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TITLE

The Diagnostic Ability of Pediatric Transthoracic Echocardiography in the Current Era: a Segmental Appraisal

ABSTRACT

Background: Transthoracic echocardiography (TTE) plays a crucial role in the care of pediatric patients with heart disease. However, despite numerous recent technological advances, there has been little re-assessment of its accuracy. We sought to systematically assess the diagnostic accuracy of pediatric TTE in the current era.

Methods: Data were prospectively gathered in consecutive patients at a single institution. TTE findings were compared to anatomic and hemodynamic catheterization/operative findings. Twelve anatomic regions of the heart were assessed, and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratios were calculated. TTE pressure estimates were compared to clinically important catheterization threshold values using ROC curve analysis. Predictors of diagnostic error, including factors pertaining to the patient, the performance of the study, and the characteristics of the reader, were examined using multiple logistic regression.

Results: Data were obtained on 2,341 patients. Specificity was excellent for all anatomic segments (>99%). Sensitivity was good overall (>95%), but less optimal for anomalies of the systemic veins (51%), pulmonary veins (67%), branch pulmonary arteries (74%) and coronary arteries (46%). TTE performed well at predicting clinically significant catheterization threshold levels. The odds of diagnostic error were increased if patient imaging was judged to be problematic (OR=3.1; 95% CI 2.3-4.1). An experienced echo reader significantly reduced the error rate (OR=0.36; 95% CI 0.3-0.5).

Conclusions: Overall, pediatric TTE performs well as a diagnostic test. However, cardiologists need to be cognizant of those anatomic regions where it has reduced sensitivity, be aware of factors influencing its accuracy, and choose appropriate echo

cutpoints to impact clinical decision making.

INTRODUCTION

Transthoracic echocardiography (TTE) plays an integral role in the care of pediatric patients with heart disease in the current era. [1-3] It is a convenient and safe test, and can be performed relatively easily in children with congenital and acquired heart disease. With the advent of advanced two-dimensional echocardiography in the early 1980's, it became integral to the care of these patients. Early studies demonstrated the value of 2-D echo in the diagnostic evaluation of children with heart disease. [4-11] The development of pulsed wave, continuous wave and color Doppler enhanced its diagnostic ability and led to further assessments of its utility, both in making anatomical diagnoses, and in quantifying gradients and pressures. [5, 12-15] Since it is a safe and convenient test compared to invasive cardiac catheterization, researchers examined its ability to replace cardiac catheterization as the sole diagnostic modality for many heart lesions. [16-19]

With improvements in the quality of color Doppler imaging and further advances in ultrasound technology and refinements in Doppler techniques, TTE's diagnostic role in more complex cardiac lesions such as total anomalous pulmonary venous return, and in delineating smaller structures such as coronary arteries, became more entrenched. [20-23]

This led to a number of studies which looked at the utility of TTE alone prior to operations in such lesions as complete AV canal defects, ventricular septal defects, and major congenital heart defects such as transposition of the great arteries and hypoplastic left heart syndrome. [24-29]

However, in many cases, these studies were essentially looking at the utility of TTE in clinical practice. In other words, how often did a preoperative diagnostic error on TTE lead to a discrepancy which altered the clinical course and outcome of a patient. These are in essence, quality assurance studies rather than diagnostic accuracy studies and were only truly able to evaluate the positive predictive value of TTE.

In an attempt to rigorously investigate the diagnostic accuracy of TTE in the current era, we chose to examine its accuracy by 12 anatomical segments, rather than solely by overall diagnosis. In this way, it allowed us to examine normal segments against the invasive reference standard of cardiac catheterization and/or surgery, and hence allow us to examine not just positive predictive value, but also examine the sensitivity, specificity and negative predictive value of TTE by anatomic segment.

Thus, this study sought to prospectively estimate in consecutive patients the diagnostic accuracy of TTE in the recent era, focusing on anatomic region, assessment of cardiac hemodynamics, and the influence of procedural and interpretive factors on its accuracy.

METHODS

Study population

Consecutive pediatric patients undergoing cardiac catheterization and/or surgery at a single tertiary cardiac referral center were prospectively enrolled over a six year period (1998 through 2003). Gathering of these data formed part of an ongoing echocardiography QA process. Consent was obtained from the institutional IRB to include these data in this study.

Echocardiography versus reference standard

Findings at cardiac catheterization and/or surgery were considered to form the reference standard. The surgical findings were obtained by the surgeon with direct inspection of the anatomical segments during the surgical procedure. On an ongoing weekly basis, verbal contact was made by the director of echocardiography and the head surgeon where all the cases were discussed. Any discrepancies in any of the 12 segments between the preoperative TTE and the surgical findings were recorded. The catheterization findings were discussed during the weekly catheterization conference. Catheterization reference standards included direct pressure and gradient measurements by catheters and also findings on angiography. If the reference standard findings were unclear, clarification was obtained during the catheterization conference.

The immediate preoperative TTE represented the index test. Findings were gleaned from the echocardiography report. The pertinent positive and negative findings for all 12 anatomic segments were recorded in the database.

