Original Article

Incidence of complications associated with deep brain stimulation surgery in patients with Parkinson's disease: An 8-year retrospective study

ABSTRACT

Background: Various complications occur in patients undergoing deep brain stimulation (DBS) surgery. The objective of this study was to determine the incidence of complications in patients with Parkinson's disease who underwent DBS surgery and identify the risk factors, especially anesthetic factors.

Methods: A retrospective cohort study was performed between May 2015 and December 2022. Based on a review of medical charts, patients aged 18 years or older who underwent DBS surgery at a tertiary neurological center in Thailand were recruited. Univariate analysis using the Chi-square test or Fisher's exact test was performed to compare patients with and without complications. Multivariate logistic regression analysis was performed to identify the predictive factors for complications.

Results: The study included 46 patients. The most common complication during DBS electrode placement was hypertension (30/46, 65.2%), and 19 patients (41.3%) who developed hypertension did not receive antihypertensive treatment. The most common complication during battery placement was clinical hypotension (14/46, 30.4%). The most common postoperative complication was delirium (6/46, 13.0%). In the multivariate analysis, no significant independent risk factors for overall complications after DBS surgery were identified.

Conclusions: Hypertension during DBS electrode insertion was the most common perioperative complication. Hemodynamic instability is preventable and manageable, and vigilant and prompt treatment should be provided during DBS surgery.

Key words: Awake craniotomy, choice of anesthesia, complication, deep brain stimulation

Introduction

Deep brain stimulation (DBS) is a surgical intervention to stimulate specific areas of the brain for treating Parkinson's disease.[1] The choice of anesthesia technique for DBS electrode placement is controversial. It is recommended to use monitored anesthesia care (MAC) with local anesthesia and sedative drugs rather than general anesthesia (GA), as it

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Jatuporn Eiamcharoenwit, Phuping Akavipat

Department of Anesthesiology, Neurological Institute of Thailand, 312 Ratchawithi Road, Thung Phaya Thai, Ratchathewi, Bangkok, Thailand

Address for correspondence: Dr. Jatuporn Eiamcharoenwit, Department of Anesthesiology, Neurological Institute of Thailand, 312 Ratchawithi Road, Thung Phaya Thai, Ratchathewi, Bangkok - 10400, Thailand.
E-mail: Jatu_air@yahoo.com

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helps in locating specific areas and performing microelectrode recording (MER) and macrostimulation testing.[2]

The incidence of complications during DBS surgery has been reported to be 5%–16%, and respiratory complications have been noted in 1.6%–2.2% of patients undergoing DBS surgery, which have been shown to be associated with excessive sedation or a sudden decrease in consciousness due to seizures or intracranial hemorrhage.[3] A venous air embolism has been reported in 0.6%–3.2% of patients, especially in patients with hypotension or those with spontaneous breathing.[3,4] Seizures have been reported in less than 1% of patients.[3,4] Intracranial hemorrhage has been noted in 0.5%–2.8% of patients.[3,4] However, rarely report perioperative complications associated with anesthetic factors. In Thailand, DBS can be performed in some institutions. This study aimed to determine the incidence of complications in patients who underwent DBS and identify the possible risk factors associated with those complications.

Materials and Methods

Ethics

This retrospective cohort study was approved by the institutional research ethics committee (approval number 66010) on December 29, 2021. Written informed consent was waived according to the approval of the ethics committee.

Study design

The study included patients aged 18 years or older who had been diagnosed with Parkinsonism and underwent DBS. Patients who had incomplete medical data were excluded. The inpatient medical records and electronic anesthesia records of the patients were reviewed over an 8-year study period (May 2015–December 2022). The first DBS procedure was in May 2015.

Patient factors included baseline characteristics and comorbidities. Anesthesia and surgical factors included expected difficult airway, scalp block, type and dosage of anesthetic drugs, duration of anesthesia, and operative time. The period of intensive care unit stay and length of hospital stay were also collected. The first stage involved the insertion of electrodes, and the intraoperative complications were divided into cardiovascular complications (hypertension, hypotension, bradycardia, and venous air embolism), respiratory complications (excessive sedation with airway obstruction and desaturation), and other complications (nausea and vomiting). The second stage involved the implantation of a programmable pulse generator, and the intraoperative cardiovascular complications included hypertension, hypotension, and bradycardia. The postoperative complications were divided into neurological complications (intracranial hemorrhage, subdural hygroma, and seizure), respiratory complications (pulmonary embolism), psychological complications (delirium), and other complications (DBS electrode migration, hematoma at the chest wall, and urinary tract infection).

