The incidence of stroke among patients undergoing elective posterior lumbar fusion: a retrospective cohort study

Patrick Arena (✉ patrick.arena@pfizer.com)

Pfizer Inc <https://orcid.org/0000-0003-3024-771X>

Jingping Mo

Pfizer Inc

Charu Sabharwal

Pfizer Inc

Elizabeth Begier

Pfizer Inc

Xiaofeng Zhou

Pfizer Inc

Alejandra Gurtman

Pfizer Inc

Qing Liu

Pfizer Inc

Rongjun Shen

Pfizer Inc

Charles Wentworth

Pfizer Inc

Kui Huang

Pfizer Inc

Research article

Keywords: Stroke, posterior lumbar fusion, epidemiology, electronic healthcare records

Posted Date: November 26th, 2019

DOI: <https://doi.org/10.21203/rs.2.17730/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Version of Record: A version of this preprint was published on September 14th, 2020. See the published version at <https://doi.org/10.1186/s12891-020-03631-5>.

Abstract

Background: Although stroke is an uncommon but life-threatening complication among spinal surgery patients, the recognition of this adverse event is critical given the aging population undergoing surgical procedures. The objective of this study was to estimate the incidence of stroke among adults undergoing elective posterior lumbar fusion (PLF) during post-operative risk windows and among different subgroups.

Methods: A retrospective cohort study using a longitudinal electronic healthcare record (EHR) database was conducted from January 1, 2007 to June 30, 2018. Elective PLF, stroke, and select clinical characteristics were defined based on International Classification of Disease codes. Patients aged 18 to 85 years with ≥ 183 days of enrollment in the database prior to undergoing elective PLF were followed from the index date until the occurrence of stroke, death, loss to follow-up, or end of study period, whichever occurred first. Incidence proportions (IPs) and rates (IRs) of stroke were estimated in the following risk windows: index hospitalization, ≤ 30 days, ≤ 90 days, ≤ 180 days, and ≤ 365 days post-operation

Results: A total of 43,063 patients were eligible for the study. The IP of stroke following elective PLF ranged from 0.29% (95% confidence interval [CI]: 0.25%, 0.35%) during index hospitalization to 1.12% (95% CI: 1.03%, 1.23%) ≤ 365 days post-operation; the IR of stroke following elective PLF per 1000 person-years decreased consistently from 229.08 (95% CI: 192.38, 272.78) during index hospitalization to 13.68 (95% CI: 12.51, 14.96) ≤ 365 days post-operation. Stratified analyses revealed that older patients had a higher incidence of stroke. Additionally, black patients had higher stroke incidences than white, Asian, or other patients. Furthermore, the incidence of post-operative stroke was higher among patients with a history of type 2 diabetes than among patients without such history.

Conclusions: The incidence of stroke following elective PLF found here using an EHR database is slightly higher than that reported in the literature; however, the discrepancy is due to differences in the variable definitions, study populations, follow-up periods, and data sources between our study and those in the literature.

Introduction

Stroke was the second leading cause of death globally in 2016, with 177,196 stroke deaths and 731,256 incident cases in the United States (US) alone [1]. Although stroke is an uncommon but life-threatening complication among spinal surgery patients [2], the recognition of this adverse event is critical given the aging population undergoing surgical procedures. The volume of elective lumbar fusion procedures in the US has increased 62.3%, from 122,679 cases in 2004 to 199,140 cases in 2015; these increases were greatest among those aged 65 years or older [3]. Furthermore, Etzioni et al. have demonstrated that the number of older people (i.e., those above the age of 65 years) undergoing surgery in general is increasing at a rate faster than the proportion of older people in the overall population [4]. For adults undergoing posterior lumbar fusions (PLFs), the incidence of stroke within 30 days post-surgery has been reported as approximately 0.2% [5–8], but there is little data during various post-operative risk windows.

It is important to have background epidemiology data about post-operative stroke during various risk windows and among different subgroups to contextualize safety data in clinical trials and the general population. This cohort study was thus designed to estimate the incidence of stroke among adults undergoing elective PLF using a large electronic healthcare record (EHR) database in the US. The objectives of this study were to estimate the incidence proportions (IPs) and incidence rates (IRs) of stroke among elective PLF patients in various post-operative time periods (as well as during the index surgical hospitalization) and within different subgroups.

Methods

Study design

A retrospective cohort study of adults undergoing elective PLF using Optum EHR, a longitudinal US EHR database, was performed. The study period was January 1, 2007 to June 30, 2018 with a length of follow-up equating to 365 days. The index surgical date was defined as the first date on or after January 1, 2007 that an adult had undergone an elective PLF. To incorporate a 183-day look-back window prior to the index surgery (for the purpose of excluding prevalent conditions), the earliest possible index surgical date was July 1, 2007. The latest index surgical date possible was June 30, 2017.

