Apparent Life-Threatening Event Admissions and Gastroesophageal Reflux Disease

The Value of Hospitalization

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Background: No standard management plan for infants with an apparent life-threatening event (ALTE) currently exists. These infants are routinely hospitalized. Benefits of hospitalization of ALTE patients with gastroesophageal reflux disease (GERD) need definition.

Objectives: The study's objectives were to determine the accuracy of a working diagnosis of GERD in infants admitted with ALTE and to describe the history and hospital course of infants with both working and discharge diagnoses of GERD.

Methods: Authors retrospectively reviewed records from a large children's hospital of infants aged 1 year old and younger hospitalized from January 1, 2004, to March 1, 2007, with an *admission* diagnosis of ALTE. Demographics, clinical presentation, testing, hospital course, and 6-month postdischarge visits were abstracted. Intensive care admissions were excluded. Univariate and multivariate analyses identified factors associated with a discharge diagnosis of GERD.

Results: Three hundred thirteen infants met inclusion. Mean age was 2.1 months; mean length of stay was 2.5 days. A discharge diagnosis of GERD was most common (n = 154, 49%); 138 (89%) were initially well appearing, 10 (6%) had in-hospital events, and only 20 (13%) had upper gastrointestinal series performed. Concordance of initial working to discharge diagnosis of GERD was 96%. Nonconcordant diagnoses evolved within 24 hours. Rescue breaths and calling 911 were independently associated with a discharge diagnosis of GERD. Within 6 months, 14 patients (9%) with a discharge diagnosis of GERD had recurrent ALTE, and 5 (3%) had significant new diagnoses.

Conclusions: Concordance of initial working diagnosis with discharge diagnosis of GERD in ALTE patients is high. However, in hospital events, evolution to new diagnoses and recurrent ALTE suggest that hospitalization of these patients is beneficial. Diagnostic studies should not be routine but should target concerns from the history, examination, and hospital course.

Key Words: apparent life-threatening event, gastroesophageal reflux disease, diagnostic methods, differential diagnosis, apnea

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Apparent life-threatening event (ALTE) is defined as "an episode that is frightening to the observer and that is characterized by some combination of apnea (central or occasionally obstructive), color change (usually cyanotic or pallid but occasionally erythematous or plethoric), marked change in muscle tone (usually marked limpness), choking, or gagging. In some cases, the observer fears that the infant has died."[1] Apparent life-threatening event incidence is estimated at 0.5% to 6% and accounts for 0.6% to 0.8% of emergency department (ED) visits for children younger than 1 year.[2–4] Although up to 50% of ALTEs are deemed idiopathic, common discharge diagnoses include gastroesophageal reflux disease (GERD, 20%–54%), lower respiratory tract infection (7%–8%), and seizure (4%–11%).[4–6] Despite the broad range of underlying causes, most infants with ALTE are well appearing when first presenting to medical attention.[4,7] Inpatient evaluation and monitoring are a current practice,[3,8,9] accounting for 2.3% of pediatric admissions in the United States.[6,10,11] At this time, no standardized management plan exists for ALTE.[9] It has been suggested that the wide variation in resource use, testing, and length of stay (LOS) in ALTE patients may be due to the lack of consensus guidelines for diagnostic approach and management.[11]

Apparent life-threatening event studies to date have been largely retrospective, using discharge data sets. McGovern and Smith[6] reviewed international citations from 1966 to 2002 using search terms that "covered a range of diagnoses in infants … after an ALTE" finding 8 of 2912 studies meeting criteria, the largest with 130 patients. This meta-analysis was limited by varied study design and data quality and the inability to ensure that patients met the definition of ALTE at initial presentation. Tieder et al[11] used a narrower set of diagnostic codes, defined by screening the 2000–2005 administrative Pediatric Health Information System using "surrogate International Classification of Diseases, Ninth Revision codes compatible with the definition of ALTE." Authors acknowledged that this method may have misclassified infants as having ALTE who did not meet the clinical definition and that exclusion of comorbid conditions may have omitted some patients.

