# Missed Diagnosis of New-Onset Systolic Heart Failure at First Presentation in Children with No Known Heart Disease

Kriti Puri, MBBS[1], Hardeep Singh, MD, MPH[2], Susan W. Denfield, MD[1], Antonio G. Cabrera, MD[1], William J. Dreyer, MD[1], Hari P. Tunuguntla, MD, MPH[1], and Jack F. Price, MD[1]

**Objective** To determine frequency of missed heart failure diagnosis at first presentation among children with no known heart disease admitted with new-onset heart failure.

**Study design** Using a retrospective design, we reviewed electronic medical records of all patients aged <21 years with no known heart disease, hospitalized with new-onset heart failure during 2003-2015 at a tertiary-quaternary care institution. We assessed records for missed diagnosis of heart failure (primary outcome), associated process breakdowns, and clinical outcomes using a structured data collection instrument.

**Results** Of 191 patients meeting inclusion criteria, 49% (94/191) were missed on first presentation. Most common incorrect diagnostic labels given to "missed" patients were bacterial infection (29%; 27/94), followed by viral illness (22%; 21/94) and gastroenteritis/hepatitis (21%; 20/94). On multivariable analysis, presentation to primary care provider (PCP), longer duration of symptoms (median 7 days), more than 2 symptoms of heart failure, and nausea/emesis were associated with missed diagnosis. On examining process breakdowns, 49% had errors in history-taking and 50% had no documentation of differential diagnoses. There was no difference in hospital mortality, length of stay, or mechanical circulatory support in missed vs not-missed cohorts. Unnecessary noninvasive and invasive tests were performed in 18% and 4% of patients, respectively.

**Conclusions** Nearly one-half of children with no known heart disease hospitalized with systolic heart failure were missed at first presentation and underwent significant nonrelevant treatment and testing. Initial presentation to the PCP, longer duration of symptoms before presentation, and nausea/emesis were associated with missed diagnosis. *(J Pediatr 2019;208:258-64)*.

The burden of heart failure is increasing worldwide.[1,2] Advanced technologies have brought new treatment options to pediatric heart failure, but timely and accurate diagnosis remains a challenge.[3-6] Children with systolic heart failure present with signs and symptoms that mimic common childhood illnesses,[7-10] which may contribute to misidentification of the source of symptoms. For instance, presenting features of heart failure such as tachypnea, feeding difficulties, abdominal pain, and nausea[9,11] may also be incorrectly ascribed to respiratory infections or gastroenteritis. The frequency of missed heart failure diagnoses in children is unknown. Identifying barriers to a correct diagnosis may allow for earlier initiation of appropriate therapies, decreased cost/morbidity associated with unnecessary testing, prevention of hospitalizations or intensive care unit admissions with associated complications, and, thus, overall better outcomes.

Children with no previously known heart disease who are hospitalized with new-onset heart failure represent an ideal population to study epidemiology of missed heart failure diagnosis. We performed a retrospective analysis of children hospitalized with new-onset heart failure and sought to determine the frequency and population characteristics of patients with missed diagnoses of heart failure at first presentation; identify factors associated with a missed diagnosis of heart failure among this population; and determine process breakdowns and barriers to making a correct diagnosis. We hypothesized that a majority of new diagnoses of heart failure among children with no known heart disease who are admitted to the hospital are missed on first presentation, a first presentation of heart failure to a primary care provider (PCP) is associated with a missed diagnosis, compared with presentation to the emergency department (ED) without a PCP referral, and children with a missed diagnosis of heart failure undergo unrelated testing for symptom work-up.

| | |
|---|---|
| BNP | B-type natriuretic peptide |
| ECG | Electrocardiogram |
| ED | Emergency department |
| GI | Gastrointestinal |
| LOS | Length of stay |
| MCS | Mechanical circulatory support |
| PCP | Primary care provider |

From the [1]Department of Pediatrics, Section of Pediatric Cardiology, Baylor College of Medicine, Houston, TX; and [2]Center for Innovations in Quality, Effectiveness and Safety, Michael E. DeBakey Veterans Affairs Medical Center and Baylor College of Medicine, Houston, TX

H.S. is supported by the VA Health Services Research and Development Service (Presidential Early Career award for Scientists and Engineers USA 14-274), the VA National Center for Patient Safety and the Agency for Health Care Research and Quality (R01HS022087), the Gordon and Betty Moore Foundation, and the Houston VA HSR&D Center for Innovations in Quality, Effectiveness and Safety (CIN 13–413). The authors declare no conflicts of interest.

Portions of this study were presented at the annual meeting of the International Society of Heart and Lung Transplantation, April 5-7, 2017, San Diego, California.


https://doi.org/10.1016/j.jpeds.2018.12.029

## Methods

We performed a retrospective study, examining records of children hospitalized with decompensated systolic heart failure from November 1, 2003 to November 30, 2015 at a large, urban, tertiary-quaternary care pediatric hospital. The study was approved by the local Institutional Review Board.

