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ORIGINAL ARTICLE **ÖZGÜN ARAŞTIRMA**

"FISHER PREVENTABLE STROKE SCORE" VERSUS "LIFE'S SIMPLE 7":

AN ANKARA ACROSS SUBGROUP STUDY

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ABSTRACT

INTRODUCTION: Modifiable risk factors constitute approximately 90% of the cumulative risk factor burden in stroke. One out of 4 strokes were preventable by optimization of these vascular risk factors according to Fisher's preventable stroke score (FPSS). However, the threshold values and coding criteria of the score are outdated. The "Life's Simple 7 score (LS7S)" schematized in the Ankara ACROSS study was designed to make this update.
METHODS: The study prospectively enrolled 787 acute ischemic stroke patients admitted to three university affiliated comprehensive stroke centers in Ankara. The preventability of stroke was evaluated according to the success attained in control of LS7S metrics (hypertension, diabetes, hyperlipidemia, active smoking, obesity, diet, physical activity), and were then compared to FPSS (0-10).
RESULTS: A total of 386 (49%) patients had highly preventable stroke according to LS7S, while 196 (25%) were classified as preventable according to the criteria of previous study. Seventy-six percent of patients with highly preventable stroke according to LS7S were not classified as such by FPSS, while 53% of patients with high preventability per FPSS were not considered as preventable according to LS7S. Young age, DM, absence of stroke history, and small artery occlusion were associated with highly preventability according to LS7S; coronary artery disease, atrial fibrillation, high NIHSS score, large artery atherosclerosis and cardio-aortic embolism were associated with highly preventability according to FPSS.
DISCUSSION AND CONCLUSION: Despite the importance of preventable stroke, its criteria has not been fully clarified yet. An ideal and practical scoring could be critical for stroke prevention strategies.
Keywords: Ischemic stroke, modifiable risk factors, preventable stroke.

"FISHER ÖNLENEBİLİR İNME SKORU''NA KARŞI "YAŞAMSAL-7":

BİR ANKARA ACROSS SUBGRUP ÇALIŞMASI

ÖZ

GİRİŞ ve AMAÇ: İnmelerin %90'ı modifiye edilebilir risk faktörleriyle ilgilidir. "Fisher Önlenebilir İnme Skoru" bu bağlantının kalitatif ölçütü olup major inmelerin en az ¼'ünün büyük oranda engellenebileceğini ortaya koymuştur. Ancak, skorun eşik değerleri ve kodlama kriterleri güncelliğini yitirmiştir. Ankara ACROSS çalışmasında şematize edilen "Yaşamsal 7 skoru" bu güncellemeyi yapmak üzere tasarlanmıştır.
YÖNTEM ve GEREÇLER: Çalışmaya, Ankara ilinde kapsamlı inme merkezi statüsündeki üç araştırma üniversite hastanesine başvurmuş 787 akut iskemik inme hastası alınmıştır. Tüm hastalarda güncel kılavuz hedefleri ışığında iskemik inmenin 7 risk faktörü ("Yaşamsal 7"; hipertansiyon, diabetes mellitus, hiperlipidemi, sigara, obezite, diyet, fiziksel

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aktivite) skorlandı ve Fisher önlenebilir inme skoru (0-10) ile karşılaştırıldı.
BULGULAR: Yaşamsal 7'ye göre yüksek oranda önlenebilir olduğu tespit edilen 386 (%49) hasta bulunmuştur. Önceki çalışmanın kriterleri kullanıldığında ise yüksek oranda önlenebilir olan hasta sayısı 196 (%25) olarak tespit edilmiştir. Yaşamsal 7'ye göre yüksek oranda önlenebilir olduğu tespit edilen hastaların %76'sının Fisher Önlenebilir İnme Skoru göre skorlandığında yüksek oranda önlenebilir inme grubuna girmediği görülmüştür. Fisher kriterlerine göre yüksek oranda önlenebilir olan hastaların ise %53'ü yaşamsal 7 kriterlerine göre skorlandığında yüksek oranda önlenebilir inme olarak tespit edilmemiştir. Genç yaş, diabetes mellitus, inme hikayesi yokluğu ve küçük arter oklüzyonu Yaşamsal 7'ye göre önlenebilirlik ile ilişkili bulunurken, koroner arter hastalığı, atriyal fibrilasyon, yüksek NIHSS skoru, büyük arter aterosklerozu ve kardiyo-aortik embolism Fisher skoruna göre önlenebilirlik ile ilişkiliydi.
TARTIŞMA ve SONUÇ: İnmenin önlenebilirliği kavramının önemine karşın günümüzde bunun belirlenmesini sağlayabilecek kriterler henüz tam olarak netleşmemiştir. İdeal ve pratik bir skorlamanın bulunması inmeden korunma stratejileri için kritik öneme haizdir.
Anahtar Sözcükler: İskemik inme, modifiye edilebilir risk faktörleri, önlenebilir inme.

