

ÖZGÜN ARAŞTIRMA

ORIGINAL ARTICLE

**THE ROLE OF EDUCATION LEVEL AND GENDER FROM THE PERSPECTIVE OF PREVENTABLE STROKE:
ANKARA ACROSS SUBGROUP ANALYSIS**

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ABSTRACT

INTRODUCTION: Recent studies have highlighted that most strokes can possibly be prevented by risk factor modification and lifestyle changes. Female gender and lower educational level are two critical sociodemographic factors that are related to increased stroke risk. In this study, we investigated the interplay between these two features, which are considered to be disadvantageous in terms of stroke, and stroke preventability.

METHODS: The study was prospectively conducted by evaluation of 787 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 "Life's simple 7" metrics (hypertension, diabetes, hyperlipidemia, active smoking, obesity, diet and physical activity) at the time of stroke. The effect of education level and gender on stroke preventability was investigated by bivariate and multivariate analysis.

RESULTS: A primary level or lower degree of education was present in 65% of the study population. Forty-two percent of our patients were female. A lower education level was significantly associated with suboptimal control of diabetes, active smoking, obesity, sedentary lifestyle and bad dietary habits. Preventable stroke (suboptimal control of ≥ 4 factors) was present among 52% of patients with lower education levels, while the corresponding proportion was 43% among those with high school or university education ($p=0.012$). The percentage of obesity and sedentary lifestyle was significantly higher in females, while active smoking was more common in males. The education level was lower among female patients in comparison to males. Preventable stroke was encountered more commonly in females (52% vs. 47%, $p=0.108$). In multivariate analysis, female gender ($p=0.021$) and lower education level ($p=0.006$) were independently associated with suboptimal control of risk factors. A lower education level mediated 31% of the relationship between female gender and preventable stroke.

DISCUSSION AND CONCLUSION: Both female gender and lower education level are closely related to preventable stroke. Patients with such sociodemographic features, who are also considered to have a higher risk of stroke, necessitate additional strategies to optimize control of preventable stroke factors.

Keywords: Preventable stroke, education level, gender, risk factors.

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Received: 10.06.2020

Accepted: 04.09.2020

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This article should be cited as following: Erkent I, Topcuoglu MA, Sorgun MH, Batur Caglayan HZ, Togay Isikay C, Nazliel B, Arsa EM. The role of education level and gender from the perspective of preventable stroke: Ankara across subgroup analysis. Turkish Journal of Cerebrovascular Diseases 2020; 26(3): 236-243. doi: 10.5505/tbdhd.2020.33254

EĞİTİM DÜZEYİ VE CİNSİYETİN İNME ÖNLENEBİLİRLİĞİ ÜZERİNDEKİ ROLÜ:

ANKARA ACROSS SUBGRUP ANALİZİ

ÖZ

GİRİŞ ve AMAÇ: Son yıllarda yapılan çalışmalar, inmelerin büyük bir kısmının risk faktörü modifikasyonu ve yaşam tarzı değişiklikleri ile önlenebilir olduğunu ortaya koymuştur. Kadın cinsiyet ve düşük eğitim seviyesi artmış inme riski ile ilişkili iki önemli sosyodemografik faktör olarak ön plana çıkmaktadır. Bu çalışmada, inme açısından dezavantajlı kabul edilen bu iki özelliğin ülkemiz özelinde inme önlenebilirliği ile etkileşimi incelenmiştir.

YÖNTEM ve GEREÇLER: Çalışmamız Ankara ilinde kapsamlı inme merkezi şeklinde fonksiyon gören üç araştırma üniversitesi bünyesinde prospektif olarak yatırılarak değerlendirilen 787 iskemik inme hastasının klinik ve laboratuvar verileri dahil edilerek gerçekleştirildi. İnme anında inmenin önlenebilirliği "Yaşamsal 7" (hipertansiyon, diyabet, hiperlipidemi, sigara, obezite, diyet ve fiziksel aktivite) faktörlerinin ne oranda kontrol altında olduğuna göre değerlendirildi. Eğitim seviyesi ve cinsiyetin inme önlenebilirliği üzerine etkileri ikili ve çok değişkenli modeller kullanılarak incelendi.

