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ORIGINAL RESEARCH

Clinical and Economic Burden Associated with Prolonged Air Leaks Among Patients Undergoing Thoracic Resection: A Retrospective Database Analysis

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Purpose: Prophylactic use of lung sealants among patients undergoing thoracic resection has been reported for the management of intraoperative air leaks and is associated with a lower incidence of prolonged air leak (PAL) and a shorter length of stay (LOS). This study estimated the incremental economic and clinical burden of PAL among patients with lung sealants used during thoracic resection in the United States.

Patients and Methods: This retrospective analysis examined hospital data (Premier Healthcare Database) for adults (age ≥18 years) with inpatient thoracic resection between October 2015 - March 2021 (first admission=index) and lung sealant used during their procedure. Follow-up extended through 90 days post-discharge. Patients were grouped by presence/absence of PAL (ie, diagnosis of post-procedural air leak or post-procedural pneumothorax with associated LOS exceeding 5 days). Outcomes included intensive care unit (ICU) days, total index hospital costs, all-cause 30-, 60-, and 90-day readmission, discharge status, and in-hospital mortality. Generalized linear models quantified associations between PAL and outcomes, accounting for hospital-level clustering, and patient, procedure, and hospital/provider characteristics.

Results: Among the 9727 patients included for study (51.0% female, 83.9% white, mean age 66 years), 12.5% had PAL, which was associated with significant incremental increases in ICU days (0.93 days, $p<0.001$) and total hospital cost ($11,119, $p<0.001$). PAL also decreased the likelihood of discharge to home (from 91.3% to 88.1%, $p<0.001$) and increased the risk of readmission within 30, 60, and 90 days by up to 34.0% (from 9.3% to 12.6%;11.7% to 15.4%;13.6% to 17.2%, respectively), all $p<0.01$. Absolute risk of mortality was low, but two times higher in patients with PAL versus those without PAL (2.4% vs 1.1%, $p=0.001$).

Conclusion: This analysis demonstrates that despite the prophylactic use of lung sealants, PAL continues to put a burden on the healthcare system, highlighting an unmet need for improved sealant technology.

Keywords: lung sealants, surgical complications, healthcare resource utilization, hospital costs

Introduction

Although prolonged air leak (PAL) is one of the most serious and common complications following thoracic resection, there is no current standard of care for prevention. PAL is typically defined as an air leak persisting longer than five days post-operatively, a definition based on the expected length of hospital stay for a lobectomy.[1,2] A recent systematic review and meta-analysis of 39 international studies comprising 89,006 patients found that pooled PAL incidence was 15% after pulmonary surgery, ranging between 5% and 60%.[3] Incidence, however, varies with PAL definition (ie, number of post-operative days) and procedural characteristics (eg, surgical approach, extent of resection, surgical indication).[1–3]

The clinical and economic consequences of PAL include increased hospital and ICU utilization, longer hospital lengths of stay (LOS), and increased risk of clinical complications such as pneumonia and pleural space infections.[2,4] Lung sealants

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are widely used in the United States to reduce the incidence of PAL during thoracic resection. Both biologic-based sealants (eg, fibrin-based and collagen-fleece bound) and synthetic sealants (eg, polyethylene glycol-based and polyglycolic acid-based) have been approved by the Food and Drug Administration (FDA) and are marketed in the U.S.[5] In various comparative studies (randomized controlled trials, retrospective studies, preclinical) several commercially-marketed sealants used in conjunction with standard of care (stitches, staples) have demonstrated clinical efficacy, lower PAL, shorter hospital LOS and lower healthcare costs compared with these outcomes in patients who received standard of care alone.[6–10] Although these sealants have been assessed individually using various study designs, to our knowledge no study has evaluated the impact of use of lung sealants in aggregate on the real-world incidence of PAL and associated healthcare resource utilization and cost outcomes. To address this knowledge gap, the current study estimated the incremental economic and clinical burden of PAL among patients with lung sealants used during thoracic resection in the United States (US).

