

Short Communication

Suicide in Deep Brain Stimulation for Parkinson's Disease: A Retrospective Case-Control Study

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Abstract. Deep brain stimulation (DBS), a treatment of Parkinson's disease (PD), has been associated with suicidality. We conducted a case-control study comparing suicide in four pairs of cohorts: PD patients with DBS or not, epilepsy patients with resection surgery or not, subjects with BMI ≥ 30 with bariatric surgery or not, and patients with chronic kidney disease with transplantation or not. PD patients with DBS demonstrated a lower risk of suicide relative to PD patients without DBS. Findings from other elective surgeries indicate that patients receiving operative treatments do not possess predictable differences in suicide rates relative to their medically managed counterparts.

Keywords: Parkinson's disease, deep brain stimulation, suicide, suicidal ideation, suicide attempted

INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder that affects up to 3% of adults over 65 years of age and is primarily characterized by motor symptoms including bradykinesia, resting tremor, and muscle rigidity [1]. In addition to motor symptoms, PD patients often experience cognitive impairment, behavioral changes, and mood disorders such as depression [2]. Both the motor and non-motor symptoms can be disabling and detrimental to quality of life, and clinicians have attempted to reduce these

symptoms with treatments such as deep brain stimulation (DBS) [3].

DBS was approved for the treatment of PD in 2002 and has been a standard of care for patients with advanced stage PD and motor fluctuations [4]. Although DBS has been a robust treatment option, some studies report an increase in neuropsychiatric symptoms after surgery, possibly secondary to dopaminergic medication withdrawal, direct subthalamic nucleus (STN) stimulation, or biopsychosocial changes following surgery [5]. The same studies also suggest that DBS treatment may increase the rate of suicidal ideation, suicide attempts, and/or suicide, although the literature is sparse with small sample sizes [1]. A perceived or actual increased risk of suicide may influence patients' and clinicians' decisions

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regarding treatment; thus, it is a pertinent question as to whether DBS is associated with a higher risk of suicide in PD. We investigated whether suicidal ideation and suicide attempts are higher with DBS, using a retrospective cohort of subjects with PD and DBS, matched to a cohort of PD subjects without DBS. To further understand the inherent impact of operative management on rates of suicidal ideation and suicide attempts, we also compared outcomes of elective surgeries in other patient populations: epilepsy resection surgery, bariatric surgery, and kidney transplantation.

METHODS

De-identified patient data was collected using the TriNetX, a federated research network containing over 85 million distinct patient records from 67 healthcare organizations (HCO) operating in the United States and internationally. Retrospective data was procured between June 9, 2002, and January 30, 2023. TriNetX, LLC is compliant with the Health Insurance Portability and Accountability Act (HIPAA), the US federal law which protects the privacy and security of healthcare data, and any additional data privacy regulations applicable to the contributing HCO [6]. Patient cohorts and outcomes were defined using International Classification of Diseases 10th Revision (ICD-10) and Current Procedural Terminology (CPT) codes.

Our main cohort included patients with PD (ICD-10: G20) and the accompanying presence of an intracranial neurostimulation procedure (CPT: 00H04MZ or 00H00MZ or 00H003MZ or 1009276). Patients in this cohort were compared to a control group of PD patients who did not have record of a neurostimulation procedure of any kind within their medical history. The outcome of suicide was defined by an ICD-10 diagnosis of suicidal ideation (R45.851) or suicide attempt (T14.91) within a 10-year window following a patient's entry into their respective cohort. Separate analyses were performed to either include or exclude patients with a history of suicidal ideation or suicide attempt prior to the 10-year outcome analysis window. To compare outcomes within other surgical procedures and understand the effect of operative management on suicide, similar methods using ICD-10 and CPT codes were utilized to define cohorts and calculate risk of suicidal ideation and suicide attempts for adults with epilepsy

resection surgery, bariatric surgery, and kidney transplantation (Supplementary Table 1).

Statistical analysis was completed using the TriNetX statistical software. In comparisons of baseline characteristics, a *t*-test was used for age, while chi squared tests were used to compare differences in sex, race, ethnicity, history of neuropsychiatric comorbidities, suicidality, and antidepressant usage. Cohorts with the surgical procedure of interest were then matched to a like cohort without the surgical procedure of interest using the TriNetX platform, which uses nearest neighbor matching with a difference between propensity scores less than or equal to 0.1 [7]. For PD cohort matching, the following variables were controlled for: antidepressant usage, suicide attempts, suicidal ideation, age, sex, race, and ethnicity. For other surgical cohorts, only age, sex, race, and ethnicity were controlled for. Comparison between cohorts based on surgical status was performed with a *t*-test to compare risk differences and relative risk (RR). Odds ratios (OR) were calculated from outcome incidence within each cohort. Significance for this study was set at $p < 0.05$. As this study contained only deidentified aggregate data, the Colorado Multiple Institutional Review Board (COMIRB) designated it as non-human research not in need of approval.

