

The Causes of Chest Pain and the Positive Rate of Myocardial Enzyme Testing in Diagnosis of Chest Pain in Children

Li Chen (✉ liliforever@163.com)

Beijing Anzhen Hospital

Hongzhou Duan

Peking University First Hospital

Xiaoyan Li

Capital Medical University

Zuozhen Yang

Zhejiang University

Meng Jiao

Beijing Anzhen Hospital

Kangtai Sun

China Rural Technology Development Center

Mei Jin

Beijing Anzhen Hospital

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Abstract

Background Chest pain is a common complaint at pediatric cardiology clinics and often leads to an extensive cardiac evaluation. In this study, we analyzed the causes of chest pain in Chinese children and developed criteria for targeted myocardial enzyme testing.

Methods We retrospectively analyzed the clinical data of patients aged below 18 years visiting our hospital for chest pain between 2005 and 2019. Based on auxiliary exams and clinical diagnosis, we analyzed the positive rate of myocardial enzyme testing in identifying the causes of chest pain in children.

Results A total of 7251 children were included in this study. The chest pain was of cardiac origin in 581 patients (8.0%). The incidence of noncardiac chest pain was significantly higher in the preschool group and the school-age group than in the adolescent group (93.5% vs 93.8% vs 90.3%, $P < 0.05$). Among children with cardiac chest pain, the most common concomitant symptom was chest tightness (67.0%). Myocardial enzyme testing was performed in 5408 patients and was abnormal in 453 (8.4%) patients.

Conclusions In children, chest pain is mostly benign and rarely cardiac. During diagnosis, targeted myocardial enzyme testing based on medical history and physical examination can effectively reduce resource use.

Introduction

Chest pain is a common complaint at pediatric clinics, accounting for approximately 6 per 1000 visits at pediatric emergency room ¹, as well as approximately 1 per 40 visits at pediatric clinics in the UK ². To date, no large studies have been conducted to investigate this topic in Chinese children. In adults, chest pain is often caused by severe cardiovascular diseases, while in children, chest pain is mostly benign and rarely cardiac ³⁻¹¹. In China, however, most parents believe that chest pain in children is cardiac and life-threatening. As a result, parents often take their children to the hospital once their children complain about chest pain. Most parents bring their child who has chest pain to an emergency room or see a pediatric cardiologist for comprehensive cardiac exams, which affects the child's life and schoolwork and increases the costs to their families. Therefore, it is important to investigate common causes of chest pain in children and develop diagnostic procedures in order to reduce stress to children and their families.

Collins et al (2014), Harahsheh et al (2017), and Etuwewe et al (2018) proposed evaluation methods and procedures for chest pain in children ¹²⁻¹⁴. They provided detailed prescriptions on positive medical history and physical examination in children with chest pain but did not provide details on how to choose the cardiac exams. In 2011, Friedman et al ¹⁵ investigated the use of echocardiography (UCG) for the diagnosis of chest pain in children and developed diagnostic and treatment procedures based on medical history, physical examination, and electrocardiogram (ECG). They found that targeted testing can reduce resource use and lead to more cost-effective care. Myocardial enzyme tests are currently widely used for

the diagnosis of many heart diseases. To date, no studies have investigated targeted cardiac enzyme testing for the diagnosis of chest pain in children. It is important to develop the criteria for targeted myocardial enzyme testing in children with potential cardiac chest pain in order to reduce the economic burden on their families and reduce resource use. In this study, we analyzed the common causes of chest pain in children and the pattern of clinical visits and the positive rate of myocardial enzyme testing in diagnosis of chest pain in children.

Methods

1. Case selection

We retrospectively analyzed the clinical data of children aged 18 years or below who visited Beijing Anzhen Hospital for chest pain between January 1, 2005 and December 31, 2019. The diagnosis was coded based on the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). Patients with incomplete clinical data or known history of heart disease were excluded from this study. We identified patients on the basis of ICD-10 billing codes for chest pain. Our study complies with the Declaration of Helsinki, and the institutional review board for clinical research at Beijing Anzhen Hospital approved the use of patient medical records for this retrospective review.

Based on patient age at the initial visit, we divided the patients into the preschool group (3 years \leq age \leq 6 years), the school-age group (6 years < age \leq 12 years), and the adolescent group (12 years < age \leq 18 years).

Positive history of past illnesses included systemic lupus erythematosus, juvenile rheumatoid arthritis, carnitine deficiency, and congenital adrenal insufficiency. Positive family history included sudden or unexplained death of a first-degree relative, severe familial hypercholesterolemia, pulmonary arterial hypertension, Marfan syndrome, and cardiomyopathy.

2. Interpretation of clinical auxiliary exams and clinical diagnosis

We retrieved and analyzed ECG reports from clinical medical records. ECG abnormalities included deviation of the electrical axis, pathological ST-segment or T-wave changes, pathological Q wave, ventricular hypertrophy, atrial enlargement, supraventricular tachycardia, frequent premature ventricular contractions, pre-excitation syndrome, and high-grade atrioventricular block.

UCG, Holter test results, chest X-ray and myocardial enzyme testing (including creatine kinase, creatine kinase-myocardial band, lactate dehydrogenase, cardiac troponin I, and myoglobin) were analyzed based on reports.