Materials and Methods

Data Source and Patient Selection

This retrospective observational study examined data from inpatient and outpatient hospital billing records contained in the Premier Healthcare Database (PHD). The PHD is a population-based research database that contains healthcare records contributed by a convenience sample of nearly 1000 US hospitals and health systems that are members of the Premier Healthcare Performance Improvement Alliance, which represents approximately 25% of annual US inpatient discharges. This database includes discharge-level information on patient demographics, diagnoses, procedures, use of medications and devices, hospital borne costs (ie, costs of each hospital encounter from the hospital perspective), length of stay, discharge disposition, as well as information on hospital and provider characteristics. Although the database excludes federally funded hospitals, contributing hospitals are nationally representative with respect to bed size, geographic region, location (urban/rural) and teaching status.

This analysis of the Premier Healthcare database was conducted under an exemption from Institutional Review Board oversight for US-based studies using de-identified healthcare records, as dictated by Title 45 Code of Federal Regulations (45 CFR 46.104(d)(4)(ii)) (https://www.ecfr.gov/current/title-45/subtitle-A/subchapter-A/part-46/subpart-A/section-46.104). As Premier Healthcare data do not contain direct identifiers of individuals, employers, households, or providers, Institutional Review Board approval is not required.

The study population included adults (age ≥18 years) with inpatient thoracic resection (ie, lobectomy, segmentectomy, wedge resection) between October 1, 2015 and March 31, 2021 and lung sealant (Progel™, Coseal®, TachoSil®, Tisseel, Evicel®, BioGlue®) used during their procedure. The earliest qualifying admission date was considered the index date. For each patient, follow-up extended through 90 days post-discharge with the hospital in which the index admission occurred contributing data to the PHD throughout that period. Patients with any of the following were excluded: admission as a transfer from another facility, missing discharge disposition, receipt of more than one branded lung sealant, or concomitant cardiac surgery.

For analysis, each patient was classified into one of two mutually exclusive cohorts based the presence or absence of PAL during the index hospitalization. PAL was defined as the diagnosis of post-procedural air leak or post-procedural pneumothorax with an inpatient LOS exceeding 5 days after the resection procedure was completed.

Measurement of Patient and Hospital/Provider Characteristics

Patients and hospital/provider characteristics measured during the index admission included age, sex, race, ethnicity, marital status, payer type, admission type (elective/non-elective), urban vs rural hospital, hospital teaching status, hospital geographic region, hospital bed size, operating physician specialty, year of surgery/index admission, annual hospital surgical volume for thoracic resection, and an indicator for whether hospital costs are derived from a cost-to-charge ratio vs procedural costing. Patient clinical characteristics measured during the index admission included the individual components of the Charlson Comorbidity (CCI) and Elixhauser Comorbidity Indices,[11–13] and their aggregate index scores. Procedural characteristics included surgical approach, type of resection (lobectomy, wedge resection, segmentectomy), lobe location, and surgical indication (malignancy/non-malignancy). The CCI and Elixhauser were measured through the presence of ICD-10-CM codes, excluding those for which there was an indication that the comorbidity was not present on admission.

Measurement of Economic and Clinical Outcomes

Primary outcomes included the total intensive care unit (ICU) days during the index hospital stay, total hospital costs from the hospital perspective, all-cause hospital readmissions within 30-, 60-, and 90-days post-procedure, patients' discharge status (home/home health vs other setting of care), and mortality. Hospital costs were inflation adjusted to 2021 US dollars using the Medical Care component of the US Bureau of Labor Statistics Consumer Price Index.

Statistical Analysis

Descriptive analyses, stratified by the absence or presence of PAL, were utilized to describe patient, procedure, and hospital/provider characteristics, and unadjusted outcomes. Data for categorical variables were summarized using counts and percentages of patients in each category. Data for continuous variables were summarized using the mean and standard deviation of the variable distribution; medians and other percentile information were reported for variables which are not normally distributed.

