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Influence of interstitial lung disease on systemic sclerosis hospitalizations, a national study (2002–2020)

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Abstract

Systemic sclerosis (SSc) is an autoimmune connective tissue disorder that can cause generalized inflammation and is characterized by fibrosis of the skin, organs, and vasculopathy. Limited SSc is more common and typically associated with a milder disease course, whereas diffuse SSc, although less common, is linked to a higher mortality rate due to more frequent visceral organ involvement. One of the most common complications of SSc is interstitial lung disease (ILD). ILD is characterized by fibrosis, scarring, and inflammation of the lungs. ILD has a 30% prevalence and a 40% 10-year mortality in patients with SSc worldwide. Hospitalizations for SSc from 2002 to 2020 were obtained using the National Inpatient Sample (NIS), an all-payer administrative database that captures 97% of hospital discharges in the United States. The primary aim was to evaluate whether inpatient mortality, length of stay (LOS), and hospital cost differed if SSc patients had underlying ILD. We estimated multivariable logistic regression and log-normal models controlling for age, biological sex, race/ethnicity, income, and hospital setting. ILD was associated with 88% greater adjusted odds of inpatient mortality (aOR 95% CI: 1.53 to 2.31, $p < 0.001$), 15% longer stays (aOR 95% CI: 1.04 to 1.28, $p = 0.001$), and 33% higher adjusted hospital costs (aOR 95% CI: 1.26 to 1.40, $p < 0.001$). These findings suggest that SSc-ILD has a significant impact on hospitalization outcomes.

Keywords Systemic sclerosis, Interstitial lung disease, Mortality, Length of stay, Hospitalizations, Healthcare costs, National, Inpatient, Sample

Background

Systemic sclerosis (SSc) is an autoimmune connective tissue disease, characterized by dysfunction of the immune system leading to gradual fibrosis of the skin and other organs [1]. It is a rare disease with a higher prevalence in middle-aged women [2]. SSc is classified as limited and diffuse subtypes. Diffuse SSc occurs less frequently than limited SSc but is associated with greater mortality due to more frequent involvement of internal organs such as the lungs, heart, and kidneys. Diffuse SSc is more commonly associated with interstitial lung disease (ILD). ILD is the leading cause of death in patients with SSc with an estimated prevalence of 30% and 10-year mortality of 40%.[2]

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In the United States, the crude incidence of isolated SSc is 16.4 per 100,000, whereas SSc with ILD (SSc-ILD) has a crude incidence of 1.2 per 100,000 [5]. Similarly, the prevalence of isolated SSc was 24.4 per 100,000 patient population compared to 6.9 per 100,000 patient population for SSc-ILD [5]. ILD typically presents with early respiratory symptoms such as exertional dyspnea and a persistent dry cough, which can be non-specific and may be overlooked in early stages. Given the aforementioned prevalence and mortality of SSc-ILD, prompt diagnosis and management in the early stages of the disease are critical to improving outcomes.

Patients with SSc and ILD contribute significantly to healthcare costs [3]. Previous research found that hospitalized patients with SSc-ILD have an average length of stay (LOS) of 6.5 days [3]. A prior retrospective study on patients hospitalized at the University of Michigan from 2011 to 2019 demonstrated that the average cost for the management of SSc-ILD was $191,107 as compared to $101,839 for isolated SSc. Prior retrospective observational studies comparing patients with isolated SSc and SSc-ILD have been critical in establishing a relationship between systemic sclerosis and ILD as well as examining how morbidity and mortality are impacted by that relationship [3]. Our study aims to take that research one step further by identifying hospitalizations specifically for SSc and evaluating the association of ILD on hospitalization outcomes using a national database. The research will provide important information about mortality and healthcare utilization associated with isolated SSc and SSc-ILD. Notably, previous studies focused on differences between isolated SSc and SSc-ILD at a single institution, whereas this study utilizes the nationally representative National Inpatient Sample (NIS) to provide generalizable, US-specific findings.

We believe this will provide specific and insightful information about how ILD impacts hospitalizations, as well as the overall burden on the healthcare system. We focused on ILD specifically because previous studies demonstrated a substantial clinical and financial impact associated with lung involvement in SSc [4]. The aim is to uncover more focused information on the impact of hospitalizations for SSc with and without ILD and how that relates to the healthcare burden. To provide a comprehensive understanding of how the presence of ILD affects SSc hospitalization outcomes, we assessed between-ILD differences in inpatient mortality, LOS, and hospital cost irrespective of whether the patients experienced ILD-specific complications.