Cohort formation

Eligible patients were 18 to 85 years of age at the time of their first elective PLF. Furthermore, patients had 183 days of continuous enrollment within the database prior to their first elective PLF (i.e., the baseline period) as well as this index surgery being performed on the day of admission to the healthcare facility or the day after admission. PLF was identified using the following six International Classification of Diseases (ICD), Ninth Revision, Procedure Classification System (ICD-9-PCS) codes: 81.05, 81.07, 81.08, 81.35, 81.37, and 81.38; these codes referred to lumbar fusion and refusion of either the posterior or anterior column using the posterior technique.

To ensure a healthy study cohort and select for elective surgeries, patients were excluded if they 1) underwent a major surgical procedure that occurred within 90 days prior to the index surgery; 2) had a surgical indication that was for an emergency procedure; 3) were pregnant; 4) were discharged on the same date of the index surgery (thereby indicating an outpatient procedure); 5) had any of the following conditions during the baseline period: anaphylactic reaction to a vaccine, cancer, end stage renal disease, congenital spleen anomalies, an immunosuppressive state, and/or receipt of corticosteroids or immunosuppressive medications; or 6) had any of the following conditions time of the index surgery: potential/presumed surgical site-related infection and/or spinal infection.

Stroke was defined based on the following ten ICD, Ninth Revision, Clinical Modification (ICD-9-CM) codes: 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, and 436; these codes referred to occlusion, stenosis, thrombosis, and embolism of arteries with cerebral infarction as well as cerebral

artery occlusion and acute cerebrovascular disease. ICD-9-PCS and ICD-9-CM codes were mapped to corresponding ICD, Tenth Revision (ICD-10) codes using General Equivalence Mapping techniques in order to account for the switch to ICD-10 coding in 2015.

Data management and analysis

All analyses were descriptive and conducted in SAS (version 9.4, SAS Institute, Cary, NC, USA). Descriptive statistics were performed to characterize the cohort in terms of demographic and clinical characteristics at the baseline. Patients were followed from the cohort entry index date until the occurrence of stroke, death, loss to follow-up, or end of study period, whichever occurred first.

IPs and IRs were estimated with associated 95% confidence intervals (CIs), assuming a Poisson distribution. Incidences were calculated overall, and in the following subgroups: age, gender, race, length of hospital stay, and selected clinical characteristics. Incidences were estimated in the following risk windows: index hospitalization (defined as the time interval from index surgery to discharge), ≤ 30 days (i.e., 0 to 30 days), ≤ 90 days (i.e., 0 to 90 days), ≤ 180 days (i.e., 0 to 180 days), and ≤ 365 days (i.e., 0 to 365 days) post-operation.

Results

Of the 80,796 patients who were 18 to 85 years of age with at least one record of elective PLF during the study period and adequate prior enrollment in the database, 37,733 met exclusion criteria; the most common reasons for exclusion were use of immunosuppressive medications (42%), receipt of systemic corticosteroids (33%), and a diagnosis of cancer (14%) during the baseline. Ultimately, 43,063 patients were included. The mean age was 59.4 years, and there were slightly more females (52.22%) than males (47.75%). The majority of the cohort members were white (89.49%), while black (5.94%) and Asian (0.52%) members were less represented. The most prevalent medical conditions were type 2 diabetes (13.86%), cardiac dysrhythmias (9.28%), and chronic ischemic disease (9.00%). Only 293 patients (0.68%) had any history of stroke during the baseline. Dementia, individual digestive disorders, deep vein thrombosis, and pulmonary embolism were also rare (i.e., each less than 1.00%). Lastly, the average length of hospital stay (for the index hospitalization) was 3.8 days. Table 1 shows the baseline demographics and clinical characteristics of the elective PLF patient population.

Table 1

Baseline demographics, clinical characteristics, and surgical characteristics of the elective posterior lumbar fusion patient population

Characteristic, N (%) except where specified	Number of patients	%
Total	43,063	
Demographic characteristics		
Age at index date		
Mean (SD)	59.4 (13.69)	
Median (Range)	61 (18, 85)	
>=18–55	15,221	35.35
56–65	11,639	27.03
66–75	11,579	26.89
76 - <86	4,624	10.74
Race		
White	38,535	89.49
Black or African American	2,556	5.94
Asian	223	0.52
Other/Unknown	1,749	4.06
Sex		
Male	20,563	47.75
Female	22,487	52.22
Unknown	13	0.03
Clinical & surgical characteristics in 183-day baseline		
Arthritis and other inflammation (or rheumatic events)		
Rheumatoid arthritis	0	0.00
Reactive arthritis	579	1.34
Psoriatic arthroplasty	42	0.10
Spondyloarthritis, including ankylosing spondylitis	1,476	3.43
Blood disorders		
Anemia/other anemia	3,494	8.11
Intracranial Hemorrhage	52	0.12
Gastrointestinal bleeding	216	0.50
Thrombocytopenia	333	0.77
Cardiovascular events and/or conditions		
Acute myocardial infarction	270	0.63
Angina	1,997	4.64
Cardiac dysrhythmias	3,997	9.28
Stroke	293	0.68
Chronic ischemic disease	3,876	9.00
Peripheral vascular disease	1,811	4.21
Dementia		
Dementia	130	0.30
Diabetes		
Diabetes, type 1	272	0.63

