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Differences in risk factors according to the site of intracranial aneurysms

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Abstract

Background and Purpose: Several risk factors for aneurysmal subarachnoid haemorrhage have been identified, but it is unknown whether some sites of aneurysms are linked to a specific risk factor. In a series of patients with aneurysmal subarachnoid haemorrhage, we compared risk factors according to the site of the ruptured aneurysm at the circle of Willis.

Methods: From our prospectively collected database of patients with aneurysmal subarachnoid haemorrhage admitted to our hospital between 2003 and 2007 we retrieved 304 patients with saccular aneurysms on the anterior communicating artery, middle cerebral artery, posterior communicating artery, basilar artery and vertebral artery. Risk factors (age, gender, smoking, no or excessive alcohol intake, hypertension and familial preponderance) were assessed per aneurysm location and compared with the anterior communicating artery as reference. We calculated odds ratios (ORs) and corresponding 95% confidence intervals (CI).

Results: In comparison with aneurysms at the anterior communicating artery, those at the middle cerebral artery were less associated with age > 55 years (OR 0.4; 95%CI 0.2-0.8), those at the posterior communicating artery were less associated with male gender (OR 0.4; 95%CI 0.2-0.9) and those at the basilar artery were more associated with no alcohol consumption (OR 5.8; 95%CI 1.1-29.9).

Conclusion: Risk factors differ according to the site of aneurysm. This heterogeneity should be kept in mind in studies on the aetiology of aneurysms, such as genetic studies.

Introduction

Risk factors for intracranial aneurysms and subarachnoid haemorrhage (SAH) include modifiable risk factors such as cigarette smoking, hypertension, excessive alcohol intake, and corticosteroid use; and non-modifiable factors such as age, female gender, positive family history, non-white ethnicity and heritable connective tissue disorder.[1-8]

In these studies on risk factors, all sites of intracranial aneurysms have always been considered together. Therefore it is unknown whether some risk factors predispose for aneurysms at a particular location, or whether some sites of aneurysms are linked to a specific risk factor. There are nevertheless indications that risk factors differ per site. Patients with a positive family history have more often an aneurysm at the middle cerebral artery (MCA) than patients without such a family history,[9] and men have been reported to have more often anterior communicating artery aneurysms than women (ACoA).[10]

We studied the relation between the prevalence of patient-related risk factors and site of aneurysm at the circle of Willis in patients with aneurysmal SAH.

Methods

Patient selection:

From the prospectively collected database of SAH patients admitted to the University Medical Centre Utrecht, we retrieved up to 75 patients per aneurysm location, from the period between January 2003 trough December 2007. We had calculated at beforehand that to find an OR of 2 with a confidence interval not including the neutral value (1.0), we needed 75 patients per aneurysm location. We used the following inclusion criteria: 1) SAH confirmed by computed tomography (CT) or lumbar puncture 2) ruptured saccular aneurysm identified on CT-angiography or conventional angiography 3) age at time of the SAH > 18 years 4) ruptured aneurysm located on the ACoA, pericallosal artery, T junction of the internal carotid artery (TCA), MCA, posterior communicating artery (PCoA), basilar artery (BA), and vertebral artery (VA). Posterior inferior cerebellar artery aneurysms were considered VA aneurysms and anterior inferior cerebellar artery aneurysms were considered BA aneurysms.

Patients with non-saccular aneurysms were excluded as well as patients with SAH and multiple aneurysms if there was any doubt about the location of the ruptured aneurysm. Furthermore, locations for which we could retrieve less than 20 patients with ruptured aneurysms were excluded from analysis.

Risk factors:

For all patients, information on age, gender, smoking, alcohol consumption, hypertension (>140/90 mmHg) and familial preponderance was retrieved from the database. If there was no information for a specific risk factor available, patients were excluded for that

particular analysis. Former smokers and sporadic alcohol consumers were excluded from the smoking- and alcohol analysis.

Data analysis:

Data was analyzed using SPSS. We calculated odds ratios (OR) with corresponding 95% confidence interval (CI) for the mentioned risk factors. We compared all locations to the ACoA, which is the most prevalent location for ruptured aneurysms in our database. Subsequently, a multivariate analysis was performed for variables with probability values <0.20 in the univariate analyses.

Results:

We were able to retrieve 75 patients for each of the following locations: ACoA, MCA and PCoA. For the BA only 42- and for the VA only 37 patients could be retrieved (table 1). The pericallosal artery and TCA were excluded from the analyses as < 20 patients were found for these locations.

