The Use of Semaglutide in Patients Undergoing Lumbar Fusion Does not Increase 90-Day Medical or 1-Year Implant Complications

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Study Design: Retrospective Cohort Study of National Database.

Objective: This study examines their effect on medical and mechanical complications within 90 days postlumbar spine surgery.

Summary of Background Data: Patients undergoing spinal procedures increasingly use glucagon-like peptide-1 receptor agonists (GLP-1 RAs), originally for type 2 diabetes and now popular for weight loss. The impact of GLP-1 RAs on spinal fusion outcomes is unknown.

Methods: This study used medical records from TriNetX, a national deidentified database, to examine diabetic patients undergoing lumbar spine procedures. Patients receiving GLP-1 RAs within 6 months preoperatively were compared with a propensity-matched control group. Propensity score matching (1:1) controlled for demographic factors and comorbidities, including type I and II diabetes, metformin use, and BMI. The study analyzed 90-day medical and 1-year implant complications using χ^2 exact tests and univariate regression in a propensity-matched cohort.

Results: The GLP-1 RA cohort and control group included 1110 and 151,440 patients, respectively. Of these, 1090 patients were propensity-matched 1:1 in each cohort. Within 90 days postoperatively, the GLP-1 RA group had higher rates of all-cause anemia (9.4% vs. 7.0%, $P=0.016$), renal failure (4.4% vs. 2.9%, $P=0.028$), opioid use (94% vs. 89%, $P<0.001$), emergency room visits (16% vs. 13%, $P=0.013$), and wound complications (0.5% vs. 0.2%, $P<0.001$). Other complications, such as infections, myocardial infarction, pulmonary embolism, deep vein thrombosis, hypoglycemic events, stroke, hospitalization, pneumonia, and transfusion, were similar between groups. One year postoperatively, pseudoarthrosis was less frequent in the GLP-1 RA group (12% vs. 16%, $P=0.002$). There were no significant differences in hospitalization, adjacent segment disease, mechanical loosening, or postlaminectomy syndrome.

Conclusion: This study found that the risk of complications in patients receiving GLP-1 RAs before lumbar spine surgery is comparable to control patients, suggesting GLP-1 RAs do not increase adverse outcomes and should not exclude patients from surgery.

Level of Evidence: Level III—therapeutic study.

Key Words: GLP-1 receptor agonists, spine surgery, postoperative complications, lumbar operations

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The utilization of glucagon-like peptide-1 receptor agonizts (GLP-1 RAs), a medication commonly prescribed to treat patients with type 2 diabetes mellitus (DM) and obesity, has surged in recent years due to their efficacy in managing blood glucose levels, promoting weight loss, and improving heart health.[1] It has been estimated that about 1 in every 8 American adults has used a GLP-1 RA with 6% of the population claiming to be actively taking the medication.[2] With 42.8% of Americans being classified as obese and over 9.5% of adults in the United States being diagnosed with type 2 diabetes, GLP-1 receptor agonizts have become common prescription choices for a large fraction of the population.[3,4] While their metabolic benefits and systemic effects are well-documented, the impact of GLP-1 receptor agonizts on surgical outcomes following spinal procedures remains largely unexplored.[1,5–8]

The number of spine surgeries, especially lumbar spinal fusions, have grown in recent years with these rates expected to further increase in the future.[9–12] Therefore, the impact of GLP-1 RAs on postoperative outcomes is increasingly important to evaluate. Complications such as infections, thromboembolic events, revisions, wound healing disorders, pseudoarthrosis, and mechanical failures can markedly affect patient recovery and overall outcomes.[13–18] In the context of orthopedic surgery, GLP-1 RAs have shown to have no significant risk of postoperative complications, and in some instances, have demonstrated less incidences of adverse postoperative events in patients undergoing arthroplasties.[19,20]

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In a retrospective study utilizing a large deidentified database of over 35,000 patients, we evaluated the risk of major medical and surgical complications following lumbar spine surgeries in patients using GLP-1 receptor agonizts. We hypothesized that postoperative outcomes would be similar or improved in patients taking GLP-1 receptor agonizts due to overall improved glycemic control and weight management. Though few studies have reported perioperative gastrointestinal side effects and bronchoaspiration risks with perioperative GLP-1 RA use or demonstrated the effects of perioperative glycemic control on complication risk profiles.[21–29] This is the first study to investigate the effects of GLP-1 RAs on spine surgery outcomes and complications.

