Risk factors of cerebral vasospasm after aneurysmal subarachnoid hemorrhage in different genders: a monocentric retrospective analysis

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Background

Cerebral vasospasm (CVS) is a feared complication in patients affected by aneurysmal subarachnoid hemorrhage (aSAH) and one of the principal causes of delayed neurological deterioration and cerebral ischemia after aSAH. The general incidence of CVS, according to literature, is around 40%, with a peak between the 4° and the 12° day after cerebral aneurysmal rupture with a resolution in the following 2-4 weeks. Its combined risk of death and disability is currently lower than 10%. At first the release of hemoglobin from subarachnoid spaces determines the acute activation of actin-myosin binding leading to vessel narrowing. However, «chronic» CVS seems associated to the endothelial disfunction due to inflammatory and thrombotic mechanisms, even in absence of elevated concentrations of calcium and adenosine triphosphate (ATP). This type of CVS is besides less responsive to the action of vasodilators and associated to vessel functional damages as well as to structural ones. Despite many studies have carried out on this topic there's still a high grade of uncertainty about which factors may influence this process.

Objectives

Our aim was to explore risk factors for CVS after SAH analysing laboratory, radiological and clinical possible biomarkers in our population and in the two genders.

Materials and Methods

We collected clinical, radiological and laboratory data of patients admitted to our Stroke Unit for aSAH from 2013 to 2025. We explored a series of possible risk factors in the whole population and then we differentiated the analysis in male and female population using Chi-squared test and Mann-Whitney test. Primary outcome was CVS, symptomatic and asymptomatic, defined by Lindegaard ratio and Sviri index, measured with transcranial doppler ultrasound.

1.0 Lindegaard ratio and Sviri index criteria

Results

We enrolled 214 patients, 126 women (mean age 58 years) and 88 men (mean age 56 years). In the general population CVS resulted associated with younger age (p <0,001), higher Fisher scale (p=0,003) and modified Fisher scale (p=0,002), drug abuse (p=0,047). Statins use before the event resulted associated with low risk of CVS (p=0,042). Of 23 women (18,2%) who developed CVS, 8 (34,7%) had prodromes, for example headache and nausea(p=0,026), and minor leak (p=0,011). We also observed a significant association with younger age (p=0,003) and a near significant association with nosocomial infections like pneumonia and urinary tract infections (p=0,08) and a high neutrophil to lymphocyte ratio (NLR) (p=0,052). In 11 men (12,5%) who developed CVS, there was an association with higher fibrinogen values (p=0,029) and platelets (p=0,026) count on admission and a near significant association with younger age (p=0,053).

1.1 General population

Variable	Population (n=214)	Vasospasm yes(n=34)	Vasospasm no(n= 180)	p-Value
Demographic features				
Gender, F	126	23	103	0,257
Mean Age	57 (23-91)	48,5	58	<0,001
Medical History				
Ipertension	99	11	88	0,076
Hyperlipemia	59	8	51	0,541
Diabetes	17	2	15	0,628
Cigarettes smoke	107	17	90	1
Drug abuse	7	3	4	0,047
Previous statins use	30	1	29	0,042
Clinical signs				
Prodromes	51	13	38	0,035
Minor leak	43	30	13	0,004
Hunt-hess				
0	2	0	2	
1	97	16	81	
2	68	10	58	0,98
3	33	6	27	
4	8	1	7	
5	5	1	4	
Radiological severity				
Fisher scale				
1	19	3	16	
2	62	2	60	
3	32	11	21	0,003
4	96	17	79	
M-Fisher scale				
1	79	5	74	
2	4	0	4	0,002
3	34	12	22	
4	94	16	78	
Complications Nosocomial infections	52	40	12	0,089

1.2 Genders

Variables	Males (n=88)	Vasospasm yes (n=11)	Vasospasm no (n=77)	p-value
Demographic features				
Mean Age	55	47	55	0,05
Medical History				
Ipertension	48	6	42	1
Hyperlipemia	25	1	24	0,129
Diabetes	10	1	9	0,8
Cigarettes smoke	46	7	39	0,42
Drug abuse	5	2	3	0,056
Previous statins use	12	0	12	0,159
Clinical signs				
Prodromes	28	5	23	0,29
Minor leak	22	5	17	0,094
Hunt-hess				
0	1	0	1	
1	51	6	45	0,367
2	21	3	18	
3	10	0	10	
4	3	1	2	
5	2	1	1	
Radiological severity				
Fisher scale				
1	11	1	10	
2	30	1	29	
3	10	4	6	0,083
4	35	5	30	
M-Fisher scale				
1	41	2	39	
2	2	0	2	
3	11	4	7	0,074
4	32	5	27	
Complications Nosocomial infections	21	3	18	0,64

Variables	Females (n=123)	Vasospasm yes (n=23)	Vasospasm no (n=103)	p-value
Demographic features				
Mean Age	59,5	50	61	0,003
Medical History				
Ipertension	51	5	46	0,043
Hyperlipemia	34	7	27	0,719
Diabetes	7	1	6	0,78
Cigarettes smoke	61	10	51	0,6
Drug abuse	2	1	1	0,241
Previous statins use	18	1	17	0,132
Clinical signs				
Prodromes	23	8	15	0,026
Minor leak	21	8	13	0,011
Hunt-hess				
0	1	0	1	
1	46	10	36	
2	47	7	40	0,59
3	23	6	17	
4	5	0	5	
5	3	0	3	
Radiological severity				
Fisher scale				
1	8	2	6	
2	32	1	31	0,015
3	22	7	15	
4	61	12	49	
M-Fisher scale				
1	38	3	35	
2	2	0	2	
3	23	8	15	
4	62	11	51	0,018
Complications Nosocomial infections	31	9	22	0,083

1.3 Laboratory data

Males with vasospasm (n=11)	Median	p-value
Basal crp	15,8	0,704
3d crp	19,1	0,645
Delta crp	0,2	0,297
Platelets	273000	0,026
Fibrinogen	486	0,029
NLR	0,2	0,406

Females with vasospasm (n=23)	Median	p-value
Basal crp	8	0,6
3d crp	28	0,3
Delta crp	22	0,04
Platelets	256500	0,63
Fibrinogen	322	0,579
NLR	0,262	0,09

Discussion

In our population we observed that patients with a higher risk of developing CVS were:

- Younger. This first data was already established by previous studies and seems to be due to arteriosclerosis typical of the elderly, leading to changes of reactivity, contractility and elasticity of cerebral arteries that might mitigate vessel narrowing and modify cerebral hemodynamic even before SAH. Moreover the weaker response in the older age to the physiological inflammatory triggers and the higher incidence of comorbidity like hypertension and hypervolemia would reduce the probability of cerebral ischemia induced by CVS.
- Affected by aSAH classified in the higher grades of Fisher scale and m-Fisher scale
- Women immediately after menopause. Probably because of the change of hormones profile and reduction of estrogens, notable vasodilators, developing in addiction more often prodromes and minor leak.
- Women with higher NLR and nosocomial infections. In fact high levels of cytokines in blood and cerebrospinal fluid would reflect the endothelial disfunction, that could be worsened by systemic inflammatory conditions. Women with these characteristics may need a strict monitoring
- Men with previous drug abuse
- Men with higher values of fibrinogen and platelets on admission.

Conclusions

CVS could be an important determinant of outcome after SAH and exploring its causes, drawing patients higher risk profiles, provides an opportunity for its prevention, monitoring and choice of more appropriate type of treatment. Its multifactorial aetiology suggests that therapies should be personalized on each patient, based on a wide variety of associated risk factors.

References

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