Multivariable generalized linear models (GLM) were used to quantify associations between incident PAL and each of the study outcomes, accounting for hospital-level clustering, and adjusting for differences in patient, procedure, and hospital/provider characteristics between the two patient cohorts. GLM with log link and negative binomial error distribution was used for ICU days, GLM with logit link and binomial error distribution was used for all-cause readmissions within 30, 60, and 90 days post-discharge, discharge status, and mortality, and a GLM with log link and gamma distribution was used for total hospital costs. Additionally, to confirm the face validity of the present study's findings in relation to prior research, we fit a multivariable logistic regression model to examine the association of patient, provider, procedure, and hospital characteristics with the incidence of PAL. Statistical analyses were performed using StataSE 16 (StataCorp, College Station, Texas, US).

Results

A total of 62,220 patients met initial selection criteria; 9727 of these patients had one lung sealant of interest used during their index thoracic resection and were included in the final study population (Table 1). Tables 2-4 display information on patient demographics/clinical characteristics, procedure characteristics, and hospital/provider characteristics, respectively. Overall, the mean age of study patients was 66 years, 51% were female, and most (84%) were of white race. Approximately 63% of patients had Medicare coverage and nearly three-quarters of patients had an Elixhauser Comorbidity Score between 1 and 4, with most of the remaining patients having scores of 5 or higher (Table 2). Most

Table 1 Patient Selection

Criteria	Patients
1. Inpatient admission carrying a primary procedure code for lung resection between October 1, 2015 and March 31, 2021	74,631
2. Restricting cohort to patients aged 18 and above	73,264
3. Restricting cohort to patients for whom their institution continues to contribute data to the database for 90 days after discharge from index admission	69,238
4. Restricting cohort to patients who were not transferred from another facility	66,744
5. Restricting cohort to patients who had ≤ 1 lung sealant	63,238
6. Restricting cohort to patients who did not have concomitant cardiac surgery	62,220
7. Restricting cohort to patients who had evidence of lung sealant use on day of thoracic resection	9,727

Table 2 Patient Demographic Characteristics and Comorbidity Burden at Index

Characteristic	Overall (N=9727)		PAL			
			Yes (N=1213)		No (N=8514)	
	N	%	N	%	N	%
Age category						
18–34	229	2.4%	13	1.1%	216	2.5%
35–44	233	2.4%	17	1.4%	216	2.5%
45–54	784	8.1%	64	5.3%	720	8.5%
55–64	2422	24.9%	315	26.0%	2107	24.7%
65–74	3791	39.0%	513	42.3%	3278	38.5%
75+	2268	23.3%	291	24.0%	1977	23.2%
Gender						
Female	4956	51.0%	575	47.4%	4381	51.5%
Male	4771	49.0%	638	52.6%	4133	48.5%
Marital status						
Married	5213	53.6%	624	51.4%	4589	53.9%
Single	4031	41.4%	532	43.9%	3499	41.1%
Other	450	4.6%	53	4.4%	397	4.7%
Unknown	33	0.3%	4	0.3%	29	0.3%
Race						
White	8159	83.9%	1045	86.2%	7114	83.6%
African American	803	8.3%	84	6.9%	719	8.4%
Other	418	4.3%	46	3.8%	372	4.4%
Asian	197	2.0%	14	1.2%	183	2.1%
Unknown	150	1.5%	24	2.0%	126	1.5%
Hispanic Indicator						
No	7909	81.3%	988	81.5%	6921	81.3%
Unknown	1148	11.8%	166	13.7%	982	11.5%
Yes	670	6.9%	59	4.9%	611	7.2%
Payer						
Medicare	6176	63.5%	825	68.0%	5351	62.8%
Commercial	2386	24.5%	226	18.6%	2160	25.4%
Medicaid	771	7.9%	106	8.7%	665	7.8%
Other	394	4.1%	56	4.6%	338	4.0%

(Continued)

Table 2 (Continued).

Characteristic	Overall (N=9727)		PAL			
			Yes (N=1213)		No (N=8514)	
	N	%	N	%	N	%
Elixhauser score						
0	230	2.4%	8	0.7%	222	2.6%
1–2	2955	30.4%	289	23.8%	2666	31.3%
3–4	4228	43.5%	591	48.7%	3637	42.7%
5 +	2314	23.8%	325	26.8%	1989	23.4%

Abbreviations: N, number; PAL, prolonged air leak.