METHODS

Cohort Selection, Study Design, and Data Source

This retrospective cohort study utilized medical records from TriNetX, a national deidentified database, to examine diabetic patients undergoing lumbar spine fusion. Patients were identified within the TriNetX Research Network database using specific procedural codes, including ICD-10-PCS codes 0SG00AJ, 0SG007J, 0SG03KJ, 0SG00KJ, 0SG00JJ, and 0SG037J, as well as CPT codes 22558, 22612, 22633, and 22630.

Patients receiving lumbar fusion were categorized into 2 cohorts. The experimental cohort consisted of patients who received glucagon-like peptide-1 receptor agonizts (GLP-1 RAs) within 3 months preoperatively, while the control cohort included patients who did not receive GLP-1 RAs as depicted in Figure 1. Propensity score matching (1:1) was utilized to statistically control for demographic factors and multiple medical comorbidities, including type I and II diabetes mellitus, metformin use, and body mass index (BMI), as shown in Table 1.

Study Outcomes

This study analyzed 90-day medical and 1-year implant complications using χ^2 exact tests and univariate regressions within the statistically controlled cohort. The primary outcomes of this study were major medical complications within 90 days postoperatively and implant-related complications within 1 year postoperatively. Within the first 90 days, outcomes assessed included wound complications, myocardial infarction, infection, pulmonary embolism, deep vein thrombosis, stroke, hospitalization, pneumonia, blood transfusion, renal failure, and emergency room visits. For the 1-year follow-up, outcomes included pseudoarthrosis, adjacent segment disease, hardware failure, reoperation rates, foot drop, and postlaminectomy syndrome.

Statistical Analysis

Risk ratios (RR) and 95% CIs for all outcomes were calculated using the advanced analytics tools provided by TriNetX, supporting robust data analysis on large-scale, deidentified data sets. Significance was assessed with a P-value threshold of <0.01. χ^2 exact tests and univariate regressions were used to analyze the outcomes within the matched cohorts. All analyzes ensured that a P-value of <0.01 was considered statistically significant.

Compliance and Ethical Considerations

This study utilized deidentified data compliant with HIPAA and other relevant regulations, ensuring adherence to stringent data privacy standards. Given the deidentified nature of the data, the study received an exemption from full Institutional Review Board (IRB) review.

RESULTS

Demographic and Clinical Characteristics

The GLP-1 RAs cohort and control group consisted of 1110 and 151,440 patients, respectively; of those, 1090 patients were 1:1 propensity-matched in each group. Before matching, the GLP-1 RAs cohort was younger (mean age: 61.7 ± 10.4 y vs. 60.1 ± 14.4 y, $P<0.001$) and had a higher percentage of females (57.6% vs. 51.5%, $P<0.001$) compared with the control group. Postmatching, these differences were no longer significant, with both groups having similar age distributions (mean age: 61.7 ± 10.4 y for GLP-1 RAs vs. 61.8 ± 11.0 y for control, $P=0.80$) and sex distributions (57.5% females in GLP-1 RAs vs. 59.4% in controls, $P=0.36$). The racial and ethnic distributions were also balanced postmatching, with no significant differences between the groups. Both groups had a high prevalence of comorbid conditions such as hypertension (78.7% vs. 79.5%, $P=0.64$), diabetes mellitus (78.0% vs. 78.3%, $P=0.84$), heart failure (9.8% vs. 8.9%, $P=0.46$), and chronic kidney disease (19.1% vs. 18.4%, $P=0.84$).

Medical Complications Within 90 Days

Within 90 days postoperatively, the GLP-1 RAs group exhibited higher rates of several medical complications compared with the control group. The incidence of renal failure was higher in the GLP-1 RAs group (5.87% vs. 3.58%, $P=0.01$), as seen in Table 2. Emergency room visits were more frequent among GLP-1 RA users (15.51% vs. 12.84%, $P=0.07$). Other complications such as wound complications (7.62% vs. 8.90%, $P=0.28$), myocardial infarction (0.98% vs. 0.96%, $P=0.96$), infection (4.41% vs. 4.31%, $P=0.91$), pulmonary embolism (0.94% vs. 0.94%, $P=0.98$), deep vein thrombosis (1.83% vs. 1.91%, $P=0.89$), stroke (1.38% vs. 1.38%, $P=1.00$), hospitalization (23.03% vs. 19.63%, $P=0.05$), pneumonia (2.02% vs. 1.74%, $P=0.64$), and transfusion (10.64% vs. 8.17%, $P=0.05$) were similar between the 2 groups.

