

EFFECT OF MODIFIABLE AND NON-MODIFIABLE RISK FACTORS AS PREDICTORS OF FUNCTIONAL OUTCOME OF STROKE REHABILITATION

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KEY WORDS: *RISK FACTORS IN STROKE, FUNCTIONAL OUTCOME OF STROKE.*

ABSTRACT

Hypothesis: *The old myth that the survival of patients with complete stroke is not sufficiently long enough to justify the great expenses and efforts of rehabilitation has been disproved by recent studies which show that at least 50 percent of the survivors lived for 7.5 years or longer. The risk factors may act as stroke outcome predictors and hence determine the intensity and type of rehabilitation program.*

Objective: *To investigate the stroke outcome predictors that will define groups of patients with maximal or minimal benefit from rehabilitation of stroke.*

Methodology: *This prospective study included 115 Ischemic stroke patients attending the Department of Rheumatology and Rehabilitation, Zagazig University Hospitals, Zagazig Health Insurance Hospital and Zagazig Rehabilitation Centre, Ministry of Social Affairs, Egypt during 2005-2006. All the patients were subjected to full history and clinical examination and routine investigations. We analyzed the influence of modifiable risk factors: diabetes mellitus (DM), hypertension (HTN), ischemic heart disease (IHD) and the duration before rehabilitation and non modifiable factors; age, sex and side of lesion on stroke outcome. All patients received regular rehabilitation and an evaluation at enrolling and*

discharge, using the modified Barthel Index. The study lasted for 9 months duration.

Results: Our results after statistical analysis showed that patients with ischemic heart disease (IHD) showed the greatest improvement after 4 months of rehabilitation. The group of patients without risk co-morbid factor followed and then patients with hypertension (HTN), patients with diabetes mellitus, patients with combined DM and HTN and patients with combined HTN and ischemic heart disease IHD. The group of patients known to have HTN, DM and IHD combined did not show significant improvement. The non modifiable risk factors age, sex and site of cerebrovascular lesion did not show any significant difference although younger patients showed better improvement without significant difference.

Conclusion: Modifiable risk factors have a strong effect as predictors of functional outcome at rehabilitation. Patients with more than 2 risk factors as well as late entry for rehabilitation may have bad prognosis.

INTRODUCTION

Stroke is the third leading cause of death and the leading cause of long-term disability in all world countries, and one of the biggest economical burdens on public health. In United States, there are approximately 4 millions patients living with sequelae of stroke.

In Europe the annual incidence of stroke including first and recurrent stroke varies from 150-280 case per 100.000. One third of stroke patients are younger, and two thirds older than 65 years age ⁽¹⁾. According to the American National Stroke Association: 10% of stroke survivors recover almost completely, 25% recover with minor impairment, 40% experience moderate to sever impairments that require special care, 10% require care in a nursing home or long-term facility, 15% die shortly after the stroke and approximately 14% of stroke survivors experience a second stroke in the first few years following a stroke ⁽²⁾.

Stroke is a well known serious condition that affects brain function, with diminution of physical and mental capacity, but there is a big variation of the extent of affection in each individual ⁽³⁾. The goal of rehabilitation is to enable an individual who has experienced a stroke to the highest possible level of independence and be as productive as possible. According to the American National Stroke Association, successful rehabilitation depends

on: amount of brain damage, skill on the part of the rehabilitation team, cooperation of family and friends. Caring family/friends can be one of the most important factors in rehabilitation and timing of rehabilitation, the earlier it begins, the more likely the restoration of abilities and skills.

PATIENTS AND METHODS

One hundred and fifteen stable stroke patients were included in this prospective study; they were 92 males and 23 females. The ages range were (27-73) with mean (52.3±4.5). The patients with transient ischemic attack (a focal neurological deficit that last few minutes to 24 hours) were excluded, as well as the patients with a reversible ischemic neurological deficit (a focal neurological deficit. The patients involved in this study were referred to the Rheumatology and Rehabilitation Department, College of Medicine, Zagazig University and to Zagazig Rehabilitation Centre, from the Internal Medicine and Neurology Departments.

