



## COMPARATIVE EVALUATION OF RISK FACTORS IN YOUNG AND MIDDLE-AGE PATIENTS WITH ACUTE ISCHEMIC STROKE

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### ABSTRACT

**Background:** Ischemic stroke (IS) in young adults has different etiologies and risk factors (RF). A better understanding of the contribution of potentially modifiable RF to the global burden of IS in young adults is crucial for successful prevention strategies.

**Objective:** To evaluate the incidence and prevalence of different RF in young and middle-age acute IS patients.

**Material and Methods:** In the study were included 63 patients with acute IS, admitted to the Neurology Clinic Pleven. They were classified in two groups: Group A (n=10) of young (18-44 y) and Group B (n=53) of middle-age (45-59 y) IS patients. Comparative evaluation of the following RF: age, sex, family history of stroke, arterial hypertension (AH), smoking, dyslipidemia, alcohol consumption, low physical activity, obesity and diabetes mellitus (DM) was done. The statistical analysis was performed with the Statistical Package for Social Sciences, version 24.0 (SPSS).

**Results:** Out of the 63 patients, 42 (66,7%) were males and 53 (84,1%) were 45-59 years old. No gender difference was found in group A, while in Group B, the prevalence of male patients (69,8%) was found, though statistically not significant (p=0.223). A first-degree family history of stroke had 30 (93.8%) of the middle-aged IS patients, as compared to only 2 of the young ones (6,3%), which was statistically significant (p=0.034). Group B showed prevalence of smoking (82,2%), alcohol consumption (83%), body overweight (90,5%), low physical activity (80%), AH (87,3%) and DM (87,3%).

**Conclusion:** The higher incidence of some RF in middle-age acute IS patients indicates that early identification and control of the RF is the best strategy for reducing stroke mortality and morbidity.

**Key words:** Ischemic stroke, risk factors, young and middle-age patients,

### INTRODUCTION

Stroke is a leading cause of death, physical and mental disability worldwide. Although stroke has been considered a privilege of the older population, recent data reveals the increasing number of “young” strokes [1, 2]. The incidence of IS in the age range 18-50 years is 10.8 to 100 000 population [3]. Approximately 10% of the young and middle-age IS patients remain severely disabled, half of them do not return to work with worsen quality of life thus causing serious economic consequences to their families and the society [4]. Annual expenses for treatment and rehabilitation of IS outpatients are assessed to 5.7 billion US dollars [4]. As the treatment of IS remains limited, the best approach to reduce stroke mortality and morbidity is the primary prevention through RF modification.

IS in young adults is considered a multifactorial disease involving genetic predisposition and a number of modifiable factors. The hypothesis that “young” stroke is associated only with rare RF is still under debate [1]. Regardless of the cumulating information that well-defined traditional RF are widely present in young male patients, undoubtedly IS in young adults has different etiologies and risk factors (RF) from the older population.

Although most of the RF for IS are potentially modifiable (smoking, low physical activity, irrational nutrition, alcohol consumption, dyslipidemia, hyperhomocysteinemia, asymptomatic carotid stenosis, AH, DM and others), their control and management are still a medical and social challenge.

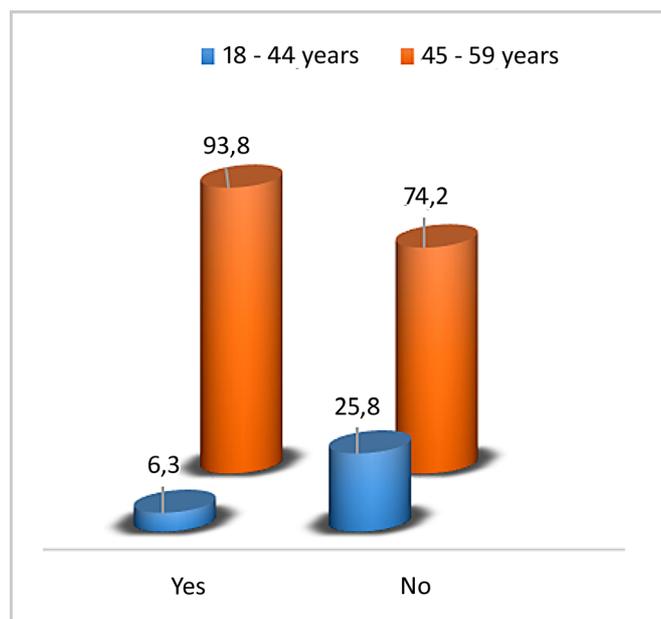
For the purpose of primary stroke prevention in young adults, a multidisciplinary approach, integrating innovative screening and educational programs for early identification and control of the specific modifiable RF, is recommended [3, 4, 5].