Anatomical regions

Periprocedural surgical and catheterization findings were compared with preoperative echo findings. Only subjects whose echocardiograms were performed at our institution were included, to reduce operator variability. Twelve different intracardiac and extracardiac regions and structures were systematically assessed. These included: 1) pulmonary veins, 2) systemic veins, 3) atrial septum, 4) atrioventricular valves, 5) ventricular septum, 6) semilunar valves, 7) central pulmonary artery, 8) branch pulmonary arteries, 9) coronary arteries, 10) ductus arteriosus, 11) aortic arch and strap vessels, and 12) aortopulmonary collateral vessels. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. The likelihood ratios for a positive test (LR+) and the likelihood ratios for a negative test (LR-), as well as 95% confidence intervals, were calculated using the following formulae: LR+ = sensitivity/ 1 – specificity; LR- = 1 – sensitivity/ specificity. [30]

Cardiac hemodynamics

Findings at cardiac catheterizations were compared to the echo findings immediately prior to the catheterization. Four hemodynamic measurements were considered: aortic stenosis gradient, pulmonic stenosis gradient, aortic coarctation gradient, and RV pressure estimate. The following cardiac catherization thresholds were chosen to represent clinically meaningful cutpoints to act as the reference standard (in other words, threshold values which affected the patient's management, such as decision to balloon the aortic valve in a patient with aortic stenosis etc.): peak to peak aortic stenosis gradient $\geq$ 50 mmHg, peak to peak pulmonic stenosis gradient $\geq$ 50 mmHg, aortic coarctation gradient $\geq$ 25 mmHg, and RV pressure estimate $\geq$ 2/3 systemic. Corresponding echocardiographic indices were used: the echo mean gradient for aortic stenosis, the peak instantaneous pressure gradient for pulmonary stenosis, the peak corrected gradient for coarctation, and the peak systolic RV pressure estimate derived from tricuspid regurgitation for RV pressure. Differing cutpoints were then created for each of the echocardiographic indices to allow for ROC curve analysis.

Factors affecting diagnostic accuracy

Periprocedural surgical and catheterization findings were compared with preoperative echo findings. We included interpretation of echocardiograms performed at outside referral institutions for this portion of the study. Significant echo omissions (such as not reporting normal pulmonary venous return) were treated as diagnostic discrepancies. A number of procedural and interpretive factors which might affect diagnostic accuracy were prospectively evaluated. These included: patient age, the time interval between the echo to the reference standard, the presence of a requisition form, whether the study was recorded digitally or on tape, the operator (sonographer verses cardiology fellow), whether the echo attending was required to obtain further images themselves, whether the patient was judged to be problematic by the scanner at the time of the study (eg. difficult acoustic windows, limited by surgical dressings, patient agitation, or patient awoke from sedation), whether the patient was sedated versus not sedated, whether the institution performing the echo does greater than 4000 echocardiograms per year, and whether the echo was interpreted by an experienced echocardiographer (i.e. a dedicated echo attending with more than three years experience at a tertiary pediatric cardiac center). Simple logistic regression was performed on each of these variables, with the odds of diagnostic error as the dependent variable. These independent variables were then entered into a multiple logistic regression model to find the factors which best explained the odds of diagnostic error.

RESULTS

During the study period, over 40 000 echocardiograms were performed (40,206). Of this total, 5 497 were read as completely normal (14%). In all, 2,341 subjects (6%) underwent reference standard testing during this time. There was a wide spectrum of congenital heart disease lesions among the 2,341 patients. These vary from a simple atrial septal defects and ventricular septal defects, to more complex forms of congenital heart disease such as transposition of the great arteries and hypoplastic left heart syndrome (a typical consecutive surgical sample from a tertiary referral pediatric cardiac center over a 6 year period).

Thus, 2,341 subjects had matched echocardiograms and surgical and/or catheterization procedures. The median age of the patients was one year (interquartile range = 63 days to 5 years). The reference standard used was surgery alone (56%), catheterization alone (40%), and both (4%). The median time interval between the echocardiogram and the reference test was 22 days.

Anatomical regions

One thousand nine-hundred and eighty two subjects had their preprocedural echocardiograms performed at our institution. The sensitivity, specificity, PPV, NPV, LR+ and LR- of echo by anatomic region are provided in Table 1. Overall, the specificity was excellent for all segments. However, the sensitivity was less optimal when evaluating the systemic veins, pulmonary veins, branch pulmonary arteries, coronary arteries and aortopulmonary collateral vessels. The reduced sensitivity for these regions is a reflection of the proportion of false negatives. Some of the more common specific anatomic diagnoses missed included: LSVC to the coronary sinus, PAPVR to the SVC, circumflex coronary artery off the right coronary artery and aberrant right subclavian artery. All the segments have a LR+ of greater than 10. This means that a positive test will significantly increase the posttest probability of true disease. The likelihood ratios for a negative test were less optimal (> 0.2) for the pulmonary veins, systemic veins, coronary arteries, and aortopulmonary collateral vessels. This means that a negative test for these segments did not significantly decrease the probability of true disease.

Cardiac hemodynamics

One thousand and thirty six patients had matched echocardiograms and cardiac catheterizations. The median interval between echo and catheterization was 21 days. Thirty five percent of the catheterizations were performed under general anesthesia, and 65% under sedation.