Mechanical Complications Within 1 Year

One year postoperatively, pseudarthrosis was less frequent in the GLP-1 RAs group compared with the control group (10.96% vs. 17.90%, $P<0.0001$). Adjacent segment disease rates were similar between the groups (6.20% vs. 5.90%, $P=0.84$), as were the incidences of hardware failure (1.17% vs. 1.26%, $P=0.84$) and reoperation (1.09% vs. 1.38%, $P=0.56$), seen in Table 3. Foot

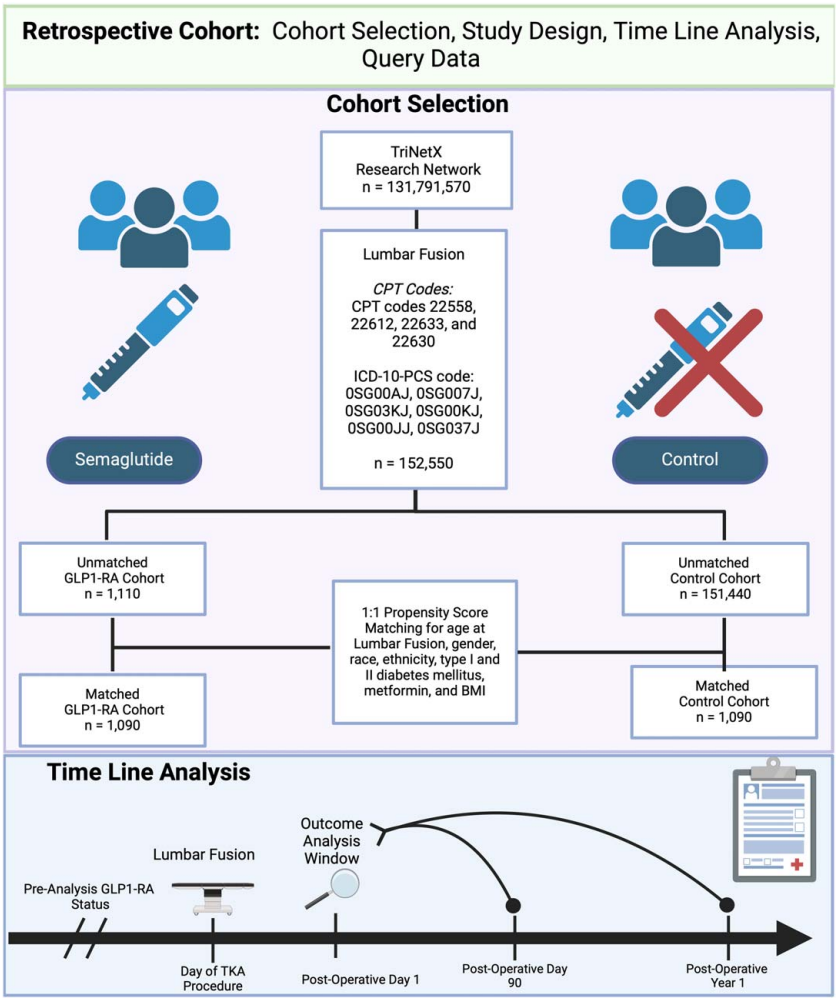

FIGURE 1. Flow diagram depicting cohort selection, study design, timeline analysis, and data query process. full color online

drop occurred in 1.85% of the GLP-1 RAs group and 0.95% of the control group ($P = 0.08$). Postlaminectomy syndrome rates were 4.8% in the GLP-1 RAs group and 3.7% in the control group ($P = 0.21$).

DISCUSSION

The objective of this study was to evaluate the risk of postoperative complications in diabetic patients undergoing lumbar spine surgeries with or without the use of GLP-1 RAs. In our matched cohort, we found that patients on GLP-1 RAs had higher rates of renal failure within 90 days of lumbar spine surgery compared with controls, however, other postoperative complications, including emergency room visits, hospitalizations, transfusion, wound complications, myocardial infarction, infection, pulmonary embolism, deep vein thrombosis, and stroke, were similar between the groups. Pseudoarthrosis was also significantly less common in the GLP-1 RA group, while other mechanical complications and reoperation rates showed no significant differences within 1 year of surgery. We report the largest study assessing postoperative adverse effects of GLP-1 RAs in diabetic patients undergoing lumbar spine surgery. Overall, our study found that using GLP-1 RAs does not increase the risk of adverse medical or mechanical outcomes following lumbar spine surgeries, and therefore, should not preclude patients from undergoing orthopedic interventions to the lumbar spine.

