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Spinal Cord Stimulation Infection Rate and Risk Factors: Results From a United States Payer Database

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Objective: Surgical site infections can cause negative clinical and economic outcomes. A recent international survey on Spinal Cord Stimulation (SCS) infection control practices demonstrated low compliance with evidence-based guidelines. This study defines infection rate for SCS implants and identifies infection risk factors.

Materials and Methods: A retrospective analysis of the MarketScan® Databases identified patients with SCS implant (2009–2014) and continuous health plan enrollment for ≥12-months (12 m) preimplant. For logistic regression analysis, patients were enrolled for 12 m postimplant. Kaplan–Meier and Cox Proportional Hazard survival analyses assessed time to infection, with infection rate reported at 12 m postimplant. Logistic regression characterized risk factors based on demographics, comorbidities, and clinical characteristics.

Results: In the logistic regression (n = 6615), 12 m device-related infection rate was 3.11%. Infection risk factors included peripheral vascular disease (OR, 1.784; 95% CI: 1.011–3.149; p = 0.0457) and infection in 12 m before implant (OR, 1.518; 95% CI: 1.022–2.254; p = 0.0386). The odds of patients experiencing an infection decreased by 3.2% with each additional year of age (OR, 0.968; 95% CI: 0.952–0.984; p < 0.0001). Survival analysis (n = 13,214) identified prior infection (HR, 1.770; 95% CI: 1.342–2.336; p < 0.0001) as a risk factor. Infection was less likely in older patients (HR, 0.974; 95% CI: 0.962–0.986; p < 0.0001). Expected risk factors including obesity, diabetes, and smoking were not identified as risk factors in this analysis. There was no significant difference between infection rate for initial and replacement implants.

Conclusions: The 3.11% SCS-related infection rate within 12 m of implant emphasizes the need for improved infection control practices. Research is needed to limit SCS infections in younger patients and those with infection history.

Keywords: Complication, healthcare utilization, infection, spinal cord stimulation

Conflict of Interest: Steven Falowski serves as a consultant for Abbott, Medtronic, and Nevro Corp. He has received research support from Abbott and Medtronic. David Provenzano has served as a consultant for Abbott, Biotronik, Bioness, Boston Scientific, Halyard, Medtronic, Nevro, and Sollis. He has received research support from Abbott and Medtronic. A.H. Doth and Y. Xia are employed by and minor shareholders of Medtronic.

INTRODUCTION

Significant interest has been placed on surgical site infections (SSIs) associated with implantable pain therapies including spinal cord stimulation (SCS). SSIs are associated with significant humanistic, economic, and clinical consequences. Recent publications have highlighted the consequences of SSIs for implantable pain therapies and the low levels of compliance with evidence-based guidelines (1–3). An analysis of the United States Closed Claims Project data base on implantable pain therapies indicated that infection was the most common damaging event (i.e., 23% of all claims) for surgical device-related claims (4).

To date, published SSI rates for SCS have ranged from 1 to 10% (1,5–11). SSI incidence rates for implantable pain therapies have been gathered from data from retrospective and prospective studies, randomized controlled trials, and systematic reviews. Two systematic reviews have reported SCS SSI rates of 3.4–4.6% (5,11). The number of patients in the primary studies are limited, ranging from 24 to 2737 patients (1,7,8).

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Emphasis has also been placed on identifying factors that modify SSI risk for implantable pain therapies, including medical comorbidities and reoperation for battery changes or revisions. Because of the limitations of existing neuromodulation data, risk factors are often extrapolated from other surgical subspecialties. For instance, in cardiac surgery, a greater number of operations for pacemaker implantation increased the risk of SSI (12). In addition to medical comorbidities, previous research has suggested that SSI infections may be higher with revision and replacement surgery, especially at the site for the implantable pulse generator (13).

The purpose of the present study is to define and compare the infection rate for both initial and replacement SCS implants by examining a large United States payer data base. Additionally, identification of patient characteristics that increase the risk for SCS infection were sought to be determined.

MATERIALS AND METHODS

Data Source

We utilized data from the Truven MarketScan® Commercial Claims and Encounters (CCAE) and Medicare Supplemental Databases for the study. These research data bases consist of fully adjudicated and paid insurance claims data for between 25 and 60 million individuals annually. They capture de-identified, patient-level health data, including clinical utilization, expenditures, patient demographic information, enrollment information, outpatient service, and outpatient prescription claims. These data bases reflect the real-world utilization of treatment patterns and costs by linking paid claims and encounter data to detailed patient information across different sites and providers.

Study Population Selection

Patient-level data were extracted from the Marketscan CCAE Database for the years 2009–2014 and Medicare Supplemental Database for the years 2011–2014. Patients were selected for inclusion in the study if they had a record of a SCS generator implant or replacement during the study period and were more than 18 years of age (Supporting Information Table S1). The date of the first observed generator implant defined the index date for each patient. Patients were excluded if they did not meet any of the inclusion criteria, or if they had a record of other neurostimulation devices or procedures or intrathecal drug delivery systems at any point during the study period (Supporting Information Table S2). Patients were classified into one of two mutually exclusive groups 1) initial implant or 2) replacement implant. Figure 1 outlines the algorithm to classify these patients. Patients were required to have at least 12 months of continuous medical and prescription enrollment prior to the index date. Patients with 12 months of continuous medical and pharmacy enrollment after index were included in the logistic regression analysis, and all patients were included in the survival analysis regardless of post-index enrollment, up to 12 months post-index date. For the survival analysis, the follow-up period was from the index date to the earliest of either 1) the end of patient enrollment in the data or 2) the date of SCS infection.