The patients included in this study were diagnosed as cerebral thrombosis with hemiparesis (first ever stroke and first rehabilitation course for stroke). According to the defined protocol, those diagnosed as cardiac embolism, hemorrhage, tumor, subdural hematoma, brain abscess and trauma as an etiological factor of hemiplegia were excluded. Diagnosis of cerebral infarction was based on clinical history and CT scan of the brain.

All the patients were examined thoroughly after full clinical history and routine laboratory investigations. Criteria for the patient's enrollment in the study were: absence of signs of further progression of neurological deficit, level of consciousness and orientation that keep good communication and direction, retained short term memory to remember and apply what was learned the day before.

The protocol for this study did not differ from the common protocol used in physical medicine and rehabilitation routine clinical practice including physiotherapy, occupational therapy for daily activities training. In addition psychological and social support was added to the patients by organized meeting to the patients and their families. Speech therapy was included in the presence of speech deficit by referral to the speech language pathologist. Simple assistance appliances as ankle foot orthoses walking cane or sticks were prescribed to the patients in need to it. Rehabilitation treatment was scheduled 3 days per week besides home program daily. Reevaluation of the program was made at the end of the week and the patients were evaluated at the beginning and at the end of 9 months of

rehabilitation program using a modified Barthel Index (MBI) ⁽⁵⁾ as shown in table (1).

Table (1): The modified Barthel Index (MBI).

Activities of daily living function	Independent I Intact	Dependent		
		II Limited	III Helper	IV Nil
Drink from cup/eat from dish	10	5	1	0
Dress upper body	5	5	3	0
Dress lower body	5	5	2	0
Done brace or prosthesis	0	0	2	0
grooming	5	5	0	0
Wash or both	4	4	0	0
Bladder incontinence	10	10	5	0
Bowel incontinence	10	10	5	0
Care of perineum/ clothing at toilet	4	4	2	0
Transfer chair	15	15	7	0
Transfer toilet	6	5	3	0
Transfer tub or shower	1	1	0	0
Walk on level 50 yards or more	15	15	10	0
Up and down stairs for one flight or more	10	10	5	0
Wheel chair/ 50 yards only if walking	15	5	0	0

Statistical analysis:

The results were analyzed by a statistician using. The SPSS Statistical Package and Analysis of Variance (ANOVA) test for age, co-morbid diseases and *t*-test for of side of stroke and sex of the patient's relation to rehabilitation outcome.

RESULTS

The age ranged between 27-73 years with a mean age (52.3±4.5) years. Table (2) shows the clinical characteristic of the patients including age, sex and co-morbid risk diseases, rehabilitation predictor's outcome and modified Barthel Index mean improvements scores (MIS).

Age as a predictor factor:

Our results showed that patients with younger age group showed better response to rehabilitation specially in group (24-45y.) but there was no significant difference $P = 0.031$ (Table 3).

Disease duration before rehabilitation:

There was a significant difference between disease duration before starting rehabilitation and the functional outcome. The improvement was better in group with disease duration $>6m$, $p < 0.05$ (Tables 2 and 3).

Table (2): Shows patient's clinical characteristics and risk factors.

