Original Article

Does neurofibromatosis 1 status impact outcomes for pediatric/young adults undergoing spinal fusion?

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ABSTRACT

Background: Although spinal deformities are common in patients with neurofibromatosis type 1 (NF1), there is a paucity of data as to how this impacts outcomes of spinal fusion surgery in pediatric/young adult patients.

Methods: Using the Nationwide Inpatient Sample (2005–2014) for all patients undergoing spinal fusion ≤26 years of age, we compared the following factors: demographics, comorbidities, and perioperative variables (e.g., between NF1 vs. non-NF1, and between NF1 and propensity score (PS)-matched non-NF1 spinal fusion patients) using univariate hypothesis tests and multivariate regression analyses. Our main interest focused on length of stay, complication rates, adverse postoperative events, and incidence of nonroutine discharges.

Results: In this study, 238 (0.92%) NF1 spine patients were compared to 25,558 (99.08%) non-NF1 spine patients. NF1 fusion patients were younger, included fewer females, and were more likely to be on Medicaid. Perioperatively, NF1 patients underwent more anterior approaches, had more vertebrae fused, required more transfusions, had a longer length of stay (LOS), and were less likely to be discharged home. However, after PS-matching, all differences between NF1 and non-NF1 groups disappeared were similar ($P > 0.05$). In PS-matched multivariate analyses, NF1-status was not a significant independent predictor of length of stay or nonroutine discharge disposition.

Conclusion: NF1-status was, therefore, not an independent predictor of complications, adverse postoperative events, longer LOS, or nonroutine hospital discharge in this cohort analysis. Further prospective studies are necessary to understand how outcomes in patients with NF1 compare to non-NF1 pediatric and young adult patients.

Keywords: Neurofibromatosis type 1, Outcomes, Spinal fusion

INTRODUCTION

Though rare, neurofibromatosis type 1 (NF1) is the most common autosomal dominant disorder found in humans. The patient presents with a heterogeneous range of clinical signs and symptoms. One of the most common and potentially debilitating factors in NF1 patients is the 38% incidence of spinal deformity (e.g., develop dystrophic or nondystrophic).[6]

Here, we evaluated whether, following spinal surgery, the short-term perioperative outcomes of pediatric/young adult patients with NF1 were inferior to those without NF1.

MATERIALS AND METHODS

Data source and patient population

Using the Healthcare Cost and Utilization Project Nationwide Inpatient Sample, we retrospectively analyzed NF1 versus non-NF1 pediatric/young adult patients undergoing elective spinal fusions (2005–2014). We focused on the following major clinical variables: patient demographics, expected payer, diagnoses (e.g., pre- and post-operative diagnoses), procedures, length of stay (LOS), pre-, peri-, and post-operative risk factors associated with prolonged LOS, and nonroutine discharges with/without NF1.

Documentation of NF1

Documenting the diagnosis of NF1 was based on: International Classification of Disease (e.g. International Classification of Diseases-9, Ninth Revision [ICD-9] and ICD-9 clinical modification (ICD-9-CM) diagnosis and procedure codes), evaluation of all hospital discharges for pediatric and young adult patients ≤26 years of age with/without NF1, Type 1 (237.71), and patients undergoing elective Spinal Fusions (Procedures codes listed in Table 1).

Data collection

Patient demographics, comorbidities, perioperative variables postoperative events/complications, outcomes, LOS, and discharge dispositions, were excluding. In-hospital death and discharge against medical advice and complications were compared between NF1 and non-NF1 patients.

Statistical analysis

Counts and percentages were described for categorical variables for NF1 versus non-NF1 patients. Two-tailed Student's *t*-tests were used to compare normally distributed continuous variables between NF1-status cohorts, while Mann–Whitney U-tests were used to compare nonnormally distributed continuous variables. Significance for all statistical tests was assessed with a threshold of $P = 0.05$. Due to the unbalanced disease status arms in our cohort, a propensity score (PS)-matched No NF1 cohort was generated.

RESULTS

Patient demographics

In our study, 238 (0.9%) had NF1 and 25,558 (99.1%) had no diagnosis of NF1 (No NF1) [Table 2], NF1 was more likely to receive an anterior surgical approach but less likely to undergo a 2–3 level vertebral fusion versus non-NF1 patients [Table 2].

Both patients groups had similar pre-, peri-, and post-operative clinical/other characteristics; age, sex, primary

Table 1: ICD-9-CM used for spinal procedures.