All patients age <21 years with first-time diagnosis of heart failure requiring hospitalization for acute decompensated heart failure were included. These patients may have presented either directly to our hospital and its associated clinics, or to an outside hospital or clinic. We excluded patients with a prior diagnosis of heart failure, and those with a neuromuscular disorder, cancer, or structural heart disease. Four criteria were used to define missed heart failure diagnosis, building on a previously applied concept of determining missed opportunities in diagnosis[12]: (1) one or more symptom of heart failure, including unexplained increased rate or work of breathing, cough, loss of appetite, nausea/emesis, abdominal pain, edema (pedal edema or ascites), diaphoresis, lethargy, syncope, or chest pain; (2) one or more signs of heart failure including unexplained tachypnea, tachycardia, diaphoresis, S3 gallop, or hepatomegaly; (3) absence of heart failure in the differential diagnosis, work-up, or management of the patient at first presentation; and (4) absence of correct diagnosis of heart failure for at least 24 hours before being diagnosed at our institution, despite a workup for signs and symptoms. All 4 criteria had to be met for a case to be classified as "missed." An echocardiogram demonstrating systolic ventricular dysfunction (ejection fraction <55%) was necessary to confirm the diagnosis of heart failure. Patients with cardiac etiology in the differential diagnosis, work-up, or management were not considered "missed" if they also had additional antimicrobial agents or broader therapies initiated.

Breakdowns in the diagnostic process were assessed using a previously validated data collection instrument that assessed 5 dimensions[13]: patient-related factors, patient-provider encounter, diagnostic test performance/interpretation, referrals, and follow-up and tracking of diagnostic test results. The instrument and testing procedures were adapted from Singh et al.[14-16]

Each patient record was independently reviewed by 2 reviewers to determine the presence or absence of missed heart failure using a structured data collection instrument. The study period excluded the practice experience of the clinician at the study institution, to minimize bias because of patient recognition. This tool was initially tested on a sample of 40 patients from the study cohort. The results were used to refine the instrument and record assessment procedures. Then, another 20 patients were reviewed There were changes to determination of missed diagnosis in 2 patients in this round, with an agreement of 90% (kappa = 0.798, 95% CI 0.532-1). After this initial testing, reviewers assessed the remainder of the cohort. In cases of discordance between the reviewers, the senior physician re-assessed the case and made the final decision.

The predictor variables analyzed for association with missed heart failure diagnosis included age at presentation, sex, race/ethnicity, setting of first presentation, and the duration and type of symptoms reported by the parent at the time of first presentation. The primary outcome was missed diagnosis of heart failure. We analyzed 2 types of secondary outcomes: measures of severity of heart failure, included intubation at admission, renal dysfunction at admission (defined as estimated glomerular filtration rate [calculated using the bedside Schwartz equation] less than the normal for age[17]), mechanical circulatory support (MCS) during index admission, total length of stay (LOS) during index admission, transplant during index admission, and death during index admission in both cohorts; and clinical impact in terms of unnecessary diagnostic and therapeutic interventions in missed cohort.

The association of symptoms at presentation with missed diagnosis was also analyzed separately after stratifying the cohort by age, because older children present more commonly with abdominal complaints, and infants present more commonly with respiratory and feeding difficulties. The age groups were decided a priori as: <1 year, 1-2 years, 2-12 years, and >12 years.

Demographics, symptoms at presentation, and admission characteristics of patients with a missed diagnosis of heart failure ("missed") were compared with patients with correctly diagnosed heart failure ("not missed"). Kappa statistic was used to analyze agreement between the 2 independent reviewers on presence/absence of missed heart failure.[18] The predictor variables were compared between the missed and the not-missed groups on univariate analysis. All factors with $P$ value of <.1 on univariate analysis were included in the model for multivariable regression analysis. Final significance was defined as $P$ value of <.05. SPSS v 22.0 (IBM SPSS Statistics, Armonk, New York) software package was used for statistical analysis.

## Results

Of 226 patients admitted with new-onset heart failure during the study period, 191 met criteria for inclusion for further analysis. Of the 35 patients excluded, 3 were found to have been diagnosed with depressed systolic function as an outpatient previously, 2 patients were found to have known repaired congenital heart disease, 3 patients were previous heart transplant recipients, and 2 patients had underlying neuromuscular disease. The remaining 25 patients did not have adequate electronic medical records available to review to assess whether the diagnosis was missed at first presentation or not. Overall, 49% (94/191) of patients had a missed diagnosis on first presentation. Interobserver agreement on presence/absence of missed diagnosis of heart failure was moderate with K = 0.782 and agreement of 89.1%.

Demographics and presenting clinical features of the missed and not-missed cohort are compared in **Table I**. Patients who were missed at first presentation were