Patient Infection Classification

SCS device-related infections were identified by either of two conditions occurring up to 365 days following SCS generator device implant.

1. A patient had the presence of device-related infection code as defined by *International Classification of Diseases Ninth Revision-CM code* (ICD-9-CM code) 996.63 (infection and inflammatory reaction due to nervous system device, implant, and graft); or
2. A patient had a record of a device-related procedure code for the removal or revision of their generator implant within 12 months after index date and the presence of at least one predefined diagnosis indicating an all-cause infection (Supporting Information Table S3) on the same date of service as the revision or removal procedure.

Variables of Interest

The primary outcomes of this study were the rate of SCS device-related infection, and the risk factors associated with SCS device-related infection. Independent variables included clinical characteristics, common comorbidities, and demographic information. Demographic information included age, gender, region, insurance type (commercial or Medicare), and group (initial implant group or replacement implant group).

The Charlson comorbidity index (CCI) was also used to estimate the health condition of patients. The CCI score uses healthcare utilization and comorbidity information recorded on the index date or <12 months before index. The CCI code listings can be found in Supporting Information Table S4.

In addition, data on 17 specific comorbidities known to be infection risk factors in other populations were also included (Supporting Information Table S5). Each of these comorbidities was recorded on the index date or <12 months before. Clinical characteristics including the site-of-service of generator implant, and the presence of any type of infection within 12 months prior to index date were examined.

Statistical Analysis

Logistic Regression

First, we examined the 6615 patients with 12 months of healthcare utilization data available after index date, which allows for a consistent picture of healthcare encounters for all patients. A descriptive analysis was performed to evaluate the infection rate at 12 months postimplant. The baseline characteristics were summarized separately for initial and replacement patients by those who experienced an infection vs. those who did not. Patient demographics, most common comorbidities, and clinical characteristics were examined using *t*-test, chi-square or Fisher's exact test. Then, a logistic regression was performed to characterize the risk factors for infection. In the logistic regression, the binary dependent variable examined was presence of infection, and other characteristics (including demographic information, comorbidities, and clinical characteristics) were assessed as independent variables in the logistic regression model. These independent variables were selected based upon previous literature suggesting their link as a potential risk factor for SSIs in the SCS, cardiac, orthopedic spine, or other literature (14–22). Analyses were performed to assess multicollinearity for all covariates; there was no evidence to show interaction among covariates.

Survival Analysis

We confirmed our results with a different patient population, including all 13,214 eligible SCS-implanted patients regardless of the amount of time available after index date, using survival analyses, capturing all healthcare utilization available after index date. This analysis allows us to examine the time to infection.

First, Kaplan–Meier curves were constructed to compare the survival patterns between the initial group and the replacement

