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" Comparison of clinical motor outcomes between unilateral pallidotomy versus subthalamotomy in patients with idiopathic Parkinson's Disease "

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ABSTRACT:

Background

Parkinson's disease is a progressive neurodegenerative disorder that primarily affects motor functions. In recent years, surgical interventions have emerged as a potential treatment approach for individuals with Parkinson's disease. Pallidotomy and subthalamotomy are two common surgical procedures that target specific brain regions to alleviate motor symptoms. This study aims to compare the clinical motor outcomes of these two surgical techniques in patients with idiopathic Parkinson's disease.

Methods

Between 2021 to 2024 in Al-Salam hospital, the general authority of healthcare, Port Said, Suez Canal University Hospital, Ismailia, and affiliated hospitals, A total of 20 patients with idiopathic Parkinson's disease were randomly divided into two equal groups of 10 patients each. One group underwent unilateral pallidotomy, while the other group was treated with subthalamotomy. The patients were evaluated preoperatively, immediately postoperatively, at 2 weeks, 3 months, and 6 months after the procedure. Assessments were performed by neurologists and neurosurgeons utilizing the Unified Parkinson's Disease Rating Scale (UPDRS) during the 'off' medication state, as well as symptom diaries to track responsiveness to medical treatment.

Results

Subthalamotomy showed significant improvement in UPDRS III from 56.60±5.04 to 28.40±6.7 (49.8%) and from 35.40±6.06 to 14.80±2.74 (58.2%) in the Off and On periods retrospectively. Schwab & England ADL score improved from 42.0±10.32 to 86.00±8.43 (51.2%) and from 70.0±9.42 to 95.0±5.27 (26.3%) in the Off and On periods retrospectively. LDED reduce by 50.65% in comparison to LDED pre-operative.

Pallidotomy showed significant improvement in UPDRS III from 48.50±8.97 to 27.0±11.48 (44.3%) and from 26.20±7.55 to 12.90±8.41 (50.8%) in the Off and On periods retrospectively. Schwab & England ADL score improved from 37.0±9.48 to 78.0±14.76 (52.6%) and from 59.0±7.37 to 90.0±12.47 (34.4%) in the Off and On periods retrospectively, No LDED reduction occurred.

Conclusion
Subthalamotomy may offer slight advantages in reducing medication requirements and improving activities of daily living. Subthalamotomy also demonstrated significantly better outcomes in specific motor domains, such as body bradykinesia, postural instability, and gait disability. Subthalamotomy was associated with a higher risk of adverse effects compared to pallidotomy. However, Pallidotomy is advised if the main complaint of patient is dyskinesia.

Keywords: Parkinson's disease, pallidotomy, subthalamotomy, motor functions,

neurosurgery, surgical interventions

INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder characterized by the classic symptoms of akinesia, stiffness, and tremor due to the degeneration of dopaminergic neurons in the substantia nigra pars compacta (1). Early symptoms are often managed effectively with L-DOPA, but chronic use can lead to various motor side effects, including "wearing off," dyskinesia, and neuropsychiatric symptoms (2). When medication becomes less effective, surgical options may be considered.

The main surgical approaches include ablative surgeries (thalamotomy, pallidotomy, subthalamotomy) and deep brain stimulation, targeting the motor thalamus, globus pallidus internus (GPi), and subthalamic nucleus (STN) (3). Studies indicate that unilateral pallidotomy and subthalamotomy can significantly reduce tremor, stiffness, and bradykinesia, with posteroventral pallidotomy showing particularly high efficacy in alleviating symptoms in up to 90% of cases with minimal complications (4,5). This paper will examine a study comparing the effects of unilateral pallidotomy and STN surgery in managing idiopathic Parkinson's disease. (6)

Methods and Study Design

To fulfill the objectives of this study, the following criteria were taken into consideration. The study was designed as a prospective, randomized, and comparative study. Between 2021 to 2024 in Al-Salam hospital, the general authority of patients diagnosed with idiopathic Parkinson's disease were chosen to receive unilateral stereotactic ablative surgery, either through unilateral pallidotomy or subthalamotomy. Computer-generated randomization numbers were utilized to randomly assign patients into two equal groups. The sealed envelope with the group assignment was opened by a different investigator who had no other involvement in the trial.