Procedure	ICD-9-CM
Spinal fusion, not otherwise specified	81.00
Atlas-axis spinal fusion	81.01
Other cervical fusion, anterior technique	81.02
Posterior other cervical fusion, posterior technique	81.03
Dorsal and dorsolumbar fusion, anterior technique	81.04
Dorsal and dorsolumbar fusion, posterior technique	81.05
Lumbar and lumbosacral fusion, anterior technique	81.06
Lumbar and lumbosacral fusion, lateral transverse process technique	81.07
Lumbar and lumbosacral fusion, posterior technique	81.08

ICD-9-CM: International classification of diseases-9 clinical modification

Table 2: Preoperative and perioperative variables.

Demographic feature	NF1 (*n*=238)	No NF1 (*n*=25558)	*P*
Age (median, IQR)	13 (10–15) (%)	15 (13–19) (%)	<0.001*
Female	48.3	38.8	<0.001*
Race			
White	49.6	54.4	0.274
Black	13.0	8.9	
Hispanic	11.3	9.5	
Asian/Pacific Islander	3.4	1.9	
Native American	1.0	1.0	
Other race	2.1	4.0	
Income quartile			
Q1	25.2	18.7	0.913
Q2	16.8	21.2	
Q3	20.6	22.6	
Q4	22.3	24.2	
Payer			
Medicare	0.4	0.6	**<0.001***
Medicaid	42.9	24.9	
Private insurance	47.9	63.8	
Self-pay	2.1	1.7	
No charge	0.8	0.3	
Other payment	5.9	8.4	
Preoperative morbidity			
Alcohol use disorder	0	0.1	0.557
Hypertension	3.4	2.3	0.249
DM	0	0.5	0.257
Obese	0	3.9	**0.002***
Smoking	0.8	6.7	**<0.001***
Hypercoagulable	0	0.2	0.546
HF	0	0.1	0.699
Atrial fibrillation	0	0	0.760
COPD	1.3	0.2	**0.002**
CKD	0	0.2	0.503
PVD	0	0	0.738
Liver disease	0.4	0.2	0.349

(Contd...)

Table 2: *(Continued)*

Demographic feature	NF1 (*n*=238)	No NF1 (*n*=25558)	*P*
Perioperative variables			
Surgical approach			
Anterior	41.2	16.1	**<0.001***
Posterior	84.9	86.7	0.411
Vertebrae fused			
2–3	12.2	30.3	**<0.001**
4–8	44.1	18.6	**<0.001**
9+	45.0	45.8	0.789
Perioperative transfusion	31.9	24.3	0.006

DM: Diabetes mellitus, HF: Heart failure, CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease, PVD: Peripheral vascular disease.

expected payers preoperative comorbidities perioperative variables, rates of complications, median LOS, or rates of nonroutine discharges [Table 2].

NF1 patients were most commonly from the 0–25% income quartile (Q1) (25.2% vs. 18.7%), were more likely to be insured through Medicaid (42.9% vs. 24.9%), and had the most prevalent preoperative morbidities including; (1) hypertension, (2) chronic obstructive pulmonary disease, and (3) smoking; in the non-NF1 group they were (1) smoking, (2) obesity, and (3) hypertension [Table 2].

Perioperative outcomes after spinal fusion

The NF1 patients had more central nervous system complications, postoperative infections, longer length of stay, and more nonroutine discharges, but spinal fusion patients with or without NF1 had similar pre-, peri-, and post-operative characteristics [Tables 1-3]. Table 4 lists the variables for propensity score-matched set data. In multivariate logistic regression analysis, there was no significant difference between the odds of being discharged nonroutinely between spinal fusion patients with NF1 and those without (Odds Ratio [OR]: 0.91, CI: 0.53–1.56; *P* = 0.73), when controlling for other factors [Table 5]. When comparing PS-matched sets data in multivariate logistic regression analysis, this difference remained statistically insignificant (OR: 0.97, CI: 0.46–2.05; *P* = 0.93) [Table 5, Figure 1].

DISCUSSION

In this study, we determined that NF1 (238 [0.9%] pediatric/ young patients undergoing spinal fusions had similar outcomes to non-NF1 patients 25,558 [99.1%]). We also found that those with NF1 were likely to have a greater number of vertebrae fused, and were more likely to receive perioperative transfusions.[1,2,4,7] In our PS-matched analysis, the observed difference in length of stay between patients

Table 3: Postoperative complications, events, and outcomes.