The single study addressing safe discharge from the ED included only previously healthy infants with ALTE younger than 1 year from a large tertiary care children's hospital.[12] Despite the greater than 90% hospitalization rate, authors stated only 14% (8/59) met the investigator's criteria for *hospitalization required*, defined as requiring resuscitation during hospitalization, having further events due to a new diagnosis, or receiving a diagnosis deemed high risk for clinical deterioration. Based on data from these 59 patients, Claudius and Keens[12] concluded that patients older than 30 days with a single ALTE in the past 24 hours could be safely discharged home from the ED. A separate study challenged the value of diagnostic testing, noting only 6% of tests contributed to the final diagnosis,[13] and another supported diagnostic testing only in infants with a suggestive history and physical examination result.[14]

These few reports suggest hospitalization may not be required and testing may be of minimal use for ALTE patients, raising the question of whether hospitalization is warranted. Gastroesophageal reflux disease, the predominant discharge diagnosis found in ALTE studies, does not require hospitalization for diagnosis or initiation of therapy.[15] Specifically, North

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American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) guidelines do not support invasive testing for diagnosis of GERD.[16] Gastroesophageal reflux disease has, however, been suggested as a risk factor for ALTE readmission.[11] Critically missing to date is the ability to capture a large number of patients at the time of ALTE presentation. Given the high percentage of discharge diagnoses attributable to GERD, accepted outpatient evaluation and treatment strategies, and possible role in ALTE readmission, this subset of ALTE patients is particularly important to examine. In this study, we aimed to determine the accuracy of the working diagnosis of GERD in infants admitted with ALTE and to define characteristics, hospital course, and posthospital events of infants hospitalized with ALTE with a discharge diagnosis of GERD.

METHODS

Study Population

This was a retrospective review of patient records of infants younger than 1 year who presented to Rady Children's Hospital San Diego (RCHSD) with an *admission* diagnosis of ALTE from January 2004 to March 2007, cared for by the Pediatric Hospital Medicine (PHM) Division. The PHM Division has practiced at RCHSD since 1978, caring for 89% of all general pediatric admissions (~3500 annually). Rady Children's Hospital San Diego is a tertiary care academic pediatric facility, with long-term stable referral patterns. It is the sole children's hospital for a large catchment area (Mexican border to South Orange County to Arizona). Readmissions or return visits, particularly for infants, are generally to the RCHSD system, which includes subspecialty clinics and urgent care centers.

Data Collection

Patients were identified from PHM Division billing records using a unique admission billing code for ALTE created in 2003. To ensure that all patients were included, the database was also searched for patients coded with an admission charge (99221–99223) and same date code for apnea (786.03), cyanosis (782.5), vomiting (787.03), respiratory problem of the newborn (770.8), altered consciousness (780.09), and transient loss of consciousness (780.02), which yielded no additional records. Rady Children's Hospital San Diego system medical records of these patients were retrospectively reviewed inclusive of initial hospitalization and all patient encounters for 6 months after discharge. Patients admitted directly to pediatric or neonatal intensive care units were excluded.

Initially, 4 investigators (A.D., E.S., L.B., C.K.) each reviewed 2 charts to ensure consistent data abstraction. All records were independently reviewed by at least 2 investigators (A.D. or E.S. and one other). Any discrepancies between reviewers were resolved jointly by A.D. and E.S. Data were entered into a spreadsheet on password-protected computers. All hospital administrative data were validated by record review.

Demographics, gestational age, chronic condition defined as preexisting disease (including congenital heart disease, genetic conditions, and preexisting known GERD but excluding prematurity <37 weeks), ALTE details, initial ED presentation, admission history and physical examination results, initial working diagnosis made by the hospitalist, hospital course, testing, and discharge diagnoses from the hospitalist discharge note were abstracted. All visits (subspecialty clinics, ED, urgent care, readmission) within a 6-month period after initial hospital discharge were recorded. The study was approved by the University of California San Diego Institutional Review Board.

