



High surgical burden for infants with severe chronic lung disease (sCLD)



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ABSTRACT

Background/purpose: Infants with severe chronic lung disease (sCLD) may require surgical procedures to manage their medical problems; however, the scope of these interventions is undefined. The purpose of this study was to characterize the frequency, type, and timing of operative interventions performed in hospitalized infants with sCLD.

Methods: The Children's Hospital Neonatal Database was used to identify infants with sCLD from 24 children's hospital's NICUs hospitalized over a recent 16-month period.

Results: 556 infants were diagnosed with sCLD; less than 3% of infants had operations prior to referral and 30% were referred for surgical evaluation. In contrast, 71% of all sCLD infants received ≥ 1 surgical procedure during the CHND NICU hospitalization, with a mean of 3 operations performed per infant. Gastrostomy insertion (24%), fundoplication (11%), herniorrhaphy (13%), and tracheostomy placement (12%) were the most commonly performed operations. The timing of gastrostomy (PMA 48 ± 10 wk) and tracheostomy (PMA 47 ± 7 wk) insertions varied, and for infants who received both devices, only 33% were inserted concurrently (13/40 infants).

Conclusions: A striking majority of infants with sCLD received multiple surgical procedures during hospitalizations at participating NICUs. Further work regarding the timing, coordination, perioperative complications, and clinical outcomes for these infants is warranted.

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Chronic lung disease (CLD) develops in approximately 25–30% of infants born prematurely and/or at very low birth weight (VLBW) [1–4]. However, chronic pulmonary morbidities are not isolated to preterm or VLBW infants as infants with conditions such as congenital diaphragmatic hernia, congenital pulmonary airway malformations, or pulmonary hypoplasia may also develop chronic pulmonary disease.

A mainstay of supportive care for infants with severe pulmonary disease is mechanical ventilation, and in cases of severe CLD, patients may require surgical intervention to support ventilation (e.g., tracheostomy) or nutrition (e.g., gastrostomy tube). In addition, many

infants with CLD have serious comorbidities affecting the nervous, cardiovascular, retinal, gastrointestinal, and the musculoskeletal systems which may also require operative procedures [5]. However, the scope, timing, and type of surgical interventions that occur during NICU hospitalization remain undefined. Operative interventions in this patient population carry significant risk, as these major comorbidities increase both anesthetic and surgical complications [6–9]. For this reason, characterization of the 'epidemiology' of the surgical needs of these infants is a critical first step to determine which infants are receiving specific interventions. These results will help determine appropriate targets for focused improvement efforts, which may mitigate risk and potentially improve perioperative care and clinical outcomes.

Therefore, we sought to determine the specific type, frequency, and timing of surgical procedures provided to infants with severe CLD

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(sCLD) cared for at 24 tertiary children's hospital NICUs during a 16 month period in 2010–11 in order to better characterize the epidemiology of surgical interventions for infants with sCLD.

1. Patients and methods

The Children's Hospital Neonatal Database (CHND) prospectively captures clinical data on all infants admitted to participating Level III children's hospital NICUs [10,11]. Prior to participating in the CHND, each NICU met specific criteria: (a) Level III designation based on published standards at the time of initiation of data collection, (b) >400 admissions annually, (c) ≥ 25 inpatient beds, and (d) >50% of admitted infants born outside the participating hospital. Each institution received institutional review board approval or waiver prior to participating in the CHND. At the time of this study, CHND included 24 academic NICUs representing 20 states from all major geographic regions of the US. Chart abstractors at each site underwent prospective training and both initial and biannual measurements of interrater agreement scores were calculated at each site; more than ninety-percent intrasite concordance in abstraction was required for participation in the CHND.

