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MAJOR ARTICLE

Deep Brain Stimulator Device Infection: The Mayo Clinic Rochester Experience

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Background. Deep brain stimulator (DBS)–related infection is a recognized complication that may significantly alter the course of DBS therapy. We describe the Mayo Clinic Rochester experience with DBS-related infections.

Methods. This was a retrospective study of all adults (≥18 years old) who underwent DBS-related procedures between 2000 and 2020 at the Mayo Clinic Rochester.

Results. There were 1087 patients who underwent 1896 procedures. Infection occurred in 57/1112 (5%) primary DBS implantations and 16/784 (2%) revision surgeries. The median time to infection (interquartile range) was 2.1 (0.9–6.9) months. The odds of infection were higher with longer operative length ($P = .002$), higher body mass index (BMI; $P = .006$), male sex ($P = .041$), and diabetes mellitus ($P = .002$). The association between infection and higher BMI ($P = .002$), male sex ($P = .016$), and diabetes mellitus ($P = .003$) remained significant in a subgroup analysis of primary implantations but not revision surgeries. Infection was superficial in 17 (23%) and deep in 56 (77%) cases. Commonly identified pathogens were *Staphylococcus aureus* (65%), coagulase-negative staphylococci (43%), and *Cutibacterium acnes* (45%). Three device management approaches were identified: 39 (53%) had complete device explantation, 20 (27%) had surgical intervention with device retention, and 14 (19%) had medical management alone. Treatment failure occurred in 16 (23%) patients. Time-to-event analysis showed fewer treatment failures with complete device explantation ($P = .015$). Only 1 individual had complications with brain abscess at failure.

Conclusions. Primary DBS implantations had higher rates of infection compared with revision surgeries. Complete device explantation was favored for deep infections. However, device salvage was commonly attempted and is a reasonable approach in select cases given the low rate of complications.

Keywords. deep brain stimulator; DBS-related infection; device-related infection; neuromodulation; neurosurgery infection.

Deep brain stimulator (DBS) implantation is an established surgical procedure for the symptomatic treatment of movement disorders [1]. The number of patients treated with DBS is expected to increase in the future, as are the complications associated with its implantation [2]. DBS-related infection is a recognized complication that can significantly alter the course of therapy.

As with other devices [3, 4], the favored approach for treating DBS-related infection involves the removal of the entire DBS system supplemented with antimicrobial therapy. However, device retention may be attempted depending on the depth of infection and patient preference [3, 4]. For example, patients with severe movement disorders who experience significant improvement with DBS may prefer to attempt device salvage, especially if DBS reimplantation after device removal is difficult.

There are few data examining outcomes following DBS-related infections and the different management approaches. In this study, we describe the clinical characteristics of patients presenting with DBS-related infection using our proposed definition. We also categorize surgical intervention into 3 clinically relevant device-management groups and compare their relative outcomes.

METHODS

We used the International Classification of Diseases, Ninth and Tenth Revision (ICD-9 and ICD-10), and Common Procedural Terminology (CPT) codes (Supplementary Data) to identify all adult patients (≥18 years old) who underwent DBS primary implantation and revision surgery from January 1, 2000, to December 31, 2020, at our institution. The study was approved

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by the Mayo Clinic Institutional Review Board. We reviewed the electronic medical records of included patients. Data collection was completed on March 1, 2022.

Definitions

Study Population

We collected and analyzed data for all DBS-related procedures performed during the study period, with some patients contributing to multiple observations (see Figure 1 for inclusion flowchart). All included procedures were followed until the next DBS-related procedure or last patient encounter, whichever came first. The postoperative period was screened for DBS-related infection.

DBS-Related Procedures

Primary DBS implantation was defined as the initial placement of DBS. The DBS system can be implanted in a single procedure, or stepwise fashion in multiple procedures—herein referred to as "single-stage" and "multistage" approaches, respectively. The latter approach involves implanting intracranial leads first, followed by an infraclavicular implantable pulse generator (IPG) in a separate operation. On the other hand, DBS revision surgery was defined as any subsequent procedure for the replacement of malfunctioning but uninfected DBS parts, such as lead exchange or IPG replacement surgery. Operative length was measured from the start of incision to the end of the operation.

Perioperative antibiotics were used before performing a surgical incision to prevent postoperative infection. The most used antibiotics were cefazolin 2 g, given <1 hour before incision, and vancomycin 15 mg/kg, given within 1–2 hours before incision. Antibiotics were stopped 24–48 hours after the procedure.

Topical antibiotics were often applied to operative wounds during DBS-related procedures at our institution. These include bacitracin, gentamicin, vancomycin, cefazolin, or levofloxacin. All antibiotics were mixed in 0.9% sodium chloride (NaCl) for irrigation, except for vancomycin, which was administered as 1 g of powder placed in the surgical bed.

DBS-Related Infection

Table 1 highlights our proposed definition for DBS-related infection based on our institutional experience. Some elements in our definition are adapted from a previously proposed definition for spinal cord stimulator infection [4].

Management of DBS-Related Infection

Based on surgical management at the time of presentation for infection, we divided treatment into 3 device management groups, defined in Table 2.

Chronic suppression was defined as oral antibiotics prescribed after an intended therapeutic antimicrobial course to suppress residual infection and prevent relapse. In our institution, this is not a routine practice but is occasionally used by some physicians when the device is retained.

Outcomes of DBS-Related Infection

Treatment failure was defined as the persistence or recurrence of infection following therapy. Persistence of infection was considered when patients continued to demonstrate clinical signs and symptoms prompting a change in initial antibiotic or surgical management. Recurrence of infection was considered when signs and symptoms of infection redeveloped after complete resolution. In patients with partial or complete device explantation, this included recurrent skin and soft tissue infection (SSTI) overlying the previous DBS device track, infection of any retained DBS parts, infection of the central nervous system (CNS) not diagnosed on initial encounter, or reinfection after reimplantation of new DBS parts.