Anesthetic procedure

Drugs used for the treatment of Parkinson's disease were withheld on the morning of the procedure to facilitate testing. Moreover, antiplatelet drugs were discontinued before the procedure. The first stage involved the insertion of electrodes into the target area of the brain. The anesthetic technique was MAC with local anesthesia and conscious sedation. Patients were monitored routinely with noninvasive blood pressure monitoring, electrocardiography, pulse oximetry, and end-tidal carbon dioxide monitoring via a nasal sponge in the operating theater. The vital signs were recorded every 2.5 min. The Ramsay sedation score was used to monitor the sedation level, and a Ramsey sedation score of 2 was considered appropriate during MER and macrostimulation testing. Oxygenation was achieved with 3 L/min of oxygen through a cannula. Local infiltration or scalp block was performed before starting the procedure. Intravenous fentanyl, propofol, and dexmedetomidine were administered for conscious sedation based on the judgment of the responsible anesthesiologist. If dexmedetomidine plus propofol was selected, propofol would be added during foley catheter insertion and the burr hole procedure, while dexmedetomidine was used mainly as a major anesthetic. Practically, we used an infusion of dexmedetomidine with fentanyl, not the combination of dexmedetomidine with fentanyl and propofol infusion, to facilitate patients' communication and cooperation during the MER. Conscious sedation was adopted during the incision and burr hole procedure, was discontinued before the MER and macrostimulation testing for electrode insertion, and was restarted for closure after macrostimulation testing. The second stage involved internalization of the leads and implantation of a programmable pulse generator under GA with an endotracheal tube immediately after placing the DBS electrodes. All patients were scheduled for routine postoperative computed tomography (CT) scans to check the electrode localization and detect intracranial hemorrhage. A single surgeon performed the DBS procedure. Stimulation was initiated 4 weeks after lead implantation.

Definitions of intraoperative and postoperative complications

The various definitions of complications adopted in this study were as follows:

1. Intraoperative hypertension was defined as an increase in blood pressure of more than 20% from baseline for more than 5 min.[5]

2. Intraoperative hypotension was defined as a reduction in blood pressure of more than 20% from baseline for more than 5 min.[6]
3. Intraoperative bradycardia was defined as a heart rate slower than 60 beats per min, and it was treated with atropine.[7]
4. Venous air embolism was defined as gas entering a venous structure and traveling through the right heart to the pulmonary circulation. The symptoms include a decrease in the end-tidal carbon dioxide concentration (ETCO2), followed by a decrease in blood pressure and an increase in heart rate.[8]
5. Excessive sedation was defined as sedation that caused a level of consciousness resembling deep sleep. The patient must respond to loud conversations or intense touch, which may need to be repeated. There may be an obstructed airway that requires support.[9]
6. Desaturation was defined as oxygen saturation of <90%.[10]
7. Vomiting was considered as the forceful retrograde expulsion of gastric contents from the body. Nausea was considered as the unpleasant sensation that precedes vomiting.[11]
8. Intracranial hemorrhage was considered as a radiographic finding of hemorrhage within the brain (intracranial hemorrhage), bleeding in the meninges (subarachnoid hemorrhage), or bleeding in the ventricles of the brain (intraventricular hemorrhage).[12]
9. A subdural hygroma was considered as a collection of cerebrospinal fluid under the dural membrane, with diagnosis confirmation by CT or magnetic resonance imaging.[13]
10. Seizure was considered as an event caused by an acute change in the function of brain cells, with abnormal electrical discharges. The signs and symptoms include movement of organs, such as the head and eyes, neck tilt, twitching or stiffening of the arms and legs, and repeated movements, such as blinking the eyes frequently or chewing in the mouth. The patient may be conscious or unconscious.[14]
11. Pulmonary embolism was diagnosed by CT pulmonary angiography.[15]
12. Postoperative delirium was considered as a change in consciousness with a hyperactive behavior, such as confusion; hypoactive behavior, such as lethargy or drowsiness; or both behaviors. The most common symptom is drowsiness. The patient usually sleeps during the daytime but is chaotic during the night. Postoperative delirium was assessed within the first 1–3 days after surgery.[16]
13. DBS electrode migration was defined as the migration of a lead to an unintended location.[17]
14. Urinary tract infection (UTI) was defined as the acute onset of UTI-associated symptoms and signs (e.g., fever, dysuria, gross hematuria, and suspected bacteremia). The minimum laboratory evaluation for suspected UTI should include urinalysis to check for pyuria.[18]

