DOI: 10.21608/pajn.2023.204191.1090

Original Article

Unilateral Combined Stereotactic Radiofrequency Pallidotomy and Thalamotomy for Idiopathic Parkinson's Disease

Ali Salah Khedr,[1] MD, PhD; Maha Abd El Fattah,[2] MD, PhD; Mohamed Khaled Elkazaz,[1] MD, PhD, MRCS
[1]Department of Neurosurgery, Faculty of Medicine, Suez Canal University, Ismailia, EGYPT
[2]Rheumatology and Physical Medicine Department, Faculty of Medicine, Suez Canal University, Ismailia, EGYPT

Received: 4 April 2023 / **Accepted:** 29 August 2023 / **Published online:** 18 December 2023

BACKGROUND: Lesioning surgeries in Parkinson's disease (PD) include target obliteration of a certain area in brain tissue to disrupt maladaptive neuronal arrangements. There was an advancement in treatment of movement disorders when stereotactic procedures were applied in lesioning. Target selections were modulated various times until in 1960s when thalamotomy was used for tremors and pallidotomy was used for bradykinesia and rigidity.

OBJECTIVE: To report the efficacy of unilateral combined stereotactic radiofrequency pallidotomy and thalamotomy for idiopathic Parkinson's disease.

PATIENTS AND METHODS: This is a prospective observational study including 62 patients with idiopathic Parkinson's disease who underwent stereotactic radiofrequency pallidotomy and thalamotomy between June 2017 and December 2019. Pre-operative clinical assessment was based on the Unified Parkinson's Disease Rating Scale (UPDRS) and Hoehn and Yahr scale for PD. Postoperative clinical assessment was based on the UPDRS and Hoehn and Yahr scale for PD in addition to complications at 1, 6, 12 and 24 months.

RESULTS: Sixty patients who completed the two-year follow-up and fulfilled our criteria were recruited. The mean age was 57.47±9.90 years. The average UPDRS off state motor assessment results showed reduction after 1 month from 60.16 to 30.88, and at 24-months follow-up it was 41.6. The average Hoehn and Yahr scale was reduced from 3.63 to 1.19 after 1-month, and at 24 months it was 1.87. The average UPDRS constancy of tremors improved after 1-month from 3.53 to 0.75. Improvement in constancy of tremors reached 75% of cases after 24-months with average 1.62. The average UPDRS rigidity score improved at 1-month follow-up from 3.31 to 1.21. Total improvement of rigidity reached 63% after 24-months. Two patients had postoperative thalamic hematoma presenting with hemiplegia, which was conservatively managed, and improved after 1-month with little deficit. Around 51.6% of the patients had gait imbalance at 6-months follow-up while 22.5% showed dysarthria immediately postoperatively which totally resolved after 1-month in 12.9%. There were no recorded cases of infection, cerebrospinal fluid (CSF) leaks or cognitive dysfunction.

CONCLUSION: Our data suggest that unilateral combined stereotactic radiofrequency Pallidotomy and Thalamotomy for idiopathic PD is an effective procedure.

KEYWORDS: Pallidotomy, Parkinson's, Radiofrequency, Spasticity, Thalamotomy, Tremors.

INTRODUCTION

Lesioning surgeries in Parkinson's disease (PD) include target obliteration of a certain area in brain tissue to disrupt maladaptive neuronal arrangements. An advancement in movement disorders occurred when stereotactic procedures were applied in lesioning. Target selections were modulated various times until in 1960s when Thalamotomy was used for tremors and Pallidotomy was used for bradykinesia and rigidity.[1,2] Though lesioning procedures were executed for numerous years in particular patients with PD, their practice reduced in the 1960s following the presentation of levodopa. However, long-term treatment with levodopa has led to newly unfavorable side effects that refreshed the era of lesioning surgeries.[3]

Correspondence:
Mohamed Khaled Elkazaz
4.5 Km Ring Road, Suez Canal University Hospitals, Neurosurgery Department 3rd floor, Ismailia, EGYPT
Email: Mohamed.elkazaz@med.suez.edu.eg

Lesioning procedures continued to develop, and currently accessible methods include invasive procedures such as thermoablation, radiofrequency and laser interstitial thermal therapy (LITT), and less invasive procedures such as magnetic resonance-guided high intensity focused ultrasound (MRgFUS) ablation, and stereotactic radiosurgery (SRS). Radiofrequency and thermaoablation are the commonly used modalities.[4,5]

