

Estimating the Proportion of Essential Tremor and Parkinson's Disease Patients Undergoing Deep Brain Stimulation Surgery: Five-Year Data From Columbia University Medical Center (2009–2014)

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Abstract: **Objective:** The aim of this study was to estimate, at a tertiary referral center, the proportion of essential tremor (ET) and Parkinson's disease (PD) patients who underwent DBS surgery.

Background: DBS surgery is an important treatment for ET and PD. Surprisingly, there are no published data on the precise proportion of such patients who are referred for this procedure.

Methods: Using the computerized billing database at the Center for Parkinson's Disease and Other Movement Disorders, Columbia University Medical Center, we searched for patients who received the diagnostic codes 333.1 (tremor) and 332.0 (PD) and who were followed by a doctor at the center during the 5-year period from 2009 to 2014. The number of patients who underwent DBS surgery for these diagnoses during this time period was also determined.

Results: Seventy-seven patients with these diagnoses (52 PD, 14 ET, and 11 ET + PD) who were followed at the center underwent DBS surgery during this time period. The proportion of ET patients who underwent DBS surgery was 2.90% (95% confidence interval [CI]: 1.78–4.02), and for PD this was 1.38% (95% CI: 1.04–1.72). The difference was significant ($P < 0.001$).

Conclusions: At a tertiary-referral center, 1 in 34 ET patients and 1 in 72 PD patients underwent DBS surgery. Similar studies from other major centers would be of additional value. These data are likely to have utility when planning health care services for patients with these diagnoses.

DBS surgery has become an important treatment for patients with essential tremor (ET) and Parkinson's disease (PD).^{1–3} Numerous studies have shown that DBS surgery of the ventralis intermedialis thalamus is an effective treatment for tremor in ET and PD patients^{4,5} and that DBS surgery of either the STN or globus pallidus internus significantly improves motor fluctuations, dyskinesias, and the cardinal motor manifestations of PD.^{6–8}

It is estimated that more than 80,000 patients have undergone DBS surgery, with the majority of these being patients with PD.⁸ Surprisingly, there are no published data on the precise proportion of patients who are referred for this procedure. The aim of this study was to estimate the proportion of ET and PD patients undergoing DBS surgery at our tertiary referral

center. These data are likely to be of value in planning health care services for patients with these diagnoses.

Methods

Study Site and Review of Electronic Medical Records

Using the computerized billing database at the Center for Parkinson's Disease and Other Movement Disorders, Columbia University Medical Center (CUMC; New York, NY), we searched for patients who received the International Classification of Diseases, Ninth Revision (ICD-9) diagnostic codes 333.1 (tremor) or 332.0 (PD) and who were followed by a

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doctor at the center during the 5-year period from 1 January 2009 to 8 May 2014. This search and subsequent electronic medical record review was approved by the CUMC Internal Review Board. Because the assignment of diagnostic codes has been shown to be incorrect in some cases,⁹ one of the authors (M.K.), a movement disorder neurologist, estimated the validity of the assigned codes by carefully reviewing 300 of the identified electronic medical records. Given that the ICD-9 code for ET is less specific than that for PD, more charts with this diagnostic code were reviewed (i.e., 200 randomly selected charts with the code 333.1 and 100 with the code 332.0). The diagnosis was considered valid when the treating physician's diagnostic impression in their electronic medical record was ET or PD. Our estimate of the number of patients with valid ET and PD diagnoses was the product of the number of cases who received each code times the validity of that code. For example, the final number of patients with a valid ET diagnosis was estimated to be 862, which was the product of 1,198 (i.e., the number of patients who had received the diagnostic code 333.1) \times 72.0% (i.e., the proportion of individuals with that code who on electronic medical record review were found to have a valid ET diagnosis).

The electronic medical records of all patients that underwent DBS surgery at CUMC in this time period were reviewed and selected data (e.g., reason for surgery) were abstracted.

