

Stroke-related erectile dysfunction: Impact of the cerebrovascular stroke site on the degree of erectile dysfunction, total testosterone and prolactin levels

Original
Article

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ABSTRACT

Background: Stroke is one of the major causes of permanent disability and mortality in the aging population worldwide. Reduced libido, and poor erection and ejaculation are among common poststroke sexual dysfunctions, which is due to multiple factors, including both organic and psychosocial factors.

Objective: We designed the study in order to detect the presence of erectile dysfunction (ED) among male patients with stroke using the International Index of Erectile Function (IIEF-5) and correlate the site of the lesion with the degree of ED. Also, we evaluated the serum total testosterone and prolactin levels among those patients and correlated their levels with the degree of ED using IIEF-5.

Patients and Methods: Eighty male patients with ischemic cerebrovascular stroke were included in the study. The patients were diagnosed and divided according to the brain site lesion of cerebrovascular stroke into seven groups. The stroke patients completed the IIEF-5. Serum testosterone and prolactin levels were obtained and compared.

Results: The mean age of the patients was 55.35±3.68 years. ED was detected in 53 patients representing 66.3% with variable degrees of severity (22.5% mild, 6.3% mild to moderate, 7.5% moderate, and 30.0% severe), while 27 (33.8%) patients had no ED. The mean testosterone level was lower than normal in basal ganglion affection and multiple areas affection only, while the mean prolactin level was higher than normal in all groups.

Conclusion: ED is a common problem that may follow cerebrovascular stroke. We do recommend that counseling by a trained professional should be made part of stroke rehabilitation.

Key Words: Cerebrovascular stroke, erectile dysfunction, international index of erectile function-5, prolactin, testosterone.

Received: 17 February 2020, **Accepted:** 09 March 2020.

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ISSN: 2090-6048, September 2019 Vol. 9, No. 3

INTRODUCTION

Stroke is thought to be one of the major causes of permanent disability (paralysis, aphasia, or dysphasia) and mortality in the aging population worldwide^[1]. It is the third leading cause of death (after heart disease and cancer) with an incidence of 5.5 million persons/year^[2].

In 1988, the WHO Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) Project defined stroke as a syndrome with symptoms of focal or global disturbance affecting brain function, for at least 24h, which may lead to death in less than 24h, with no apparent cause other than of vascular origin^[3].

Irreversible brain insult occurs as a result of hypoxic or ischemic damage to the brain, which was mediated through multiple factors such as apoptosis, inflammation, oxidative damage, neuronal death, and others^[4].

Reduced sex drive (libido), and poor erection and ejaculation are among common poststroke sexual dysfunctions, due to multiple factors, including both organic (lesion localization, premorbid medical conditions, and medications) and psychosocial (fear, low self-esteem, anxiety, and depression) factors^[5].

Diabetes mellitus, arterial hypertension, cigarette smoking, and dyslipidemia, which are the main risk factors for erectile dysfunction (ED), are also considered to be the main risk factors for cerebrovascular stroke, especially in developed countries^[6,7]. They exert their damaging effect through promoting arteriosclerotic changes with its subsequent dysfunction on the endothelium of the erectile penile tissue, which in turn leads to impairment of the vasodilation within the erectile penile tissue and accounts for vasculogenic ED^[8].

We designed the study on patients with cerebrovascular

stroke in order to detect the presence of ED and its degree and to correlate the location of brain injury to the degree of ED. We also analyzed the relationship between the levels of both testosterone and prolactin and both the degree of ED and the site of brain affection.

PATIENTS AND METHODS

The study was a prospective hospital-based cross-sectional study which was performed at the Department of Dermatology, Venerology and Andrology, in collaboration with the Department of Neuropsychiatry, Assiut, Egypt, during the period from April 2017 to May 2018. We included all male patients with different types of ischemic cerebrovascular stroke who had attended the Neuropsychiatry Department during that period. Eighty male patients were included in the study. The concept of the study was explained to all participants and a written informed consent was obtained from each patient. The study protocol was approved by the Assiut Medical School Ethics Review Board (Ethics Committee N:IRB 17100862).