BULGULAR: Çalışmamıza dahil olan hastaların %65'i ilk öğretim düzeyi veya altında eğitim almışlardı; %41 hastamız ise kadın idi. Düşük eğitim seviyesi "Yaşamsal 7" faktörlerinden, kötü diyabet kontrolü, aktif sigara kullanımı, obezite, sedanter yaşam ve kötü beslenme alışkanlıkları ile anlamlı bağlantı göstermekteydi; bu grupta önlenebilir inme varlığı (≥ 4 faktörde kontrolsüzlük) %52 oranında mevcut iken, lise veya daha üstü seviyede eğitilmiş grupta bu oran %43 olarak saptandı ($p=0,012$). Kadın hastalarda obezite varlığı ve sedanter yaşam anlamlı olarak fazla iken, daha az sigara kullanımı mevcuttu. Genel olarak eğitim seviyesi açısından da erkeklere göre daha dezavantajlı olan kadınlarda önlenebilir inme oranı sayısal olarak daha fazlaydı (%52'ye %47; $p=0,108$). Çok değişkenli analiz sonucunda kadın cinsiyet ($p=0,021$) ve düşük eğitim seviyesi ($p=0,006$) önlenebilir inme açısından bağımsız risk faktörleri olarak gözlemlendi; kadın cinsiyet ve önlenebilir inme arasındaki ilişkinin %31'inden kadınlarda daha sık oranda gözlenen düşük eğitim seviyesinin sorumlu olduğu saptandı.

TARTIŞMA ve SONUÇ: Gerek kadın cinsiyet, gerekse düşük eğitim düzeyi inme önlenebilirliği ile ilişkili faktörlerdir. Aynı zamanda yüksek inme riski de taşıyan bu hasta gruplarında önlenebilir inme faktörlerinin gözden kaçırılmaması için ilave stratejilere ihtiyaç vardır.

Anahtar Sözcükler: Önlenebilir inme, eğitim düzeyi, cinsiyet, risk faktörleri.

INTRODUCTION

Recent studies have drawn attention to the importance of preventable risk factors both for all cardiovascular diseases and for stroke (1-3). There is limited epidemiological data on the frequency and distribution of stroke-related risk factors in our country (4-6). Determination of the relevant patient profile in our country would be an important step in developing treatment strategies for the prevention of primary and secondary stroke. As a matter of fact, relevant studies have demonstrated that stroke risk factor profiles differ according to countries, and different policies have been determined accordingly (7).

Sociodemographic factors are also of great importance in terms of the frequency and control of risk factors (3, 8, 9). There are different opinions in studies on the epidemiology of stroke; however, an increase in the risk of stroke has been reported for middle-aged females in general. In addition, it is known that stroke burden is higher in females, which is associated with higher life expectancy and the incidence of stroke at later ages in females (10, 11).

Socioeconomic factors consist of parameters such as education level, profession, income level, social security status, possession of material assets/wealth and the characteristics of the living environment. The effects of these factors on disease risk and mortality have been examined in terms of general cardiovascular diseases and stroke. Among these effects, education level is of particular importance due to being a parameter that does not vary in the case of various diseases and can be easily measured (12). In addition, since education is often completed in early adulthood and is mainly related to parental characteristics, it reflects the socioeconomic status in the early period of life (11, 13). In the literature, poor education level is often associated with the presence and lack of control of cardiovascular risk factors, increased risk of stroke, and increased mortality after stroke (12, 14-16).

In this study, we aimed to investigate the effects of education level and gender on the preventability of stroke, stroke subtypes, and post-stroke prognosis in a city cohort, considering the

long-term benefit of disease management.

METHODS

The study was conducted in accordance with the Helsinki Declaration ethical standards and approved by the Hacettepe University Faculty of Medicine Noninterventional Clinical Studies Ethics Committee (Number: GO 16/717-09, Date: 24.11.2016).

This study was conducted at three research universities in Ankara operating as comprehensive stroke centers [Ankara Academic Comprehensive stROke centerS conSortium (ACROSS)] by evaluating the clinical and laboratory data of 787 patients, who presented prospectively with acute ischemic stroke between November 2016 and October 2018 (17). Patients admitted within the first 5 days of the symptom onset were included. All patients signed informed consent form firstly. Patients with severe aphasia and dementia, history of transient ischemic episodes, and those with no relatives for obtaining reliable information about their medical history were excluded.

