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The utility of combined cardiopulmonary exercise stress testing in the evaluation of pediatric patients with chest pain

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Abstract

Introduction: A cardiac cause is an extremely rare etiology of pediatric chest pain. Despite its low sensitivity/specificity, exercise stress testing (EST) is widely used to determine the prognosis in patients with suspected/established coronary disease. We aimed to look at the utility of a combined cardiopulmonary EST in the evaluation of pediatric patients with chest pain.

Methods: After institutional review board approval, a retrospective chart review was performed of all pediatric patients who were referred for an EST for chest pain from January 2014 to 2017. Patients with incomplete records, severe congenital heart disease, and a prior EST were excluded.

Results: A total of 389 patients met the inclusion criteria. Echocardiogram (ECHO) was performed on 333 (85.6%) patients and 43 (11%) previously unknown structural cardiac anomalies were identified. A total of 76 (19.5%) patients had an abnormal EST with the 3 most common causes being related to the respiratory system. Only four patients had both an abnormal exercise stress test and an incidental structural anomaly on ECHO but none of them had their symptoms recreated during the EST.

Conclusion: Only 1% of patients previously undiagnosed with heart disease had an abnormal stress test and an incidental anomaly on ECHO. These ECHO anomalies were unlikely to be the cause of chest pain. Furthermore, since the majority of abnormal stress tests were secondary to a pulmonary cause, a complete cardiopulmonary EST may be an effective screening tool for certain patients presenting with chest pain. Our study emphasizes the need for performing a complete cardiopulmonary EST instead of an isolated cardiac stress test to maximize diagnostic efficiency and yield.

KEYWORDS

chest pain, exercise stress test, pulmonary function test

1 | INTRODUCTION

Chest pain is a common presenting complaint in the pediatric population.[1,2] Musculoskeletal causes and pulmonary abnormalities account for the majority of cases while cardiac causes are extremely rare, accounting for <1%.[3] The workup of chest pain, even among pediatric cardiologists, is quite variable[2-5] and there is no standard protocol for evaluation. The specific etiologies to exclude via cardiac evaluation are previously undiagnosed structural abnormalities associated with ischemic pain, acquired myopericardial or coronary disease, and arrhythmias with palpitations and/or tachycardia described as pain by the child.[6] The concerning history of exertional

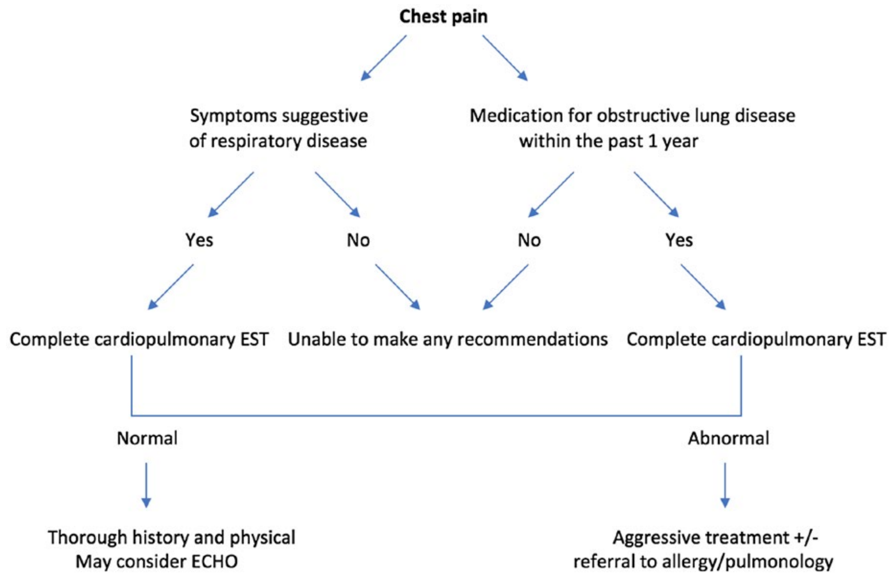

FIGURE 1 A screening algorithm for the initial evaluation of pediatric patients with chest pain [Colour figure can be viewed at wileyonlinelibrary.com]

chest pain or exercise-associated symptoms such as palpitations, lightheadedness, and syncope often leads to evaluation with an exercise stress test (EST).