Statistical Analysis

Frequency counts and percentages were used for categorical variables, while medians (interquartile ranges [IQRs]) were used for continuous variables. Comparisons of groups were made using the chi-square or Fisher exact test for categorical variables, the Wilcoxon-Mann-Whitney test for continuous variables when comparing 2 groups, and the Kruskal-Wallis H test for continuous variables when comparing >2 groups. A Kaplan-Meier curve was used to determine DBS-related infection rates and compare treatment failure rates between the 3 device management groups. Statistical analyses were performed using BlueSky Statistics, version 7.40 (BlueSky Statistics LLC, Chicago, IL, USA). *P* values of <.05 were considered significant.

RESULTS

During the study period, 1087 patients underwent 1896 DBS-related procedures performed by 5 different surgeons: 1112 primary implantations and 784 revision surgeries. A multistage approach was used in 598/1112 (54%) primary implantations. Revision surgeries consisted of replacing IPG alone in 759/784 (97%) procedures and replacing both IPG and lead(s) in 25/784 (3%) procedures. All revision surgeries were carried out to replace depleted batteries or malfunctioning DBS parts. None of the revision surgeries were for infection. The median operative length (IQR) was 3.1 (2.2–4.4) hours for primary DBS implantation and 0.5 (0.4–0.7) hours for DBS revision surgery ($P < .001$). Table 3 provides an overview of the clinical and surgical profiles of these procedures.

Rates of DBS-Related Infection

DBS-related infection developed in 73 patients following 57/1112 (5%) primary DBS implantations and 16/784 (2%)

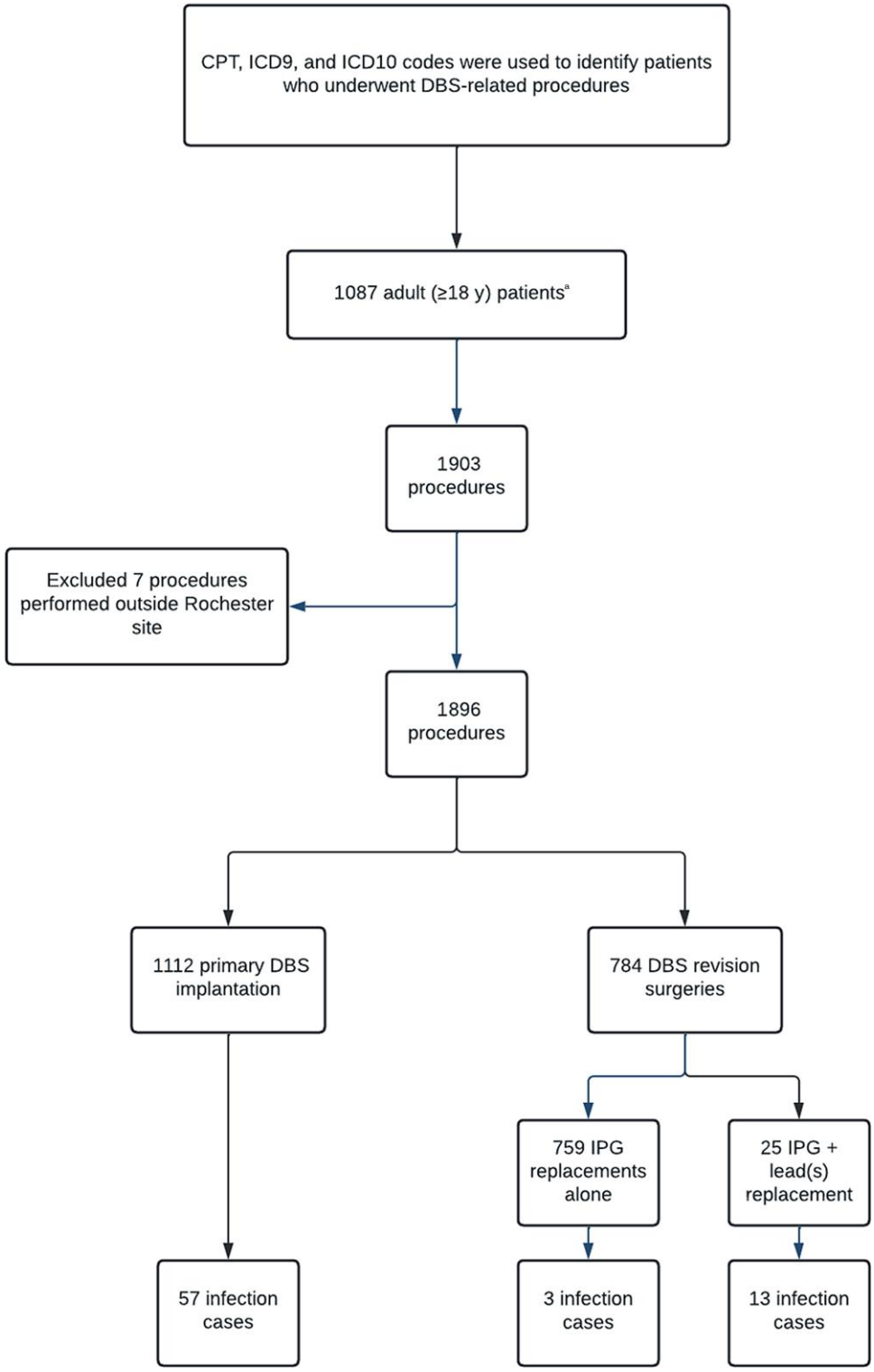

Figure 1. Inclusion flowchart. All adult patients who underwent implantation of intracranial leads and infraclavicular IPG were included, while patients who had implantation of vagal nerve stimulators and responsive neurostimulators were excluded. [a]Minnesota law requires that patients grant permission for medical chart review, a process called research authorization. Therefore, only patients with research authorization were included. Abbreviations: CPT, Common Procedural Terminology; DBS, deep brain stimulator; ICD9, International Classification of Diseases, Ninth Revision; ICD10, International Classification of Diseases, Tenth Revision; IPG, implantable pulse generator.

