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Pseudomonas aeruginosa and post-tracheotomy bacterial respiratory tract infection readmissions

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Abstract

Objective—Identify risk factors for readmission due to a bacterial tracheostomy-associated respiratory tract infection (bTARTI) within 12 months of discharge after tracheotomy.

Design/Methods—We performed a retrospective cohort study of 240 children who underwent tracheotomy and were discharged with tracheotsomy in place between 1/1/2005 and 6/30/2013. Children with prolonged total or post-tracheotomy length of stay (LOS), less than 12 months of follow-up, or who died during the index hospitalization were excluded. Readmission for a bTARTI (e.g., pneumonia, tracheitis) treated with antibiotics, as ascertained by manual chart review, was the outcome variable. We used multivariate logistic regression to identify the independent association between risk factors and hospital readmission for bTARTI within 12 months.

Results—At index hospitalizations for tracheotomy, the median admission age was 5 months [interquartile range (IQR) 2–43 months] and median LOS was 73 days (IQR 43–121 days). Most patients were of Hispanic ethnicity (n=162, 68%) and were publicly insured (n=213, 89%). Nearly half (n=112, 47%) were discharged on positive pressure mechanical ventilation. Many (n=103, 43%) were admitted for bTARTI within 12 months of discharge. Only Hispanic ethnicity [adjusted odds ratio (AOR) 2.0; 95% confidence interval (CI): 1.1–3.9; p=0.03)] and acquisition of

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Pseudomonas aeruginosa between tracheotomy and discharge from index hospitalization (AOR 3.2; 95% CI: 1.2–8.3; p=0.02) were independently associated with increased odds of bTARTI readmission, while discharge on gastrointestinal pro-motility agents was associated with decreased risk (AOR=0.4; 95% CI: 0.2–0.8; p=0.01).

Conclusions—Hispanic ethnicity and post-tracheotomy acquisition of *Pseudomonas aeruginosa* during initial hospitalization are associated with bTARTI readmission.

Keywords

Tracheitis; Pneumonia; Bacterial; Child; hospitalized; Readmission; Pediatric; *Pseudomonas aeruginosa*

Introduction

Hospitalizations in pediatric patients with pre-existing tracheostomy amounted to $1.4 billion in hospital charges in 2012[1]. Of these hospitalizations, bacterial pneumonia is the most common ambulatory care sensitive condition (conditions for which appropriate ambulatory care prevents or reduces admission to the hospital)[2] requiring hospitalization[3]. Previous research has shown that the wide diagnostic and therapeutic variations of pediatric patients hospitalized with bacterial tracheostomy-associated respiratory tract infections (bTARTIs) are not associated with length of stay (LOS) or readmission[4]. Because children with tracheostomy account for high utilization of health care resources[3,5–7], identification of high-risk subpopulations and modifiable factors may assist in development of evidence-based best practices for the prevention and treatment of these infections and decrease hospital admissions and healthcare expenditures.

One reason for frequent pneumonia hospitalizations is that up to 90% of pediatric patients with tracheostomy have respiratory cultures positive for *Pseudomonas aeruginosa (P. aeruginosa)*, a multidrug resistant bacterium with limited oral treatment options, at some point post-tracheotomy[8]. Indeed, over 70% of pediatric patients hospitalized bTARTIs receive empiric antibiotics that target *P. aeruginosa)*[4]. While previous literature in patients with cystic fibrosis (CF) demonstrated associations between *P. aeruginosa* acquisition and both increased CF exacerbation rates[9] and declining pulmonary status and greater mortality[10–14], the relationship between *P. aeruginosa* and outcomes in pediatric patients with tracheostomy remains unclear.

Because of the large number of children who undergo tracheotomy at our center each year, we saw an opportunity to further investigate risk factors for a bTARTI requiring readmission after tracheotomy surgery in pediatric patients, with a focus on acquisition of *Pseudomonas aeruginosa.* The objective of the current study was to identify risk factors for readmission due to a bTARTI within 12 months of hospitalization for tracheotomy.