In 1954, Hassler and Reichert used thalamotomy to treat tremors associated with PD. Ventrolateral thalamotomy has been considered the neurosurgical treatment of choice for disabling, drug-resistant parkinsonian and other types of tremors. Tremors could be relieved not only by a thalamic lesion but also by a lesion in the posteroventral portion of the medial (Internal) Globus Pallidum (GPi) and ventralis intermedius (VIM) nucleus of the Thalamus. Hassler and Reichert proved that thalamotomy controls the tremors related to PD.[2] Various studies had shown the role of VIM lesioning in control of PD medically refractory tremors or other types of tremors.[6–8]

One of the studies retrospectively reviewed the results in 60 patients with PD tremors, cerebellar tremors, essential tremors and post-traumatic tremors. All these patients had unilateral VIM thalamotomy with mean follow-up of 53.4 months. Patients with PD tremors had marked improvement in 86% of the cases while patients with essential tremors had similar improvement in 83% of cases. Results were not as favorable for those patients with post-traumatic tremors (50%) or cerebellar tremors (67%). Temporary complications of thalamotomy were seen in 60% of cases including dysarthria, dysphasia, confusion, dystonia, contralateral paresis or sensory disturbances.[9]

Lesion of the posteroventral segment of the internal Globus Pallidus (GPi) is efficient at treating contralateral tremor, rigidity, dyskinesia and bradykinesia.[10] Various studies supported this opinion. The first of these studies described an improvement in the off-state Unified Parkinson's Disease Rating Scale (UPDRS) motor score of 65% at 1 year following the surgery.[11] Lozano et al. study showed UPDRS motor score improved in the off state by 30% at 6 months postoperatively, although the UPDRS akinesia score improved only by 33%. The gait score showed 15% improvement in the off-state with decrease in contralateral dyskinesias by 92%.[12] Baron et al. described a 25% improvement in the motor score in the off state at 3 months postoperatively.[13] Shannon et al. described an improvement in 15% in the off-state motor score 6 months postoperatively.[14] This study aims to evaluate the role of unilateral combined Thalamotomy and Pallidotomy in improving the symptoms in patients with PD.

PATIENTS AND METHODS

This prospective observational study included patients suffering from idiopathic Parkinson's disease treated at Suez Canal University between June 2017 and December 2019. Total number of 62 patients underwent stereotactic unilateral combined Pallidotomy "GPi" and Thalamotomy "VIM" using radiofrequency ablation for the management of Parkinson related tremors, bradykinesia and rigidity, after careful counseling and acquiring informed consent from the patients. All patients have signed a consent for the publication purpose. This article followed the world medical association declaration of Helsinki ethical principles. The study was approved by our institutional review board (IRB), and consent was obtained from all patients.

We included only patients diagnosed with idiopathic PD, with medication induced motor signs and refractory tremors, and Hoehn and Yahr >2 off stage. Exclusion criteria included multiple comorbidities that increase morbidity and mortality risk of surgery, neuropsychiatric diseases, dementia, postural instability and atypical PD such as supranuclear gaze palsy, early postural instability or severe early dysautonomia. We excluded patients who failed to complete 24-months follow-up.

A multidisciplinary presurgical assessment was done by neurosurgery and neurology team, including complete physical and mental assessment of the patients presented with PD. Neurology team was responsible for diagnosis confirmation and assessment of the medication trials the patients were offered. The off state was outlined as the state after withdrawal of anti PD treatment by 12 hours, based on the Core Assessment Program for Intracerebral Transplantations (CAPIT) committee definition.[15] The objective clinical test used in this study was the UPDRS in off state motor assessment, tremors and rigidity, both preoperatively and at 1, 6, 12 and 24 months postoperatively.[16] Patients were also staged using Hoehn and Yahr scale in off state preoperatively and postoperatively at 1, 6, 12 and 24 months.[17] Preoperative imaging included magnetic resonance imaging (MRI) and computed tomography (CT) brain one day prior to surgery.

Operative details

After admission, patients were preoperatively assessed by the anesthesia team. Stereotactic system Cosman-Robert Wells (CRW) (Integra, NJ, USA) application was performed under local anesthesia by scalp block. Patients then underwent CT brain with the frame and fiducials applied to it. Data was analyzed and target selection was done by waypoint navigator software (FHC, Bowdoin, ME, USA), selecting the preferred points after fusion between preoperative MRI, CT brain and post fiducials CT brain as follows.