INTRODUCTION

Stroke ranks the 4th among causes of death and the first among causes of disability (1). In the treatment of ischemic stroke, the etiology of stroke should be identified and appropriate antithrombotic treatment should be initiated. In addition, studies have demonstrated that the incidence of stroke would decrease in case the risk factors of stroke are checked as well. Of the strokes, 90% are associated with modifiable risk factors (hypertension, diabetes mellitus (DM), obesity and metabolic syndrome, atrial fibrillation (AF), hyperlipidemia, cardiovascular diseases, smoking and drinking alcohol, physical inactivity, unhealthy diet) (1,2). As the qualitative measure of this relation, the "Fisher Preventable Stroke Score" has demonstrated that at least ¼ of the strokes are largely preventable (3). However, the threshold values and rating criteria of the score are out of date.

The "Life's Simple 7 score" (LS7S), which was schematized in the Ankara ACROSS study, was designed to perform this updating (4). In the present study, it was aimed to compare the definition of preventable stroke made according to the risk factor modification principles in line with the objectives of the current guideline and the criteria in the previous study, and to examine the differences between the definitions in terms of sociodemographic and clinical characteristics of stroke.

METHODS

The study included 787 patients, who presented to the three university affiliated research hospitals with comprehensive stroke center status due to acute (first 5 days) first or recurrent stroke and whose etiological examinations were completed between November 2016 and October 2018. The approval of the ethics committee was obtained for the study (Date: 24 November 2016, Decision number GO16/717-09), and the study was started after obtaining the approval of the ethics committee. The informed consent forms were signed by all patients. Clinical and laboratory parameters were evaluated in terms of demographic characteristics (age, gender, height, weight, drugs used by the patients at the time of admission and their regular usage) and risk factors (hypertension, diabetes, hyperlipidemia, atrial fibrillation and other cardiovascular diseases, smoking). The presence/absence of previous strokes before the current clinical picture of stroke were recorded along with the data regarding diet and physical activity. The severity of the stroke at the time of admission was determined according to the NIHSS (National Institutes of Health Stroke Scale) score (5). The findings of the patients in the electrocardiography, echocardiography, 24-hour Holter, computed tomography of the brain, cranial magnetic resonance imaging and angiography were evaluated. To determine the etiological type of ischemic stroke, the automated Causative Classification System (CCS) was used (6). Patient follow-up data were obtained by using modified Rankin scores in the 3rd month through the phone calls with the patients or their relatives.

In all patients, the 7 risk factors of ischemic stroke ("Life's Simple 7"; hypertension, diabetes mellitus, hyperlipidemia, smoking, obesity, diet and physical activity) were scored (2,4,7-9) and compared to the Fisher preventable stroke score (0-10)(3). The Life's Simple 7 and Fisher preventable stroke scores are presented in Table I.

Statistical Analysis: Descriptive statistics are shown as mean ± standard deviation (SD) for variables with normal distribution, and as median (interquartile range) for variables with non-normal distribution. The nominal variables were shown as the number of cases and (%). When the number of groups was two, the significance of the difference between the groups in terms of means was investigated with the t test, and the significance of the difference in terms of median values was investigated with the Mann Whitney U test. When the number of groups was more than two, the significance of the difference between the groups in terms of means was investigated with one-way analysis of variance, and the significance of the difference in terms of median values was investigated with the Kruskal Wallis test. Nominal variables were evaluated using the Chi-Square or Fisher's exact test. The threshold value for both preventable stroke definitions was determined as ≥4 in the light of the previous studies. Logistic regression test was used for multivariate analysis. Where p<0,05, the results were considered statistically significant. All statistical analyses were performed using the SPSS® 16.0 software.