Previous studies have looked at the utility of the cardiac EST in the outpatient evaluation of pediatric patients with chest pain and have correlated echocardiographic findings with the EST results.[7] Published data suggest that pulmonary abnormalities may be a large cause of chest pain in the pediatric population.[6] However, there is extremely limited data regarding the utility of pulmonary function testing along with the EST in this population. Hence, the purpose of this study was to examine the utility of a combined cardiopulmonary EST in the evaluation of pediatric patients with chest pain in a large single-center cohort.

2 | MATERIALS AND METHODS

A retrospective chart review was performed of all pediatric patients (<21 years) who were referred for an EST for symptoms of chest pain over a 3-year period (January 2014-2017). This included both outpatient and inpatient referrals. To address the variability in the evaluation of patients with chest pain, our center has instituted a screening algorithm especially for those with an indication of an underlying respiratory pathology. The algorithm suggests an EST under certain clinical scenarios (Figure 1). The approval for this study was obtained from the institutional review board at the Children's Healthcare of Atlanta. Electronic medical records were obtained and reviewed for all patients who had an EST as a part of their evaluation for chest pain. Patients' age, gender, ethnicity, weight, height, and the current medications were recorded. EST results were reviewed by an exercise physiologist/cardiologist while echocardiograms were reviewed by a separate imaging cardiologist. Patients with incomplete records, severe congenital heart disease such as those with single ventricle physiology, and those with a prior EST were excluded from our study.

2.1 | Testing method

Treadmill exercise testing was performed using the Bruce protocol.[8,9] In this protocol, there is a rise in speed (baseline speed 1.7 mph) and incline (baseline incline 10%) every 3 minutes. For those unable to exercise on a treadmill or for those under 8 years of age, the bike was used for testing. Our stress lab uses the James protocol most commonly for bike testing. The James Protocol separates patients into three categories based on body surface area (BSA) and gender-termed James Large (>1.2 m^2), James Medium (1.0-1.2 m^2), and James Small (BSA < 1.0 m^2). Each stage is of 3 minutes duration similar to the Bruce protocol. Heart rate and EKG monitoring was performed every minute with supplementary analysis if arrhythmias were noted.

The parameters that were recorded for the cardiac portion of the EST included supine heart rate (HR), exercise duration, maximum HR, maximum HR% predicted, lowest and peak oxygen saturation, supine systolic and diastolic blood pressure, maximal systolic and diastolic blood pressure, peak oxygen consumption (VO_2), peak VO_2% predicted, anaerobic threshold, and anaerobic threshold % predicted (Table 1).

Pulmonary function testing was performed using the Children's Healthcare of Atlanta Exercise Laboratory Spirometry Guidelines. This involves pre- and postexercise spirometry which entails performing forced vital capacity (FVC). After obtaining a baseline FVC, we perform FVCs 10 minutes post-exercise. Acceptability criteria for an adequate PFT were defined as plateau in one second, expiratory time >6 seconds, back extrapolated volume less than 5% or 1.5 L, smooth and continuous exhalation, and maximal effort based on

TABLE 1 Cardiac parameter findings of the exercise stress test

Parameters of EST	Mean ± SD		
	5-9 Years	10-14 years	15-19 years
Exercise duration	9.3 ± 2.2	10.3 ± 1.6	10.5 ± 2.2
Supine HR	86.3 ± 15.6	79.9 ± 15.4	78.3 ± 16.9
Maximal HR	194.9 ± 12.3	194.8 ± 11.8	194.1 ± 12.1
Maximal HR % predicted	91.2 ± 6.0	93.2 ± 6.2	94.5 ± 6.3
Lowest SpO_2	93.5 ± 2.4	95.3 ± 3.1	95.8 ± 2.1
Peak SpO_2	99.3 ± 0.8	98.8 ± 1.7	98.8 ± 1.1
Supine BP systolic	109.8 ± 13.9	119.8 ± 14.4	123.0 ± 17.1
Supine BP diastolic	63.1 ± 10.6	64.8 ± 10.5	67.5 ± 11.4
Maximal BP systolic	157.8 ± 26.4	174.0 ± 25.0	184.4 ± 28.6
Maximal BP diastolic	66.5 ± 9.9	69.9 ± 13.4	69.1 ± 14.0
Peak VO_2	41.9 ± 9.4	41.7 ± 10.1	39.5 ± 9.8
Peak VO_2 % predicted	104.3 ± 18.9	99.0 ± 21.4	94.3 ± 16.9
Anaerobic threshold	20.6 ± 5.6	19.6 ± 6.3	19.2 ± 5.3
Anaerobic threshold % predicted	51.6 ± 10.9	47.3 ± 14.3	46.1 ± 11.7