The causes of cardiac chest pain in children include myocarditis, pericarditis, cardiomyopathy, anomalous origin of the coronary artery, moderate or severe left ventricular outflow tract obstruction, pulmonary arterial hypertension, aortic dissection, pulmonary embolism, large ventricular septal defect, and arrhythmia^{3-7,9-13,15}. In China, many children with chest pain do not meet the diagnostic criteria for myocarditis as per their clinical symptoms and auxiliary exams; however, they meet the diagnostic criteria of suspected myocarditis, which may also cause chest pain. Therefore, according to the 2019 guidelines for the diagnosis of myocarditis in children developed by the Subspecialty Group of Cardiology, the Society of Pediatrics, Chinese Medical Association¹⁶, we included suspected myocarditis as one of the causes of cardiac chest pain in children.

3. Targeted myocardial enzyme testing for chest pain in children

We gave suggestion for targeted myocardial enzyme testing in children with chest pain based on our study and the diagnostic procedures for chest pain in children from literature reports^{15,17-18}.

4. Patient and Public Involvement

It was not appropriate or possible to involve patients or the public in our research.

5. Statistical analysis

SPSS20.0 was used for statistical analysis. Measurement data are presented as mean \pm standard deviation ($\bar{x} \pm SD$) and count data are expressed as frequency (percentage). The χ^2 test was performed to analyze sex distribution and the causes of chest pain. $P < 0.05$ was considered statistically significant.

Results

1. Demographics

A total of 7251 children were included in this study, including 4293 boys (59.2%) and 2958 girls (40.8%), aged 3–18 years (mean: 12.1 ± 4.0). Chest pain was more common in school-age children and adolescents. Most patients in the preschool group were girls (55.5%) while most patients in the school-age and adolescent groups were boys (60.6%, 61.3%) ($P < 0.05$) (Table 1).

Table 1
The sex and causes of chest pain in children with different ages

	n	3yrs ≤ age ≤ 6yrs	6yrs < age ≤ 12yrs	12yrs < age ≤ 18yrs
Total	7251	784	2779	3688
Age (yrs)	12.1 ± 4.0	5.1 ± 0.9	9.6 ± 1.7	15.5 ± 1.7
Male	4293 (59.2%)	349 (44.5%)	1685 (60.6%)	2259 (61.3%)
Female	2958 (40.8%)	435 (55.5%)	1094 (39.4%)	1429 (38.7%)
χ^2			64.846	74.513
<i>P</i>			0.000*	0.000*
Cardiac	581 (8.0%)	51 (6.5%)	171 (6.2%)	359 (9.7%)
Non-cardiac	6670 (92.0%)	733 (93.5%)	(93.8%)	3329 (90.3%)
χ^2		8.096	27.011	
<i>P</i>		0.004#	0.000#	
* stands for $P < 0.01$ contrast to 3yrs ≤ age ≤ 6yrs group; # stands for $P < 0.05$ contrast to 12yrs < age ≤ 18yrs group.				

2. Pattern of clinical visits in children with chest pain

The number of children who saw a doctor for chest pain was increasing each year from 2005 to 2019 (Fig. 1). 6312 patients (87.0%) visited a clinic, and 926 patients (12.8%) went to an emergency room. Only 13 patients (0.2%) were admitted to the hospital. At the initial visit, most children saw a pediatric cardiologist (n = 3477, 55.09%).

3. General information

Four patients had a positive family history, including two patients whose fathers had dilated cardiomyopathy, one patient whose sibling had Marfan syndrome, and one patient whose father had died suddenly. Physical examination was positive in 795 children. Among them, 75 patients had pathological heart murmur, including systolic murmur (n = 25), diastolic murmur (n = 32), accentuated P2 (n = 3), splitting of the second heart sound (n = 12), and continuous machine-like murmur (n = 3); 33 had arrhythmia; 62 had a tachycardia; 77 had a bradycardia; 198 patients had fever and bibasilar crackles in both lungs; six had fever and wheezing sounds in both lungs; 327 only had fever; 15 only had wheezing sounds in both lungs; two had hepatomegaly.

Among children with cardiac chest pain (n = 581, 8.0%), the most common concomitant symptom was chest tightness (n = 389, 67.0%). Among patients with noncardiac chest pain (n = 6670, 72.0%), most (n = 4899, 73.4%) had no concomitant symptoms (Table 2).

Table 2
The associated symptoms of chest pain in children

Associated symptoms	n (%)
Cardiac-related Chest Pain	581
No Associated symptoms	116 (20.0%)
Chest oppression	389 (67.0%)
Palpitation	43 (7.4%)
Fatigue	32 (5.5%)
Syncope	5 (0.9%)
Dizzy	4 (0.7%)
Headache	2 (0.3%)
Fever	4 (0.7%)
Respiratory symptoms	11 (1.9%)
Gastrointestinal symptoms	5 (0.9%)
Non-cardiac related chest pain	6670
No Associated symptoms	4899 (73.4%)
Chest oppression	666 (10.0%)
Palpitation	102 (1.5%)
Fatigue	35 (0.5%)
Syncope	14 (0.2%)
Dizzy	46 (0.7%)
Headache	11 (0.2%)
Joint pain	2 (0.03%)
Fever	238 (3.6%)
Respiratory symptoms	562 (8.4%)
Gastrointestinal symptoms	103 (1.5%)

4. Auxiliary exams

All 7251 patients (100%) underwent ECG, 5352 (73.8%) underwent UCG, 128 (1.8%) underwent Holter test, 1037 (14.1%) underwent chest X-ray, and 5408 (74.6%) underwent myocardial enzyme testing.

