the EPIC database and Syngodynamics Echocardiographic database (Siemens Medical Solutions, Malvern, PA) for having a history of primary or secondary pulmonary hypertension from 1/1/2007 through 6/1/18. All patients from newborn through 21 years of age were included. Subjects with small intracardiac shunts were included, but subjects with other structural heart defects were excluded. Age matched controls who were undergoing cardiac catheterization for atrial septal defect device closure and had normal pulmonary artery pressures were selected. Echocardiograms were performed within 90 days prior to catheterization. Echocardiograms were reviewed and measured by 2 blinded readers. Studies were assessed for overall quality, presence and velocity of tricuspid regurgitation, pulmonary insufficiency, pulmonary stenosis, peripheral pulmonary artery stenosis, atrial level shunt, ventricular level shunt, and ventricular systolic function. The "septal positional angle" (see figure 1) was made in the parasternal short axis at peak systole at the level of the papillary muscles by drawing a primary midpoint line (M) that bisects the right and left ventricular area equally. A secondary perpendicular line (S) was drawn at the widest dimension of the left ventricle. A third line (A) was drawn which intersected the secondary line at the inferior portion of the left ventricular epicardium and the right ventricular side of the interventricular septum along the midpoint line. The angle (α) was calculated utilizing the angle tool in the Syngodynamics software, from the intersection of the second and third line and defined as the echocardiographically-derived septal positional angle (EDSPA). Data was obtained from the Epic electronic medical record database for these patients including dose and duration of medical therapy, other co-morbidities, and quantitative assessment of right ventricular systolic pressures from cardiac catheterization (RV systolic and diastolic pressures, LV systolic and diastolic pressures, mean pulmonary artery pressure, qualitative ventricular systolic function assessment, Qp:Qs, cardiac index and response to therapy).

Statistical analysis

Median values with range were calculated for each patient variable with numerical data. Percentage of total patients was calculated for categorical characteristics. Welch's t-test, unpaired t-test and chi-square was used for comparison of ASD and pulmonary hypertension hemodynamic measurements on echocardiogram and catheterization. Inter-observer variability and concordance of the EDSPA measurements were calculated using the sign of Pearson's r and the Lin's concordance. Receiver operating characteristic curves were utilized to display the predictive ability of EDSPA to discriminate select groups.

Results

A total of 159 children were included in this study, 150 of which had useable echocardiographic data. 39 children were identified as having clinically-diagnosed pulmonary hypertension while 111 children had an atrial septal defect requiring closure in the cardiac catheterization laboratory. Slightly over half (56%) of patients were less than 5 years of age, approximately 13% of patients were between the age of 5-10 years, 20% between the age of 10-15, and 11% were between 15-21 years. The mean age of the total group of patients was 7.1 years (SD=5.3), with a minimum age of 54 days and a maximum of 19.1 years. The echo was obtained at a median of 6.5 days (0-88 days) prior to the catheterization.

A table summarizing the echocardiographic and catheterization findings of the two groups (ASD and pulmonary hypertension patients) is provided below (Table 1).

An EDSPA of [?]39° predicted a mean MPA pressure >20 mmHg (as measured by cardiac catheterization) with a 76% sensitivity and 76% specificity (AUC 0.85) (Figure 3) and an EDSPA of [?]37deg predicted a mean MPA pressure >40 mmHg (as measured by cardiac catheterization) with a 80% sensitivity and 81% specificity (AUC 0.85). A graphical depiction of the EDSPA values in those with MPA pressures less than and greater than 40 mmHg is seen in figure 4. In addition an EDSPA [?]40deg predicted a RV/LV systolic pressure ratio >0.5 (as measured by cardiac catheterization) with a 76% sensitivity and 77% specificity (AUC 0.888) (Figure 5).

Inter-observer variability between the two readers was small with a Pearson correlation coefficient of 0.913 (p <0.001) and the Lin's correlation coefficient of 0.907 when using a mean of the 3 measurements per observer (Figure 3). In addition, intra-observer variability was low with an intraclass correlation coefficient (ICC) for each observer of 0.95 (0.9-0.97 95% CI) for reader 1 and 0.94 (0.89-0.97) for reader 2.