Methods

Study setting and population

We conducted a single-center retrospective cohort study of pediatric patients who underwent initial tracheotomy at Children's Hospital Los Angeles (CHLA). CHLA is a university-based children's hospital with 365 beds and over 15,000 annual admissions annually. We identified all patients between 0–18 years of age admitted with an *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM)* procedure code for tracheotomy previously used in studies examining pediatric tracheotomy[15,16] (*ICD-9-CM*: 31.1, 31.2, 31.21, 31.29) who: (1) were discharged from the hospital with tracheostomy between 1/1/2005 and 6/30/2013 and; (2) had at least one year of documented follow-up at CHLA. We excluded patients who died during the index hospitalization or who underwent decannulation within 12 months of discharge post-tracheotomy, or those patients with outlier overall LOS (>400 days) or excessive LOS post-tracheotomy (>200 days).

Data collection

We conducted manual chart review of each patient's individual medical records for demographic data including gender, race/ethnicity, insurance; details of index tracheotomy hospitalization including age and LOS; prematurity, defined as gestational age <37 weeks; date of first respiratory culture with *Pseudomonas aeruginosa*; and discharge details including discharge on home positive pressure ventilation as well as respiratory (e.g. bronchodilators, inhaled corticosteroids, glycopyrrolate, ipratroprium) and gastrointestinal (e.g. acid blockers such as histamine-2 receptor antagonists and proton pump inhibitors, as well as pro-motility agents such as erythromycin and metoclopromide) discharge medications. We also manually recorded date of tracheostomy decannulation, date of death (if applicable), and last date of hospital follow-up. Respiratory cultures are done at the discretion of the ordering physician and are generally ordered in response to symptoms. Because of the lack of evidence for surveillance cultures[17], at CHLA, there is no general policy for obtaining surveillance cultures.

We augmented manual chart review with administrative data from the Pediatric Health Information System (PHIS) database for the encounter in which tracheotomy occurred. The PHIS database contains de-identified inpatient, emergency room, ambulatory surgery and observation unit data from 48 freestanding children's hospitals.[18] The PHIS data contains a blinded medical record number for each patient. After data download, we unblinded the PHIS medical record number to link the PHIS data to the CHLA medical record data. Data obtained from the PHIS database included previously validated *ICD-9-CM* codes for medical comorbidities associated with tracheotomy (e.g. upper airway obstruction, chronic lung disease, neuromuscular disease, trauma)[5,16], cardiac surgery (*ICD-9-CM* procedure codes 35–37.XX])[19], as well as gastrostomy tube dependence at discharge (e.g., *ICD-9-CM* diagnoses codes v44.1, v55.1, and 536.4x, and gastrostomy tube placement *ICD-9-CM* procedure codes 43.0, 43.1x, 97.02)[20,21].

Primary outcome variable

Through chart review, we identified the outcome variable as the first hospitalization for a bTARTI, defined as a discharge diagnosis of a bacterial respiratory tract infection (e.g. pneumonia, tracheitis) on review of the discharge summary, treated with a complete course of antibiotic therapy (as defined by the primary team) or discharge home to complete antibiotic therapy. One medical student and one research staff member trained in medical chart abstraction identified the outcome variables; discrepancies were resolved through a secondary review by the principal investigator (C.R.).

Statistical methodology

Descriptive statistics and bivariate analyses were first used to assess the association between predictor variables and covariates with readmission for bTARTI. Bivariate logistic regressions for binary outcomes and linear regressions for continuous outcomes were reported through unadjusted odds ratios (UOR) with 95% confidence intervals (CI). Predictor variables that maintained a $p<0.15$ significance level, or had demographic or medical justification for inclusion in the multivariate analysis (male gender, public insurance, age at admission) were used. Adjusted odds ratios (AOR) with 95% CI were reported in the final, multivariable logistic regression model. For those patients readmitted with a bTARTI, chi-square tests were used posteriori to investigate whether significant differences existed between the timing of first *P. aeruginosa*-positive respiratory culture and respiratory culture results on bTARTI readmission. All models were analyzed using SPSS Statistics for Windows, version 23. The study was reviewed by the Children's Hospital Los Angeles Institutional Review Board and was approved per 45 CFR 46.110/21 CFR 56.110.