Target selection

VIM target is 14 mm lateral and 6 mm anterior from the posterior commissural point in the same anterior commissure - posterior commissure (AC-PC) plane and GPi point is 21 mm lateral and 3 mm anterior from the mid commissural point at the mid-commissure (MC) plane **(Fig. 1).** Specific adjustments were done in relation to the lateral ventricular wall and internal capsule with the fusion images. Afterwards, selected targets were transferred to Stereocheck application (Mevis Informatica Medica Ltda, Sao Paulo, Brazil) **(Fig. 2),** where both entry and lesion targets were transformed into X, Y and Z numbers. Preoperative placement of the patient on the Mayfield (Integra, NJ, USA) was done. Patient was connected with neurophysiological monitoring for motor assessment. Sterile shaving and surgical draping was done. Data gained from Stereocheck was then transferred to phantom stereotaxis system and confirmed, then the arc and ring was fixed upon patients' frame. Burr hole guided by trajectory from the software was performed followed by durotomy.

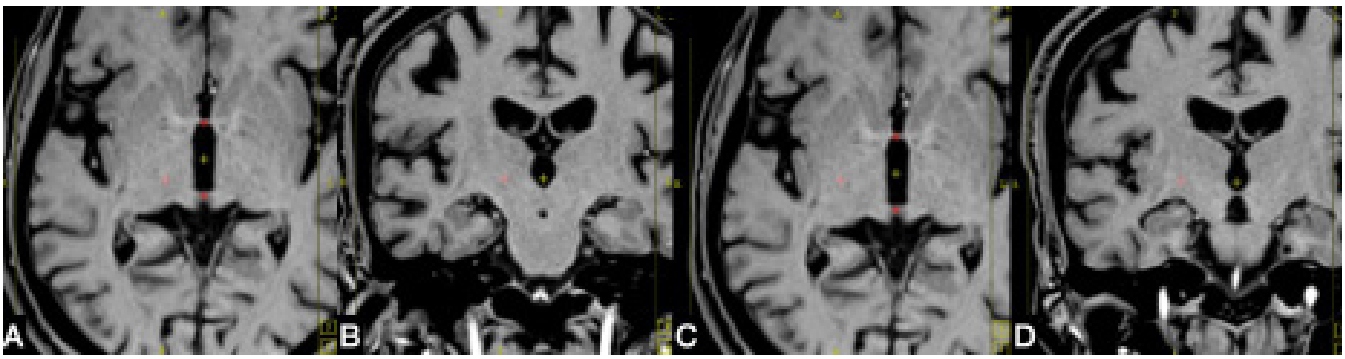


Fig 1: A case of a 56 years old male patient with PD planning for right unilateral combined VIM and GPi lesioning. (A) Axial MRI brain T1WI with VIM target "red crosshair right to third ventricle". (B) Coronal MRI brain T1WI with VIM target "red crosshair right to third ventricle". (C) Axial MRI brain T1WI with GPi target "red crosshair right to third ventricle". (D) Coronal MRI brain T1WI with GPi target "red crosshair right to third ventricle".

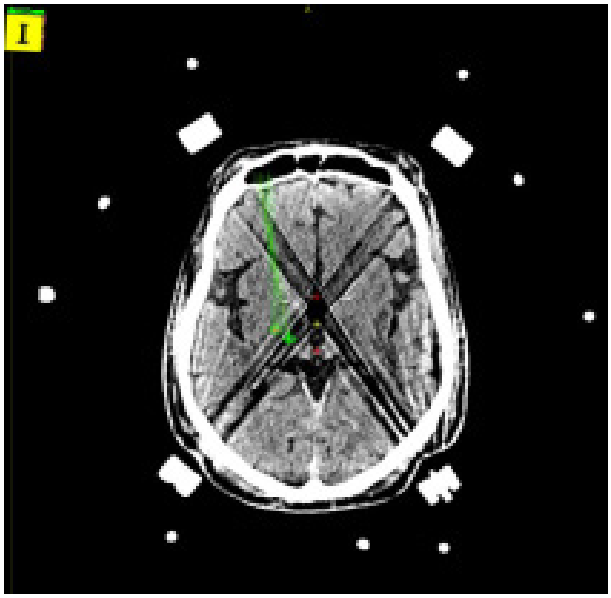


Fig 2: Axial CT brain with ring and fiducial marks for planning in Stereocheck.

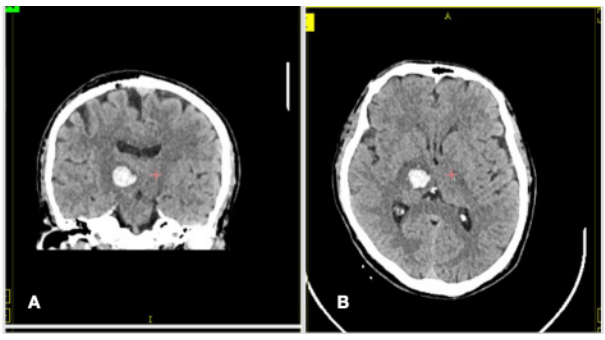


Fig 3: (A) Coronal and (B) axial CT brain showing thalamic hematoma post-lesioning.