Statistics

Descriptive statistics have been reported as frequency, percentage, mean, and interquartile range. Univariate analysis was performed to compare patients with and without complications using the Chi-square test or Fisher's exact test as appropriate for the data. The variables associated with complications and having a *P* value of <0.2 in the univariate analysis were included in the multivariate logistic regression analysis to identify the predictive factors. *P* values, odds ratios (ORs), adjusted ORs, and 95% confidence intervals (CIs) are reported. A *P* value of <0.05 was considered statistically significant. SPSS version 16 (SPSS Inc., Chicago, IL, USA) was used to analyze the data. There were no missing data in this study.

Results

Among 56 Parkinson's disease patients who were eligible, 10 patients were excluded because they underwent pallidotomy. The remaining 46 patients were enrolled during the study period, and there was no incomplete medical data. All patients underwent DBS (frame-based subthalamic nucleus DBS) for Parkinson's disease. Of the 46 patients, 44 (95.65%) underwent bilateral DBS. The incidences of complications are shown in Table 1. The most common intraoperative complication during the insertion of DBS electrodes was hypertension (30/46, 65.2%), and 19 patients (41.3%) who developed hypertension did not receive antihypertensive treatment. The most common intraoperative complication during the internalization of the leads and implantation of the programmable pulse generator was hypotension (14/46, 30.4%), and all patients received ephedrine injections. The most common postoperative complication was delirium (6/46, 13.0%), which developed on days 2–3 postoperatively. Moreover, three patients (6.5%) were found to have intracranial hemorrhage immediately postoperatively on routine brain CT, and all patients received conservative treatment. Furthermore, one patient (2.2%) had a subdural hygroma and underwent a bilateral burr hole procedure with irrigation, one patient (2.2%) developed a pulmonary embolism on day 5 postoperatively and was referred to another hospital for continued pulmonary embolism treatment on postoperative day 8, one patient (2.2%) had DBS electrode migration and underwent frame-based stereotactic proper DBS revision under MAC with sedation (data for the DBS revision were not collected and analyzed), one patient (2.2%) had a hematoma at

the chest wall and underwent hematoma drainage under GA, and one patient (2.2%) developed a fever on postoperative day 3 and had a UTI. There was no event of venous air embolism or seizure. We found that patients with complications had a significantly longer hospital stay than those without complications, with a median (IQR) of 6.00 (5.00–9.00) and 4.50 (4.00–5.00), respectively (OR = 4.42, 95% CI = 1.19–16.44; $P = 0.002$). However, there was no significant difference in ICU stay between the groups, with a median (IQR) of 1.00 (1.00–1.00) and 1.00 (1.00–1.00) in the patients without and with complications, respectively ($P = 0.283$).

Table 1: Incidence of complications (*n*=46)

Events	*n* (%)
Intraoperative complications	
First stage	
Hypertension	
Not received antihypertensive treatment	19 (41.3)
Received antihypertensive treatment	11 (23.9)
Hypotension	3 (6.5)
Bradycardia	5 (10.9)
Excessive sedation	1 (2.2)
Desaturation	1 (2.2)
Nausea/vomiting	2 (4.3)
Second stage	
Hypertension	11 (23.9)
Not received antihypertensive treatment	7 (15.2)
Received antihypertensive treatment	4 (8.7)
Hypotension	14 (30.4)
Bradycardia	3 (6.5)
Postoperative complications	
Intracranial hemorrhage	3 (6.5)
Subdural hygroma	1 (2.2)
Pulmonary embolism	1 (2.2)
Delirium	6 (13)
DBS electrode migration	1 (2.2)
Hematoma at the chest wall	1 (2.2)
Urinary tract infection	1 (2.2)

Data are presented as number of patients (percentage)

With regard to the anesthetic technique, DBS was performed under local anesthesia without a sedative drug in one patient (2.17%), MAC with fentanyl in seven patients (15.22%), MAC with fentanyl, and propofol plus dexmedetomidine in nine patients (19.57%), MAC with fentanyl and dexmedetomidine in 11 patients (23.91%), and MAC with fentanyl and propofol in 18 patients (39.13%). Univariate analysis results of patient factors are shown in Table 2. Univariate analysis results of anesthesia and surgical factors for complications during the first and second stages are shown in Tables 3 and 4, respectively. Univariate analysis revealed that the total dose of propofol and dexmedetomidine infusion during the first stage was significantly associated with the development of complications [Table 3]. Multivariate analysis did not identify risk factors associated with the development of complications in patients who underwent DBS [Table 5].