The Ann & Robert H. Lurie Children's Research Center of Chicago's Institutional Review Board approved this study. The CHND was accessed on 10-11-2011 to identify infants with sCLD that were admitted to 24 participating children's hospital NICUs over a 16-month period during 2010–11. The definition of sCLD was contingent on the gestational age at birth (GA), the postnatal chronological age (CA), the postmenstrual age (PMA), and the level of respiratory support received at prespecified time points [12]. Infants born <32 weeks GA were classified with sCLD if they received positive pressure or supplemental $\text{FiO}_2 \geq 0.3$ at 36 weeks PMA. Infants born 32^{0/7}–36^{6/7} weeks GA were diagnosed with sCLD if they received any positive pressure, including more than 2 liters-per-minute (LPM) of nasal cannula flow rate, or $\text{FiO}_2 \geq 0.3$ at 56 days CA. For infants born at term (≥ 37 weeks GA), sCLD was assigned if infants received positive pressure, >2 LPM of nasal cannula flow rate, or $\text{FiO}_2 \geq 30\%$ for at least 7 days after admission/referral to the CHND NICU.

The primary outcome measures were the number and distribution of surgical procedures performed in infants with sCLD prior to discharge. Maternal and demographic variables were characterized by parity, race/ethnicity, and pregnancy complications. Infant variables included reason for referral, respiratory interventions, timing of surgical procedures, device utilization, central line-associated bloodstream infections (CLABSI; in accordance with the National Healthcare Safety Network definitions) [13], and discharge disposition.

Because more than 95% of infants were born outside of the hospitals participating in the CHND, selected variables were summarized to describe the clinical course prior to referral and the severity of illness of the eligible cohort. These variables included the presence of prematurity-associated morbidities at the time of referral and therapies utilized prior to transport. Infants born at CHND hospitals were also included in the analysis.

Bivariable analysis was performed using Student's *t* test or chi-squared tests, stratified by gestational age strata (≤ 27 , 28–33, and ≥ 34 weeks). Student's *t* test, chi-squared, and nonparametric testing were used, as appropriate. All statistical tests were two-tailed and $p = 0.05$ was used to define statistical significance. Analyses were performed with SAS v9.3 (Cary, NC).

2. Results

22,084 patients were enrolled in the CHND during this time period, and 556 infants were diagnosed with severe CLD (3% of all NICU patients; Table 1). Most sCLD infants were born prior to 37 weeks gestation (92%), and were referred at approximately 3 weeks of age. The median length of stay after referral was

Table 1
Patient demographic and admission characteristics.

Variable	
N	556 (100%)
General characteristics	
Mean gestational age at birth (wk, \pm SD)	27 \pm 4
Mean birth weight (grams, \pm SD)	1088 \pm 749
Median age on admission (days)	22
Mean postmenstrual age at admission (wk, \pm SD)	33 \pm 7
Mean weight on admission (grams, \pm SD)	1857 \pm 1211
Male sex	63%
SGA (<10th percentile weight)	21%
Maternal race/ethnicity (%)	
Non-Hispanic White	47%
Black	30%
Hispanic White	7%
Other race/ethnicity	16%
Perinatal conditions/treatments	
Multiple gestation	21%
Any antenatal steroids	56%
Surfactant in the delivery room	50%
Primary reason for referral	
Surgical evaluation	30%
Respiratory	26%
Preterm birth without existing comorbidities	13%
Patent ductus arteriosus	6%
Cardiac	6%
ROP	3%
Morbidities present on admission	
Bronchopulmonary dysplasia	25%
Any intraventricular hemorrhage	22%
Any retinopathy of prematurity	18%
Therapy delivered during transport or on referral	
Intermittent positive pressure ventilation	71%
Continuous vasoactive agents	12%

94 days, with discharge occurring on average at 20 \pm 9 weeks CA. The majority (71%) were referred from Level 3 NICUs, and the overall survival rate was 90%.

Selected demographic and referral characteristics are described in Table 1; affected infants were born quite preterm, referred well after birth, and both male gender and black race were overrepresented relative to the national birth cohort [12]. Infants that developed sCLD were most commonly referred for surgical evaluation, treatment of respiratory failure, or management of prematurity (Table 1). Excluding intervention for retinopathy of prematurity, less than 3% of infants had undergone surgical procedures prior to referral/admission. Of those, peritoneal drainage (0.4%) and bowel ostomy creation (2%) for necrotizing enterocolitis were most common.

As expected, infants with sCLD received significant support related to their pulmonary disease while hospitalized. Intermittent positive pressure ventilation, high-frequency ventilation, and systemic corticosteroids were commonly used, and the majority required supplemental oxygen at the time of discharge. The frequency of other applied pulmonary treatments is described in Table 2.