Methods

Data source

Data were abstracted from the 2002–2020 National Inpatient Sample (NIS), an all-payer administrative database sponsored by the Agency for Healthcare Research and Quality (AHRQ) as part of the Healthcare Cost and Utilization Project (HCUP). The NIS covers over 97% of the U.S. population and includes data on approximately 35 million hospital discharges annually [13]. Importantly, the NIS is de-identified and Health Insurance Portability and Accountability Act (HIPAA) compliant. Creighton University's Institutional Review Board acknowledged this study as Not Human Subjects Research (InfoEd record number: 2004587). The NIS is publicly available; information about purchasing the NIS can be found at: https://hcup-us.ahrq.gov/tech_assist/centdist.jsp.

Aim

The primary aim of the study was to evaluate whether inpatient mortality, LOS, and hospital cost differed by whether the patient suffered from ILD in hospitalizations for SSc. Additionally, we evaluated if age, biological sex, race/ethnicity, and hospital setting moderated the effect of ILD on these outcomes.

Cohort identification

Hospitalizations for SSc were identified using the hospitalization's primary diagnosis code. From January 2002 through September 2015, *International Classification of Disease*, *Ninth Revision* (*ICD-9*: 710.1) codes were used. From October 2015 through December 2020, *International Classification of Diseases*, *Tenth Revision* (*ICD-10*: M34) codes were used. Next, among the hospitalizations for SSc, we stratified by whether the hospitalization also carried a diagnosis for ILD on either admission or discharge. (ICD-9: 517.2; ICD-10: M34.81). Hospitalizations of patients younger than 18 years were excluded.

Descriptives

To describe the study cohort, we identified patient- and facility-level characteristics. Patient-level descriptives included age, biological sex (male, female), race/ethnicity (White, Black, Hispanic, other), income quartile (I, II, III, IV), and insurance type (Medicare, Medicaid, private, other). Facility-level descriptives included region (Northeast, Midwest, South, West), bed size (small, medium, large), and facility type (rural, urban nonteaching, urban teaching). These descriptives were presented overall and stratified by whether the SSc hospitalization also carried a diagnosis of ILD.

Statistical analysis

To evaluate the association between concomitant ILD and inpatient mortality, we estimated a logistic regression model. We estimated log-normal regression models to evaluate the association between (1) concomitant ILD and LOS and (2) concomitant ILD and cost. Cost was inflation adjusted to mid-year 2020 US dollars [14]. Next,

we assessed whether patient and facility factors (age, biological sex, race/ethnicity, facility type) moderated the effect of ILD on inpatient mortality, LOS, and cost using two-way interaction effects. For each factor we estimated an ILD-by-factor interaction effect (e.g., ILD-by-age, ILD-by-biological sex, etc.) in the respective regression model. Categorical variables were summarized as percentages and compared using Rao-Scott chi-square tests. Continuous variables were summarized as medians with interquartile ranges and compared using multivariable regression models.

The sampling design of the NIS was accounted for in all analyses. We evaluated the nonlinear functional form of age using restricted cubic splines with knots at the 10th, 50th, and 90th percentiles [15]. Statistical significance was indicated as two-tailed $p < 0.05$.

Results

Cohort descriptives

In the US from 2002 to 2020, there were an estimated 33,549 (95% CI: 31,613 – 35,485) hospitalizations for SSc; of those, 34.14% ($N = 11,453$, 95% CI: 10,554 – 12,351) also had ILD. Cohort descriptives are presented in Table 1. Briefly, hospitalizations for SSc included patients that were commonly middle-aged, white, female, and insured through Medicare. Most hospitalizations occurred at urban teaching hospitals and facilities with large bed sizes.

In-patient mortality

Table 2 presents the unadjusted and adjusted odds of inpatient mortality by ILD status. After adjusting for age, sex, race/ethnicity, income quartile, and facility type,

Table 1 Demographics of systemic sclerosis hospitalizations stratified by concomitant interstitial lung disease (ILD)

	Overall	ILD		*p*
		Yes	No	
Age, median [interquartile range]	55.91 [45.56, 66.56]	56.27 [46.64, 66.26]	55.65 [44.69, 66.71]	0.006
Biological Sex, %				
Male	19.98	21.94	18.97	0.007
Female	80.02	78.06	81.03	
Race/ethnicity, %				
White	57.94	55.18	59.38	0.018
Black	23.21	25.37	22.09	
Hispanic	12.74	13.60	12.30	
Other	6.10	5.85	6.23	
Income Quartile, %				
0-25th	26.03	26.30	25.90	0.299
26th-50th	23.88	22.35	24.67	
51st-75th	23.10	23.71	22.78	
76th-100th	26.99	27.64	26.65	
Insurance, %				
Medicare	45.74	46.61	45.29	0.483
Medicaid	13.34	13.04	13.50	
Private	34.23	34.30	34.19	
Other	6.69	6.05	7.02	
Facility Region, %				
Northeast	22.79	21.48	23.46	0.184
Midwest (North Central)	23.91	22.69	24.55	
South	35.54	37.04	34.77	
West	17.76	18.79	17.22	
Facility Bed Size, %				
Small	9.36	7.54	10.31	0.001
Medium	19.98	18.90	20.54	
Large	70.66	73.56	69.15	
Facility Type, %				
Rural	6.43	4.87	7.25	0.003
Urban nonteaching	24.38	23.83	24.67	
Urban teaching	69.19	71.30	68.09	