RESULTS

We identified 11,390 PD patients with DBS and created a matched cohort of 11,390 PD patients without DBS. After propensity score matching, these two cohorts displayed no significant differences in suicidal ideation, suicide attempts, antidepressant usage, age, sex, race, or ethnicity. Prior to DBS surgery, the cohort undergoing DBS had a significantly higher prevalence of depressive episodes and anxiety disorder, while the cohort without DBS had a higher prevalence of bipolar disorder and schizophrenia. The two cohorts did not show significant differences in history of suicidal ideation or suicide attempts (Table 1). Following DBS surgery, PD patients with DBS had a significantly lower risk of both suicidal ideation (RR: 64%; OR: 0.632; $p < 0.0001$) and suicide attempts (RR: 60%; OR: 0.596; $p < 0.001$) compared to PD patients without DBS (Table 2). When excluding patients with a prior history of suicidal ideation or suicide attempt from analysis, PD patients with DBS still displayed a significantly lower risk of suicidal ideation (RR: 71%; OR: 0.699;

Table 1
Comparison of baseline characteristics between PD subjects with DBS and PD subjects without DBS after matching for age, sex, race, and ethnicity

Variable	PD with DBS N = 11,390	PD without DBS N = 11,390	<i>p</i>
Age (y), mean (+/-SD)	71.5 (11.0)	71.5 (10.9)	0.886
% Of Cohort Male Sex (n)	64.5% (7,346)	64.5% (7,349)	0.967
% Of Cohort Female Sex (n)	35.5% (4,044)	35.5% (4,041)	0.967
Race (n)			
White	85.2% (9,700)	85.2% (9,707)	0.896
Black or African American	2.0% (223)	1.9% (219)	0.848
Ethnicity (n)			
Hispanic or Latino	4.2% (473)	4.1% (463)	0.739
Neuropsychiatric History Prior to DBS and/or PD Diagnosis (n)			
Anxiety Disorder	19.2% (2,187)	15.5% (1,762)	<0.001
Bipolar Disorder	1.7% (190)	4.4% (498)	<0.001
Depressive Episode	25.4% (2,895)	20.4% (2,324)	<0.001
Schizophrenia	0.4% (41)	1.8% (205)	<0.001
Suicidal Ideation	2.4% (277)	2.5% (280)	0.898
Suicide Attempts	0.4% (47)	0.3% (39)	0.387
Medications			
Antidepressants	47.8% (5,448)	47.8% (5,446)	0.979

PD, Parkinson's disease; DBS, deep brain stimulation.

Table 2
Risk of suicidal ideation and suicide attempt in patient populations who have undergone elective surgeries versus control populations that have not undergone elective surgeries (inclusive of subjects with prior history of suicidal ideation and/or suicide attempt)

Cohort	N	Risk of Suicidal Ideation (R45.851)				Risk of Suicide Attempt (T14.91)			
		Risk	Relative Risk	Odds Ratio (95% CI)	<i>p</i>	Risk	Relative Risk	Odds Ratio (95% CI)	<i>p</i>
PD with DBS	11,390	2.4%	64%	0.632 (0.541, 0.738)	<0.0001	0.6%	60%	0.596 (0.440, 0.807)	0.001
PD without DBS	11,390	3.7%				1.0%			
Other Elective Surgeries									
Cohort	N	Risk of Suicidal Ideation (R45.851)				Risk of Suicide Attempt (T14.91)			
		Risk	Relative Risk	Odds Ratio (95% CI)	<i>p</i>	Risk	Relative Risk	Odds Ratio (95% CI)	<i>p</i>
Resection Surgery in Epilepsy									
Epilepsy with Resection Surgery	2,431	4.6%	90%	0.891 (0.686, 1.157)	0.3866	1.1%	84%	0.842 (0.503, 1.410)	0.5125
Epilepsy without Resection Surgery	2,431	5.1%				1.3%			
Bariatric Surgery in BMI \geq 30									
BMI 30 – 39 with Bariatric Surgery	120,371	2.3%	134%	1.344 (1.269, 1.424)	<0.0001	0.5%	134%	1.342 (1.188, 1.515)	<0.0001
BMI 30 – 39 without Bariatric Surgery	120,371	1.7%				0.4%			
Kidney Transplant in Chronic Kidney Disease									
CKD with Kidney Transplant	35,218	1.6%	36%	0.347 (0.315, 0.384)	<0.0001	0.3%	31%	0.304 (0.240, 0.384)	<0.0001
CKD without Kidney Transplant	35,218	4.3%				0.9%			

PD, Parkinson's Disease; DBS, Deep Brain Stimulation; BMI, Body Mass Index; CKD, Chronic Kidney Disease.