RESULTS

There were 386 patients (49%, 170 female [53%], mean age 67 ± 13 years) who were found to be highly preventable according to Life's Simple 7. Using the criteria of the previous study, the number of highly preventable patients was determined as 196 (25%, 109 women [34%], mean age 74 ± 11 years). The demographic data of the patients, their risk factor frequencies, NIHSS at the time of admission, follow-up mRS, appropriate antithrombotic usage and distribution of the CCS subtypes are presented in Table II.

The definition of preventable stroke in the context of Life's Simple 7 and Fisher scores overlapped in about half of the cases. Of patients, who were found to be highly preventable according to Life's Simple 7, 76% were not included in the highly preventable stroke group when they were scored according to the Fisher Preventable Stroke Score. Of the patients, who were found to be highly preventable according to the Fisher criteria, 53% were not determined to be listed among the highly preventable stroke group when scored according to the Life's Simple 7 criteria (Table III).

The inconsistencies between scores were evaluated in the light of multivariate analyses; and it was found that the young age, presence of diabetes, absence of the history of stroke, and the presence of small artery occlusion were associated with preventability according to Life's Simple 7, while coronary artery disease, atrial fibrillation, high NIHSS score, large artery atherosclerosis and cardio-aortic embolism were associated with preventability according to the Fisher score (Figure).

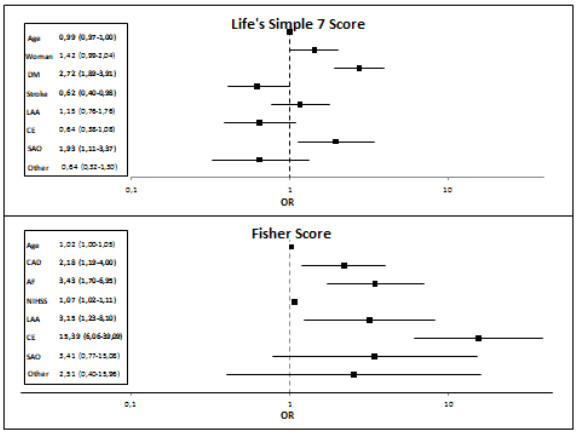

Figure. Factors related to the different definitions of preventable stroke - results of the multivariate analysis. Factors with statistical significance were written in bold letters. The horizontal axis has a distribution within the logarithmic scale. AF: Atrial fibrillation; LAA: Large Artery Atherosclerosis; DM: Diabetes Mellitus; CAD: Coronary Artery Disease; SAO: Small Artery Occlusion, CE: Cardioaortic embolism.

DISCUSSION AND CONCLUSION

The presence of patients with recurrent stroke despite appropriate antithrombotic treatment indicates that risk factors should also be reviewed and controlled within the treatment plan. A total of 889 patients were included in the RESQUE study; and, it was found that 79% of the patients with recurrent acute stroke were under antiaggregant treatment while 21% were under anticoagulant treatment (10). In the study, which involved 94,474 patients with AF who had acute stroke, it was observed that 30% of the patients were under oral anticoagulant treatment, and 16% had a stroke under the therapeutic range of INR or a regular effective dose of new generation oral anticoagulants (11). In the EUROASPIRE III study, which included 881 patients with ischemic stroke, only 62.4% of hypertensive patients had high blood pressure, 75.7 % had high LDL-C values,

Table I. Life's Simple 7 and Fisher preventable stroke score.

