Congenital Diaphragmatic Hernia Defect Size and Infant Morbidity at Discharge

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abstract

BACKGROUND AND OBJECTIVE: Survival for infants with congenital diaphragmatic hernia (CDH) has gradually improved, yet substantial burden of disease remains. Although larger CDH defect sizes increase mortality, the association between defect size and morbidity has not been reported. Our objective was to evaluate the association of defect size with pulmonary, neurologic, and gastrointestinal morbidity at the time of hospital discharge.

METHODS: An international, prospective cohort study was performed. Patient demographics, intraoperative defect size, and clinical outcomes were reviewed. The primary outcome was morbidity at the time of discharge, which entailed supplemental oxygen requirement, abnormal neurologic clinical and radiographic findings, gastroesophageal reflux, supplemental nutrition, or pulmonary-, neurologic-, or gastrointestinal-related medications.

RESULTS: A total of 3665 patients were included in the study cohort. Overall survival was 70.9%, and 84.0% of survivors were discharged from the hospital (16.0% transferred). Median age at discharge was 38 days (interquartile range [IQR] 23–69) and ranged from 22 (IQR 16–32) days for "A" (smallest) defects to 89 (IQR 64–132) days for "D" (largest) defects ($P < .001$). Of those discharged from the hospital, 1522 (74.2%) had pulmonary ($n = 660$, 30.2%), neurologic ($n = 446$, 20.4%), or gastrointestinal ($n = 1348$, 61.7%) morbidities, and multiple morbidities were diagnosed in 701 (34.7%) patients. On multivariable regression analyses incorporating key patient characteristics, defect size was consistently the greatest predictor of overall morbidity, hospital length of stay, and duration of ventilation.

CONCLUSIONS: Infants with CDH are commonly discharged with ≥1 major morbidities. The size of the diaphragmatic defect appears to be the most reliable indicator of a patient's hospital course and discharge burden of disease.

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WHAT'S KNOWN ON THIS SUBJECT: Among infants with congenital diaphragmatic hernia, neurologic, gastrointestinal, and pulmonary morbidity at the time of discharge are significant. Diaphragmatic defect size is a strong predictor of infant mortality, but its association with morbidity and other clinical outcomes remains unknown.

WHAT THIS STUDY ADDS: Morbidity at the time of discharge is common in this patient population. Defect size was the strongest predictor of neurologic, gastrointestinal, and pulmonary morbidity as well as duration of ventilation and length of stay.

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Infants with congenital diaphragmatic hernia (CDH) are surviving at a steadily increasing rate.[1–3] Improved survival is probably related to reduction in iatrogenic or ventilator-associated lung injury, protocol-driven management, and the appropriate application of therapies such as extracorporeal membrane oxygenation (ECMO) and anti–pulmonary hypertension medications.[4–8] Despite these advances in care, it is well recognized that patients with CDH suffer from substantial ongoing morbidity.[9,10] Currently, the frequency and types of morbidity in these patients are unclear and may be a reason why standardized care and follow-up for this patient population are not well defined.

In an effort to more accurately risk stratify patients with CDH, a group of >50 international children's hospitals in the Congenital Diaphragmatic Hernia Study Group (CDHSG) recently developed a staging system to describe the size of the diaphragmatic defect.[3] This system was subsequently shown to correlate strongly with mortality in patients with CDH.[4] Given the association with mortality, we sought to understand the association between the CDHSG staging system and patient morbidity.

The purpose of this study was twofold. First, we aimed to describe the types of major morbidities present in patients with CDH who survived until the time of discharge. Second, we sought to identify patient characteristics that may predict discharge morbidity. We hypothesized that infants with CDH commonly have ongoing pulmonary, neurologic, and gastrointestinal morbidity at the time of discharge and that defect size would be the strongest predictor of morbidity, duration of ventilation, and length of stay.