ECG was abnormal in 574 of 7251 children (7.9%). The most common abnormality was pathological ST-segment or T-wave changes (n = 537, 93.6%), followed by frequent premature ventricular contractions (n = 7, 1.2%), pre-excitation syndrome (n = 10, 1.8%), supraventricular tachycardia (n = 7, 1.2%), deviation of the electrical axis (n = 6, 1.0%), pathological Q wave (n = 6, 1.0%), and left atrial enlargement (n = 1, 0.2%).

UCG was abnormal in 331 of 5352 children (6.2%). The abnormality was unrelated to chest pain in 221 of these patients (66.8%) (Table 3) and was related to chest pain in 110 of them (33.2%), including aortic sinus enlargement with aortic sinus aneurysm (n = 3, 2.7%), coronary artery dilation (n = 3, 2.7%), generalized cardiomegaly with reduced left ventricular systolic function (n = 4, 3.6%), pericardial effusion (n = 2, 1.8%), large ventricular septal defect (n = 2, 1.8%), severe pulmonary valve stenosis with pulmonary valve regurgitation (n = 1, 0.9%), quadricuspid aortic valve with aortic sinus aneurysm (n = 1, 0.9%), aortic valve stenosis (n = 3, 2.7%), coronary-pulmonary arterial fistula (n = 4, 3.6%), anomalous origin of the left coronary artery from the pulmonary artery (n = 6, 5.5%), anomalous origin of the right coronary artery from the left sinus (n = 3, 2.7%), pulmonary arterial hypertension (n = 6, 5.6%), and left ventricular enlargement with normal left ventricular systolic function (n = 72, 65.5%).

Table 3
Incidental Echocardiographic Findings

	n
Mild tricuspid regurgitation	69
Patent foramen ovale	62
Atrial septal defect	23
Mild mitral regurgitation	14
Patent ductus arteriosus	10
Mild aortic regurgitation	9
LV hypertrabeculation/noncompaction*	9
Small ventricular septal defect	5
Bicuspid aortic valve	5
Mitral valve prolapse	3
Mild dilated aortic sinus	2
Mild LV hypertrophy	2
Mild pulmonary stenosis	2
Subaortic septum	1
Mild pulmonary regurgitation	1
Small ventricular septal defect with double-chambered RV	1
Tetralogy of Fallot	1
Tetralogy of Fallot with atrial septal defect and patent ductus arteriosus	1
Partial anomalous pulmonary venous connection with atrial septal defect	1
LV indicates left ventricular.	
RV indicates right ventricular.	
* Normal LV function.	

The Holter test was abnormal in only 6 of 128 children (4.7%), all of whom had frequent premature ventricular contractions. Chest X-ray was abnormal in 643 of 1037 children (62.0%). Myocardial enzyme tests were abnormal in 453 of 5408 children (8.4%).

5. Diagnosis

Based on medical history, physical examination, and auxiliary exams, 581 patients (8.0%) were diagnosed with cardiac chest pain, and 6670 patients (92.0%) were diagnosed with noncardiac chest pain. (Fig. 2). The incidence of noncardiac chest pain was significantly higher in the preschool group and the school-age group than in the adolescent group (93.5% vs 93.8% vs 90.3%, $P < 0.05$) (Table 1).

Among the 581 cases of cardiac chest pain, the most common cause was suspected myocarditis (n = 431, 74.2%) (Fig. 3).

Among the 660 cases of chest pain due to respiratory diseases, the most common cause was bronchitis (n = 357, 54.1%) (Fig. 4).

Among the 44 cases of chest pain due to gastrointestinal diseases, the most common cause was gastritis (n = 28, 63.6%) (Fig. 5). Among the 12 cases of chest pain due to mental diseases, the causes included anxiety (n = 5), depression (n = 4), and hysteria-like attacks (n = 3). Among the three cases of chest pain due to other disorders, the causes included breast mass (n = 1), dysmenorrhea (n = 1), and poor wound healing (n = 1).

6. Suggestion for targeted myocardial enzyme testing for chest pain in children

For children with chest pain, clinicians should collect detailed information about the history of the present illness, past medical history, and family history and perform a comprehensive physical examination. Patients with potential cardiac chest pain should be referred to a pediatric cardiologist and undergo ECG or ECG plus UCG if they have a pathological heart murmur or hypoxemia, respectively. Based on the ECG or UCG results, targeted myocardial enzyme testing merely should be conducted for children with chest pain probably be induced by myocarditis or suspected myocarditis.