Electrode placement

The macroelectrode with bipolar 2-mm width, 3-mm length and 3-mm tip was inserted through a guiding tube with 2mm diameter, then it was connected to the radiofrequency apparatus "Neuro N50" (Inomed, Germany) with impedance monitoring until reaching the target. Functional localization was done by macrostimulation with 2 Hertz and 50 Hertz in both points to assess proximity of the VIM target to ventral caudal (VC) nucleus and internal capsule, and proximity of the GPi target to the internal capsule. After confirmation of the target, VIM underwent a temporarily lesioning "50° C for 50 seconds" followed by careful assessment of the patient. If there was no deficit it was followed by permanent lesion "65° C for 60 seconds" then withdrawal by 2-mm and reapplying permanent lesion. GPi underwent a temporarily lesioning "50° C for 50 seconds" followed by careful assessment of the patient, then followed by permanent lesion "72° C for 60 seconds", withdrawal by 2-mm then reapplying permanent lesion. Hemostasis and skin closure were done.

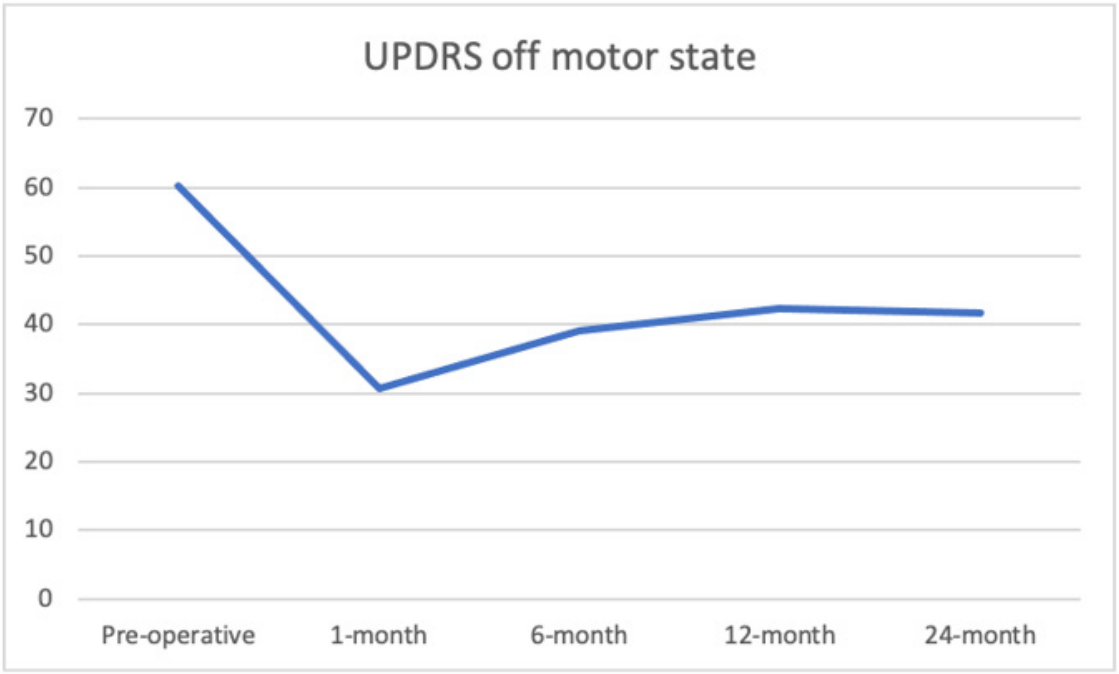
Postoperative assessment was done at 1, 6, 12 and 24 months for both the UPDRS off state and the Hoehn and Yahr scale. Intraoperative and postoperative complications were reported. Statistical analysis was done using the statistical packages for the social sciences (SPSS) version 26 (IOS, Chicago, IL, USA). Paired t-test was implemented between means of variables.