METHODS

The CDHSG is a voluntary, international collaborative of children's hospitals dedicated to the study of CDH. Predefined data are prospectively collected by individual centers, and deidentified data from contributing centers are entered into the registry. Several iterations of the standardized data collection and entry form used by the registry have been adopted since the registry's inception, and each iteration incorporates specific data points to prospectively evaluate clinically important questions. This study used data from version 3, which was instituted in 2007, and includes data on CDH defect size. Standardized defect sizes were determined through international consensus and are described in the CDHSG Staging System.[3] The smallest defects are categorized as "A" defects and the largest as "D" defects (Fig 1).

After institutional review board approval was obtained (HSC-MS-15-0724), patient data from 2007 to 2014 in the CDHSG registry were queried. Only patients who survived until the time of discharge were included in the analyses. Patient and operative characteristics including sex, prenatal diagnosis, birth location (inborn or outborn), estimated gestational age (EGA), birth weight, major cardiac or chromosomal anomalies, 5-minute Apgar scores, side of defect, size of defect, and use of ECMO were reviewed.

Pulmonary, neurologic, and gastrointestinal morbidity at the time of patient discharge were determined from several criteria (Table 1). Pulmonary morbidity entailed the need for supplemental oxygen at discharge, administered through continuous positive airway pressure, nasal cannula, tracheostomy collar, or ventilator support. Additionally, patients discharged from the hospital with pulmonary-specific medications such as inhaled steroids, β-2 agonists, endothelin receptor antagonists, and pulmonary vasodilators were also categorized as having pulmonary morbidity. Patients with an abnormal neurologic examination or needing neurologic-specific medications at the time of discharge were classified as having a neurologic morbidity. An abnormal neurologic examination consisted of ≥1 abnormal findings on the following tests: eye examination, hearing evaluation, head ultrasound, computed tomography or MRI. Gastrointestinal morbidity was determined if the patient was noted to need supplemental nutrition, have gastroesophageal reflux (GER), or be discharged with gastrointestinal medications. Antacids including histamine receptor antagonists and proton pump inhibitors were excluded from consideration because they are often started reflexively for patients with CDH and may not accurately reflect a GER diagnosis. Additional details of how diagnosis of GER was determined and whether medical or surgical therapy was needed were recorded.

The duration of mechanical ventilation and total hospital length of stay for patients surviving to hospital discharge were also determined.

Dichotomous variables were described in terms of frequencies, and continuous data were described in terms of means ± SD or medians (interquartile range [IQR]) based on their distribution. χ^2 and Fisher's exact tests were used for frequency data, and Student's *t* tests, Mann–Whitney *U* tests, analyses of variance, and Kruskal–Wallis tests were used for continuous data. The Cochran–Armitage test of trend was performed to evaluate survival and morbidity trends during the study period. Mixed-effects, multivariable logistic, and linear regression models were constructed in forward, stepwise fashion, and center was treated as a random effects variable. All statistical testing was performed in Stata/IC 13.1 (Stata Corp, College Station, TX).