The aim of the present study was to evaluate the incidence and prevalence of different RF in young (18-44 y) and middle-age (45-59 y) acute IS patients.

## MATERIALS AND METHODS

In the prospective study initially were enrolled 80 patients with acute IS admitted to the Neurology Clinic of UMHAT “Dr Georgi Stranski” Pleven from September 2018 to September 2019. From the study were excluded 17 patients with rhythmic disorders, concomitant systemic, infectious and psychiatric diseases. The remaining 63 patients that fulfilled the inclusion criteria of the study were subdivided into two groups: Group A (n=10) with age range 18-44 years and Group B (n=53) with age range 45-59 years. All the patients were diagnosed with first or recurrent acute IS.

**Fig. 1.** Family history of IS



The experiments were conducted in accordance with the rules and regulations approved by the University Research Ethics Committee. Informed consent was obtained by the patients or their authorized relatives.

Detailed information concerning history of disease, family history, behavioral and risk factors, previous and concomitant medication, was collected.

The National Institute of Health Stroke Scale (NIHSS) was used to assess the neurological deficit on admission and the modified Rankin Scale (mRS) was used to evaluate the outcome at discharge.

All the patients underwent CT examination of the brain on admission. Routine blood tests were done on admission, including serum lipid profile (total cholesterol, LDL, HDL and triglycerides), blood glucose and C-reactive protein (CRP).

For the identification of RF for ischemic stroke different categorical and quantitative variables were used. The categorical variables (AH, DM, IS, family history of stroke, smoking, alcohol consumption, low physical activity, overweight) were defined by their absolute and relative frequency. The quantitative variables (LDL, HDL, CRP, blood glucose, systolic and diastolic blood pressure) were presented by median (Mdn), minimal and maximal values (Min÷Max). The statistical analysis was performed with the Statistical Package for Social Sciences, version 24.0 (SPSS). Pearson’s chi-squared test ( $\chi^2$ ) and Mann-Whitney U test were also used. A value of  $p \leq 0.05$  was considered statistically significant.

## RESULTS

Data concerning the distribution of patients by sex and age are given in Table 1. The results showed that 42 (66.7%) of the patients with IS were male and 53 (84.1%) were middle-aged. The incidence of stroke was similar for both sexes in the group of young patients (n=5; 50%) while 37 (69,8%) of middle-age cases were predominantly males, statistically nonsignificant difference ( $p=0.223$ ). Family history of stroke was found in 30 (93.8%) of the middle-aged patients with acute IS and only in 2 (6,3%) of the young ones ( $\chi^2=4.510$ ;  $df=1$ ;  $p=0.034$ ). (Fig.1)

**Table 1.** Distribution of patients with IS by sex and age (n, %)

Variable	n (%)	Variable	n (%)
<b>Sex</b>		<b>Age</b>	
<b>Male</b>	42 (66.7)	18-44 y	10 (15.9)
<b>Female</b>	21 (33.3)	45-59 y	53 (84.1)
<b>Total</b>	63 (100.0)	<b>Total</b>	63 (100.0)

The most common behavioral RF for IS (total and for the two subgroups) are presented on Table 2. Smokers dominated in the middle-age B group (n=45; 71,4%), though the difference was not statistically significant ( $p=0,380$ ). About 51% of the smokers had history of tobacco smoking >10 years. Comparatively higher (31,8%) was the number of young heavy smokers (>20 cigarettes/daily). Alcohol consumption was declared by 83% of the middle-age IS patients ( $p=0.869$ ), but everyday alcohol consumption was more common for the young IS patients (92,9%). Body overweight was more frequent in the middle-age patients (90,5%). Low physical activity (less than 30 min daily walking) had only 20 % of the young IS patients and 80% of the middle-age IS cases ( $p=0,619$ ).