Table 3 Procedure Characteristics

Characteristic	Overall (N=9727)		PAL			
			Yes (N=1213)		No (N=8514)	
	N	%	N	%	N	%
Surgical indication						
Malignancy	7897	81.2%	1054	86.9%	6843	80.4%
Non-malignancy	1830	18.8%	159	13.1%	1671	19.6%
Robotic surgery						
Yes	3080	31.7%	294	24.2%	2786	32.7%
Lung approach						
Open	3385	34.8%	570	47.0%	2815	33.1%
VATS	3262	33.5%	349	28.8%	2913	34.2%
Robotic	3080	31.7%	294	24.2%	2786	32.7%
Conversion to open surgery						
Yes	196	2.0%	36	3.0%	160	1.9%
Type of resection						
Lobectomy	5647	58.1%	768	63.3%	4879	57.3%
Wedge	2608	26.8%	209	17.2%	2399	28.2%
Multiple resections	1455	15.0%	235	19.4%	1220	14.3%
Segmentectomy	17	0.2%	1	0.1%	16	0.2%
Secondary resection on different procedure day						
Yes	68	0.7%	32	2.6%	36	0.4%
Lobe position						
Right upper	3050	31.4%	495	40.8%	2555	30.0%
Left upper	2230	22.9%	278	22.9%	1952	22.9%

(*Continued*)

Table 3 (Continued).

Characteristic	Overall (N=9727)		PAL			
			Yes (N=1213)		No (N=8514)	
	N	%	N	%	N	%
Right lower	2073	21.3%	248	20.4%	1825	21.4%
Left lower	1480	15.2%	119	9.8%	1361	16.0%
Right middle	752	7.7%	67	5.5%	685	8.0%
Lingula	56	0.6%	3	0.2%	53	0.6%
Right, not specified	46	0.5%	2	0.2%	44	0.5%
Left, not specified	39	0.4%	1	0.1%	38	0.4%
Other	1	0.0%		0.0%	1	0.0%
Admission Year						
2015	523	5.4%	85	7.0%	438	5.1%
2016	2288	23.5%	302	24.9%	1986	23.3%
2017	1781	18.3%	231	19.0%	1550	18.2%
2018	1344	13.8%	164	13.5%	1180	13.9%
2019	2205	22.7%	263	21.7%	1942	22.8%
2020	1586	16.3%	168	13.8%	1418	16.7%

Abbreviations: N, number; PAL, prolonged air leak; VATS, video-assisted thoracoscopic surgery.

Table 4 Hospital and Provider Characteristics

Characteristic	Overall (N=9727)		PAL			
			Yes (N=1213)		No (N=8514)	
	N	%	N	%	N	%
Geography						
Urban	8892	91.4%	1084	89.4%	7808	91.7%
Rural	835	8.6%	129	10.6%	706	8.3%
Teaching status						
Yes	5651	58.1%	679	56.0%	4972	58.4%
No	4076	41.9%	534	44.0%	3542	41.6%
Provider region						
South	5101	52.4%	638	52.6%	4463	52.4%
Midwest	2149	22.1%	280	23.1%	1869	22.0%
Northeast	1256	12.9%	128	10.6%	1128	13.2%
West	1221	12.6%	167	13.8%	1054	12.4%

(*Continued*)

Table 4 (Continued).

Characteristic	Overall (N=9727)		PAL			
			Yes (N=1213)		No (N=8514)	
	N	%	N	%	N	%
Number of hospital beds						
000–099	82	0.8%	12	1.0%	70	0.8%
100–199	322	3.3%	50	4.1%	272	3.2%
200–299	1651	17.0%	218	18.0%	1433	16.8%
300–399	1074	11.0%	162	13.4%	912	10.7%
400–499	1564	16.1%	220	18.1%	1344	15.8%
500+	5034	51.8%	551	45.4%	4483	52.7%
Hospital costing type						
Procedural	7255	74.6%	850	70.1%	6405	75.2%
Ratio of cost to charges	2472	25.4%	363	29.9%	2109	24.8%
Procedural physician specialty						
Pulmonary/thoracic surgeon	4701	48.3%	559	46.1%	4142	48.6%
Cardiovascular surgeon	3319	34.1%	467	38.5%	2852	33.5%
General surgeon	959	9.9%	116	9.6%	843	9.9%
Other specialty/Unknown	748	7.7%	71	5.9%	677	8.0%
Provider procedure volume						
0–100	6442	66.2%	883	72.8%	5559	65.3%
101–200	2360	24.3%	262	21.6%	2098	24.6%
201–300	819	8.4%	58	4.8%	761	8.9%
301–400	106	1.1%	10	0.8%	96	1.1%

Abbreviations: N, number; PAL, prolonged air leak.