Discussion

The goals of anesthesia for DBS are to provide good surgical conditions, stable hemodynamics, and patient comfort, and to facilitate intraoperative MER and macrostimulation testing.[5] It is essential to select the right patient and optimize the patient's preoperative condition, especially in

Table 2: Univariate analysis of patient risk factors for complications (*n*=46)

Variables	Without complications (*n*=8)	With complications (*n*=38)	Odds ratio	95% confidence interval	*P*
Age, years	58 (53–65)	59 (55–65)	1.03	0.93–1.14	0.337
Age, years					1.000
<65	6 (75)	28 (73.7)	1		
≥65	2 (25)	10 (26.3)	1.07	0.19–6.20	
Sex					0.243
Male	7 (87.5)	24 (63.2)	1		
Female	1 (12.5)	14 (36.8)	4.08	0.45–36.72	
Body mass index, kg/m^2	20.93 (20.42–22.97)	21.48 (18.87–22.93)	1.02	0.81–1.28	0.977
Body mass index; kg/m^2					N/A
<30	8 (100)	38 ((100)	N/A†	N/A	
≥30	0	0			
Comorbidities					
Hypertension	2 (25)	16 (42.1)	2.18	0.39–12.25	0.453
Diabetes mellitus	0	5 (13.2)	N/A	N/A	0.569
Ischemic heart disease	0	1 (2.6)	N/A	N/A	1.000
Aspirin use	0	4 (10.5)	N/A	N/A	1.000
Pulmonary disease	0	1 (2.6)	N/A	N/A	1.000
Previous cerebrovascular disease	0	2 (5.3)	N/A	N/A	1.000

Data are presented as median (interquartile range) or number of patients (percentage). *P<0.05, statistically significant. †NA: not applicable

Table 3: Univariate analysis of anesthesia and surgical factors for complications during the first stage of DBS Surgery (*n*=46)

Variables	Without complications (*n*=8)	With complications (*n*=38)	Odds ratio	95% confidence interval	*P*
Expected difficult airway	0	2 (5.3)	N/A†	N/A	1.000
Scalp block	0	7 (18.4)	N/A	N/A	0.325
Anesthetic drugs					
Propofol used	6 (75)	21 (55.3)	0.41	0.07–2.30	0.440
Total dose of propofol, mg	45 (27.50–52.50)	70 (50.00–100.00)	1.04	0.99–1.10	0.030*
Total dose of propofol, mg					0.555
≤100	6 (100)	16 (76.2)			
>100	0	5 (23.8)	N/A	N/A	
Dexmedetomidine used	0	20 (52.6)	N/A	N/A	0.006*
Total dose of dexmedetomidine, μg	0	127 (68.00–164.50)	N/A	N/A	N/A
Total dose of dexmedetomidine, μg/kg/h					N/A
≤0.6	0	15 (75)			
>0.6	0	5 (25)	N/A	N/A	
Dexmedetomidine plus propofol used	0	9 (23.7)	N/A	N/A	0.324
Fentanyl used	6 (75)	35 (92.1)	3.89	0.53–28.39	0.203
Total dose of fentanyl, μg	90 (68.75–112.50)	80 (50–100)	1.00	0.99–1.01	0.548
Total dose of fentanyl, μg/kg/h					1.000
≤1	6 (100)	34 (97.1)			
>1	0	1 (2.9)	N/A	N/A	
Duration of anesthesia, min	208.50 (173.25–365.25)	249.00 (203.50–305.75)	1.00	0.99–1.01	0.602
Duration of anesthesia, min					0.451
≤240	5 (62.5)	17 (44.7)	1		
>240	3 (37.5)	21 (55.3)	2.06	0.43–9.87	
Operative time, min	173.50 (138.00–320.25)	219.50 (171.50–262.00)	1.00	0.99–1.01	0.592
Operative time, min					0.105
≤180	5 (62.5)	11 (28.9)	1		
>180	3 (37.5)	27 (71.1)	4.09	0.83–20.14	