Discussion

Chest pain is a common symptom. With the improvement of living standards and attention to quality of life, more children are seeing a doctor for chest pain. In 2011, Saleeb et al¹⁹ analyzed the clinical data of children who visited Boston Children's Hospital for chest pain between 2000 and 2009 and found that the number of children who saw a doctor for chest pain increased each year. This study showed a similar trend at our hospital between 2005 and 2019, suggesting that parents are paying more attention to their children's symptoms and that many parents believe that chest pain in children is cardiac and life-threatening, due to a lack of knowledge in the common causes of chest pain in children. As a result, they often take their children to an emergency or a pediatric cardiologist. In fact, most cases of chest pain in children are noncardiac and benign^{3-7,9-11,15,18-19}. In 2011, Saleeb et al¹⁹ retrospectively analyzed the pattern of visits, causes, and mortality of chest pain in 3700 children and found that 18% of the patients visited an emergency room and that 99% of the cases were noncardiac. During the 4.4-year follow-up,

only three patients died of non-cardiac diseases. This indicates that mortality is low in children with chest pain, with few cardiac deaths. In 2020, Gesuete et al analyzed the clinical data of 761 children who went to an emergency for chest pain and found that only 1% of the cases were cardiac¹¹. Our study showed that 92.0% of the cases were noncardiac, 12.8% of the patients went to an emergency, and 55.09% saw a pediatric cardiologist, suggesting that most parents believe that their children's chest pain is critical and has a cardiac cause. Therefore, it is important to educate the public about chest pain in children, investigate the causes of chest pain in children, and develop standard diagnostic procedures, in order to reduce resource use.

Chest pain in children may be cardiac or noncardiac^{5,16}. The causes of cardiac chest pain include coronary artery diseases, arrhythmia, inflammatory diseases and structural abnormalities^{5,16}. Noncardiac causes include respiratory diseases, gastrointestinal diseases, skeletomuscular diseases, mental diseases, and idiopathic factors. In 2011, Saleeb et al analyzed the causes of chest pain in 3700 children and found that 52% of the cases were idiopathic, 36% were related to skeletomuscular diseases, 7% were related to gastrointestinal diseases, 1% were related to mental disorder, and only 1% were cardiac. The most common cause of cardiac chest pain was inflammatory disease, such as pericarditis and myocarditis¹⁹. In 2008, Lin et al analyzed the causes of chest pain in 103 children who went to an emergency room between 2002 and 2005. They found that the most common cause was idiopathic chest pain (59.2%), followed by respiratory diseases (24.3%), skeletomuscular diseases (6.7%), gastrointestinal diseases (5.8%), cardiac chest pain (2.0%), and other conditions (2.0%)⁷.

This is the first large study to investigate the causes of chest pain in Chinese children. We analyzed the causes of chest pain in 7251 children during a 15-year period and found that 53.0% of the cases were idiopathic, 29.1% were related to skeletomuscular diseases, 9.1% were related to respiratory diseases, 8.0% were cardiac, 0.6% were related to gastrointestinal diseases, 0.16% were related to mental diseases, and 0.04% were related to other conditions. These data indicate that idiopathic chest pain is the most common cause of chest pain in Chinese children, which is consistent with foreign reports.

At their initial visit, most patients with chest pain see a pediatric cardiologist. Moreover, parents often request cardiac auxiliary exams to exclude cardiac chest pain. As a result, most children with chest pain undergo various unnecessary auxiliary exams. Therefore, it is important to develop diagnostic procedures for chest pain in children in order to reduce resource use. Collins et al (2014), Harahsheh et al (2017), and Etuwewe et al (2018) proposed evaluation methods and procedures for chest pain in children¹²⁻¹⁴. The researchers stressed the importance of detailed medical history and physical examination to determine the potential cause of chest pain, followed by necessary exams. But they did not describe how to choose the auxiliary exams. In 2011, Friedman et al¹⁵ reported that they developed standard clinical evaluation and treatment procedures for chest pain in children and applied these procedures in children who saw a pediatric cardiologist at Boston Children's Hospital for chest pain between 2000 and 2009. The researchers believed that patients with exercise-related chest pain or positive family history should undergo comprehensive cardiac evaluation, including UCG, for further diagnosis. With these procedures,

UCG usage was reduced by 20% without missing any case of cardiac chest pain, thereby reducing resource use and the costs to the families.

Myocardial enzyme testing is widely used in clinical practice to help diagnose heart conditions. In China, many doctors order myocardial enzyme tests at the initial visit to exclude myocarditis or suspected myocarditis in children with chest pain. However, the test result is normal in most cases. In 2020, the Subspecialty Group of Cardiology, Society of Pediatrics, Chinese Medical Association, issued recommendations for the diagnosis of myocarditis in children and clearly stated the diagnostic criteria for myocarditis and suspected myocarditis in children¹⁶. No past studies have investigated how to choose the myocardial enzyme test and reduce their use without missing any case of cardiac chest pain in children. The present study showed that for children with cardiac chest pain, the most common concomitant symptom was chest tightness (67.0%) while most patients with noncardiac chest pain had no concomitant symptoms, and respiratory or gastrointestinal symptoms were the main concomitant symptoms (if any). Therefore, concomitant symptoms may help evaluate the potential cause of chest pain in children, followed by auxiliary exams. In this study, among the 7251 children with chest pain, the positive rate of myocardial enzyme tests was merely 8.4%, suggesting that myocardial enzyme testing is unnecessary in patients without symptoms or signs of myocarditis or suspected myocarditis during the initial evaluation. Such an approach would help reduce resource use and unnecessary treatment.