The majority (71%) of infants diagnosed with sCLD required at least one surgical procedure after referral, with a mean of 3 procedures per patient (Table 3). The percent of sCLD infants requiring operative intervention was similar across GA categories, although the type of procedure varied. Gastrostomy tube placement, fundoplication, tracheostomy, PDA ligation, and ventricular shunt placement were most frequently performed. Intestinal procedures including laparotomy, small and large bowel resection, ostomy, peritoneal drain placement, and stoma takedown were also common, with a total of 317 surgical procedures performed in 103 patients. Patients referred for surgical evaluation were, not surprisingly, more likely to have surgery than those referred for other indications (89% vs 64%, $p < 0.0001$), and had a higher mean number of surgeries per patient (3.5 vs 2.2; $p < 0.0001$). Interestingly, the group of patients with tracheostomy performed was less likely to have been referred

Table 2

Frequency of applied respiratory treatments delivered to sCLD patients during admission at CHND hospitals.

Treatments	
Number of infants	556 (100%)
Caffeine (% treated)	53%
Surfactant (during this hospitalization) (%)	10%
Conventional Mechanical Ventilation (%)	91%
HFOV (%)	32%
HFJV (%)	6%
nCPAP (%)	52%
siPAP (%)	21%
Nasal cannula support	
<1 LPM (%)	63%
1–1.99 LPM (%)	59%
≥ 2 LPM (%)	67%
Median duration of mechanical ventilation (days, [IQR])	35 [13–64]
Any corticosteroid (%)	71%
Inhaled steroid for CLD (%)	32%
Supplemental oxygen at discharge (%)	72%

Median [IQR] or percent of patients, n = 556.

for surgical evaluation (8%) than referred for other indications (14%; $p = 0.04$), and the time of tracheostomy placement did not vary based on indication for referral.

Because certain interventions may predict the potential need for others, we describe the synchrony in which tracheostomy, gastrostomy tube (GT) placement, and fundoplication were performed in this cohort. Sixty percent of infants receiving a tracheostomy also had a GT inserted (41/68), and those insertions (GT: CA 20 ± 11 wk; and tracheostomy: CA 18 ± 8 wk) were performed as separate procedures in 68% of patients requiring both (28/41). More than half of sCLD patients who had tracheostomy and GT placement also had a fundoplication (23/41), and fundoplications were largely performed concurrently with GT insertions (21/23). However, for infants receiving all three procedures, only 17% were performed concurrently (7/23) and 9% were performed as three separate operative procedures.

In addition, less invasive procedures such as bronchoscopy and cardiac catheterization were frequently performed in patients with sCLD (Table 3). The frequency of central line insertion was high, as 82% of sCLD patients had at least one central line placed (mean 2.5 ± 1.4 central lines per patient). Bloodstream infections occurred in 21% of sCLD patients, and of these infections, 28% were designated as central line associated blood stream infection (CLABSI). The CLABSI rate for sCLD patients was 2 infections per 1000 catheter days. Ventilator-associated pneumonia occurred in 23% of sCLD infants during their NICU hospitalization.

Table 3

Surgical interventions performed during NICU hospitalization.

	≤27 wk	28–33 wk	≥34 wk	All
Number of patients (N)	375	118	63	556
Number of surgical procedures (N)	888	252	158	1298
Infants with ≥1 surgery (N, %)	264 (70%)	82 (69%)	51 (81%)	397 (71%)
Mean procedures per patient (N ± SD)	3.3 ± 2.6	3.7 ± 3.2	2.5 ± 2.8	3.3 ± 2.7
Gastrostomy (N, % infants)	88 (23%)	21 (18%)	22 (35%)	131 (24%)
Fundoplication (N, %)	43 (11%)	10 (8%)	8 (13%)	61 (11%)
(% performed as open procedure)	(47)	(20)	(50)	(43)
Herniorrhaphy (N, %)	43 (11%)	10 (8%)	8 (13%)	70 (13%)
Tracheostomy (N, %)	46 (12%)	15 (13%)	7 (11%)	68 (12%)
Intraventricular drain (N, %)	62 (17%)	5 (4%)	5 (8%)	72 (13%)
Ductus arteriosus ligation (N, %)	78 (21%)	9 (8%)	2 (3%)	89 (16%)
Mean age at gastrostomy tube insertion (PMA, wk ± SD)	48 ± 10	43 ± 10	51 ± 10	48 ± 10
Mean age at tracheostomy placement (PMA, wk ± SD)	46 ± 6	48 ± 10	52 ± 7	47 ± 7
Central line utilization ratio (central line days/patient days)	0.45	0.55	0.63	0.49
Bronchoscopy (N, %)	82 (22%)	29 (25%)	12 (19%)	123 (22%)
Cardiac catheterization (N, %)	12 (3%)	7 (6%)	4 (6%)	23 (4%)