The study included a total of 20 patients with idiopathic Parkinson's disease, who were randomly split into two equal groups of 10 patients each. One group was treated by

unilateral pallidotomy, while the other group was treated by subthalamotomy. All 20 patients were followed up on and their outcomes were analyzed statistically.

Evaluations were conducted by neurologists and neurosurgeons with expertise in movement disorders. The assessment timeline included pre-operative, immediate post-operative, two weeks post-discharge (for suture removal), as well as 3-month and 6-month follow-ups.

To assess disease severity, we employed video-recorded evaluations of the Unified Parkinson's Disease Rating Scale (UPDRS) in the 'off' medication state, both before and after surgery. Additionally, a symptom diary was used to monitor responses to medical treatment. (7)

The neurosurgeon's main responsibilities involve re-assessing the patient's clinical status, confirming the diagnosis, evaluating surgical eligibility, providing counseling to the patient and their family, and choosing an appropriate surgical target. During the preoperative consultation, the neurosurgeon outlines the preoperative process, discusses the available surgical options (including targets and techniques), and provides a thorough review of the associated risks and realistic expectations for the surgery. Informed consent is subsequently obtained from the patient. It is essential to establish realistic patient expectations early in the process to avoid any misconceptions that could lead to unsuccessful surgical outcomes. The potential risks associated with the surgical procedures, which were communicated to the patients and their families, included intracranial hemorrhage, infection, neurological deficits, and seizures. Furthermore, general contraindications to surgery were assessed to confirm the patient’s suitability for the procedure.

Preoperative neuroimaging, ideally using magnetic resonance imaging (MRI), was deemed essential for assessing patients prior to surgery.

Inclusion criteria

- Idiopathic Parkinson`s Disease.
- L-Dopa responsive at least 30% improvement in Unified Parkinson`s
- Disease Rating Score: Unified Parkinson’s Disease Rating Scale (UPDRS).
- Good “on” function from medication
- Realistic expectations
- Main symptoms not adequately controlled:
- Dyskinesia or motor fluctuations
- Refractory tremors

- Frequent or severe “off” periods.
- Off period disability from: Bradykinesia, rigidity, tremors.

Exclusion criteria

- Atypical parkinsonism or Parkinson plus.
- Age>75 years.
- Lack of response to levodopa, dementia, major depression,
- Levodopa-induced psychosis, severe personality disorder.
- Convulsions.
- Contraindications for magnetic resonance imaging (MRI).
- Previous brain surgery for Parkinson’s disease PD.
- Other central nervous system diseases.
- Focal abnormalities on MRI and unstable medical conditions.
- Declined informed consent.

The last step before surgery was obtaining medical clearance, which usually included standard preoperative blood tests and electrocardiography as needed, followed by an assessment by the anesthesiologist to evaluate the patient's condition. Furthermore, patients were advised to stop taking vitamin E, aspirin, and any other medications that could affect normal blood clotting for at least 2 weeks prior to the surgery to minimize the risk of hemorrhage. (8)

Surgical Procedure:

Whenever possible, the surgery is conducted after the patient has refrained from taking medications overnight and without sedation. This ensures the patient is in a relatively "off" state, allowing for a clearer clinical assessment of the effects during the surgical procedure. An MRI scan is obtained, including a 3D SPGR volumetric sequence and an SWI sequence, to allow for reconstruction in multiple planes and to clearly delineate the globus pallidus nuclei or the subthalamic nucleus from the internal capsule. (9)

Ipsilateral intravenous (IV) access is established to provide freedom of movement for the limb of interest. Oxygen is administered through a nasal cannula, while ECG, pulse oximetry, and blood pressure are continuously monitored. Arterial line placement and bladder

catheterization are not routinely conducted. The surgery is performed under local anesthesia, and maintaining well-controlled blood pressure during and after the procedure is essential to minimize the risk of hemorrhage.