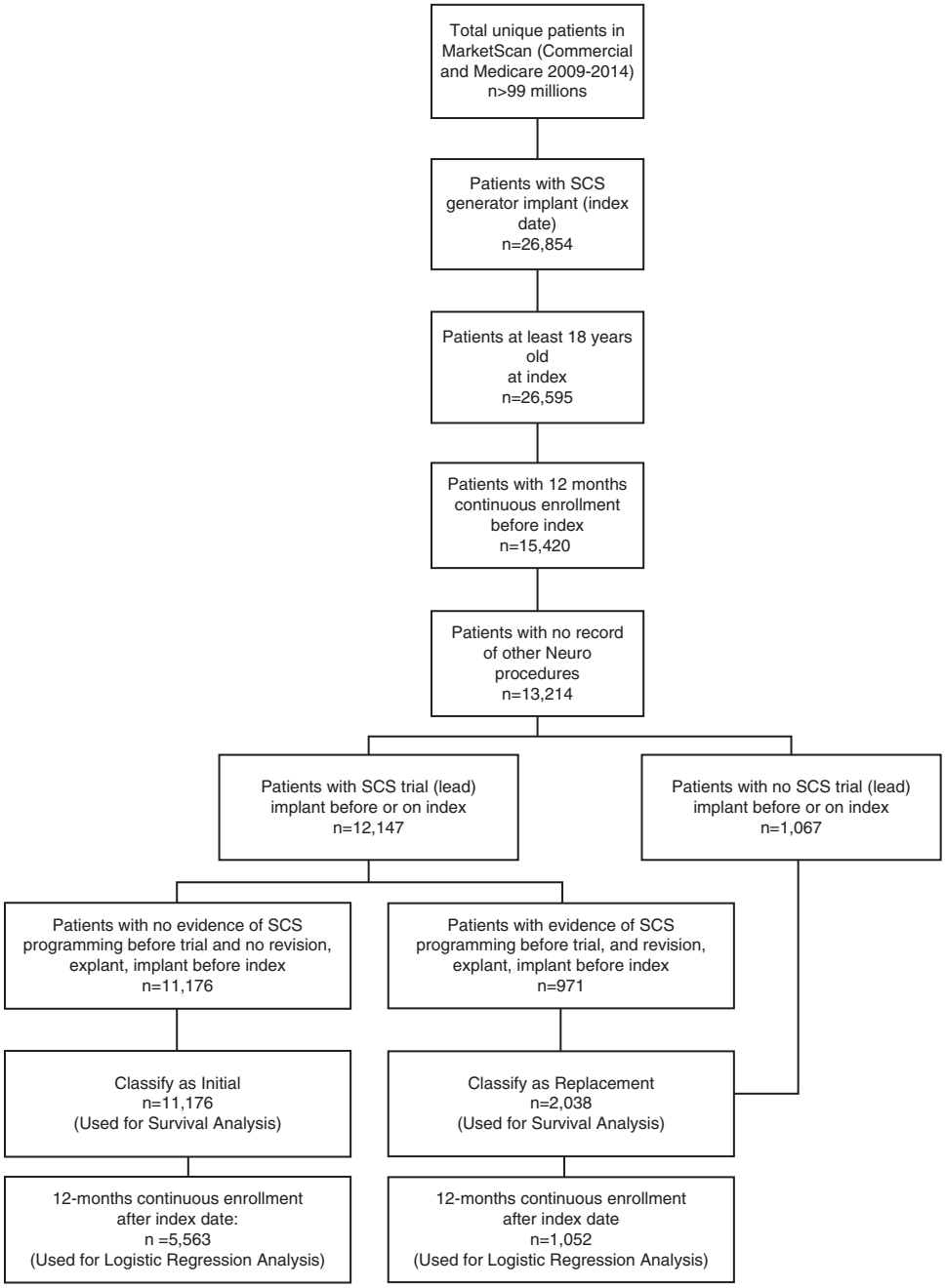

Figure 1. Attrition diagram for study patients.

group, and a log-rank test was used to indicate whether there was any statistically significant difference between the survival curves. Then, a Cox proportional hazard regression was applied to determine the effect of various risk factors on SCS infection. The dependent variables were time and censor (value of censor was 1, which indicated an event of SCS infection, while 0 indicated censoring). The time represented follow-up time, measured in days. The independent variables included patient demographic information (age, gender, region, etc.), comorbidities, and clinical characteristics. The Cox proportional hazard model allowed us to consider covariates in the model, thus providing us with hazard ratios (HRs) for each potential risk factor. HRs and confidence intervals were calculated and reported. Analyses were performed which confirmed that the proportional hazards assumption was satisfied.

All data were imported and maintained as SAS data files. All statistical tests used a significance level of 0.05 (p value <0.05). All analyses were performed using SAS Software, Version 9.2 (SAS Institute, Inc., Cary, NC, USA).

RESULTS

Logistic Regression

A total of 26,854 patients had a record of SCS generator implant or replacement during the study period. The final study population was 6615 patients after applying all inclusion and exclusion criteria. A total of 5563 (84.1%) patients were identified

Table 1. Baseline Patient Demographics and Descriptive Analysis for Initial and Replacement Cohorts by Infection Status.

	Initial group (N = 5563)			Replacement group (N = 1052)		
	Infection	Infection		Infection	Infection	
	Yes (N = 172)	No (N = 5391)	p value	Yes (N = 34)	No (N = 1018)	p value
Age (Mean [SD])	51.0 [13.6]	53.9 [12.7]	0.0033*	49.8 [9.9]	54.3 [13.0]	0.0429*
Gender						
Male	40.12%	39.60%	0.8922	41.18%	39.10%	0.8069
Female	59.88%	60.40%		58.82%	60.90%	
Region						
Northeast	6.40%	8.53%	0.1304	14.71%	12.18%	0.1690
North Central	29.07%	27.73%		17.65%	25.93%	
South	52.33%	46.34%		35.29%	43.91%	
West	8.72%	14.84%		26.47%	15.52%	
Unknown	3.49%	2.56%		5.88%	2.46%	
Insurance type						
Commercial	84.88%	82.06%	0.3416	94.12%	80.94%	0.0695
Medicare	15.12%	17.94%		5.88%	19.06%	
Charlson Comorbidity Index						
0	51.16%	50.23%	0.1562	44.12%	50.39%	0.2614
1	22.67%	25.41%		26.47%	25.54%	
2–3	21.51%	16.51%		14.71%	17.78%	
≥4	4.65%	7.85%		14.71%	6.29%	
Cardiac dysrhythmias						
Yes	8.14%	10.89%	0.2529	0.00%	11.89%	0.0259*
No	91.86%	89.11%		100.00%	88.11%	
Congestive heart failure						
Yes	2.33%	3.06%	0.8202	2.94%	3.93%	1.0000
No	97.67%	96.94%		97.06%	96.07%	
COPD						
Yes	10.47%	11.09%	0.7963	14.71%	10.12%	0.3841
No	89.53%	88.91%		85.29%	89.88%	
Depressive disorders						
Yes	50.00%	46.87%	0.4188	44.12%	36.35%	0.3547
No	50.00%	53.13%		55.88%	63.65%	
Diabetes type 1						
Yes	4.07%	3.32%	0.5904	8.82%	3.63%	0.1352
No	95.93%	96.68%		91.18%	96.37%	
Diabetes type 2						
Yes	24.42%	22.02%	0.4551	20.59%	19.74%	0.9033
No	75.58%	77.98%		79.41%	80.26%	
GERD						
Yes	18.60%	21.59%	0.3479	14.71%	21.41%	0.3464
No	81.40%	78.41%		85.29%	78.59%	
Hyperlipidemia						
Yes	43.02%	42.48%	0.8868	41.18%	39.69%	0.8613
No	56.98%	57.52%		58.82%	60.31%	
Hypertension						
Yes	58.14%	55.26%	0.4544	50.00%	50.10%	0.9910
No	41.86%	44.74%		50.00%	49.90%	
Hypothyroidism						
Yes	13.95%	16.06%	0.4574	20.59%	15.72%	0.4445
No	86.05%	83.94%		79.41%	84.28%	
Lumbar disk disease						
Yes	75.58%	69.67%	0.0964	58.82%	50.69%	0.3506
No	24.42%	30.33%		41.18%	49.31%	
Overweight and obesity						
Yes	14.53%	13.56%	0.7133	14.71%	11.49%	0.5649
No	85.47%	86.44%		85.29%	88.51%	
Osteoarthritis						
Yes	70.35%	67.35%	0.4091	73.53%	54.22%	0.0261*
No	29.65%	32.65%		26.47%	45.78%	