There were 108 patients with valvar aortic stenosis. Mean echo cutpoint gradients were compared to a catheterization peak-to-peak gradient threshold of ≥ 50 mmHg. The resultant ROC curve is shown in Figure 1. Higher echo mean gradient cutpoints resulted in lower sensitivity but higher specificity. There were 154 patients with valvar pulmonic stenosis. Peak instantaneous pressure gradients were compared to a catheterization peak-to-peak gradient threshold of ≥ 50 mmHg. The ROC curve (Fig. 2) shows that a higher echo cutpoint results in decreased sensitivity. There were 69 patients with aortic coarctation. Peak corrected echo gradients were compared to a catheterization peak-to-peak gradient threshold of ≥ 20 mmHg. The ROC curve is shown in Figure 3. The echo derived RV pressure estimate was compared to a direct catheterization measurement of > 2/3 systemic pressure in 162 patients with a spectrum of congenital heart disease. The resultant ROC curve shows that the echo cutpoint of 2/3 systemic pressure is close to the flexion point of the curve, with reasonably good sensitivity and specificity (Figure 4).

Factors affecting diagnostic accuracy

The method of image storage was digital in 17%, reflecting a transition to digital archiving during the course of this study. A requisition form was present 97% of the time. The proportion of studies done solely by sonographers was 57%, by fellows 29%, and with additional imaging by an attending in 32%. Eighty-five percent of the echocardiograms were performed at a center doing > 4000 echo's per year. Sixty-six percent of the studies were interpreted by an experienced echocardiographer. The patient was judged to be problematic 16% of the time by the person performing the study.

The odds of diagnostic error for each of the independent study and interpretation variables are demonstrated in Table 2. Univariate predictors that increased the odds of diagnostic error included digital versus tape recording (OR 1.28, CI 0.96-1.69), if the patient was judged problematic (OR 2.28, CI 1.74-2.98), and if the patient was sedated (OR 1.22, CI 0.69-2.16). Univariate predictors that reduced the odds of diagnostic error included a high volume institution (OR 0.69, CI 0.52-0.93), an echo reader that trained at a high volume institution (OR 0.64, CI 0.48-0.85), and an experienced echo reader (OR 0.43, CI 0.34-0.53).

Table 3 demonstrates the final multiple logistic regression model which best explained the overall diagnostic error rate. If the patient was judged to be problematic at the time of the study, there was a 3-fold increased risk of diagnostic error (CI 2.27-4.09). An experienced echo reader decreased the error rate by 64% (OR 0.36, CI 0.28-0.47). The odds of diagnostic error were increased with digital acquisition (OR 1.38, CI 1.01-1.90). Both the presence of a requisition slip and the performance of the study at a high volume center resulted in a decreased error rate, which did not reach statistical significance (OR 0.63, CI 0.33-1.22; OR 0.76, CI 0.38-1.5 respectively).

DISCUSSION

This study confirms that transthoracic echocardiography performs very well as a diagnostic test in pediatric patients with heart disease, exhibiting excellent specificity and negative predictive value. It has reduced sensitivity and positive predictive value for certain extracardiac anatomic regions such as branch pulmonary arteries, coronary arteries, pulmonary veins and systemic veins. It can accurately predict important cardiac hemodynamics obtained at catheterization, dependent upon threshold echocardiographic cutpoints. The diagnostic error rate is significantly raised when patients are judged problematic at the time of imaging, and is reduced when studies are interpreted by experienced readers.

Accuracy by anatomical region

Similar to this study, other investigators have reported a higher rate of diagnostic errors when evaluating extracardiac structures. Tworetzky et al. looked at 503 children with major congenital heart diseases such as transposition of the great arteries, tetralogy of Fallot, double chamber right ventricle, interrupted aortic arch, aortic coarctation, atrioventricular septal defect, truncus arteriosus, aortopulmonary septal defect and totally anomalous pulmonary venous return.[27] This was a similar sample as our study. These investigators found that 82% of the subjects underwent surgery after echocardiography alone. They did not strictly assess accuracy, but rather recorded the number of errors made by echocardiography when compared to catheterization and/or surgery. They classified these as major errors if they necessitated a change in the operative procedure, or minor if they did not. In the echocardiography-alone group, diagnostic errors were made in 19 out of 412, 8 major and 11 minor. They found that the single most common type of significant diagnostic error was incorrect definition of the coronary artery anatomy in patients with transposition of the great arteries (13 cases). This is similar to the findings in our study. Methodologically, this study utilized error rate, and there was significant potential for verification bias. In addition, they did not use sensitivity, specificity, PPV and NPV in their analysis.

Pfammatter et al. examined 209 open-heart procedures over a 30 month study period. Nonivasive preoperative diagnosis using echocardiography exclusively was done in 142 patients (68%). Of these, the surgeons were confronted with a previously undiagnosed finding in 12 patients (8.5%) and unexpected findings were obtained at catheterization in 4 subjects (6%) Similar to our study, errors were more common when assessing extracardiac structures such as the coronary arteries and pulmonary and systemic veins (such as missing partial anomalous pulmonary venous return and a left superior vena cava).[28] Again, the investigators calculated an error rate as opposed to utilizing the more rigorous methods of assessing accuracy.

The likelihood ratios from our study show that if echo detects any anatomical abnormality, it significantly raises the post-test probability of true disease. However, when assessing extracardiac structures such as systemic and pulmonary veins, branch pulmonary arteries, coronary arteries and collateral vessels, a normal echo (negative test) less optimally reduces the post-test probability of true disease. Hence, sonographers should take particular care when imaging these structures, and echocardiographers should be particularly vigilant when evaluating these regions.