After the infiltration of local anesthetic at the pin insertion sites, the stereotactic frame is fixed to the outer table of the skull, positioned 3 cm above the supraorbital ridge while avoiding the supraorbital nerve, vessels, and the temporalis muscle. We used Zamorano–Dujovny (ZD) stereotactic frame (Inomed Instruments, Emmendingen, Germany), Cosman Roberts Wells (CRW) rigid stereotactic frame (Integra, Burlington, MA, USA) and Brown Roberts Wells (BRW) stereotactic guidance system (Radionics, Inc., Burlington, MA) all over the study. Once the frame is applied, a CT scan is performed using 1-mm contiguous slices, a 512 × 512 matrix, and no gantry tilt.

The stereotactic CT is fused with preoperative MRI images to pinpoint the target by using Microtargeting Waypoint Planner 3.0 FHC, Inc., 2009 software.

(1) Globus Pallidus Internus (GPi): The target is identified both indirectly in relation to the midcommissural point and directly by visualizing the GPi on the MRI. A line is drawn along the pallidocapsular border at the AC-PC level, with the target positioned one-third of the distance from the posterior end, 3 mm lateral to the border. The final target is selected near the bottom of the GPi, just lateral and 2 mm above the optic tract. The trajectory is planned to avoid the lateral ventricle and sulci, remaining as close to the parasagittal plane as possible. (figure 1)

(2) Subthalamic nucleus (STN) boundaries are identified on the MRI scans and co-registered in 3D to define the stereotactic target coordinates. The target is typically 10-12 mm lateral to midline, 1-3 mm posterior to the midcommissural point, and 3-5 mm inferior to the AC-PC line. This target appears as a small, almond-shaped, hypointense structure anterior to the red nucleus and superior/lateral to the substantia nigra reticulata.

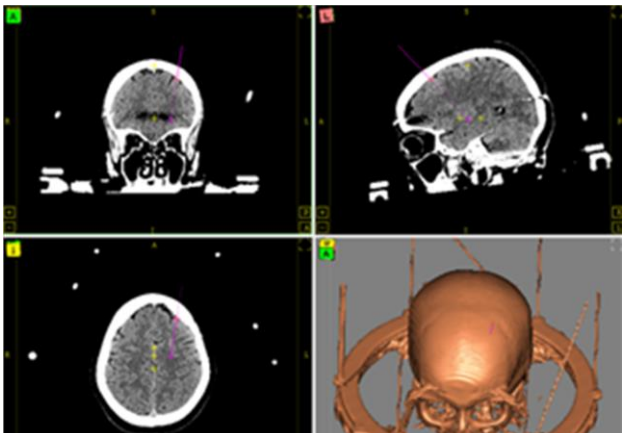

Figure (1): Entry localization 1: axial view 2: coronal view 3: sagittal view 4: 3D skull view.

The patient is positioned in a semi-sitting posture with their head secured in a stereotactic head holder. Prophylactic antibiotics and dexamethasone are administered, and a grounding pad is applied. A linear incision is made in the coronal direction, followed by the creation of a burr hole using local anesthesia. The dura and pia are then sealed and incised, and a guide tube is inserted into the burr hole. (10)

Figure (2): During insertion of the monopolar probe towards the target using ZD-arch.

Macrostimulation with a bipolar probe is employed to confirm the target location, instead of microelectrode recording, which is a subject of active debate. During the pallidotomy procedure, high-frequency stimulation (100 Hz) is used to evaluate proximity to the optic tract, assess speech dysfunction, and monitor symptom improvement. Low-frequency stimulation (5 Hz) helps identify motor thresholds and proximity to the internal capsule. Adjustments may be made if the visual or motor thresholds are too low, suggesting the electrode needs to be repositioned laterally or anteriorly. (figure 2)

Once the target site is confirmed, a test lesion is created at a 46-degree angle for 60 seconds. The patient's motor, speech, and visual functions are then evaluated, and if there are no adverse effects, a therapeutic lesion is made at a 72-degree angle for 70 seconds. (13) Additional lesions are created 2 mm and 4 mm above the target site, using the same parameters (72 degrees for 70 seconds). The patient’s response regarding rigidity, bradykinesia, tremor, and any potential side effects is assessed after each procedure. If additional therapeutic benefit is needed, expanding the lesion through a parallel trajectory may be considered using similar techniques. Once satisfactory results are achieved, the electrode is removed, and the wound is closed. (11)

A CT brain scan is conducted immediately after surgery to check for any hemorrhage. Following this, a brain MRI is obtained to evaluate the lesion site and identify any clinically silent complications. Patients are monitored overnight in the hospital, with careful attention to blood pressure to prevent hypertension, and most are discharged the day after surgery.