RESULTS

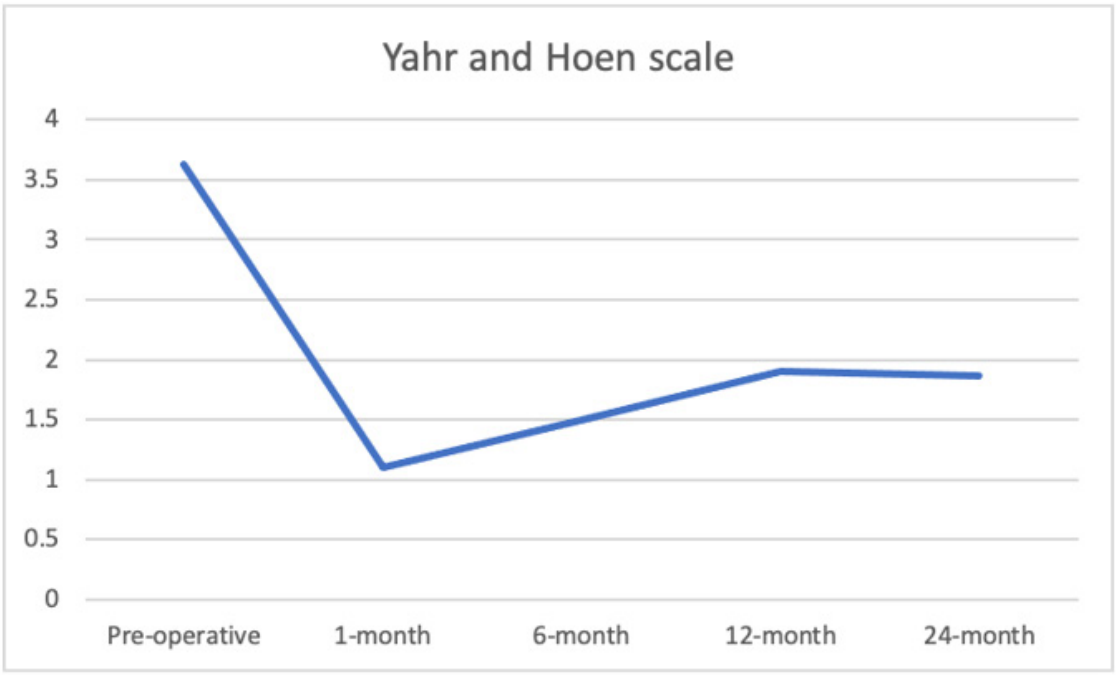
Sixty-two patients were enrolled in the study; 37 males and 25 females and the mean age was 57.47±9.90 years. Two patients failed to complete follow-up and were excluded from the study. The average UPDRS off motor assessment results showed marked reduction after 1 month from 60.16 to 30.88. At 6-months and 1-year follow-up there was a non-significant rise in the average UPDRS off motor assessment to 39.1 and 42.3, respectively. At 24-months follow-up, the average UPDRS off motor was 41.6. The average Hoehn and Yahr scale was reduced from 3.63 to 1.19 after 1-month. At 6-months and 12-months follow-up, there was a non-significant rise to 1.5 and 1.9, respectively. At 24 months postoperatively, the average Hoehn and Yahr scale was 1.87 **(Table 1) (Graphs 1,2).**

The average UPDRS constancy of tremors **(Graph 3)** was analyzed and showed a significant improvement after 1-month duration from 3.53 to 0.75. There was a non-significant rise at 6 months and 12 months to 1.23 and 1.72, respectively. Total improvement in constancy of tremors reached up to 75% of cases after 24-months with average 1.62. In addition, the average UPDRS rigidity score **(Graph 4)** also showed significant improvement at 1-month follow-up from 3.31 to 1.21. There was a non-significant rise at 6 months and 12 months to 1.9 and 2.3, respectively. At 24-months follow-up, the average reached 2.1. Total improvement of rigidity reached up to 63% of cases after 24-months.