Table 1. Definition of DBS-Related Infection

Depth of DBS-Related Infection	Definition
1. Superficial skin and soft tissue infection related to DBS	A patient is considered to have superficial DBS-related SSTI if ≥2 of the following signs are present around the DBS parts: skin erythema, skin swelling, tenderness, wound dehiscence, and wound drainage; with or without positive intraoperative wound cultures AND no evidence of deep infection as defined below. Infection must involve parts overlying the DBS components to be considered related to the DBS device.
2. Deep uncomplicated DBS-related infection	A patient is considered to have deep uncomplicated DBS-related infection if any of the following is present: 1. Device exposure to the outside or sinus tract communicating with the device. 2. Deep purulent collection surrounding DBS parts detected intraoperatively or by ultrasound-guided needle aspiration. 3. Positive growth of microorganisms in cultures from any of the following: (a) Deep intraoperative tissue or fluid surrounding DBS parts; (b) DBS device parts; (c) Deep fluid aspirate from IPG pocket; AND no evidence of complications as defined below.
3. Deep complicated DBS-related infection	A patient is considered to have deep complicated DBS-related infection if criteria for deep uncomplicated are met AND they have evidence of ≥1 of the following: intracranial pus, intracranial organized abscess, meningitis, or encephalitis.[a]

Abbreviations: DBS, deep brain stimulator; SSTI, skin and soft tissue infection.

[a]Growth of microorganisms in cultures from intracranial leads in the absence of intracranial pus, intracranial organized abscess, meningitis, or encephalitis is considered deep uncomplicated infection.

Table 2. Device Management Groups

Device Management	Definition
1. Medical management	Antimicrobial therapy alone without surgical intervention.
2. Complete device explantation	Removal of the entire DBS system at time of presentation.
3. Surgical intervention with device retention	Complete or partial retention or immediate replacement of DBS parts at time of presentation. Such as with: (a) Incision and debridement. (b) Single-stage replacement, defined as immediate replacement of infected DBS part(s) with new part(s). (c) Partial device explanation, defined as removal of grossly infected part(s) with retention of other DBS parts.

All 3 device management groups included antimicrobial therapy.

Abbreviation: DBS, deep brain stimulator.

revision surgeries (log-rank test $P = .0022$) (Kaplan-Meier curve in Supplementary Figure 1). The median time from procedure to infection (IQR) was 2.1 (0.9–6.9) months. Our hospital experienced an increase in DBS-related procedures during the study period met by a decline in operative length and DBS-related infections (Supplementary Figure 2).

Table 3 compares DBS-related procedures complicated by infection (n = 73) with procedures remaining infection free (n = 1823). The former group had higher body mass index (BMI; $P = .006$) and longer operative length ($P = .002$). Infection was more likely to develop with male sex ($P = .041$) and diabetes mellitus ($P = .002$). Notably, the median age at index procedure was lower for infected cases ($P = .003$). Perioperative intravenous (IV) antibiotics were used in all procedures, with no significant difference between groups in antibiotics used. Similarly, there was no significant difference for most topical antibiotics administered during the index procedure, with exception for bacitracin ($P = .015$), which was more commonly used in procedures followed by infection.

A subgroup analysis of primary DBS implantations continued to show a significant association between infection and male sex ($P = .016$), higher BMI ($P = .002$), and diabetes mellitus ($P = .003$) (Supplementary Table 1). However, the associations between infection and operative length and infection and topical bacitracin were no longer statistically significant. Furthermore, the odds of infection seemed higher following multistage as opposed to single-stage primary implantations but did not meet statistical significance. In contrast to primary implantations, no significant associations were found on subgroup analysis of revision surgeries (Supplementary Table 2).

Clinical Presentation of DBS-Related Infection

The median duration of symptoms before presentation (IQR) was 7.0 (3.0–14.0) days. Hospitalization occurred in 69 (95%) cases of infection, with a median length of stay (IQR) of 4.0 (3.0–5.0) days. All remained hemodynamically stable during infection. Infection was superficial in 17 (23%) cases and deep in 56 (77%) cases (uncomplicated in 53 and complicated in 3). Of the 3 cases with deep complicated infection, 1 presented with cerebritis, 1 with brain abscess, and 1 with purulence around the intracranial electrodes at the time of explantation.

Symptoms included localized erythema in 45 (62%) cases, localized pain in 43 (59%), wound drainage in 31 (43%), wound dehiscence in 19 (26%), device exposure in 16 (22%), fever in 11 (15%), headache in 4 (6%), and altered mentation in 1 (1%). On physical examination, 20 (27%) had evidence of infection limited to IPG pocket, 30 (41%) to lead track, and 23 (32%) to both IPG pocket and lead track. Of the 53 cases with lead track infection, 46 (87%) involved the scalp region.

When tested, C-reactive protein was elevated in 32/54 (59%) cases (normal ≤8 mg/dL), sedimentation rate was elevated in 16/35 (46%) cases (normal 0–22 mm/h), and white blood cell count was elevated in 20/56 (36%) cases (normal 3.5–10.5 × 10^9/L).

Nine (45%) of the 20 cases with infection limited to the IPG pocket had computed tomography (CT) of the head, and 2