Data from the table is based off an estimated 33,549 patients hospitalized for systemic sclerosis between 2002–2020 in the US. The table presents the percentage of patients with systemic sclerosis, categorized by key demographic factors such as race, sex, income quartile, ect. Data is also stratified into two groups: patients with systemic sclerosis and ILD, and patients with systemic sclerosis without ILD. Comparisons highlight demographic differences between these two patient populations. A p-value < 0.05 indicates a significant difference in the % of patients with SSc for the respective demographic factor

Table 2 In-patient mortality by concomitant interstitial lung disease and demographic factors

	Unadjusted				Adjusted	
	ILD: Yes	**ILD: No**	**Ratio (95% CI)**	***p***	**Ratio (95% CI)**	***p***
***In-patient mortality*, %**	12.11	6.38	1.90 (1.55–2.32)	< 0.001	1.88 (1.53–2.31)	< 0.001
By age	Varied, see Fig. 1			0.021	Varied, see Fig. 1	0.021
By biological sex				0.087		0.128
Female	13.32	5.94	2.07 (1.65–2.61)	< 0.001	2.05 (1.62–2.59)	< 0.001
Male	11.42	8.34	1.37 (0.90–2.08)	0.141	1.41 (0.93–2.15)	0.108
By race				0.218		0.222
White	14.01	7.20	2.15 (1.68–2.76)	< 0.001	2.10 (1.64–2.70)	< 0.001
Black	8.65	8.10	1.30 (0.85–1.98)	0.232	1.27 (0.82–1.95)	0.279
Hispanic	10.35	6.91	2.18 (1.19–4.01)	0.012	2.21 (1.20–4.08)	0.011
Other	14.13	10.97	1.89 (0.79–4.39)	0.152	1.83 (0.77–4.34)	0.169
Income quartile				0.569		0.581
I	11.36	6.69	1.70 (1.16–2.48)	0.006	1.69 (1.16–2.48)	0.007
II	12.28	5.24	2.34 (1.52–3.61)	< 0.001	2.31 (1.49–3.58)	< 0.001
III	12.39	5.94	2.09 (1.37–3.17)	0.001	2.10 (1.38–3.20)	< 0.001
IV	12.49	7.50	1.66 (1.17–2.37)	0.005	1.65 (1.15–2.35)	0.006
By facility type				0.557		0.524
Rural	7.48	6.42	1.17 (0.45–3.04)	0.754	1.11 (0.42–2.93)	0.830
Urban nonteaching	14.31	7.78	1.84 (1.28–2.64)	0.001	1.83 (1.27–2.63)	0.001
Urban teaching	11.74	5.88	1.99(1.55–2.57)	< 0.001	1.97 (1.53–2.55)	< 0.001

The table presents the In-patient mortality percentage of patients with systemic sclerosis with and without ILD. The table contains both the unadjusted and adjusted odds of In-patient mortality by ILD status. The unadjusted data includes the raw results and direct relationship between variables without control for confounding factors. The adjusted data is statistically modified to control for possible confounding factors including age, sex, race, ect. A p value < 0.05 indicates a significant difference between In-patient mortality % by the respective demographic factor

