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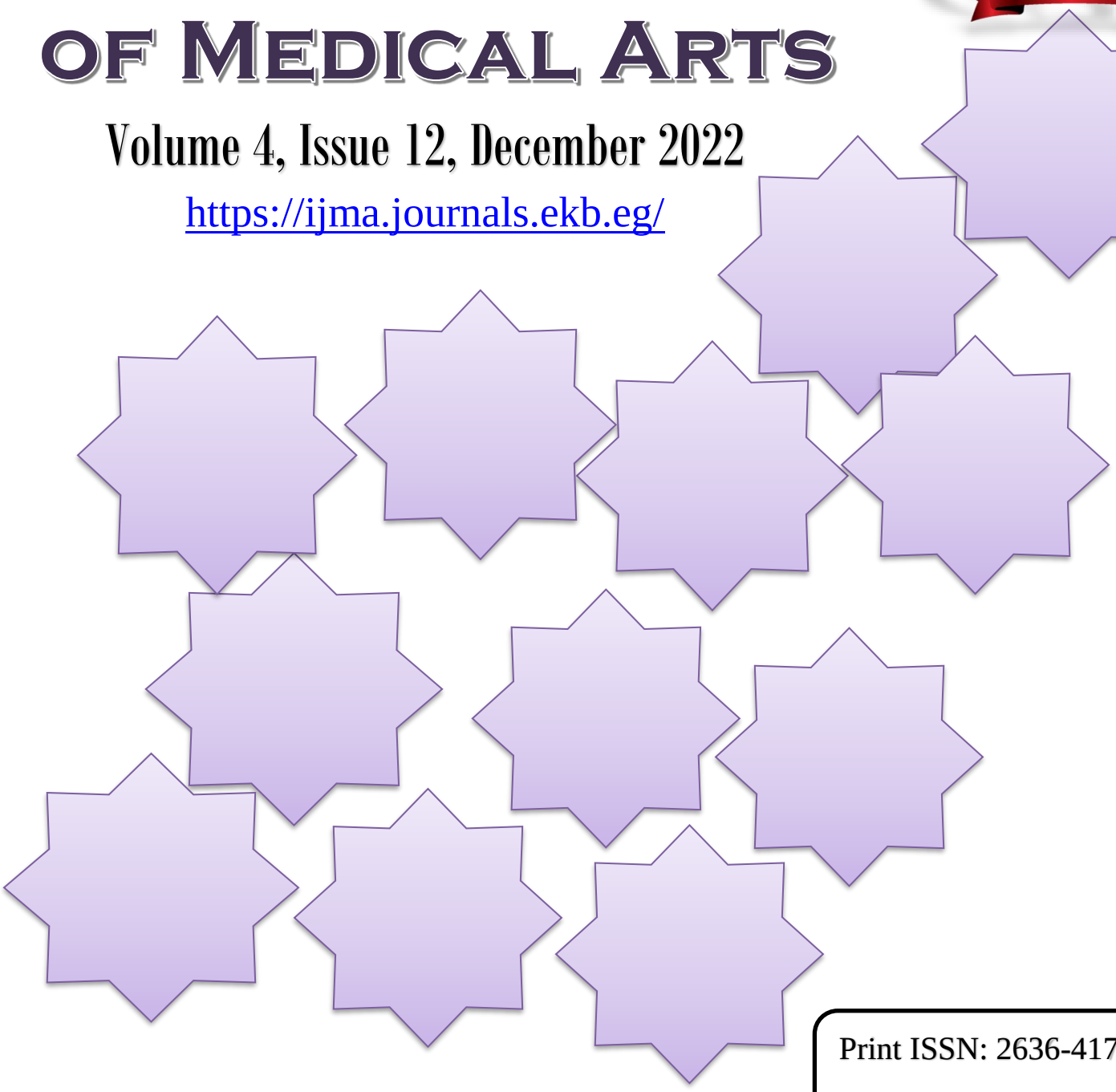

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Original Article

Assessment of the Outcome of Stereotactic Unilateral Pallidotomy Surgery for Parkinson's Disease

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ABSTRACT

Background: The principal type of Parkinsonism that occurs most often is Parkinson's disease [PD]. Pallidotomies decrease stiffness, tremor, and dyskinesias, however bilateral pallidotomies have a higher risk of consequences, including cognitive decline and dysarthrias.