Characteristic, N (%) except where specified	Number of patients	%
Diabetes, type 2	5,970	13.86
Digestive disorders		
Crohn's disease	73	0.17
Ulcerative colitis	71	0.16
Peptic ulcer disease	240	0.56
Hepatic disorders		
Liver disease and cirrhosis	607	1.41
Nervous system disorders		
Guillain-Barre syndrome	0	0.00
Multiple sclerosis	105	0.24
Respiratory disorders		
Asthma/wheezing/bronchospasm	3,353	7.79
Bronchitis/chronic obstructive pulmonary disease	2,315	5.38
Obstructive asthma	1,126	2.61
Surgical characteristics		
Existing permanently implanted device or prosthesis at baseline	1,270	2.95
Total length of hospital stay		
Mean (SD)	3.8 (3.4)	
Median (Min, Max)	3 (1, 90)	
History of allogenic blood transfusion during surgery	1	0.00
Revisional surgery on the same day as index surgery	320	0.74
Use of implanted material during surgery on the same day as index surgery	2,667	6.19
Thrombotic events		
Deep vein thrombosis	386	0.90
Pulmonary embolism	170	0.39
Thyroid disorders		
Grave's disease	37	0.09
Autoimmune thyroiditis	55	0.13
Hyperthyroidism	109	0.25
Hypothyroidism	3,455	8.02
Thyroiditis	6	0.01

[Insert Table 1 here]

The IP of stroke following elective PLF was 0.29% (95% CI: 0.25%, 0.35%) during index hospitalization, 0.44% (95% CI: 0.38%, 0.50%) $\leq$ 30 days, 0.59% (95% CI: 0.52%, 0.67%) $\leq$ 90 days, 0.76% (95% CI: 0.68%, 0.85%) $\leq$ 180 days, and 1.12% (95% CI: 1.03%, 1.23%) $\leq$ 365 days post-operation. The IR of stroke following elective PLF decreased consistently from index hospitalization to $\leq$ 365 days post-operation; these IRs per 1000 person-years (PYs) were 229.08 (95% CI: 192.38, 272.78) during index hospitalization, 52.79 (95% CI: 45.72, 60.95) $\leq$ 30 days, 25.63 (95% CI: 22.65, 28.99) $\leq$ 90 days, 17.48 (95% CI: 15.68, 19.48) $\leq$ 180 days, and 13.68 (95% CI: 12.51, 14.96) $\leq$ 365 days post-operation. Tables 2 and 3 show the IP and IR of stroke in patients undergoing elective PLF, respectively.

Table 2
Incidence proportion of stroke in patients undergoing elective posterior lumbar fusi

Stroke incidence type	During index hospitalization				Up to 30 days post-operation				Up to 90 days post-operation			
	Number of patients at risk	Number of cases	Years at risk	Incidence proportion (95% confidence interval)	Number of patients at risk	Number of cases	Years at risk	Incidence proportion (95% confidence interval)	Number of patients at risk	Number of cases	Years at risk	Incidence proportion (95% confidence interval)
Crude	42,742	126	550.03	0.29% (0.25%, 0.35%)	42,744	186	3523.41	0.44% (0.38%, 0.50%)	42,745	252	9833.32	0.59% (0.52%, 0.67%)
Stratifications by:												
Age												
>=18–55	15,181	17	179.62	0.11% (0.07%, 0.18%)	15,181	25	1251.95	0.16% (0.11%, 0.24%)	15,181	36	3498.67	0.24% (0.17%, 0.33%)
56–65	11,588	22	146.04	0.19% (0.12%, 0.29%)	11,590	39	956.04	0.34% (0.24%, 0.46%)	11,591	53	2662.86	0.46% (0.34%, 0.60%)
66–75	11,438	51	157.62	0.45% (0.33%, 0.59%)	11,438	71	942.84	0.62% (0.49%, 0.78%)	11,438	90	2634.55	0.79% (0.63%, 0.97%)
76 - <86	4,535	36	66.74	0.79% (0.56%, 1.10%)	4,535	51	372.57	1.12% (0.84%, 1.48%)	4,535	73	1037.24	1.61% (1.26%, 2.02%)
Gender												
Male	20,404	64	256.25	0.31% (0.24%, 0.40%)	20,405	96	1680.10	0.47% (0.38%, 0.57%)	20,405	129	4681.68	0.63% (0.53%, 0.75%)
Female	22,325	62	293.61	0.28% (0.21%, 0.36%)	22,326	90	1842.21	0.40% (0.32%, 0.50%)	22,327	123	5148.73	0.55% (0.46%, 0.66%)
Unknown	13	0	0.17	0.00% (0.00%, 0.00%)	13	0	1.10	0.00% (0.00%, 0.00%)	13	0	2.91	0.00% (0.00%, 0.00%)
Race												
White	38,246	113	487.13	0.30% (0.24%, 0.36%)	38,248	160	3154.63	0.42% (0.36%, 0.49%)	38,249	218	8814.21	0.57% (0.50%, 0.65%)
Black or African American	2,545	9	36.89	0.35% (0.16%, 0.67%)	2,545	17	210.81	0.67% (0.39%, 1.07%)	2,545	23	585.70	0.90% (0.57%, 1.35%)
Asian	212	0	3.33	0.00% (0.00%, 0.00%)	212	0	17.43	0.00% (0.00%, 0.00%)	212	1	49.07	0.47% (0.01%, 2.60%)
Other/Unknown	1,739	4	22.68	0.23% (0.06%, 0.59%)	1,739	9	140.54	0.52% (0.24%, 0.98%)	1,739	10	384.34	0.58% (0.28%, 1.06%)
Type 1 Diabetes during baseline												
Yes	270	1	3.85	0.37% (0.01%, 2.05%)	270	2	22.56	0.74% (0.09%, 2.65%)	271	3	64.50	1.11% (0.23%, 3.20%)
No	42,472	125	546.17	0.29% (0.25%, 0.35%)	42,474	184	3500.85	0.43% (0.37%, 0.50%)	42,474	249	9768.82	0.59% (0.52%, 0.66%)
Type 2 Diabetes during baseline												