This is the first study to analyze the positive rate of myocardial enzyme testing in diagnosis of chest pain in children. Through analyzing the clinical data of 7251 children who visited our hospital for chest pain during a 15-year period and referencing the diagnostic procedures from literature reports, we recommend that clinicians evaluate the potential cause of chest pain based on the history of the present illness, past medical history, family history, and physical examination. Patients with potential cardiac chest pain should undergo ECG or ECG plus UCG if they have a pathological heart murmur or hypoxemia, respectively. Based on the ECG or UCG results, targeted myocardial enzyme testing merely should be conducted for children with chest pain probably be induced by myocarditis or suspected myocarditis. These suggestions could reduce unnecessary myocardial enzyme tests, thereby reducing resource use.

Conclusions

This large retrospective study shows that chest pain is more common in school-age children and adolescent children than in preschool children. For preschool children, chest pain is more common in girls; for school-age children and adolescents, chest pain is more common in boys. For Chinese children with chest pain, the most common cause is idiopathic chest pain. Few cases are cardiac chest pain, which is usually accompanied by chest tightness, while most patients with noncardiac chest pain have no concomitant symptoms. Detailed medical history and comprehensive physical examination can help the physician determine the potential cause of chest pain in children and refer the patient to an appropriate specialist for auxiliary exams, diagnosis, and treatment. Patients with potential cardiac chest pain should undergo ECG or ECG plus UCG if they have a pathological heart murmur or hypoxemia, respectively. Based on the ECG or UCG results, targeted myocardial enzyme testing merely should be

conducted for children with chest pain probably be induced by myocarditis or suspected myocarditis. These suggestions could reduce unnecessary myocardial enzyme tests, thereby reducing resource use.

List Of Abbreviations

UK: United Kingdom

UCG: echocardiography

ECG: electrocardiogram

ICD-10: the 10th revision of the International Statistical Classification of Diseases and Related Health Problems

Declarations

Ethics approval and consent to participate

Our study complies with the Declaration of Helsinki, and the institutional review board for clinical research at Beijing Anzhen Hospital approved the use of patient medical records for this retrospective review. The study was approved by the the ethics committee of Beijing Anzhen Hospital, and the committee's reference number was 2020088X. Informed consent was obtained from a parent and/or legal guardian of patients.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LC, HD, XL, ZY, MJ, KS and MJ made substantial contributions to the conception or design of the work or the acquisition, analysis or interpretation of data. LC drafted the work. HD, XL, ZY, MJ, KS and MJ revised the work critically for important intellectual content. All authors read and approved the final manuscript.

