THE COMPARED ANALYSIS OF THE NEUROLOGICAL EVOLUTION IN SUBJECTS THAT ASSOCIATE ACUTE MYOCARDIAL INFARCTION AND STROKE VS. STROKE ONLY SUBJECTS

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Cuvinte cheie: *infarct miocardic acut, accident vascular cerebral ischemic, factori de prognostic*

Rezumat: *Asocierea unui accident vascular cerebral ischemic (AVCi) la un infarct miocardic acut (IMA) poate fi considerată o consecinţă a ischemiei miocardice, dar şi o entitate separată de aceasta. Scop: De a aprecia evoluţia pe temen scurt (30 de zile) a subiecţilor care asociază un AVCi la un IMA la un interval de minim 1, maxim 6 zile de la instalarea IMA. Material şi metodă: Au fost incluşi 97 de subiecţi, între anii 2005-2008, împărţiţi în două grupe:grupul A-asociere de AVCi la un IMA; grupul B-grup case-control, subiecţi fără IMA, dar cu AVCi. Rezultate: Încărcătura de factori de risc vasculari nu diferă semnificativ între cele două grupe studiate. La analiza intra-grup, prezenţa bolii arteriale periferice, un raport cholesterol total/HDL-colesterol ridicat, precum şi fibrilaţia atrială post-IMA se corelează cu un status neurologic mai sever (p<0.05, CI95%). Asocierea la un IMA a unui AVCi în mod paradoxal conduce la o apreciere a statusului neurologic la 30 de zile (p<0.05, CI95%). Concluzii: Asocierea unui AVCi la un IMA nu reprezintă un factor de prognostic neurologic negativ pentru evoluţia pe termen, fără a influenţa semnificativ mortalitatea*

Keywords: *acute myocardial infarction, stroke, prognostic factors*

Abstract: *The association of stroke to acute myocardial infarction(AMI)may be considered either a consequence of the myocardial ischemia, or a separate entity.Purpose:To appreciate the short term(30-days)evolution of the subjects that associate an ischemic cerebral stroke to an AMI within minimum one and maximum 6 days from the onset of the myocardial infarction.Material and Methods:There were included 97subjects during 2005–2008,divided in two groups:group A–association of stroke to AMI; groupB–case control, subjects with stroke and no AMI.Results:The cardiovascular burden did not differ significantly in the two groups. In the intra-group analysis the presence of peripheral arterial disease, high total cholesterol/HDL-cholesterol ratio and post-AMI atrial fibrillation correlated to a more severe neurological status(p<0.05,CI95%).The association of stroke to the AMI paradoxically leads to an appreciation of the neurological status at 30 days(p<0.05,CI95%).The mortality did not differ significantly.Conclusions:The association of an ischemic stroke to a myocardial infarction is not a negative shot term neurological prognostic factor,without significantly influencing the mortality.*

INTRODUCTION

The association of myocardial infarction (MI) and cerebral ischemic stroke is known by at least a few decades, both entities playing a dual role of risk factors for each other. Epidemiological studies show that the link between the two is multi-factorial and represents mainly the catastrophic consequence of atherosclerosis (1,2).

The myocardial infarction is the principal cause of death world wide. Most of the complications of a myocardial infarction may be efficiently approached in clinical practice, resulting in a reduction in morbidity and mortality.

The etiology of a cerebral stroke as a complication of a myocardial infarction is well disputed. In the pre-trombolytic era, before the use of anticoagulants, the incidence of stroke was 2.4% in acute myocardial infarction (AMI) subjects (3). The studies of that epoch did not distinguish among hemorrhagic or ischemic strokes. Once with the development of AMI therapeutical approach, by the use of thrombolytics and anticoagulants, the incidence of cerebral stroke modified, by simply separating the two entities of ischemic and hemorrhagic strokes, as a consequence of the etiopathogenic mechanisms. Several studies report an incidence of 1.4% for ischemic strokes, 1.6% for hemorrhagic ones, whereas the hemorrhagic stroke was considered as a complication of the therapeutical approach of AMI (trombolysis, anticoagulation) (4,5,6).

The purpose of the hereby study is to appreciate the evolution of the neurological deficit at the subject that associates an AMI and a cerebral ischemic stroke in the first 6 days from the onset of the acute coronary syndrome compared to the subjects that suffer of only cerebral ischemic stroke, at short term (30 days).

MATERIAL AND METHODS

The design of the hereby study is an observational, case-control, longitudinal one, during a period of 3 years, 2005-2008, comprising a studied population of 97 subjects, composed of two groups of subjects admitted in the Neurology Clinic of Arad, Romania.