3. Discussion

Severe CLD in infancy is typically a consequence of either extreme prematurity or congenital pulmonary anomalies. The respiratory outcomes of these patients are well described, but little is known about the nonpulmonary morbidities they may endure. Although only 30% of these infants were referred specifically for surgical consultation, most infants with sCLD (71%) required at least one operative procedure after referral to the participating children's hospital NICUs, with a mean of three procedures per patient. The type of surgical procedures varied, but tracheostomy, surgical feeding tube placement, fundoplication, ductus arteriosus ligation, and/or ventricular drain placement were most commonly performed.

Infants with sCLD represent a vulnerable patient population. Developmental abnormalities and acquired lung injury predispose these infants to disordered pulmonary vascular and alveolar development, frequently leading to cardiopulmonary complications such as pulmonary hypertension [14–16]. Current evidence suggests that sCLD infants assume significantly greater perioperative risks and have a higher likelihood of adverse events associated with surgical intervention and anesthetic exposure [7–9,14–17]. Furthermore, prolonged intensive care can confer a risk of hospital associated infections (e.g., CLABSI and ventilator-associated pneumonia), which we found to be significantly higher than expected for typical NICU patients [18,19]. We believe that this study highlights an area in which multidisciplinary approaches to perioperative care and targeted quality improvement work are likely to improve the care and outcomes for these critically ill infants in children's hospital NICUs.

Several clinical practices may mitigate surgical risk in these infants. Although most sCLD patients had multiple surgical procedures performed during their NICU hospitalization, these were infrequently performed in a coordinated fashion. This may simply be related to the timing in which complications arose during the hospital course, and may have been unavoidable. Furthermore, use of fundoplication as a means to reduce the risk of chronic aspiration may be a reasonable strategy to reduce chronic lung injury and long-term mechanical ventilation need. However, certain procedures may predict the need for others (e.g., tracheostomy and surgical feeding tube) and efforts directed at anticipating future clinical needs and improving coordination of multiple surgical procedures could reduce patient anesthetic and surgical risks and improve perioperative outcomes.

This study has limitations. Infants included in the study represent a specific cohort of infants that were referred to and cared for at children's hospital NICUs, and may not be representative of or generalizable to the entire population of infants with sCLD. Also, the definition of sCLD closely parallels the NICHHD definition for severe bronchopulmonary dysplasia among infants born preterm [12].

However for term infants, this definition was reached by consensus prospectively and the validation of this definition on any pediatric short- or long-term adverse outcome is not known. The findings of this study do lead to several areas for future study, including the comparison of this cohort to age-matched control subjects, determination of interinstitutional variance as it relates to surgical outcomes, and analyses of clinical outcomes and resource utilization related to improved coordination of perioperative care.

In conclusion, we found that infants diagnosed with sCLD referred to children's hospital NICUs have a high surgical burden, as more than 70% required at least one surgical procedure during their NICU stay. The variation in timing of tracheostomy suggests that standardizing the decision to provide chronic ventilation as well as the timing of tracheostomy could decrease the length of stay of these patients. We have identified opportunities to improve perioperative care through close attention to underlying cardiopulmonary morbidity, prevention of hospital-associated infection, and consideration of coordination of multiple surgical procedures. Focus on these and other questions will likely provide new areas for potential improvement, and with analytic, prospective studies, offers the opportunity to improve the perioperative outcomes of infants with sCLD.

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