Data are presented as median (interquartile range) or number of patients (percentage). *$P<0.05$, statistically significant. †NA: not applicable

Table 4: Univariate analysis of anesthesia, surgical factors for complications during the second stage of DBS Surgery (*n*=46)

Variables	Without complications (*n*=8)	With complications (*n*=38)	Odds ratio	95% confidence interval	*P*
Anesthetic drugs					
Total dose of propofol, mg	120 (100–150)	100 (80–130)	0.99	0.96–1.01	0.129
Total dose of fentanyl, μg	100 (81.25–142.50)	100 (67.50–100.00)	0.99	0.97–1.01	0.122
Duration of anesthesia, min	101 (90–117)	105 (88–120)	1.00	0.97–1.04	0.850
Operative time, min	60 (59–86)	60 (50–70)	0.97	0.93–1.02	0.469

Data are presented as median (interquartile range). *$P<0.05$, statistically significant

Table 5: Multivariate analysis of risk factors for complications

Variables	Adjusted odds ratio	95% confidence interval	*P*
First stage			
Total dose of propofol, mg	1.09	1.00–1.21	0.074
Fentanyl used	0.15	0.01–7.67	0.347
Operative time, min			
≤180	1		
>180	21.83	0.78–610.23	0.070
Second stage			
Total dose of propofol, mg	0.95	0.89–1.01	0.117
Total dose of fentanyl, μg	1.00	0.95–1.06	0.989

a patient with Parkinson's disease who is of old age and has comorbidities.

In previous studies, perioperative complications occurred in 2.8%–42.6% of patients undergoing DBS.[4,19-25] In our study, intraoperative complications occurred in 2.2%–65.2% of patients, and postoperative complications occurred in 2.2%–13% of patients. There are vast differences in the incidence range among various studies owing to differences in the types of complications collected.

In our study, intraoperative hypertension during electrode insertion was the most common complication, which occurred in 65.2% of patients, and 41.3% of the patients did not receive antihypertensive treatment. In the study by Chowdhury *et al*.,[20] the incidence of hypertension during this stage was 50.6%, and 57% of cases underwent treatment.

Hypertension should be controlled to minimize the risk of intracerebral hemorrhage during electrode insertion. The recommendation is to control the systolic blood pressure below 140 mmHg or within 20% of the patient's baseline systolic blood pressure.[5,20,26] No detection of venous air embolism (VAE) in our study can be attributed to the fact that we defined VAE based on the clinical diagnosis. If the monitorings with high sensitivity for VAE were used, the incidence of VAE should be detected more. Although transesophageal echocardiography is the most sensitive monitor for venous air embolism, but it is still not suitable for patients undergoing awake procedures.[8] In addition, the study by Chowdhury *et al*.[20] found that hypotension was the most common hemodynamic perturbation during the battery placement period. Similarly, we found that hypotension was the most common complication during battery placement, which occurred in 30.4% of patients. This is because patients with Parkinson's disease have autonomic dysfunction and develop hypotension during GA.[5]

We found that delirium was the most common postoperative complication, which occurred in 13.0% of patients. Similarly, the study by Lu *et al*.[25] reported that the incidence of postoperative delirium was 16.8%. A low preoperative Mini-Mental State Examination score (OR = 0.855, 95% CI = 0.768–0.951; $P = 0.004$) and a high unified Parkinson's disease rating scale part 3 (on the state) score (OR = 1.061, 95% CI = 1.02–1.104; $P = 0.003$) were independent risk factors for delirium after DBS surgery in Parkinson's disease patients under total intravenous anesthesia.[25] Moreover, Strapasson *et al*.[27] reported that advanced age was a risk factor for postoperative delirium after DBS surgery.

In our study, intracranial hemorrhage after DBS surgery occurred in 6.5% of patients. This incidence is similar to the incidence reported in the study by Fenoy *et al*. (5%)[4] but is higher than the incidences reported in the studies by Yang *et al*. (3.13%)[21] and Jung *et al*. (0.7%).[24] The study by Jung *et al*.[24] found that male sex and underlying hypertension were risk factors for intracranial hemorrhage after DBS surgery in patients with Parkinson's disease.