Statistical Analysis

For data analysis, diagnoses of GERD and an isolated choking episode were combined and labeled as GERD. Frequencies and percentages for demographics, clinical presentation, and procedures are presented. The main outcome of interest was a discharge diagnosis other than GERD. Differences in study variables related to a discharge diagnosis of GERD versus other than GERD were assessed using χ^2 tests. Logistic regression was used to identify potential independent associations with a discharge diagnosis of GERD and included factors found to be significant in the univariate analyses or of interest based on previous studies. The agreement between an initial working diagnosis and a final discharge diagnosis of GERD was determined. Odds ratios, 95% confidence intervals, and P values are presented. Significance was defined as $P \leq 0.05$. Data were analyzed with SPSS version 16.0 (SPSS, Inc, Chicago, Ill).

RESULTS

Three hundred thirteen patient records met inclusion criteria. Average age was 2.1 months, with 39% (124/313) and 64% (203/313) younger than 30 and 60 days, respectively. Boys and premature infants represented 54% and 27% of patients, respectively. Hispanics accounted for 45% of patients, with whites accounting for 30%, other/mixed race accounting for 17%, and Asian/Pacific Islanders and African Americans each accounting for 3%.

Average LOS was 2.5 days, ranging from 1 to 66 days. Seventy patients (22%) had a preexisting chronic condition, with 25 (8%) attributed to chronic gastroesophageal reflux. Discharge diagnoses are presented in Figure 1. Gastroesophageal reflux disease was the most common discharge diagnosis (49%).

For the 154 patients with a discharge diagnosis of GERD, average age was 1.7 months, with 62 (40%) and 109 (71%) younger than 30 and 60 days, respectively. Race/ethnicity percentages paralleled the total study population, with 43% (67/154) Hispanic and 31% (48/154) white. Comparisons between GERD and all other patients are noted in Table 1. Chronic condition frequencies were similar to the total study population, present in 21% (31/146), with 12% (17/146) listed as preexisting chronic gastroesophageal reflux. Compared with all other patients, GERD patients were more likely to have received rescue breaths (P = 0.005) or the patients are not calling 911 (P = 0.030) but also to be well appearing upon hospital presentation (P < 0.001). Gastroesophageal reflux disease patients were less likely to have a nonchoking event or signs or symptoms upon hospital presentation (P values both <0.001). Factors independently associated

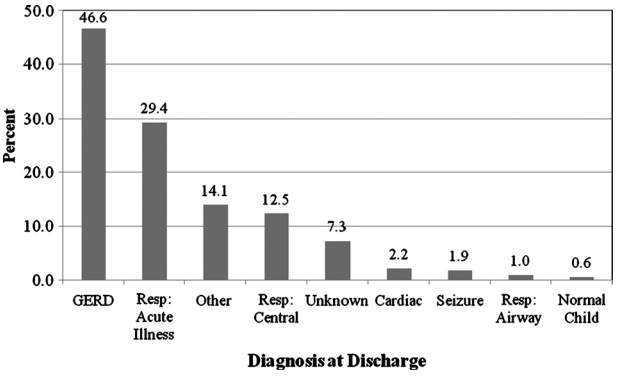

FIGURE 1. All ALTE admissions: diagnosis at discharge (N = 313). Resp indicates respiratory.

TABLE 1. Comparison of Demographic and Patient Characteristics of Patients With a Discharge Diagnosis of GERD Versus All Other Patients (N = 313)

	GERD (n = 154)		Other Than GERD (n = 159)		
Patient Characteristics	**n**	**%**	**n**	**%**	***P***
Sex (male)	77	50.0	94	59.1	0.105
Premature	48	31.2	38	23.9	0.150
Chronic condition	33	21.4	37	23.3	0.696
Abnormal family history findings	24	15.6	24	15.1	0.904
Nonchoking event	56	36.4	125	78.6	<0.001
Well appearing upon presentation to hospital	138	89.6	111	69.8	<0.001
Signs or symptoms upon presentation to hospital	25	16.2	63	39.6	<0.001
Working diagnosis of GERD	132	85.7	5	3.1	<0.001
Rescue breaths	28	18.5	12	7.5	0.005
Called 911	54	35.1	38	23.9	0.030
EMS intervention	13	8.4	11	6.9	0.613
Patients with consults	10	6.5	45	28.3	<0.001
Consult tests performed	7	4.5	18	11.3	<0.001
At least 1 abnormal test result	23	14.9	77	48.4	<0.001

EMS indicates emergency medical services.

with a discharge diagnosis of GERD are shown in Table 2. After adjusting for covariates, having rescue breaths was significantly associated with increased odds of being discharged with a diagnosis of GERD. Having a nonchoking event, subspecialty consultation, or an abnormal test result were each significantly associated with decreased odds of being discharged with a diagnosis of GERD.

