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Original Article

CORRELATIONS BETWEEN ACUTE ISCHEMIC STROKE AND ITS ASSOCIATED CARDIOVASCULAR DISEASES

Daniela Y. Arabadzhieva, Ara G. Kaprelyan, Zdravko D. Slavov[1], Zhaneta T. Georgieva[2], Aleksandra Zh. Tsukeva

First Clinic of Neurology, St. Marina University Hospital of Varna
[1]Chernorizets Hrabar Varna Free University, Varna
[2]Department of Propedeutics of Internal Medicine, St. Marina University Hospital of Varna

Summary

The objective of this study was to analyze the association between some cardiovascular diseases and acute ischemic stroke. A total of 258 acute ischemic stroke patients (mean age 70.59±7.22 years) were examined. The presence of eight cardiovascular diseases and pathological conditions was analyzed: arterial hypertension, hypertensive heart, atrial fibrillation, myocardial infarction, ischemic heart disease, effort angina pectoris, coronary atherosclerosis, and heart failure. Data were statistically processed by variation and correlation analysis. Most male and female patients presented with four accompanying cardiovascular diseases (27 or 20.93% and 31 or 24.03% of the cases, respectively). There were two groups of four variables each - with a relatively strong and a moderate, as well as with a weak correlation ($r<0.4$), to the presence of acute ischemic stroke in the corresponding patients. Ischemic heart disease was strongly associated with effort angina pectoris ($r=0.667$) and to a lesser extent - with coronary atherosclerosis ($r=0.470$), whereas myocardial infarction was associated with coronary atherosclerosis ($r=0.604$) and ischemic heart disease ($r=0.378$), respectively. Arterial hypertension was moderately related to hypertensive heart ($r=0.300$). In conclusion, there were relatively close associations between acute ischemic stroke and these heart diseases. These patients should strictly and regularly be followed up by general practitioners.

Key words: acute ischemic stroke, associated cardiovascular diseases, cardiovascular risk, correlation analysis

Introduction

There is rising evidence of the mutual relationships between cardiovascular and cerebrovascular diseases. In this respect, atherosclerosis, myocardial damage, ischemic heart disease (IHD), arterial hypertension (AH), and heart failure (HF) belong to the most socially important cardiovascular diseases and pathological conditions. They are closely related to the risks of development of stroke and of ischemic stroke (IS), in particular [1, 2]. In addition, emerging data suggest that left atrial disease may cause IS in the absence of atrial fibrillation (AF).

Corresponding Author:
Daniela Y. Arabadzhieva
First Clinic of Neurology
St. Marina University Hospital of Varna
1, Hristo Smirnenski blvd
Varna, 9010
Bulgaria
e-mail: d.arabadzhieva@abv.bg

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The purpose of this study was to analyze the association between some cardiovascular diseases and acute IS (AIS).

Materials and Methods

A total of 258 AIS patients (mean age 70.59±7.22 years, range 49-92 years) were examined. There were 129 males aged 69.60±7.80 years (range, 49-87 years) and 129 females aged 71.59±6.65 years (range 58-92 years). The diagnosis of AIS was confirmed by Doppler sonography and computed tomography of cerebral circulation. The presence of eight cardiovascular diseases and pathological conditions was analyzed: AH, hypertensive heart (HH), coronary atherosclerosis (CA), IHD, effort angina pectoris (AP), myocardial infarction (MI), AF, and HF.

Data were statistically processed by variation (ANOVA as *t*-criterion was considered significant if p<0,05) analysis and correlation (Pearson's coefficient) analysis as well. SPSS, version 13.0 software was applied.

Results

Distribution of the patients according to age is shown on Table 1. The number of AIS patients with a various number of other accompanying diseases is presented on Table 2. It is noteworthy that the absolute number and relative share of the patients with four, two and five accompanying cardiovascular diseases and pathological conditions prevailed.

Pearson's coefficients, illustrating the relationships between eight cardiovascular diseases among AIS patients, are presented on Table 3. They deal mainly with weak and moderate, positive and negative correlations. There were two groups of four variables each: with a relatively strong and a moderate, as well as with a weak correlation (r<0.4) to AIS presence in the corresponding patients. IHD was strongly associated with AP and to a lesser extent - with CA, whereas MI - with CA and IHD, respectively. AH was moderately related to HH.