Aim of the Work: The clinical motor results of stereotactic pallidotomy procedures for Parkinson's disease and possible complications.

Patients and Methods: This research, which included 20 patients who received stereotactic unilateral pallidotomies for Parkinson's disease, was carried out in both a retrospective and prospective manner at the Department of Neurosurgery Al-Azhar University Hospitals.

Results: This study demonstrated a comparison of Unified Parkinson's Disease Rating Scale [UPDRS] 3 [motor symptoms]. There was very statistical substantial [p-value < 0.001] decreased UPDRS 3 post-operative [33.0 ± 8.5] and 6 months post-operative [33.3 ± 9.02] when compared with pre-operative UPDRS 3 [45.8 ± 10.4]. As regards Post-Hoc test for multiple comparisons and UPDRS 3, there was very statistical substantial variation [p-value < 0.001] between pre-operative and post-operative UPDRS 3 and 6 months post-operative UPDRS. As regards comparison of activity daily life [ADL] [UPDRS 2], there was statistically substantial [p-value = 0.009], decreased ADL [UPDRS 2] post-operative [25.6 ± 6.02] and 6 months post-operative [24.7 ± 5.5] when compared with pre-operative ADL [UPDRS 2] [31.8 ± 7.7]. As regards Post-Hoc test for multiple comparisons and ADL [UPDRS 2], there was statistically substantial variation [p-value = 0.004] between pre-operative and post-operative ADL [UPDRS 2]. Considering comparison of dyskinesia, there was highly statistical substantial variation [p-value < 0.001] of dyskinesia.

Conclusion: Stereotactic Unilateral pallidotomy for Parkinson's Disease had good effect on improving motor functions assessed by Unified Parkinson's disease rating scale especially the motor functions in follow up after operation with little prevalence of complications.

Keywords: Parkinson's disease; Pallidotomy; Dyskinesia

INTRODUCTION

The majority of Parkinsonism cases seen in clinics are caused by Parkinson's disease [PD], the most prevalent primary or idiopathic type of Parkinsonism. With a frequency of 1% to 2% in persons over 65, it is the second most prevalent neurodegenerative condition after Alzheimer disease [1].

Parkinson's disease is a degenerative condition brought on by the death of nerve cells in the region of the brain that regulates movement, the substantia nigra. These nerve cells pass away or suffer damage, losing their capacity to make dopamine [2].

Although the clinical course and presentation of Parkinson's disease vary, the general natural history is marked by a slow deterioration and increasing impairment. Despite significant progress in medical and surgical care, PD is still an unstoppably progressing condition without a known cause or effective neuroprotective treatments [3].

PD surgery was not often carried out at this period. Due to the growing awareness of the limits of PD drugs and the side effects of L-dopa, interest in the neurosurgical therapy for PD did not return until the late 1980s. This resulted in a rise in lesioning procedures like pallidotomies for Parkinson's disease. Modifications were made to the original Leksell target of pallidal lesions for the treatment of Parkinson's disease [4, 5].

Although thalamotomies are mostly effective, they may have unfavorable outcomes including speech problems or cognitive impairment. Pallidotomies decrease stiffness, tremor, and dyskinesias, however bilateral pallidotomies have a higher risk of consequences, including cognitive decline and dysarthrias [6].

Medications currently available for PD treatment fall into three groups: dopamine enhancers, acetylcholine inhibitors, and drugs for non-motor symptoms [7].

PATIENTS AND METHODS

Study population: This research, which evaluated the results of stereotactic unilateral pallidotomies for Parkinson's disease, was carried out at the Department of Neurosurgery Al-Azhar University Hospitals from 9/2021 to 6/2022.

Methods

Patients complaining of Parkinson`s fulfilling inclusion criteria were offered stereotactic pallidotomy lesioning procedure and all patients who accepted the procedure were included in the study and informed written consent from all patients, we recruited the patients according to the following criteria;

Inclusion criteria: 1] Idiopathic PD. 2] Medically intractable PD [severe response fluctuations, dyskinesias and painful dystonias]. 3] Bradykinesia and rigidity predominant PD.

Exclusion criteria: 1] Refusal to participate in the study. 2] Drug induced parkinsonism. 3] Medically responsive patients. 4] History of alcoholism or drug abuse. 5] Age more than 75 years.