Stroke incidence type	During index hospitalization				Up to 30 days post-operation				Up to 90 days post-operation			
	Number of patients at risk	Number of cases	Years at risk	Incidence proportion (95% confidence interval)	Number of patients at risk	Number of cases	Years at risk	Incidence proportion (95% confidence interval)	Number of patients at risk	Number of cases	Years at risk	Incidence proportion (95% confidence interval)
Yes	5,923	23	82.24	0.39% (0.25%, 0.58%)	5,923	42	492.66	0.71% (0.51%, 0.96%)	5,924	58	1394.58	0.98% (0.74%, 1.26%)
No	36,819	103	467.78	0.28% (0.23%, 0.34%)	36,821	144	3030.75	0.39% (0.33%, 0.46%)	36,821	194	8438.74	0.53% (0.46%, 0.61%)
Existing permanently implanted device or prosthesis at baseline												
Yes	1,242	0	17.80	0.00% (0.00%, 0.00%)	1,242	1	102.71	0.08% (0.00%, 0.45%)	1,242	1	287.33	0.08% (0.00%, 0.45%)
No	41,500	126	532.23	0.30% (0.25%, 0.36%)	41,502	185	3420.70	0.45% (0.38%, 0.51%)	41,503	251	9545.98	0.60% (0.53%, 0.68%)
Total length of hospital stay												
1–5 days	37,077	60	393.57	0.16% (0.12%, 0.21%)	37,079	104	3053.66	0.28% (0.23%, 0.34%)	37,080	148	8514.74	0.40% (0.34%, 0.47%)
6–10 days	4,530	43	98.86	0.95% (0.69%, 1.28%)	4,530	57	375.63	1.26% (0.95%, 1.63%)	4,530	70	1054.52	1.55% (1.21%, 1.95%)
> 10 days	1,135	23	57.60	2.03% (1.29%, 3.03%)	1,135	25	94.11	2.20% (1.43%, 3.23%)	1,135	34	264.06	3.00% (2.08%, 4.16%)
Use of implanted material during surgery on the same day as index surgery												
Yes	3,095	11	44.45	0.36% (0.18%, 0.64%)	3,095	16	255.45	0.52% (0.30%, 0.84%)	3,095	19	714.26	0.61% (0.37%, 0.96%)
No	39,647	115	505.58	0.29% (0.24%, 0.35%)	39,649	170	3267.96	0.43% (0.37%, 0.50%)	39,650	233	9119.06	0.59% (0.51%, 0.67%)
Medical history of stroke												
Yes	291	39	4.59	13.40% (9.71%, 17.86%)	292	58	20.47	19.86% (15.44%, 24.91%)	292	77	54.44	26.37% (21.41%, 31.82%)
No	42,451	87	545.43	0.20% (0.16%, 0.25%)	42,452	128	3502.94	0.30% (0.25%, 0.36%)	42,453	175	9778.87	0.41% (0.35%, 0.48%)

Table 3
Incidence rate of stroke in patients undergoing elective posterior lumbar fusion