Discussion

This study shows that the EDSPA is a reliable and reproducible, but non-invasive estimate of right ventricular systolic pressure. Importantly, it can be quickly and easily measured using widely available echocardiographic processing software like Syngo Dynamics and can be measured post-acquisition in standard echocardiographic views. An EDSPA of < 39deg suggests a main pulmonary artery mean systolic pressure of > 20 mmHg. As such, it can be used as an indication for more invasive measures in the cardiac catheterization laboratory prior to treatment with anti-pulmonary hypertensives or in titrating anti-pulmonary hypertensive therapies. As such, it is an excellent tool for use in outpatient and inpatient screening for pulmonary hypertension.

EDSPA has some significant potential advantages over other published measurements such as the Eccentricity Index (EI). The measured angle is independent of left ventricular dimensions or normal left ventricular free wall motion, so it can be used for patients with abnormal left ventricular size and function. This is especially important in patients with left sided obstructive cardiac disease that can lead to pulmonary hypertension, patients with volume loaded left ventricles, patients with regional wall motion abnormalities, and patients with cardiac dysynchrony. These are critical populations to track non-invasively. As well, it is easy to reproduce and had low intra and interobserver variability. Like the eccentricity index, it can be quickly measured with common echocardiographic processing software already being used in clinical care.

The limitations of our study include the interval between the echocardiogram and cardiac catheterization which could lead to variation in pulmonary pressures at different times and under different conditions (i.e. level of sedation). However, given that echocardiograms are usually performed in an outpatient non-sedated setting, these results may be more generalizable and relevant to outpatient decision-making. Also, although EDSPA does not precisely calculate right ventricular systolic pressure, it does effectively triage patients into those who qualify for at least mild pulmonary hypertension, and those who have significantly elevated pressures who may need earlier direct assessment or medication adjustment. Further studies with simultaneous echocardiographic and catheterization measurements are indicated. As well, there may have been variation in the level of sedation versus anaesthesia under which the cardiac catheterizations were performed in the pulmonary hypertension and atrial septal defect groups but this was not studied. Finally, we excluded patients with concurrent congenital heart disease and pulmonary hypertension in our study population. These patients should be evaluated in the future to increase generalizability.

In conclusion, EDSPA is a useful and easily performed and interpreted echocardiographic method for obtaining a semi-quantifiable measurement of right ventricular pressure that is useful for identifying and managing patients at risk for pulmonary hypertension.

Author Contributions

Jennifer Huang and Erin Madriago participated in the concept/design, data analysis/interpretation, drafting of the article, critical revision of article, approval of article, statistics, securing of funding, and data collection.

Zach Hutchinson participated in the data analysis/interpretation, drafting article, critical revision of article, approval of article, securing funding, and data collection.

Brendan Kelly participated in concept/design, critical revision of article, approval of article.

Grant Burch participated in concept/design, critical revision of article, approval of article, data collection.

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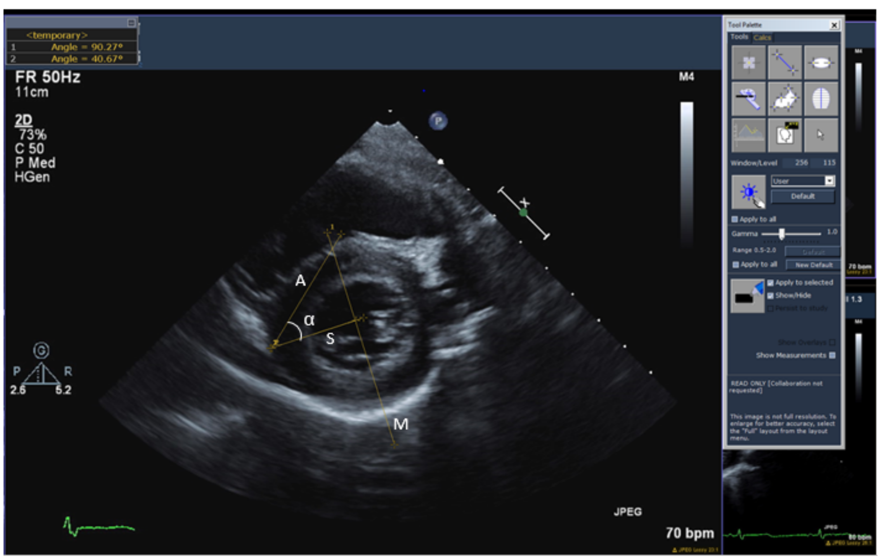
Table 1: Hemodynamic Findings in Pulmonary Hypertension and ASD Subgroups

Hemodynamic Findings	**Pulmonary Hypertension**
Number of Patients	39
Age (years)	2.1 (0.2-19.1)
Gender female (%)	48.7%%