**Table I. Demographic and clinical characteristics of patients with correct and missed diagnoses of systolic heart failure**

| Characteristics | Missed (n = 94) | Not missed (n = 97) | OR (95% CI) | *P* value |
|---|---|---|---|---|
| Age at admission, y (median, IQR) | 4.1 (0.9-9.8) | 0.830 (0.1-9.5) | | **.007** |
| Sex | | | 0.73 (0.41-1.28) | .270 |
| Male, n (%) | 40 (43) | 49 (51) | | |
| Female, n (%) | 54 (57) | 48 (50) | | |
| Race/ethnicity | | | | .690 |
| Non-Hispanic white, n (%) | 28 (30) | 27 (28) | | |
| Hispanic white, n (%) | 38 (40) | 34 (35) | | |
| Black, n (%) | 19 (20) | 28 (29) | | |
| Asian, n (%) | 2 (2) | 1 (1) | | |
| Unknown, n (%) | 7 (7) | 7 (7) | | |
| Site of initial presentation | | | | **<.001** |
| ED, n (%) | 33 (35) | 60 (62) | | |
| PCP, n (%) | 60 (64) | 31 (32) | | |
| In-patient, n (%) | 1 (1) | 6 (6) | | |
| Duration of symptoms before presentation, d (median, IQR) | 7 (4-14) | 3 (1.5-7) | | **<.001** |
| Number of encounters before correct diagnosis (median, IQR) | 2 (1-2) | 0 (0) | | **<.001** |
| Time to correct diagnosis from first presentation to medical care, d (median, IQR) | 3 (1.5-7) | 0 (0-1) | | **<.001** |
| Symptoms | | | | |
| Fever, n (%) | 3 (3) | 7 (7) | 0.42 (0.11-1.69) | .331 |
| Tachypnea/work of breathing, n (%) | 61 (65) | 61 (63) | 1.09 (0.60-1.97) | .773 |
| Cough, n (%) | 24 (26) | 20 (21) | 1.32 (0.67-2.60) | .420 |
| Loss of appetite, n (%) | 50 (53) | 34 (35) | **2.11 (1.18-3.77)** | **.012** |
| Abdominal pain, n (%) | 26 (28) | 11 (11) | **2.99 (1.38-6.48)** | **.004** |
| Nausea/emesis, n (%) | 51 (54) | 29 (30) | **2.78 (1.53-5.04)** | **.001** |
| Diaphoresis, n (%) | 9 (10) | 4 (4) | 2.46 (0.73-8.29) | .135 |
| Palpitations or syncope, n (%) | 13 (14) | 12 (12) | 1.14 (0.49-2.64) | .765 |
| Edema of peripheries or ascites, n (%) | 12 (13) | 6 (6) | 2.22 (0.80-6.18) | .120 |
| Headache, n (%) | 3 (3) | 1 (1) | 3.17 (0.32-30.98) | .363 |
| Lethargy or tiredness, n (%) | 32 (34) | 27 (28) | 1.34 (0.72-2.48) | .353 |
| More than 1 heart failure symptom, n (%) | 83 (88) | 62 (64) | **4.26 (2.01-9.05)** | **<.001** |
| More than 2 heart failure symptoms, n (%) | 62 (66) | 26 (27) | **5.29 (2.85-9.83)** | **<.001** |

Values in bold indicate $P < .05$ on univariate analysis.

correctly diagnosed after a median of 2 encounters (IQR 1-2) with medical services, and had a median time delay of 3 days in getting a correct diagnosis (IQR 1.5-7). Among the missed patients, 64% (60/94) first presented to a PCP, and 35% (33/94) presented to an ED. Missed patients were more likely to have presented to a PCP and not-missed patients were more likely to present directly to an ED (Table I). Patients with a missed diagnosis were older at presentation (median age 4.1 years vs 0.8 years; $P = .007$) and had a longer duration of symptoms (median 7 vs 3 days, $P < .001$) than not missed patients. Further, missed patients had a higher frequency of gastrointestinal (GI) symptoms, including abdominal pain, loss of appetite, and nausea/emesis.

Table II (available at www.jpeds.com) summarizes the diagnoses (other than heart failure) assigned to the missed patients at their first presentation. The diagnosis of a bacterial illness such as pneumonia, sinusitis, or otitis media was made in 29% (27/94) of the patients, for which antibiotics were prescribed. Twenty-two percent (21/94) were diagnosed with a viral illness and symptomatically managed with cough suppressants, decongestants, and/or allergy medication. Another 21% (20/94) were diagnosed with gastroenteritis or hepatitis, and were managed with anti-emetic or antispasmodic agents or underwent additional testing. A diagnosis of asthma or reactive airway disease was made in 10% (9/94), and bronchodilators and antiallergic medications were prescribed. When comparing frequency of missed diagnosis by site of presentation, patients who presented to the PCP office were more often incorrectly diagnosed with a viral syndrome (27% at PCP vs 15% in ED, $P = .004$), and those presenting to the ED or inpatient at time of first diagnosis of heart failure had a higher frequency of incorrect diagnosis of bacterial infection with prescription of antibiotics (35% vs 25.0%, $P = .004$).

There was no significant difference in the distribution of the various etiologies of heart failure between the missed and not-missed groups ($P = .110$), and dilated cardiomyopathy was the most common etiology of heart failure in the cohort. Among the missed group, 54% of the patients had dilated cardiomyopathy (51/94), followed by myocarditis in 28% (26/94). The remainder of the group included left ventricular noncompaction in 5% (5/94), restrictive cardiomyopathy in 3% (3/94), anomalous origin of the left coronary artery from pulmonary artery in 3% (3/94), hypertrophic obstructive cardiomyopathy in 2% (2/94), and connective tissue disease in 2% (2/94). The remaining 2 patients were presumed to have myocarditis. Among the not-missed group, dilated cardiomyopathy was again the most common diagnosis, 43% (42/97), followed by myocarditis in 31% (30/97). The remainder of the cohort included tachycardia-induced cardiomyopathy in 7% (7/97), anomalous origin of the left coronary artery from pulmonary artery