Results

The study cohort included 240 patients, 103 (43%) of whom were readmitted for bTARTI within 12 months of discharge post-tracheotomy. Of the 103 patients readmitted, 39% (n=40) were diagnosed with bacterial tracheitis, 34% (n=35) with bacterial pneumonia, and 27% (n=28) with both bacterial tracheitis and pneumonia. The most common bacteria identified by respiratory culture on readmission included *P. aeruginosa* (45.5%), *Staphylococcus aureas* (21.8%), *Stenotrophomonas maltophilia* (18.4%), *Serratia marcascens* (16.8%) and *Moraxella catarrhalis* (12.9%). Patient demographics and details of index hospitalization are presented in Table 1. The cohort was predominantly male (n=144, 60%), of Hispanic ethnicity (n=162, 68%), and publicly insured (n=213, 89%) and had a median age at index hospitalization of five months [interquartile range (IQR)=1–37 months]. The most common medical comorbidities associated with indication for tracheotomy included chronic lung disease (n=141, 59%) and neuromuscular disease (n=129, 54%). A minority had a respiratory culture with *P. aeruginosa* prior to tracheotomy (n=50, 21%) or acquired *P. aeruginosa* between tracheotomy and discharge (n=26, 11%). Additional surgical procedures included cardiac surgery (n=23, 10%) and gastrostomy tube placement (n=117, 49%). Many patients were discharged on positive-pressure home mechanical ventilation (n=112, 47%). The majority of patients were discharged on bronchodilators (n=191, 80%), inhaled corticosteroids (n=128, 53%), or gastrointestinal acid suppressive medications (n=147; 61%); use of pro-motility agents was less frequent (n=83, 35%).

Unadjusted odds ratios (UOR) for factors associated with hospitalization for bTARTI are presented in Table 1. In bivariate analysis, risk factors statistically significantly associated with increased odds for readmission with bTARTI within 12 months of tracheotomy included: Hispanic ethnicity (UOR 2.1, 95% CI: 1.2–3.8, p=0.01), acquisition of *P. aeruginosa* between tracheotomy and discharge (UOR=3.0; 95% CI: 1.2,7); p=0.01), the presence of gastrostomy tube at hospital discharge (UOR=1.8; 95% CI: 1.1–3.2) and discharge on inhaled ipratropium (UOR=2.2; 95% CI 1.1–4.4). Discharge on gastrointestinal pro-motility agents was associated with decreased odds of bTARTI readmission within 12 months (UOR=0.5; 95% CI: 0.3–0.9; p=0.02). Other variables that met our inclusion cutoff and were entered in the multivariable model included: admission age, prematurity, discharge on home positive-pressure ventilation, and discharge on inhaled corticosteroids.

The multivariable logistic regression model is presented in Table 2. Risk factors independently associated with increased odds for readmission for bTARTI within 12 months of tracheotomy included: Hispanic ethnicity (AOR=2.0; 95% CI 1.1, 3.9; p=0.03) and acquisition of *P. aeruginosa* between tracheotomy and discharge (AOR=3.1; 95% CI 1.2–8.3; p=0.02). Discharge on gastrointestinal pro-motility agents (AOR=0.4; 95% CI 0.0.20.8; p=0.01) was associated with decreased odds for readmission for bTARTI within 12 months of tracheotomy. Other main predictors, including age, prematurity and discharge on chronic positive pressure ventilation were not associated with odds of readmission for a TARTI within 12 months.