Stroke incidence type	During index hospitalization				Up to 30 days post-operation				Up to 90 days post-operation			
	Number of patients at risk	Number of cases	Years at risk	Incidence rate per 1000 years (95% confidence interval)	Number of patients at risk	Number of cases	Years at risk	Incidence rate per 1000 years (95% confidence interval)	Number of patients at risk	Number of cases	Years at risk	Incidence rate per 1000 years (95% confidence interval)
Crude	42,742	126	550.03	229.08 (192.38, 272.78)	42,744	186	3523.41	52.79 (45.72, 60.95)	42,745	252	9833.32	25.63 (22.65, 28.99)
Stratifications by:												
Age												
>=18–55	15,181	17	179.62	94.64 (58.83, 152.24)	15,181	25	1251.95	19.97 (13.49, 29.55)	15,181	36	3498.67	10.29 (7.42, 14.26)
56–65	11,588	22	146.04	150.64 (99.19, 228.78)	11,590	39	956.04	40.79 (29.80, 55.83)	11,591	53	2662.86	19.90 (15.21, 26.05)
66–75	11,438	51	157.62	323.56 (245.90, 425.74)	11,438	71	942.84	75.30 (59.68, 95.02)	11,438	90	2634.55	34.16 (27.79, 42.00)
76 - <86	4,535	36	66.74	539.42 (389.10, 747.82)	4,535	51	372.57	136.89 (104.03, 180.12)	4,535	73	1037.24	70.38 (55.95, 88.53)
Gender												
Male	20,404	64	256.25	249.76 (195.49, 319.10)	20,405	96	1680.10	57.14 (46.78, 69.79)	20,405	129	4681.68	27.55 (23.19, 32.74)
Female	22,325	62	293.61	211.16 (164.63, 270.84)	22,326	90	1842.21	48.85 (39.74, 60.07)	22,327	123	5148.73	23.89 (20.02, 28.51)
Unknown	13	0	0.17	0.00 (0.00, 0.00)	13	0	1.10	0.00 (0.00, 0.00)	13	0	2.91	0.00 (0.00, 0.00)
Race												
White	38,246	113	487.13	231.97 (192.91, 278.94)	38,248	160	3154.63	50.72 (43.44, 59.22)	38,249	218	8814.21	24.73 (21.66, 28.24)
Black or African American	2,545	9	36.89	243.99 (126.95, 468.92)	2,545	17	210.81	80.64 (50.13, 129.72)	2,545	23	585.70	39.27 (26.10, 59.09)
Asian	212	0	3.33	0.00 (0.00, 0.00)	212	0	17.43	0.00 (0.00, 0.00)	212	1	49.07	20.38 (2.87, 144.69)
Other/Unknown	1,739	4	22.68	176.39 (66.20, 469.96)	1,739	9	140.54	64.04 (33.32, 123.08)	1,739	10	384.34	26.02 (14.00, 48.36)
Type 1 Diabetes during baseline												
Yes	270	1	3.85	259.59 (36.57, 1,842.88)	270	2	22.56	88.64 (22.17, 354.43)	271	3	64.50	46.51 (15.00, 144.22)
No	42,472	125	546.17	228.86 (192.06, 272.72)	42,474	184	3500.85	52.56 (45.49, 60.73)	42,474	249	9768.82	25.49 (22.51, 28.86)
Type 2 Diabetes during baseline												

Stroke incidence type	During index hospitalization				Up to 30 days post-operation				Up to 90 days post-operation			
	Number of patients at risk	Number of cases	Years at risk	Incidence rate per 1000 years (95% confidence interval)	Number of patients at risk	Number of cases	Years at risk	Incidence rate per 1000 years (95% confidence interval)	Number of patients at risk	Number of cases	Years at risk	Incidence rate per 1000 years (95% confidence interval)
Yes	5,923	23	82.24	279.66 (185.84, 420.84)	5,923	42	492.66	85.25 (63.00, 115.36)	5,924	58	1394.58	41.59 (32.15, 53.80)
No	36,819	103	467.78	220.19 (181.52, 267.09)	36,821	144	3030.75	47.51 (40.35, 55.94)	36,821	194	8438.74	22.99 (19.97, 26.46)
Existing permanently implanted device or prosthesis during baseline												
Yes	1,242	0	17.80	0.00 (0.00, 0.00)	1,242	1	102.71	9.74 (1.37, 69.12)	1,242	1	287.33	3.48 (0.24, 24.71)
No	41,500	126	532.23	236.74 (198.81, 281.91)	41,502	185	3420.70	54.08 (46.82, 62.47)	41,503	251	9545.98	26.29 (23.23, 29.76)
Total length of hospital stay												
1–5 days	37,077	60	393.57	152.46 (118.38, 196.36)	37,079	104	3053.66	34.07 (28.11, 41.28)	37,080	148	8514.74	17.39 (14.80, 20.42)
6–10 days	4,530	43	98.86	434.95 (322.58, 586.48)	4,530	57	375.63	151.74 (117.05, 196.72)	4,530	70	1054.52	66.38 (52.52, 83.90)
> 10 days	1,135	23	57.60	399.33 (265.37, 600.93)	1,135	25	94.11	265.64 (179.49, 393.12)	1,135	34	264.06	128.76 (92.00, 180.20)
Use of implanted material during surgery on the same day as index surgery												
Yes	3,095	11	44.45	247.47 (137.05, 446.87)	3,095	16	255.45	62.63 (38.37, 102.24)	3,095	19	714.26	26.60 (16.97, 41.70)
No	39,647	115	505.58	227.46 (189.47, 273.08)	39,649	170	3267.96	52.02 (44.76, 60.46)	39,650	233	9119.06	25.55 (22.47, 29.05)
Medical history of stroke												
Yes	291	39	4.59	8,494.19 (6,206.12, 11,625.81)	292	58	20.47	2,833.29 (2,190.40, 3,664.87)	292	77	54.44	1,414.1 (1,131, 1,786.6)
No	42,451	87	545.43	159.51 (129.28, 196.80)	42,452	128	3502.94	36.54 (30.73, 43.45)	42,453	175	9778.87	17.90 (15.43, 20.75)