**Table III. Univariate and multivariable analysis of characteristics associated with missed diagnosis of systolic heart failure**

| Characteristics | *P* value (univariate) | *P* value (multivariable) | OR (95%CI) |
|---|---|---|---|
| Age at admission | .007 | .963 | 1.00 (0.94-1.07) |
| Site of initial presentation (PCP or not) | <.001 | **.001** | **3.32 (1.61-6.82)** |
| Duration of symptoms before presentation, d, (median, IQR) | <.001 | **.022** | **1.04 (1.01-1.07)** |
| Loss of appetite | .012 | .405 | 1.42 (0.63-3.21) |
| Abdominal pain | .004 | .078 | 2.39 (0.91-6.30) |
| Nausea/emesis | .001 | **.022** | **2.44 (1.13-5.23)** |
| Edema | .120 | .607 | 1.40 (0.39-5.03) |
| Diaphoresis | .135 | .434 | 1.76 (0.43-7.26) |
| More than 2 symptoms | <.001 | **.033** | **2.51 (1.08-5.86)** |

Values in bold indicate $P < .05$ on univariate analysis.

in 6% (6/97), left ventricular noncompaction in 4% (4/97), restrictive cardiomyopathy in 2% (2/97), and connective tissue disease in 1% (1/97). Five patients were presumed to have myocarditis in this group.

On multivariable analysis, initial presentation to PCP ($P = .001$), longer duration of symptoms before presentation ($P = .022$), nausea/emesis ($P = .022$), and presence of 2 or more symptoms ($P = .033$) remained associated with a missed diagnosis of heart failure (Table III).

The only difference in the frequency of symptoms between missed and not-missed patients within age groups was observed in infants and adolescents (Table IV; available at www.jpeds.com). Among infants, those with missed diagnosis were more likely to present with diaphoresis (36% vs 8%, $P = .03$). Among adolescents, those with missed diagnosis were more likely to have abdominal pain (47% vs 17%, $P = .046$).

There was no difference in clinical outcomes (MCS, LOS, mortality, or cardiac transplant) of the index hospitalization between the missed and not-missed groups (Table V; available at www.jpeds.com).

At initial presentation, 87% (82/94) of missed patients were prescribed some type of medication (not targeting heart failure), including antibiotics, bronchodilators, antiemetics, and decongestants (Table VI). Further, 22% (21/94) of the cohort were admitted for medical management not targeted to heart failure. Eighteen percent (17/94) underwent noninvasive testing not relevant to heart failure (strep test, abdominal radiograph, ultrasound, computed tomography scans), and 4% (4/94) underwent invasive testing not relevant to heart failure (eg, pH study, lumbar puncture, esophagogastroduodenoscopy, and liver biopsy). Some of these instances led to harm. For instance, a patient was evaluated in an ED for respiratory complaints, had a chest radiograph that revealed cardiomegaly and slightly prominent pulmonary vascular markings, and was subsequently discharged home with bronchodilator therapy. However, the patient presented a few weeks later in acute cardiorespiratory failure and died, with postmortem examination revealing dilated cardiomyopathy. Two patients were referred for surgical intervention for heart failure symptoms: 1 for cholecystectomy because of right upper quadrant abdominal pain and an ultrasound showing gall bladder sludge, and 1 for exploratory laparotomy because of suspected appendicitis attributable to right-sided abdominal tenderness. The patient referred for cholecystectomy had an enlarged cardiac silhouette seen on the admission abdominal radiograph at our institute and was correctly diagnosed with heart failure before surgery. The patient planned for laparotomy suffered cardiac arrest on anesthesia induction at the outside hospital, which prompted a cardiac evaluation demonstrating cardiomegaly on chest radiograph and severely depressed systolic function on echocardiography. On evaluation at our center, that patient was also noted to have a gallop rhythm and hepatomegaly on examination. Another patient had been started on dialysis prior to referral to our center for further management of their renal failure. However, abdominal radiograph revealed cardiomegaly, which eventually led to a correct diagnosis of dilated cardiomyopathy and heart failure.

Overall, 5% (5/94) suffered complications from the testing/therapeutic measures, including 1 cardiac arrest after intubation for planned laparotomy, 1 patient started on dialysis for management of renal failure, 1 patient undergoing liver biopsy because of concern for hepatomegaly, and 2

**Table VI. Clinical impact related to unnecessary testing and management of patients with missed diagnosis of new-onset systolic heart failure**

| Management | n = 94 |
|---|---|
| Medical management | |
| Outpatient medical management for incorrect diagnosis, n (%) | 82 (87) |
| Admission for management of incorrect diagnosis, n (%) | 21 (22) |
| Nonrelevant testing | |
| Noninvasive diagnostic testing, n (%)* | 17 (18) |
| Invasive diagnostic testing, n (%)† | 4 (4) |
| Complication because of testing or therapy for incorrect diagnosis, n (%)‡ | 5 (5) |

*Includes 8 computed tomography scan of abdomen or pelvis, 3 computed tomography scan of head, 3 abdominal ultrasound, 2 hepatobiliary iminodiacetic acid scan, and 1 allergy testing.
†Includes 1 liver biopsy, 1 nonrelevant lumbar puncture (of the 3 lumbar punctures in the cohort, 2 were in the setting of neonatal sepsis work-up), 2 esophagogastroduodenoscopy (1 in the patient who also underwent liver biopsy) and 1 pH probe study.
‡Includes 1 cardiac arrest after intubation for planned laparotomy, 1 patient instituted on dialysis for renal failure, which was secondary to low cardiac output and heart failure, 1 patient undergoing liver biopsy because of concern for hepatomegaly, and 2 patients receiving more than 60 mL/kg of fluid resuscitation in the setting of heart failure.