Table 1. Age distribution of AIS patients

Age (years)	males		females		total	
	n	%	n	%	n	%
⩽60	8	6.20	6	4.65	14	5.43
61-65	33	25.58	21	16.28	54	20.93
66-70	36	27.91	27		63	24.42
71-75	22	17.05	36	27.91	58	22.48
76-80	19	14.73	27	20.93	46	17.83
⩾81	11	8.53	12	9.30	23	8.91
total	129	100.00	129	100.00	258	100.00

Discussion

Our study outlined the importance of enlarging the scope of cardiovascular diseases which are a possible risk for AIS among the adult population. Only 1.94% of our patients presented with a single cardiovascular disease. In contrast, there were four accompanying cardiovascular diseases in 22.48% of them, and two - in 20.15% of the AIS patients. It should be added that a special attention should be paid by general practitioners, cardiologists and their patients themselves to the correlations in AIS between IHD, on the one hand, and AP and CA, on the other hand (r=0.643 and r=0.363, respectively).

Numerous recent publications are devoted to the etiopathogenetic role of cardiovascular diseases for AIS. AIS is influenced by gender, age, and the brain site affected.

Demographics, prestroke conditions, etiology, subtypes, specific hospital outcome, clinical and laboratory parameters, and mortality rates were prospectively registered in 105 southern Italian patients [3]. Association of AIS

Table 2. AIS patients with a various number of other accompanying diseases

Number of diseases	Patients					
	males		females		total	
	n	%	n	%	n	%
no one	1	0.77	4	3.10	5	1.94
one	17	13.18	10	7.75	27	10.46
two	22	17.05	30	23.26	52	20.15
three	14	10.85	16	12.40	30	11.63
four	27	20,93	31	24.03	58	22.48
five	22	17.05	20	15.50	42	16.28
six	15	11.63	8	6.20	23	8.91
seven	11	8.53	7	5.43	18	6.98
eight	0	0	1	0.77	1	0.38
nine	0	0	2	1.55	2	0.77
total	129	100.00	129	100.00	258	100.00

Table 3. Correlations between eight cardiovascular diseases among 258 AIS patients

	AH	HH	CA	IHD	AP	MI	AF	HF
AH	1	0.166	-0.013	0.006	0.026	-0.007	0.096	0.040
HH	0.166	1	0.177	0.136	0.140	0.037	0.069	0.130
CA	-0.013	0.177	1	0.367	0.215	0.257	0.096	0.169
IHD	0.006	0.136	0.367	1	0.643	0.243	0.163	0.246
AP	0.026	0.140	0.215	0.643	1	0.073	0.021	0.228
MI	-0.007	0.037	0.257	0.243	0.073	1	0.019	0.081
AF	0.096	0.069	0.096	0.163	0.021	0.019	1	0.148
HF	0.040	0.130	0.169	0.246	0.228	0.081	0.148	1

with AH, diabetes mellitus and previous MI increased with age, whereas that with active smoking decreased with age, independently of sex and cerebral site.

The examination of 58 IS patients showed that left atrial dysfunction was an independent risk factor for IS even in patients without baseline AF [4]. The left atrial function index, a validated formula incorporating left atrial volumes at end-atrial systole and diastole, was the strongest predictor of IS. The study of 211 AIS patients aged 68±10 years showed that short stature was associated with occurrence of IS and diastolic dysfunction in patients with AF and preserved systolic function [5]. Height is a non-modifiable risk factor of IS and might be more important than obesity in Asian AF patients, who are relatively thinner than Western populations. The association between markers of left atrial abnormality and the subsequent risk of IS was examined among 6 741 participants in the Multi-Ethnic Study of Atherosclerosis, who were free of clinically apparent cerebrovascular or cardiovascular disease at baseline [6]. During a median follow-up of 8.5 years, IS was diagnosed in 121 participants and AF - in 541. There was an association between baseline P-wave morphology and incident IS even after accounting for AF suggesting that atrial cardiopathy could lead to IS in the absence of AF.

Data of 4 781 patients with AF from the National Health Insurance Research Database in Taiwan were analyzed in terms of IS risk and mortality [7]. The use of digoxin was associated with an increased risk of clinical events, with an adjusted hazard ratio of 1.41 (95% CI 1.17-1.70) for IS and 1.21 (95% CI 1.01-1.44) for all-cause mortality. Besides, digoxin was a risk factor for adverse events in patients without HF but not in those with HF (interaction $p<0.001$ for either end point).