Assessment of cardiac hemodynamics

Previous studies have looked at correlations between echocardiographic measures of cardiac hemodynamics and invasive measurements. Typically these have been in the form of "artificial" simultaneous validation studies under controlled conditions. [31, 32] In this study, however, echocardiographic values and catheterization values were compared under "real world" conditions where the data were obtained during routine preoperative assessment. In our analyses, rather than evaluating how well echo can mimic cardiac catheterization measures, we utilized ROC curve analyses to evaluate a range of echo cutpoints. These then allows clinicians to "trade-off" sensitivity verses specificity, depending on the clinical scenario, and positively impact management decisions. For instance, it may be more beneficial to use a mean echo aortic stenosis gradient of 60 mmHg as a threshold for taking a patient for balloon angioplasty, since it is highly specific at predicting a catheterization gradient of ≥50 mmHg. If one used 50 mmHg as an echo threshold, this would result in more "false positives" (in other words, patients who in the catheterization lab have peak-to-peak gradients less the 50 mmHg, and have the angioplasty aborted). These patients would have then undergone general anesthesia and a cardiac catheterization needlessly. These same principles can be applied to pulmonic stenosis, aortic coarctation and the assessment of right ventricular pressure. In this way, clinicians can utilize the ROC curves and pick the optimal cutpoints to use, dependent on the clinical decision (i.e. the trade-off between sensitivity and specificity).

Factors affecting diagnostic accuracy

Investigators have explored factors which affect the accuracy of pediatric echocardiograms. In a study by Stanger et al, pediatric echocardiograms performed in adult echo labs were evaluated for their accuracy. [33] Sixty-six pediatric patients who underwent echocardiograms at adult facilities had repeat echocardiograms done at a tertiary pediatric cardiac referral center. The adult echocardiographic diagnoses were compared with either catheterization and/or surgery, or with echocardiographic verification by blinded duplicate-observer review (done by pediatric cardiologists). In 35 of 66 adult lab echocardiograms (53%), moderate or major diagnostic errors occurred (71% were interpretive, 17% were technical, and 11% both). However, the overall number of subjects in the study was small, and not all the findings were verified by the reference standard of surgery or catheterization. Another study in Australia looked at the diagnostic error rate among echocardiograms undertaken by individuals other than pediatric cardiologists. [34] Similarly, they found diagnostic errors in 47 out of 110 patients (44% of the externally studied group).

We explored a number of factors which might impact accuracy, some of which are specific to a tertiary training facility. Age did not impact diagnostic accuracy. This could be explained by the deterioration in image quality as patients age, which may offset the degree of complexity which is more common in neonates. A requisition form helped to decrease the error rate, likely by increasing the care with which specific areas were examined, and hence indirectly raising the pre-test probability. This was not statistically significant, possibly since the vast majority did have requisition forms (which is a policy of our laboratory). Digital acquisition appeared to increase the error rate in this study. However, our lab transitioned to a digital lab near the end of the study period, and thus this might reflect a relative inexperience at the time. It did not appear to matter whether a cardiology fellow or sonographer performed the study, or whether further imaging needed to be obtained by the echo attending. The most significant factor which increased the error rate was whether the patient was judged to be problematic at the time of the study. The most cited reasons for this were lack of sedation, restlessness, poor acoustic windows, or the presence of surgical dressings. This highlights how important it is to optimize imaging conditions in pediatric patients. Our echo lab has a policy of sedating patients between the ages of 1 month to 4 years for complete studies, which helps to ensure optimal imaging conditions. The effect of volume of echocardiograms per year was examined (by comparing volumes between referral centers). The accuracy was better in centers performing greater than 4000 pediatric echocardiograms per year.

We investigated echo interpretation factors. Studies interpreted by echo readers who trained at higher volume centers (>4000 studies per year), appeared to have a lower error rate. In addition, experienced echo readers who were defined as "echo subspecialists" (> 3 years as a dedicated echo attending at a tertiary cardiac center), had lower diagnostic discrepancy rates.

Strengths and Limitations

The main strength of this study was that the data were gathered prospectively as part of a quality assurance process. This ensured the completeness of the reference test findings (cardiac catheterization and findings at surgery). In addition, the patients were collected consecutively, which helped to avoid selection bias. Finally, the significant number of patients collected helped to improve the precision of the findings.

The problem of verification bias is usually unavoidable in situations where the reference standard is invasive, and when it is performed as a result of the index test. For instance, the echocardiograms read as normal obviously would not be verified by cath or surgery. However, since this study assessed the regions systematically, often our normal findings (like normal systemic venous return) were confirmed when the reference standard was performed for the other more significant anatomic abnormalities (such as an ASD or VSD). We feel that this helped to minimize the impact of verification bias on our findings.

The surgeons and the catheterizers were not blinded to the echo reports, and this could have influenced interpretation of the reference standard. However, results from direct inspection by the surgeon (for example of a VSD) and invasively measured catheterization data and angiography, we feel are not prone to significant diagnostic bias.