**Table 2.** Distribution of the behavioral RF for acute IS (n, %), total and by groups.

Variable (n, %)	Total	Group A (18-44 y)	Group B (45-59 y)	p
Smoking (smokers)	45 (71.4)	8 (17.8)	37 (82.2)	0.513
Number of smoked cigarettes e"20 cigarettes/daily	26 (41.3)	20 (31.8)	6 (26.1)	0.380
Alcohol consumption (AC) Patients with AC	30 (47.6)	5 (16.7)	25 (83.3)	0.869
Frequency of AC Everyday AC	14 (22.2)	13 (92.9)	1 (7.1)	0.434
Body overweight Patients with body overweight	21 (33.3)	2 (9.5)	19 (90.5)	0.326
Low Physical activity (LPA) LPA	27 (42.9)	5 (18.5)	22 (81.5)	0.619

Data about the incidence and prevalence of traditional RF for ischemic stroke are given in Table 3. Hypertension was the major risk factor in 90% of the acute IS patients, 7 times more frequent in the middle-age (87,3%) compared to the young (12,7%) IS patients, though the difference was not statistically significant (p=0,073). Young patients had mean blood pressure (BP) 135/90 mmHg (systolic BP 110÷220 and diastolic BP

75÷120), while middle-age patients had mean BP 140/90 (systolic BP 110÷250 and diastolic 70÷130) (p>0,05). Diabetes had 20 (31,8%) patients with acute IS and it was more frequently associated with the middle-age cases (87.3%) (p=0.541). The lipid profiles of both groups were similar. Though CRP mean values were higher in group A (6.2; 1.4÷41.8) compared to group B (3.9; 0.5÷29.1), a statistical significance was not found (p=0.130).

**Table 3.** Distribution of the traditional RF for IS, total and by groups

Variable (n, %)	Total	Group A (18-44 y)	Group B (45-59 y)	p
Arterial hypertension (AH) Yes, present	55(87.3)	7(12.7)	48(87.3)	0.073
Diabetes mellitus (DM) Yes, present	20 (31.8)	4 (65.7)	16 (87.3)	0.541
Mean values of Total Cholesterol (Mdn, Min÷Max)	6,10 (3.6÷11.2)	6,10 (4.4÷9.5)	6,10 (3.6÷11.2)	0.836
Mean values of HDL (Mdn, Min÷Max)	1,20 (0.2÷2.4)	1,20 (0.8÷2.4)	1,10 (0.2÷1.9)	0.292
Mean values of LDL (Mdn, Min÷Max)	3,70 (1.6÷7.8)	3,50 (2.1÷5.7)	3,90 (1.6÷7.8)	0.586
Mean values of Triglycerides (Mdn, Min÷Max)	1,90 (0.4÷7.3)	1,20 (0.9÷5.1)	2,10 (0.4÷7.3)	0.176
Mean values of C-reactive protein (Mdn, Min÷Max)	4.0 (0.5÷41.8)	6,20 (1.4÷41.8)	3,90 (0.5÷29.1)	0.130

## DISCUSSION

In the present study we compared the incidence and prevalence of RF in young and middle-age acute IS patients. We found that in the middle-aged group male patients prevailed, while in the group of young patients both sexes had a similar frequency of IS (p=0.223). According to the study of Miri Lutski et al. the young patients with IS were predominantly male smokers with a family his-

tory of IS. [6] A research on 15 257 patients confirmed that the incidence of IS increased with age, but in young patients, less than 44 years old, it was higher for the female ones (53%) [7]. Although family history of stroke was defined as independent nonmodifiable risk factor, current data concerning the association between family history and the risk for developing IS have been controversial [8]. We found high percentage of first-degree fam-

ily history of stroke only in the middle-age IS patients (Group B).