Abbreviations: BP, blood pressure; HR, heart rate; SpO_2, oxygen saturation; VO2, peak oxygen consumption.

TABLE 2 Pulmonary function testing findings of the exercise stress test

Parameters of PFT	Mean (SD)
Maximal RR	53.2 ± 14.4
End tidal CO_2	36.1 ± 11.2
FVC	3.5 ± 1.7
FEV_1	3.0 ± 1.0
FEV_1/FVC	84.6 ± 6.8
FEF 25%-75%	3.2 ± 1.1
FVC% predicted	100.6 ± 15.1
FEV_1% predicted	97.7 ± 14.5
FEV_1/FVC% predicted	87.5 ± 7.6
FEF 25%-75% predicted	90.9 ± 23
% Change FVC	−1.3 ± 5.1
% Change FEV_1	−0.8 ± 6.1
% Change FEV_1/FVC	−12.5 ± 5.0
% Change FEF 25%-75%	−1.4 ± 16.3

Abbreviations: FEF, forced expiratory flow; FEV_1, forced expiratory volume in the 1st second; FVC, forced vital capacity; RR, respiratory rate.

peak flow. Normal FVC and FEV_1 were defined as >85% predicted and normal FEV_1/FVC was defined as >85% for kids, >80% for teenagers, and >75% for adults. The PFT parameters that were recorded were maximal respiratory rate, end tidal CO_2, forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1), FEV_1/FVC, FEF 25%-75%, FVC % predicted, FEV_1 % predicted, FEV_1/FVC % predicted, FEF 25%-75% predicted, % change in FVC, FEV_1, FEV_1/FVC, and FEF 25%-75% post-exercise (Table 2).

Absolute indications to terminate the test included: (i) ST segment elevation (>1.0 mm) in leads without Q waves (other than V_1 or aVR), (ii) drop in systolic BP >10 mmHg, (iii) moderate-to-severe angina (grade 3 to 4), (iv) central nervous systems (ataxia, dizziness, or near syncope), (v) signs of poor perfusion (cyanosis or pallor), (vi) sustained ventricular tachycardia, (vii) technical difficulties monitoring the EKG or systolic BP, and (viii) subject's request to stop.

2.2 | Analysis

Electronic medical records were obtained for all patients included in the study. Data regarding clinical evaluation by the referring a pediatric cardiologist, electrocardiograms (EKGs), echocardiogram, previous exercise, or pulmonary testing as available were collected and analyzed using descriptive statistics. An adequate EST was based on certain performance criteria including heart rate (>85% predicted) and respiratory exchange ratio (>1.09 in a child >13 years age and >1.0 in a child <13 years of age).[10] A normal EST was defined as one without evidence of ischemia, arrhythmias, pathological changes in corrected QT interval, or abnormalities on PFT. Descriptive statistics were used to analyze all results.

3 | RESULTS

Three hundred eighty-nine patients who underwent exercise testing between January 2014 and 2017 met the inclusion criteria. The mean age of our cohort was 13.6 ± 3.2 years with a range of 5-19 years. There were 237 (60.9%) males and 152 (39.1%) females. Two hundred and ten patients (54.0%) were Caucasian, 146 (37.5%) were African American, 29 (7.5%) were Hispanic, and 2 (0.5%) were of Asian descent. Ethnicity was unknown in two patients (0.5%). Mean height and weight of all patients were 160.2 ± 16.1 cm and 57.1 ± 21.2 kg, respectively.