Multiple echocardiographers were responsible for reading the TTE's which were incorporated in this study. This likely introduced inter-observer variability. However, this did allow us to make comparisons between the levels of experience of the echocardiographers. In addition, the incorporation of multiple echocardiographers in fact increases the external validity and generalizability of the findings. Finally, these findings are in the setting of a single tertiary pediatric cardiac center, and may not be applicable to other tertiary centers, or to other pediatric cardiology settings.

Conclusions

Overall, pediatric transthoracic echocardiography performs well as a diagnostic test. However, cardiologists need to be cognizant of those anatomic regions where it has reduced sensitivity, be aware of factors influencing its accuracy, and choose appropriate echo cutpoints to impact clinical decision making.

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TABLES

Table 1. Comparison of Diagnostic Accuracy of Transthoracic Echocardiography by Anatomic Region in 2,341 subjects with matched echocardiograms and surgical and/or catheterization procedures.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR +ve	LR -ve
Pulmonary Veins	66.7 (64.6-68.7)	99.9 (99.8-100)	96.6 (95.7-97.3)	99.3 (98.9-99.7)	667 (518-858)	0.33 (0.2-0.6)
Systemic Veins	51.2 (49.0-53.4)	99.9 (99.8-100)	95.5 (94.5-96.3)	98.9 (98.5-99.4)	512 (384-682)	0.49 (0.3-0.8)
Atrial Septum	98.0 (97.4-98.6)	99.9 (99.8-100)	99.7 (99.4-99.9)	99.6 (99.3-99.9)	980 (835-1150)	0.02 (0.01-0.05)
AV Valves	97.7 (97.0-98.3)	99.9 (99.7-100)	99.2 (98.8-99.6)	99.7 (99.3-99.9)	977 (831-1148)	0.02 (0.01-0.05)
Ventricular Septum	98.9 (98.4-99.3)	99.7 (99.5-99.9)	99.1 (98.6-99.5)	99.7 (99.4-99.9)	329 (282-385)	0.01 (0.01-0.02)
Semilunar Valves	98.3 (97.7-98.9)	99.8 (99.6-100)	99.2 (98.7-99.5)	99.6 (99.3-99.9)	492 (419-576)	0.02 (0.01-0.04)
Main PA	98.4 (97.8-98.9)	99.8 (99.6-100)	98.8 (98.3-99.2)	99.8 (99.5-99.9)	492 (419-576)	0.02 (0.01-0.03)
Branch PA's	74.1 (72.1-76.0)	99.5 (99.1-99.7)	86.3 (84.7-87.8)	98.9 (98.3-99.3)	148 (117-187)	0.26 (0.14-0.49)
Coronary Arteries	45.8 (43.6-48.0)	99.5 (99.2-99.8)	55.0 (52.8-57.1)	99.3 (98.9-99.6)	92 (68-123)	0.54 (0.3-0.9)
PDA	97.8 (97.1-98.4)	99.8 (99.6-100)	96.7 (95.9-97.5)	99.9 (99.7-100)	489 (416-574)	0.02 (0.01-0.05)
Aortic Arch	83.1 (81.4-84.7)	99.5 (99.1-99.8)	94.6 (93.5-95.5)	98.2 (97.6-98.8)	166 (135-205)	0.17 (0.09-0.33)
Collateral Vessels	35.5 (33.3-37.5)	100 (99.9-100)	100 (99.9-100)	98.9 (98.5-99.4)	355 (258-488)	0.64 (0.41-1.00)

PPV – positive predictive value, NPV – negative predictive value, LR+ve = likelihood ratio of a positive test, LR-ve = likelihood ratio of a negative test; 95% confidence intervals are shown in brackets.

Table 2. Univariate Predictors of Diagnostic Error of Transthoracic Echocardiography.

	Odds Ratio	Std. Error	P-value	95% C.I.
Patient age (days)	1.00	0.0002	0.161	0.99-1.00
Time from echo to reference standard (days)	0.99	0.0006	0.51	0.99-1.00
Presence of a requisition form	0.64	0.21	0.16	0.34-1.2
Digital verses tape recording	1.28	0.18	0.092	0.96-1.69
Study performed by sonographer	0.99	0.11	0.97	0.79-1.25
Study performed by cardiology fellow	0.87	0.11	0.26	0.67-1.11
Additional images obtained by echo attending	0.78	0.11	0.07	0.59-1.02
Patient judged problematic at time of study (by operator and/or reader)	2.28	0.31	<0.001*	1.74-2.98
Patient cooperative verses restless	0.89	0.16	0.49	0.63-1.25
Patient sedated verses not sedated	1.22	0.36	0.49	0.69-2.16
Institution performing echo does > 4000 echos per year	0.69	0.11	0.016*	0.52-0.93
Echo reader trained at tertiary pediatric cardiac center doing > 4000 echos per year	0.64	0.09	0.002*	0.48-0.85
Echo reader with > 3 years experience as dedicated echo attending at a tertiary pediatric cardiac center	0.43	0.05	<0.001*	0.34-0.53

* P-value <0.05

Table 3. Multivariate Regression Model Predicting Diagnostic Error of Transthoracic Echocardiography.