(81%) patients' surgical indication was for malignancy and surgical approach was evenly distributed (open 35%, video-assisted thoracoscopic surgery [VATS] 34%, robotic 32%). Out of all resections, 5647 (58%) were lobectomies, and the right upper was the most prevalent (31%) lobe position (Table 3). Patients were predominantly treated in urban hospitals (91%) and nearly half (48%) underwent surgery by a pulmonary/thoracic surgeon (Table 4).

Incident PAL was identified in 12.5% (n=1213) of patients after the index procedure. In unadjusted analysis, mean (SD) age was not meaningfully different between patients with and without PAL (67.4 years [10.0] and 65.9 years [11.7], respectively) although the age distribution of patients with PAL was shifted upward with a larger proportion aged 65 years or older and covered by Medicare. Patients with PAL also carried a greater comorbidity burden; 76% had an Elixhauser Comorbidity Score of 3 or higher compared with 66% of patients without PAL.

After adjusting for differences in demographics, clinical characteristics, procedural and hospital characteristics, incident PAL was found to significantly increase resource utilization and costs (Table 5). Specifically, PAL was associated with significant incremental increases in ICU days (0.93 days, p<0.001) and incrementally higher total hospital costs ($11,119, p<0.001). The presence of PAL also significantly decreased patients' chance of being discharged

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Table 5 Adjusted Cost and Utilization Outcomes

Adjusted Outcome	PAL	No PAL	Difference	95% CI		P-value
Cost	$39,160	$28,041	$11,119	$9444	$12,796	<0.001
ICU days	2.499	1.569	0.930	0.661	1.199	<0.001
Discharge to Home	88.1%	91.3%	−3.2%	−4.9%	−1.6%	<0.001
30-day readmission	12.6%	9.4%	3.2%	1.1%	5.2%	0.003
60-day readmission	15.4%	11.7%	3.7%	1.5%	5.9%	0.001
90-day readmission	17.2%	13.6%	3.6%	1.4%	5.8%	0.001
In-hospital mortality	2.4%	1.0%	1.4%	0.6%	2.2%	0.001

Abbreviations: CI, confidence interval; PAL, prolonged air leak.

to home vs other setting (eg, skilled nursing facility) from 91.3% to 88.1% (3.6%, p<0.001). Patients' risk of being readmitted also significantly increased with the presence of PAL from 9.3% to 12.6% at 30 days, from 11.7% to 15.4% at 60 days, and from 13.6% to 17.2% at 90 days, all p<0.01. Additionally, although the absolute risk of in-hospital mortality was low in the study population, it was two times higher in patients with PAL compared with patients without evidence of PAL (2.4% vs 1.1%, p=0.001).

In the multivariable logistic regression model fit to examine the association of patient, provider, procedure, and hospital characteristics with the incidence of PAL, male sex, resection of the right upper lobe, lobectomy (compared to wedge, segmentectomy), and multiple resections were significantly associated with increased risk of PAL (Table 6). Minimally invasive surgery was significantly associated with decreased risk of PAL.

Table 6 Predictors of Prolonged Air Leaks

Reference	Variable Evaluated	Odds Ratio	95% Confidence Interval		P-value
Age (years) Reference: 65–74	18–34	0.526	0.277	0.998	0.049
	35–44	0.766	0.44	1.332	0.344
	45–54	0.599	0.435	0.824	0.002
	55–64	0.936	0.766	1.145	0.522
	75+	0.95	0.808	1.118	0.541
Sex Reference: Female	Male	1.199	1.049	1.369	0.008
Race Reference: White	African American	0.807	0.628	1.036	0.092
	Asian	0.592	0.33	1.062	0.079
	Other	0.75	0.53	1.059	0.102
	Unknown	1.64	1.02	2.636	0.041
Hispanic Ethnicity Indicator Reference: No	Unknown	1.242	1.018	1.514	0.033
	Yes	0.982	0.721	1.337	0.907
Marital Status Reference: Married	Other	1.086	0.792	1.491	0.608
	Single	1.127	0.985	1.289	0.083

(*Continued*)

Table 6 (Continued).