	Life's Simple 7	**Fisher 10**
Hypertension	0; Admission SBP <160 mmHg 1; Admission SBP ≥160 mmHg	0; Admission SBP <180 mmHg 1; Admission SBP 180-199 mmHg 2; Admission SBP >= 200 mmHg
Diabetes mellitus	0; HbA1c<7 1; HbA1c ≥ 7	-
Atrial fibrillation	-	0; None or if present, under appropriate treatment 2; Present and under treatment; however, INR<2 4; Present, not receiving any treatment
Hyperlipidemia	0; LDL-C <100 mg/dl 1; LDL-C≥100 mg/dl	0; TC<180 mg/dl or LDL-C 100 mg/dl 1; TC 180-199 mg/dl or LDL-C 100-149 mg/dl 2; TC≥200 mg/dl or LDL-C ≥150 mg/dl
Previous stroke/Transient ischemic attack/myocardial infarction	-	0; None, or if present, underantiaggregant or anticoagulant treatment 2; Present and not under underantiaggregant or anticoagulant treatment
Obesity	0; Body mass index<30 kg/m^2 1; Body mass index≥30 kg/m^2	-
Smoking	0; Never or has quit smoking (>Having quitted 6 months ago) 1; active smoker (including smoking within the last 6 months)	-
Physical activity	0: Sweating physical activity at least once a-week 1: No sweating physical activity	
Diet	0: Mediterranean type diet score>12 1: Mediterranean type diet score ≤12	-
Preventable Stroke	**Score ≥4**	**Score ≥4**

SBP; Systolic blood pressure, TC; Total cholesterol , LDL-C; Low-density lipoprotein – Cholesterol.

Table II. Sociodemographic and clinical characteristics of the patients in the light of both preventable stroke definitions.

	Life's Simple 7			**Fisher**		
	patients < 4 n=401	**patients ≥ 4 n=386**	**p**	**patients < 4 n=591**	**patients ≥ 4 n=196**	**p**
Age, year, *Mean±SD*	69±15	67±13		66±14	74±11	
Female, *n(%)*	154 (38)	170 (44)	0.108	215 (36)	109 (56)	< 0.001
Risk factors						
Hypertension,*n(%)*	269 (67)	281 (73)	0.081	385 (65)	165 (84)	< 0.001
Diabetes mellitus, *n(%)*	104 (26)	186 (48)	< 0.001	214 (36)	76 (39)	0.519
Known AF, n(%)	67 (17)	34 (9)	0.001	34 (6)	67 (34)	< 0.001
Dyslipidemia, *n(%)*	103 (26)	122 (32)	0.066	155 (26)	70 (36)	0.011
CAD, *n(%)*	119 (30)	127 (33)	0.329	151 (26)	95 (48)	< 0.001
Previous history of stroke *n(%)*	87 (22)	73 (19)	0.332	108 (18)	52 (27)	0.013
Admission NIHSS, *Median (IQR)*	4 (2-10)	4 (2-8)	0.952	4 (2-8)	6 (3-14)	< 0.001
Follow-up mRS at 3 months, *Median (IQR)*	2 (0-4)	1 (0–3)	0.540	1 (0–3)	2 (1–4)	< 0.001
CCS						
LAA	112 (28)	124 (32)	< 0.001	201 (34)	35 (18)	< 0.001
CE	128 (32)	75 (19)		94 (16)	109 (56)	
SAO	30 (8)	60 (6)		80 (14)	10 (5)	
Other causes	28 (7)	21 (5)		45 (8)	4 (2)	
Undetermined causes	103 (26)	106 (27)		171 (29)	38 (19)	

SS: standard deviation, NIHSS: National Institutes of Health Stroke Scale, mRS: modified Rankin Scale, DM: Diabetes Mellitus, AF: Atrial Fibrillation, CAD: Coronary artery disease, CCS: Causative Classification System, LAA: Large artery atherosclerosis, CE: Cardioaortic embolism, SAO; Small artery occlusion.

Table III. Patients in need of risk factor optimization for the Life's Simple 7 and Fisher Preventable Stroke Score after ischemic stroke.