RESULTS

A total of 3665 patients from 60 international centers in 13 countries

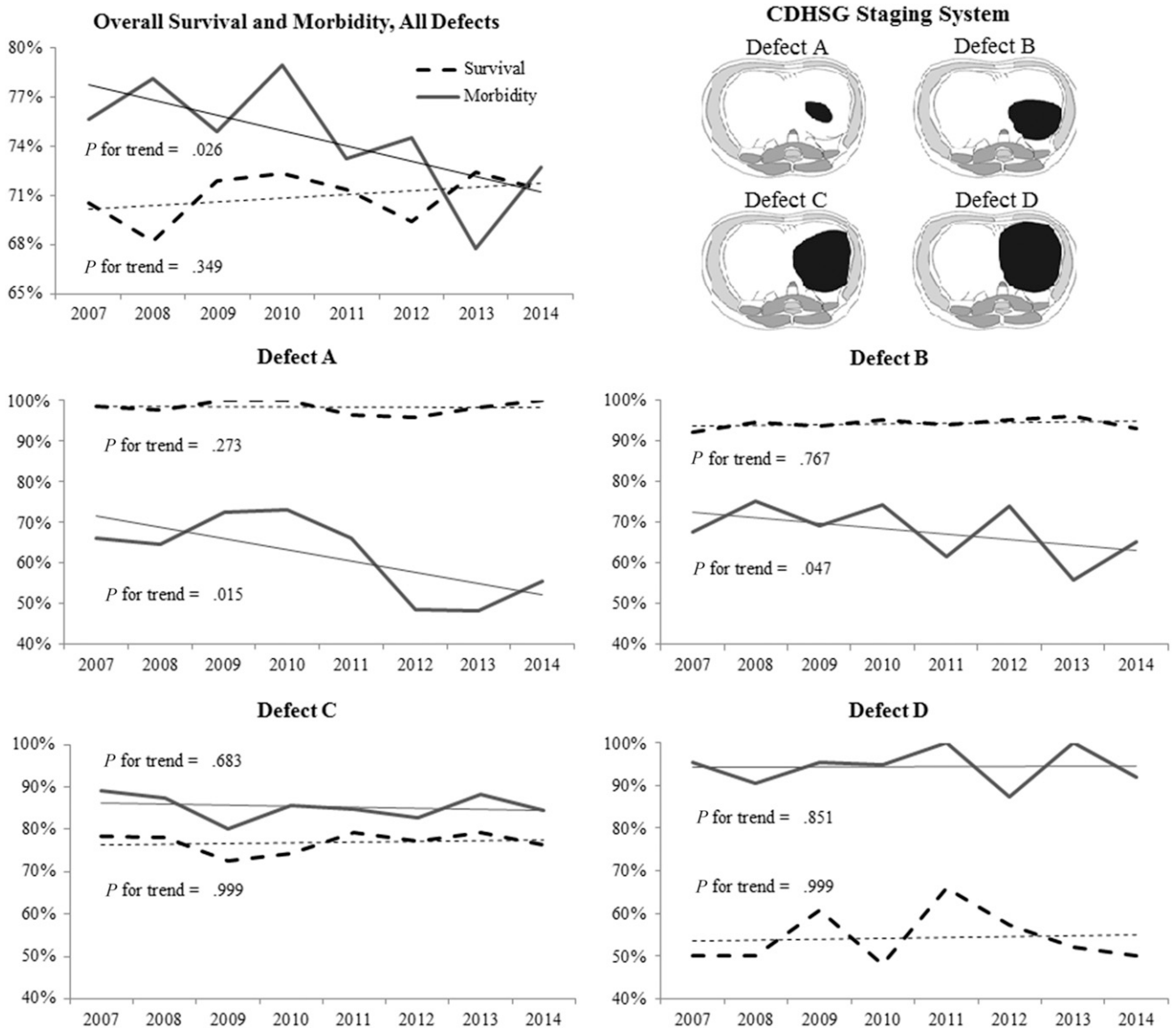

FIGURE 1
Although overall survival has not significantly changed in the last 8 years, overall morbidity at the time of discharge has significantly decreased. However, only patients with smaller defects (A, B) have experienced decreased morbidity, whereas morbidity in patients with larger defects (C, D) has remained unchanged.

TABLE 1 Criteria for Morbidity at the Time of Discharge

System	Conditions	Medication Types
Pulmonary	Supplemental oxygen (continuous positive airway pressure, nasal cannula, tracheostomy collar, ventilator)	Inhaled steroids, β-2 agonists, endothelin receptor antagonists, pulmonary vasodilators
Neurologic	Abnormal eye examination, head imaging, or hearing tests	Sedatives, antiepileptics, antiapneics, controlled analgesics
Gastrointestinal	Supplemental feeding, GER	Prokinetics, anticholestatics
Overall	Any patient with ≥1 of the conditions listed above	Any patient with ≥1 of the medication types listed above

were included in the study cohort. A median of 464 (IQR 431–476) patients were entered into the registry annually. The median number of total patients contributed by each center was 22 (IQR 10–38).

Overall survival during the study period was 70.9%. Of those who survived, 2183 (84.0%) were discharged from the hospital, and 417 (16.0%) were transferred to another hospital or long-term care facility on median day of life 30 (IQR 17–52). There was a nonsignificant trend in increased survival during the study period (range 68.2%–72.5%, $P = .484$).