Estimating the Proportion of ET and PD Patients Who Had Undergone DBS Surgery

For our primary estimate of the proportion of ET and PD patients who had undergone DBS surgery, we included only those who had been followed by a doctor at CUMC and who had been referred by one of these doctors for DBS during this time period. Thus, patients that were referred directly from outside the center for a DBS evaluation and who then underwent surgery were excluded. For each of the two diagnoses, ET and PD, we divided the number of patients that had undergone DBS surgery by the estimate of the total number of patients with valid ET and PD diagnoses who were followed.

Statistical Analyses

Statistical analyses were performed using SPSS software (version 21.0; SPSS, Inc., Chicago, IL). For each proportion, we also calculated a 95% confidence interval (CI). The proportion of ET versus PD patients who had undergone DBS surgery was compared using a chi-square test.

Results

During the 5-year time interval, 81 patients (52 PD, 14 ET, 11 ET and PD, and 4 generalized dystonia) who were followed at the center before the DBS referral and surgery underwent DBS surgery at CUMC. The most common indications for referral of PD patients to DBS surgery were tremor (52 [82.5%]/63 PD patients), wearing off motor fluctuations (50 [79.3%] patients),

and dyskinesia (50 [79.3%] patients). All of the ET patients referred for DBS had tremor that impaired activities of daily living (ADLs).

The total number of patients at the center during that time period who received the diagnostic codes 333.1 and 332.0 was 1,198 and 5,191, respectively. The validity of the ET and PD diagnoses, estimated based on review of electronic medical records of 200 patients who received the diagnostic code 333.1 and 100 patients who received the diagnostic code 332.0, was 72% and 88.0%, respectively. Hence, the above values were adjusted from 1,198 to 862 (for ET) and from 5,191 to 4,568 (for PD).

The proportion of ET patients referred for DBS was 25 of 862 or 2.90% (95% CI: 1.78–4.02). This included 14 patients with ET and 11 with both ET and PD. For PD, this value was 63 of 4,568 or 1.38% (95% CI: 1.04–1.72). This included 52 patients with PD and 11 with both ET and PD. The difference between these proportions (2.90% vs. 1.38%) was significant ($P < 0.001$).

For our primary estimate, we included only those patients who had been followed by a doctor at CUMC and who had been referred by one of these doctors for DBS during this time period. In a secondary analysis, we also considered patients referred from outside of CUMC who underwent DBS. There were 105 additional patients from outside of CUMC who were referred for DBS, for a total of 186 patients who underwent DBS. Of these, 121 had PD, 35 had ET, and 15 had ET and PD. Hence, the proportion of ET patients referred for DBS was 50 of 862 or 5.80% (95% CI: 4.24–7.36). For PD, this value was 136 of 4,568 or 2.97% (95% CI: 2.48–3.46). The difference between these proportions (5.80% vs. 2.97%) was significant ($P < 0.001$).

Discussion

To our knowledge, this is the first study that attempts to estimate the proportion of ET and PD patients undergoing DBS surgery. Approximately 1 in 34 ET patients (2.90%) and 1 in 72 PD patients (1.38%) who were followed in CUMC before referral for surgery underwent DBS surgery.

Several study limitations should be addressed up front. Because CUMC is a large tertiary referral center, numerous patients were referred from outside the center for consideration of DBS surgery. We provide data regarding the proportion of all PD and ET patients undergoing DBS and data regarding only the patients that were followed at CUMC before the surgery. For our primary analysis, we excluded patients who were referred directly from outside the center for DBS evaluation and surgery, in order to prevent a biased overestimation of the proportion of patients undergoing DBS surgeries. Yet, we recognize that even the patients that were followed at CUMC before DBS surgery might not represent the PD and ET populations observed outside of a tertiary referral center, given that it is likely that patients followed at a tertiary center are more medically complicated and are resistant or intolerant of the typical standard therapies. This could influence the proportion of

patients undergoing DBS. Hence, additional studies at other centers, some of which are not tertiary, would be instructive as well. It should also be mentioned that patients who are referred for consideration of DBS surgery are occasionally found not to be suitable candidates for surgery. This study did not directly assess the proportion of patients who were referred for surgery who decided against surgery or were considered poor surgical candidates. Though interesting, this is a separate question from the one our study was designed to address. Finally, it is possible that a small number of patients who were initially cared for at our medical center decided to have their DBS surgery at another center; this could have lowered the estimates we provide.