Predictor	Patients				SD
	Group	No.	%	MIS (mean)	
Age (years)	27-45	24	(20.8)	46.35	25.91
	46-65	63	(54.8)	37.2	26.06
	66-75	28	(24.3)	28.8	25.2
Total		115			
Sex	Male	92	(80)	37.8	27.5
	Female	23	(20)	35.9	27.2
Side of stroke	Right	56	(48.6)	34.8	26.8
	Left	59	(51.4)	33.9	26.6
Duration before rehabilitation/ months	<6m.	62	54	44.32	13.21
	6-9m.	28	24.3	40.1	12.1
	>9m.	25	21.7	29.2	8.9
Co-morbid risk factors	DM	21	18.3	34.2	19.5
	IHD	10	8.7	65	38.2
	HTN	35	30.4	38.2	29.4
	DM+HTN	20	17.4	22.9	23.2
	DM+IHD	8	6.9	18.3	24.8
	HTN+IHD	8	6.9	22.1	23.7
	DM+HTN+IHD	7	6	0	0
	No co-morbid diseases	6	5.2	44.2	26.2

DM = diabetes mellitus, IHD = Ischemic heart disease.

HTN= hypertension, MIS: mean improvement score.

SD: standard deviation.

Co-morbidity risk factors:

Our results showed that co-morbid risk factors showed significant burden on rehabilitation outcome $p < 0.005$ (Table 3).

The group of ischemic heart diseases and those without any co-morbid disease showed the highest scores of improvement after rehabilitation followed by hypertension group patients, diabetes, mellitus, the combined hypertension and diabetes mellitus and the group of ischemic heart disease and hypertension. The group of 3 co morbid risk factor did not show improvement.

Table (3): Analysis of variance (ANOVA) for the predictors, age, duration, of disease and the co morbid risk factors.

Factor	Source	Sum of square	Mean square	F-ratio	p-value
Age	Between groups	1504.524	753.248	0.962	0.39
	Within groups	84664.262	784.824		
Duration before rehabilitation	Between groups	803.264	18.816	2.024	<0.05
	Within groups	2525.26	798.402		
Co-morbidity risk factors	Between groups	15088.188	2026.284	2.856	<0.001
	Within group	6209.384	898.678		

Table (4): Analysis of t-test for the side of the stroke and sex of the patients.

Factor	No	Mean improvement score (MIS)	SD	T-value
Side of stroke:				
Rt side	56	34.8	26.8	0.30
Lt side	59	33.9	26.6	
Sex:				
Males	92	37.8	27.5	0.62
Females	23	35.9	27.2	

DISCUSSION

Stroke is one of the most common cause of morbidity and mortality and the leading cause of long term disability in the community⁽¹⁾. The goal of rehabilitation is to enable an individual who has experienced a stroke to get the highest level of independence and to be as a productive as possible. The advent of new promising therapies for acute ischemic stroke led to higher expectations for rapid recovery and good outcome. Nevertheless, poor outcome may prevail because ischemic stroke is a heterogeneous disease and many factors may influence its rehabilitation outcome^(1, 6 and 7).

In health and medicine field, there is an emphasis on the role of prophylaxis in such diseases which result in a catastrophic functional disability and its management is difficult and needs a group of different specialties to deal with and its outcome is usually disappointing with high cost. In this study we studied the risk factors modifiable and the non modifiable to estimate if stroke outcome can be modifiably improved through management of the modifiable risk factors or at least controlling these risk factors.

Until recently, proposals suggested that modifiable and non modifiable risk factors can act as predictors of stroke outcome and hence can determine the importance to identify the impact of risk factors on functional outcome before embracing a system that limits access to rehabilitations because of such factors. Among the non modifiable risk factor, we studied the age, sex and side of stroke, right or left and among the modifiable risk (co-morbid medical diseases) factors, hypertension, diabetes mellitus, ischemic heart disease and the time passed starting before rehabilitation.

The results of our study showed that the non modifiable risk factors; age, sex and the side of the lesion has no significant effect on functional outcome of stroke rehabilitation although, the younger patients showed better response to rehabilitation compared to the older patients. Recent studies are in disagreement to the results of our study and concluded that older patients had a poor outcome^(8, 9). However we can not separate the poor outcome of rehabilitation due to advanced age from co-morbidities, and the initial severity of stroke and age are the most powerful predictors of functional recovery.