Of all patients surviving to discharge, 1522 (74.2%) were determined to have pulmonary, neurologic, or

gastrointestinal morbidities. Multiple morbidities were diagnosed in 701 (34.7%) patients. Over the 8-year study period, overall morbidity at the time of discharge significantly decreased (range 67.8%–79.0%, P = .027). When stratified by defect size, patients with smaller defects (A, B) experienced decreased morbidity over time, whereas morbidity and mortality remained largely unchanged in patients with larger defects (Fig 1).

Pulmonary morbidity was present in 660 (30.2%) patients at the time of discharge. Compared with patients without morbidities, patients with pulmonary morbidity were more likely to be diagnosed prenatally; have lower EGA, birth weight, and 5-minute Apgar scores; and have higher rates of chromosomal anomalies than patients without morbidities. Not surprisingly, patients with pulmonary morbidity were more likely to receive a diagnosis of major cardiac anomalies than patients without morbidities or those with neurologic or gastrointestinal morbidities (Table 2). Larger defect sizes were more common in patients with pulmonary morbidity. In fact, more than half of patients with D defects needed both supplemental oxygen and pulmonary-directed medications at the time of discharge. Additionally, patients with the largest defects (C, D) needed mechanical ventilation 2 times and 3 times longer than those with A and B defects, respectively (Table 3).

Neurologic morbidity was present in 446 (20.4%) patients at the time of discharge. Compared with patients without morbidities, these patients were more often diagnosed prenatally with CDH; had lower EGA, birth weights, and 5-minute Apgar scores; and had higher rates of cardiac and chromosomal anomalies. Similar to patients with pulmonary morbidity, patients with neurologic morbidity were found more often to have right-sided and larger defects compared with patients without morbidity (Table 2). Patients with larger defects (C, D) were diagnosed with neurologic morbidities 2 and 3 times as often, respectively, as patients with A and B defects (Table 3).

TABLE 2 Baseline Characteristics of Patients Discharged With and Without Morbidities

Baseline Characteristics	Patients Discharged (n = 2183)	No Morbidity (n = 513)	Pulmonary Morbidity (n = 660)	Neurological Morbidity (n = 446)	Gastrointestinal Morbidity (n = 1348)
Female	854 (39.1)	207 (40.4)	250 (37.9)	179 (39.7)	523 (38.8)
Prenatal diagnosis	1357 (62.2)	246 (49.0)	504 (76.3)[a]	323 (72.3)[a]	908(67.4)[a]
Outborn	1209 (55.4)	277 (54.1)	327 (49.5)	228 (51.0)	787(58.3)
Preterm (<37 wk EGA)	385 (17.6)	78 (15.2)	163 (24.7)[a]	121 (27.1)[a]	248 (18.4)
Low birth wt (<1500 g)	25 (1.2)	2 (0.4)	14 (2.1)[a]	16 (3.6)[a]	14 (1.0)
Major cardiac anomaly	83 (3.8)	8 (1.6)	58 (8.8)[a]	21 (4.7)[a]	50 (4.5)[a]
Chromosomal anomaly	73 (3.4)	8 (1.6)	46 (7.0)[a]	31 (6.9)[a]	57 (4.2)[a]
Low 5-min Apgar score (<7)	605 (29.3)	102 (20.8)	276 (43.5)[a]	186 (42.9)[a]	411 (32.6)[a]
Left-sided defect	1856 (85.1)	445 (86.7)	511 (77.5)[a]	360 (80.7)[a]	1139 (84.4)
ECMO	435 (19.9)	14 (2.7)	269 (40.7)[a]	212 (47.4)[a]	362 (26.8)[a]
Patch repair	980 (45.0)	108 (21.1)	480 (77.0)[a]	294 (66.2)[a]	736 (54.6)[a]
Defect site			[b]	[b]	[b]
A	370 (17.1)	129 (25.3)	44 (6.7)	40 (9.1)	183 (13.6)
B	979 (45.1)	283 (55.5)	181 (27.6)	137 (31.2)	543 (40.4)
C	644 (29.7)	88 (17.3)	312 (47.5)	183 (41.7)	474 (35.3)
D	177 (8.2)	10 (2.0)	120 (18.3)	79 (18 0)	144 (10.7)

Data are presented as n (%). ECMO, extracorporeal membrane oxygenation.
[a] $P < .01$ when compared with patients without morbidities via χ^2.
[b] $P < .01$ when all defect sizes are compared with patients without morbidities via the χ^2 test.