Table 1. *Continued*

	Initial group (*N* = 5563)			Replacement group (*N* = 1052)		
	Infection	Infection		Infection	Infection	
	Yes (*N* = 172)	No (*N* = 5391)	*p* value	Yes (*N* = 34)	No (*N* = 1018)	*p* value
Other coronary artery disease						
Yes	13.37%	12.32%	0.6788	11.76%	10.90%	0.7816
No	86.63%	87.68%		88.24%	89.10%	
Peripheral vascular disease						
Yes	6.98%	5.12%	0.2792	11.76%	4.72%	0.0821
No	93.02%	94.88%		88.24%	95.28%	
Sleep apnea						
Yes	21.51%	15.66%	0.0384*	11.76%	14.83%	0.8070
No	78.49%	84.34%		88.24%	85.17%	
Smoking						
Yes	14.53%	14.43%	0.9697	20.59%	12.28%	0.1502
No	85.47%	85.57%		79.41%	87.72%	
Evidence of prior infection within 12-month period before index date						
Yes	12.79%	9.98%	0.2277	29.41%	11.59%	0.0018*
No	87.21%	90.02%		70.59%	88.41%	
Setting of service on the index date						
Outpatient	68.02%	71.55%	0.6166	44.12%	63.36%	0.0994
ASC	10.47%	10.41%		14.71%	10.31%	
Inpatient	5.81%	5.79%		8.82%	6.29%	
Other	5.81%	3.67%		2.94%	4.42%	
Unknown	9.88%	8.59%		29.41%	15.62%	

*$p < 0.05$.

as the initial group, and 1052 (15.9%) patients were identified as the replacement group (Fig. 1).

A total of 3.11% of SCS patients (206/6615) experienced an infection event within 12 months after index date. In addition, the difference of infection rates between the initial group (3.09%; 172/5563) and the replacement group (3.23%, 34/1052) was not statistically significant ($p = 0.8104$).

The baseline characteristics for SCS patients and the results from the descriptive analysis are shown in Table 1. The demographic information, comorbidities, and clinical characteristics were shown by groups (initial group vs. replacement group) and by infection status (whether these patients experienced an infection event within 12 months after index date). The descriptive analysis examines factors individually to identify differences between those with and without infection. Across both cohorts, patients who experienced a device-related infection within 12 months after generator implant were slightly younger (initial group: 51.0 [13.6]; replacement group: 49.8 [9.9]; mean [standard deviation]) than those who did not (53.9 [12.7] for initial group, and 54.3 [13.0] for replacement group). For patients in the initial group, patients with sleep apnea had a higher rate of infection compared with patients without (21.51 vs. 15.66%, $p = 0.0384$). For patients in the replacement group, the infection rates were higher in patients with osteoarthritis or those who had evidence of a prior infection in the 12 months before their index date than patients without (osteoarthritis: 73.53 vs. 54.22%, $p = 0.0261$; prior infection: 29.41 vs. 11.59%, $p = 0.0018$). In addition, patients with cardiac dysrhythmias had a lower rate of infection than those without (0.00 vs. 11.89%, $p = 0.0259$).

Logistic regression results ($n = 6615$) are shown in Table 2 and demonstrate which characteristics are most likely to be risk factors when considering all factors together. The regression identified that risk factors for SCS device-related infection include a comorbidity of peripheral vascular disease (OR, 1.784; 95% CI: 1.011–3.149; $p = 0.0457$) as well as a history of previous (all-cause) infection in the 12-month period prior to SCS implant (OR, 1.518; 95% CI: 1.022–2.254; $p = 0.0386$). Elderly patients were less likely to have infection; for each additional year of age at any timepoint, patients are 3.2% less likely to have an infection (OR, 0.968; 95% CI: 0.952–0.984; $p < 0.0001$; Table 3) which is true regardless of age group division chosen. Notably, there were no observed differences for rate of infection when looking at insurance type or setting of service of the index implant.