[Insert Table 2 here]

Stratified analyses revealed that older patients consistently had higher incidences of post-operative stroke during all surgical risk windows. For example, the IR of post-operative stroke per 1000 PYs $\leq$ 365 days post-operation was 4.87 (95% CI: 3.79, 6.25) among those aged $\geq$ 18 to 55 years, 11.12 (95% CI: 9.18, 13.46) among those aged 56 to 65 years, 20.25 (95% CI: 17.56, 23.34) among those aged 66 to 75 years, and 33.41 (95% CI: 28.02, 39.84) among those aged 76 to < 86 years. Moreover, men had higher incidences of stroke than women; for instance, the IR of post-operative stroke per 1000 PYs during index hospitalization was 249.76 (95% CI: 195.49, 319.10) for men and 211.16 (95% CI: 164.63, 270.84) for women. Additionally, black patients had higher stroke incidences than

white, Asian, or other patients: the IR of post-operative stroke per 1000 PYs $\leq$ 365 days post-operation was 13.29 (95% CI: 12.08, 14.63) among white adults, 20.36 (95% CI: 15.05, 27.55) among black adults, 17.43 (95% CI: 5.62, 54.04) among Asian adults, and 12.11 (95% CI: 7.42, 19.76) among other adults.

[Insert Table 3 here]

The incidence of post-operative stroke was higher among patients with a history of type 2 diabetes than among patients without such history; for instance, the IR per 1000 PYs of stroke was 24.47 (95% CI: 20.51, 29.20) for those with a history of type 2 diabetes and 11.88 (95% CI: 10.71, 13.18) for those without such history $\leq$ 365 days post-operation. The incidence of post-operative stroke was much higher among patients with a history of stroke than among patients without a history of stroke during all risk windows. For example, the IR of post-operative stroke per 1000 PYs during index hospitalization was 8,494.19 (95% CI: 6,206.12, 11,625.81) among those with a history of stroke and 159.51 (95% CI: 129.28, 196.80) among those without such history. Lastly, patients with longer hospital stays had a higher incidence of stroke. However, it should be emphasized that these longer hospital stays could be a result of stroke instead of a reverse relationship (i.e., where stroke is the consequence of a longer hospital stay).

Discussion

Stroke incidence

Minhas et al. examined the incidence of peri-operative cerebrovascular accidents (CVAs) among patients undergoing elective orthopedic procedures from 2006 to 2012 within the National Surgical Quality Improvement Program (NSQIP) database and reported that the 30-day IP of CVA was 0.35% for single-level/multilevel PLF (n = 2,895) [9]. In our study, a 30-day IP for post-operative stroke of 0.44% (95% CI: 0.38%, 0.50%) was observed; however, it should be noted the authors defined their procedures using Current Procedure Terminology (CPT) codes and their definition for CVA was based on medical record review [9]. In a 2012 retrospective database study, 2015 PLF patients were identified from a nationwide Taiwanese cohort from 2000 to 2005 using The National Health Insurance Research Database and followed up for three years. The IR of stroke per 1000 PYs was 10.22 (95% CI: 7.94, 13.17). In their study, Wu et al. used ICD-9-CM codes 430–435 for stroke and ICD-9-PCS codes 81.0 and 81.38 to identify PLF [10]. The IR of stroke per 1000 PYs in our study was 13.68 (95% CI: 12.51, 14.96) $\leq$ 365 days post-operation, which was in line with their finding.

A 2014 retrospective cohort study performed by Marquez-Lara et al. used the Nationwide Inpatient Sample (NIS) database from 2002 to 2011 to identify patients undergoing elective lumbar fusion procedures and found a post-operative CVA incidence of 0.15% among the PLF patients (n = 214,837) [11]. In our study, the IP of stroke following elective PLF ranged from 0.29% (95% CI: 0.25%, 0.35%) to 1.12% (95% CI: 1.03%, 1.23%). It should be noted that only patients with ICD-9 code 81.08 were included and that CVA was defined with only one ICD-9 code (997.02) in their study. However, the researchers also found that increased length of hospital stay was associated with post-operative CVA [11]. Furthermore, a variety of studies examined 30-day outcomes following lumbar spinal fusion within both the NIS and NSQIP databases and generally found that the 30-day overall incidence of post-operative stroke was about 0.20% [5–8, 12].

Our finding that the risk of stroke increased with age was consistent with the literature within the general population [13]. Furthermore, studies evaluating the risk of stroke among adults undergoing lumbar spinal fusion also found an association between increased age and the risk of stroke [9, 11, 14]. With regards to sex, Minhas et al. and Marquez-Lara et al. found no significant difference in the sex-specific incidence of stroke [9, 11], which is in line with our findings. Stratified analyses revealed that black patients had a higher stroke incidence compared to other ethnic groups. This finding is consistent with the literature as numerous studies have illustrated that African-Americans have significantly higher risk of stroke in the general population [15–17]. Among populations undergoing elective PLF though, there was no published data on the incidence of post-operative stroke by race.