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Figures

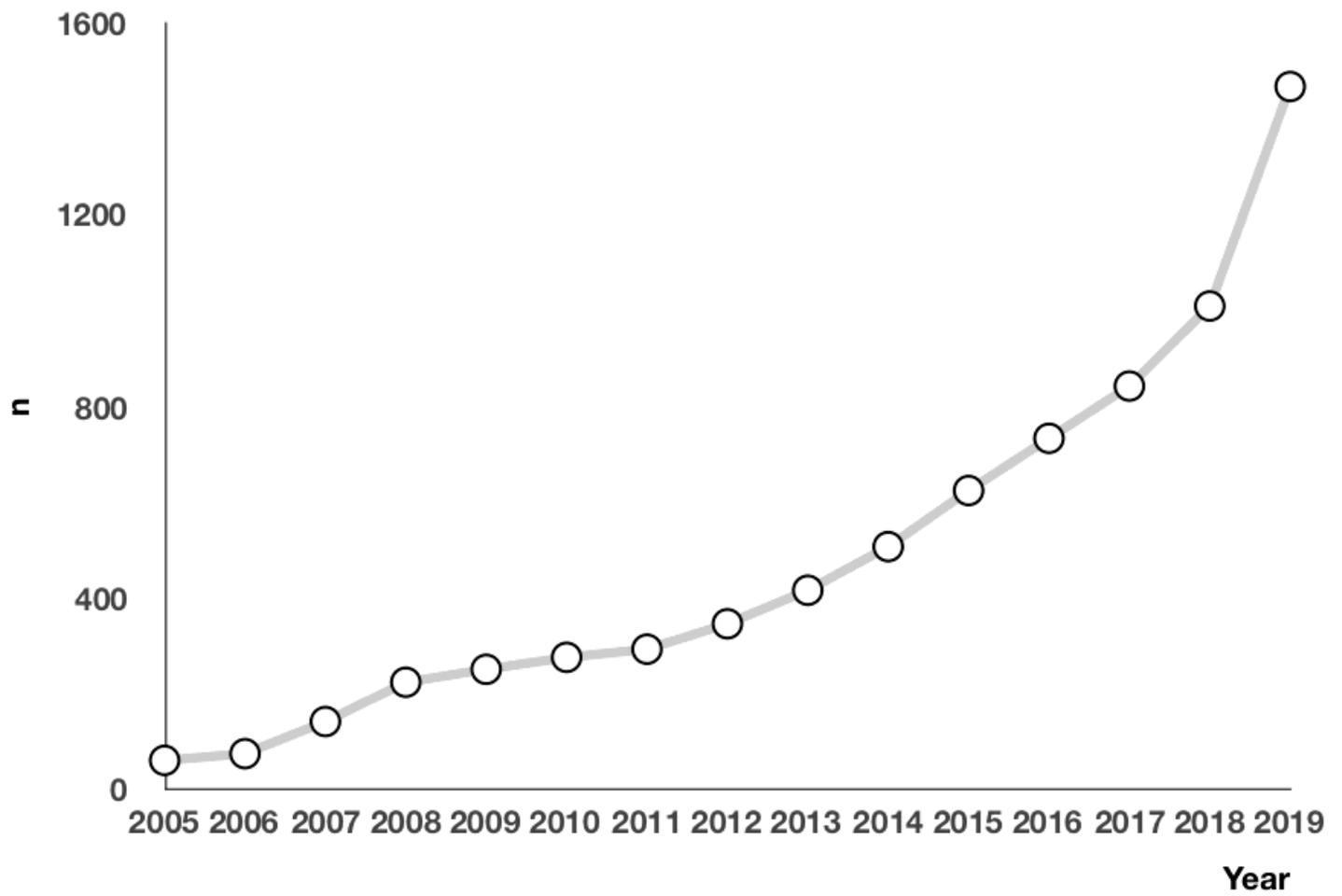


Figure 1

Number of initial evaluations of chest pain in children per year.

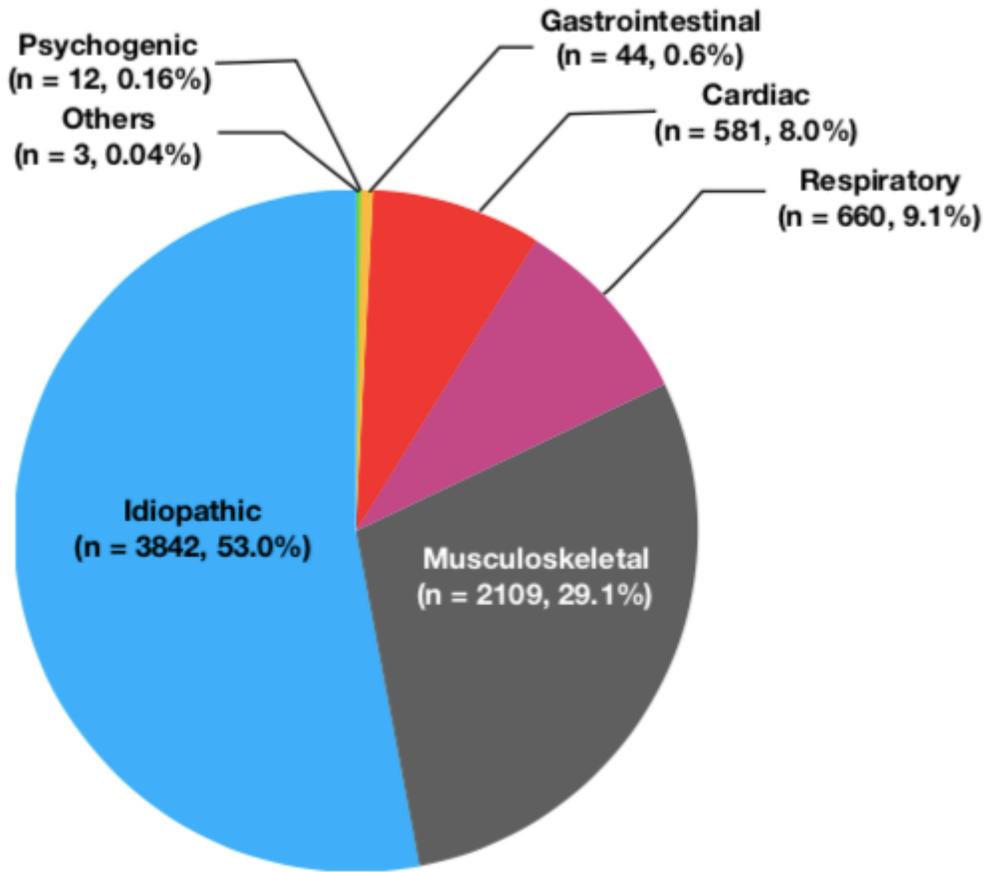


Figure 2

The diagnosis of chest pain in children.