Hemodynamic Findings	Pulmonary Hypertension
Echo Data	
Presence of tricuspid regurgitation	82.0%
TR velocity (m/s)	3.6 (2.6-6.3)
Presence of pulmonary insufficiency	56.4%
Presence of mild pulmonary valve acceleration	.03%
Presence of mild peripheral pulmonary artery stenosis	5.2%
Atrial level shunt	18
Cath Data	
Median RV systolic pressure (mmHg)	25 (16-50)
Median mean pulmonary artery pressure (mmHg)	40 (13-120)
Qp:Qs	1 (.55-3)
PVR (dynes/sec/cm^5)	6.4 (2-34.4)
SVR (dynes/sec/cm^5)	13.6 (7.1-38)
Cardiac Index (l/min/m^2)	3.9 (2-7.6)
Numbers expressed are totals, median (range) and percentages	*Numbers expressed are totals, median (range) and percenta*

Figure 1. A) Diagram of line placement for measurement of Echocardiographically-Derived Septal Position Angle (EDSPA) in subject without pulmonary hypertension. B) Diagram of line placement for measurement of EDSPA in a subject with pulmonary hypertension.



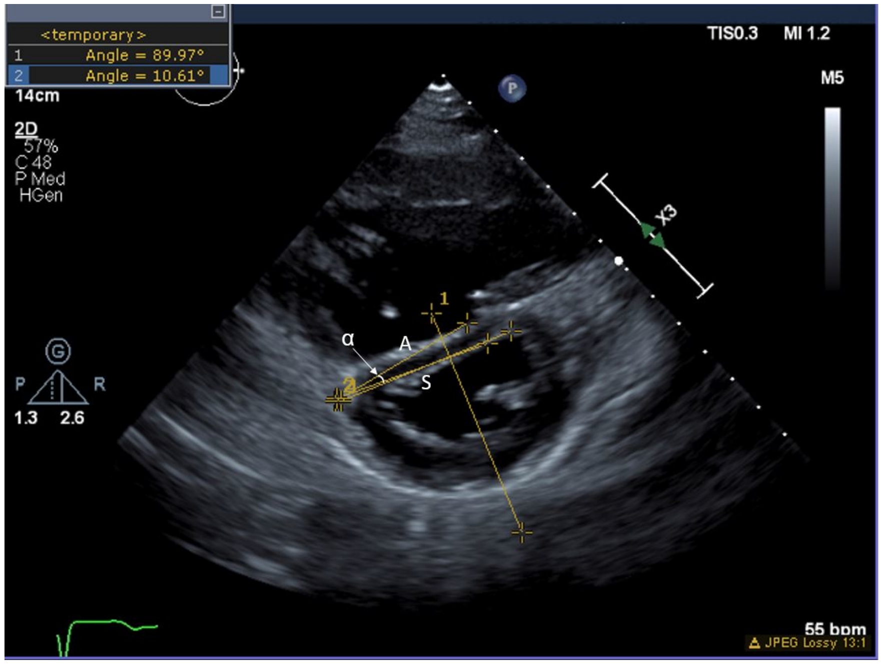


Figure 2. Mean EDSPA Inter-Observer Variability or Concordance

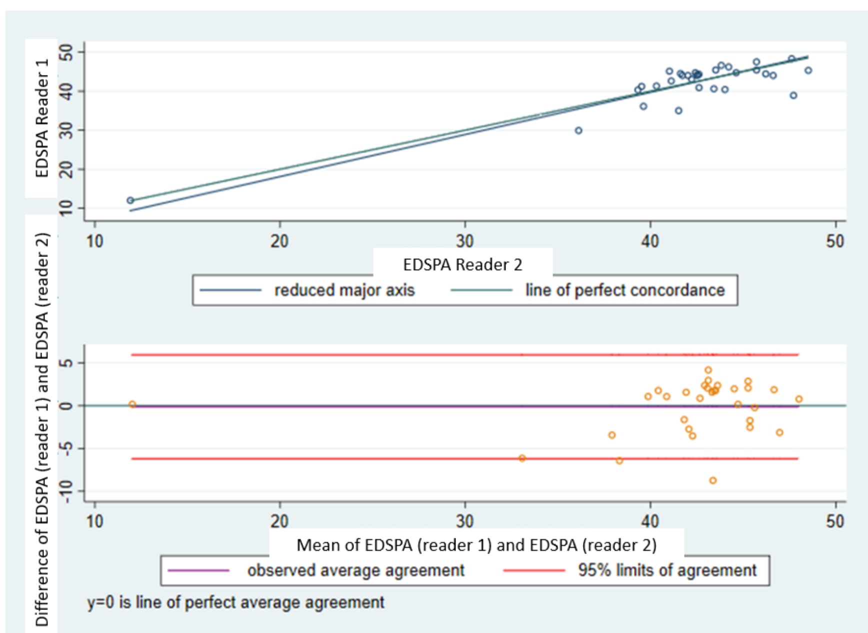


Figure 3. Receiver Operating Characteristic Curve of EDSPA vs. Mean Main Pulmonary Artery Pressure >20 mmHg