Survival Analysis

For the survival analysis, we identified all SCS-implanted patients, but we did not require that patients have any period of continuous enrollment after index date. After all inclusion and exclusion criteria, the final study population was 13,214 patients. A total of 11,176 (84.6%) patients were identified as the initial group, and 2038 (15.4%) patients were identified as the replacement group. The attrition of SCS population selection for this study is shown in Figure 1.

The patient demographic information and other baseline characteristics for patients in the survival analysis cohort are shown in Table 4. In the initial group, patients who experienced the SCS infection events were slightly younger than patients who did not (51.6 [13.5] vs. 54.2 [12.8], respectively). Except for age, we identified that there were no statistically significant demographic differences between patients with SCS infection and patients without in either group. Across both cohorts, if patients had evidence of an infection in the 12 months before their index date, they had a significantly higher likelihood to experience SCS infection than

Table 2. The Result of Logistic Regression for Infection Within 12 Months After Index Date.

	Odds ratio	95% confidence interval		*p* value
Age	0.968	0.952	0.984	<0.0001*
Gender				
Male	0.975	0.723	1.316	0.8697
Female	Reference			
Region				
Northeast	0.808	0.470	1.388	0.4403
North Central	0.974	0.695	1.366	0.8797
South	Reference			
West	0.760	0.481	1.200	0.2389
Unknown	1.404	0.665	2.964	0.3738
Insurance type				
Commercial	0.729	0.419	1.269	0.2639
Medicare	Reference			
Charlson Comorbidity Index				
0	Reference			
1	0.868	0.583	1.292	0.4855
2–3	1.108	0.682	1.801	0.6780
≥4	0.659	0.300	1.445	0.2979
Group				
Initial group	0.882	0.602	1.295	0.5225
Replacement group	Reference			
Setting of service on the index date				
Outpatient	Reference			
Ambulatory surgical center	1.229	0.779	1.938	0.3747
Inpatient	1.204	0.671	2.160	0.5330
Other	1.457	0.772	2.750	0.2454
Unknown	1.521	0.987	2.344	0.0572
Cardiac dysrhythmias				
Yes	0.588	0.334	1.034	0.0653
No	Reference			
Congestive heart failure				
Yes	0.773	0.297	2.011	0.5973
No	Reference			
Chronic obstructive pulmonary disease (COPD)				
Yes	1.072	0.650	1.766	0.7857
No	Reference			
Depressive disorders				
Yes	1.057	0.794	1.407	0.7035
No	Reference			
Diabetes 1				
Yes	1.335	0.642	2.775	0.4391
No	Reference			
Diabetes 2				
Yes	1.124	0.716	1.762	0.6121
No	Reference			
GERD				
Yes	0.779	0.537	1.129	0.1869
No	Reference			
Hyperlipidemia				
Yes	1.061	0.774	1.454	0.7145
No	Reference			
Hypertension				
Yes	1.245	0.903	1.718	0.1814
No	Reference			
Hypothyroidism				
Yes	0.974	0.651	1.458	0.8987
No	Reference			
Lumbar disk disease				
Yes	1.298	0.936	1.799	0.1177
No	Reference			
Overweight and obesity				
Yes	0.942	0.621	1.428	0.7781
No	Reference			
Osteoarthritis				
Yes	1.346	0.976	1.856	0.0699
No	Reference			
Other coronary artery disease				
Yes	1.221	0.765	1.950	0.4031
No	Reference			
Peripheral vascular disease				
Yes	1.784	1.011	3.149	0.0457*
No	Reference			
Sleep apnea				
Yes	1.268	0.869	1.849	0.2175
No	Reference			
Smoking				
Yes	0.992	0.667	1.476	0.9682
No	Reference			
Evidence of prior infection within 12-month period before index date				
Yes	1.518	1.022	2.254	0.0386*
No	Reference			

*$p < 0.05$.

patients without an infection before index (in the initial group: 18.09 vs. 10.98%, $p = 0.0001$; in the replacement group: 23.08 vs. 12.29%, $p = 0.0205$). For patients in the replacement group, the infection rates were higher patients who smoked than patients who did not smoke (25.00 vs. 12.29%, $p = 0.0169$).

The Kaplan–Meier curves (Fig. 2), indicate that the SCS infection rates were 3.15% in the initial group and 2.96% in the replacement group at the end of 12 months after index date. The result of the log-rank test showed the difference in infection rates between the initial group and the replacement group was not statistically significant ($p = 0.7916$). Approximately, 40% of infections occurred within the first 30 days and approximately three-quarters occurred within the first 90 days after generator implant.

From Table 5, the result of the COX proportional hazard regression ($n = 13{,}214$) identified risk factors for SCS device-related infection when all factors were considered together, including a comorbidity of lumbar disk disease (HR, 1.302; 95% CI: 1.015–1.671; $p = 0.0381$) as well as a history of prior infection (HR, 1.770; 95% CI: 1.342–2.336; $p < 0.0001$). In addition, elderly patients were less likely to have an infection (HR, 0.974; 95% CI:

Table 3. Infection Rate Distribution by Age Group.

	Infection Yes ($N = 206$)	Infection No ($N = 6409$)	% w/ Infection in this age group
18–29	8	139	5.44
30–44	60	1277	4.49
45–64	113	3900	2.82
≥65	25	1093	2.24
Total	206	6409	3.11

Table 4. Patient Demographics and Comorbid Conditions for Initial and Replacement Cohorts by Infection Status, Survival Analysis.