For the 103 patients readmitted with a bTARTI, we found an association between initial timing of first *P. aeruginosa*-positive respiratory culture and *P. aeruginosa* identification on hospital readmission for first bTARTI. Patients with a *P. aeruginosa*-positive respiratory culture prior to post-tracheotomy discharge were more likely to have a *P. aeruginosa*-positive respiratory culture on bTARTI readmission, when compared to patients without a *P. aeruginosa*-positive respiratory culture (64.1% vs. 35.9%; p=0.003). However, there was no difference in subsequent *P. aeruginosa*-positive bTARTI readmission respiratory culture for those patients with *P. aeruginosa* prior to tracheotomy, when compared to those who acquired *P. aeruginosa* between tracheotomy and discharge (59.1% vs. 70.6%; p=0.46)

Discussion

In this single center retrospective study of pediatric patients undergoing tracheotomy, nearly half of patients undergoing tracheotomy are readmitted within 12 months for a bacterial tracheostomy-associated respiratory tract infection (bTARTI). Hispanic ethnicity and hospital-acquired *P. aeruginosa* after tracheotomy and before discharge are independently associated with increased odds, while discharge on pro-motility agents was associated with decreased odds of bTARTI readmission after controlling for potential confounders. Finally, acquisition of respiratory tract *P. aeruginosa* prior to post-tracheotomy discharge was associated with subsequent readmission for a *P. aeruginosa* bTARTI.

Our finding of poorer outcomes for those who acquire *P. aeruginosa* after tracheotomy but prior to initial post-tracheotomy discharge is consistent with poorer outcomes after *P. aeruginosa* acquisition in other respiratory diseases. As noted previously, up to 90% of

pediatric patients with tracheostomy demonstrate *P. aeruginosa* in a respiratory culture at some time[8]. Our study demonstrates that *P. aeruginosa* acquisition while hospitalized after tracheotomy is associated with poorer healthcare outcomes, and may be considered a healthcare-acquired infection. In pediatric CF, another disease of impaired airway clearance, eradication of *P. aeruginosa* is feasible after antibiotic administration via inhalation antibiotics, oral/parenteral antibiotics, or a combination of both delivery methods[22–25], and leads to reductions in chronic *P. aeruginosa* infection[26]. Further, failure to eradicate *P. aeruginosa* after initial acquisition is associated with greater exacerbation risk[27]. Given that *P. aeruginosa* acquisition may be potentially modifiable, we believe that acquisition during the post-tracheotomy recovery period may warrant aggressive eradication measures to prevent readmission.

Results showing poorer outcomes in Hispanic patients are also consistent with past literature demonstrating health care disparities in Hispanics. Previous studies have shown that Hispanic ethnicity is associated with increased odds of hospitalization for an ambulatory care sensitive condition[28] and decreased use of home care or facilities[29] in pediatric patients. Further, Hispanic ethnicity is associated with higher mortality rate in patients with other respiratory diseases (e.g. cystic fibrosis[30]) and in those undergoing surgical procedures (e.g. congenital heart surgery repair[31]). The poorer outcomes may be due to biological differences, socioeconomic differences (e.g. access to care, language difficulties), decreased use of home health services and post-acute facilities or a combination.

Pro-motility agents may decrease both frank aspiration and undetectable micro-aspiration of gastrointestinal contents into the respiratory tract and decreased odds of aspiration-related respiratory infection. Despite this finding, the side effect profile of certain medications (e.g., metoclopramide and irreversible tardive dyskinesia) may limit its long-term use for motility. Given these findings, improving gastrointestinal motility may decrease admissions for TARTIs and presents an area of future investigation. Unlike previous studies showing an increased risk of lower respiratory tract infections in pediatric patients treated with acid suppression[32,33], our study showed no relationship between hospital discharge on acid suppression medications and subsequent bTARTI readmission.