Preoperative Parkinson's medications are resumed, and the response to levodopa therapy remains consistent after the pallidotomy. (12) (figure 3)

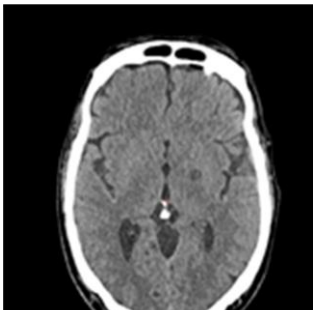

Figure (3): Post-op CT scan showing lesion after left pallidotomy. A case from our study

The most common side effects in pallidotomy include temporary confusion and mild transient weakness, particularly in facial muscles, which typically resolve within 7-10 days. Patients experiencing brief weakness generally show excellent outcomes following pallidotomy. None of the patients who underwent lesioning procedures experienced any visual field deficits, and there have been no cases of infection reported. One patient required a craniotomy to remove an acute intracerebral hematoma. In the subthalamotomy group, two patients experienced complications of hemiballismus. One case was mild and showed improvement within 2 weeks, while the other was severe and took 2 months to recover.

Results

The study population consisted of a total of 20 patients with Parkinson's disease, with an age range of 28 to 75 years and a mean age of 50.35 ± 11.79 years. There was a male predominance, with 14 male patients out of the total 20. Of the 20 patients, 12 underwent surgery on the left side, while 8 had surgery on the right side. The duration of Parkinson's disease ranged from 5 to 15 years, with a mean duration of 10.85 ± 3.25 years.

The study participants were further divided into two groups based on the specific surgical intervention performed. Ten patients underwent pallidotomy, with a male predominance of 7 cases. The age range for the pallidotomy group was 35 to 75 years, with a mean age of 51.6 ± 11.28 years. Five patients had pallidotomy performed on the left side, and another 5 on the right side. The duration of Parkinson's disease in the pallidotomy group ranged from 7 to 15 years, with a mean of 11.8 ± 3.19 years. The remaining 10 patients underwent subthalamotomy, again with a male predominance of 7 cases. The age range for the subthalamotomy group was 28 to 62 years, with a mean age of 49.1 ± 12.77 years. Seven patients had a subthalamotomy performed on the left side, and 3 on the right side. The duration of Parkinson's disease in the subthalamotomy group ranged from 5 to 13 years, with

a mean of 9.9 ± 3.18 years. The baseline characteristics of the two groups were not statistically significantly different.

Table 1: UPDRS III of the studied groups

UPDRS III	Pallidotomy group (n=10)	Sub-thalamotomy group (n=10)	Independent t test	P value (groups)
"OFF" state				
Preoperative	48.50±8.97	56.60±5.04	2.48	0.023*
Postoperative	27.0±11.48	28.40±6.7	0.333	0.026*
P value (pre vs post)	**t=8.66 p<0.001***	**t=6.37 p<0.001***		
"ON" state				
Preoperative	26.20±7.55	35.40±6.06	**3.01**	**0.008***
Postoperative	12.90±8.41	14.80±2.74	**0.679**	**0.506**
P value (pre vs post)	**t=19.03 p<0.001***	**t=8.93 p<0.001***		

In each group (patients treated by pallidotomy and those treated by Sub-thalamotomy), UPDRS III was significantly decreased after surgery than before during both "OFF and ON" states (P<0.05).