	Initial group (*N* = 11,176)			Replacement group (*N* = 2038)		
	Infection	No infection	*p* value	Infection	No infection	*p* value
	N = 293	*N* = 10,883		*N* = 52	*N* = 1986	
Age (Mean [SD])	51.6 [13.5]	54.2 [12.8]	0.0006*	51.3 [12.1]	54.0 [13.4]	0.1603
Gender						
Male	38.23%	40.49%	0.4367	63.46%	61.28%	0.7497
Female	61.77%	59.51%		36.54%	38.72%	
Region						
Northeast	10.24%	9.72%	0.5134	17.31%	13.70%	0.2505
North Central	27.65%	26.89%		21.15%	26.23%	
South	48.46%	46.87%		34.62%	42.75%	
West	10.58%	14.09%		23.08%	15.21%	
Unknown	3.07%	2.43%		3.85%	2.11%	
Insurance type						
Commercial	84.98%	82.00%	0.1889	86.54%	81.72%	0.3738
Medicare	15.02%	18.00%		13.46%	18.28%	
Setting of service on the index date						
Outpatient	70.99%	71.92%	0.3948	50.00%	64.80%	0.0747
ASC	9.22%	11.46%		19.23%	11.23%	
Inpatient	5.80%	5.59%		5.77%	5.99%	
Other	5.12%	3.51%		1.92%	4.33%	
Unknown	8.87%	7.53%		23.08%	13.65%	
Charlson Comorbidity Index						
0	47.78%	47.95%	0.2086	40.38%	48.39%	0.1305
1	21.84%	25.90%		23.08%	25.73%	
2–3	21.84%	17.72%		21.15%	18.73%	
≥4	8.53%	8.43%		15.38%	7.15%	
Cardiac dysrhythmias						
Yes	12.29%	12.02%	0.8893	11.54%	11.78%	0.9570
No	87.71%	87.98%		88.46%	88.22%	
Congestive heart failure						
Yes	4.10%	3.75%	0.7582	5.77%	4.28%	0.4893
No	95.90%	96.25%		94.23%	95.72%	
COPD						
Yes	10.24%	11.61%	0.4677	11.54%	12.19%	0.8880
No	89.76%	88.39%		88.46%	87.81%	
Depressive disorders						
Yes	50.17%	48.41%	0.5529	44.23%	39.12%	0.4566
No	49.83%	51.59%		55.77%	60.88%	
Diabetes type 1						
Yes	4.44%	3.41%	0.3405	7.69%	3.73%	0.1351
No	95.56%	96.59%		92.31%	96.27%	
Diabetes type 2						
Yes	25.60%	22.95%	0.2887	23.08%	21.35%	0.7643
No	74.40%	77.05%		76.92%	78.65%	
GERD						
Yes	21.84%	23.29%	0.5620	13.46%	23.56%	0.0889
No	78.16%	76.71%		86.54%	76.44%	
Hyperlipidemia						
Yes	44.37%	44.72%	0.9047	42.31%	43.76%	0.8353
No	55.63%	55.28%		57.69%	56.24%	
Hypertension						
Yes	59.73%	56.86%	0.3280	48.08%	52.92%	0.4898
No	40.27%	43.14%		51.92%	47.08%	
Hypothyroidism						
Yes	13.31%	16.17%	0.1884	17.31%	17.72%	0.9381
No	86.69%	83.83%		82.69%	82.28%	
Lumbar disk disease						
Yes	75.77%	70.98%	0.0745	59.62%	52.22%	0.2915
No	24.23%	29.02%		40.38%	47.78%	
Overweight and obesity						
Yes	17.41%	15.85%	0.4723	17.31%	13.80%	0.4698
No	82.59%	84.15%		82.69%	86.20%	

Table 4. *Continued*

	Initial group (N = 11,176)			Replacement group (N = 2038)		
	Infection	No infection	p value	Infection	No infection	p value
	N = 293	N = 10,883		N = 52	N = 1986	
Osteoarthritis						
Yes	72.35%	70.04%	0.3922	65.38%	56.95%	0.2249
No	27.65%	29.96%		34.62%	43.05%	
Other coronary artery disease						
Yes	12.63%	13.10%	0.8120	11.54%	11.68%	0.9747
No	87.37%	86.90%		88.46%	88.32%	
Peripheral vascular disease						
Yes	6.83%	5.41%	0.2927	9.62%	4.63%	0.0957
No	93.17%	94.59%		90.38%	95.37%	
Sleep apnea						
Yes	20.48%	16.88%	0.1054	15.38%	16.16%	0.8803
No	79.52%	83.12%		84.62%	83.84%	
Smoking						
Yes	13.99%	16.81%	0.2031	25.00%	13.44%	0.0169*
No	86.01%	83.19%		75.00%	86.56%	
Evidence of prior infection in 12-month period before index date						
Yes	18.09%	10.98%	0.0001*	23.08%	12.29%	0.0205*
No	81.91%	89.02%		76.92%	87.71%	

*$p < 0.05$.

0.962–0.986; $p < 0.0001$). In other words, for each additional year of age at any timepoint, patients were 2.6% less likely to have a SCS infection. Several factors that were significant in the descriptive analysis were not significant when examined along with the other factors in the COX proportional hazard regression analysis.