Table 3. Clinical and Surgical Profile of DBS-Related Procedures

	No Infection (n = 1823)	Infection (n = 73)	Total (n = 1896)	Median Difference/OR[a]	*P* Value
(A) Age at procedure, y	67.0 (57.0–74.0)	61.0 (53.0–68.0)	66.0 (57.0–73.0)	5.00 (2.00–8.00)	.003
(B) Gender (male)	1081 (59.3)	52 (71.2)	1133 (59.8)	1.70 (1.02–2.85)	.041
(C) Race (White)	1751 (96.1)	73 (100.0)	1824 (96.2)		.558
(D) BMI, kg/m^2	26.7 (23.7–30.7)	28.8 (24.5–33.4)	26.9 (23.7–30.9)	2.00 (0.60–3.42)	.006
(E) Comorbidities					
• Myocardial infarct	50 (2.7)	2 (2.7)	52 (2.7)		1.000
• Congestive heart failure	80 (4.4)	1 (1.4)	81 (4.3)		.369
• CVA or TIA	250 (13.7)	6 (8.2)	256 (13.5)		.221
• Connective tissue disease	166 (9.1)	11 (15.1)	177 (9.3)		.086
• Diabetes mellitus	311 (17.0)	23 (31.5)	334 (17.6)	2.24 (1.34–3.72)	.002
• Moderate to severe CKD	146 (8.0)	7 (9.6)	153 (8.1)		.627
• Cancer	160 (8.8)	7 (9.6)	167 (8.8)		.810
• Solid tumor	125	6	131		
• Leukemia	14	1	15		
• Lymphoma	28	0	28		
• Transplant	13 (0.7)	1 (1.4)	14 (0.7)		.520
• BMT	9	0	9		
• Heart	2	0	2		
• Liver	0	1	1		
• Renal	2	0	2		
(F) CCI score	3.0 (2.0–5.0)	4.0 (2.0–5.0)	3.0 (2.0–5.0)		.235
(G) Indication for DBS					.969
• Essential tremor	742 (40.7)	27 (37.0)	769 (40.6)		
• Parkinson's disease	499 (27.4)	23 (31.5)	522 (27.5)		
• Dystonia	421 (23.1)	18 (24.7)	439 (23.2)		
• Epilepsy	107 (5.9)	3 (4.1)	110 (5.8)		
• Obsessive compulsive disorder	30 (1.6)	1 (1.4)	31 (1.6)		
• Tourette's	11 (0.6)	0	11 (0.6)		
• Cluster headache	7 (0.4)	1 (1.4)	8 (0.4)		
• Intractable face pain	2 (0.1)	0	2 (0.1)		
• Poststroke pain	2 (0.1)	0	2 (0.1)		
• Phantom limb pain	1 (0.1)	0	1 (0.1)		
• SUNCT	1 (0.1)	0	1 (0.1)		
(H) Perioperative IV antibiotics					
• Cefazolin	1646 (90.3)	64 (87.7)	1710 (90.2)		.461
• Vancomycin	170 (9.3)	8 (11.0)	178 (9.4)		.639
• Cefepime	48 (2.65)	1 (1.4)	49 (2.6)		1.000
• Clindamycin	6 (0.3)	0	6 (0.3)		1.000
(I) Intraoperative topical antibiotics					
• Bacitracin	1465 (80.4)	67 (91.8)	1532 (80.8)	2.7 (1.17–6.34)	.015
• Vancomycin	600 (32.9)	28 (38.4)	628 (33.1)		.333
• Gentamicin	725 (39.8)	33 (45.2)	758 (40.0)		.353
• Levofloxacin	105 (5.8)	7 (9.6)	112 (5.9)		.174
• Cefazolin	98 (5.4)	7 (9.6)	105 (5.5)		.123
(J) Operative length, h	1.9 (0.5–3.4)	2.6 (2.0–3.4)	2.0 (0.6–3.4)	0.66 (0.21–1.22)	.002
(K) Wound type (type I clean)	1823 (100.0)	73 (100.0)	1896 (100.0)		
(L) Follow-up from procedure, y	2.3 (1.1–3.8)	4.8 (2.4–7.3)	2.3 (1.1–3.8)	2.32 (1.65–3.05)	< .001

Abbreviations: BMI, body mass index; BMT, bone marrow transplant; CCI, Charlson comorbidity index; CKD, chronic kidney disease; CVA or TIA, cerebrovascular accident or transient ischemic attack; DBS, deep brain stimulator; IV, intravenous; OR, odds ratio; SUNCT, short-lasting, unilateral, neuralgiform headache attacks with conjunctival injection and tearing.

The Mann-Whitney *U* test was used to compare continuous variables between both samples. The chi-square or Fisher exact test was used to compare categorical variables between both samples. Continuous variables are represented by median (interquartile range), while categorical variables are represented by frequency and column or subheading percentages.

[a]Values are reported only for variables with a significant difference between groups.

(10%) had brain magnetic resonance imaging (MRI). One of these cases had a brain abscess, while all others had normal brain imaging. On the other hand, head CT and brain MRI were performed in 31 (58%) and 2 (4%) of the 53 cases with lead track involvement, respectively. In this group of cases, head imaging mostly revealed nonspecific inflammatory changes around the extracranial lead track. Only 1 case had evidence of intracranial infection in the form of cerebritis seen on head CT.

Microbiology

Cultures for microbiological diagnosis were available for 62 cases but absent for the remaining 11 cases, all of which had superficial infections managed medically. Overall, 60/62 (97%) cases had positive microbiology, including positive intraoperative cultures alone in 37 cases, positive aspirate cultures alone in 3, and a combination of both in 20. The 2 remaining cases had sterile intraoperative cultures, 1 of which had superficial SSTI, while the other had deep infection with wound dehiscence and lead exposure. Of the 62 patients, 13 (21.0%) had received antibiotics before obtaining cultured specimens but still had microbial growth. The cultured specimen was considered deep and surrounding DBS parts in 56/73 (77%) infected cases.

Microbial growth occurred in ≥2 cultured specimens in 53/60 (88%) cases with positive microbiology and was polymicrobial in 37/60 (62%). A total of 114 bacterial isolates were identified and are listed in Table 4: 105 (92%) were gram-positive, and 9 (8%) were gram-negative. *Staphylococcus aureus* was identified in 39/60 (65%) cases, while 31 different coagulase-negative staphylococci (CoNS) were identified in 26/60 (43%). A methicillin-resistant *S. aureus* or CoNS was identified in 10/60 (17%). *Cutibacterium acnes* was identified in 27/60 (45%) patients, 14 of whom had growth of *C. acnes* from ≥2 specimens. All *C. acnes* isolates grew in a polymicrobial setting. Blood cultures were drawn in 34/73 (47%) infected cases, and all remained without growth.

Table 4. Microbiology of DBS-Related Infections (n = 114)

Gram-Positive Pathogens	No. of Isolates (%)	Gram-Negative Pathogens	No. of Isolates (%)
S. aureus	39 (34.2)	*Citrobacter koseri*	2 (1.8)
• Methicillin resistant	4	*P. aeruginosa*	2 (1.8)
• Methicillin susceptible	35	*K. aerogenes*	2 (1.8)
CoNS	31 (27.2)	*Klebsiella pneumoniae*	1 (0.9)
• S. epidermidis	11	*Serratia marcescens*	1 (0.9)
• S. capitis	11	*S. maltophilia*	1 (0.9)
• S. lugdunensis	2		
• S. hominis	1		
• S. intermedius	1		
• S. devriesei/ haemolyticus	1		
• Other CoNS	4		
C. acnes	27 (23.7)		
Streptococcus viridans group	1 (0.9)		
S. agalactiae	1 (0.9)		
Bacillus spp.	1 (0.9)		
C. amycolatum	1 (0.9)		
C. kroppenstedtii	1 (0.9)		
Peptoniphilus	1 (0.9)		
E. faecalis	1 (0.9)		
Finegoldia magna	1 (0.9)		

Values in parentheses represent percentages of the 114 isolates. In 52/60 (87%) cases, cultured specimen grew gram-positive bacteria only, as opposed to 1/60 (2%) case where cultured specimen grew gram-negative bacteria only. The remaining 7/60 (12%) cases had a mixed growth of both gram types. No fungal organisms were identified.