Demographic, clinical, and laboratory data were collected at the time of admission using a standardized questionnaire. Education level was categorized under two groups, which were primary education level and below, and high school and university degree. Medical history of hypertension was evaluated based on the individual statement of the patient, use of antihypertensive drugs or blood pressure $\geq 140/90$ mmHg at home measurements. Medical history of diabetes was evaluated based on the individual statement of the patient and the use of antidiabetic drugs. Medical history of hyperlipidemia was evaluated according to the use of antihyperlipidemic drugs or a total cholesterol value of ≥ 240 mg/dl in previous measurements. Also, patients were inquired for their medical history of coronary artery disease, atrial fibrillation, and stroke and their previous medical records were reviewed. The etiology of stroke was determined through the "Causative Classification of Stroke System (CCS)" (18). Follow-up evaluation was performed on the 90th day using the modified Rankin Score (mRS). The evaluation on the 90th day was performed via phone calls for patients who were not able to come to the hospital.

In our patients admitted to the hospital with

stroke, the preventability of stroke was evaluated on the basis of "Life's simple 7" (hypertension, diabetes mellitus, hyperlipidemia, smoking, obesity, diet and physical activity), which focuses on seven significant modifiable risk factors determined by the American Heart Association (2). The presence or absence of each risk factor, and the need for additional medical treatment to control this risk factor at the time of admission were evaluated in line with the recommendations in the guidelines for the prevention of secondary stroke (19). The criteria used for these evaluations are summarized in Table 1 (17). The degree of preventability of stroke was evaluated by determining the number of risk factors requiring additional intervention (from 0 to 7) to be checked in each patient. Accordingly, the stroke experienced by the patient group, whose number of risk factors was higher than the median value (≥ 4) of the population, was categorized as preventable (17).

Categorical variables were presented as percentages; numerical variables were presented as mean and standard deviation, or median and interquartile range. Education level and gender were analyzed in terms of their effects on the preventability of stroke, stroke subtypes, and prognosis, using binary and multivariate models. Logistic regression analysis was used for determining independent risk factors. The p value < 0.05 was considered statistically significant. All statistical analyses were made using the SPSS version 23.0. Ethics Committee Approval was obtained for the study.

RESULTS

A total of 787 (463 male, 324 female) patients were included in the study. The patients in our study were distributed according to their education levels as follows: 130 (17%) were illiterate, 382 (49%) had primary education degrees, 172 (22%) had high school degrees, and 103 (13%) had university degrees. Preventable stroke, which was defined as a condition in which four or more risk factors were not controlled at the optimum level, was present in 386 (49%) of the patients.

The distribution of the characteristics of the study group by education level is summarized in Table 2. Individuals with low educational levels

Table 1. Risk factor criteria indicating the need for modification in terms of stroke preventability.

Uncontrolled hypertension*	Systolic blood pressure value at the time of admission ≥ 160 mmHg
Uncontrolled diabetes	HbA1c $\geq 7\%$
Uncontrolled dyslipidemia	LDL-C value ≥ 100 mg/dl
Obesity	Body mass index value ≥ 30 kg/m ²
Active smoking	Continued smoking (including the patients who had quit in less than 6 months)
Non-compliance with the Mediterranean diet*	MDS score ≤ 12
Sedentary life [^]	Patients who did not have intensive weekly physical activity to cause sweating

*Evaluation was made considering that the value at presentation after ischemic stroke was approximately 20 mmHg higher compared to the most recently measured systolic blood pressure value at home.

+The "Mediterranean Diet Score" (MDS), which was used in a global study investigating diet patterns in individuals with coronary artery disease, was adapted and evaluated.

[^]The evaluation of the frequency of physical activity during the period before the stroke was based on the REGARDS study.