The inclusion criteria for group A were: subjects with AMI (clinical, enzymological and ECG confirmation) which associate within 24 hours up to 6 days an ischemic stroke, or a stroke in progression (positive clinic diagnostic, neurological status evaluation with persistence of neurological deficits more than 24 hours, CT scan, or MRI exam positive for ischemia). There were excluded he subjects that associated a stroke to an AMI at less than 24 hours because of high mortality (83%) reported in the literature (7).

The group B is a case-control group. The subjects that

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presented only cerebral ischemic stroke were selected by an aleatory manner, with respect to age groups and sex.

The subjects were evaluated at admission, 15 and 30 days using: neurological clinical exam, CT scan exam, or MRI exam, neurological deficit quantification using the NIHSS (National Institute of Health Stroke Scale), ECG, ankle-brachial index (ABI), blood pressure and laboratory tests.

RESULTS

The demographical data, the cardiovascular history, as well as some cardiovascular risk factors for the two groups are illustrated in table 1.

Table no. 1. Comparative presentation of the demographical data and of the cardiovascular disease historical, and of the vascular risk factors in the subjects of the two groups

		Group A		Group B	
No. of subjects (n)		47		50	
Male: female ratio		1.94:1		1.63:1	
Average age ± SD		64.17 ± 6.850		64.22 ± 6.891	
History of:		**n**	**%**	**n**	**%**
HBP		32	68.09	26	52.00
Dyslipidemia		9	19.90	6	12.00
Diabetes mellitus (DM)		18	37.60	8	16.00
Peripheral arterial disease (PAD)		22	46.80	16	32.00
Atrial fibrillation (FA)		5	10.64	9	18.00
Smoking status	Actual	15	31.91	18	36.00
	Never	20	42.55	23	46.00
	Ex-smoker	12	25.53	9	18.00

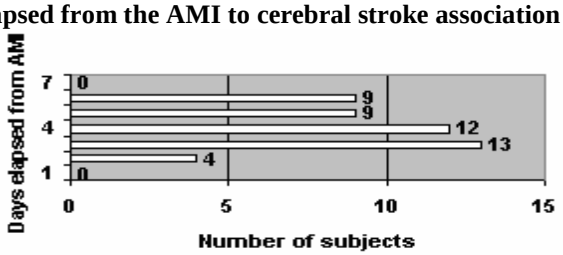
In the intra-group analysis, the following parameters have a negative predictor role in the evolution of the subjects of the two groups: ABI value, TC/HDL-c ration, AF associated to MI (table 2), and no influence at all for the prognostic of stroke at 30 days: history of AF, HBP, puls pressure, the Killip class and the ACS type (STEMI/nSTEMI).

In group A the STEMI ACS determines a 4 points on the NIHSS more severe neurological status at admission vs. nSTEMI ACS subjects (p<0.05, CI 95%, 1.541 la 6.435).

The topography of the stroke varies in the two groups. In group A most of the ischemic lesions are located in the territories of the ICA and the MCA (n=33), whereas in group B the rate of the vertebrobasilar (n=11 vs. 4) and ACA strokes (n=10 vs. 7) is much higher, but with no statistical significance.

The majority of subjects in group A (n=25, 53.2%) associated a stroke during the 3rd and the 4th day of evolution after the AMI, the lowest number strokes being in the 2nd day following the AMI (n=2, 8.5%) (graphic 1), with a median at 5.27.

Figure no. 1. The graphical representation of the subjects in group A in respect to the number of days elapsed from the AMI to cerebral stroke association



The analysis of the NIHSS scores in group A and B shows statistically significant differences in evolution (table 3) since the onset of stroke up to the 30th day of evolution:

- At admission group A subjects had an NIHSS score with in average 4 points lower than the control subjects (p<0.001, CI95%, -6.08 la -1.77);
- At 15 days of evolution there is always a 5 points advantage on the NIHSS for group A subjects (p<0.001, CI95%, -6.06 la -1.79);
- At 30 days of evolution there is a 3 points advantage on the NIHSS for group A individuals (p<0.001, CI95%, -4.19 la -1.27).

It is worth to notice that the history of HBP, DM, PAD certified by an ABI < 0.9, dyslipidemia did not alter in a significantly statistical manner the compared evolution of the two groups on the NIHSS scale. The group A subjects had a milder and a better neurological rehabilitation at 30 days, independently of other vascular risk factors, as illustrated in table 3.

The mortality was 6.40% (n=3) in group A vs. 4.00% (n=2) in group B, without a statistical significance. The mortality was not influenced by any of the studied parameters in this study.

DISCUSSIONS

The myocardial infarction represents the worldwide leading cause of death and the cerebral stroke the leading cause of disability (8,9).