Primary investigations of GLP-1 RAs have shown that these medications are safe in patients undergoing elective orthopedic surgeries with some instances of decreased postoperative complications. Magruder et al[19,20] completed a series of retrospective studies investigating diabetic patients taking a GLP-1 RA at the time of total knee arthroplasty (TKA) or total hip arthroplasty (THA) and propensity-matched them to controls not taking the medication. The patients in the GLP-1 RA cohort undergoing TKA showed a reduction in severe postoperative complications, such as sepsis, prosthetic joint infections, and 90-day readmissions; however, they were found to have elevated postoperative risk of myocardial infarction, acute kidney injury, hypoglycemic events, and pneumonia compared with the control.[20] In the THA study completed

TABLE 1. Demographic Characteristics of Unmatched and 1:1 Propensity-matched Cohorts in GLP-1-RA Patients Compared With Control

		Unmatched			Matched		
Demographics	**Cohort**	**Patients mean (SD)**	**% of cohort**	***P***	**Patients mean (SD)**	**% of cohort**	***P***
Age at lumbar fusion	GLP1-RA	1091 61.7 (10.4)	100	<0.001	1090 61.7 (10.4)	100	0.799
	Control	142419 60.1 (14.4)	100		1090 61.8 (11.0)	100	
Male	GLP1-RA	404	37.0	<0.001	404	37.1	0.246
	Control	63,389	44.5		378	34.7	
Female	GLP1-RA	628	57.6	<0.001	627	57.5	0.361
	Control	73,413	51.5		648	59.4	
White	GLP1-RA	793	72.7	0.012	792	72.7	0.885
	Control	108,156	75.9		795	72.9	
Black	GLP1-RA	127	11.6	<0.001	127	11.7	0.84
	Control	11,263	7.9		124	11.4	
Asian	GLP1-RA	17	1.6	0.135	17	1.6	0.737
	Control	3174	2.2		19	1.7	
Native Hawaiian	GLP1-RA	10	0.9	0.001	10	0.9	1
	Control	493	0.3		10	0.9	
American Indian	GLP1-RA	10	0.9	<0.001	10	0.9	1
	Control	345	0.2		10	0.9	
Other race	GLP1-RA	35	3.2	0.187	35	3.2	0.303
	Control	3664	2.6		27	2.5	
Not Hispanic	GLP1-RA	826	75.7	0.145	825	75.7	0.881
	Control	105,050	73.8		822	75.4	
Hispanic	GLP1-RA	67	6.1	0.032	67	6.1	0.407
	Control	6769	4.8		58	5.3	
Comorbidities							
Hypertension	GLP1-RA	859	78.7	<0.001	858	78.7	0.635
	Control	70,116	49.2		867	79.5	
Osteoporosis	GLP1-RA	108	9.9	<0.001	108	9.9	0.42
	Control	9904	7.0		97	8.9	
Osteoporosis with current pathologic fracture	GLP1-RA	16	1.5	0.9	16	1.5	0.237
	Control	2024	1.4		10	0.9	
Heart failure	GLP1-RA	107	9.8	<0.001	107	9.8	0.462
	Control	5340	3.7		97	8.9	
Diabetes mellitus	GLP1-RA	851	78.0	<0.001	850	78.0	0.836
	Control	24,804	17.4		854	78.3	
Chronic kidney disease (CKD)	GLP1-RA	209	19.2	<0.001	208	19.1	0.701
	Control	9090	6.4		201	18.4	
Medications							
Metformin	GLP1-RA	481	44.1	<0.001	480	44.00	0.635
	Control	9535	6.7		469	43.00	
Body mass index	GLP1-RA	837 34.8 (6.5)	76.7	<0.001	836 34.8 (6.5)	76.7	<0.001
	Control	102,553 29.9 (6.3)	72.0		793 33.5 (6.8)	72.8	
25–30 kg/m^2	GLP1-RA	227	20.8	<0.001	227	20.8	0.488
	Control	43,506	30.5		214	19.6	
30–35 kg/m^2	GLP1-RA	359	32.9	<0.001	358	32.8	0.383
	Control	36,086	25.3		339	31.1	
35–40 kg/m^2	GLP1-RA	312	28.6	<0.001	311	28.5	0.924
	Control	18,972	13.3		309	28.3	

by the same group, patients in the GLP-1 RA cohort also reported a reduction in 90-day readmissions and 2-year prosthetic joint infections without significant differences in other medical complications rates, length of hospital stay, or cost, but less acute kidney injuries and hypoglycemic events.[19] The differences between the Magruder and colleagues studies and ours could be due to limitations of generalizable cohorts and the inability to assess the specific postoperative parameters in further detail.