DISCUSSION

Prevention of infection with SCS implants and replacement procedures is of the utmost importance. Consequences of these events have been well reported and are a detriment to the field, although levels of compliance with evidence-based guidelines remain low (1,3). SSI rates have been reported in the literature and can range from 1 to 10%, but have most commonly been accepted to be 3–4.6% (1,3,7,9,23–28). However, most studies are retrospective and have smaller sample sizes. In addition, there is limited attention to the characteristics involved that lead to infection, as well as differences between initial and replacement procedures.

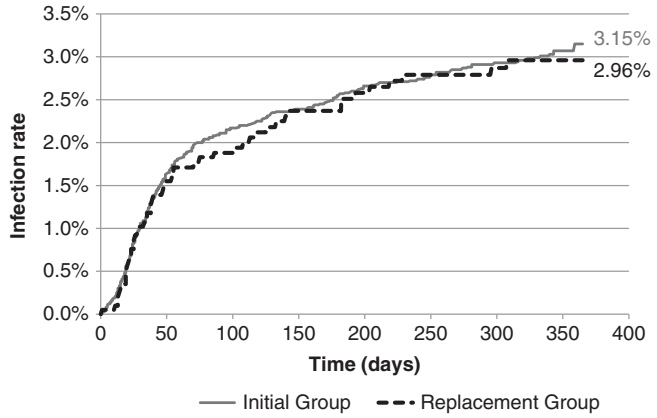

Figure 2. Kaplan–Meier curves of infection rate among initial and replacement groups.

Our present study sought to define and compare the infection rates for both initial and replacement SCS implants and identify patient characteristics that increase the risk for SCS infection. This is the largest study to date that examines the SCS device-related infection rate. We examined a large United States payer data base to provide real-world data in which the survival analysis included 13,214 patients while the logistic regression included 6615 patients. The data demonstrated a 3% device-related infection rate within 12 months of SCS implant, with most infections occurring within the first 90 days following device implantation (Fig. 2). This infection rate is in line with previous published data, while the time to occurrence of infection is similar to the reported rate by Hayek et al. which demonstrate a median time to infection of 1.99 months(1,7,24). In addition, our data demonstrated no statistically significant difference between the likelihood of infection for patients with initial implants and replacement implants.

Attention in this analysis is largely placed on identifying the factors that may contribute to an increased risk of SSI for SCS, including medical comorbidities and revisions. Many of these risk factors have been identified by extrapolating data from other surgical procedures, such as pacemaker implantation, which demonstrated higher risk of SSI with replacement procedures, but this did not hold true in our analysis. The logistic regression analysis included patients with 12 months of continuous enrollment after the index date and identified a comorbidity of PVD as well as history of a previous infection in the 12-month period prior to index as risk factors for SCS infection. Interestingly, it also demonstrated that older patients were less likely to have infections and that infection was less likely with increasing age. This has been identified in other procedures; two recent analysis of total ankle arthroplasties concluded that age also had a protective effect against infections (16,29). Future research is needed to further explore the impact of age on infection risk in this patient population.

Table 5. The Result of COX Proportional Hazard Regression Model.

	Hazard ratio	95% confidence interval		*p* value
Age	0.974	0.962	0.986	<0.0001*
Gender				
Male	0.861	0.685	1.083	0.2010
Female	Reference			
Region				
Northeast	1.103	0.775	1.572	0.5861
North Central	1.017	0.785	1.318	0.8985
South	Reference			
West	0.877	0.624	1.233	0.4501
Unknown	1.282	0.695	2.367	0.4265
Insurance type				
Commercial	0.803	0.534	1.208	0.2923
Medicare	Reference			
Charlson Comorbidity Index				
0	Reference			
1	0.898	0.665	1.213	0.4833
2–3	1.327	0.939	1.874	0.1089
≥4	1.198	0.710	2.021	0.4988
Group				
Initial group	1.006	0.744	1.358	0.9710
Replacement group	Reference			
Setting of service on the index date				
Outpatient	Reference			
Ambulatory surgical center	1.004	0.708	1.423	0.9834
Inpatient	1.057	0.669	1.671	0.8129
Other	1.238	0.744	2.060	0.4105
Unknown	1.296	0.914	1.837	0.1454
Cardiac dysrhythmias				
Yes	1.016	0.724	1.426	0.9259
No	Reference			
Congestive heart failure				
Yes	1.065	0.606	1.874	0.8261
No	Reference			
Chronic obstructive pulmonary disease (COPD)				
Yes	0.816	0.556	1.196	0.2976
No	Reference			
Depressive disorders				
Yes	1.018	0.820	1.264	0.8719
No	Reference			
Diabetes 1				
Yes	1.147	0.668	1.972	0.6185
No	Reference			
Diabetes 2				
Yes	1.014	0.730	1.409	0.9327
No	Reference			
GERD				
Yes	0.840	0.643	1.098	0.2028
No	Reference			
Hyperlipidemia				
Yes	1.031	0.811	1.310	0.8024
No	Reference			
Hypertension				
Yes	1.172	0.914	1.501	0.2105
No	Reference			
Hypothyroidism				
Yes	0.804	0.587	1.101	0.1744
No	Reference			
Lumbar disk disease				
Yes	1.302	1.015	1.671	0.0381*
No	Reference			
Overweight and obesity				
Yes	1.027	0.767	1.376	0.8581
No	Reference			
Osteoarthritis				
Yes	1.207	0.944	1.544	0.1329
No	Reference			
Other coronary artery disease				
Yes	0.976	0.677	1.407	0.8975
No	Reference			
Peripheral vascular disease				
Yes	1.385	0.891	2.151	0.1476
No	Reference			
Sleep apnea				
Yes	1.191	0.895	1.585	0.2293
No	Reference			
Smoking				
Yes	0.903	0.670	1.217	0.5029
No	Reference			
Evidence of prior infection within 12-month period before index date				
Yes	1.770	1.342	2.336	<0.0001*
No	Reference			