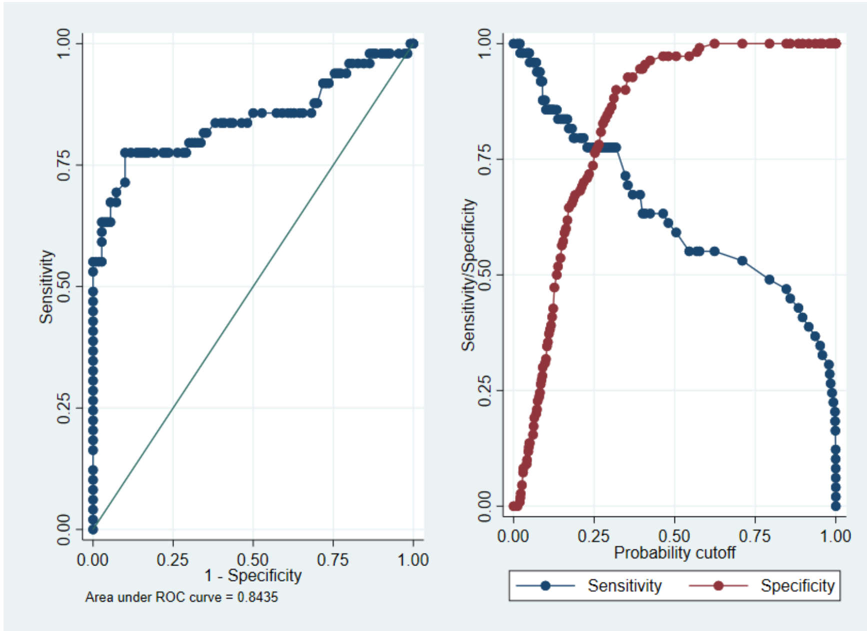


Figure 4. Echocardiographically-derived septal position angle versus mean main pulmonary artery pressure >40 mmHg

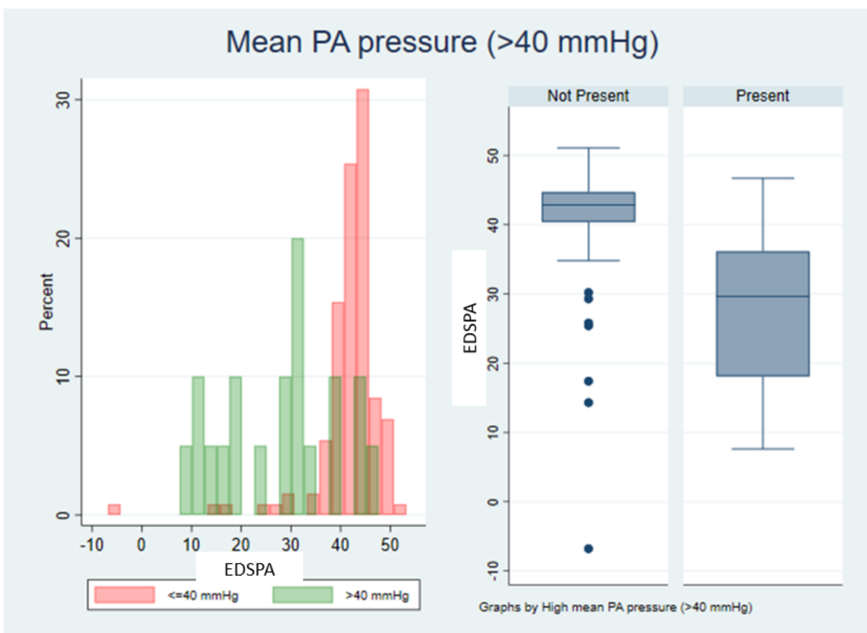
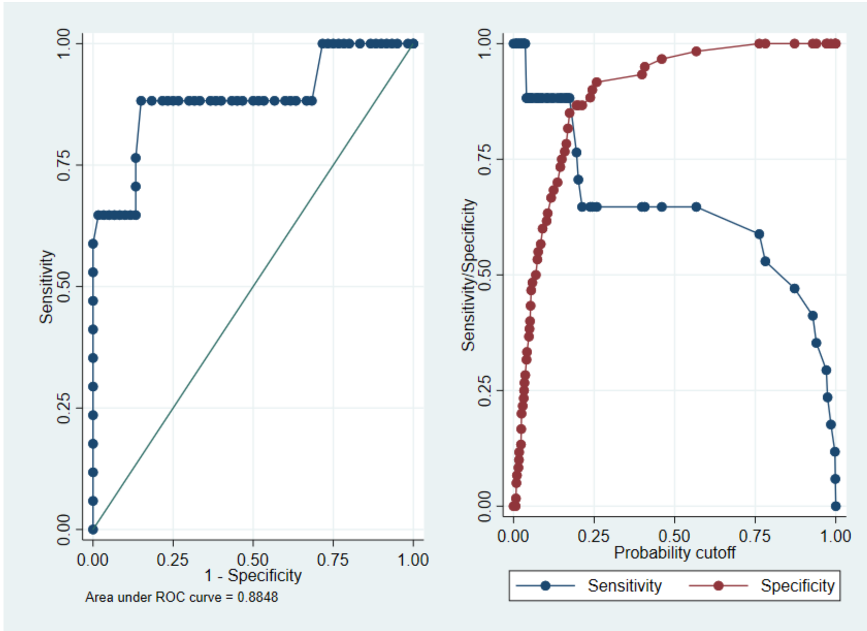