Complication	NF1 (*n*=238) (%)	No NF1 (*n*=25558) (%)	*P*
VTE	0.4	0.2	0.46
Sepsis	1.3	0.6	0.19
UTI	0.8	2.1	0.18
Pulmonary complication	3.8	4.1	0.78
Peripheral vascular complications	0	0	0.83
CNS complication	4.2	0.7	**<0.001***
Cardiac complication	0.8	1.0	0.86
Myocardial infarction	0	0	0.77
Stroke	0	0	0.72
Hematomas	2.9	2.0	0.32
Cut, puncture, or hemorrhage	0.8	0.6	0.72
Wound complication	2.1	1.1	0.12
Postoperative infection	2.1	0.7	**0.009***
Other complication	1.3	1.0	0.74
CSF leak	0.4	0.4	0.97
Carotid vertebral injury	0	0	0.76
Hoarseness	0	0.1	0.57
Dysphagia	0	0.1	0.56
Outcomes			
Length of stay (median, IQR)	6 (5–10.75)	5 (3–6)	**<0.001***
Nonroutine discharge	6.3	3.7	**0.038***

VTE: Venous thromboembolism, UTI: Urinary tract infection, CNS: Central nervous system, CSF: Cerebrospinal fluid.

Table 4: Pre-, peri-, and post-operative variables for propensity score-matched set data.

Demographic	NF1 (*n*=238) (%)	No NF1 (*n*=238) (%)	*P*
Age (median, IQR)	13 (10–15)	13 (10–15)	0.32
Female	51.7	51.7	1.0
Payer			
Medicare	0.4	0.4	0.71
Medicaid	42.9	41.2	
Private insurance	47.9	52.1	
Self-pay	2.1	1.3	
No charge	0.8	0.0	
Other payment	5.9	4.6	
Preoperative morbidity			
Smoking	0.8	0.8	1.0
Perioperative variables			
Surgical approach			
Anterior	41.2	38.2	0.51
Vertebrae fused			
2–3	12.2	11.8	0.89
4–8	44.1	50.4	0.17
Perioperative transfusion	31.9	31.1	0.84
Complications			
CNS complication	4.2	2.9	0.46
Postoperative infection	2.1	0.4	0.10
Outcomes			
Length of stay (median, IQR)	6 (5–11)	6 (5–8)	0.25
Nonroutine discharge	6.3	5.9	0.85

CNS: Central nervous system

Table 5: Propensity score matched predictors of home discharge: multivariate linear and logistic regression models and multivariate doubly-robust PS-matched linear and logistic regression models.

Length of stay	Risk ratio	Lower 95% CI	Upper 95% CI	P
NF1	3.02	2.16	3.87	**<0.001***
NF1 PS-matched	1.36	−0.93	3.65	0.24
Nonroutine discharge	**Odds ratio**	**Lower 95% CI**	**Upper 95% CI**	**P**
NF1	0.91	0.53	1.56	0.73
NF1 PS-matched doubly robust	0.97	0.46	2.05	0.93
NF1: Neurofibromatosis type 1				
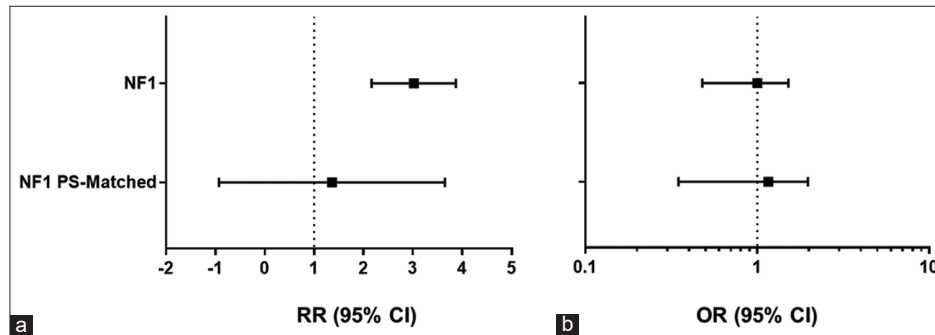
Figure 1: Forest plots representing relative risks and odds ratios for the regression models in Table 4. (a) Multivariate linear regression models of neurofibromatosis (NF1) status on length of stay and (b) multivariate logistic regression models of NF1-status on nonroutine discharge.

with and without NF1 did not reach significance. Similarly, we applied a multivariate logistic regression to explore the likelihood of nonroutine discharge in patients with and without NF1 and again found no difference between the two groups.

CONCLUSION

Comparing outcomes for NF1 versus non-NF1 pediatric/young patients (≤26 years old) undergoing spinal fusion, we found that NF1 patients were no more likely than their counterparts without NF1 to experience inferior surgical outcomes.

Declaration of patient consent

Patients consent not required as patients idenity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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