	Odds Ratio	Std. Error	P-value	95% C.I.
Echo reader with > 3 years experience as dedicated echo attending at a tertiary pediatric cardiac center	0.36	0.05	<0.001*	0.28-0.47
Digital verses tape recording	1.38	0.22	0.045*	1.01-1.90
Presence of a requisition form	0.63	0.21	0.17	0.33-1.22
Institution performing echo does > 4000 echos per year	0.76	0.27	0.43	0.38-1.50
Patient judged problematic at time of study (by operator and/or reader)	3.05	0.46	<0.001*	2.27-4.09

* P-value <0.05

FIGURE LEGENDS

Figure 1. ROC curve depicting the accuracy of different echocardiographic mean gradient cutpoints at predicting a catheterization-derived peak-to-peak gradient of >50mmHg in patients with aortic stenosis (echo values are in mmHg).

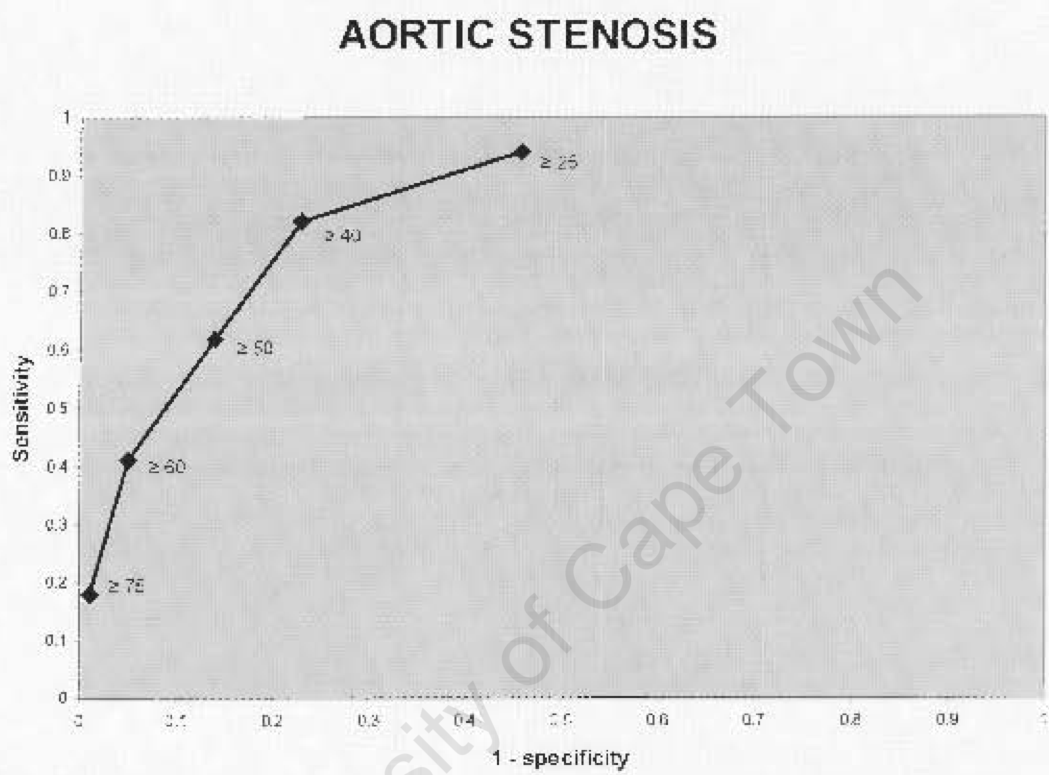
Figure 2. ROC curve depicting the accuracy of different peak echocardiographic gradient cutpoints at predicting a catheterization-derived peak-to-peak gradient of >50mmHg in patients with pulmonic stenosis (echo values are in mmHg).

Figure 3. ROC curve depicting the accuracy of different peak echocardiographic gradient cutpoints at predicting a catheterization-derived peak-to-peak gradient of ≥25mmHg in patients with aortic coarctation (echo values are in mmHg).

Figure 4. ROC curve depicting the accuracy of different echocardiographic cutpoint values of RV pressure derived from tricuspid regurgitation compared to catheterization measurements of RV pressure (echocardiographic values are provided as a proportion of systemic pressure).