*$p < 0.05$

The survival analysis included a very large sample size, nearly doubling the population of patients compared to the logistic regression analysis, given that continuous enrollment for 12 months after the procedure was not necessary. This is an important way to look at patients when exploring a safety endpoint to validate that the safety event does not cause patients to drop out of the data. The results are similar to the logistic regression analysis, confirming that history of prior infection was identified as a risk factor for an infection and that younger patients were more likely to have an infection. The rate of infection also was consistent in the two different patient populations.

In this study, some factors such as smoking, cardiac dysrhythmias, or sleep apnea were individually significant in the descriptive analysis for either the initial or replacement group of patients but were no longer statistically significant in the final regression models. The descriptive analysis is designed to assess differences between the groups, while the multiple regression model is used to evaluate risk factors driving the occurrence of infection while looking at all the characteristics together. Characteristics are considered risk factors when they are found to be significant in these regression models. The physician authors recommend that clinicians closely examine patients with the factors that were individually significant and assess them in context with other comorbidities to determine if the overall combination may warrant additional infection prevention mechanisms, particularly as some of these factors have been identified as associated with infection in other disease states (30).

As confirmed in both the logistic regression and survival analysis, the expected risk factors for developing an SSI such as obesity, diabetes, and smoking were not identified as risk factors with this dataset, although smoking was found to individually increase the risk in those undergoing replacement procedures. A recent large retrospective chart analysis demonstrated similar conclusions (7). Future prospective studies with large study populations are needed

to further assess the impact of these individual risk factors on SSIs with implantable pain therapies. The evolving consideration of appropriate candidates for elective surgery and related management of chronic disease characteristics prior to surgery may be at play in this recent dataset compared with prior analyses (1).

The current study is a retrospective analysis of SCS device-related infection. A large international survey indicated low compliance with evidence-based infection control practices by implanting physicians during the timeframe under review in this study (3). Evidence-based guidelines have been published to increase adherence to established standards (1). This article identifies patients in whom greater care may be appropriate. Clinicians should consider following best-practice recommendations to prevent and control infections in all patients, particularly patients at greater risk for infection.

This study examining a United States payer data base demonstrates that research is warranted on methods to limit SCS infection rates. This is especially true in those with a comorbidity of PVD, history of previous infection, and those of younger age. Future studies utilizing a different time period may identify the impact of increased compliance with infection control practices and the evolving infection control field. This research also highlights the need for a prospective analysis in the field of SCS to further understand patients at higher risk for infection. Ultimately, this study highlights the need for strong infection prevention, especially in those with prior infections.

Limitations do exist in this study despite the large sample size looking at real-world data. This study is a retrospective cohort analysis using administrative claims data sourced for billing purposes and is therefore reliant on proper coding and documentation. This assumption may not always include accurate and complete coding. Perhaps, the most important limiting factor is that important comorbidities such as obesity and smoking history may not be properly or accurately coded leading to underreporting; these factors are known to be underreported in administrative claims data (31–34). Infection classification using ICD-9 diagnosis codes from claims data does not permit further classification of device-related infection reasons or severity in a similar manner to clinical studies, which may categorize factors contributing to device-related infection into hardware, therapy, biological, procedure, medication, or human-related factors; this classification is not possible in this claims dataset and likely includes instances of all of those factors grouped together. Some factors identified as SSI risk factors in previous studies such as surgical time are not available in this dataset (35). Last, this analysis follows patients for a 12 month period after implantation which does not account for potential bacterial seeding of the implant far after the implant. Despite these limitations, this study is a valuable contribution to understanding infection rates, examining real-world effectiveness and complications of SCS therapy.

CONCLUSION

The approximate 3% device-related infection rate within 12 months of SCS implant determined from a large administrative data base further emphasizes the need for improvement in SCS infection control practices. Based on these results, research is warranted on methods to limit SCS infection rates in patients with a history of prior infection, as well as younger patient populations. Further research is needed to evaluate these patient factors in a prospective manner for SCS.

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Authorship Statements

Drs. Falowski, Provenzano, Xia, and Ms. Doth designed the study. Dr. Xia performed the statistical analysis. All authors contributed to the interpretation of the data and preparation of the manuscript. All authors approved the final manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the supporting information tab for this article.

COMMENT

This study provides useful clinical information that identifies those patients at a potentially higher risk of surgical site infections after implantation of spinal cord stimulators (SCS). Specifically, this study highlights that we must be cognizant of the higher infection risk of young patients, and those with a prior infection history receiving a SCS implant.

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Comments not included in the Early View version of this paper.