Table 2. Distribution of demographic and clinical characteristics of the study cohort by education level

	High education level (n= 275)	Low education level (n= 511)	p
Age (mean \pm standard deviation)	62 \pm 15 y	71 \pm 12 y	<0.001
Female gender (n, %)	65 (24%)	259 (51%)	<0.001
Hypertension (n, %)	164 (60%)	386 (75%)	<0.001
Diabetes (n, %)	89 (32%)	201 (39%)	0.056
Dyslipidemia (n, %)	68 (25%)	157 (31%)	0.079
Coronary artery disease (n, %)	74 (27%)	172 (34%)	0.054
History of previous stroke (n, %)	55 (20%)	105 (21%)	0.866
Uncontrolled hypertension (n, %)	108 (39%)	203 (40%)	0.918
Uncontrolled diabetes (n, %)	61 (22%)	160 (31%)	0.007
LDL ≥ 100 mg/dl at the time of admission (n, %)	192 (70%)	363 (71%)	0.777
Body mass index ≥ 30 kg/m ² (n, %)	49 (18%)	145 (28%)	0.001
Active smoking (n, %)	74 (27%)	98 (19%)	0.012
Non-compliance with Mediterranean diet (n, %)	214 (78%)	457 (89%)	<0.001
Sedentary life (n, %)	205 (75%)	426 (83%)	0.002
Insufficient risk factor control (n, %)	118 (43%)	268 (52%)	0.012
NIHSS score at the time of admission (median, IQR)	3 (2-8)	5 (2-10)	<0.001
CCS stroke subtype (n, %)			0.015
Large artery atherosclerosis	72 (26%)	164 (32%)	
Cardio-aortic embolism	66 (24%)	137 (27%)	
Small-artery occlusion	32 (12%)	58 (11%)	
Other causes	23 (8%)	26 (5%)	
Cryptogenic	78 (28%)	106 (21%)	
Unclassified	4 (1%)	21 (4%)	
3rd month mRS ≥ 3 (n, %)*	67 (25%)	192 (40%)	<0.001

*Analyses were performed on 747 patients, who could be reached.

were predominantly the female and the elderly. When examined in terms of the presence of risk factors, a higher rate of hypertension, diabetes, hyperlipidemia and coronary artery disease was observed in the group with a low education level. Lower education levels exhibited a statistically significant correlation with uncontrolled diabetes management, active smoking, obesity, sedentary lifestyle, and non-compliance with Mediterranean diet among the "Life's simple 7" factors. The rate of preventable stroke decreased linearly as education level increased (Figure 1). In total, the presence of preventable stroke in the illiterate and primary school group was 52%, while it was 43% in the high school or the group with higher education (p=0.012).

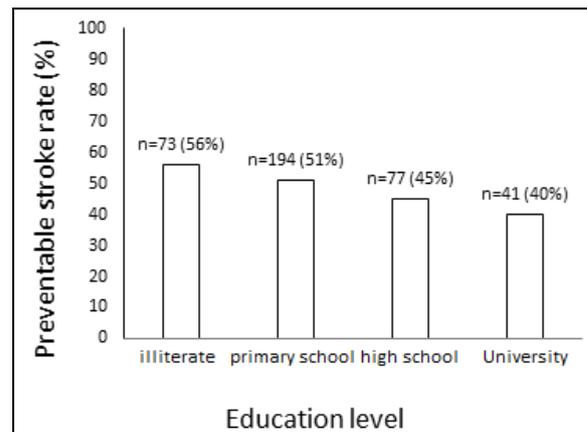


Figure. The relationship between educational background and preventable stroke.

The distribution of the characteristics of the study group by gender is summarized in Table 3. It was noted that female patients in the study were older than males, and the rates of chronic diseases such as hypertension, diabetes, and dyslipidemia were higher in female patients. When evaluated in terms of "Life's simple 7" factors, active smoking was higher in males with statistical significance, while obesity and sedentary lifestyle were more common in females. Although preventable stroke rate was numerically higher in female patients, this finding did not have statistical significance (53% vs 47%; p= 0.108).

When the groups were examined in terms of stroke subtypes, large artery atherosclerosis and cardio-embolism were observed with a higher rate, and the cryptogenic stroke was found with a lower rate in the group with low education

Table 3. Distribution of demographic and clinical characteristics of the study cohort by gender.