**Table VII. Errors in different realms of patient-provider encounter and care in cases with missed diagnosis of systolic heart failure**

| | n = 94 |
|---|---|
| Patient-provider encounter | |
| No patient-provider encounter, n (%) | 0 (0) |
| Problems in ordering further diagnostic test for workup, n (%) | 73 (78) |
| Error related to medical history, n (%) | 46 (49) |
| Error related to physician examination performance, n (%) | 51 (54) |
| Failure to review previous documentation, n (%) | 1 (1) |
| None, n (%) | 0 (0) |
| Documentation-related | |
| Failure to review previous documentation, n (%) | 0 (0) |
| Failure to acknowledge heart failure history or family history of cardiomyopathy, n (%) | 4 (4) |
| Failure to document the provider visit, n (%) | 0 (0) |
| No evidence of differential diagnosis, n (%) | 47 (50) |
| None, n (%) | 43 (46) |
| Diagnostic testing | |
| Ordered test not performed at all, n (%) | 1 (1) |
| Ordered test not performed correctly, n (%) | 0 (0) |
| Ordered test not interpreted correctly, n (%) | 9 (10) |
| Misidentification, n (%)* | 0 (0) |
| None, n (%) | 84 (89) |
| Follow-up and tracking | |
| Problem with timely follow-up of abnormal diagnostic test results, n (%) | 11 (12) |
| Problems with scheduling of appropriate and/or timely follow-up visits, n (%) | 46 (49) |
| None, n (%) | 37 (39) |
| Referrals | |
| Problem initiating referral, n (%) | 65 (69) |
| Lack of appropriate actions on requested consultation, n (%) | 3 (3) |
| Communication breakdown from consultant to referring provider, n (%) | 0 (0) |
| None, n (%) | 26 (28) |

*Includes mislabeling or incorrect test being performed.

patients receiving more than 60 mL/kg of fluid resuscitation in the setting of heart failure.

Table VII shows diagnostic error-related breakdowns in the missed cohort.[12,13] In the patient-provider encounter dimension, tests were not ordered in 78% of patients at initial assessment (ie, they did not receive relevant testing including a chest radiograph, electrocardiogram [ECG] or a B-type natriuretic peptide [BNP] level measurement). Forty-nine percent of the records had an error related to medical history, including nature and duration of symptoms, and family history of sudden death or cardiomyopathy. In 54% of the cases, there were errors related to physical examination, including absence of recorded vital signs, or lack of comment about abnormal vital signs in the "assessment"/"plan" sections. Fifty percent of the cases lacked a differential diagnosis, and in 4% of the cases, a significant family history concerning for cardiac disease (which might have prompted further cardiac investigation) was not documented in the initial presentation, but documented in the subsequent admission note in the hospital. In 10% (9 patients) of the cases, testing was not interpreted correctly by the ordering caregiver (eg, failure to detect cardiomegaly or increased pulmonary vascular markings on chest/abdominal radiographs). In 8 of the 9 cases, the test interpretation was performed by the ordering provider, without a final radiology read available prior to initiation of nonheart failure management and/or transfer. In the remaining patient, the final test read from radiology was communicated to the care team 48 hours after the test. Appropriate follow-up, such as early PCP visit or close follow-up at the ED, was lacking in nearly one-half of patients (49%). Sixty-nine percent of the patients met clinical criteria for referral to a cardiology clinic or inpatient cardiology consult, but it was never made.

## Discussion

Our findings suggest that children who present with GI symptoms rather than cardiovascular features of heart failure are more likely to be missed. GI symptoms are known to be common in children with heart failure, especially in adolescents.[8,9] In a review of children with a new diagnosis of dilated cardiomyopathy, Hollander et al found that GI complaints such as nausea, vomiting, abdominal pain, decreased appetite, or weight loss were frequently described in infants (42%), children aged 1-10 years (28%), and adolescents (65%).[11] Macicek et al reported that over 80% of children with decompensated heart failure in the ED presented with at least one GI sign or symptom.[10] Our study confirms that GI symptoms remain an underappreciated feature of decompensated heart failure.[10,11,19] We recommend that curriculum to train future pediatricians should emphasize these clinical features and encourage inclusion of heart failure in the differential diagnosis of children presenting with GI complaints.