Discrepancies between various studies that associate age with outcome might be to the correlation between age and co-morbidities⁽¹⁰⁾. For example, we can associate a history of diabetes or ischemic heart disease with poor outcome, the impact of which is increased with old age. Although age greater than 65 years has a significant negative effect on hospital discharge, it may not be an independent predictor factor of functional recovery. In our study although younger patients showed a small trend to better outcome, the age variable did not reach statistical significance as we could not separate age from other co-morbidities and this coincide with results of *Bagg et al.*⁽¹⁰⁾.

Our results also showed that there is a significant correlation between duration of disease before starting the rehabilitation program and the functional outcome, the early entry into rehabilitation, the better

outcome, this can be explained by that early rehabilitation minimize bed immobility complications, prevent joint contracture, improve sensory input to enhance CNS integrity.

The importance of gender in predicting stroke outcome is conflicting and less apparent. Animal studies suggest that the outcome is dependent on gender⁽⁸⁾. This might be a result of estrogen that seems to mediate improvement in outcome after ischemic brain injury. Several human studies associated males with a poorer outcome.¹⁰ Contrary to mentioned results, the study performed in Sweden showed that after 3 months, more women were physically and mentally impaired, and dependent on other persons. However, case fatality ratios during the first 3 months were similar in men and women¹¹. In another study, *Jaume et al.*⁽¹²⁾ found that women more often suffered aphasic disorders, visual field disturbances and dysphagia. Our study showed no significant difference in rehabilitation outcome between male and female patients.

Research on the influence of lesion side on functional outcome has yielded contradictory results. Recent literature reviews suggest that the hemisphere of stroke does not predict outcome, which is consistent with our results. However, *Tur et al.*⁽¹⁵⁾ found that patients with aphasia and depression had a lower Functional Independence Measures (FIM) score. If we consider aphasia as a consequence of left hemisphere lesion, we can conclude that this location is a less favorable prognostic factor. On the other side, *Laufer et al.*⁽¹⁶⁾ found that functional ability and balance control are equally affected in both right and left hemisphere lesions.

The existence of co-morbid disorders such as DM, HTN or IHD has been associated with poorer outcome after stroke⁽⁸⁾. Ischemic heart disease was a prominent predictor of survival in multiple studies⁽³⁾.

In our study, the group of patients suffering from multiple disorders such as DM, HTN and IHD did not show any signs of improvement during and after, rehabilitation. Those with single medical conditions, such as IHD showed the best improvement. Only 10 (8.7%) patients represented this group in our study and as a consequence, the samples of patients with combined DM and IHD, combined HTN and IHD, and combined DM, HTN and IHD, were also relatively small. Nonetheless, the groups of patients with HTN and DM were well represented in the study and showed improvement after rehabilitation. Statistical analysis between and within the various groups with co-morbid disorders was highly significant.

However, there are limitations to our study including the relatively small sample size and short duration. We need further research on bigger samples to draw conclusions that are more valid.

Conclusion:

Ischemic stroke is a heterogeneous disease. We found that many factors influence rehabilitation outcome. Our study confirmed that in patients with ischemic stroke, non-modifiable risk factors like age, gender and the side of lesion (right or left) do not play a significant role in functional outcome, except that the younger group of patients showed a tendency for better improvement. The results in some studies were inconsistent with our findings, probably due to differences in the tested samples and methodology.

However, most of the studies are consistent with our results. Regarding modifiable risk factors such as DM, HTN and IHD, we found that patients with IHD showed the greatest improvement after the rehabilitation program. The HTN, DM, combined DM and HTN and combined HTN and IHD groups followed this. Those suffering from multiple diseases such as DM, HTN and IHD did not show improvement. Although it cannot reverse the neurological deficits, rehabilitation plays a significant role in functional recovery and improvement of quality of life in stroke patients.