	Female (n= 324)	Male (n= 463)	p
Age (mean ± SD)	71± 14 y	66±13 y	<0.001
Hypertension (n, %)	242 (75%)	308 (67%)	0.014
Diabetes (n, %)	132 (41%)	158 (34%)	0.058
Dyslipidemia (n, %)	107 (33%)	118 (26%)	0.021
Coronary artery disease (n, %)	97 (30%)	149 (32%)	0.504
History of previous stroke (n, %)	59 (18%)	101 (22%)	0.216
Uncontrolled hypertension (n, %)	139 (43%)	172 (37%)	0.104
Uncontrolled diabetes (n, %)	97 (30%)	124 (27%)	0.319
LDL ≥100 mg/dl at the time of admission (n, %)	224 (69%)	331 (72%)	0.487
Body mass index ≥30 kg/m ² (n, %)	113 (35%)	81 (18%)	<0.001
Active smoking (n, %)	35 (11%)	137 (30%)	<0.001
Non-compliance with Mediterranean diet (n, %)	282 (87%)	389 (84%)	0.240
Sedentary life (n, %)	278 (86%)	353 (76%)	<0.001
Insufficient risk factor control (n, %)	170 (53%)	216 (47%)	0.108
NIHSS score at the time of admission (median, IQR)	6 (2-11)	4 (2-8)	<0.001
CCS stroke subtype (n, %)			<0.001
Large artery atherosclerosis	86 (27%)	150 (32%)	
Cardio-aortic embolism	108 (33%)	95 (21%)	
Small-artery occlusion	32 (10%)	58 (13%)	
Other causes	18 (6%)	31 (7%)	
Cryptogenic	64 (20%)	120 (26%)	
Unclassified	16 (5%)	9 (2%)	
3rd month mRS ≥3 (n, %)*	137 (46%)	122 (27%)	<0.001

*Analyses were performed on 747 patients, who could be reached.

level ($p=0.015$). The distribution of stroke subtypes differed significantly between male and female patients ($p<0.001$). While cardio-embolism was observed with the highest rate in female patients, large artery atherosclerosis was the most common etiological cause in male patients. As a consequence of the heterogeneity in etiologies between the groups, female patients, and patients with low education level had more severe stroke symptoms at the time of admission, and worse functional outcomes in the 3rd month.

In multivariate analysis, female gender (Odds ratio: 1.45, 95% CI: 1.06-1.99; $p= 0.021$) and low education level (Odds ratio: 1.59, 95% CI: 1.14-2.21; $p= 0.006$) were observed as independent risk factors for preventable stroke. When the relationship between female gender and preventable stroke was re-examined with mediator analysis, it was found that low education level, which was observed more frequently in female patients, was responsible for 31% of the total effect.

DISCUSSION AND CONCLUSION

There are variations in epidemiological studies according to different countries, cultures and education systems; however, an overall increase has been reported in the risk of stroke due to low education level, and the relationship between the two factors have been associated with the lifestyle (health behavior), psychosocial factors, occupational characteristics and biological stroke risk factors (cardiovascular disease, smoking and alcohol consumption) (7,8,10). Similar to our findings, low education level is associated with active smoking, obesity, diabetes, hypertension, and sedentary life in patients with stroke in the literature (8). In addition, the relationship of low education level with uncontrolled hypertension and diabetes was determined; an increase in routine exercise rates and a decrease in obesity prevalence have been reported due to high education level (15). In a multi-center study, low education level was found to cause a 26-28% increase in stroke mortality, which was attributed to risk factors such as hypertension and smoking. While this effect was more pronounced in the female population in certain populations, there was no difference between the genders in general (7). In another study, it was found that low education level increased the risk of stroke twice, and it was observed that more than 50% of this effect disappeared when the depressive symptoms, social connections, physical / cognitive functionality were adjusted for diabetes (20). High education level positively affects social, psychological and economic skills. These features cause a positive approach to general health and facilitate access to preventive health services (15,21). This study demonstrates a direct impact of education level on stroke preventability and morbidity, and shows that missed opportunities in the context of risk factor control or lifestyle changes are greater in individuals with lower education, who had a stroke. Despite the fact that education level is not usually a changeable factor after young adulthood, developing and implementing training programs that include new and appropriate techniques (such as the importance of exercise, Mediterranean diet, smoking cessation trainings) in order to deliver effective messages to the target audience can be a successful strategy in reducing the increased cardiovascular risk (15,21).