Of the patients in the missed cohort, 87% were prescribed medicines not related to heart failure. Awaiting response to these medications which would be ineffective for heart failure symptoms may have contributed to the delay in institution of appropriate therapies. Twenty-two percent of the patients were admitted for medical management with nonheart failure strategies, which is important as it indicates multiple medical teams missed the diagnosis of heart failure in these patients. Further, 18% of the patients underwent nonrelevant noninvasive testing, and 4% underwent nonrelevant invasive testing. Advanced imaging such as computed tomography scans and sedated magnetic resonance imaging scans as well as procedures such as liver biopsy, lumbar puncture, and esophagogastroduodenoscopy performed on children with a missed heart failure diagnosis exposed them to risk of morbidity or radiation. Further, 5% had a complication related to an unnecessary procedure. Conversely, relatively inexpensive cardiovascular testing that might provide important diagnostic clues such as chest radiograph, ECG, or BNP testing were often not performed or sometimes misinterpreted when performed.

Unexpectedly, and despite the potential consequences of a missed diagnosis of heart failure, children in the missed cohort did not suffer worse outcomes, including MCS, LOS, transplant, or mortality. One potential reason could be that children with a missed diagnosis were more likely to present to their PCP rather than the ED and were not as acutely ill. It is also possible that the patients in the missed

cohort who suffered mortality may have had better outcomes if the heart failure had been diagnosed on time and management initiated earlier. Nevertheless, this finding is similar to that in adults in which a diagnosis of chronic heart failure was missed but had no impact on heart failure-related mortality or readmission.[20]

Diagnostic errors in pediatric cardiology are understudied. Previously, Benavenidez et al reviewed diagnostic errors in the echocardiography laboratory (defined as missing a finding or a diagnosis on an echocardiogram), and found 254 errors in 6 years (0.17% of 147 000).[21] In pediatrics, new-onset heart failure is an uncommon clinical syndrome, and hence may be expected to have some error in its recognition. However, in our cohort, 88% of the children with missed heart failure had 2 or more symptoms of heart failure, which should result in heart failure being included in the differential diagnosis even if it occurs rarely. Performing chest radiograph, ECG, or serum BNP testing to investigate that possibility, while attempting other symptomatic management, should be considered.[22,23]

Process breakdowns largely involved basic clinical skills, from incorrect history of symptoms, missed family history of cardiomyopathy, errors in physical examination including missing vital signs, and lack of a differential diagnosis. An adult primary care study found 80% of diagnostic error cases had no differential diagnoses documented.[24] Several strategies to improve data gathering and interpretation skills and use of differential diagnosis could be useful.[25] Although this study was not planned as a quality assessment project, the findings of the study spurred us to carry out a community workshop to increase awareness about pediatric heart failure for providers in the clinics and urgent care facilities affiliated with our institution.

Our study was limited to a single site. We did not have information about accreditation or training level of providers involved. We were also limited in our assessment by provider documentation where thought processes may be incompletely conveyed. Hindsight bias can occur with retrospective reviews.[26] A prospective quality assessment study to examine each case of heart failure admitted will better capture some of this information through real-time case analysis, debriefs with the PCP or ED physicians and knowledge of systems issues involved.[27] We identified several areas where interventions can be focused to reduce missed heart failure, including strategies to improve data gathering and clinical reasoning based on history and physical examination. ■

Submitted for publication Aug 17, 2018; last revision received Dec 7, 2018; accepted Dec 10, 2018.

Reprint requests: Kriti Puri, MBBS, Department of Pediatrics, Section of Pediatric Cardiology, Baylor College of Medicine, Texas Children's Hospital, 6621 Fannin St, MC 19345C, Houston, TX 77030. E-mail: puri.kriti@gmail.com; kriti.puri@bcm.edu

## Data Statement

Data sharing statement available at www.jpeds.com.