Few patients with a discharge diagnosis of GERD had events, studies, or consultations. Only 6% (10/154) of these patients had events while hospitalized (Table 3). All 10 were younger than 3 months; 6 patients were premature. Events included apnea, choking, desaturation, and cyanosis. The 7 patients requiring support needed only brief intervention for events or supplemental oxygen for respiratory tract infection. Four patients were discharged with both GERD and respiratory tract infection diagnoses. Of the 154, only 20 had upper gastrointestinal (UGI) series performed of which 10 had an abnormal result (9 GER, 1 pylorospasm). One patient had a pH probe test performed, the result of which was abnormal. Thirteen consultations from 6 subspecialties occurred in only 9 patients (6%), with only 1 gastroenterology consultation. Reasons for consultation included response to events during hospitalization (4 of the 10 patients noted previously), ruling out a potential alternate diagnosis (seizure), confirmation of a potentially related comorbidity (panhypopituitarism, thyroglossal duct cyst, stridor), allaying parental concern for seizure, and assessing known heart failure. Consultants did not make a new unanticipated diagnosis in any of the 9 patients.

An initial working diagnosis of GERD was used for 137 (44%) of the 313 total patients and accounted for the majority (86%) of patients with a final diagnosis of GERD. These patients represented all 10 with events in the hospital, 17 of the 20 with UGI series, the patient with the pH probe test, and 8 of the 9 patients receiving consultation. Concordance of initial working diagnosis of GERD to discharge diagnosis of GERD was 96% (132/137). Nonconcordant discharge diagnoses included

TABLE 2. Factors Associated With a Discharge Diagnosis of GERD Using Logistic Regression

		95.0% CI		
	OR	**Lower**	**Upper**	***P***
Rescue breaths (yes/no)	6.33	2.65	15.11	<0.001
Nonchoking event (yes/no)	0.14	0.08	0.24	<0.001
Consult (yes/no)	0.16	0.07	0.38	0.005
Abnormal test result (yes/no)	0.28	0.15	0.54	0.013

Variables removed: called 911, consult tests ordered, well appearing upon presentation to hospital, and signs and symptoms upon presentation to hospital.

CI indicates confidence interval; OR, odds ratio.

TABLE 3. Characteristics of the 10 Patients With a Discharge Diagnosis of GERD Who Had Events During Hospitalization

Characteristic	**n**	**%**
Aged <30 d	6	60.0
Premature	6	60.0
Sex (male)	4	40.0
Race/ethnicity		
White	4	40.0
Hispanic	2	20.0
Mixed race/other	4	40.0
Preexisting chronic condition		
GERD	3	30.0
GERD/VSD/panhypopituitarism	1	10.0
GERD/AOP	1	10.0
Acute intercurrent respiratory tract infection	4	40.0
Events attributed to		
Prematurity	5	50.0
Respiratory tract infection	4	40.0
GERD	1	10.0
Consultant	4	40.0
New diagnosis within 6 months	0	0.0

AOD indicates apnea of prematurity; VSD, ventricular septal defect.

TABLE 4. Discharge Diagnosis of GERD: New Diagnoses at 6-Month Follow-Up (n = 5)

Diagnosis	Time to Diagnosis	Diagnostic Evaluation	Suggestive Findings on Initial Admission?	Comments From Initial Admission
Seizure	2 wk	Observed events, EEG (normal finding)	Yes	Family history of seizure, abnormal movements/tone
Seizure	3 wk	EEG	No	None
Seizure	5 mo	Observed events, EEG (normal finding)	Yes	Family history of seizure
Double aortic arch	2 wk	Chest CT, UGI series	Yes	Chronic wheeze
Anomalous subclavian artery	7–8 wk	UGI series, bronchoscopy, neck CT	Yes	Chronic noisy breathing, failure to thrive

CT indicates computed tomography.