Abbreviations: CoNS, coagulase-negative staphylococci; DBS, deep brain stimulator.

Management of DBS-Related Infection

Complete device explantation was performed in 39/56 (70%) deep infections, surgical intervention with device retention in 14/56 (25%), and medical management in 3/56 (5%). The last 3 cases managed medically were considered deep infections due to growth of a virulent microorganism from 1 IPG pocket aspirate in each; *S. aureus* was isolated in 2 patients and *Stenotrephomonas maltophilia* in 1. On the other hand, surgical intervention with device retention was performed in 6/17 (35%) superficial infections and medical management in 11/17 (65%), while none had complete device explantation. Figure 2 summarizes all surgical interventions performed in the 73 infected cases.

Antimicrobial therapy was prescribed in all infection cases. The median duration of antibiotic therapy (IQR) was 15.0 (14.0–18.0) days, 15.0 (14.0–21.8) days for deep infection compared with 14.0 (11.0–16.0) days for superficial infection ($P = .017$). IV antibiotics were used more frequently with deep infection (98% vs 82%; $P = .012$). The median duration of IV antibiotics (IQR) was 14.0 (6.8–16.3) days for deep infection compared with 3.0 (2.0–10.0) days for superficial infection ($P < .001$). Chronic suppression was prescribed in 11/73 (15%) cases, including 3/14 (21%) cases treated with medical management and 8/20 (40%) cases treated with surgical intervention with device retention. Suppression was continued until last encounter in 8 cases. For the remaining 3, suppression duration ranged from 91 to 400 days. Supplementary Figure 3 summarizes all antibiotics used for the treatment and suppression of DBS-related infections.

After completion of therapy and resolution of symptoms, DBS reimplantation occurred in 27/39 (69%) cases treated with complete device explantation and 7/12 (58%) treated with partial device explantation. The median time to reimplantation (IQR) was 2.9 (2.1–5.1) months and 2.3 (1.4–6.8) months, respectively.

Outcomes of DBS-Related Infection

The median follow-up from infection (IQR) was 4.2 (1.9–6.9) years. Treatment failure occurred in 4/39 (10%) cases treated with complete device explantation, 7/20 (35%) cases treated with surgical intervention with device retention, and 5/14 (36%) cases treated with medical management. Supplementary Figure 4 shows the distribution of treatment failure events according to type of surgical intervention.

Table 5 compares between cases who failed treatment (n = 16) and those who did not (n = 57). There was no difference in depth

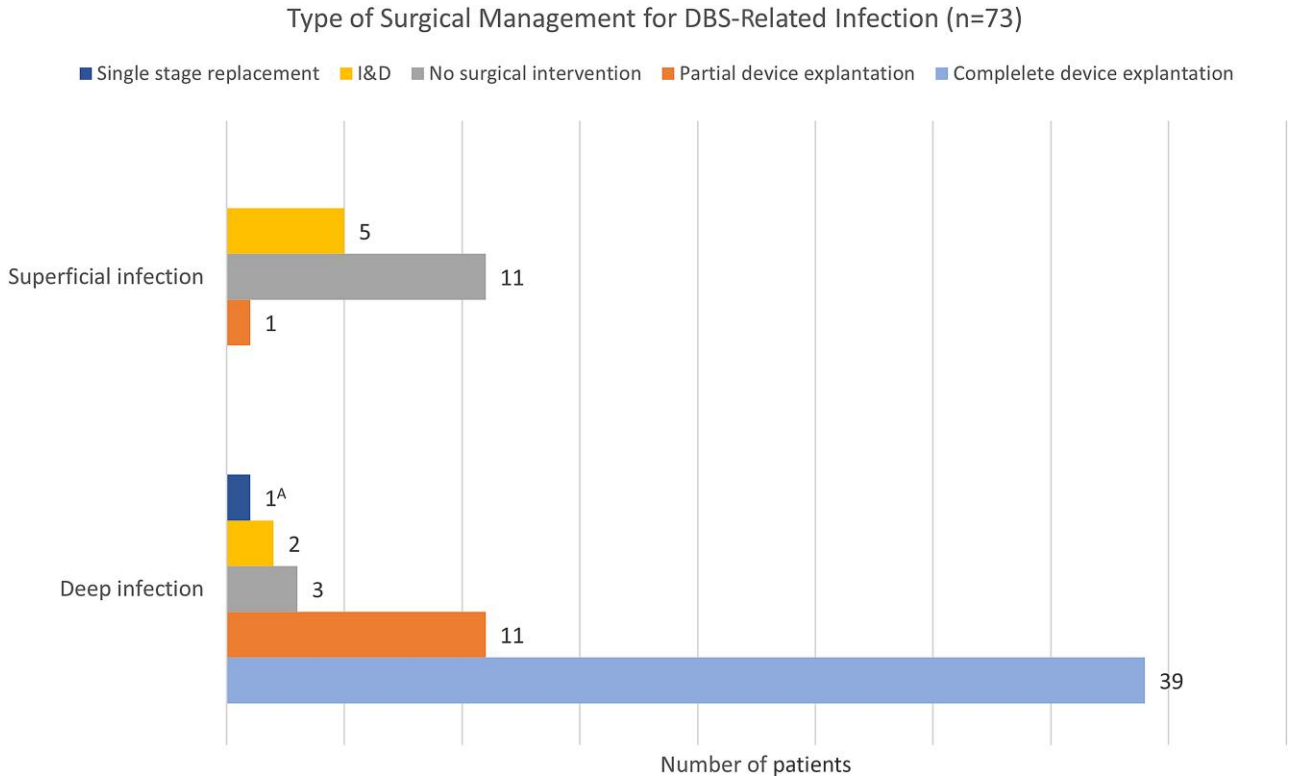

Figure 2. List of surgical interventions performed for DBS-related infections, stratified based on the depth of infection. [a]Patient had exposure of cranial plate and screws and so is considered to have a deep infection based on our definition despite the absence of deep pus. The exposed plate and screws were replaced with new hardware to secure a malpositioned DBS lead. Cultures from the previous hardware grew *C. acnes* and *S. capitis*. Abbreviations: DBS, deep brain stimulator; I&D, incision and drainage.