## References

1. Savarese G, Lund LH. Global public health burden of heart failure. Card Fail Rev 2017;3:7-11.
2. Rossano JW, Kim JJ, Decker JA, Price JF, Zafar F, Graves DE, et al. Prevalence, morbidity, and mortality of heart failure-related hospitalizations in children in the United States: a population-based study. J Card Fail 2012;18:459-70.
3. Skinner TR, Scott IA, Martin JH. Diagnostic errors in older patients: a systematic review of incidence and potential causes in seven prevalent diseases. Int J Gen Med 2016;9:137-46.
4. Kümler T, Gislason GH, Kirk V, Bay M, Nielsen OW, Køber L, et al. Accuracy of a heart failure diagnosis in administrative registers. Eur J Heart Fail 2008;10:658-60.
5. Barents M, van der Horst IC, Voors AA, Hillege JL, Muskiet FA, de Jongste MJ. Prevalence and misdiagnosis of chronic heart failure in nursing home residents: the role of B-type natriuretic peptides. Neth Heart J 2008;16:123-8.
6. Issa VS, Dinardi LF, Pereira TV, de Almeida LK, Barbosa TS, Benvenutti LA, et al. Diagnostic discrepancies in clinical practice: an autopsy study in patients with heart failure. Medicine (Baltimore) 2017;96:e5978.
7. Rosenthal D, Chrisant MR, Edens E, Mahony L, Canter C, Colan S, et al. International Society for Heart and Lung Transplantation: practice guidelines for management of heart failure in children. J Heart Lung Transplant 2004;23:1313-33.
8. Kantor PF, Lougheed J, Dancea A, McGillion M, Barbosa N, Chan C, et al. Children's Heart Failure Study Group. Presentation, diagnosis, and medical management of heart failure in children: Canadian Cardiovascular Society guidelines. Can J Cardiol 2013;29:1535-52.
9. Ross RD. The Ross classification for heart failure in children after 25 years: a review and an age-stratified revision. Pediatr Cardiol 2012;33:1295-300.
10. Macicek SM, Macias CG, Jefferies JL, Kim JJ, Price JF. Acute heart failure syndromes in the pediatric emergency department. Pediatrics 2009;124:e898-904.
11. Hollander SA, Addonizio LJ, Chin C, Lamour JM, Hsu DT, Bernstein D, et al. Abdominal complaints as a common first presentation of heart failure in adolescents with dilated cardiomyopathy. Am J Emerg Med 2013;31:684-6.
12. Singh H. Editorial: helping health care organizations to define diagnostic errors as missed opportunities in diagnosis. Jt Comm J Qual Patient Saf 2014;40:99-101.
13. Singh H, Sittig DF. Advancing the science of measurement of diagnostic errors in healthcare: the Safer Dx framework. BMJ Qual Saf 2015;24:103-10.
14. Singh H, Hirani K, Kadiyala H, Rudomiotov O, Davis T, Khan MM, et al. Characteristics and predictors of missed opportunities in lung cancer diagnosis: an electronic health record-based study. J Clin Oncol 2010;28:3307-15.
15. Al-Mutairi A, Meyer AN, Thomas EJ, Etchegaray JM, Roy KM, Davalos MC, et al. Accuracy of the safer Dx instrument to identify diagnostic errors in primary care. J Gen Intern Med 2016;31:602-8.
16. Davalos MC, Samuels K, Meyer AN, Thammasitboon S, Sur M, Roy K, et al. Finding diagnostic errors in children admitted to the PICU. Pediatr Crit Care Med 2017;18:265-71.
17. Schwartz GJ, Haycock GB, Edelmann CM Jr, Spitzer A. A simple estimate of glomerular filtration rate in children derived from body length and plasma creatinine. Pediatrics 1976;58:259-63.
18. McHugh ML. Interrater reliability: the kappa statistic. Biochem Med (Zagreb) 2012;22:276-82.
19. Clark BJ III. Treatment of heart failure in infants and children. Heart Dis 2000;2:354-61.
20. Akosah KO, Moncher K, Schaper A, Havlik P, Devine S. Chronic heart failure in the community: missed diagnosis and missed opportunities. J Card Fail 2001;7:232-8.
21. Benavidez OJ, Gauvreau K, Geva T. Diagnostic errors in congenital echocardiography: importance of study conditions. J Am Soc Echocardiogr 2014;27:616-23.

22. Cantinotti M, Law Y, Vittorini S, Crocetti M, Marco M, Murzi B, et al. The potential and limitations of plasma BNP measurement in the diagnosis, prognosis, and management of children with heart failure due to congenital cardiac disease: an update. Heart Fail Rev 2014;19:727-42.
23. Maher KO, Reed H, Cuadrado A, Simsic J, Mahle WT, Deguzman M, et al. B-type natriuretic peptide in the emergency diagnosis of critical heart disease in children. Pediatrics 2008;121:e1484-8.
24. Singh H, Giardina TD, Meyer AN, Forjuoh SN, Reis MD, Thomas EJ. Types and origins of diagnostic errors in primary care settings. JAMA Intern Med 2013;173:418-25.
25. Singh H, Zwaan L. Annals for hospitalists inpatient notes—reducing diagnostic error: a new horizon of opportunities for hospital medicine. Ann Intern Med 2016;165:HO2-4.
26. Fischhoff B. Hindsight not equal to foresight: the effect of outcome knowledge on judgment under uncertainty. Qual Saf Health Care 2003;12:304-11. discussion 311-2.
27. Zwaan L, Thijs A, Wagner C, van der Wal G, Timmermans DR. Design of a study on suboptimal cognitive acts in the diagnostic process, the effect on patient outcomes and the influence of workload, fatigue and experience of physician. BMC Health Serv Res 2009;9:65.

**Table II. Diagnoses (incorrectly) assigned to patients with a missed diagnosis of systolic heart failure**

| Incorrectly assigned diagnoses | Overall (n = 94) n (%) | PCP (n = 60) n (%) | ED or in-patient (n = 34) n (%) | *P* value* |
|---|---|---|---|---|
| Bacterial infection-pneumonia/sinusitis/otitis media | 27 (29) | 15 (25) | 12 (35) | .004 |
| Viral syndrome | 21 (22) | 16 (27) | 5 (15) | |
| Gastroenteritis or hepatitis | 20 (21) | 11 (18) | 9 (27) | |
| Asthma/reactive airway disease | 9 (10) | 6 (10) | 3 (9) | |
| Behavioral/no diagnosis | 10 (11) | 7 (12) | 3 (9) | |
| Constipation | 2 (2) | 1 (2) | 1 (3) | |
| Metabolic disorder | 2 (2) | 1 (2) | 1 (3) | |
| Renal disorder | 1 (1) | 1 (2) | 0 (0) | |
| Delay in referral/nonspecific cardiology referral | 2 (2) | 2 (3) | 0 (0) | |

*$\chi^2$ test for distribution of incorrect diagnoses between sites of presentation.