Intraoperative airway and respiratory complications are concerns in a patient undergoing DBS under MAC with sedation, especially when the patient's head is immobilized in the stereotactic head frame. Excessive sedation or a sudden decrease in consciousness due to intracranial hemorrhage or seizures may cause loss of airway patency.[5] Our study found that the incidence of airway complications, including excessive sedation causing upper airway obstruction and desaturation, was 4.4%. This incidence is higher than the incidence in the study by Khatib *et al*.,[19] who reported that airway obstruction and respiratory distress occurred in 1.6% of patients who underwent DBS surgery, with 91% of patients receiving an intravenous infusion of propofol as the sole agent.

Although univariate analysis showed that the total dose of propofol and dexmedetomidine infusion during the first stage was significantly associated with the occurrence of complications, multivariate analysis did not identify the independent risk factors for complications after DBS surgery in patients with Parkinson's disease. Our result is contrary to the result in the study by Khatib *et al*.,[19] who found that age was an independent risk factor for complications during DBS. Even though hypertension was the most common comorbidity, the results in univariate and multivariate analyses were insignificant. On the other hand, Xu *et al*.[23] reported hypertension (OR = 3.33, 95% CI = 1.14–9.71; $P = 0.027$) and surgery in the year 2017–2018 (OR = 11.04, 95% CI = 2.42–50.45; $P = 0.002$) as independent risk factors for overall postoperative complications (operation-related and hardware-related complications). A possible reason for the absence of independent risk factors for complications in our study is the small sample size. Moreover, all patients were cared for since the beginning of DBS surgery. Studying a larger sample and identifying risk factors for specific complications instead of overall complications may provide better results. However, our study showed that the clinical outcomes considerably varied among patients with and without complications, and patients in the complications group had a longer hospital stay.

The choice of anesthesia for inserting the electrodes varies depending on the anesthesiologist and neurosurgeon. Venkatraghavan *et al*.[5] preferred using MAC with sedation more than GA to facilitate MER and macrostimulation testing. The meta-analysis by Liu *et al*.[28] comparing MAC with GA found that both GA and MAC did not differ in improving symptoms and the incidence of complications. Careful preoperative assessments include toleration of awake and difficult airway problems, impaired respiratory reserve, poor cough reflex, and increased risk for aspiration, especially in patients with long-standing Parkinson's disease, before deciding on MAC with sedation.[5] Our results showed no independent risk factors for complications. Using MAC with sedation (intravenous fentanyl, propofol, dexmedetomidine, or propofol plus dexmedetomidine administered for conscious sedation) did not increase the incidence of complications. Low-dose infusion of dexmedetomidine (0.2–0.7 μg/kg/h) provides sedation with easy arousal and no effect on MER.[29] Propofol needs to be stopped in advance before MER testing to avoid interference with MER. Short-acting opioids, such as fentanyl and remifentanil, are

commonly used because of their minimal effect on MER. In addition, using opioids plus propofol may increase the risk of respiratory depression.[30] Optimization of modifiable factors, such as primarily controlled hypertension, controlled disease-specific considerations of Parkinson's disease, experienced anesthesiologists and surgeons, and prompt treatment of perioperative and postoperative adverse events, should be considered in patients undergoing DBS. It is essential to rely on the cooperation of multiple specialty teams (neurosurgery, neurology, radiology, and anesthesiology).

Our study highlights the importance of reporting perioperative complications and identifying the contributing anesthetic factors. This area is yet to be extensively studied. However, our retrospective cohort study has some limitations. First, our data were from a single center, and the sample size was small for patients who underwent DBS. Second, we assessed mainly anesthesia and some surgical factors without hardware-related complications. Third, anesthetic and surgical techniques gradually develop over time, which could decrease complication incidence. More studies need to be conducted in the future.

Conclusion

MAC with local anesthesia and sedation is commonly used for DBS surgery. The potential complications of DBS include airway/respiratory, neurologic, and cardiovascular complications. Hemodynamic instability was the most common perioperative complication, especially hypertension during insertion of the DBS electrodes. Hemodynamic instability is preventable and manageable, and vigilant and prompt treatment should be provided during DBS surgery.

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Conflicts of interest

There are no conflicts of interest.

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