of infection between both groups. Patients who received IV antibiotics had lower odds of failure ($P = .008$). The median duration of IV antibiotics was also longer for the group without failure (not statistically significant). Similarly, patients receiving chronic suppression had lower rates of treatment failure (not statistically significant). For the 11 cases prescribed chronic suppression for device retention, the median follow-up from infection (IQR) was 3.3 (1.8–5.3) years. Only 1 case had treatment failure, which occurred 3 months after stopping suppression. Patients treated with complete device explantation had lower odds of failure (log-rank test $P = .015$) (Kaplan-Meier curve in Supplementary Figure 5). No association was depicted between treatment failure and other tested variables. Notably, the analysis was limited by the small size of the compared subgroups.

The median time to treatment failure (IQR) was 4.5 (2.7–6.8) months. Five (31%) of the 16 cases who failed treatment had persistence of infection, and 11 (69%) had recurrence. Seven of the recurrences were reinfections following DBS reimplantation, indicating a cumulative rate of 7/34 (21%) with reinfection after reimplantation: 4/27 (15%) with reinfection following reimplantation after complete device explantation, and 3/12 (25%) with reinfection after partial explantation. Notably, all the failure events following complete device explantation were reinfections following reimplantations. Of the 7 patients with reinfections following reimplantation, 5 patients had surgical debridement and complete device removal, of whom 3 had reinfection with similar pathogens as their index infection, while 2 had reinfection with different pathogens.

Treatment failure led to subsequent extraction of the entire DBS system in 13/16 (81%) cases. Complications from failure were rare, occurring in only 1 of the failed cases. This was a patient who originally presented with deep infection of the IPG pocket and underwent IPG removal with retention of leads. He completed 14 days of antibiotic therapy without chronic suppression and presented 3 months later with bacterial meningitis. His meningitis resolved after explantation of the leads and 14 days of IV antibiotics.

DISCUSSION

Our study highlights several key points on the epidemiology of DBS-related infections. We found a higher rate of infection following primary DBS implantation compared with revision surgery. This is plausible given the higher complexity of primary implantation. Furthermore, we saw a decrease in DBS infection rate over time. This is likely a result of multiple factors, which may include advances in DBS design and surgical expertise over time. The latter is evident by the decline in operative length.

Table 5. Treatment Outcomes of DBS-Related Infection

	No Treatment Failure (n = 57)	Treatment Failure (n = 16)	Total (n = 73)	Median Difference/OR[a]	*P* Value
(A) Age at procedure, y	63.0 (54.0–70.0)	59.5 (48.3–62.0)	61.0 (53.0–68.0)		.102
(B) Gender (male)	42 (73.7)	10 (62.5)	52 (71.2)		.383
(C) BMI, kg/m^2	28.8 (25.7–33.4)	29.2 (24.3–32.9)	28.8 (24.5–33.4)		.729
(D) Comorbidities					
• MI	1 (1.8)	1 (6.2)	2 (2.7)		.393
• CHF	1 (1.8)	0 (0.0)	1 (1.4)		1.000
• CVA or TIA	6 (10.5)	0 (0.0)	6 (8.2)		.328
• Liver disease	9 (15.8)	2 (12.5)	11 (15.1)		1.000
• Diabetes mellitus	18 (31.6)	5 (31.2)	23 (31.5)		.980
• Moderate to severe CKD	7 (12.3)	0 (0.0)	7 (9.6)		.335
• Cancer	6 (10.5)	1 (6.2)	7 (9.6)		1.000
• Transplant	1 (1.8)	0 (0.0)	1 (1.4)		1.000
(E) CCI score	4.0 (2.0–5.0)	3.5 (2.0–4.0)	4.0 (2.0–5.0)		.490
(G) DBS-related procedure					.734
• Battery replacement	12 (21.1)	4 (25.0)	16 (21.9)		
• Primary implantation	45 (78.9)	12 (75.0)	57 (78.1)		
(H) Time from index procedure to infection, mo	2.2 (1.0–6.6)	1.5 (0.8–7.7)	2.1 (0.9–6.9)		.689
(I) Duration of symptoms, d	7.0 (2.0–14.0)	7.0 (6.0–21.0)	7.0 (3.0–14.0)		.459
(J) Depth of infection					1.000
• Deep	44 (77.2)	12 (75.0)	56 (76.7)		
• Superficial	13 (22.8)	4 (25.0)	17 (23.3)		
(K) Device exposure	11 (19.3)	5 (31.2)	16 (21.9)		.307
(L) IPG infection	34 (59.6)	9 (56.2)	43 (58.9)		.807
(M) Lead track infection	43 (75.4)	10 (62.5)	53 (72.6)		.305
(N) Scalp lead infection	38 (66.7)	8 (50.0)	46 (63.0)		.222
(O) Antibiotic course					
• Received IV antibiotics only	37 (64.9)	7 (43.8)	44 (60.3)		.154
• Received oral antibiotics only	1 (1.8)	3 (18.8)	4 (5.5)	12.92 (1.24–134.46)	.008
• Transitioned from IV to oral antibiotics	19 (33.3)	6 (37.5)	25 (34.2)		.772
(P) Duration of antibiotics, d	15.0 (14.0–18.0)	14.5 (14.0–22.2)	15.0 (14.0–18.0)		.466
• IV antibiotics	56 (98.2)	13 (81.2)	69 (94.5)	0.08 (0.01–0.81)	.008
• Duration of IV antibiotics, d	14.0 (4.0–16.0)	8.0 (1.8–14.0)	14.0 (3.0–15.0)		.073
• Oral antibiotics	22 (38.6)	9 (56.2)	31 (42.5)		.257
• Duration of oral antibiotics, d	0.0 (0.0–14.0)	8.5 (0.0–12.5)	0.0 (0.0–14.0)		.308
(Q) Chronic suppression	10 (17.5)	1 (6.2)	11 (15.1)		.437
(R) Culture-driven therapy	48 (84.2)	12 (75.0)	60 (82.2)		.463
• Polymicrobial	29 (60.4)	8 (66.7)	37 (61.7)		.752
• ≥2 positive specimens	43 (89.6)	10 (83.3)	53 (88.3)		.619
• Gram-positive pathogens	47 (97.9)	12 (100.0)	59 (98.3)		1.000
• Gram-negative pathogens	6 (12.5)	2 (16.7)	8 (13.3)		.655
• *S. aureus*	33 (68.8)	6 (50.0)	39 (65.0)		.223
• CoNS	19 (39.6)	7 (58.3)	26 (43.3)		.241
• *C. acnes*	21 (43.8)	6 (50.0)	27 (45.0)		.697
(S) Surgical intervention	48 (84.2)	11 (68.8)	59 (80.8)		.165
• Intraoperative pus	31 (64.6)	8 (72.7)	39 (66.1)		.734
(T) Device management group					.036
• Complete device explantation	35 (61.4)	4 (25.0)	39 (53.4)		
• Surgical intervention with device retention	13 (22.8)	7 (43.8)	20 (27.4)		
• Medical management	9 (15.8)	5 (31.2)	14 (19.2)		
(U) Follow-up from infection, y	4.5 (1.8–6.9)	4.0 (2.6–6.8)	4.2 (1.9–6.9)		.631