Gastrointestinal morbidity was the most common morbidity noted in infants with CDH who survived to discharge (n = 1348, 61.7%). Although these infants were more likely to receive a diagnosis prenatally than patients without morbidities, a similar percentage of patients were premature and found to have left-sided defects. Like the infants with pulmonary and neurologic morbidities, patients with gastrointestinal morbidities were diagnosed more frequently with cardiac and chromosomal anomalies, had lower 5-minute Apgar scores, and had larger defects (Table 2). Although the majority of patients with CDH were found to have gastrointestinal morbidities irrespective of defect size, the frequency of this morbidity increased significantly with larger sizes (Fig 2). Of patients diagnosed with GER, most (76.9%) were diagnosed clinically, and the remainder were diagnosed by nuclear scans, upper gastrointestinal series, or pH probes. Patients with larger defects were significantly more likely to undergo surgical therapy for GER (range, A: 3.1%; D: 40.5%; P < .001) (Table 3).

On multivariable regression analyses incorporating the patient characteristics described previously, larger defect size was consistently the greatest predictor of morbidity (Table 4). Other characteristics that were frequently associated with increased pulmonary, neurologic, and gastrointestinal morbidity included a prenatal diagnosis, the presence of major cardiac or chromosomal anomalies, and lower 5-minute Apgar scores.

Finally, the median age at discharge for all patients was 38 (IQR 23–69) days and ranged from a median of 22 (IQR 16–32) days for A defects to 89 (IQR 64–132) days for D defects (P < .001) (Table 3).

DISCUSSION

Infants with CDH are now surviving at a rate >70%. Unfortunately, although these cases are often deemed successes, these patients remain at significant risk for ongoing morbidity and are often discharged

TABLE 3 Morbidity Outcomes at Discharge Based on CDH Defect Size

	All Patients (*N* = 2183)	No. Missing Data	Defect A (*n* = 370)	Defect B (*n* = 979)	Defect C (*n* = 644)	Defect D (*n* = 177)	*P*[a]
Any morbidity	1503 (74.6)	167	209 (61.8)	612 (68.4)	514 (85.4)	159 (94.1)	<.001
Pulmonary morbidity	661 (30.4)	6	44 (12.0)	181 (18.5)	312 (48.5)	120 (68.2)	<.001
Supplemental oxygen	417 (19.2)	7	20 (5.5)	95 (9.7)	204 (31.8)	94 (53.4)	<.001
Pulmonary medication	524 (24.0)	0	30 (8.1)	133 (13.6)	246 (38.2)	111 (62.7)	<.001
Neurologic morbidity	447 (21.7)	125	40 (11.7)	137 (15.0)	183 (29.8)	79 (45.7)	<.001
Abnormal neurologic examination	437 (21.2)	125	40 (11.7)	134 (14 6)	177 (28.8)	78 (45.1)	<.001
Neurologic medication	40 (1.8)	0	3 (0.8)	8 (0.8)	18 (2.8)	10 (3.6)	<.001
Gastrointestinal morbidity	1349 (65.2)	114	183 (51.7)	543 (58.8)	474 (77.7)	144 (85.2)	<.001
Supplemental tube feeds	660 (30.5)	22	45 (12.2)	183 (18.9)	309 (48.6)	119 (68.8)	<.001
Gastroesophageal reflux	1227 (58.8)	97	162 (45.6)	496 (53.3)	437 (70.9)	128 (74.4)	<.001
Diagnosed clinically	903 (76.9)	52	144 (90.6)	393 (83.3)	298 (72.7)	62 (50.0)	<.001
Diagnosed radiologically	272 (23.1)		15 (9.4)	80 (16.7)	112 (27.3)	62 (50.0)	<.001
Nuclear scan	33 (12.1)		3 (20.0)	8 (10.0)	12 (10.7)	9 (14.5)	
Upper gastrointestinal series	219 (80.5)	0	10 (66.7)	69 (36.3)	90 (80.4)	48 (77.4)	.564
pH probe	20 (7.4)		2 (13.3)	3 (3.7)	10 (8.9)	5 (8.1)	
Medical therapy	1008 (84.4)		154 (96.3)	450 (92.4)	328 (78.3)	74 (58.7)	
Surgical therapy	184 (15.4)	32	5 (3.1)	35 (7.2)	91 (21.7)	51 (40.5)	<.001
No therapy given	3 (0.2)		1 (0.6)	1 (0.2)	0 (0)	1 (0.8)	
Gastrointestinal medication	353 (16.2)	0	54 (14.6)	145 (14.8)	110 (17.1)	43 (24.3)	.012
Median time on ventilator, d	13 (7–24)	37	7 (4–10)	10 (7–16)	22 (14–34)	30 (22–50)	<.001
Median hospital length of stay, d	38 (23–69)	4	22 (16–32)	31 (22–47)	62 (39–96)	89 (64–132)	<.001