Reference	Variable Evaluated	Odds Ratio	95% Confidence Interval		P-value
Payer Type Reference: Medicare	Commercial	0.84	0.681	1.036	0.103
	Medicaid	1.156	0.874	1.528	0.31
	Other	1.119	0.807	1.551	0.5
Hospital Bed Size Reference: 500+	0–99	1.141	0.593	2.193	0.693
	100–199	1.513	1.06	2.161	0.023
	200–299	1.105	0.899	1.359	0.342
	300–399	1.228	0.987	1.527	0.065
	400–499	1.128	0.928	1.372	0.225
Hospital Teaching Status Reference: Yes	No	0.887	0.761	1.032	0.121
Hospital Geography Reference: Urban	Rural	1.044	0.83	1.314	0.71
Hospital Costing Type Reference: Procedural	Ratio of cost to charges	1.257	1.073	1.472	0.005
Provider Procedure Volume Reference: 0–100	1–200	0.919	0.772	1.095	0.347
	201–300	0.586	0.425	0.807	0.001
	301–400	0.897	0.441	1.826	0.764
Provider Region Reference: South	Midwest	0.921	0.775	1.094	0.349
	Northeast	0.798	0.636	1.002	0.052
	West	1.011	0.817	1.251	0.922
Procedural Physician Specialty Reference: Pulmonary/ Thoracic Surgeon	Cardiovascular Surgeon	0.964	0.825	1.127	0.646
	General Surgeon	0.824	0.648	1.049	0.116
	Other Specialty	0.553	0.303	1.007	0.053
	Unknown	0.711	0.527	0.959	0.026
Surgical Indication Reference: Malignancy	Non-Malignancy	0.789	0.57	1.092	0.153
Surgical Approach Reference: Open	Robotic	0.625	0.529	0.74	<0.001
	Video Assisted Thoracic Surgery	0.658	0.564	0.769	<0.001
Lobe Position Reference: Right Upper	Left Lower	0.477	0.384	0.592	<0.001
	Left Upper	0.766	0.65	0.901	0.001
	Left Other	0.327	0.117	0.914	0.033
	Right Lower	0.705	0.595	0.836	<0.001
	Right Other	0.469	0.355	0.618	<0.001

(*Continued*)

Table 6 (Continued).

Reference	Variable Evaluated	Odds Ratio	95% Confidence Interval		P-value
Type of Resection Reference: Lobectomy	Multiple Resections	1.426	1.2	1.694	<0.001
	Others	0.65	0.548	0.772	<0.001
Elixhauser Score Reference: 3–4	0	0.65	0.39	1.081	0.097
	1–2	0.949	0.766	1.176	0.633
	5 +	1.055	0.808	1.378	0.692
Admission Year Reference: 2016	2015	1.238	0.94	1.629	0.128
	2017	0.931	0.769	1.127	0.465
	2018	0.913	0.738	1.129	0.399
	2019	0.925	0.767	1.115	0.412
	2020	0.817	0.661	1.01	0.061

Discussion

Greater risk of clinical complications, longer postoperative and ICU stays as well as higher costs have been documented previously for air leaks in general and PAL in various settings and patient populations,[8,14–17] but to our knowledge, this is the first real-world study to quantify the incremental healthcare resource utilization and cost impacts of PAL in patients who have received prophylactic lung sealants.