We excluded patients older than 70 years, patients on phosphodiesterase type 5-inhibitors or any other drugs modifying erectile function, patients with systemic diseases (diabetes mellitus, chronic liver, and kidney diseases), patients with hypogonadism, and patients having communication problems (severe aphasia, dementia, or dysarthria) due to their inability to be interviewed.

After complete medical history and meticulous clinical examination, complete neurological examination by an expert neurologist, the stroke location was determined by either cranial computed tomography or MRI. All patients were subdivided into seven subgroups (from A to G) according to the affected brain site.

Each patient was asked to complete the Arabic version of The International Index of Erectile Function (IIEF-5) for assessment of male sexual function. The IIEF-5 addresses the five domains of sexual functions (erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction). The IIEF-5 score is the sum of the responses to the five items; thus, the score ranges between 5 and 25 as follows: 5–7 (severe ED), 8–11 (moderate ED), 12–16 (mild to moderate ED), 17–21 (mild ED), and 22–25 (no ED).

Venous blood samples were obtained early morning from all patients to measure total testosterone levels by enzyme-linked immunosorbent assay using Thermo Scientific Multiskan FC kits (Finland, Vantaa). Normal value ranges from 2.50 to 11.00 ng/ml. Also, prolactin levels were measured by enzyme-linked immunosorbent assay using Thermo Scientific Multiskan FC kits (Finland). Normal value ranges from 4.04 to 15.20 ng/ml.

Statistical analysis

Analysis of the data was performed using the Statistical Program for the Social Sciences (SPSS.18.0, SPSS Inc., Chicago, Illinois, USA) software program. Quantitative data were expressed as mean \pm SD. Qualitative data were expressed as frequency and percentage. Independent samples *t* test of significance was used when comparing between two means. Pearson's correlation coefficient (*r*) test was used for correlating data, and one-way analysis of variance when comparing between more than two means. A *P* value of less than 0.05 was considered statistically significant. *P* value less than 0.001 was considered as highly significant, while *P* value more than 0.05 was considered insignificant.

RESULTS

Our study included 80 male patients with ischemic cerebrovascular stroke. The mean age of the stroke patients was 55.35 ± 3.68 years and the mean duration of stroke in them was 12.72 ± 4.85 months. The patients were subdivided into seven subgroups according to the affected brain site (Table 1) as follows:

Group A included 17 patients with middle cerebral artery (MCA) affection. The mean age of those patients is 55.71 ± 3.37 years and the mean duration of stroke is 18.24 ± 7.27 months. The mean testosterone is 4.45 ± 4.43 ng/ml and the mean prolactin is 20.48 ± 13.06 ng/ml.

Group B included 13 patients with posterior cerebral artery (PCA) affection. The mean age of those patients is 56.23 ± 3.77 years and the mean duration of stroke is 13.59 ± 5.88 months. The mean testosterone is 4.26 ± 3.73 ng/ml and the mean prolactin is 20.04 ± 13.07 ng/ml.

Group C included 12 patients with anterior cerebral artery (ACA) affection. The mean age of those patients is 55.58 ± 3.58 years and the mean duration of stroke is 11.06 ± 5.71 months. The mean testosterone is 4.23 ± 3.67 ng/ml and the mean prolactin is 20.03 ± 11.40 ng/ml.

Group D included 11 patients with brain stem affection. The mean age of those patients is 54.00 ± 2.72 years and the mean duration of stroke is 12.58 ± 4.73 months. The mean testosterone is 3.44 ± 3.96 ng/ml and the mean prolactin is 21.17 ± 13.19 ng/ml.

Group E included 10 patients with cerebellum affection. The mean age of those patients is 52.90 ± 2.47 years and the mean duration of stroke is 10.44 ± 3.42 months. The mean testosterone is 4.75 ± 3.55 ng/ml and the mean prolactin is 16.82 ± 12.10 ng/ml.

Group F included nine patients with basal ganglion affection. The mean age of those patients is 53.44 ± 3.91 years and the mean duration of stroke is 9.81 ± 4.56 months. The mean testosterone is 2.06 ± 2.85 ng/ml and the mean prolactin is 28.37 ± 13.20 ng/ml.

Group G included eight patients with multiple areas affection. The mean age of those patients is 60.00 ± 2.07 years and the mean duration of stroke is 16.55 ± 6.80 months. The mean testosterone is 0.64 ± 0.28 ng/ml and the mean prolactin is 44.79 ± 2.01 ng/ml.