IS occurrence was evaluated in 1 191 elderly treated AH patients aged between 60 and 90 years [8]. After adjustment for various covariables such as clinical signs, left ventricular hypertrophy and ambulatory blood pressure parameters, Cox regression analysis indicated that left atrial enlargement was significantly associated with increased risk of IS (hazard ratio 1.54; 95% CI 1.05-2.27; $p=0.03$) and represented an independent predictor of this disease. After mean follow-up of 3.19 years, 847 Chinese patients (21.82%) with nonvalvular AF without antithrombotic therapy developed IS (annual risk 9.28%, 95% CI 8.89%-9.70%) [9]. The annual risk of IS progressively increased with increasing CHADS2 and CHA2DS2VASc scores. Administration of aspirin and warfarin reduced the annual risk of IS by 18.7% and 52.7%, respectively ($p<0.05$). The CHADS2 and CHA2DS2-VASc scores for IS risk stratification were compared in 10 999 AF patients with end-stage renal disease undergoing renal replacement therapy [10]. The median (interquartile) CHADS2 and CHA2DS2-VASc scores were 3 (2-5) and 5 (4-7), respectively. IS occurred in 1 217 patients (11.7%), with an incidence rate of 6.9 per 100 person-years. In Cox regression models, the CHADS2 and CHA2DS2-VASc scores were significant predictors of IS.

Conventional risk factors for IS (i.e., cerebral infarction, embolism and small-vessel disease) were investigated with 5 935 AH patients during a community-based cross-sectional study in 60 communities in Shenzhen, China [11]. Total plasma homocysteine was significantly higher in IS patients than in non-IS male and female controls. Its greater level was dose-dependently associated with an increased risk of IS presence in both of them.

Twenty-nine single-nucleotide polymorphisms were genotyped in 3 677 IS cases and in 2 415 controls included in the Lund Stroke Register, the Malmö Diet and Cancer study and the Sahlgrenska Academy Study on Ischemic Stroke [12]. The analysis was conducted on the combined sample and separately for the three studies. After adjustment for AH, diabetes mellitus and smoking habits, the genetic risk scores were associated with IS in the combined sample and with similar trends in all three samples. A blood pressure genetic risk score was independently associated with IS risk in these Swedish case-control studies.

During an average follow-up of 19.0±5.1 months (0.6-26.8 months) of 373 patients with large artery atherosclerosis, a total of 69 (20.4%) cardiovascular events occurred in 339 IS patients [13]. Kaplan-Meier analysis showed that daytime systolic blood pressure variability was associated with cardiovascular outcomes in IS patients without rather than in those with diabetes mellitus.

The analysis of 249 consecutive patients (133 with and 116 without cerebrovascular disease) who required or underwent invasive cardiac treatment, failed to reveal any significant relationship with significant cerebrovascular stenosis in the patients with or without coronary artery disease [14]. The incidence of previous IS was significantly higher in the cerebrovascular disease group (12.8 versus 3.4%; $p=0.017$). A previous IS event had increased the odds (3.919; $p=0.006$) of having significant cerebrovascular stenosis.

Within the REGARDS study, a population-based cohort of 28 832 American adults aged $\geqslant$ 45 years were followed-up in terms of IS incidence [15]. A previous IS/transient ischemic attack ($p=0.0004$), diabetes mellitus ($p=0.03$), and AH ($p=0.046$) were associated with increased IS risk in participants with HF without AF. Among these participants, IS incidence was highest in those with previous IS/TIA and diabetes mellitus (2.4: 1.1- 4.0) per 100 person-years.

Knowledge of the cardiovascular health status of the inhabitants allows for the implementation of policies directed to reduce the burden of IS and cardiovascular diseases in Atahualpa, a rural village in coastal Ecuador [16]. The realization of a three-phase epidemiologic survey, the Atahualpa Project, determined the prevalence and incidence of IS and ischemic heart disease and improved the status of these people. The assessment of this status and the presence of the metabolic syndrome in Atahualpa (rural coastal Ecuador) residents aged $\geqslant$ 40 years with IS and ischemic heart disease demonstrated a poor

cardiovascular health status (according to the American Heart Association) in 87.5%, and metabolic syndrome in 58.3% of case-patients [17].

Systematic analysis of multiple databases to identify randomized controlled trials or observational studies devoted to the relations between the consumption of nuts and legumes and risk of IHD, IS, and diabetes mellitus indicated inverse associations between eating nuts and eating legumes, on the one hand, and incident IHD and diabetes mellitus and incident IHD only, respectively, on the other hand, but there was no association with IS at all [18].

Conclusions

We identified relatively close associations between AIS and some of these cardiovascular diseases in adult patients. These patients should strictly and regularly be controlled by general practitioners in order to avoid the development of IS.

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