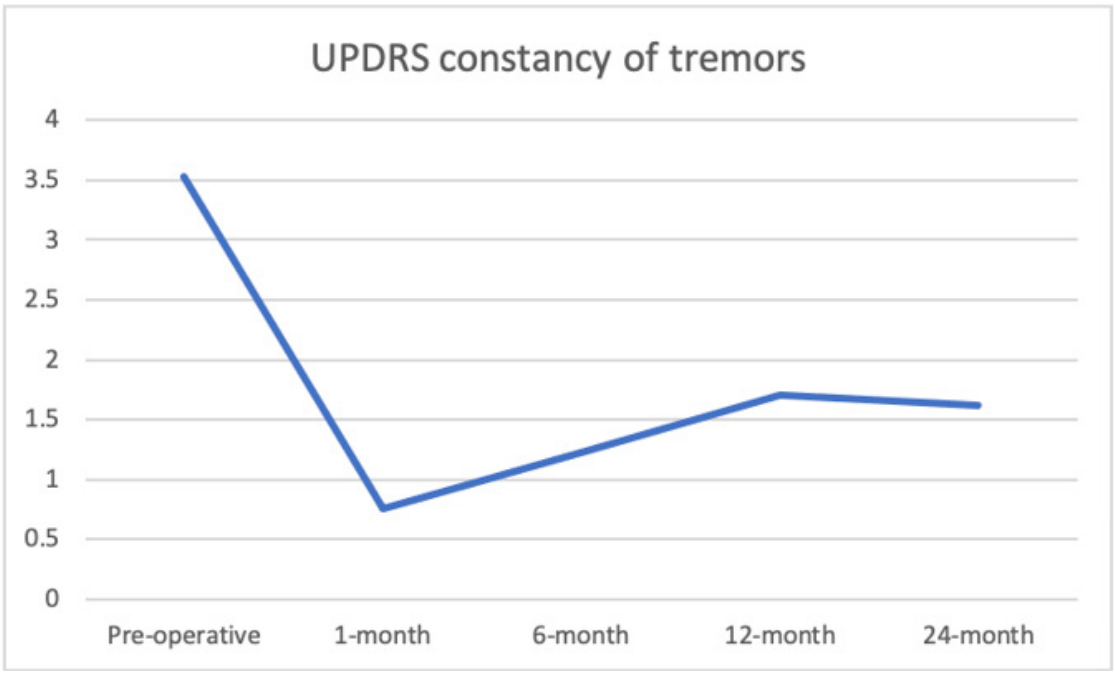
Two patients (3.2%) had thalamic hematoma that was discovered postoperatively with hemiplegia **(Fig. 3)**. The patients were managed conservatively, and they improved after 1-month with little residual deficit. Also noticed in the study that 32 patients (51.6%) had gait imbalance noticed at 6-months follow-up with leaning towards the contralateral side to the lesioning. Fourteen patients (22.5%) showed dysarthria immediately postoperative and 8 of these patients (12.9%) totally recovered after 1-month. There were no recorded cases of infection, CSF leaks or cognitive dysfunction.



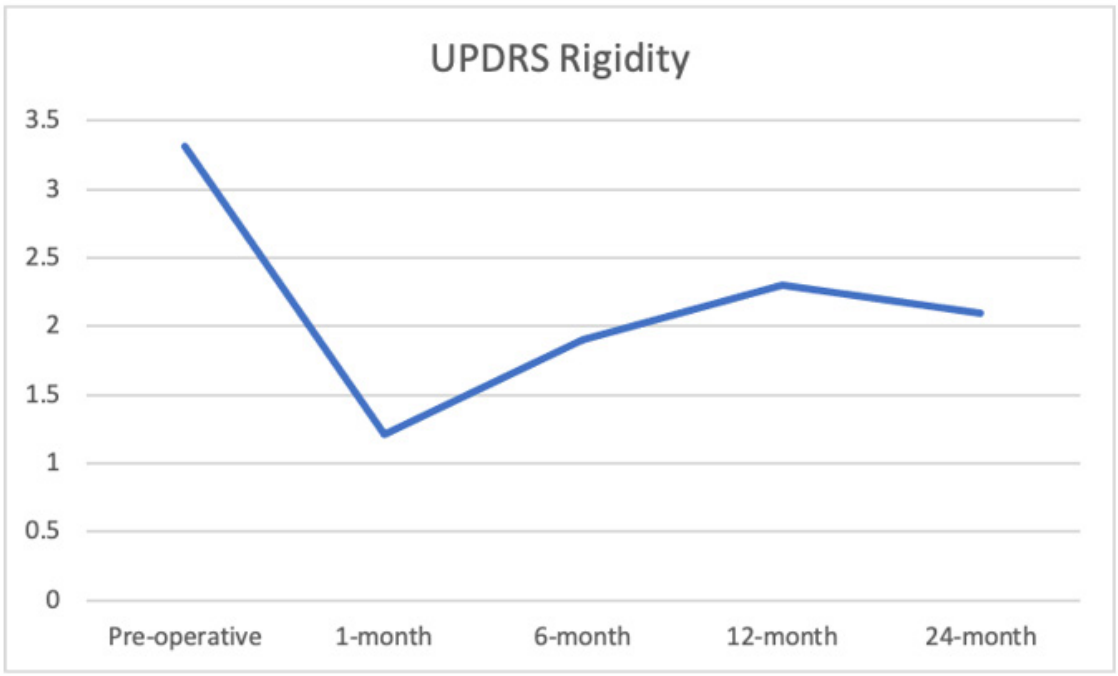
Graph 1: UPDRS off motor state assessment.



Graph 2: Hoehn and Yahr assessment.