Although findings from these earlier studies cannot be directly compared with ours given differences in study populations and air leak definitions used, they do provide important historical and clinical context for our results. One 6-year retrospective study reported that post-operative air leaks lasting more than 6 days occurred in 6.7% of all patients who underwent lung resection between January 2002 and December 2007 in the Liverpool Heart and Chest Hospital NHS Foundation Trust (United Kingdom). In that study, PAL was associated with increased length of stay (p<0.0001), in-hospital mortality (p=0.003) and intensive care unit readmission (p=0.05).[16] An administrative claims data study of patients who underwent a lobectomy, segmentectomy or wedge resection in 2009–2011 found that PAL added $15,000 per patient. Consistent with the current study's findings, the authors also reported that video-assisted thoracoscopic surgery was associated with a reduced risk of PAL, which subsequently resulted in lower total hospital costs, length of stay, and risk of readmission.[17]

Another, more recent study, examined the impact of air leak complications, defined as any air leak plus pneumothorax in patients who had undergone primary lobectomy, segmentectomy, or wedge resections in 2012 through 2014 and found associated increased utilization burden, hospital costs and mortality risk.[14] This study found adjusted mean hospital costs were approximately $6500 higher in patients with air leak complications compared to costs for patients without such complications.

Yotsukura et al quantified the impact of PAL in 2278 patients who underwent pulmonary resection for lung cancer from 2014 to 2018. PAL occurred in 4.0% of those patients and was associated with the development of additional complications (p < 0.001) and a 32% increase in hospital costs (p<0.001).[15] In another retrospective analysis of 982 patients undergoing lobectomy or segmentectomy between 2014 and 2018, PAL occurred in 27% of patients. Incidence of 90-day readmission was twice that in patients with PAL compared to patients without PAL and those with PAL had 27% higher index hospital costs (p<0.0001).[18] Significant risk factors for PAL in the current study are consistent with prior literature, including male sex, resection of the right upper lobe, and an open surgical approach.[15,16,18,19]

Limitations of the present study include those inherent in using a hospital billing database for research purposes. Search/text mining techniques were used to identify the use of lung sealants; however, the absence of device identification through such techniques does not necessarily rule out the use of the device. It must be assumed that misclassification is non-differential between the group of patients using sealants who experienced PAL as compared to those who did not. The PHD does not include an ICD-10 diagnosis date, so the exact onset and duration of PALs is unknown. Additionally, the PHD does not capture nutritional status which is a significant prognostic factor for PAL.[20] Other unmeasurable variables such as provider skill, surgical technique, overall patient health, product availability in hospitals, hospital practices, and other factors (eg, forced expiratory volume, presence of incomplete or fused fissures) may lead to residual confounding after adjusted analyses. It is important to note that in the hospital readmissions that do not occur within the same hospital as the index hospital admission are not captured in the PHD and therefore may be underestimated. Lastly, the study results will not necessarily be generalizable to all hospitals in the US.

Conclusion

This analysis demonstrates that despite the use of lung sealants, PAL continues to put a burden on the healthcare system, highlighting an unmet need for improved sealant technology.

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Disclosure

Barbara H. Johnson, Stephen Johnston and Walter Danker III are employees of Johnson & Johnson and Johnson & Johnson stockholders. Mosadoluwa Afolabi is an employee under contract with Johnson & Johnson. Pranjal Tewari is an employee of Mu Sigma under contract with Johnson & Johnson. The authors report no other conflicts of interest in this work.