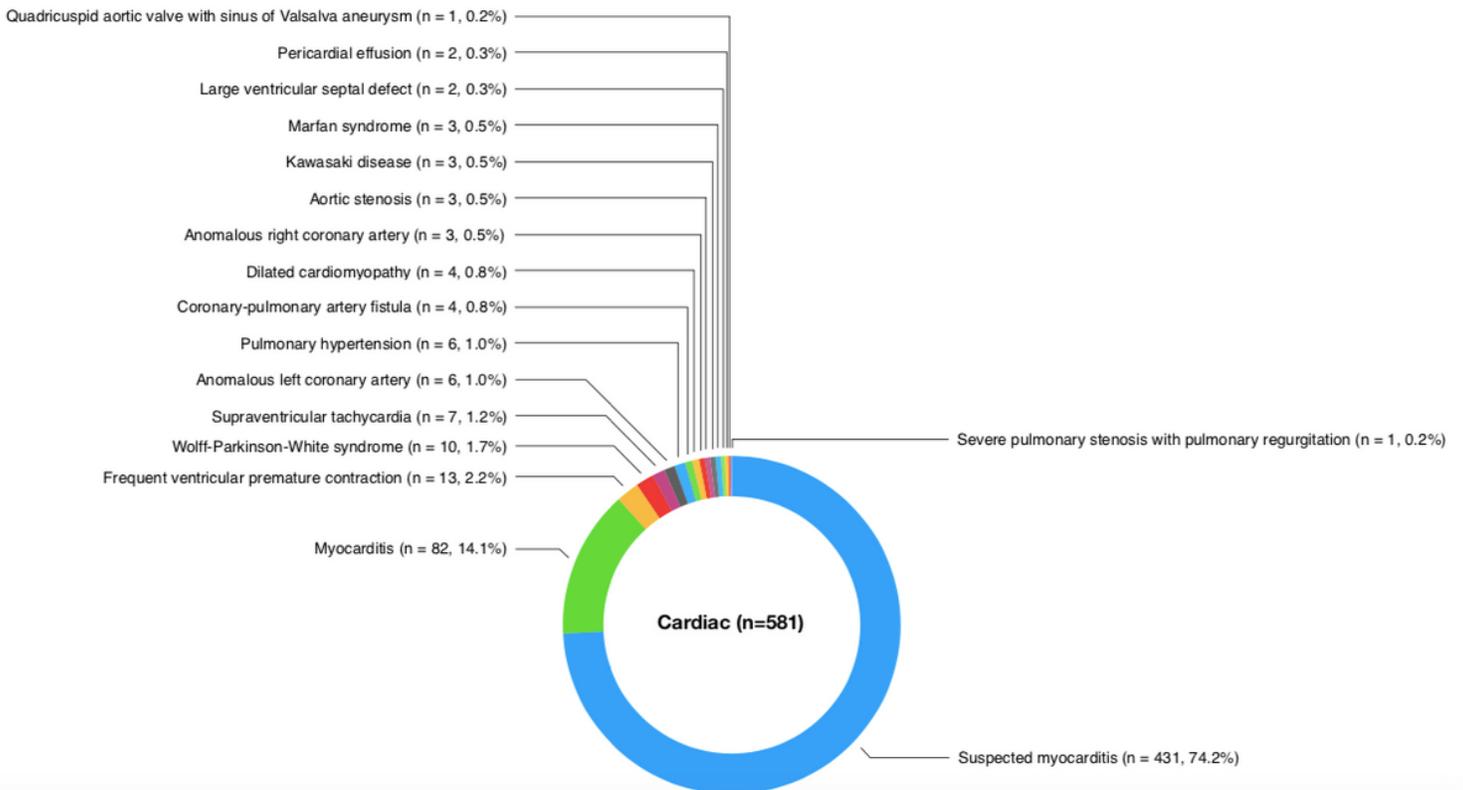


Figure 3

The cardiac causes in children with chest pain.