FIGURES

Figure 1

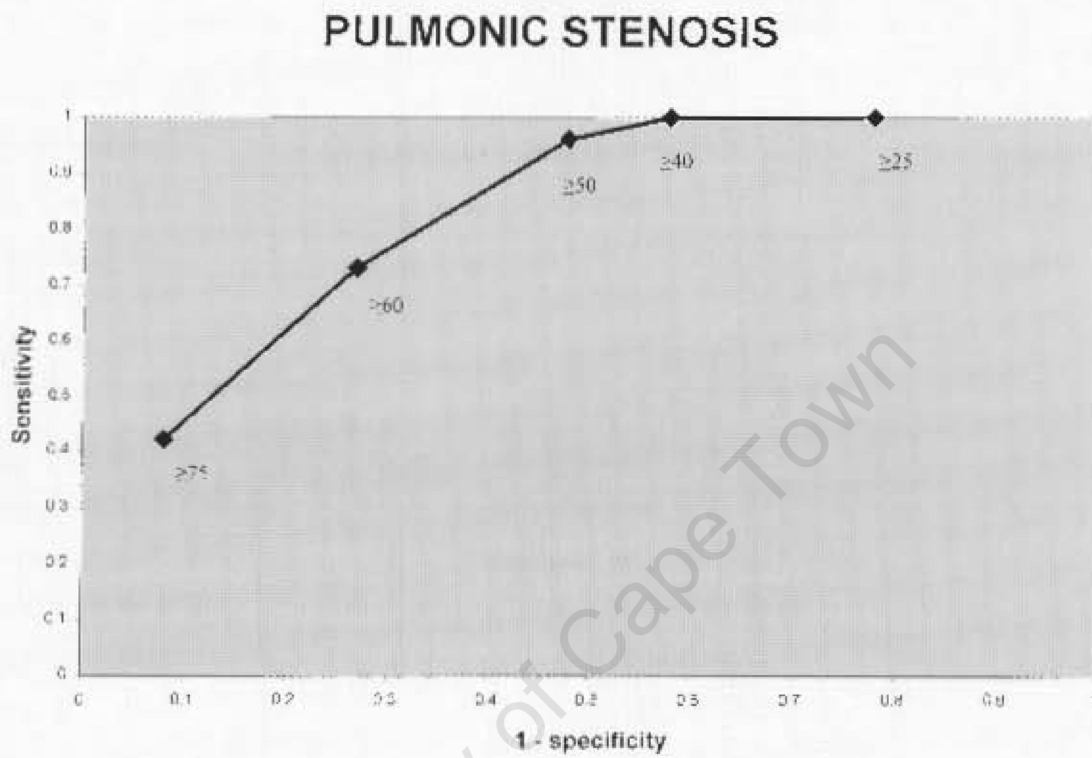


Aortic stenosis peak-to-peak gradient ≥ 50 mmHg (n=108)

Echo mean gradient cutpoint (mmHg)	**Sens (%)**	**Spec (%)**	**PPV (%)**	**NPV(%)**	**Area under ROC**	**LR+**	**LR-**
≥ 25	94 *(90-99)	54 (45-63)	49 (39-58)	95 (91-99)	0.74 (0.7-0.8)	2.0	0.11
≥ 40	82 (75-90)	77 (69-85)	62 (53-71)	90 (85-96)	0.80 (0.7-0.9)	3.6	0.22
≥ 50	62 (53-71)	86 (80-93)	68 (59-77)	83 (76-90)	0.74	4.6	0.44
≥ 60	41 (32-50)	95 (90-99)	78 (70-86)	78 (70-86)	0.68 (0.6-0.8)	7.6	0.62
≥ 75	18 (10-25)	99 (96-99)	86 (79-92)	72 (64-81)	0.58 (0.5-0.6)	13.1	0.83

* Bracketed values represent 95% confidence intervals

Figure 2

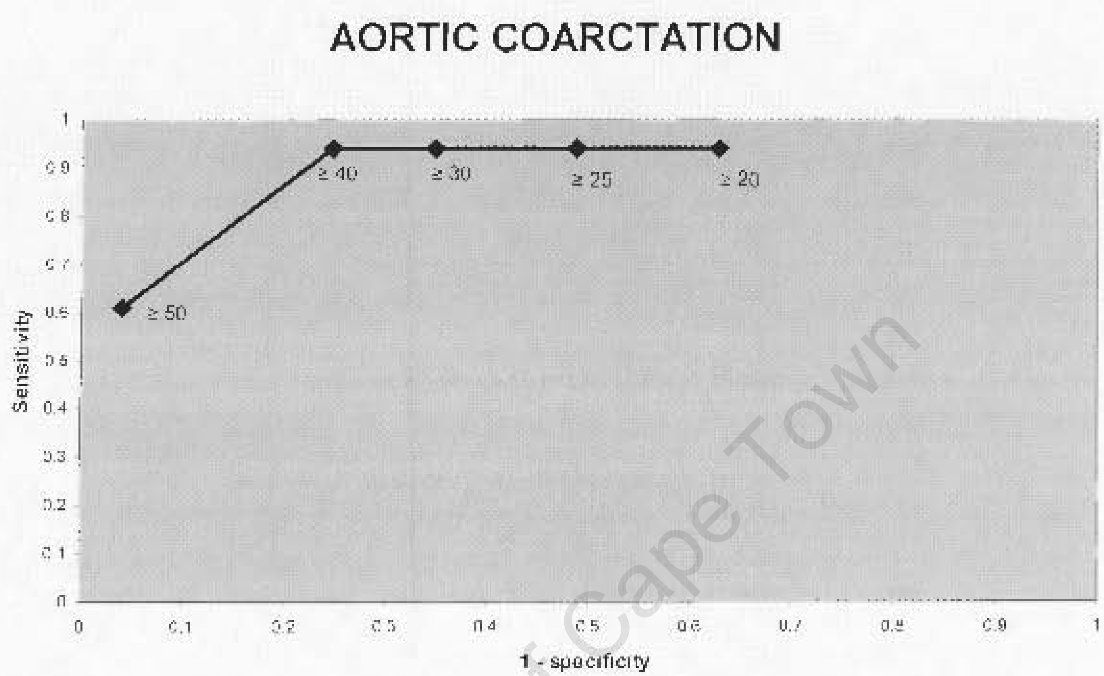


Pulmonic stenosis peak-to-peak gradient ≥ 50 mmHg (n=154)