$p < 0.0001$) and suicide attempts (RR: 65%; OR: 0.643; $p = 0.012$).

To investigate whether differences in suicidal ideation and suicide attempt were dependent upon the event of operative treatment, alternative surgeries were analyzed. Overall, the risk of suicide

within elective surgeries varied with the type of procedure that was performed (Table 2). Between epilepsy patients receiving resection surgery, and those not receiving resection surgery, there was no significant difference in outcomes of suicidal ideation (RR: 90%; OR: 0.891; $p = 0.3866$) and sui-

cide attempts (RR: 84%; OR: 0.842; $p=0.5125$). In patients with a body mass index (BMI) ≥ 30 , patients who had undergone bariatric surgery displayed a significantly higher risk of suicidal ideation (RR: 134%; 1.344; $p<0.0001$) and suicide attempts (RR:134%; OR:1.342; $p<0.0001$). In patients with chronic kidney disease (CKD), there was a significantly lower risk of suicidal ideation (RR: 36%; OR: 0.347; $p<0.0001$) and suicide attempt (RR: 31%; OR:0.304; $p<0.0001$) in patients who had undergone a kidney transplant. Thus, with the surgical procedures assessed in this study, there was no clear association between the inherent nature of operative vs non-operative management and trends in suicide.

DISCUSSION

Despite the suggested concern of increased suicidal behavior following DBS in PD, our study contradicted this notion by revealing a lower risk of suicidal ideation and suicide attempts in PD patients with DBS compared to those without. Other research has suggested elective surgery itself may be a risk factor for suicidal ideation due to the failure of stress processing mechanisms to adapt to the physical, psychological, and social post-surgical demands [8]. Our investigations of different elective surgeries indicate that the nature of the procedure, combined with the characteristics of the population receiving elective surgical treatment, ultimately influences differences in risks of suicide. For example, transplantation within CKD was associated with a lower risk of suicide, bariatric surgery with a higher risk, while resection surgery for epilepsy revealed no statistical differences. Of note, these findings support previous studies of suicide in bariatric surgery [9], while the effects of epilepsy resection surgery and kidney transplantation on suicidality require further characterization [10, 11]. Overall, patients receiving operative treatments do not necessarily display predictable differences in suicide rates when compared to medically managed counterparts, raising our confidence that the lower risk of suicidal ideation and suicide attempts is related to DBS specifically within the PD population.

The greatest limitation of our study is the lack of randomization due to the nature of retrospective cohort studies. Additionally, other factors such as social determinants of health and outside stressors are known contributors to suicidal behavior [12], and

due to the database utilized, we are unable to characterize how patients seeking operative treatments may differ in these confounding factors. Another limitation is the nature of ICD-10 coding, which the clinician utilizes for the purposes of billing, rather than as a diagnostic framework. Thus, a clinician may not enter the multitude of billing codes that pertain to a patient's medical condition, which may have the effect of underreporting the absolute risk of suicidal ideation and suicide attempts in populations experiencing these phenomena. Yet, this degree of imprecision is likely similar across cohorts and thus does not present a major confound in statistical comparisons among case-control subjects. The CPT codes used in this study also possess inherent limitations, as currently available DBS CPT codes do not distinguish whether leads are targeted to the STN versus the globus pallidus interna (GPi). While previous randomized controlled trials have demonstrated similar rates of suicidal ideation among STN-DBS versus GPi-DBS at 6 months [13], this study is unable to characterize differences between these DBS subgroups, illustrating the need for further study in this area.

These findings provide valuable insight to the neurology community at large and further the discussion around suicide and DBS. This is the largest study showing a cohort of PD patients after DBS having incidentally lower suicide rates relative to PD patients without this elective treatment, even after controlling for confounding factors such as antidepressant usage. We postulate the mechanisms underlying these findings are unlikely to be due to DBS alone, while PD symptom reduction may attribute to an increased quality of life, these findings may also reflect that there is increased healthcare attention to cognitive and mood symptoms both prior to and following DBS treatment. Although suicide risk should always be monitored, our findings indicate DBS should not be declined solely in an effort to avoid suicidal ideation and suicide attempts.

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CONFLICT OF INTEREST

RD provides consulting for Medtronic, Inc.

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OK is a full-time employee of Neurocrine Biosciences Inc.

SUPPLEMENTARY MATERIAL

The supplementary material is available in the electronic version of this article: <https://dx.doi.org/10.3233/JPD-225049>.

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