One hundred thirty patients had chest pain with exertion alone and 156 patients had chest pain at rest and with exercise. Echocardiogram (ECHO) was performed on 333 (85.6%) of these patients and 43 (11%) previously unknown structural cardiac anomalies were identified. Of them, 8 patients were considered to have a lesion significant enough to warrant further follow-up, evaluation, or care (8/333, 2.4%). These included unicuspid aortic valve, left ventricular noncompaction, and coronary artery abnormalities. The significant coronary artery anomalies included right coronary off left sinus (n = 2), left coronary off right sinus (n = 1), and atresia of the left main coronary artery with collateralization from the right coronary (n = 1).

TABLE 3 Incidental structural anomalies on echocardiogram and anomalies on the exercise stress test

Incidental structural anomalies on ECHO	Abnormalities on EST
Patent foramen ovale (6)	Obstructive pattern (34)
Bicuspid aortic valve without obstruction (6)	Exercise induced bronchospasm (22)
Mild left ventricular hypertrophy (5)	Restrictive pattern (6)
Mild valvar pulmonary stenosis (3)	ST segment changes (5) [elevation (4), depression (1)
Coronary anomalies (8) [RCA off left sinus (2), LCA off right sinus (1), atresia of left main CA (1), acute angulation of RCA (2), small LCA to pulmonary artery fistula (2)]	Arrhythmias (3) [severe PACs (1), atrial fibrillation (1), wide complex tachycardia (1)]
Mitral valve disease (4) [mild mitral stenosis (2), trivial mitral valve prolapse (1), trivial mitral insufficiency (1)]	Vocal cord dysfunction (2)
Trivial aortic insufficiency (2)	Obstructive sleep apnea (2)
Tiny patent ductus arteriosus (2)	Syncope (1)
Aberrant right subclavian artery (2)	QT prolongation (1)
Unicupsid aortic valve (1)	
LV noncompaction (1)	
Tiny AP collaterals (1)	
Small secundum ASD (1)	
Trivial pericardial effusion (1)	

Abbreviations: AP, aortopulmonary; ASD, atrial septal defect; LCA, left coronary artery; LV, left ventricle; PAC, premature atrial complex; RCA, right coronary artery.

None of these patients had chest pain with exertion and all of them had a normal EST. Two other patients had an acute takeoff of the RCA and 1 patient had a small fistula from the LCA to the pulmonary artery. The 3 most common incidental anomalies identified on ECHO were patent foramen ovale [*n* = 6], bicuspid aortic valve (BAV) [*n* = 6], and left ventricular hypertrophy (LVH) [*n* = 5]. The complete list of incidental anomalies identified on ECHO is listed in Table 3.

A total of 76/389 (19.5%) patients had an abnormal EST with 16 of them having an abnormal PFT pre-exercise. Seventy patients with an abnormal EST had an ECHO. The 3 most common causes of an abnormal EST were all related to the respiratory system (obstructive pattern on spirometry [*n* = 34], exercise induced asthma [*n* = 22], and restrictive pattern on spirometry [*n* = 6]). Seventy percent of these patients (*n* = 53) had symptoms consistent with a respiratory cause upon further questioning and 60% (*n* = 46) had taken medications to treat obstructive lung disease within the past 1 year. Of the 53 patients, 40 complained of coughing with the onset of exercise or shortly after, 5 patients complained of wheezing, and 8 patients had nonspecific complaints (throat tightness, increased use of B2 agonists over the next 24 hours). None of these patients had an abnormal ECHO. Twenty-two of the patients with exertional chest pain (22/130 = 16.9%) had an abnormal EST and 21 of them were related to the respiratory system. Only one patient had a significant arrhythmia but had a normal ECHO and cardiac MRI. Thirty-eight patients with chest pain at rest and with exercise had an abnormal EST (38/156 = 24.4%) and all but two patients had abnormalities on the PFTs. One patient had ST segment depression with a normal ECHO and the other had ST segment elevation with LVH on ECHO but no symptoms were recreated during the EST. The complete list of abnormal ESTs is listed in Table 3.