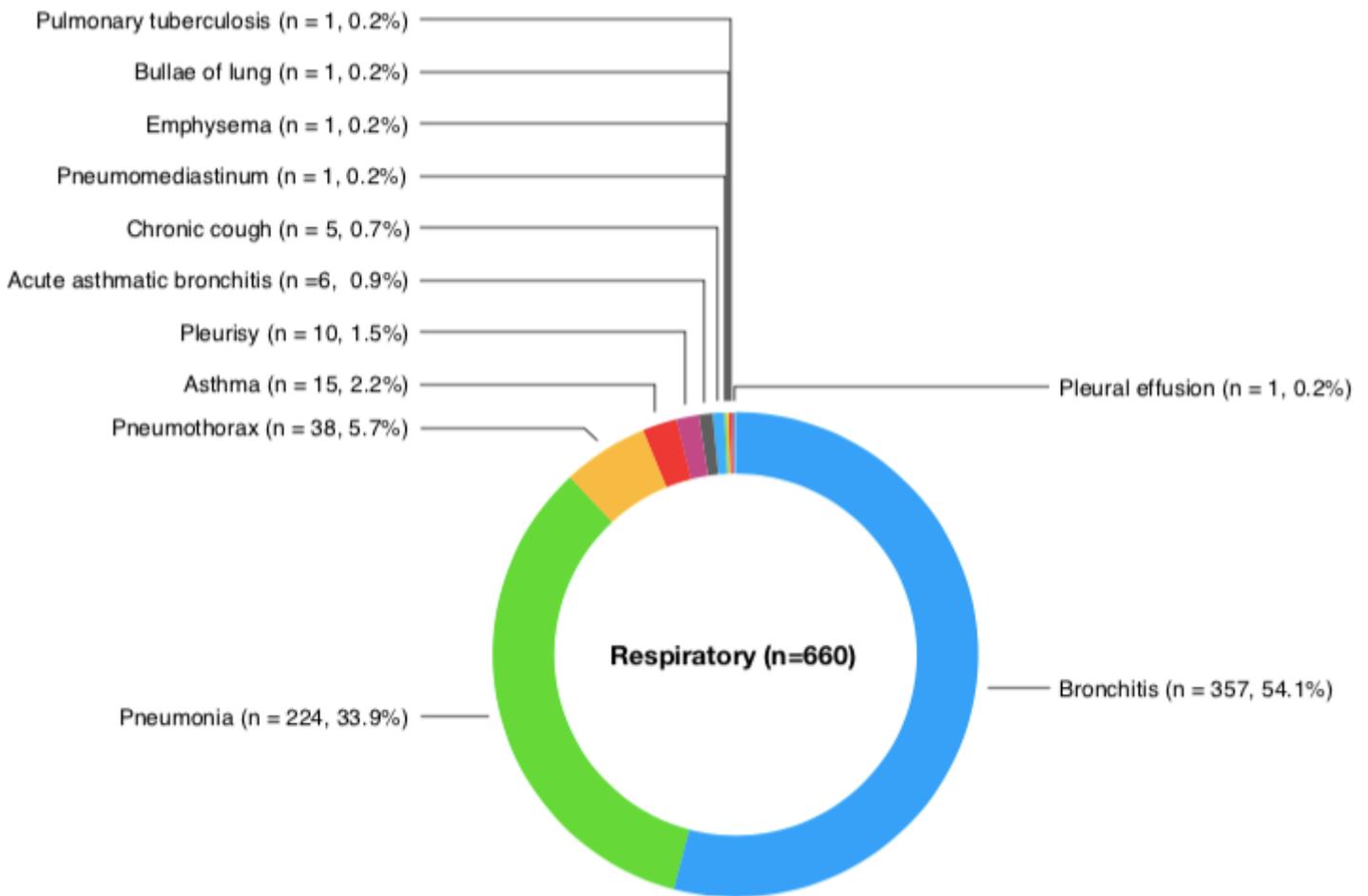


Figure 4

The respiratory causes in children with chest pain.

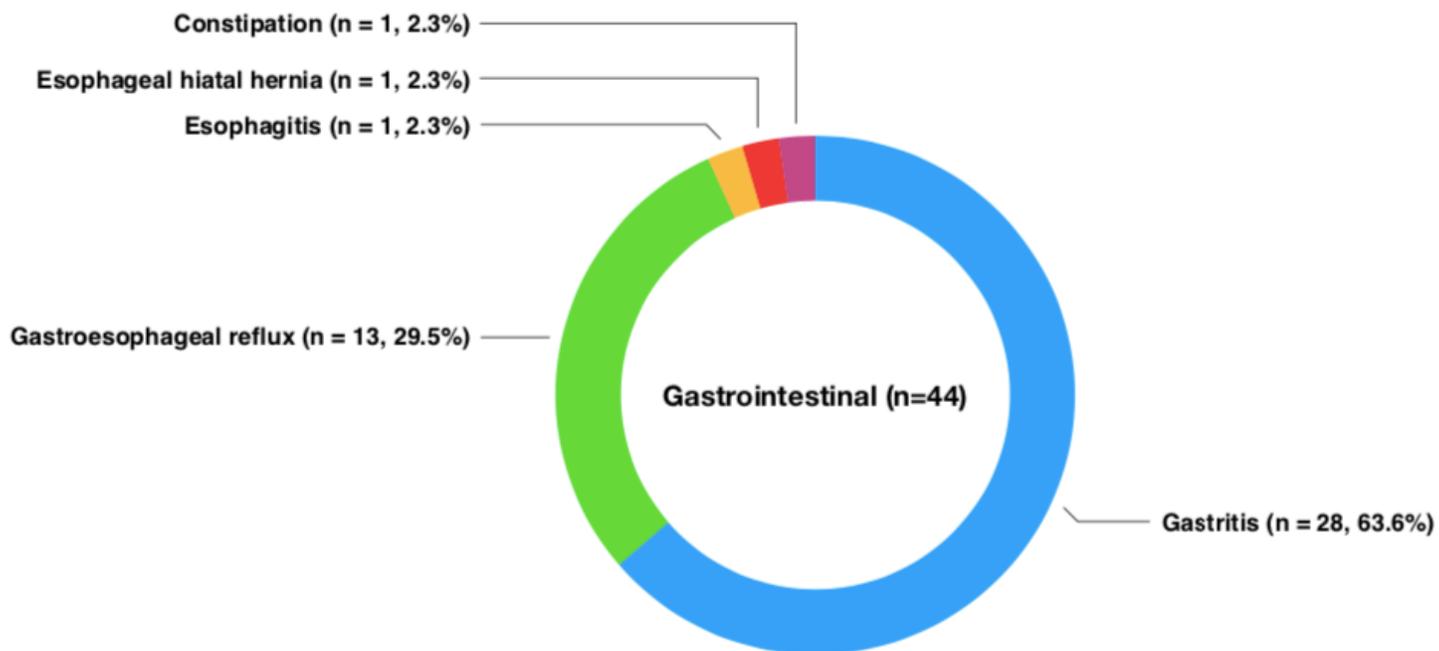


Figure 5

The gastrointestinal causes in children with chest pain.