

Introduction

Delayed cerebral ischemia (DCI) is a major contributor to the high morbidity in patients with aneurysmal subarachnoid haemorrhage (aSAH). Spreading depolarizations may play a role in DCI pathophysiology. Migraine with aura (MA) increases the risk of ischemic stroke, possibly due to increased susceptibility to SDs in patients with migraine

In this study we investigated in a large prospectively collected cohort of aSAH patients whether patients with migraine are at increased risk of developing DCI compared with patients without migraine.

Conclusion

In the overall aSAH population we found no association between DCI development and history of migraine. However, we found an interaction between migraine and age suggesting that young migraine patients may have an increased risk of DCI.

Future studies with a larger number of young aSAH patients are needed to further study the association between migraine and DCI in this particular subgroup.

Results

In total, 809 patients were eligible for the study. Of these patients, 542 had complete data on both migraine and DCI and were included. Mean age of the included patients was 57 ± 13 (SD) years and 391 (72%) were women. (Table 1)

Patients with a history migraine were not at increased risk of developing DCI compared to patients without migraine (22% versus 28%, aHR: 0.78; 95% CI: 0.49 – 1.25). However, we found an interaction between migraine and age ($p_{\text{interaction}} = 0.011$). (Table 2)

Presence of DCI (n/N (%))	Migraine	No migraine	Migraine vs. no migraine
All patients (n=542)	23/103 (22%)	123/439 (28%)	0.78 (0.49 - 1.25)*
Women (n=391)	20/87 (23%)	94/304 (31%)	0.72 (0.43 - 1.21)
Men (n=151)	3/16 (19%)	29/135 (22%)	1.35 (0.39 - 4.61)
Age <50 years (n=142)	12/33 (36%)	26/109 (24%)	1.62 (0.77 - 3.42)
Age ≥50 years (n=400)	11/70 (16%)	97/330 (29%)	0.52 (0.27 - 1.00)

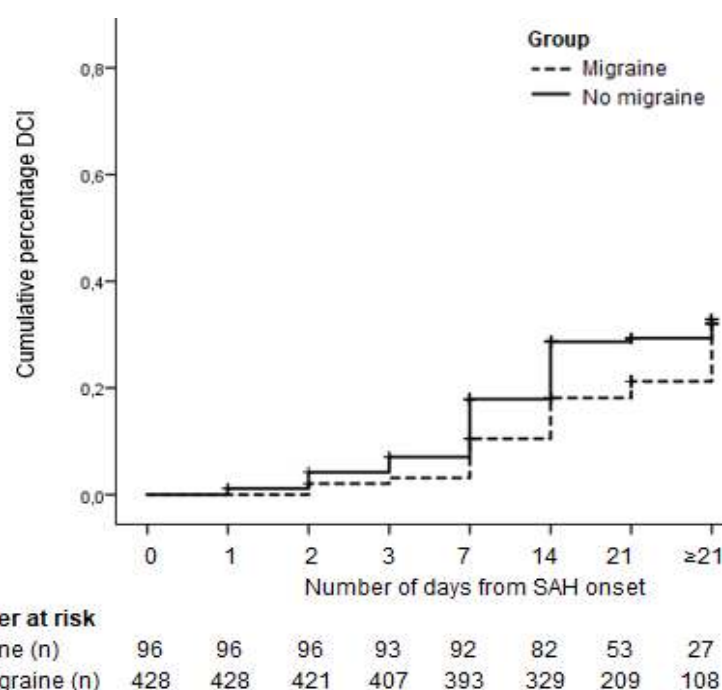


Table 2. Risk for delayed cerebral ischemia in patients with and without migraine, stratified by age and sex.

*Interaction between migraine and sex: $p = 0.376$ and between migraine and age (continuous): $p = 0.011$

Figure. DCI-free survival of patients with and without migraine

Characteristics	Migraine (n=103)	No migraine (n=439)
Demographics		
Age, mean years ± SD	55 ± 13	58 ± 13
Women, n (%)	87 (85%)	305 (69%)
History, n (%)		
Hypertension	36 (36%)	169 (39%)
Diabetes mellitus	4 (4%)	19 (4%)
Hyperlipidemia	16 (16%)	85 (20%)
Cardiovascular disease*	11 (11%)	45 (10%)
aSAH	5 (5%)	12 (3%)
aSAH in family history	3 (5%)	11 (5%)
Intracranial hemorrhage	1 (1%)	2 (1%)
Smoking: current**	22 (22%)	85 (20%)
Smoking: past**	52 (51%)	208 (49%)
Alcohol use**	50 (50%)	265 (63%)
Medication use, n (%)		
Oral anticoagulation	1 (1%)	10 (4%)
Oral contraceptive	10 (17%)	15 (9%)
Platelet aggregation inhibitor	11 (15%)	30 (12%)
GCS at admission (IQ range)	15 (13 - 15)	15 (13-15)
GCS at admission < 13, n (%)	16 (17%)	94 (23%)

Table 1. Clinical characteristics

Methods

We included patients from two university hospitals and one large teaching hospital. In all three participating centers research nurses recorded a migraine screener.

DCI was defined as the occurrence of focal neurological impairment or a decrease of at least 2 points on the Glasgow Coma Scale. The symptoms had to last for at least 1 hour, were not present immediately after aneurysm occlusion, and could not be attributed to other causes.

Because the development of DCI is time dependent we performed a survival analysis to investigate whether migraine is associated with occurrence of DCI. Adjustments were made for possible confounders (age, sex, GCS at admission) in a multivariable Cox regression analysis, and hazard ratios (HR) and adjusted HR (aHR) with 95% confidence intervals (CI) were calculated.

Acknowledgments

Prof. Dr. Wermer was supported by a personal Zon-Mw VIDI grant, a Dekker Junior Staff Member Grant from the Netherlands Heart Foundation (2011T055) and a Fellowship grant from the Netherlands Brain Foundation (F2014(1)-22).