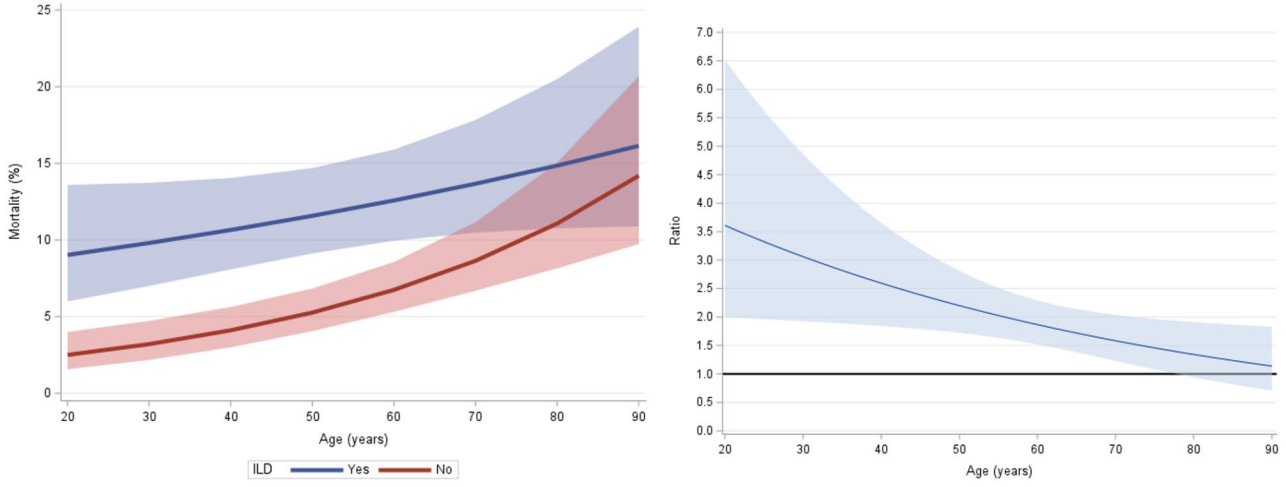

Fig. 1 Mortality rate (left) and adjusted odds ratio (right) by interstitial lung disease and age

SSc-ILD was associated with 88% greater adjusted odds of inpatient mortality compared to isolated SSc (aOR: 1.88, 95% CI: 1.53 to 2.31, $p < 0.001$; Table 2). Age moderated the effect of ILD on inpatient mortality (interaction $p = 0.021$); as age increased, the difference in mortality between SSc-ILD and isolated SSc decreased (Fig. 1). Biological sex, race/ethnicity, income quartile, and facility type did not moderate the effect of ILD on inpatient mortality (interaction $p = 0.128$, $p = 0.222$, $p = 0.581$, $p = 0.524$, respectively). Thus, the association between ILD and inpatient mortality did not vary by biological sex, race/ethnicity, income quartile, or facility type. Main effects are provided in Table 2.

Length of stay

Table 3 presents the unadjusted and adjusted LOS by ILD status. After adjusting for age, sex, race/ethnicity, income quartile, and facility type, SSc-ILD was associated with 15% longer hospital stays compared to isolated SSc (aOR: 1.15, 95% CI: 1.04 to 1.28, $p = 0.008$; Table 3). Age moderated the effect of ILD on LOS (interaction $p < 0.001$); in hospitalizations of young and middle-aged

Table 3 Length of stay by concomitant interstitial lung disease and demographic factors

	Unadjusted				Adjusted	
	ILD: Yes	**ILD: No**	**Ratio (95% CI)**	***p***	**Ratio (95% CI)**	***p***
Length of stay, days	5.16	4.38	1.18 (1.06–1.31)	0.002	1.15 (1.04–1.28)	0.008
By age	Varied, see Fig. 2			< 0.001	Varied, see Fig. 2	< 0.001
By biological sex				0.121		0.047
Female	5.06	4.42	1.14 (1.03–1.27)	0.009	1.11 (1.01–1.23)	0.038
Male	5.51	4.20	1.31 (1.08–1.60)	0.006	1.33 (1.09–1.63)	0.006
By race				0.322		0.278
White	5.00	4.10	1.22 (1.05–1.42)	0.010	1.20 (1.03–1.39)	0.020
Black	5.77	5.06	1.14 (1.01–1.29)	0.041	1.12 (0.98–1.27)	0.097
Hispanic	5.11	4.39	1.16 (1.05–1.29)	0.004	1.18 (1.06–1.31)	0.003
Other	4.35	4.87	0.89 (0.66–1.21)	0.461	0.88 (0.66–1.18)	0.417
Income quartile				0.210		0.243
I	5.31	4.73	1.12 (1.00-1.25)	0.042	1.08 (0.96–1.20)	0.197
II	5.39	4.43	1.22 (1.09–1.36)	0.001	1.19 (1.06–1.33)	0.002
III	5.17	4.89	1.06 (0.94–1.18)	0.333	1.05 (0.94–1.17)	0.417
IV	4.84	3.65	1.33 (0.98–1.80)	0.071	1.31 (0.97–1.78)	0.079
By facility type				0.165		0.188
Rural	3.23	3.27	1.01 (0.77–1.33)	0.915	1.00 (0.76–1.31)	0.988
Urban nonteaching	4.19	4.15	1.01 (0.83–1.23)	0.907	1.01 (0.83–1.23)	0.905
Urban teaching	5.66	4.59	1.23 (1.08–1.40)	0.002	1.22 (1.07–1.39)	0.003