Data are presented as *n* (%) or median (IQR).

[a] χ^2 or Kruskal–Wallis rank tests comparing these patients with patients without morbidities.

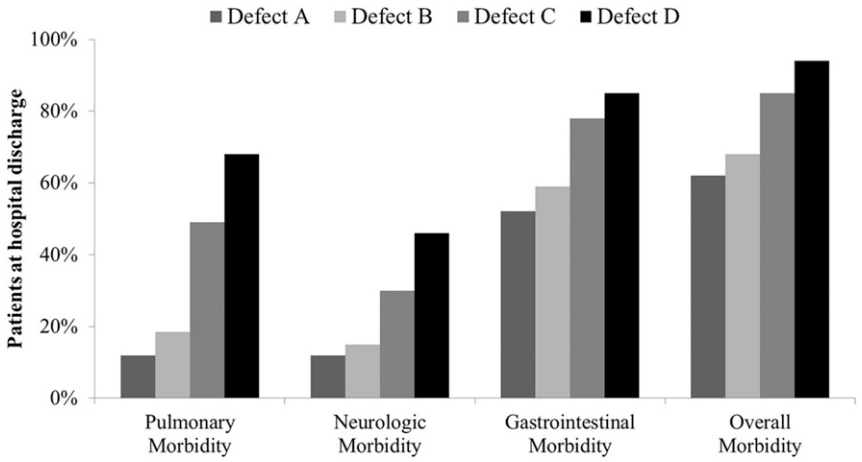

FIGURE 2

Pulmonary, neurologic, and gastrointestinal morbidity at the time of discharge is common among infants with CDH. Although patients with larger defects (C, D) experience greater pulmonary and neurologic morbidity, gastrointestinal morbidity affects the majority of all patients with CDH.

with a substantial burden of disease. We found that patients with CDH suffer from significant pulmonary, neurologic, and gastrointestinal morbidity at the time of discharge. Furthermore, gastrointestinal morbidity was the most prevalent. Several patient characteristics including prenatal diagnosis and major cardiac or chromosomal anomalies predicted the types and frequency of morbidity that affect these infants, yet diaphragmatic defect size at the time of repair was consistently the strongest predictor of morbidity at discharge. Defect size also showed a strong association with duration of mechanical ventilation and hospital length of stay. These data advance our understanding of the morbidity associated with CDH, allow clinicians to screen for and identify specific morbidity based on the CDHSG staging system, enable early in-hospital counseling regarding specific morbidity and length of stay, and prepare the pediatrician for potential screening and management at postdischarge follow-up.