The Mann-Whitney *U* test was used to compare continuous variables between both samples. The chi-square or Fisher exact test was used to compare categorical variables between both samples. Continuous variables are represented by median (interquartile range), while categorical variables are represented by frequency and column or subheading percentage.

Abbreviations: BMI, body mass index; BMT, bone marrow transplant; CCI, Charlson comorbidity index; CKD, chronic kidney disease; CoNS, coagulase-negative staphylococci; CVA or TIA, cerebrovascular accident or transient ischemic attack; DBS, deep brain stimulator; IV, intravenous; OR, odds ratio.

[a]Values are reported only for variables with a significant difference between groups.

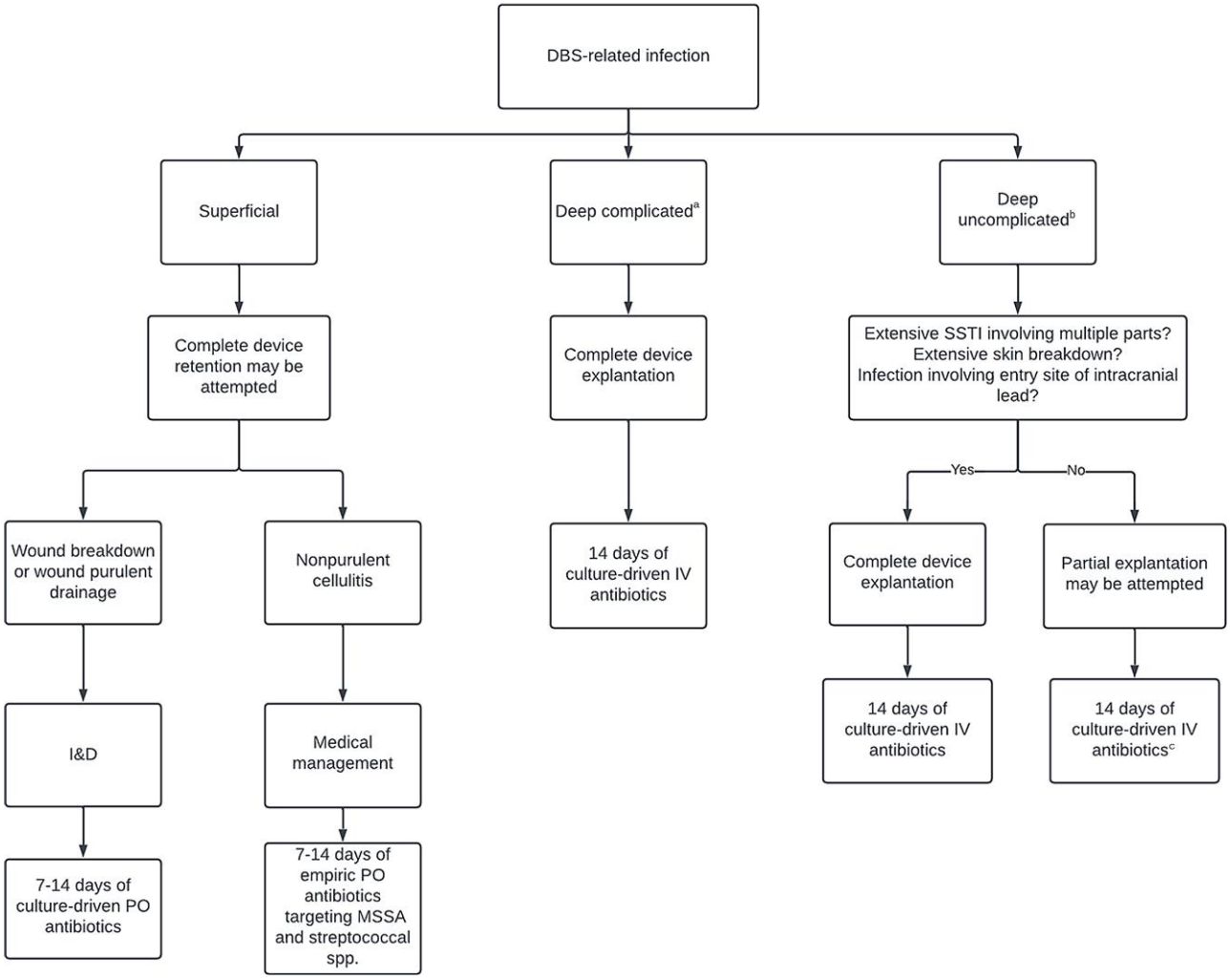

Figure 3. Management algorithm for DBS-related infections. This algorithm describes our preferred approach based on clinical experience and does not represent evidence-based guidelines. The optimal duration of antimicrobial therapy is not defined; we suggest a total duration of 7–14 days depending on the depth of infection. However, a definite duration should be individualized and may be extended depending on the clinical response. [a]We favor an empiric antibiotic regimen that includes a combination of IV agents effective against *P. aeruginosa* and methicillin-resistant *S. aureus*. Antibiotics can then be adjusted according to culture results. [b]We favor a narrow empiric antibiotic regimen. Depending on local rates of methicillin resistance, this may include a second- or third-generation IV cephalosporin (such as IV cefazolin or IV ceftriaxone) or IV vancomycin. Antibiotics can then be adjusted according to culture results. [c]Switching to culture-driven oral antibiotics may be considered if there is adequate debridement of infected tissue. Chronic suppression with oral antibiotics can also be considered after completing therapy. If prescribed, duration of chronic suppression should be determined by consultation with infectious diseases and neurosurgery teams. Abbreviations: DBS, deep brain stimulator; I&D, incision and drainage; IV, intravenous; MSSA, methicillin-susceptible *S. aureus*; PO, per os; SSTI, skin and soft tissue infection.

DBS-related infection typically occurred early postoperatively in our cohort and was predominantly caused by gram-positive bacteria commonly found on skin. Most of our patients were free of systemic symptoms. Infection was associated with male sex, higher BMI, and diabetes mellitus. We found no reduction in rates of infection with the use of topical antibiotics. Finally, we saw lower rates of treatment failure with complete device explantation.

The rate of DBS-related infection ranges from 2.6% to 9.3% in the current literature [5–15]. The variation in reported rates is due to heterogeneity in how DBS-related infection is defined and analyzed. Most studies used a definition of surgical site infection to identify DBS-related infection within a specified postoperative period [8–10]. This period was limited to 6 months in some studies [5, 8] and 1 year in other studies [9]. Moreover, some studies excluded superficial infections [5, 7, 10]. In contrast to these prior reports, our observation was not restricted to a prespecified surveillance period and included both superficial and deep infections.

Some of our findings are unique to our study. In a prior investigation, females were more likely to develop DBS infection compared with males, which contrasts with our findings [10].

Our study was the first to depict an association between infection and both BMI and diabetes mellitus [9, 11, 12]. We saw a higher infection rate following multistage primary implantations, albeit not statistically significant. The current literature on this is mixed, with 1 study confirming a significant association between infection and a multistage approach [13] while others refute this [5, 10]. Importantly, we found no reduction in infection rates with the use of topical antibiotics. The most used topical antibiotic was bacitracin, which has been in use since the beginning of the study period. On the other hand, topical vancomycin has been inconsistently used since 2010. While we were unable to prove a benefit from topical antibiotics, the efficacy of this practice in preventing postoperative infection, particularly topical vancomycin, is supported by some studies [10]. In a prior single-center investigation, rates of DBS-related infection dropped from 9.7% before to 3.3% after implementing topical vancomycin [10]. Future prospective studies to confirm the role of topical antibiotics in preventing DBS-related infections are highly encouraged.