TABLE 4 Corresponding structural anomaly on echocardiogram in patients with an abnormal exercise stress test

Abnormality on stress test	Incidental structural anomaly on ECHO
ST elevation	Left ventricular hypertrophy
ST elevation	Left ventricular hypertrophy
Abnormality on spirometry	Mild valvar pulmonary stenosis
Abnormality on spirometry	Aberrant right subclavian artery

There were four patients who had both an abnormal exercise stress test and an incidental structural anomaly on ECHO—two patients with ST elevations during stress testing had left ventricular hypertrophy on ECHO while the other two patients had mild valvar pulmonary stenosis and an aberrant right subclavian artery but only pulmonary anomalies on the stress test (Table 4). None of these patients had their symptoms recreated during the EST and hence the findings on ECHO were not believed to be the cause of the abnormal EST or the chest pain.

4 | DISCUSSION

Chest pain is a common presenting complaint to pediatric cardiologists. This study focuses on a complete cardiopulmonary EST including gas metabolics and its utility in the evaluation of pediatric patients with chest pain. This study suggests that noncardiac etiologies continue to be the most common cause of chest pain in pediatric patients. A combined cardiopulmonary EST uncovered pathology in approximately 20% of the patients in our study (mostly related to the respiratory system). This suggests that it may be an effective screening tool in the evaluation of patients with chest pain.

EST is utilized most frequently in children to determine exercise capacity and sufficiency of coronary perfusion and to evaluate exercise-associated arrhythmias. An abnormality in any of these processes may cause chest pain. However, it is well known that chest pain in the pediatric population is rarely cardiac in origin. One concerning lesion in the pediatric patient with chest pain is an anomaly in which the right or left coronary artery originates from the opposite sinus and courses between the great arteries. Basso et al studied patients with this lesion who died suddenly.[11] Six of the 27 patients in their study had an EST performed prior to their death, and all 6 ESTs were normal. More limited ESTs were performed on 6 of the other patients, and all were normal. In their review of other published cases with the same coronary anomaly, 18 patients had an EST and 14 (78%) were normal. Thus, even a negative EST cannot offer complete reassurance when considering a high-risk lesion such as this. We had three patients with similar lesions and all of them had a normal EST. Patients found to have coronary anomalies received an ECHO at the discretion of the outpatient cardiologist. Upon retrospective chart review of these patients, we were unable to discern a specific finding on history or physical examination which would have hinted at this diagnosis. This highlights the fact that a patient may have a significant coronary lesion in the presence of a normal physical examination and EST. It emphasizes the need for a complete multimodality evaluation and maintaining a high clinical suspicion for this condition.

The occurrence of classic adult-type anginal chest pain in the pediatric population is exceedingly rare. However, chest pain occurring only with exercise frequently raises the suspicion for an anginal type of chest pain in the pediatric population.[12] For this reason, an EST is often ordered. The findings of this study support other reports that most children with chest pain who undergo exercise testing will have normal cardiac anatomy.[6,7] Kyle et al evaluated 176 patients who had an EST performed for chest pain.[6] In their cohort, 124 patients had an ECHO performed and 17 patients (14%) had abnormalities, but none of the abnormalities found were thought to contribute to the patients' chest pain. There were only 4 (2.2%) abnormal EST, but none were thought to be diagnostic for the patients' symptoms of chest pain. However, their study did not perform PFTs and hence the abnormal EST did not include abnormalities on PFT. If we exclude abnormal PFTs as a cause of the abnormal EST, our study demonstrated similar rates of abnormal EST (10/333 = 3.3%). Anwar et al. evaluated 118 pediatric patients with chest pain (7). PFTs were also performed as part of the EST evaluation in their study. Ninety-six percent of patients (113/118) had an ECHO performed as a part of their initial evaluation, and 11/113 (9.7%) had minor, hemodynamically insignificant abnormalities. Three patients had nonpulmonary abnormalities on the EST while 28% had abnormalities on the PFT. This was slightly higher as compared to the percentage of patients with abnormalities on the PFT in our study (66/389 = 17%).