2 with apnea of prematurity and one each of seizure, bronchiolitis, and viral sepsis. Both apnea of prematurity patients had known central apnea, but on presentation, their ALTEs were attributed to GERD. Both underwent pneumocardiography, one in response to hospital events; both demonstrated central apnea. The clinical course of the patients with seizure, bronchiolitis, and viral sepsis evolved during hospitalization. One patient had an observed hypotonic event, with normal pneumocardiogram and abnormal electroencephalogram (EEG) findings. Apneic and bradycardic events progressed acutely to bronchiolitis with acute respiratory distress syndrome within 18 hours of admission in the second patient. The third infant with viral sepsis developed poor perfusion on hospital day 1, with subsequent disseminated intravascular coagulation and sepsis. Time to final diagnosis was less than 24 hours for all.

At 6-month follow-up, 14 (9%) of the patients with a discharge diagnosis of GERD had a recurrent ALTE, 8 again due to GERD and one each due to pertussis and apnea of prematurity. All 14 had a working diagnosis of GERD. More clinically concerning were the patients with seizure (3) and anomalous subclavian artery (1). These 4 patients and a fifth patient evaluated with double aortic arch who did not re-present with ALTE comprised the 5 patients initially evaluated with GERD who received a new pathologic diagnosis within 6 months (Table 4). Average LOS in these patients was 1 day. Time to final diagnosis ranged from 2 weeks to 5 months. Diagnostic tests performed included EEG, UGI series, chest computed tomography, and bronchoscopy. History and physical examination at initial hospitalization noted minor elements such as noisy breathing or a subtle abnormal tone.

DISCUSSION

In this study of patients presenting with an admission diagnosis of ALTE, we found that a small but not insignificant number of patients with a working diagnosis of GERD experienced events or evolved to a new diagnosis during hospitalization. To the best of our knowledge, this is the largest study to date of patients presenting with physician-validated ALTE. Similar to previously published studies,[4,6,7] GERD was a predominant discharge diagnosis in our patients, and the majority were well appearing upon presentation. Of these patients discharged with GERD, 12% had preexisting GERD, suggesting that more than 1 in 10 admissions are due to a significant repeated GERD event. Chronic conditions were equally represented in both total and discharge diagnosis GERD groups.

The differences in rates of calling 911 and giving rescue breaths were statistically significant between the group with a discharge diagnosis of GERD and all others. Premature infants were not overly represented in patients in whom 911 was called or rescue breaths were given. The higher rate noted with the GERD group suggests the severity of the event as witnessed does not equate with underlying pathologic diagnosis. This highlights that although GERD is generally recognized as benign, associated incidents are or, in the minimum, are perceived as eventful. The influence of parental perceptions on the decision to hospitalize is substantial.[4,8] The fear induced by the event may be associated in part to inference that the severity of the event equates with a morbid diagnosis. The data here suggest that such an inference is not founded, which may be helpful when offering support to families during hospitalization.

Patients with a working diagnosis of GERD rarely underwent diagnostic studies, consistent with NASPGHAN guidelines.[15] The few UGI series performed were done to evaluate for anatomic abnormality, not to diagnose GERD. Despite the limited testing done on these patients, concordance of working diagnosis with discharge diagnosis of GERD was quite high. This suggests that the pediatric hospitalists' diagnosis of GERD formed with information available at the time of initial history and physical examination, without further testing, is highly reliable.

A few common considerations lead to admission for ALTE patients.[3,4,14] The most basic is the observation time needed to validate the working diagnosis or assess for evolution of symptoms or for clinical support of active or anticipated events. Other reasons may include the need to expeditiously confirm or refute diagnoses with testing or subspecialist consultation. Of the patients with a working diagnosis of GERD in this study, 10 had events, and 5 demonstrated unanticipated evolution to a new diagnosis during a 24-hour period. Although the data in Table 3 reflect some characteristics of the 10 patients with events, half of these patients were completely well appearing at presentation. Apart from our high concordance rate between working and discharge diagnosis of GERD, the 5 nonconcordant diagnoses found were clinically significant. Although prior diagnosis of apnea of prematurity was known for the 2 patients ultimately again evaluated with apnea of prematurity, the ALTE was initially attributed to GERD. The other 3 patients were evaluated only through the process of hospital observation. In patients with a working diagnosis of GERD, testing was performed infrequently and was nondiagnostic, and consultations did not offer unexpected information. Despite this, approximately 10% of patients with a working diagnosis of GERD had a substantial benefit from admission.