The highest risk for stroke in AMI subjects is during the first month post-AMI (2.4%). A series of clinical studies and meta-analysis show that the incidence of stroke in AMI subjects with anticoagulant medication ranges between 0.7 – 25%. Less data are available for nSTEMI subjects. The OASIS study showed an incidence of 1.3% of stroke at 6 months after an AMI (10). The highest risk for a stroke following an AMI is during the first 30 days of evolution.

The mechanism through which the incidence of stroke following an AMI is constantly diminishing is partially known; the inflammatory response plays an important role in the extension of the atherogenic process (11), determining the instability of the atheroma. Another supposed mechanism is represented by the sympatic activation following an AMI which represents a promoter of the coagulation, by the augmentation of the expression of the factor VIII and the facilitation of the platelet aggregation, with a diminution of fibrinolysis (12) Other parameters are capable of influencing the evolution of a subject with stroke, with / without an associated AMI, determining a predictable cardio-vascular risk, as follows:

- Low ABI values are associated in the present study to an unfavorable neurological evolution at 30 days (2.2 points more severe on the NIHSS in group A vs. 4.1 in group B). Values less than 0.9 are associated to a higher risk for death and to a higher incidence of cardiovascular diseases, coronary disease, heart failure and PAD (13). The risk of death by any cause is 2 tp 4 times higher in subjects with ABI <0.9, and the risk for coronary disease increases 6 folds (14);
- the puls pressure (PP), measured as the difference between SBP and DBP at rest shows the arterial compliance. It was one of the monitored parameters in this study, but without having any statistical significant differences in the two groups. A PP>40 was met in 19 subjects (40.42%) in group A, with a mean value of 43.4 ± 12.03 vs. 47.5 ± 13.10 in group B, where a PP>40 was noticed in 50% of the subjects. Values higher than 40 are considered as suggestive markers for arterial rigidity due to atherosclerosis and lipohialinotic degeneration, but also to aortic regurgitation, arterial-venous malformations, or hyperthyroidism (15). An increase by 10 in PP leads to an increase in cardiovascular complications and death by 20% (16,17);

Table no. 2. Intra-group analysis: The impact of some monitored parameters on the short term (30 days) neurological evolution appreciated on the NIHSS in the studied groups

Parameter	Group	Mean NIHSS difference at 30 days	Confidence interval 95%		p
			Maximum	Minimum	
ABI < 0.9	A	2.206	.443	3.970	.015
	B	4.134	1.931	6.338	.000
TC/HDL-c*	A	2.342	.606	4.077	.009
	B	3.524	1.476	5.573	.001
AF post AMI	A	3.122	1.517	4.727	.000
	B	**	**	**	**

* cut-point value for group A at 5.4, the mean of the ratio for this groups and 5.9 for group B; ** not applicable.

Table no. 3. The comparison of the NIHSS scored in group A subjects vs. group B for the whole study length

Variable	Mean difference	Confidence interval 95%		p
		Minimum	Maximum	
NIHSS at admission	-3.925	-6.082	-1.767	.000
NIHSS at 15 days	-4.621	-6.613	-2.628	.000
NIHSS at 30 days	-2.727	-4.187	-4.187	.000

- the TC/HDL-c ratio – the results of the Prospective Studies Collaboration (PSC) and those of the Multiple Risk Factor Intervention Trial (MRFIT) underline that the absolute values for TC, HDL-c and LDL-c do not have a predictive value for the mortality by ischemic coronary syndromes, or cerebral ischemic stroke. Furthermore, a TC/HDL-c ratio above 4.6 has a predictive value for the cardio and cerebro-vascular mortality (6). This aspect is certified by the actual study, noticing that a high TC/HDL-c ratio represents a negative neurological prognostic factor for the studied group (see table 2);
- the history of AF – the Framingham Study reports an incidence of AF history in stroke subjects of 14.5% (7), and the International Stroke Trial (IST) an incidence of 17%, (18). In the present study the association of AF post-AMI represents a negative predictor factor (see table 2).

The results of the present study show that in the case of an AMI followed by a cerebral ischemic stroke at 24 hour, but not more than 6 days from the ACS onset, the short term neurological evolution (at 30 days) is better than the one of a subject that presents an isolated cerebral ischemic stroke, without an ACS. A possible explanation would be the concept of remote ischemic preconditioning, the vascular cerebral territory responding by a "defense reaction" secondarily to the late myocardial ischemic preconditioning cascade, protein dependent phase.

CONCLUSIONS

The data of the present study show that the short term clinical evolution, at 30 days, of the subjects that associate a cerebral ischemic stroke to an AMI, within 24 hours up to 6 days from the onset of the ACS, is more favorable when compared to the one of isolated cerebral ischemic stroke subjects and is independent of the influence of other vascular risk factors. Thus, the myocardial infarction becomes a positive prognostic factor for stroke subjects in this well limited context.

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