There are several limitations to the current study. This is a single center study with a large proportion of Hispanic patients and patients who are on chronic positive pressure mechanical ventilation; thus, our patient population may not be representative of the entire population of pediatric patients with tracheostomy. Our results may not generalize to patients treated at non-children's hospitals. While our patient numbers were large, we may have had limited power to detect smaller differences in odds ratios for some predictor variables. Because of the retrospective nature of the study, there are potential confounders, including smoking exposure at home, school/daycare attendance, other siblings in the home, use of home nursing, and discharge to a sub-acute facility, that may affect risk of bTARTI exposure and hospital readmission. For reference, in addition to primary care, the usual care for patients with tracheostomy at CHLA is for follow-up appointments with the pulmonology clinic every 3–6 months and with pediatric otorhinolaryngology every 6–12 months. Lastly, there is no standard definition nor guidelines for diagnosis of bTARTIs in pediatric patients; thus, some patients identified as having at bTARTI readmission may have

been given antibiotics for chronic bacterial colonization in the setting of a viral or other non-bacterial respiratory tract illness. Strengths include detailed chart reviews to identify the primary outcome and availability of detailed clinical information not available through administrative data (e.g. discharge medications, *P. aeruginosa* respiratory culture results).

Despite these limitations, this study demonstrates that among pediatric patients who undergoing tracheotomy, those of Hispanic ethnicity and those who acquire *P. aeruginosa* are at increased odds of being readmitted for a bacterial tracheostomy-associated respiratory tract infection. Our findings suggest further exploration is needed into care delivery to Hispanic pediatric patients with tracheostomy. Larger, multicenter studies are needed confirm our findings of the association between *P. aeruginosa* acquisition and subsequent respiratory infections. Should these findings be replicated, this may support intervention trials (e.g. inhaled antibiotics) in pediatric patients recovering from tracheotomy to investigate the association between *P. aeruginosa* prevention or eradication and subsequent respiratory infections.

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Abbreviations

AOR	adjusted odds ratio
bTARTI	bacterial tracheostomy-associated respiratory tract infection
CHLA	Childrens Hospital Los Angeles
CI	confidence interval
CF	cystic fibrosis
ICD-9-CM	*International Classification of Diseases, Ninth Revision, Clinical Modification*
IQR	interquartile range
LOS	length of stay
PHIS	Pediatric Health Information System
UOR	unadjusted odds ratio

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Table 1

Characteristics of pediatric patients undergoing tracheostomy in the study cohort, stratified by hospital admission for a bacterial tracheostomy-associated respiratory tract infection

	Admitted for Bacterial Tracheostomy-Associated Respiratory Tract Infection within 12 months					Unadjusted Odds Ratio (95% CI)	p-value
	Total	**No**	**Percent**	**Yes**	**Percent**		
	240	137	57.1	103	42.9		
Gender							
Male	144 (60.0%)	80	58.4	64	62.1	1.17 (.69 to 1.97)	.56
Female	96 (40.0%)	57	41.6	39	37.9		
Ethnicity							
Hispanic	162 (67.5%)	83	60.6	79	76.7	2.14 (1.21 to 3.79)	.01
Non-Hispanic	78 (32.5%)	54	39.4	24	23.3	REF	
Insurance							
Public	213 (88.8%)	120	87.6	93	90.3	1.32 (.58 to 3.01)	.51
Other	27 (11.3%)	17	12.4	10	9.7		
Admit Age (Months)							
0 months	46 (19.2%)	22	16.1	24	23.3	REF	
1 – 12 months	107 (44.6%)	60	43.8	47	45.6	.72 (.36 to 1.44)	.35
1 – 4 years	41 (17.1%)	26	19.0	15	14.6	.53 (.22 to 1.25)	.15
5 – 12 years	24 (10.0%)	15	10.9	9	8.7	.55 (.20 to 1.51)	.25
13 – 18 years	22 (9.2%)	14	10.2	8	7.8	.52 (.18 to 1.49)	.23
Length of Stay, Days (Median, (IQR))	72.5 (43, 121)	69 (39.5, 121)		73 (47, 120)		1.00 (1.00 to 1.00)	.62
Comorbidities associated with Indication for Tracheostomy							
Prematurity	85 (35.4%)	54	39.4	31	30.1	.66 (.39 to 1.14)	.14
Upper Airway Obstruction	89 (37.1%)	50	36.5	39	37.9	1.06 (.63 to 1.80)	.83
Chronic Lung Disease	141 (58.8%)	82	59.9	59	57.3	.90 (.54 to 1.51)	.69
Neuromuscular Disease	129 (53.8%)	70	51.1	59	57.3	1.28 (.77 to 2.14)	.34
Trauma	8 (3.3%)	3	2.2	5	4.9	2.28 (.53 to 9.76)	.27
Pseudomonas-positive respiratory culture							
None before discharge	164 (68.3%)	100	72.3	64	62.1	REF	
Before tracheotomy	50 (20.8%)	28	20.4	22	21.4	1.23 (.65 to 2.33)	.53