With more than 50% of the US population estimated to be obese by 2030 and the overall prevalence of type 2 diabetes on the rise,[3,30] the utilization of GLP-1 RAs before elective orthopedic surgery is of great interest, especially with weight loss and glycemic control being modifiable risk factors known to influence postoperative outcomes in arthroplasty and lumbar spine surgery patients.[10,27,31,32] Given that GLP-1 RAs have shown strong correlations with weight loss and glycemic control in both diabetic and nondiabetic patients,[1,23] these medications can be considered in diabetic or overweight patients undergoing elective orthopedic surgeries as a means of reducing postoperative risks and influencing perioperative optimization. However, the use of these medications may be more evident in populations with poorer glycemic control and heightened lipid levels compared with those not requiring additional medication management.

TABLE 2. Major Medical Complications In 1:1 Propensity-Matched Cohort 90 Day Postoperatively

90 d postoperative medical complications					
Complication	GLP-1-RA (%)	Control (%)	RR	95% CI	*P*
Wound complications	7.6	8.9	0.9	(0.65–1.13)	0.28
Myocardial infarction	1.0	1.0	1.0	(0.43–2.44)	0.96
Infection	4.4	4.3	1.0	(0.68–1.55)	0.91
Pulmonary embolism	0.9	0.9	1.0	(0.42–2.4)	0.98
Deep vein thrombosis	1.8	1.9	1.0	(0.51–1.80)	0.89
Stroke	1.4	1.4	1.0	(0.49–2.04)	1.00
Hospitalization	23.0	19.6	1.2	(1.00–1.38)	0.05
Pneumonia	2.0	1.7	1.2	(0.63–2.13)	0.64
Transfusion	10.6	8.2	1.3	(1.00–1.67)	0.05
Renal failure	5.9	3.6	1.6	(1.11–2.42)	0.01
Emergency department visit	15.5	12.8	1.2	(0.98–1.5)	0.07

Therefore, patients prescribed GLP-1 RAs with poorly controlled diabetes, higher BMI levels, or concomitant health issues may have an increased likelihood of postoperative complications compared with patients that do not require GLP-1 RA supplementation, as supported by the Magruder et al studies.[19,20] These potential variances in diabetic control and weight management could lead to different postoperative courses and complications.

Notably, our study found that patients taking GLP-1 RAs demonstrated lower rates of pseudoarthrosis at 1 year. Diabetes and obesity have historically been shown to be risk factors for persistent pseudarthrosis in patients undergoing lumbar fusions.[32,33] Hills et al[34] demonstrated that pre-existing endocrine-related disorders, including diabetes, were identified in 82% of pseudarthrosis cases. As GLP-1 RAs have demonstrated better glycemic control than insulin alone in type 2 diabetics undergoing elective orthopedic surgeries,[35] it could be hypothesized that GLP-1 RA-induced improvements to glycemic control and obesity, both known risk factors of postoperative spinal procedure complications,[13] can be a potential reason for improved bone healing or various other significant findings in our study.

There are various limitations to our study. The large sample size collected from a retrospective database of deidentified electronic medical records across various health care organizations may permit external generalizability of our study findings. The utilization of current procedural terminology (CPT) codes for data collection, procedure identification, case discernment, and supplemental comorbidities created limited verification processes or ability to delineate specific aspects of lumbar operations or medication adherence that could affect our results, including but not limited to perioperative complications, medication compliance, number of levels fused, specific medication type, dosing, glycemic control, preoperative medication hold, and extent of weight loss. Due to this study's retrospective design, provider-dependent or institution-based components may also have impacted procedure processes, overall outcomes, or inherent biases. Future studies could include the evaluation of perioperative effects, cervical spine cohorts, or outcomes in non-diabetic patients.

TABLE 3. 1:1 Propensity-Matched Cohort Mechanical Complications 1 Year Postoperatively

Mechanical complications 1 y after surgery					
Complication	GLP-1-RA (%)	Control (%)	RR	95% CI	*P*
Pseudarthrosis	11.0	17.9	0.6	(0.49–0.77)	<0.0001
Adjacent segment disease	6.2	5.9	1.1	(0.66–1.67)	0.84
Hardware failure	1.2	1.3	1.3	(0.42–2.01)	0.84
Foot drop	1.9	0.9	2.0	(0.91–4.20)	0.08
Reoperation	1.1	1.4	1.1	(0.36–1.74)	0.56
Postlaminectomy syndrome	4.8	3.7	1.3	(0.86–2.02)	0.21

CONCLUSIONS

In conclusion, the effects of GLP-1 receptor agonizts on patients undergoing lumbar spine surgery do not increase the risk of adverse outcomes and should not be a reason to exclude patients from undergoing lumbar spinal procedures. Our current study demonstrates that the risk of medical and mechanical complications in patients receiving GLP-1 RAs before lumbar spine surgery is comparable to that of control patients when statistically controlled for other comorbidities with no notable increase of various other postoperative adverse outcomes.

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