Before the CDHSG Staging System, standardized criteria for describing the defect size did not exist. Rather, investigators simply described defect sizes by the type of repair performed (primary versus patch) or whether agenesis was present.[11] This method made it challenging to accurately risk stratify patients because the surgeon's choice to perform a primary or patch closure is subjective. The CDHSG Staging System addresses this shortcoming by using predefined definitions for each defect size. For example, A defects are those entirely surrounded by muscle, and B defects are those with <50% of the hemithorax chest wall being devoid of diaphragm tissue.[4] Using this system of standardized classification adds clarity and

TABLE 4 Patient Characteristics and Associations with Morbidity - Multivariable Regression Analyses

Patient Characteristics	Any Morbidity		Pulmonary Morbidity		Neurologic Morbidity		Gastrointestinal Morbidity	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Outborn	NI		1.25 (0.85–1.84)	.247	1.04 (0.73–1.47)	.848	1.64 (1.11–2.42)	.013
Premature	1.24 (0.87–1.77)	.237	1.57 (1.15–2.13)	.004	1.82 (1.36–2.43)	<.001	NI	
Prenatal diagnosis	1.85 (1.39–2.45)	<.001	2.21 (1.57–3.09)	<.001	1.44 (1.02–2.02)	.036	2.05 (1.48–2.84)	<.001
Major cardiac anomaly	6.15 (2.26–16.75)	<.001	9.18 (4.79–17.71)	<.001	NI		2.94 (1.41–6.21)	.005
Chromosomal anomaly	4.24 (1.62–11.78)	.006	3.24 (1.66–6.33)	.001	2.35 (1.33–4.14)	.003	4.12 (1.75–9.69)	.001
5-min Apgar <7	1.74 (1.26–2.41)	.001	2.09 (1.59–2.75)	<.001	1.78 (1.36–2.32)	<.001	1.44 (1.08–1.92)	.013
Right-sided defect	1.01 (0.69–1.48)	.951	NI		1.23 (0.89–1.72)	.211	NI	
Defect size								
A	Reference		Reference		Reference		Reference	
B	1.56 (1.11–2.19)	.012	1.97 (1.29–2.99)	.001	1.26 (0.83–1.91)	.277	1.42 (1.03–1.96)	.033
C	4.54 (2.93–7.05)	<.001	8.37 (5.36–13.07)	<.001	2.27 (1.47–3.51)	<.001	4.53 (3.03–6.76)	<.001
D	11.23 (4.81–26.24)	<.001	15.54 (8.79–27.47)	<.001	4.28 (2.53–7.26)	<.001	7.26 (3.81–13.88)	<.001

CI, confidence interval; NI, not included in multivariable model because *P* > .2 on univariate analysis; OR, odds ratio.

simplicity to communication while allowing interinstitutional disease stratification, data alignment, and reporting, in addition to the previously reported association with patient survival. This study demonstrates that the staging system also correlates strongly with duration of ventilation, hospital length of stay, and patient morbidity at the time of discharge.

Morbidities at the time of discharge varied significantly between patients with smaller (A, B) and larger (C, D) defects. In fact, 25% to 35% of patients with smaller defects did not have any morbidities that necessitated ongoing treatment at the time of discharge. Additionally, only a minority of patients with smaller defects had major pulmonary or neurologic morbidities (17% and 14%, respectively), whereas patients with larger defects were commonly found to have major pulmonary and neurologic morbidities (53% and 33%, respectively). Patients with both smaller and larger defects were commonly diagnosed with gastrointestinal morbidity, and this was the most common morbidity overall. These general trends have important implications for discharge planning and multidisciplinary follow-up to optimize long-term patient outcomes, family satisfaction, and resource utilization.