Echo peak gradient cutpoint (mmHg)	Sens (%)	Spec (%)	PPV (%)	NPV(%)	Area under ROC	LR+	LR-
≥ 25	100 *(100)	22 (15-28)	39 (32-47)	100 (100)	0.61 (0.6-0.7)	1.3	0.00
≥ 40	100 (100)	42 (34-50)	47 (39-55)	100 (100)	0.71 (0.7-0.8)	1.7	0.00
≥ 50	96 (93-99)	52 (44-60)	51 (43-58)	96 (93-99)	0.74 (0.7-0.8)	2.0	0.07
≥ 60	73 (66-80)	73 (66-80)	58 (50-65)	84 (78-90)	0.73 (0.7-0.8)	2.7	0.37
≥ 75	42 (35-50)	92 (88-96)	73 (66-80)	76 (69-83)	0.67 (0.6-0.7)	5.4	0.63

*Bracketed values represent 95% confidence intervals

Figure 3

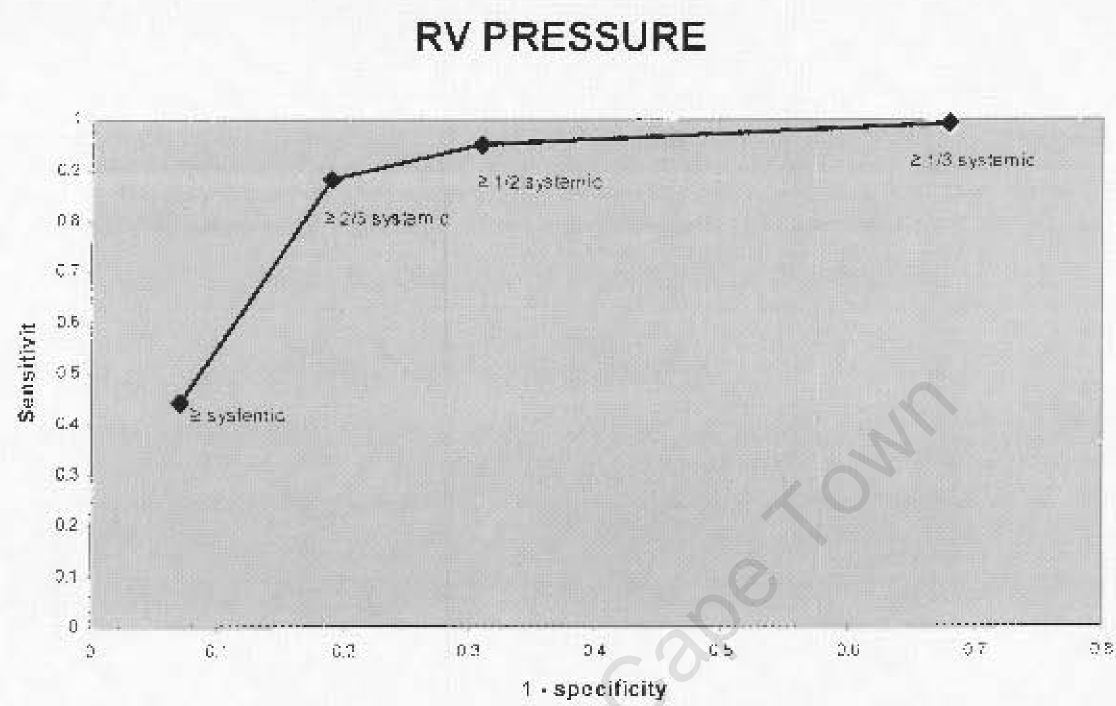


Aortic coarctation peak gradient ≥ 25 mmHg (n=69)

Echo peak gradient cutpoint (mmHg)	Sens (%)	Spec (%)	PPV (%)	NPV(%)	Area under ROC	LR+	LR-
≥ 20	94 *(89-99)	37 (26-49)	35 (23-46)	95 (90-100)	0.66 (0.6-0.7)	1.5	0.15
≥ 25	94 (89-99)	51 (39-63)	40 (29-52)	96 (92-100)	0.73 (0.6-0.8)	1.9	0.11
≥ 30	94 (89-99)	65 (53-76)	49 (37-60)	97 (93-100)	0.80 (0.7-0.8)	2.7	0.09
≥ 40	94 (89-99)	75 (64-85)	57 (45-68)	97 (94-100)	0.84 (0.8-0.9)	3.7	0.07
≥ 50	61 (50-73)	96 (92-100)	85 (76-93)	88 (80-95)	0.79 (0.7-0.9)	15.6	0.41

* Bracketed values represent 95% confidence intervals

Figure 4



Right ventricular pressure ≥ 2/3 systemic pressure (n=162)

Echo RVp estimate from TR cutpoint	**Sens (%)**	**Spec (%)**	**PPV (%)**	**NPV(%)**	**Area under ROC**	**LR+**	**LR-**
≥ 1/3 systemic	99 *(97-100)	32 (25-39)	59 (52-67)	96 (93-99)	0.65 (0.6-0.7)	1.5	0.04
≥ 1/2 systemic	95 (92-98)	69 (62-76)	75 (69-82)	93 (89-97)	0.82 (0.8-0.9)	3.1	0.07
≥ 2/3 systemic	88 (83-93)	81 (76-87)	83 (77-88)	87 (82-92)	0.85 (0.8-0.9)	4.7	0.15
≥ systemic	44 (36-51)	93 (89-97)	85 (80-91)	63 (55-70)	0.68 (0.6-0.7)	5.9	0.61

* Bracketed values represent 95% confidence intervals