Table 1: Descriptive data of all patients with cerebrovascular stroke.

Groups	Brain site	No. (N=80) [n(%)]	Age (years)	Duration (months)
Group A	MCA	17 (21.3)	55.71 ± 3.37	18.24 ± 7.27
Group B	PCA	13 (16.3)	56.23 ± 3.77	13.59 ± 5.88
Group C	ACA	12 (15.0)	55.58 ± 3.58	11.06 ± 5.71
Group D	Brain stem	11 (13.8)	54.00 ± 2.72	12.58 ± 4.73
Group E	Cerebellum	10 (12.5)	52.90 ± 2.47	10.44 ± 3.42
Group F	Basal ganglion	9 (11.3)	53.44 ± 3.91	9.81 ± 4.56
Group G	Multiple lesions	8 (10.0)	60.00 ± 2.07	16.55 ± 6.80

ACA, anterior cerebral artery; MCA, middle cerebral artery; PCA, posterior cerebral artery.

The scores of the IIEF-5 questionnaire showed that 53 (66.3%) patients had ED with varying severity (22.5% mild, 6.3% mild to moderate, 7.5% moderate, and 30.0% severe), while no evidence of ED was detected in 27 (33.8%) patients. The scores of the IIEF-5 questionnaire in all groups is presented in Table 2, Fig.1.

A comparison between the IIEF-5 in all stroke patients was performed; and revealed a statistically significant difference between the IIEF-5 score in each group (Table 3).

Regarding endocrinal evaluation of all patients, measurement of total testosterone level showed that the mean testosterone level in stroke groups was 3.64 ± 3.72 ng/ml (Table 4), while that of serum prolactin

levels was 23.30 ± 14.00 ng/ml (Table 5).

Correlation analysis of the IIEF-5 score with the age of patients, serum testosterone, and prolactin levels showed that there was statistically significant positive correlation between IIEF-5 score and serum testosterone, while significant negative correlation between IIEF-5 score and both age and serum prolactin (Table 6).

Another correlation analysis was performed between age with serum testosterone and prolactin levels, and showed that there was statistically significant negative correlation is present between age and serum testosterone ($r = -0.414$, $P = 0.000$), while statistically significant positive correlation between age and serum prolactin ($r = 0.511$, $P = 0.000$).

Table 2: The International Index of Erectile Function-5 scores in all patient groups

Groups	Group A (N=17) [n (%)]	Group B (N=13) [n (%)]	Group C (N=12) [n (%)]	Group D (N=11) [n (%)]	Group E (N=10) [n (%)]	Group F (N=9) [n (%)]	Group G (N=8) [n (%)]	Total (N=80) [n (%)]
IIEF-5								
No ED	7 (41.2)	5 (38.5)	5 (41.7)	4 (36.4)	5 (50.0)	1 (11.1)	0	27 (33.8)
Mild	3 (17.6)	4 (30.8)	3 (25.0)	2 (18.2)	3 (30.0)	3 (33.3)	0	18 (22.5)
Mild to moderate	0	1 (7.7)	1 (8.3)	1 (9.1)	1 (10.0)	1 (11.1)	0	5 (6.3)
Moderate	1 (5.9)	2 (15.4)	1 (8.3)	2 (18.2)	0	0	0	6 (7.5)
Severe	6 (35.3)	1 (7.7)	2 (16.7)	2 (18.2)	1 (10.0)	4 (44.4)	8 (100.0)	24 (30.0)

IIEF-5, The International Index of Erectile Function.