Recently INTERSTROKE study proved the major role of the following RF for IS: current smoking, alcohol consumption, stress, low physical activity, irrational nutrition, obesity, dyslipidemia, DM, AH and cardiac diseases. All of them were defined as modifiable RF, responsible for 90% of strokes [9]. Our results demonstrated that arterial hypertension was the major IS risk factor (87,3%), followed by current smoking (71,4%); low physical activity (42,9%); body overweight (33,3%); diabetes mellitus (31,8%) and daily alcohol consumption (22,2%) (Table 2 and 3). This finding is different from the data published by Bettina von Sarnowski et al., where smoking was the leading RF (55,5%), followed by low physical activity (48,2%), AH (46,6%), dyslipidemia (34,9%) and obesity (22,3%) [5].

The risk of IS was found to be 2 to 4 times greater in smokers [10, 11], what is more, it was defined as dose dependent, especially for patients younger than 44 years [12]. In our study 71% of all the patients with acute IS were smokers, with a distinct prevalence of the middle-age patients.

Alcohol consumption was 5 times higher in the group of middle-age IS patients compared to the young ones ( $p=0.8369$ ). More than 90% of the young strokes declared everyday alcohol consumption, to as only 7 % of the middle-age cases ( $p=0.434$ ). Everyday alcohol consumption was associated with increased risk of IS [13], and that risk was greater for patients, younger than 65 years [14, 15]. A disadvantage of the present study was the lack of detailed information concerning the quantity and type of alcohol intake, which should be corrected in future prospective studies.

Obesity is considered a significant modifiable risk factor, especially for young IS patients [16]. According to our results, body overweight was found in 90% of the middle-age IS patients, not in the young ones.

Low physical activity is another risk factor for IS that offers an excellent option for primary prevention in young adults [17, 18, 19]. The prevalence of low physical activity in the middle-age group was 4 times higher than in young IS patients ( $p=0.619$ ).

AH was 7 times more frequent risk factor in the middle-age IS patients, compared to the young ones ( $p=0.073$ ). Recent data revealed that 41,8% from the Bulgarian population have AH and 72% of the patients with stroke have AH, too [20]. According to Michael McManus and David S Liebeskind AH is the major modifiable risk

factor present in about 84% of IS patients. [21]. Our results are identical with the published data, showing similar mean BP values of the compared groups with systolic BP on admission  $>140\text{mmHg}$  being registered in more than 50% [21].

DM is an important modifiable RF for IS as patients with  $\text{DM}<65$  years old have 5 times higher risk of IS compared to those without DM at the same age [22]. J. Putaala et al. also reported that younger patients with IS and DM had increased vascular risk [23]. We found that middle-age IS patients had a higher incidence of DM (87.3%), but statistically nonsignificant.

Dyslipidemia is associated with atherosclerotic plaque formation of the extra- and intracranial vessels, thus increasing the risk of IS [24, 25]. Dyslipidemia is intimately connected with cerebrovascular disease because of the strong dependence between the total cholesterol level ( $>7\text{mmol/l}$ ), LDL cholesterol and the risk of IS [26]. The comparative analysis of our patients' lipid profiles showed elevated total cholesterol ( $p=0.836$ ), lower HDL-cholesterol ( $p=0.292$ ) and higher LDL-cholesterol ( $p=0.586$ ) for both of the studied groups. Epidemiological studies have provided conflicting findings regarding the association of dyslipidemia with ischemic stroke [26].

C-reactive protein is a nonspecific biomarker of inflammation, being defined lately as a predictor of increased vascular risk for IS [27]. From our results young IS patients had higher mean values of CRP, compared to those of the middle-age group, but statistically nonsignificant ( $p=0,130$ ).

## CONCLUSION

Our results confirm data from previous research, but are limited by the small sample size. At the same time, some interesting relations were found. A prevalence of the modifiable risk factors as smoking, alcohol consumption, obesity, low physical activity, AH and DM was found in the group of middle-aged acute IS patients compared to the young ones. Alcohol consumption and heavy smoking were identified as significant risk factors for the young acute IS patients.

Future prospective large population-based studies could improve our basic knowledge on the potentially modifiable risk factors specific for young adults.

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