	Admitted for Bacterial Tracheostomy-Associated Respiratory Tract Infection within 12 months					Unadjusted Odds Ratio (95% CI)	p-value
	Total	**No**	**Percent**	**Yes**	**Percent**		
Between tracheotomy & discharge	26 (10.8)	9	6.6	17	16.5	3.00 (1.24 to 7.02)	.01
Surgical comorbidities							
Heart Surgery	23 (9.6%)	12	8.8	11	10.7	1.25 (.53 to 2.95)	.62
Discharge Details							
Discharge on home PPV	112 (46.7%)	71	51.8	41	39.8	.62 (.37 to 1.03)	.07
Discharge respiratory medications							
Bronchodilators	191 (79.6%)	105	76.6	86	83.5	1.54 (.80 to 2.96)	.19
Inhaled corticosteroids	128 (53.3%)	66	48.2	62	60.2	1.63 (.97 to 2.73)	.07
Glycopyrrolate	17 (7.1%)	8	5.8	9	8.7	1.54 (.57 to 4.15)	.39
Ipratropium	39 (16.3%)	16	11.7	23	22.3	2.17 (1.08 to 4.37)	.03
Discharge Gastrointestinal Medications							
Acid Blockage	147 (61.3%)	83	60.6	64	62.1	1.07 (.63 to 1.81)	.81
Pro-Motility Agents	83 (34.6%)	56	40.9	27	26.2	.51 (.30 to .90)	.02

CI = confidence interval; PPV= positive pressure ventilation

Table 2

Multivariable logistic regression analysis of readmission for a bacterial tracheostomy-associated respiratory tract infection among pediatric patients undergoing tracheotomy

	Adjusted Odds Ratio (95% CI)	p-value
Demographics		
Male	.92 (.51 to 1.66)	.79
Hispanic	2.02 (1.06 to 3.85)	.03
Public Insurance	1.16 (.44 to 3.05)	.76
Admission age, in months		
0 months	REF	
1 – 12 months	.86 (.39 to 1.91)	.71
1 – 4 years	.44 (.17 to 1.15)	.09
5 – 12 years	.59 (.19 to 1.80)	.35
13 – 18 years	.38 (.12 to 1.28)	.12
Comorbidities associated with Indication for Tracheostomy		
Premature	.72 (.37 to 1.40)	.33
Pseudomonas-positive respiratory culture		
None	REF	
Before tracheotomy	1.19 (.58 to 2.42)	.64
Between tracheotomy & discharge	3.20 (1.23 to 8.31)	.02
Discharge Details		
Gastrostomy tube at discharge	1.72 (.93 to 3.18)	.09
Discharge on home PPV	.61 (.33 to 1.12)	.11
Respiratory medications		
Inhaled corticosteroids	1.46 (.78 to 2.74)	.24
Ipratropium	1.89 (.86 to 4.15)	.11
Gastrointestinal Medications		
Pro-Motility Agents	.43 (.23 to .80)	.01

CI = confidence interval; PPV= positive pressure ventilation