Graph 3: UPDRS constancy of rest tremors assessment.



Graph 4: UPDRS rigidity assessment.

Table 1: Clinical assessment preoperatively and at the final follow-up (After 24-months)

Item	Preoperative (Mean±SD)	24-months (Mean±SD)	T-score	P-value
UPDRS off state motor score	60.16±3.8	41.6±4.49	10.23	<0.05*
Hoehn and Yahr scale	3.63±0.66	1.87±0.61	7.8	<0.05*

SD: standard deviation.

UPDRS: Unified Parkinson's disease rating scale.

*p-value <0.05 is statistically significant.

DISCUSSION

Spiegel et al. in 1947 introduced the era of brain stereotactic surgery.[18] Later it became an evolution in this field in the management of PD. Hassler successfully managed to control PD symptoms by Thalamotomy.[19] Traditionally, Thalamotomy alone was used as a maneuver for PD, but after Leksell's evolutionary introduction of the GPi lesioning, rigidity and bradykinesia were managed along with tremors.[6] Long-term studies on isolated Thalamotomies had shown that patients were still disabled with rigidity. In addition studies which favored that isolated lesion in GPi could control both rigidity and tremors, was found later to be insufficient to control the tremors.[20,21] VIM lesioning aims to disrupt the rubro-thalamo-cortical circuit controlling abnormal impulses initiating tremors,[22,23] while GPi lesioning disconnect the inhibitory outflow of the GPi to the ventralis oralis anterior (VOa) nucleus and the pedunculopontine nucleus (PPN).[22,24]

In this series we had a success rate in improving patients UPDRS and experiencing less relapse and complications. Linhares et al. reported success of thalamotomy procedure in suppressing tremors in PD with 75% improvement in upper limb and 73% improvement in lower limb tremors.[25] Fayed et al. reported successful results in combined Pallidotomy and Thalamotomy over Pallidotomy alone in improving patients functional state and controlling PD.[26] Several mechanisms were postulated regarding the persistence of tremors after lesioning the GPi alone as the GPi lesioning does not directly disconnect the rubro-thalamo-cortical loop. In addition, it may exacerbate the tremors by the disinhibition of the reticulospinal system.[23,27] Iacono et al. stated that combined VIM and GPi lesioning could treat broad range of symptoms in PD immediately with no or little risk on the patients.[22]

Study Limitations

The small sample size affected the statistical testing of the results.

CONCLUSION

Unilateral combined VIM/GPi lesioning had shown to be very effective in controlling PD symptoms and improving the overall functional state of the patients. Despite being a successful technique, few studies were focusing on it. It showed to be potent and carries little risk for the patients. We advocate that case-control studies should be directed to assess this technique.

List of abbreviations

AC: Anterior commissure.
CAPIT: Core Assessment Program for Intracerebral. Transplantations.
CRW: Cosman Roberts Wells.
CSF: Cerebrospinal fluid.
CT: Computed tomography.
GPi: Globus pallidus internus.
IRB: Institutional review board.
LITT: Laser interstitial thermal therapy.
MC: Mid-commissure.
MRgFUS: Magnetic resonance -guided high intensity focused ultrasound.
MRI: Magnetic resonance imaging.
PC: Posterior commissure.
PD: Parkinson's disease.
PPN: Pedunculopontine nucleus.
SPSS: Statistical packages for the social sciences
SRS: Stereotactic radiosurgery.
UPDRS: Unified Parkinson's Disease Rating Scale.
VC: Ventral caudal.
VIM: Ventralis intermedius.
VOa: Ventralis oralis anterior.

Disclosure

The authors report no conflict of interest in the materials or methods used in this study or the findings specified in this paper.

Funding

The authors received no financial support for the research, authorship, and/or publication of this paper.

Acknowledgements

Special thanks to the Neurosurgery Department in Suez Canal University for the continuous support.

REFERENCES

1. Svennilson E, Torvik A, Lowe R, et al. Treatment of parkinsonism by stereotactic thermolesions in the pallidal region. A clinical evaluation of 81 cases. *Acta Psychiatr Scand.* 1960;35(3):358-377.

2. Hassler R, Riechert T. Indications and localization of stereotactic brain operations [Article in German]. *Nervenarzt.* 1954;25(11):441-447.

3. Marsden CD, Parkes JD. Success and problems of long-term levodopa therapy in Parkinson's disease. *Lancet.* 1977;1(8007):345-349.

4. Walters H, Shah BB. Focused ultrasound and other lesioning therapies in movement disorders. *Curr Neurol Neurosci Rep.* 2019;19(9):66.