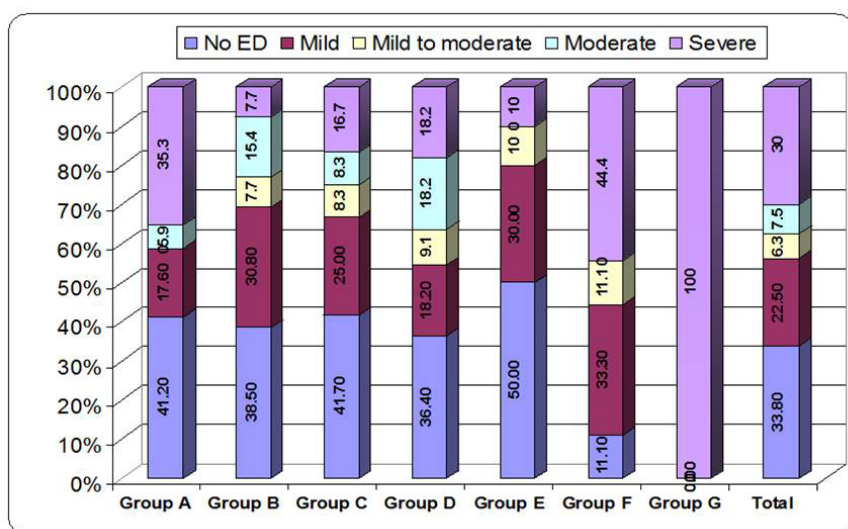


Fig. 1: Distribution of ED percentage inpatients with stroke.ED, erectile dysfunction.

Table 3: Comparison between the mean, median, and range of International Index of Erectile Function-5 in all patient groups.

IIEF-5	Brain Site							P value
	Group A	Group B	Group C	Group D	Group E	Group F	Group G	
Mean ±SD	15.5±8.2	17.2±6.4	16.9±6.5	15.7±7.2	18.6±5.6	13.0±7.2	6.4±0.7	0.037
Median (range)	19 (5–25)	18(5–24)	19.5(6–23)	17(5–24)	20(5–24)	13(5–23)	6.5(5–7)	

Comparison between the IIEF-5 in all patient groups.
 IIEF-5, International Index of Erectile Function.
 Statistically significant difference ($P < 0.05$) Kruskal–Wallis test

Table 4: Serum total testosterone level in all patient groups

Groups	Testosterone (ng/ml)
Total patients	3.64±3.72
Group A	4.45±4.43
Group B	4.26±3.73
Group C	4.23±3.67
Group D	3.44±3.96
Group E	4.75±3.55
Group F	2.06±2.85
Group G	0.64±0.28
P value	0.030

Data are expressed in the form of mean ±SD.

Table 5: Serum prolactin level in all patient groups

Groups	Prolactin (ng/ml)
Total patients	23.30±14.00
Group A	20.48±13.06
Group B	20.04±13.07
Group C	20.03±11.40
Group D	21.17±13.19
Group E	16.82±12.10
Group F	28.37±13.20
Group G	44.79±2.01
P value	0.001

Data are expressed in the form of mean±SD.

Table 6: Correlation of The International Index of Erectile Function-5) with age, testosterone level, and prolactin levels.

Variables	IIEF-5	
	r value	P value
Age	-0.474	0.001
Testosterone level	0.962	0.003
Prolactin level	-0.920	0.002

IIEF-5, International Index of Erectile Function.

DISCUSSION

Various types of disabilities are known to occur following cerebrovascular stroke, which include physical problems such as walking difficulties, aphasia, etc. and psychological problems such as depression, low self-esteem, etc., which in turn negatively affect the overall daily activities, including sexual activity^[9,10]. A plenty of studies and reviews have proven that sexual function is disturbed in poststroke patients^[9,11-14]; however, few studies have assessed and correlated hormonal profile in those patients.

During the last century, Monga *et al.*^[15], and Korpelainen *et al.*^[16] reported ED in 62 and 75% of post-stroke patients, respectively. Then, during the current century, Kimura *et al.*^[9] reported ED in 58.6% of male stroke patients, followed by Bener *et al.*^[11] who reported ED in 48.3% of male stroke patients, lastly, Koehn *et al.*^[7] reported ED in 78.9% of stroke patients.

In our study, we included 80 patients with stroke patients, the mean age of them was 55.35±3.68 years. A similar study by Purwata *et al.*^[17], who included 74 stroke patients with stroke. They found that the mean age of poststroke patients sampled was 52.19±4.37 years. Also, the study conducted by Akinpelu *et al.*^[18] found that the mean age of poststroke patients sampled was 59.4±9.49 years.