The predilection of DBS-related infection to occur early postoperatively seen in our cohort is consistent with the current literature [5, 8–11, 16, 17]. Like prior reports, the most frequently isolated pathogens in our study were *S. aureus, C. acnes,* and CoNS [5, 7, 9, 10, 13, 15, 16]. The high prevalence of *C. acnes* is not unique to our study [10]. It is a known colonizer of the skin, and its pathogenic role is well established in other prosthetic infections such as CNS shunt infections [18] and infections of shoulder arthroplasties [19]. The pathogenic role of *C. acnes* in DBS infections could be supported when heavy growth is detected. In our series, 52% of patients with *C. acnes* had growth in ≥2 cultured specimens.

The optimal management for DBS-related infection is unknown, but several important observations from our study and current literature could help guide physicians. Figure 3 outlines our preferred management approach.

The rate of treatment failure following device salvage may reach 27%–40% [5, 10]. Like our study, prior reports showed more treatment success with complete device explantation, making it the most efficacious approach from a curative standpoint [5, 10]. However, DBS is a last resort intervention for movement disorders refractory to pharmacotherapy, and its removal could have a negative impact on patients' quality of life. The low rate of complications from DBS-related infection seen in our study and prior series is reassuring [5, 10]. This means that partial or complete device salvage may be attempted in certain patients (Figure 3) [5, 10].

Considering the known microbiology and the low acuity of DBS-related infections, a broad empiric antimicrobial regimen is often not needed in otherwise stable patients without CNS infection. If CNS infection is suspected, then broad empiric coverage with agents effective against *Pseudomonas aeruginosa* and methicillin-resistant *S. aureus* is preferred [20]. Antibiotics could later be tailored toward the isolated pathogen(s). Device-related infections are typically treated for 2–6 weeks with antibiotics [3–5, 10], but the optimal duration remains undefined for DBS-related infection. Most patients in our series had resolution of infection with only 2 weeks of antibiotics. The optimal route of treatment is also unknown. While patients who failed treatment in our cohort overall had shorter duration of IV antibiotics, this was not statistically significant. We favor finishing the entire course with IV antibiotics in patients with evidence of CNS involvement and in patients with extensive skin and soft tissue inflammation (Figure 3). Finally, chronic suppression might be effective in preventing infection relapse. While our study did not confirm a significant role, the analysis was limited due to the infrequent use of chronic suppression. The optimal duration for chronic suppression for DBS infection and its adverse effects are unknown. Long courses of chronic suppression are not feasible in patients with long life expectancy but may otherwise be attractive for elderly patients with multiple comorbidities who are managed with a device salvage.

CONCLUSIONS

DBS-related infections typically occur a few months after an index procedure. Infection can be classified as superficial, deep uncomplicated, or deep complicated. Depth of infection and patient-related factors should be taken into consideration to individualize the best therapeutic surgical approach. Our study's retrospective nature and the overall small number of infection events are limitations. We were unable to confirm the role of topical antibiotics, the optimal route and duration of antimicrobial therapy, and the role of chronic suppression. Larger observational studies that consider multiple potential confounders are needed to better assess risk factors for DBS-related infections and prognostic determinants affecting the outcome.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Patient consent. The study does not include factors necessitating patient consent. The design of the work has been approved by the Mayo Clinic Institutional Review Board.

Availability of data and material. Data are not publicly available.

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