With regards to the other subgroups, limited information among PLF patients is available in the literature. However, Minhas et al. reported that patients with insulin-dependent diabetes mellitus (IDDM) had 3.08 times the odds of a post-operative CVA compared to those without IDDM [9]. Furthermore, recent reviews have demonstrated that diabetes mellitus is an established risk factor for stroke in the general population [18–19]. Thus, our finding that post-operative stroke incidence was higher among patients with a history of type 2 diabetes is consistent with the literature. Lastly, it is known that the incidence of stroke among those with a medical history of stroke is increased (i.e., there is a high risk of recurrent stroke) [18–19]; our results are thus in line with the standard medical knowledge regarding recurrent stroke.

Variable and database considerations

A 2012 review by Andrade et al. examined the validity of algorithms for identifying CVAs using administrative/claims data among 35 identified studies and ultimately concluded that the algorithms and definitions used to identify CVAs using administrative/claims data differ greatly in the published literature. However, the authors determined that studies reported the highest positive predictive values for inpatient ICD-9 codes 430.x, 431.x, 434.x, and 436.x for acute stroke while algorithms that included ICD-9 codes 433.x1, 434 (excluding 434.x0), and 436 performed well (85% or higher) for transient ischemic stroke [20].

Lastly, it is noteworthy that our study used Optum EHR while most studies in the literature used NSQIP or NIS. Because of differences in these data sources, it may not be surprising that our results would not exactly align with the incidence information found in the literature. For instance, a 2016 study evaluated the variability in standard outcomes of PLF between the University HealthSystem Consortium (UHC) and the NIS and found that the databases had similar patient populations undergoing PLF, but that the UHC database reported significantly higher complication rates and longer lengths of hospital [21]. Additionally, recent studies have also shown that certain variables have changed over time within both NIS and NSQIP [8, 14]; thus, even comparisons within the same database can be fraught.

Strengths and limitations

The Optum EHR database has both inpatient and outpatient data as well as a large sample size that enabled us to generate real-world incidence estimates that are generalizable to a segment of the commercially insured US population (i.e., those in the Optum network). Like other studies utilizing secondary data sources without validation (e.g., medical chart review), exposure and outcome misclassification are possible; diagnosis codes may have been incorrect or included as part of the diagnostic rule-out process rather than an indication of disease or surgery itself. Furthermore, patients may have sought healthcare outside Optum EHR prior to the index surgery, so it is possible that a patient developed a stroke prior to the index surgery; similarly, some incident events may have been missed if a patient sought care outside the system after surgery. Additionally, as we used a broad set of ICD codes to identify stroke events, we may have overestimated its incidence.

Conclusion

This study estimated the incidence of stroke using an EHR database among adults undergoing elective PLF during various post-operative risk windows and among different subgroups. This incidence is slightly higher than that reported in the literature; however, the discrepancy is due to differences in the variable definitions, study populations, follow-up periods, and data sources between our study and those in the literature.

List Of Abbreviations

CI	Confidence interval
CPT	Current Procedure Terminology
CVA	Cerebrovascular accident
EHR	Electronic healthcare record
ICD	International Classification of Diseases
ICD-9-PCS	International Classification of Diseases, Ninth Revision, Procedure Classification System
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
ICD-10	International Classification of Diseases, Tenth Revision
IDDM	Insulin-dependent diabetes mellitus
IP	Incidence proportion
IR	Incidence rate
NIS	Nationwide Inpatient Sample
NSQIP	National Surgical Quality Improvement Program
PLF	Posterior lumbar fusion
PY	Person-year
UHC	University HealthSystem Consortium
US	United States

Declarations

Ethics approval and consent to participate

As this study involved anonymized structured data, which according to applicable legal requirements do not contain data subject to privacy laws, obtaining informed consent from patients was not required.

Consent for publication

Not applicable.

Availability of materials

The data that support the findings of this study are available from Optum but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Optum.

Competing interests

All authors are employees of Pfizer Inc., New York, NY, USA.

Funding

This work was funded by Pfizer Inc.

Authors' contribution

PA, JM, CS, EB, AG, and KH contributed to the study design. PA, KH, XZ, QL, RS, and CW contributed to data analyses. PA and KH drafted the manuscript with input from JM, CS, EB, AG, XZ, QL, RS, and CW. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

References

- [1] GBD 2016 Stroke Collaborators. Global, regional, and national burden of stroke, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol.* 2019;18(5):439-458. [https://doi.org/10.1016/S1474-4422\(19\)30034-1](https://doi.org/10.1016/S1474-4422(19)30034-1).
- [2] Yang F, Zhao J, Xu H. Characteristics of hemorrhagic stroke following spine and joint surgeries. *Biomed Res Int.* 2017;5390839. <https://doi.org/10.1155/2017/5390839>.
- [3] Martin BI, Mirza SK, Spina N, Spiker WR, Lawrence B, Brodke DS. Trends in lumbar fusion procedures rates and associated hospital costs for degenerative spinal diseases in the United States, 2004 to 2015. *Spine (Phila Pa 1976).* 2019;44(5):369-376. <https://doi.org/10.1097/BRS.0000000000002822>.
- [4] Etzioni DA, Liu JH, Maggard MA, Ko CY. The aging population and its impact on the surgery workforce. *Ann Surg.* 2003;238(2):170-7. <https://doi.org/10.1097/01.SLA.0000081085.98792.3d>.
- [5] Bronheim RS, Oermann EK, Cho SK, Caridi JM. Coagulation profile as a risk factor for 30-day morbidity and mortality following posterior lumbar fusion. *Spine (Phila Pa 1976).* 2017;42(12):950-957. <https://doi.org/10.1097/BRS.0000000000001935>.
- [6] Chung AS, Campbell D, Waldrop R, Crandall D. Metabolic syndrome and 30-day outcomes in elective lumbar spinal fusion. *Spine (Phila Pa 1976).* 2018;43(9):661-666. <https://doi.org/10.1097/BRS.0000000000002397>.