	Life's Simple 7	
Fisher	*patients <4 n(%)*	*patients ≥ 4 n(%)*
patients <4 n(%)	297 (38)	294 (37)
patients ≥ 4 n(%)	104 (13)	92 (12)

17.6% patients continued active smoking after stroke, 79.2% were overweight, and % 35.5 of them were found to be obese. In these patients, the percentage of the administration of antiaggregant and anticoagulant treatment was around 87.2%. In a study, which included 279 patients and aimed at optimizing blood pressure and lipid levels after minor stroke, it was observed that 78.1% of the patients were receiving antihypertensive and 84.6% statin treatments; however, none of the patients achieved the treatment goals specified in the guideline (12). In the ASPIRE-S study, where 302 patients with stroke were included, approximately 95% of the patients were under statin treatment and 75% were under antihypertensive treatment during the 6-month follow-up period; however, it was found that 63.4% of the patients did not achieve the treatment goals for HT, 23% for HL and 28% for DM. Of these patients, 97% were under appropriate antithrombotic treatment (13). Despite the high rates of antithrombotic use reported in these studies, insufficiency of the risk factor modification indicates that the high risk continues in of cardiovascular and cerebrovascular terms (14).

The concept of preventable stroke was used in the study of Fisher et al.; and in the study that included 274 patients who had ischemic stroke, all risk factors were scored over 10 points (0-not preventable stroke, 10-most preventable stroke, hypertension 0-2, hyperlipidemia 0-2, atrial fibrillation 0-4, antithrombotic treatment 0-2) according to the preventability criteria. Of the patients, 25.9% were found to be highly preventable; however, the scoring used in this study does not fully match the target values recommended by the current guideline (3).

Of the patients, who were found to be highly preventable according to Life's Simple 7, 76% were not included in the highly preventable stroke group when they were scored according to the Fisher Preventable Stroke Score. Of the patients, who were found to be highly preventable according to the Fisher criteria, 53% were not determined to be listed among the highly preventable stroke group when scored according to the Life's Simple 7 criteria. This was due to the scoring of different parameters in both models as well as the emphasis placed on different preventable aspects of stroke in this context. The history of stroke and AF was not evaluated in Life's Simple 7; and the factors regarding the life style such as DM, smoking and obesity, physical activity and eating habits were not scored in Fisher preventable stroke score. As a result, while the large artery atherosclerosis and cardioembolic processes were prominent in terms of preventability in the Fisher score, which attached importance to the antithrombotic treatment and cardiac pathologies, small vessel occlusion stood out as an etiological cause in Life's Simple 7. These etiological differences were reflected in other parameters related to preventability in multivariate models. Strong stroke severity, which was more common on the basis of advanced age, cardiac comorbidity and atrial fibrillation, appeared as a criterion for preventability according to the Fisher score (15). On the other hand, demographic groups such as the younger group or female gender, who were more incompatible in terms of risk factor optimization or had difficulty in accessing treatment, were at risk of preventable stroke in the Life's Simple 7.

The result of this study should be interpreted by considering various limitations. The scoring of different parameters in both models and the fact that only hospitalized patients were evaluated constituted the weaknesses of this study. In addition, the information regarding the diet and physical activity collected in relation to Life's Simple 7 was obtained by talking with the patient and relatives; therefore, they contained a margin of error in terms of reliability.

Despite the importance of the concept of preventability of stroke, the criteria for identification have not yet been clarified. The inconsistency between the criteria sets that has been defined in the literature so far was noted. As a matter of fact, inconsistency is not an unexpected finding in a heterogeneous entity such as stroke. Both scoring methods that were examined in the study had both strengths and shortcomings. Finding a practical and an ideal scoring method that includes many different aspects of stroke with the studies to be carried out in this field would be critical for the development of stroke prevention strategies.

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Ethics

Ethics Committee Approval: The study was approved by the Hacettepe University Faculty of Medicine Noninterventional Clinical Studies Ethics Committee (Date: 24.11.2016, Number: GO16/717-09).

Informed Consent: It was declated that signed informed consent was obtained from all cases.

Authorship Contributions: Surgical and Medical Practices: MHS, IE, MAT, HZBC, CTI, BN, EMA. Concept: MHS, IE, MAT, HZBC, CTI, BN, EMA. Data Collection or Processing: MHS, IE, MAT, HZBC, CTI, BN, EMA. Analysis or Interpretation: MHS, IE, MAT, HZBC, CTI, BN, EMA. Literature Search: MHS, IE, MAT, HZBC, CTI, BN, EMA. Writing: MHS, IE, MAT, HZBC, CTI, BN, EMA.

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