The table presents the length of stay in days for patients with systemic sclerosis with and without ILD. The table contains both the unadjusted and adjusted odds of LOS by ILD status. The unadjusted data includes the raw results and direct relationship between variables without control for confounding factors. The adjusted data is statistically modified to control for possible confounding factors including age, sex, race, ect. A p value < 0.05 indicates a significant difference between LOS by the respective demographic factor

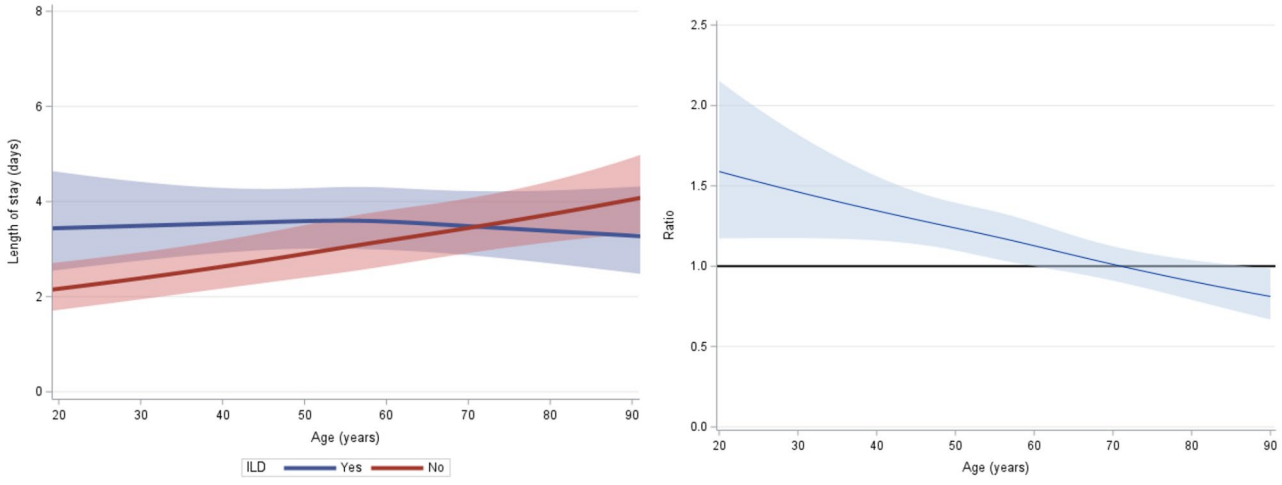

Fig. 2 Adjusted length of stay (left) and difference ratio (right) by interstitial lung disease and age

patients, LOS was longer in those with ILD (Fig. 2). Biological sex also moderated the effect of ILD on LOS (interaction $p = 0.047$). Compared to isolated SSc, SSc-ILD was associated with longer hospital stays in female and male patients; in females SSc-ILD was associated with 11% longer adjusted stays and in males SSc-ILD was associated with 33% longer stays compared to isolated SSc (Female- aOR: 1.11, 95% CI: 1.01 to 1.23, $p = 0.038$; Male- aOR: 1.33, 95% CI: 1.09 to 1.63, $p = 0.006$, Table 3). Race/ethnicity, income quartile, and facility type did not moderate the effect of ILD on LOS (interaction $p = 0.278$, $p = 0.243$, $p = 0.188$, respectively); main effects are provided in Table 3.

Cost

Table 4 presents the unadjusted and adjusted cost by ILD status. After adjusting for age, sex, race/ethnicity, income quartile, and facility type, SSc-ILD was associated with 33% greater adjusted cost compared to isolated SSc (aOR: 1.33, 95% CI: 1.26 to 1.40, $p < 0.001$; Table 4). Age moderated the effect of ILD on cost (interaction $p < 0.001$); as age increased, the difference in cost between

Table 4 Hospital cost by concomitant interstitial lung disease and demographic factors