Sample size: 20 patients fulfilling the inclusion criteria and underwent stereotactic unilateral pallidotomy.

Data collection

Full detailed systemic history including [sex, age, occupation, smoking, and co-morbid medical conditions] and Past history of chronic diseases as [Diabetes mellitus, hypertension, chronic kidney or liver disorders, cardiac issues, neurological complaint, prior injuries or procedures, and heart difficulties were all documented] besides, full medication history, onset of the disease and time of diagnosis, compliance on medications and presence of complications of medications such as L-Dopa induced dyskinesia. Full examinations were done, the severity of Parkinson's disease was assessed by video recorded Unified Parkinson`s Disease Rating Score [UPDRS] during off state preoperatively, early postoperative and 6 months postoperative and for dyskinesia we assessed using clinical dyskinesia rating scale from [0-4] assessing the head, face, trunk and the four limbs preoperatively, early postoperative and 6 months postoperative.

Imaging studies: The preoperative radiographic evaluation consisted of 1] CT brain to detect any secondary pathology, skull bone abnormalities and any possible infarctions 2] MRI brain to check for secondary pathology 3]

High-resolution MRI T1 protocol on DICOM format to visualize targets and assess anterior-posterior commissure reference [AC-PC].

Surgical procedure: Before the procedure the next morning, medications ceased at midnight. In order to precisely pinpoint the anterior commissure-posterior commissure plane [AC-PC plane] and identify the globus pallidus, we collected high resolution T1 Brain MRI on a DICOM format the day before surgery. The ZD-RM stereotactic frame was then attached to the patient's head while they were under local anesthetic. After that we fused MRI and CT using brain navigation and localize the target of interest and trajectory by X, Y, Z. From the mid-commissural position, the GPi was aimed at 17–20 mm laterally, 0–3 mm anteriorly, and 0–3 mm inferiorly. The intended target was located right above the optic tract in the posteroventral portion of the GPi. The final targets in both GPi will be determined by intraoperative macrostimulation. Under Local anesthesia, skin incision was done, burr hole was done and the stereotactic electrode was introduced towards the target after confirmatory check with the phantom ring. We used Neuro N50 lesion generator for macrostimulation and lesion production. Regular stimulations at 2 Hz, 2.0 mA, and 50 Hz, 0.4 mA, were employed to prevent any potential invasion of the internal capsule or the optic tract. Through a burr hole 3 cm laterally to the midline and immediately anterior to the coronal suture, the electrode [1.8 mm in diameter, 2-mm uninsulated tip] was inserted toward the estimated target. Lesions were created gradually, adjusting for variations in the major parkinsonian symptoms. The electrode was continuously monitored for motor performance, visual fields, and mental state while being heated sequentially to 45, 50, 60, 70, and 80°C for 30 s. The stimulation and lesion paradigm were then performed when the electrode was inserted 2 mm deeper. Depending on the clinical response of stiffness, tremor, and speed of extremities movements, more lesion extension will be carried out.

Post-operative Imaging: Regular CT scans were performed to confirm the location of the lesion or lead and to rule out bleeding.

Post-operative Evaluation: Preoperative and postoperative medication-free status, UPDRS III and motor sub scores, and medication-free status six months after surgery.

Statistical analysis: Version 24 of the Statistical Program for Social Science [SPSS] was utilized to analyze the data. Quantitative information was presented as mean ±SD. Frequency and percentage were utilized to convey qualitative data. The mean [average] is the middle value in a collection of discrete numbers; it is the sum of values divided by the total number of values. To compare the baseline test results with the results from the immediate postoperative and six-month postoperative periods, paired t tests will be performed. If $p < 0.05$, the analysis' findings will be deemed substantial.

RESULTS

Twenty Parkinson's disease patients participated in our research and underwent stereotactic pallidotomy lesioning. There were 12 male patients [60%] and 8 female patients [40%] in the study's patient population. The average age of all patients in the study was 62.5 ±6.03 years, with a minimum age of 53 and a maximum age of 72. With a minimum age of 7 years and a maximum age of 14, the average duration of all patients in the study was 10.1± 2.1 years. As regard handedness, there were 18 patients [90%] right-handed and 2 patients [5%] left-handed in all studied patients. As regard more affected side, there were 8 patients [40%] right side affected and 12 patients [60%] left side affected in all studied patients as shown in table [1].