**Table IV. Clinical characteristics of patients with correct and missed diagnosis of systolic heart failure stratified by age**

| | <1 y | | | 1-2 y | | | 2-12 y | | | >12 y | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n = 25 | n = 50 | | n = 13 | n = 7 | | n = 37 | n = 22 | | n = 19 | n = 18 | |
| | Missed | Not missed | *P* value (OR, 95% CI) | Missed | Not missed | *P* value (OR, 95% CI) | Missed | Not missed | *P* value (OR, 95% CI) | Missed | Not missed | *P* value (OR, 95% CI) |
| Tachypnea/increased work of breathing, n (%) | 18 (72) | 33 (66) | .600 (1.33, 0.46-3.79) | 12 (92) | 7 (100) | 1 (1.08, 0.93-1.27) | 22 (60) | 13 (59) | .978 (1.02, 0.35-2.97) | 9 (47) | 8 (44) | .858 (1.13, 0.31-4.11) |
| Cough, n (%) | 9 (36) | 8 (16) | .051 (2.95, 0.97-8.99) | 3 (23) | 3 (43) | .613 (0.40, 0.06-2.89) | 8 (22) | 6 (27) | .622 (0.74, 0.22-2.50) | 4 (21) | 3 (17) | 1 (1.33, 0.25-7.01) |
| Loss of appetite, n (%) | 17 (68) | 24 (48) | .101 (2.30, 0.84-6.30) | 7 (54) | 1 (14) | .158 (7.00, 0.65-75.74) | 18 (49) | 6 (27) | .106 (2.53, 0.81-7.89) | 8 (42) | 3 (17) | .091 (3.64, 0.78-16.93) |
| Abdominal pain, n (%) | 0 (0) | 0 (0) | NA | 1 (8) | 1 (14) | 1 (0.50, 0.03-9.46) | 16 (43) | 7 (32) | .384 (1.63, 0.54-4.95) | 9 (47) | 3 (17) | **.046 (4.50, 0.97-20.83)** |
| Nausea/vomiting, n (%) | 10 (40) | 15 (30) | .386 (1.56, 0.57-4.24) | 8 (62) | 1 (14) | .070 (9.60, 0.88-105.17) | 22 (60) | 8 (36) | .086 (2.57, 0.86-7.62) | 11 (58) | 5 (28) | .065 (3.58, 0.90-14.15) |
| Syncope/palpitations | 2 (8) | 4 (8) | 1 (1, 0.17-5.87) | 1 (8) | 0 (0) | 1.000 (1.08, 0.93-1.27) | 4 (11) | 1 (5) | .641 (2.55, 0.27-24.36) | 6 (32) | 7 (39) | .642 (0.73, 0.19-2.81) |
| Diaphoresis, n (%) | 9 (36) | 4 (8) | **.003 (6.45, 1.75-23.93)** | 0 (0) | 0 (0) | NA | 0 (0) | 0 (0) | NA | 0 (0) | 0 (0) | NA |
| Edema, n (%) | 0 (0) | 0 (0) | NA | 1 (8) | 0 (0) | 1.000 (1.08, 0.93-1.27) | 8 (22) | 2 (9) | .294 (2.76, 0.53-14.38) | 3 (16) | 4 (22) | .693 (0.66, 0.13-3.45) |
| Headache, n (%) | 0 (0) | 0 (0) | NA | 0 (0) | 0 (0) | NA | 2 (5) | 1 (5) | 1 (1.2, 0.10-14.06) | 1 (5) | 0 (0) | 1 (1.06, 0.95-1.17) |
| Lethargy/tiredness, n (%) | 5 (20) | 15 (30) | .356 (0.58, 0.18-1.85) | 3 (23) | 1 (14) | 1.000 (1.80, 0.15-21.48) | 13 (35) | 5 (23) | .317 (1.84, 0.55-6.14) | 11 (58) | 6 (33) | .134 (2.75, 0.72-10.48) |
| More than 2 symptoms | 13 (52) | 16 (32) | .094 (2.302, 0.860-6.160) | 6 (46.2) | 1 (14.3) | .329 (5.14, 0.48-55.64) | 27 (73) | 5 (23) | **<.001 (9.18, 2.68-31.51)** | 16 (84) | 4 (22) | **<.001 (18.67, 3.55-98.17)** |

NA, not applicable.

**Table V. Severity measures and secondary outcomes of missed and correct diagnoses of systolic heart failure**

| Outcome/severity | Missed (n = 94) | Not missed (n = 97) | *P* value | OR (95% CI) |
|---|---|---|---|---|
| Renal dysfunction at admission, n (%) | 34 (36) | 31 (32) | .683 | 1.14 (0.62-2.08) |
| Intubation at admission, n (%) | 54 (57) | 51 (53) | .499 | 1.22 (0.69-2.16) |
| MCS in index admission, n (%) | 29 (31) | 21 (22) | .148 | 1.62 (0.84-3.10) |
| LOS in d, (median, IQR) | 22 (12-61.5) | 21 (12.5-41) | .504 | |
| Transplant in index admission, n (%) | 11 (12) | 10 (10) | .758 | 1.15 (0.47-2.86) |
| Death in index admission, n (%) | 11 (12) | 11 (11) | .915 | 1.05 (0.43-2.55) |