Pulmonary, neurologic, and gastrointestinal morbidity among patients with CDH have been widely recognized,[10,12–18] yet this is the first study to focus exclusively on the multisystem burden of disease at the time of discharge. Furthermore, when patients are classified by their defect size, the varying rates of morbidity at the time of discharge can be clearly delineated, as opposed to grouping all patients with CDH together and reporting their overall rates of morbidity. Among our cohort of patients, the need for supplemental oxygen or pulmonary medication at the time of discharge ranged from 5.5% to 63% based on defect size. Longitudinal studies of patients with CDH suggest that pulmonary morbidity may improve after discharge, with rates of pulmonary sequelae such as recurrent respiratory tract infections and chronic lung disease ranging from 10% to 22%.[19,20] One study with a mean patient follow-up of ~30 years found that only 4% of patients continued to have recurrent respiratory tract infections.[21] Abnormal neurologic examinations and the need for neurologic medications were documented in 1% to 45% of our patients. A literature review in 2007 by Bagolan et al[12] found that the reported rates of neurodevelopmental sequelae at follow-up times ranging from 30 days to 13 years varied substantially (8%–54%). A more recent multi-institutional study with a minimum of 24 months' follow-up demonstrated that 27% of patients suffered from ongoing neurologic morbidity, the most common of which was related to speech and language.[22]

Gastrointestinal morbidity was commonly present at the time of discharge, with supplemental tube feeds, GER, or the need for gastrointestinal medications noted for 52% to 85% of the patients depending on defect size. Most of this morbidity was caused by clinically or radiographically diagnosed GER (46%–74% by defect size); however, the majority (69%) of patients with D defects needed supplemental tube feeds at the time of discharge. This wide variability in ongoing gastrointestinal morbidity is supported in the literature, with rates of persistent GER alone ranging from 15% to 55% at 2 to 10 years of follow-up.[12,19,23] Interestingly, although gastrointestinal morbidity was the most prevalent morbidity among our patient cohort at the time of discharge, studies suggest that after 2 years of age, neurologic disability may become more common than both gastrointestinal and pulmonary disabilities.[22]

We were surprised to find that although the overall trend in survival in patients with CDH appeared to be increasing over time, overall morbidity at the time of discharge did not. These findings made more

sense when we analyzed them by defect size, which showed largely unchanged survival benefit but improvement in morbidity among patients with smaller defects. Therefore, it does not appear that the more severely ill infants are now surviving at a greater rate with greater morbidity but that infants with less severe CDH are surviving to discharge with fewer major morbidities. Decreasing ventilator-associated lung injury among infants with mild or moderate pulmonary hypoplasia is a good example. This change may suggest that care for infants with mild to moderately severe CDH has continued to improve while care for infants with more severe forms of CDH has remained stagnant. It is also possible that trends in management strategy could be shifting, creating an illusion of trends in morbidity. Management and diagnosis of GER have shifted dramatically over the last decade, possibly resulting in decreased treatment of GER and decreased detection based on our study definitions. More analysis of the diagnostic and treatment strategies for infants with CDH is warranted.

There were several limitations in this study. Reliable entry of defect size into the registry could not be audited, but simple and clear definitions and a user-friendly diagram have been widely accepted and published to help minimize reporting variability. The lack of standardized protocols for diagnostic testing between centers and clinicians may lead to overestimation or underestimation of the true morbidity rate; however, this variation is more likely to underestimate overall morbidity because clinicians tend to do fewer tests on children with smaller defects and those who are asymptomatic. Long-term morbidities are not currently captured by the registry, so they could not be reported in this study. Although we found that morbidity in patients with smaller defects may be gradually decreasing, whether this affects longer-term quality of life is a crucial question that has yet to be determined.[24] We are hopeful that standardized, multidisciplinary follow-up targeting morbidity at discharge will provide opportunities to closely follow and report on longer-term outcomes.

CONCLUSIONS

Infants with CDH are commonly discharged with ≥1 major gastrointestinal, pulmonary, or neurologic morbidities. Although several patient characteristics may help clinicians and caretakers anticipate the types of morbidities these patients will encounter during their initial hospital stay and at discharge, the size of the diaphragmatic defect at the time of repair appears to be the most reliable indicator of a patient's hospital course and discharge burden of disease.

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ABBREVIATIONS

CDH: congenital diaphragmatic hernia
CDHSG: Congenital Diaphragmatic Hernia Study Group
ECMO: extracorporeal membrane oxygenation
EGA: estimated gestational age
GER: gastroesophageal reflux
IQR: interquartile range

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