The proportion of ET patients undergoing DBS surgery was roughly twice as much, compared to the PD patients, although in absolute numbers, many more PD than ET patients underwent DBS surgery. Yet, the proportion of PD and ET patients that underwent DBS surgery is surprisingly low considering the fact that DBS has been shown to be very effective in treating tremor, wearing off motor fluctuations and dyskinesias, which are common in PD patients, and in treating tremor in ET patients. A number of reasons could explain the low number of patients undergoing DBS surgery, including relatively mild, nondisabling symptoms, medical treatments that have not been exhausted, good persistent response of symptoms to medication, the presence of symptoms that do not respond to DBS surgery (i.e., freezing of gait and falls and severe speech impairment), the presence of medical comorbidities that prevent surgery, significant cognitive impairment, patient preference of not being operated on, and personal preference of the treating physician.

The guidelines used for DBS surgery referrals at CUMC are stringent, aimed at deriving the best medical outcomes. Our criteria for DBS surgery referral for PD patients are: an excellent response to a single supratherapeutic dose of levodopa; severe wearing off motor fluctuations and dyskinesia that cannot be improved by further medication adjustment; or medication-refractory tremor. The relative contraindications for DBS surgery referral include patients whose main problem is freezing of gait or imbalance, dementia with a Montreal Cognitive Assessment¹⁰ score lower than 23/30, depression, psychosis, or poor social support. Our inclusion criterion for DBS surgery referral for ET patients is a medication refractory tremor that interferes with basic ADLs.

A study using a questionnaire to estimate the percentage of PD patients that are suitable candidates for DBS surgery showed that only 1.6% of PD patients fulfilled the strict DBS surgery criteria, thus making them good surgical candidates.¹¹ Most patients were excluded because of absence of severe motor disability, lack of motor complications, presence of cognitive impairment, presence of systemic illness or major depression, and lack of personal motivation to undergo DBS surgery. These data, although different in nature from ours, are in keeping with our results showing that only a small subgroup of PD patients are suitable candidates for DBS surgery, probably explaining the reason for the low proportion of PD patients undergoing DBS surgery.

Although it is intriguing to entertain the possibility of conducting a study such as this using a large administrative (e.g., Medicare) data set, given the low validity of the ICD code for ET (72% here and 49% in an earlier study),⁹ the results would have been problematic. This is because the denominator for ET could not have been determined with any degree of precision.

According to published data, the estimated total number of DBS surgeries performed in the United States for PD and ET between the years 1998 and 2007 was 24,000, with the majority of surgeries done because of PD.¹² This number, although only an estimate based on data from 20% of the hospitals in the United States, suggests that fewer than 2% of PD patients underwent DBS in a 9-year time period. This is in keeping with our data of a low referral rate for DBS surgeries. Unlike our study, however, that work used an administrative data set, which is potentially problematic for reasons noted above. Furthermore, that study did not formally assess the number of ET or PD patients from which DBS patients were selected (i.e., there was no denominator); hence, it did not address the main question which we sought to answer: What is the proportion of ET and PD patients undergoing DBS surgery?

This study had additional limitations. First, the design of this study was aimed at estimating the proportion of PD and ET patients undergoing DBS surgery during a 5-year period from 2009 to 2014. It was not a longitudinal, prospective study that assessed the yearly or lifetime risk of DBS surgery among PD or ET patients. Hence, it does not assess the proportion of PD and ET patients undergoing DBS at some point during the course of their disease. Rather, it assessed the proportion of PD or ET patients who were referred at one center for DBS surgery. Second, our analyses were limited to a single 5-year time period. Additional studies could look at longer time periods as well as time trends for DBS surgery. It is likely that the approval of new treatments might influence the proportion of patients referred for DBS surgery.

In summary, at a tertiary referral center, 1 in 34 ET patients and 1 in 72 PD patients underwent DBS surgery. Similar studies from other major centers would be of additional value. These data are likely to have utility when planning health care services for patients with these diagnoses.

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

M.K.: 1B, 1C, 2B, 3A

B.F.: 1B, 3B

E.D.L.: 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B

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