References

1. Lazarus DR, Casal RF. Persistent air leaks: a review with an emphasis on bronchoscopic management. *J Thorac Dis*. 2017;9:4660–4670. doi:10.21037/jtd.2017.10.122
2. Clark JM, Cooke DT, Brown LM. Management of Complications After Lung Resection: prolonged Air Leak and Bronchopleural Fistula. *Thorac Surg Clin*. 2020;30(3):347–358. doi:10.1016/j.thorsurg.2020.04.008
3. Zheng Q, Ge L, Zhou J, et al. Risk factors for prolonged air leak after pulmonary surgery: a systematic review and meta-analysis. *Asian J Surg*. 2022. doi:10.1016/j.asjsur.2022.01.001
4. Stolz AJ, Schützner J, Lischke R, Simonek J, Pafko P. Predictors of prolonged air leak following pulmonary lobectomy. *Eur J Cardio-Thoracic Surg*. 2005;27:334–336. doi:10.1016/j.ejcts.2004.11.004
5. Gondé H, Le Gac C, Gillibert A, et al. Feedback on the use of three lung sealants for preventing prolonged air leak after robot-assisted anatomical lung resection. *J Thorac Dis*. 2019;11:2705–2714. doi:10.21037/jtd.2019.06.43
6. Lequaglie C, Giudice G, Marasco R, Morte AD, Gallo M. Use of a sealant to prevent prolonged air leaks after lung resection: a prospective randomized study. *J Cardiothorac Surg*. 2012;7:106. doi:10.1186/1749-8090-7-106
7. Tansley P, Al-Mulhim F, Lim E, Ladas G, Goldstraw P. A prospective, randomized, controlled trial of the effectiveness of BioGlue in treating alveolar air leaks. *J Thorac Cardiovasc Surg*. 2006;132:105–112. doi:10.1016/j.jtcvs.2006.02.022
8. Mortman KD, Corral M, Zhang X, Berhane I, Soleas IM, Ferko NC. Length of stay and hospitalization costs for patients undergoing lung surgery with P ROGEL pleural air leak sealant. *J Med Econ*. 2018;21:1016–1022. doi:10.1080/13696998.2018.1499519
9. Pedersen TB, Honge JL, Pilegaard HK, Hasenkam JM. Comparative Study of Lung Sealants in a Porcine Ex Vivo Model. *Ann Thorac Surg*. 2012;94:234–240. doi:10.1016/j.athoracsur.2012.03.050
10. Anegg U, Lindenmann J, Matzi V, Smolle J, Maier A, Smolle-Jüttner F. Efficiency of fleece-bound sealing (TachoSil®) of air leaks in lung surgery: a prospective randomised trial☆. *Eur J Cardio-Thoracic Surg*. 2007;31:198–202. doi:10.1016/j.ejcts.2006.11.033
11. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992;45(6):613–619. doi:10.1016/0895-4356(92)90133-8
12. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care*. 1998;36(1):8–27. doi:10.1097/00005650-199801000-00004
13. van Walraven C, Austin PC, Jennings A, Quan H, Forster AJ. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. *Med Care*. 2009;47(6):626–33.11. doi:10.1097/MLR.0b013e31819432e5

14. Yoo A, Ghosh SK, Danker W, Kassis E, Kalsekar I. Burden of air leak complications in thoracic surgery estimated using a national hospital billing database. *Clinicoecon Outcomes Res*. 2017;9:373–383. doi:10.2147/CEOR.S133830
15. Yotsukura M, Okubo Y, Yoshida Y, Nakagawa K, Watanabe S-I. Predictive factors and economic impact of prolonged air leak after pulmonary resection. *Gen Thorac Cardiovasc Surg*. 2022;70:44–51. doi:10.1007/s11748-021-01677-3
16. Elsayed H, McShane J, Shackcloth M. Air leaks following pulmonary resection for lung cancer: is it a patient or surgeon related problem? *Ann R Coll Surg Engl*. 2012;94:422–427. doi:10.1308/003588412X13171221592258
17. Swanson S, Miller D, McKenna R, et al. Economic Burden of Prolonged Air Leak After Lung Resection: open Versus Video-Assisted Thoracoscopic Surgery (VATS). *Value in Health*. 2014;17:A80. doi:10.1016/j.jval.2014.03.466
18. Brunelli A, Chapman K, Pompili C, et al. Ninety-day hospital costs associated with prolonged air leak following lung resection. *Interact Cardiovasc Thorac Surg*. 2020;31(4):507–512. doi:10.1093/icvts/ivaa140
19. Bhora F, Ghosh SK, Kassis E, et al. Association of tumor location with economic outcomes and air leak complications in thoracic lobectomies: results from a national hospital billing dataset. *Clinicoecon Outcomes Res*. 2019;Jun(11):373–383. doi:10.2147/CEOR.S190644
20. Attaar A, Tam V, Nason KS. Risk Factors for Prolonged Air Leak After Pulmonary Resection. *Ann Surg*. 2020;271(5):834–844. doi:10.1097/SLA.0000000000003560