In terms of comparison of UPDRS 3 [motor symptoms], there was a statistically significant [P: < 0.001] decreased UPDRS 3 post-operative [33.0 ± 8.5] and 6 months post-operative [33.3 ± 9.02] when compared with pre-operative UPDRS 3 [45.8 ± 10.4]. Regarding comparison of activity daily life [ADL] [UPDRS 2] there was a statistically significant [p-value = 0.009] decreased ADL [UPDRS 2] post-operative [25.6 ± 6.02] and 6 months post-operative [24.7 ± 5.5] when compared with pre-operative ADL [UPDRS 2] [31.8 ± 7.7] as shown in table [2].

As regards Post-Hoc test for multiple comparisons as regard UPDRS 3, there was highly statistical substantial variation [p-value < 0.001] between pre-operative and post-operative UPDRS 3, highly statistical substantial variation [p-value < 0.001] between pre-operative and 6 months post-operative UPDRS 3. No statistical substantial variation [p-value = 0.920] between 3 post-operative and 6 months post-operative

UPDRS 3. Regarding Post-Hoc test for multiple comparisons as regard ADL [UPDRS 2] there was a statistically substantial variation [p-value = 0.004] between pre-operative and post-operative ADL [UPDRS 2]. Statistically substantial variation [p-value = 0.001] between pre-operative and 6 months post-operative ADL [UPDRS 2]. No statistical substantial variation [p-value = 0.662] between post-operative and 6 months post-operative ADL [UPDRS 2] as shown in table [3].

As regards comparison of dyskinesia, there was a highly statistical substantial variation [p-value < 0.001] of dyskinesia in studied patients as shown in table [4]. As regards comparison of dementia rating scale, there was no statistical substantial variation [p-value > 0.05] of dementia rating scale as shown in table [5]. Regarding description of complications, there was 1 patient [5%] with intracranial hemorrhage [ICH] and 1 patient [5%] with transient confusion shown in table [6].

Table [1]: Demographic and clinical data of studied cases

Variables	Total [n=20]	
Age [years]	Mean ± SD Min - Max	62.5 ± 6.03 53 – 72
Sex [n, %]	Males Females	12 [60%] 8 [40%]
Duration of symptoms [years]	Mean ± SD Min - Max	10.1 ± 2.1 7-14
Handedness	Right Left	18 [90%] 2 [10%]
More affected side	Right Left	8 [40%] 12 [60%]

Table [2]: Comparison of UPDRS 3 [motor symptoms] and activity daily life [ADL] [UPDRS 2] in all studied patients

		Follow up [n = 20]			Test	P-value
		Pre-op	**Post-op**	**Post-op 6 months**		
UPDRS 3	Mean ± SD	45.8 ± 10.4	33 ± 8.5	33.3 ± 9.02	KW = 16	**< 0.001**
ADL [UPDRS 2]	Mean ± SD	31.8 ± 7.7	25.6 ± 6.02	24.7 ± 5.5	KW = 9.4	**0.009**

Table [3]: Post-Hoc test for multiple comparisons as regard UPDRS 3 and ADL [UPDRS 2]

		Pre-op vs Post-op	Pre-op vs Post-op 6 months	Post-op vs Post-op 6 months
UPDRS 3	LSD	12.8	12.5	0.3
	p-value	**< 0.001**	**< 0.001**	0.920
UPDRS 2 [ADL]	LSD	6.2	7.1	0.9
	p-value	**0.004**	**< 0.001**	0.662

Table [4]: Comparison of dyskinesia in all studied patient

Dyskinesia	Pre-op	Post-op	Post-op 6 months	Test	P-value
Absent	0 [0%]	2 [10%]	2 [10%]	**X^2 = 34.4**	**< 0.001**
Occasionally	2 [10%]	12 [60%]	8 [40%]		
Frequently	6 [30%]	6 [30%]	10 [50%]		
Mostly	8 [40%]	0 [0%]	0 [0%]		
Always	4 [20%]	0 [0%]	0 [0%]		