In our study, we found that among 80 patients with stroke, 53 (66.3%) patients suffered from ED with different grades of severity. According to the result of IIEF-5, the grades of severity were as follows: 24 (30.0%) patients had severe degree of ED, six (7.5%) patients had moderate degree of ED, five (6.3%) patients had mild-to-moderate degree of ED, and 18 (22.5%) patients had mild degree of ED. These results were in accordance to the results of Koehn *et al.*^[7] who found that 20 (35.1%) patients had severe degree of ED; four (7%) patients had moderate ED; four (7%) patients had mild-to-moderate degree of ED; and 17 (29.8%) patients had mild degree of ED.

Studies explained the occurrence of poststroke ED on the basis of disruption of central autonomic nerves and

tracts^[10]; physical impairments such as motor weakness, spasticity, bladder, or bowel dysfunction^[19]; psychological factors such as depression^[16], and lack of self-confidence and self-esteem^[20].

In our study, we divided all patients into seven groups (A–G) according to the site of the brain injury; we found that affection of the MCA is the most common type of injury, followed by PCA, ACA, brain stem, cerebellum, basal ganglia, and lastly multiple areas affection was the least common type. Koehn *et al.*^[7] also found that MCA affection is the most common type of brain injury, followed by PCA, ACA, brain stem, cerebellar, basal ganglia, and lastly multiple areas affection.

Regarding the percentage of ED in all seven groups, it was as follows: 58.8, 61.5, 58.3, 63.7, 50, 88.9, and 100% for group A, B, C, D, E, F, and G, respectively, in our study, while in the study performed by Koehn *et al.*^[7] it was as follows: 78.8, 80.0, 100, 100, 80, 40, and 100 for patients with MCA, PCA, ACA, basal ganglia infarction, brain stem infarction, cerebellar and multiple area affection, respectively.

The medial and the inferior frontal lobes, which are both supplied by the MCA, are among the cortical areas contributing to erection^[21], so ischemia affecting these MCA-supplied autonomic structures will affect the erectile function, thus explaining the high prevalence of ED in our patients with MCA stroke.

As normal erection depends on contribution from ACA-supplied centers (as the anterior cingulate gyrus, the nucleus accumbens, the fornix, and the medial preoptic area and paraventricular nuclei of the hypothalamus), we found that 58.3% of patients with ACA affection develop ED^[21].

Regarding patients with PCA affection, ED was detected in 61.5% of them. This occurs due to deterioration of the functions of the thalamic nuclei, the midbrain ventral tegmental area, substantia nigra, and afferent and efferent structures, which mediate arousal and erection^[21].

In our study and in patients with brain stem affection, ED was present in 63.7% of patients. This occurs due to interruption of signals that travel from the genital areas

through the brain stem toward supraspinal areas that control male sexual behavior.

Regarding patients with multiple area affection, our study results confirmed the presence of ED, which was detected in all patients, and this was in accordance with the results of Jea-Hun *et al.*^[22] who claimed that patients with multiple brain lesions had a significant decrease in ED compared with patients with one lesion.

Regarding the IIEF-5 score, we found a significant negative correlation between the IIEF-5 score and the age of patients, which means that ED prevalence increases with increasing patient age. This is in agreement with Koehn *et al.*^[7] who established a negative correlation between age and IIEF-5 score in stroke patients.

The mean level of total testosterone blood samples taken from stroke patients was lower than normal in group F and group G basal ganglion affection and multiple areas affection only, while the mean prolactin level was higher than normal in all groups. This was in contrast with Reshmi *et al.*^[23] who found that there was no association between endogenous testosterone and incident clinical stroke or ischemic brain changes in men.

The mean level of serum prolactin blood samples taken from the stroke patients was higher than normal ranges in all groups. This is in agreement with Fikri *et al.*^[24] and Sankalp *et al.*^[25], who found 'that men with stroke had higher serum prolactin levels than age-matched men without stroke.'

Raaz *et al.*^[26] suggested that prolactin contributes to the pathophysiology of ischemic cerebrovascular event through increasing activation of platelets.

CONCLUSION

We conclude that ED is a common complication that may follow cerebrovascular stroke, especially in patients with multiple areas affection. The presence of ED increases with increasing age, and multiplicity of brain lesions in poststroke patients and high prolactin level. Serum testosterone level decreases with the advancement of age and multiplicity of brain lesions.

We do recommend that counseling by an expert physician in that field should be a part of rehabilitation of poststroke patients.

CONFLICT OF INTEREST

There are no conflicts of interest.

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