In our study, female gender was also determined as a disadvantageous group in terms of stroke preventability. The increase in the risk of stroke in female patients is biologically related to the lack of estrogen in the postmenopausal period. This effect is attributed to the vasodilator effects of endogenous estrogen on the endothelium as well as its antioxidant and anti-apoptotic properties (22). The protective effect of hormone replacement therapy on stroke has not been demonstrated; however, there are studies demonstrating that it increases the risk of stroke in the postmenopausal period (23-26). These contradictory results are associated with the different effects of nitric oxide synthase activity, which is the target of estrogen in the endothelium, in different age groups. While it has positive effects in the young female thanks to nitric oxide production, it has a negative effect due to the increase of superoxide radicals in the elderly (27). In addition, although diabetes and metabolic syndrome increase the risk of stroke in both genders, it has been reported that this effect is higher in the female compared to the male, and subclinical atherosclerosis caused by metabolic syndrome develops earlier in the female (26,28,29). These findings are consistent with our current data.

In addition, the relationship between age and gender seems to be a prominent factor in the context of stroke risk. The incidence of stroke in the female between the ages of 55 and 74 is lower compared to the male; however, a higher risk of stroke was found in the female aged 75 years in some studies, and in the female aged 85 and above in some other studies (30,31). Age-specific stroke rates are higher in the female compared to the male; this is believed to be due to the high life expectancy in the female and the increased incidence of stroke at later ages (10,11,26). In our study, female patients, who had a stroke, consisted of older individuals at a statistically significant level.

In a study about a 10-year follow-up of a large female population, a healthy life index (no smoking, low body mass index, moderate consumption of alcohol, regular exercise and healthy diet) was determined, and the risk ratio of ischemic stroke was determined as 0.29 in the female with a high health index compared to hemorrhagic stroke (95% Confidence interval; 0.14-0.63). When the factors were evaluated

separately, non-smoking and low body mass index were found to be associated with a more significant reduction in the risk of stroke. It has been found that the female with low health index have low education and income levels (32). The low education level in the female also seems to be responsible for part of the interaction between the female gender and the preventability of stroke risk/stroke.

A study conducted on the reasons why education on female health was more important associated this situation with the lower socioeconomic resources (income level, authority, power and wealth) available to the female. In addition, similar to the findings of our study, there are opinions that low education level in female patients is associated with an increase in obesity prevalence; and this may explain the higher rate of morbidity and mortality in women. Furthermore, advanced age, functional status before the stroke, stroke subtype and accompanying comorbidities have been reported as factors that increase mortality in the female (7,33). In terms of preventable factors, we believe that the measures to be taken regarding public health should be different in these patient groups, since obesity and sedentary life are predominant in the female and active smoking is predominant in the male.

In conclusion, the control level of stroke risk factors is insufficient in terms of education level and gender. In addition, it is necessary to develop strategies specific to these patient groups in our country in order to prevent preventable stroke. The components effective on stroke risk factor control are clearly important in terms of stroke prophylaxis. Considering the burden of stroke in the society in terms of morbidity and mortality, determining the target patient group and risk profiles appropriately should be taken into account in terms of its social benefit.

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- Ethics**
Ethics Committee Approval: The study was approved by the Hacettepe University Faculty of Medicine Noninterventional Clinical Studies Ethics Committee (Number: GO 16/717-09, Date: 24.11.2016).
Informed Consent: Informed consent was signed by all included patients.
Authorship Contributions: Surgical and Medical Practices: IE, MAT, MHS, HZBC, CTI, BN, EMA. Concept: IE, MAT, MHS, HZBC, CTI, BN, EMA. Design: IE, MAT, MHS, HZBC, CTI, BN, EMA. Data

Erkent et al.

Collection or Processing: IE, MAT, MHS, HZBC, CTI, BN, EMA.

Analysis or Interpretation: IE, MAT, MHS, HZBC, CTI, BN, EMA.

Literature Search: IE, MAT, MHS, HZBC, CTI, BN, EMA. Writing:

IE, MAT, MHS, HZBC, CTI, BN, EMA.

Copyright Transfer Form: Copyright Transfer Form was signed by all authors.

Peer-review: Internally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.