Figure 5. Receiver Operating Characteristic Curve of EDSPA vs. RV/LV systolic pressure ratio >0.5



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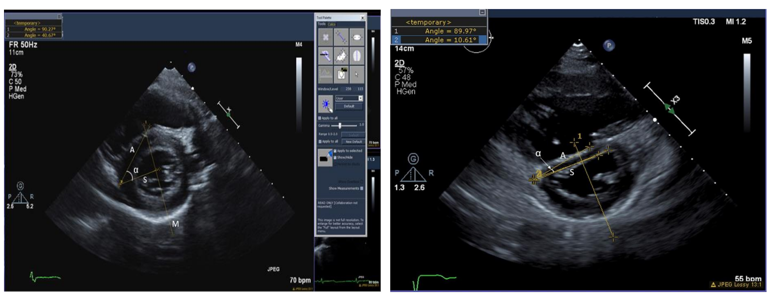

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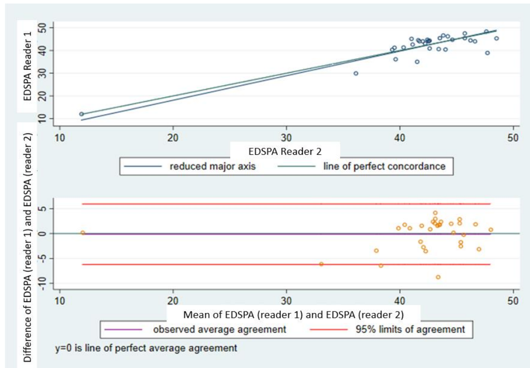

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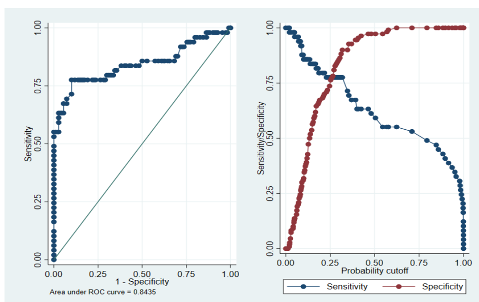

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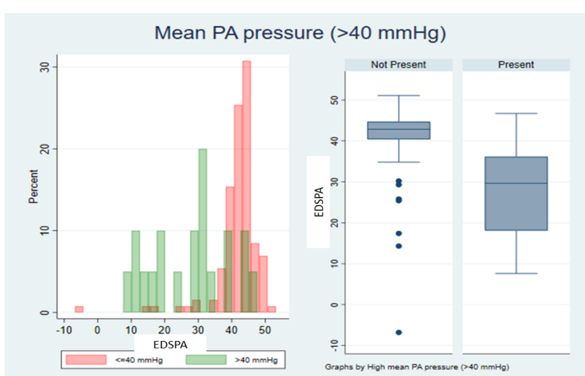

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