5. Jourdain VA, Schechtmann G. Health economics and surgical treatment for Parkinson's disease in a world perspective: Results from an international survey. *Stereotact Funct Neurosurg.* 2014;92(2):71-79.

6. Laitinen L V, Bergenheim AT, Hariz MI. Leksell's posteroventral pallidotomy in the treatment of Parkinson's disease. *J Neurosurg.* 1992;76(1):53-61.

7. Nagaseki Y, Shibazaki T, Hirai T, et al. Long-term follow-up results of selective VIM-thalamotomy. *J Neurosurg.* 1986;65(3):296-302.

8. Fox MW, Ahlskog JE, Kelly PJ. Stereotactic

ventrolateralis thalamotomy for medically refractory tremor in post-levodopa era Parkinson's disease patients. *J Neurosurg.* 1991;75(5):723-730.

9. Jankovic J, Cardoso F, Grossman RG, et al. Outcome after stereotactic thalamotomy for parkinsonian, essential, and other types of tremor. *Neurosurgery.* 1995;37(4):680-687.
10. Lai EC, Jankovic J, Krauss JK, et al. Long-term efficacy of posteroventral pallidotomy in the treatment of Parkinson's disease. *Neurology.* 2000;55(8):1218-1222.
11. Dogali M, Fazzini E, Kolodny E, et al. Stereotactic ventral pallidotomy for Parkinson's disease. *Neurology.* 1995;45(4):753-761.
12. Lozano AM, Lang AE, Galvez-Jimenez N, et al. Effect of GPi pallidotomy on motor function in Parkinson's disease. *Lancet.* 1995;346(8987):1383-1387.
13. Baron MS, Vitek JL, Bakay RA, et al. Treatment of advanced Parkinson's disease by posterior GPi pallidotomy: 1-year results of a pilot study. *Ann Neurol.* 1996;40(3):355-366.
14. Shannon KM, Penn RD, Kroin JS, et al. Stereotactic pallidotomy for the treatment of Parkinson's disease: Efficacy and adverse effects at 6 months in 26 patients. *Neurology.* 1998;50(2):434-438.
15. Langston JW, Widner H, Goetz CG, et al. Core assessment program for intracerebral transplantations (CAPIT). *Mov Disord.* 1992;7(1):2-13.
16. Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. The Unified Parkinson's Disease Rating Scale (UPDRS): Status and recommendations. *Mov Disord.* 2003;18(7):738-750.
17. Hoehn MM, Yahr MD. Parkinsonism: Onset, progression, and mortality. 1967. *Neurology.* 1998;50(2):318-333.
18. Spiegel EA, Wycis HT, Marks M, et al. Stereotaxic apparatus for operations on the human brain. *Science.* 1947;106(2754):349-350.
19. Hassler R. Extrapyramidal cortical systems and central regulation of motor function [Article in German]. *Dtsch Z Nervenheilkd.* 1956;175(3):233-258.
20. Okun MS, Vitek JL. Lesion therapy for Parkinson's disease and other movement disorders: Update and controversies. *Mov Disord.* 2004;19(4):375-389.
21. Taha JM, Favre J, Baumann TK, et al. Tremor control after pallidotomy in patients with Parkinson's disease: Correlation with microrecording findings. *J Neurosurg.* 1997;86(4):642-647.
22. Iacono RP, Henderson JM, Lonser RR. Combined stereotactic thalamotomy and posteroventral pallidotomy for Parkinson's disease. *J Image Guid Surg.* 1995;1(3):133-140.
23. Narabayashi H. Neurophysiological ideas on pallidotomy and ventrolateral thalamotomy for hyperkinesis. *Confin Neurol*. 1962;22:291-303.
24. Ohye C. Depth microelectrode studies. In: Schaltenbrand G, Walker AE, eds. Stereotaxy of the Human Brain: Anatomical, Physiological and Clinical Applications. *2nd ed. Thieme*. 1982:510–514.
25. Linhares MN, Tasker RR. Microelectrode-guided thalamotomy for Parkinson's disease. *Neurosurgery.* 2000;46(2):390-398.
26. Fayed ZY, Radwan H, Aziz M, et al. Combined unilateral posteroventral pallidotomy and ventral intermediate nucleus thalamotomy in tremor-dominant Parkinson's disease versus posteroventral pallidotomy alone: A prospective comparative study. *Stereotact Funct Neurosurg.* 2018;96(4):264-269.
27. Sandyk R, Iacono RP. The relationship of the reticular system to the primary pathoetiology of Parkinson's disease. *Int J Neurosci.* 1988;42(3-4):297-300.