In line with the finding of Tieder et al[11] of GERD as a risk factor for readmission, we found 8 patients (5%) in our study with a discharge diagnosis of GERD who presented within 6-month follow-up with recurrent ALTE, again due to GERD. In addition, 12% of our patients with a discharge diagnosis of

GERD had known GERD on initial admission. The standard of care is to provide GERD education to families in ambulatory and hospital settings. However, these findings suggest there may be an opportunity for improvement. Greater emphasis should be placed on the natural history of GERD, the likelihood of recurrent events, and when to seek medical attention. Physicians should also recognize that hospitalization may not relieve parental anxiety about future events or decrease the likelihood of occurrence of a future severe event. Prevention of readmissions may therefore be limited.

All 5 nonconcordant patients demonstrated evolution of symptoms leading to a new diagnosis within 24 hours of admission. In contrast, those given a new pathologic diagnosis after discharge presented from 2 weeks to 5 months after initial hospitalization. It is unlikely that prolonged hospitalization would have expedited diagnosis for these patients.

Several aspects of this study design offer advantages over existing ALTE studies. The use of a custom-created admission billing code for ALTE identified study patients with ALTE at presentation, rather than working backward from discharge diagnoses that may have potentially presented as ALTE. This avoided potential misclassification of patients, which limited previous discharge data-based studies. Importantly, we used diagnoses as noted on the hospitalists' history and physical examination and discharge summary for working and discharge diagnoses, ensuring clinical relevance. Patients with known chronic conditions were included to ensure that the population reflected all ALTE patients encountered by physicians.

Limitations

Most patients had undergone common ED testing such as basic laboratory studies or chest radiography before evaluation by the pediatric hospitalist. However, given the previously demonstrated low rate of abnormal test results in ALTE patients and the even lower rate of tests contributing to diagnosis,[12,14] it is unlikely that the available results of testing done in the ED were a factor in shaping the hospitalists' initial working diagnosis.

Study patients were associated with a single PHM division. Because 89% of RCHSD general pediatric patients are admitted to this service, most patients admitted to our institution with ALTE were likely captured. Referring EDs may have discharged some ALTE patients; however, the standard of care in our community is to admit all patients with ALTE, and therefore, the likelihood of missing patients for this reason is quite low.

Working and discharge diagnoses of GERD were determined clinically by the attending physician, usually without testing, as consistent with NASPGHAN guidelines. This may have resulted in misdiagnosis of GERD. However, data from 6-month follow-up of the patients likely captured patients whose GERD diagnosis was later changed.

It is also not possible to ensure that all interventions done in the hospital would have occurred outside the hospital setting. However, interventions are assumed to have been done after nursing standard responses to alarms or clinical events.

Patients may have been lost to follow-up after discharge or may have presented elsewhere for return visits, skewing our data. However, RCHSD is the sole children's hospital in the region as previously noted with a large catchment area and consistent referral patterns, minimizing the possibility of missed visits.

CONCLUSIONS

Concordance of working diagnosis of GERD to discharge diagnosis of GERD in infants presenting with ALTE is high. However, occurrence of in-hospital events, evolution of new diagnoses, the clinical severity of these nonconcordant diagnoses, and the value of consultation in certain cases suggest that discharge of these patients from the ED should be approached with caution. Rescue breaths and 911 calls are notably more often associated with GERD, supporting that these events are significant to the observer. Admission and readmission with ALTE due to GERD are not uncommon; improved parent education may help reduce these numbers. Testing and consultation are useful for evaluation of alternate diagnoses rather than for assessment of GERD. Hospitalization should be considered to allow for observation, education, and evolution of new diagnoses rather than to rule in GERD.

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