The comparison between both groups showed a statistically significant difference during "OFF", "ON" state, as patients treated by sub-thalamotomy had higher UPDRS III than those treated by pallidotomy pre and postoperatively except for postoperative "ON" state. **[Table 1, Figure 4]**

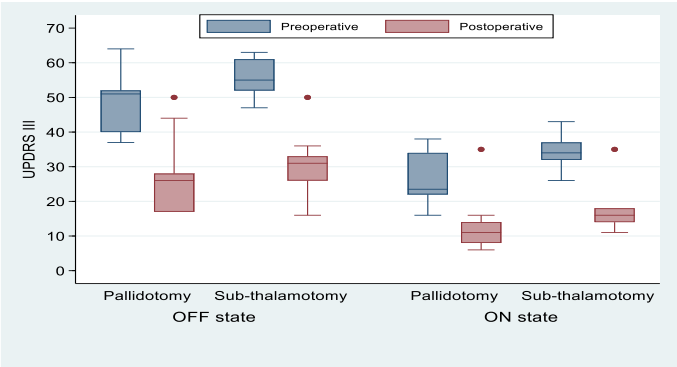

Figure 4: UPDRS III of the studied groups

Table 2: Schwab & England ADL scale of the studied groups

Schwab & England ADL	Pallidotomy group (n=10)	Sub-thalamotomy group (n=10)	independent t test	P value (groups)
"OFF" state				
Preoperative	37.0±9.48	42.0±10.32	1.12	0.274
Postoperative	78.0±14.76	86.00±8.43	1.49	0.154
P value (pre vs post)	**t=10.08 p=0.001***	**t=9.86 p=0.001***		
"ON" state				
Preoperative	59.0±7.37	70.0±9.42	**2.91**	**0.009***
Postoperative	90.0±12.47	95.0±5.27	1.17	0.258
P value (pre vs post)	**t=12.94 p=0.001***	**t=8.14 p=0.001***		

Data are presented as mean ±SD *: Statistically significant as P value<0.05, ADL: Activities of Daily Living

In each group of patients, Schwab & England ADL scale was significantly increased 6 months after surgery than before during both "OFF and ON" states (P<0.05).

The comparison between both groups showed a statistically significant difference only during "ON" state preoperatively, as patients treated by sub-thalamotomy had higher Schwab & England ADL scale than those treated by pallidotomy (P=0.009). **[Table 2, Figure 5]**

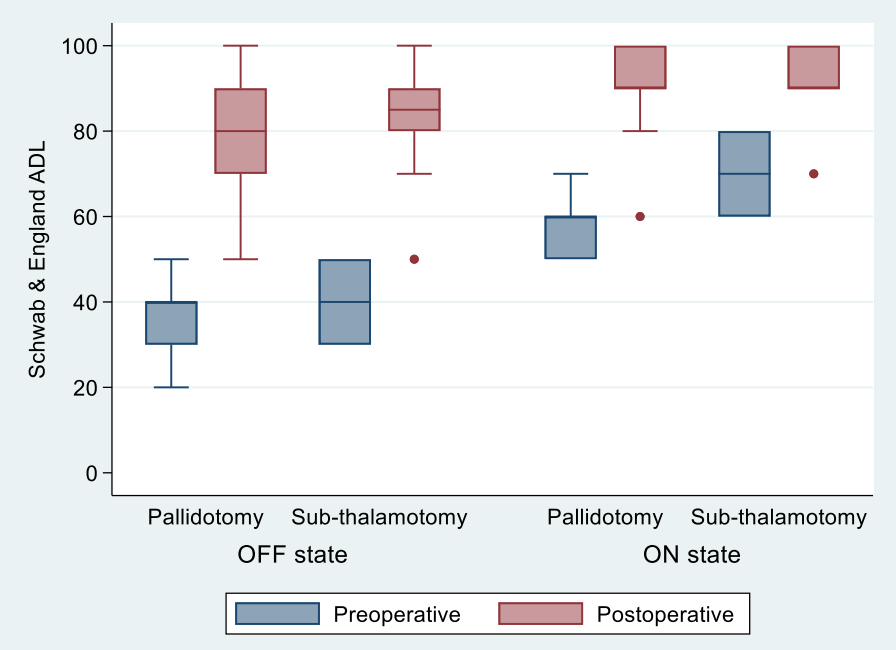

Figure 5: Schwab & England ADL scale of the studied groups

We used Levodopa Equivalent Daily Dose (LEDD) to show how much L-Dopa dose can be reduced after lesioning surgery. The results were as follows**: [Table 3, Figure6]**

-Mean of LDED:

- **In subthalamotomy group** was 770 and 380 pre and post-operative respectively.
- **In pallidotomy group** was 765 for both pre and post-operative.