Clinicians should be aware of the importance of different factors on rehabilitation outcome of ischemic stroke. It will offer not only realistic expectations to stroke patients and their families, but also contribute to the development of adequate rehabilitation strategies and improve cost effectiveness. It will also support important decisions that we should contemplate and greatly enrich our understanding of ischemic stroke and its treatment. However, due to the ethical concerns, we should give each patient the chance to undergo rehabilitation, regardless of his or her age, sex, side of infarction and co-morbid disorders. Nevertheless, we should document well these clinical attributes.

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تأثير العوامل القابلة للتعديل وغير القابلة للتعديل من عوامل الخطر كعوامل تنبؤ للنتائج الوظيفية عند تأهيل مرضى الجلطات الدماغية

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الهدف من البحث: دراسة العوامل القابلة للتعديل وغير القابلة للتعديل من عوامل الخطر لحدوث الجلطات وتأثيرها على النتائج الوظيفية عند تأهيل مرضى الجلطات الدماغية.

المرضى والبحث: أجري هذا البحث على 115 مريضاً بالجلطات الدماغية من الحالات المستقرة طبياً والذين كانوا يرتدون أقسام التأهيل بمستشفيات جامعة الزقازيق ومستشفى التأمين الصحي ومركز التأهيل الاجتماعي بالزقازيق. وتم فحص هؤلاء المرضى بعد أخذ التاريخ الطبي للمرضى جيداً وتم عمل الفحوصات الروتينية المطلوبة للمرضى وكذلك تحويلهم إلى الأقسام الطبية المختلفة لإستكمال تأهيلهم. تم تقييم عوامل الخطر القابلة للتعديل وهي: مرض السكر، وارتفاع ضغط الدم، ومرض نقص تروية القلب وكذلك العوامل الغير قابلة للتعديل من عوامل الخطر وهي العمر والجنس ومكان حدوث الجلطة (يمنى او يسرى).

وقد تم وضع برنامج التأهيل الطبي الملائم لمثل هذه الحالات وذلك لمدة 9 أشهر وتم تقييم الحالات قبل وبعد إنتهاء البرنامج مستخدمين المؤشر المعدل لبارثل.

النتائج: أظهرت النتائج بعد تحليلها إحصائياً أن مرض نقص التروية القلبية كانوا هم الأفضل في التحسن بعد برنامج التأهيل فقد تحسنا بصورة ملحوظة بعد 4 أشهر من بداية البرنامج وقد تلا ذلك مجموعة المرضى بدون أي عوامل للخطر ثم تبعهم مرضى ارتفاع ضغط الدم ثم مرضى السكر ثم بعد ذلك مجموعة مرضى ضغط الدم مع مرضى السكر (عاملين) ثم مرضى نقص تروية القلب مع ارتفاع ضغط الدم (عاملين) أما المرضى الذين كلن لديهم 3 عوامل (ضغط الدم والسكر ونقص تروية القلب) فلم يطرأ عليهم ملحوظ بعد نهاية البرنامج.

بالنسبة للعوامل الغير قابلة للتعديل فلم يلحظ لها تأثير قوي مفيد إحصائياً غير أنه لوحظ أن المرضى صغار السن كانوا أفضل النتائج من كبار السن غير أن عددهم الصغير نسبياً ربما أدى إلى هذه النتيجة غير المقيدة إحصائياً أو ربما يكون للعمر تأثير آخر غير مباشر وذلك بزيادة العوامل الأخرى من عوامل الخطر.

الإستنتاج: عوامل الخطر القابلة للتعديل هامة في التأثير على نتائج التأهيل لمرضى الجلطات الدماغية حيث يمكن الحصول على نتائج أفضل لو تم السيطرة أو تعديل هذه العوامل وكذلك يمكن القول بأنه كلما زادت عدد عوامل الخطر عند المريض كلما ساء النتائج الوظيفية، وفي حالة وجود أكثر من عاملين من هذه العوامل ربما لا يحدث أي تحسن وظيفي للمريض.