We demonstrated a similar percentage of incidental findings on ECHO as compared to other reports and only a small percentage (2.4%) of them needed further cardiac evaluation. Almost all of these patients had a normal EST. A large proportion of patients with an abnormal EST received an ECHO in our study (70/76). On hindsight, this was likely because of the majority of these patients having chest pain with exertion. The cardiac anomaly found with an abnormal EST did not explain the chest pain. This suggests that a thorough history and physical is likely the most useful and cost-effective method for the evaluation of chest pain in the pediatric population and a limited cardiac EST may have limited utility in this cohort. However, interestingly, 81.5% of patients with an abnormal stress test had an abnormal PFT. Furthermore, patients who had symptoms referable to the respiratory system upon detailed questioning or those who had used medications to treat obstructive lung disease in the recent past were more likely to have pulmonary abnormalities detected on a complete cardiopulmonary EST. Reactive airway disease has a well-established association with complaints of chest pain in children.[13,14] Our institutional practice, in general, has been to perform PFTs immediately prior to and upon completion of the EST in these patients, especially those with respiratory symptoms or those on medications to treat obstructive lung disease to increase efficiency and diagnostic yield. This study provides the justification for this continued practice. Aggressive treatment of the underlying respiratory cause along with follow-up with the pediatrician and/or subspecialty referral is an adequate outcome of the testing. While the general guidelines suggest further cardiac workup (cardiology referral, ECHO) in patients without respiratory symptoms and certain red flags such as syncope, significant family history, an abnormal physical examination, and an abnormal electrocardiogram,[15] we did not evaluate the baseline characteristics of all patients undergoing an EST. Because of this limitation, we are unable to make any specific recommendations regarding further workup of patients without a clear indication of respiratory pathology.

There are no clear guidelines regarding when an EST should be performed and there is no consensus statement regarding the use of PFTs during an EST. The current AHA guidelines for an EST in the pediatric population describe 6 indications for which an EST is commonly performed.[16] These are evaluation of signs or symptoms induced or aggravated by exercise, assessment of cardiac/pulmonary or other organ disorders, assessment of efficacy of medical/surgical therapy, assessment of functional capacity for recreational/athletic activities, evaluation of prognosis with baseline and serial testing, and establishment of baseline data for institution of cardiac/pulmonary or musculoskeletal rehabilitation. Based on our results, only three patients with chest pain with exercise had an abnormal EST which was not related to the pulmonary system (3/286 = 1%) and only one of them had an incidental anomaly of LVH on ECHO. This would suggest that when an EST is performed for evaluation of signs/symptoms induced or aggravated by exercise, a complete cardiopulmonary test including PFTs may be of higher yield. This stands in contrast to using cardiac stress test alone, which by itself has been shown to be of extremely low yield. Our experience described here could support the utilization of complete cardiopulmonary exercise testing as the standard of care to improve efficiency and yield.

4.1 | Limitations

This is a single-center study and may therefore warrant validation via a larger pooled data or multicenter study. It is however the largest study published to date. As in most previous studies, we anticipate a referral bias and we did not define the baseline characteristics of all patients referred for an EST (physical examination, electrocardiogram findings). However, the patients referred for testing in this cohort were all derived from the same group of referral cardiologists who adopt similar testing algorithms. This is however somewhat difficult to ascertain.

5 | CONCLUSION

A very low percentage of patients previously undiagnosed with heart disease had an abnormal stress test and an incidental anomaly on ECHO (1%). The ECHO anomalies found were unlikely to be the cause of chest pain in these patients. This reiterates the fact that chest pain in the pediatric population is rarely cardiac in origin. Furthermore, since the majority of abnormal stress tests were secondary to a pulmonary cause, a complete cardiopulmonary EST may be an effective screening tool for certain patients presenting with chest pain. Our study emphasizes the need for performing a complete cardiopulmonary EST instead of an isolated cardiac stress test to maximize diagnostic efficiency and yield.

CONFLICT OF INTEREST

The authors declare that they have no potential conflict of interest.

AUTHOR CONTRIBUTIONS

Each author contributed equally to the genesis of the research design, analysis and interpretation of data, initial drafting of the manuscript, and review and approval of the submitted and final version.

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