Table 3: Comparison of mean LDED between studied groups pre and post operative.

Mean LDED	Pallidotomy group (n=10)	Sub-thalamotomy group (n=10)	P value #(groups)
Preoperative	765±12.5	770±10.5	**P=0.001***
Post operative	765±12.5	380±10.5	**P=0.001***
##	P=1.0	P<0.001*	

Used test Student t test, ##Paired t test, *statistically significant

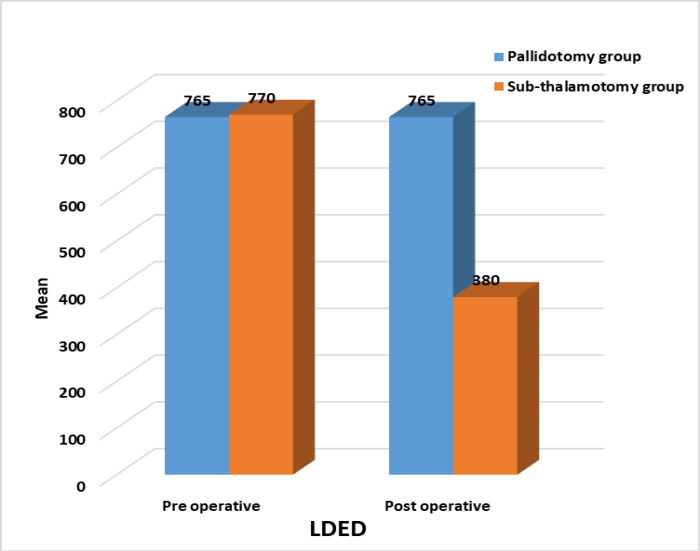

Figure 6: Comparison of mean LDED between studied groups pre and post operative.

Discussion

Parkinson's disease (PD) is a neurodegenerative disorder characterized by a clinical triad of akinesia, stiffness, and tremor due to dopaminergic neurodegeneration. While medical therapy can initially manage symptoms, long-term use leads to complications like dyskinesia and motor fluctuations. Surgical treatments like ablative surgery (thalamotomy, pallidotomy, subthalamotomy) and deep brain stimulation are options when medical therapy fails.

This study compared the clinical outcomes of 20 PD patients treated with two different surgical techniques - unilateral pallidotomy (10 patients) and unilateral subthalamotomy (10 patients). The subthalamotomy group showed significant improvement in UPDRS III from 56.60±5.04 to 28.40±6.7 (49.8%) and from 35.40±6.06 to 14.80±2.74 (58.2%) in the Off and On periods retrospectively. There was a dramatic improvement in rigidity, body bradykinesia and tremors 52%,47%, and 57% respectively 6 months after surgery during "OFF and 67%, 52% and 70% during "ON" states ($P<0.05$). Dyskinesia reduced from 6.10±1.52 to 3.40±1.07 (44.3%) in the On period.

In this group, Schwab & England ADL score improved from 42.0±10.32 to 86.00±8.43 (51.2%) and from 70.0±9.42 to 95.0±5.27 (26.3%) in the Off and On periods retrospectively. Modified H&Y scale was significantly decreased 6 months after surgery during both "OFF and ON" states ($P<0.05$). LDED reduce by 50.65% in comparison to LDED pre-operative.