- [7] Basques BA, Diaz-Collado PJ, Geddes BJ, Samuel AM, Lukasiewicz AM, Webb ML et al. Primary and revision posterior lumbar fusion have similar short-term complication rates. *Spine (Phila Pa 1976)*. 2016;41(2):E101-6. <https://doi.org/10.1097/BRS.0000000000001094>.
- [8] Shultz BN, Bovonratwet P, Ondeck NT, Ottesen TD, McLynn RP, Grauer JN. Evaluating the effect of growing patient numbers and changing data elements in the National Surgical Quality Improvement Program (NSQIP) database over the years: a study of posterior lumbar fusion outcomes. *Spine J*. 2018;18(11):1982-1988. <https://doi.org/10.1016/j.spinee.2018.03.016>.
- [9] Minhas SV, Goyal P, Patel AA. What are the risk factors for cerebrovascular accidents after elective orthopaedic surgery? *Clin Orthop Relat Res*. 2016;474(3):611-8. <https://doi.org/10.1007/s11999-015-4496-2>.
- [10] Wu JC, Chen YC, Liu L, Huang WC, Thien PF, Chen TJ et al. Lumbar spine fusion surgery and stroke: a national cohort study. *Eur Spine J*. 2012;21(12):2680-7. <https://doi.org/10.1007/s00586-012-2405-x>.
- [11] Marquez-Lara A, Nandyala SV, Fineberg SJ, Singh K. Cerebral vascular accidents after lumbar spine fusion. *Spine (Phila Pa 1976)*. 2014;39(8):673-7. <https://doi.org/10.1097/BRS.0000000000000197>.
- [12] Memstoudis SG, Kirksey M, Ma Y, Chiu L, Mazumdar M, Pumberger M et al. Metabolic syndrome and lumbar spine fusion surgery: epidemiology and perioperative outcomes. *Spine (Phila Pa 1976)*. 2012;37(11):989-95. <https://doi.org/10.1097/BRS.0b013e31823a3a13>.
- [13] Kelly-Hayes M. Influence of age and health behaviors on stroke risk: lessons from longitudinal studies. *J Am Geriatr Soc*. 2010;58 Suppl 2:S325-8. <https://doi.org/10.1111/j.1532-5415.2010.02915.x>.
- [14] Shen Y, Silverstein JC, Roth S. In-hospital complications and mortality after elective spinal fusion surgery in the united states: a study of the nationwide inpatient sample from 2001 to 2005. *J Neurol Surg Anesthesiol*. 2009;21(1):21-30. <https://doi.org/10.1097/ANA.0b013e31818b47e9>.
- [15] Cruz-Flores S, Rabinstein A, Biller J, Elkind MSV, Griffith P, Gorelick PB et al. Racial-ethnic disparities in stroke care: the American experience: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2011;42:2091–2116. <https://doi.org/10.1161/STR.0b013e3182213e24>.
- [16] Park JH, Ovbiagele B. Association of black race with recurrent stroke risk. *J Neurol Sci*. 2016;365:203-206. <https://doi.org/10.1016/j.jns.2016.04.012>.
- [17] Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. *Circulation*. 2015;131:e29–e322. <https://doi.org/10.1161/CIR.0000000000000152>.
- [18] Hankey GJ. Stroke. *Lancet*. 2017;11;389(10069):641-654. [https://doi.org/10.1016/S0140-6736\(16\)30962-X](https://doi.org/10.1016/S0140-6736(16)30962-X).
- [19] Isabel C, Calvet D, Mas JL. Stroke prevention. *Presse Med*. 2016;45(12 Pt 2):e457-e471. . <https://doi.org/10.1016/j.lpm.2016.10.009>.
- [20] Andrade SE, Harrold LR, Tjia J, Cutrona SL, Saczynski, Dodd KS et al. A systematic review of validated methods for identifying cerebrovascular accident or transient ischemic attack using administrative data. *Pharmacoepidemiol Drug Saf*. 2012;21 Suppl 1:100-28. <https://doi.org/10.1002/pds.2312>.

[21] Joseph JR, Smith BW, Park P. Variability in standard outcomes of posterior lumbar fusion determined by national databases. *World Neurosurg.* 2017;97:236-240. <https://doi.org/10.1016/j.wneu.2016.09.117>.