	Unadjusted				Adjusted	
	ILD: Yes	ILD: No	Ratio (95% CI)	*p*	Ratio (95% CI)	*p*
***Cost*, $**	14,625	10,744	1.36 (1.29–1.44)	< 0.001	1.33 (1.26–1.40)	< 0.001
By age	Varied, see Fig. 3			< 0.001	Varied, see Fig. 3	< 0.001
By biological sex				0.006		0.002
Female	13,967	10,672	1.31 (1.23–1.39)	< 0.001	1.28 (1.18–1.38)	< 0.001
Male	17,145	11,052	1.55 (1.39–1.74)	< 0.001	1.54 (1.38–1.72)	< 0.001
By race				0.598		0.599
White	14,128	10,159	1.39 (1.29–1.50)	< 0.001	1.36 (1.27–1.47)	< 0.001
Black	14,785	11,422	1.29 (1.17–1.43)	< 0.001	1.26 (1.15–1.39)	< 0.001
Hispanic	15,824	11,618	1.36 (1.23–1.51)	< 0.001	1.33 (1.20–1.48)	< 0.001
Other	16,304	12,782	1.28 (1.08–1.51)	0.005	1.27 (1.08–1.50)	0.004
Income quartile				0.469		0.273
I	13,845	10,274	1.35 (1.22–1.49)	< 0.001	1.28 (1.16–1.41)	< 0.001
II	13,118	10,213	1.28 (1.18–1.40)	< 0.001	1.26 (1.16–1.37)	< 0.001
III	15,269	11,141	1.37 (1.24–1.52)	< 0.001	1.35 (1.23–1.60)	< 0.001
IV	16,251	11,360	1.43 (1.29–1.59)	< 0.001	1.42 (1.28–1.58)	< 0.001
By facility type				0.009		0.008
Rural	9,066	7,222	1.26 (1.09–1.45)	0.001	1.23 (1.06–1.42)	0.006
Urban nonteaching	10,799	9,080	1.19 (1.10–1.28)	< 0.001	1.18 (1.10–1.28)	< 0.001
Urban teaching	16,584	11,864	1.40 (1.30–1.50)	< 0.001	1.39 (1.30–1.49)	< 0.001

The table presents the hospital cost in dollars for patients with systemic sclerosis with and without ILD. The table contains both the unadjusted and adjusted hospital cost by ILD status. The unadjusted data includes the raw results and direct relationship between variables without controlling for confounding factors. The adjusted data is statistically modified to control for possible confounding factors including age, sex, race, ect. A p value < 0.05 indicates a significant difference between hospital cost by the respective demographic factor

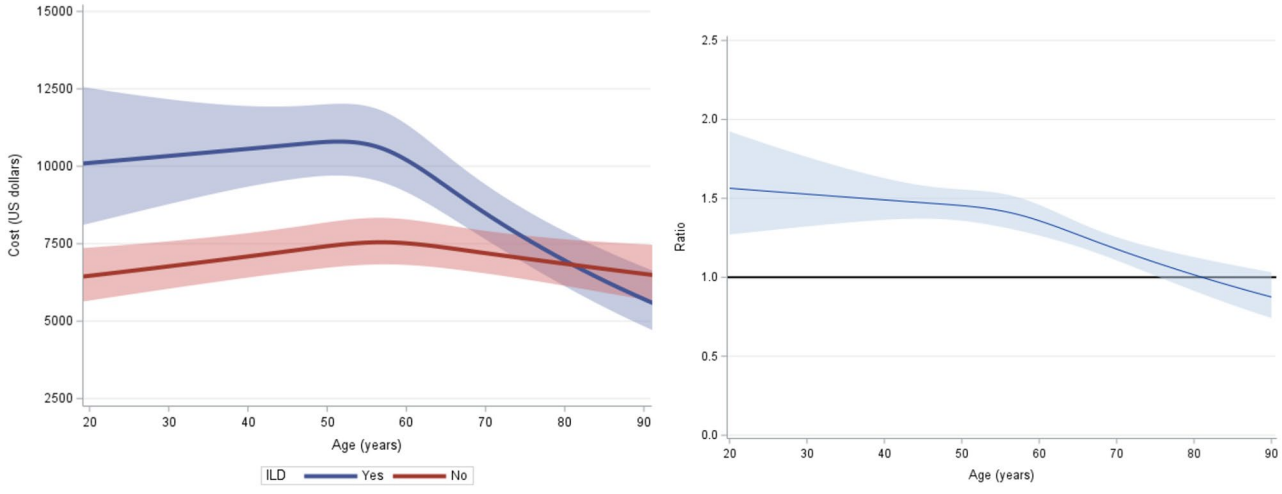

Fig. 3 Adjusted hospital cost (left) and difference ratio (right) by interstitial lung disease and age