In Su et al., 2002 study, subthalamotomy had effective results in Schwab & England ADL score which improved by 38% and 27% in the Off and On periods retrospectively. LDED reduce by 38% in comparison to LDED pre-operative. (14)

L. Alvarez et al., 2001 study showed that unilateral subthalamotomy is effective in treatment of advanced PD. His results showed improvement in UPDRS III by 50% and 39% in Off and On periods retrospectively. There was a dramatic improvement in rigidity, body bradykinesia and tremor by 70.84%, 51.16% and 86.61% retrospectively in Off periods. (15)

The pallidotomy group showed significant improvement in UPDRS III from 48.50±8.97 to 27.0±11.48 (44.3%) and from 26.20±7.55 to 12.90±8.41 (50.8%) in the Off and On periods retrospectively. There was a dramatic improvement in rigidity and body bradykinesia 35% and 26% respectively 6 months after surgery during "OFF" state and 49% and 41% during "ON" state ($P<0.05$). Dyskinesia reduced from 4.80±2.29 to2.20±2.14 (54.2%) in the On period.

In this group, Schwab & England ADL score improved from 37.0±9.48 to 78.0±14.76 (52.6%) and from 59.0±7.37 to 90.0±12.47 (34.4%) in the Off and On periods retrospectively. Modified H&Y scale was significantly decreased 6 months after surgery during both "OFF and ON" states ($P<0.05$). No LDED reduction occurred.

Lozano & Lang, 1995 study showed that pallidotomy improved rigidity and body bradykinesia was 30 %, and 22 % retrospectively in Off period. Tremor was not prominent in patients here so was not assessed. Schwab & England ADL score improved by 50% in Off period. Dyskinesia reduced by 92 % in the On period. There was no significant LDED reduction changes. (16)

In Schuurman and Speelman et al., 1999 study, UPDRS III improved by 31.91% in off period. Dyskinesia reduced by 50% in On period. Schwab & England ADL score improved by 50% in Off period. These results are near to the results of our study. (17)

The complication rates were low in both groups. In the subthalamotomy group, 2 patients developed transient hemiballismus, one mild and one severe. No other major complications like hemorrhage or cognitive issues were observed. In the pallidotomy group, one patient had a small hemorrhage, and another had a missed lesion leading to temporary improvement.

Overall, both subthalamotomy and pallidotomy were effective in managing the motor symptoms of PD, with subthalamotomy having a slight advantage. The choice between the two procedures may depend on the specific symptoms and patient characteristics. Careful patient selection and surgical technique are crucial to minimize complications and optimize outcomes.

Ethical Considerations

When conducting surgical management of Parkinson's disease, it is critical to consider a range of ethical considerations to ensure the patient's well-being and rights are protected. First and foremost, the study protocol was approved by the hospital's ethics committee. This ensures that the proposed procedures and study design meet the necessary standards for

patient safety and ethical conduct. Equally important is obtaining the patient's informed consent. Patients must be fully informed about the objectives of the study, the operative procedures that will be performed, and the potential complications that may arise. A written consent form was obtained from all patients, and they were made aware of their right to withdraw from the study at any time without having to provide a reason. The safety and security of the patient is paramount. Particular attention was paid to the patient's exposure to radiation during any imaging or treatment procedures. Measures were in place to ensure that radiation exposure is within safe limits and that the patient's data is managed securely to protect their confidentiality. It is well-established that functional lesioning, such as thalamotomy, pallidotomy, and subthalamotomy, can be safe and effective for the management of Parkinson's disease. However, the research team still carefully reviewed the existing literature and ensured that the planned procedures are well-suited to the individual patient's needs and risks. Finally, the patient's identity was kept anonymous throughout the study, and their confidentiality was guaranteed. This ensures that the patient's personal and medical information remains protected and secure. By carefully considering these ethical principles, the research team ensured that the surgical management of Parkinson's disease is conducted in a manner that respects the patient's rights, safety, and well-being.

Limitations: small sample size, the duration of follow-up in this study was relatively short.

Conclusion

Both Posteroventral Pallidotomy and Subthalamotomy have been shown to result in improvements in the major symptoms of Parkinson's disease. Subthalamotomy may offer slight advantages in reducing medication requirements and improving activities of daily living. Subthalamotomy also demonstrated significantly better outcomes in specific motor domains, such as body bradykinesia, postural instability, and gait disability. Subthalamotomy was associated with a higher risk of adverse effects compared to pallidotomy. However, Pallidotomy is advised if the main complaint of patient is dyskinesia.

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