Table [5]: Comparison of dementia rating scale in all studied patient

UPDRS 2 [ADL]		Pre-op	Post-op 6 months	Test	P- value
Dementia rating scale	No dementia	14 [70%]	12 [60%]	**X^2 = 0.44**	**0.507**
	Mild dementia	6 [30%]	8 [40%]		

Table [6]: Description of complications in all studied patients

		Studied patients [N = 20]
Complication	ICH	1 [5%]
	Transient confusion	1 [5%]

DISCUSSION

In functional neurosurgery, destructive techniques include stereotactic radiofrequency ablation, radiosurgery [Gamma Knife], and high intensity focused ultrasound [8]. Despite of its non-invasiveness, the radio surgical technique is unsafe and entails complications. The efficacy and safety of unilateral pallidotomy in treatment of motor disorders in PD has been previously recognized by many authors [9].

This study was a retrospective and prospective study that was conducted in the Department of Neurosurgery Al-Azhar University Hospitals to assess the outcome of surgery for Parkinson's. The study included 20 patients with Parkinson's disease underwent stereotactic unilateral pallidotomy.

In our study, the demographic characteristics as regard age, the mean age of all investigated patients was 62.5 ± 6.03 years with minimum age of 53 years and maximum age of 72 years. As regard duration, the mean duration of all studied patients was 10.1 ± 2.1 years with minimum age of 7 years and maximum age of 14 years.

As regard handedness, there were 18 patients [90%] right-handed and 2 patients [5%] left handed in all studied patients. As regard more affected side, there were 8 patients [40%] right side affected and 12 patients [60%] left side affected in all studied patients.

The current study revealed statistically substantial [p-value < 0.001] decreased UPDRS 3 post-operative [33.0 ± 8.5] and 6 months post-operative [33.3 ± 9.02] when compared with pre-operative UPDRS 3 [45.8 ± 10.4]. This is in line with the results of **de Bie *et al.*** [10], and **Valldeoriola *et al.*** [11].

This also agrees with another study by **Yen *et al***. [12] was conducted on PD patients too and revealed statistically substantial decreased UPDR3 postoperatively after 6 months, 1 year and 2 years with p-value=0.028.

The current study found statistically substantial [p-value = 0.009] decreased ADL [UPDRS 2] post-operative [25.6 ± 6.02] and 6 months post-operative [24.7 ± 5.5] when compared with pre-operative ADL [UPDRS 2] [31.8 ± 7.7]. This goes with This goes in run with **Haffenden *et al.*** [13] study which was conducted on 19 patients who underwent unilateral pallidotomy and revealed statistically substantial decreased ADL [UPDRS 2] after 1 year and 2 years follow up after unilateral pallidotomy for PD patients with p-value<0.01.

Lang *et al.* [14] analyzed the results of 11 on evaluation of the efficacy of unilateral pallidotomy and found a substantial improvement of motor functions assessed by UPDRS III and daily activity by UPDRS II.

The current study revealed a statistical substantial variation [p-value < 0.001] of dyskinesia in studied patients. Another study by **Strutt *et al.*** [15] revealed drug induced dyskinesia after unilateral pallidotomy decreased by 68% on contralateral side and 50% on ipsilateral side. In the same study, ipsilateral dyskinesia recurred within a year after surgery.

Another study by **Intemann *et al.*** [16] demonstrated that sustained improvement after treatment of dyskinesia was retained up to 12 years.

Similarly, **Elkazaz *et al.*** [17] conducted a study on 62 PD patients who underwent unilateral pallidotomy and revealed statistically substantial decreased UPDRS after 24 months with p-value <0.05.

The current research reported that there was 1 patient [5%] with small ICH and 1 patient [5%] with transient confusion in the studied patients. Compared to study by **Horisawa *et al.*** [18] which was performed on 69 patients underwent unilateral pallidotomy and revealed 5/69 [7.2%] had hemorrhage as side effects, 3/65 [4.6%] had cerebral infarction, 2/65 [3.07%] had hemiparesis and 1/65 [1.5%] had visual disturbances.

Conclusion

Unilateral pallidotomy for Parkinsonism patients had good effect in improving motor functions assessed by Unified Parkinson's disease rating scale especially the motor functions in follow up after operation with little prevalence of complications including intracranial hemorrhage [only 1 patient] and little confusion [only 1 patient].

Conflict of Interest and Financial Disclosure: None.

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