patients with and without ILD decreased (Fig. 3). Biological sex moderated the effect of ILD on cost (interaction $p = 0.002$). Compared to isolated SSc, SSc- ILD was associated with greater adjusted cost in males relative to females; in females, SSc-ILD was associated with 28% greater adjusted cost and in males SSc-ILD was associated with 54% greater adjusted cost compared to isolated SSc (Female- aOR: 1.28, 95% CI: 1.18 to 1.38, $p < 0.001$; Male- aOR: 1.54, 95% CI: 1.38 to 1.72, $p < 0.001$, Table 4). Facility type moderated the effect of ILD on cost (interaction $p = 0.008$). Compared to isolated SSc, SSc-ILD was associated with greater adjusted cost in rural, urban nonteaching, and urban teaching facilities; in rural facilities SSc-ILD was associated with 23% greater adjusted cost, in urban nonteaching facilities SSc-ILD was associated with 18% greater adjusted cost, and in urban teaching facilities SSc-ILD was associated with 39% greater adjusted cost compared to isolated SSc (Rural- aOR: 1.23, 95% CI: 1.06 to 1.42, $p = 0.006$; Urban nonteaching- aOR: 1.18, 95% CI: 1.10–1.28, $p < 0.001$; Urban teaching- aOR: 1.39, 95% CI: 1.30 to 1.49, $p < 0.001$). Race/ethnicity and income quartile did not moderate the effect of ILD on

cost (interaction $p = 0.599$ and $p = 0.273$, respectively). Main effects are provided in Table 4.

Discussion

In this retrospective, nationally representative U.S. analysis, SSc-ILD was associated with 88% greater adjusted odds of inpatient mortality compared to isolated SSc (aOR 95% CI: 1.53 to 2.31). The unadjusted inpatient mortality rate for SSc-ILD was 12.11% compared to 6.38% for isolated SSc. Although the relative difference in mortality between SSc-ILD and isolated SSc appeared to diminish with age, this may reflect survivor bias. For example, older patients with SSc-ILD may represent a more resilient subgroup who survived earlier complications. Alternatively, age-related comorbidities in all SSc patients may overshadow the added mortality risk conferred by ILD alone. Notably, the increased mortality in patients with SSc-ILD compared to isolated SSc was experienced by patients in all income quartiles. These findings underscore the significant, widespread impact of ILD on mortality outcomes across diverse socioeconomic backgrounds. Our study found that males with systemic sclerosis-associated interstitial lung disease (SSc-ILD) had longer hospital stays and higher costs than females, suggesting more severe disease. Despite these indicators, we observed no significant difference in inpatient mortality between sexes. This could be due to men presenting later in the disease course, leading to more severe manifestations at hospitalization, or the possibility that the most severely ill male patients died before hospitalization, resulting in selection bias. Additionally, ILD was associated with increased adjusted odds of inpatient mortality in hospitalizations of White and Hispanic patients, highlighting a differential impact of SSc-ILD on mortality ($p < 0.001$, $p = 0.011$, respectively). The demographic-specific associations between ILD and inpatient mortality suggest potential areas of targeted interventions and healthcare policies such as more widespread use of interpreter services and more specific disease counseling and education.

Previous studies have explored the relationship between SSc and ILD without distinguishing between inpatient and outpatient data. There is also limited research on differences in inpatient hospitalization outcomes: including mortality, LOS, and cost. In addition, most work on SSc-ILD focused on single-centers whereas our study used data from a national database (i.e., NIS). A Brazilian observational study of 380 patients with SSc demonstrated a significant increase in overall mortality for patients with SSc-ILD ($p < 0.001$) [6].: of the 72 patients that died, 57 had SSc-ILD. Similarly, a Norwegian study in 2019 documented cumulative mortality rates at 1, 5, and 10 years of 39% for SSc patients with lung fibrosis and 19% for SSc patients without lung fibrosis [7]. These findings are consistent with our study which found an inpatient mortality rate of 12.1% hospitalized patients with SSc-ILD compared to a 6.4% for isolated SSc ($p < 0.001$). In contrast, a single center study from the University of Pennsylvania Hospital following a retrospective cohort of SSc patients from 2001 to 2011 found that the presence of ILD in patients with SSc was not significantly associated with higher inpatient mortality [8]. While this contradicts the findings we present, as previously mentioned, our study is based on a national level with data from hospitals across the United States.

In terms of LOS, SSc-ILD was associated with 15% longer adjusted stays compared to isolated SSc (aOR 95% CI: 1.04 to 1.28). The prolonged LOS associated with SSc-ILD emphasizes the complexity of managing these patients and the need for comprehensive care strategies to address their healthcare needs. This increased LOS in SSc-ILD hospitalizations remained significant in males, females, and Black, White, and Hispanic populations. Additionally, LOS was increased in all income quartiles, however the increase was statistically significant in income quartiles I and II. These findings suggest that the financial impact of SSc-ILD (e.g., the cost associated with staying in the hospital longer) may be felt more acutely by patients in lower income brackets thereby highlighting disparities in financial burden.

Similar to our findings, a 2002–2003 NIS study found that SSc-ILD was associated with increased odds of inpatient mortality and LOS; specifically, SSc-ILD was associated with 2.63 greater odds of inpatient mortality and 7.25% longer stays compared to isolated SSc [9]. In contrast to this, a 2020 study out of England documented a median LOS of less than one day consistent across all clinical groups [10]. Our study demonstrated that SSc-ILD was associated with 15% increased adjusted LOS compared to isolated SSc hospitalizations (aOR 95% CI: 1.04 to 1.28).

Relatedly, we showed a nearly $4,000 increase in hospital associated costs for SSc-ILD hospitalizations versus isolated SSc ($p < 0.001$). SSc-ILD was associated with greater costs compared to isolated SSc for all ages, genders, races, income quartiles, and hospital facility types (rural and urban). These cost differentials underscore the substantial economic burden imposed by SSc-ILD on both patients and the healthcare system, necessitating cost-effective interventions and healthcare resource allocation strategies to mitigate financial strain.

Inpatient visits are associated with a large portion of hospital costs in the US; across all diagnoses and illnesses, the average adjusted cost per inpatient stay at a community hospital was an estimated $14,101. Relatedly, 5.2% of people under 65 years had at least one hospital stay in the US in 2018 [16]. Regarding SSc and ILD, a 2018 US study found that 53% of patients with SSc-ILD

had at least 1 inpatient admission over a 5-year period while only 43% of isolated SSc patients had an inpatient admission over that same time period [12]. The same study demonstrated increased healthcare costs for patients with SSc-ILD, with most of the cost attributed to inpatient visits. Similarly, a 2020 study in Australia found that SSc-ILD patients used healthcare services averaging approximately $48,368 AUD per patient with SSc-ILD vs. $33,657 AUD for patients with SSc without ILD [11]. These findings all align closely with the results presented in our study.

SSc-ILD has a significant prevalence and impact on patients and the healthcare system. Our study demonstrated statistical differences between isolated SSc and SSc-ILD on inpatient mortality, LOS, and hospital cost. Despite our significant findings, there were limitations. One limitation of using the NIS database is that it provides only inpatient-level information with no post-hospitalization information. In addition, our database search did not specify whether an ILD diagnosis was present on admission or discharge so it is possible that some ILD cases may have been undiagnosed at admission and only identified during hospitalization. Similarly, the database does not provide information on cause of death for the patients included in our study. The NIS also provides limited information on clinical characteristics and relies on administrative billing codes to identify diagnoses and procedures. This reliance on administrative billing codes makes it difficult to distinguish between complications and comorbidities in any given patient population. Despite these limitations, this study provides valuable insight into national trends in SSc-ILD that may inform strategies to improve patient outcomes.

Conclusions

Our study highlights the substantial impact of SSc-ILD, demonstrating significantly higher inpatient mortality, longer hospital stays, and greater costs compared to hospitalizations for isolated SSc. These differences were consistent across age groups, biological sex, race/ethnicity, income quartiles, and hospital facility types. Our findings, drawn from the National Inpatient Sample (NIS) database, reinforce and expand upon previous research by providing a broad, nationally representative perspective on the implications of SSc-ILD. The increased mortality and hospital burden associated with SSc-ILD underscore the need for heightened awareness, early diagnosis, and improved treatment strategies for managing this complex condition. Future studies should aim to build on these findings, exploring the mechanisms behind these disparities and identifying specific strategies to improve outcomes for SSc-ILD patients.

Abbreviations

ILD	Interstitial lung disease
SSc	Systemic sclerosis
LOS	Length of stay
NIS	National inpatient sample
HCUP	Healthcare cost and utilization project
AHRQ	The agency for healthcare research and quality
ICD	International classification of disease

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Author contributions

J.J -Innovation of the idea, paper writing, study Design. N.F.-Innovation of the idea, writing the paper. A.J.-Writing the paper, proofreading the paper, finalizing the conclusion. D.D.-Data analysis with methods and results writing N.A.-Study design, innovation of the idea. M.M.-Literature review and helping with paper reviewing. J.N.-Literature reviewed for selection of articles for manuscript and final revision. A.T.- Innovation of the topic, study design, literature review and final interpretation with implementation.

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Data availability

Data is provided within the manuscript. The National Inpatient Sample (NIS) is publicly available through the Healthcare Cost and Utilization Project (HCUP).

Declarations

Ethics approval and consent to participate

Creighton University's Institutional Review Board acknowledged this study as Not Human Subjects Research (InfoEd record number: 2004587).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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