Table 1: Baseline characteristics

	Total no of patients (%)	ACoA (%)	PCoA (%)	MCA (%)	BA (%)	VA (%)
No of patients	304 (100%)	75 (100%)	75 (100%)	75 (100%)	42 (100%)	37 (100%)
Age > 55 years	164 (53.9%)	47 (62.6%)	50 (66.7%)	30 (40%)	14 (33.3%)	23 (62.2%)
Men	75 (24.7%)	25 (33.3%)	13 (17.3%)	17 (22.7%)	14 (33.3%)	6 (16.2%)
Smoking (n=245)*						
Never	84 (34.3%)	25 (41.7%)	25 (39.0%)	19 (33.9%)	6 (17.6%)	9 (29.0%)
Former	21 (8.6%)	3 (5.0%)	7 (10.9%)	4 (7.1%)	3 (8.8%)	4 (12.9%)
Current	140 (57.1%)	32 (53.3%)	32 (50.0%)	33 (58.9%)	25 (73.5%)	18 (58.1%)
Alcohol (n=206)*						
Never	69 (33.5%)	15 (27.8%)	14 (31.1%)	20 (38.5%)	10 (34.5%)	10 (38.5%)
<1/day	59 (28.6%)	17 (31.4%)	10 (22.2%)	12 (23.1%)	12 (41.4%)	8 (30.8%)
1-3/day	52 (25.2%)	16 (29.6%)	16 (35.6%)	11 (21.2%)	3 (10.3%)	6 (23.1%)
>3/day	26 (12.6%)	6 (11.1%)	5 (11.1%)	9 (17.3%)	4 (13.8%)	2 (7.7%)
Hypertension (n=294)*	77 (26.2%)	19 (25.7%)	18 (24.7%)	20 (28.2%)	11 (26.8%)	9 (25.7%)
≥1 affected relative (n=198)*	5 (2.5%)	0 (0.0%)	4 (7.7%)	0 (0.0%)	1 (3.7%)	0 (0.0%)

*Less than 304 because of missing data

In the univariate analyses (figure 1) and compared with patients with ACoA aneurysms, those with BA aneurysms were less often older than the median age (OR 0.3; 95%CI 0.1-0.7) and smoked more often (OR 3.3; 95%CI 1.2-9.1); those with MCA aneurysms were less often older than the median age (OR 0.4; 95%CI 0.2-0.8), and those with PCoA aneurysms were less often men (OR 0.4; 95%CI 0.2-0.9). Other risk factors had no statistical significant relation with location of the aneurysm. The relation between men and ruptured MCA and VA aneurysms and between no alcohol users (teetotallers) and ruptured BA aneurysms had p-values < 0.2 and were therefore included in the multivariate analysis.

In the multivariate regression analysis, patients with MCA aneurysms were less often older than the median age (OR 0.4; 95%CI 0.2-0.8), those with PCoA aneurysms were less often men (OR 0.4; 95%CI 0.2-0.9), and those with BA aneurysms more often teetotallers (OR 5.8; 95%CI 1.1-29.9). The other associations found in the univariate analyses were no longer significant in the multivariate analysis: patients with MCA aneurysms were less often men (OR 0.6; 95%CI 0.3-13), patients with BA aneurysms were less often older than the median age (OR 0.5; 95%CI 0.2-1.3) en more often smokers (OR 2.8 95%CI 0.8-9.6) and patients with VA aneurysms were less often men (OR 0.4; 95%CI 0.1-1.0).

Discussion:

Some risk factors predispose for ruptured aneurysms at a particular location. Within the subset of patients with SAH, MCA aneurysms are less likely to occur in older patients, PCoA aneurysms are less likely to occur in men, and BA aneurysms are more common among teetotallers. Excessive use of alcohol and hypertension did not seem to influence the site of aneurysms.

MCA aneurysms occur more often in patients with a family history of SAH than in patients without a positive family history.[9] Patients with a positive family history are also of a younger age at time of SAH than patients without a positive family history. This may explain why in the current study, patients with MCA aneurysms were more often young than patients with ACoA aneurysms. In the present study, we found no relation between family history and site of aneurysms, possibly because of the small number of patients with a positive family history in our sample. This small number is explained by the fact that in the present sample not all families were scrutinized for a familial occurrence of SAH.[11]

Our study demonstrates that men have ruptured aneurysms more often at the ACoA compared to the PCoA. This same result was found by Park et al who did a gender comparison study about ruptured aneurysms.[10] We did not find other studies comparing the relation between different risk factors and site of aneurysms, so we could not further compare our results to those of the literature.

Some limitations can be noticed for this study. First, the relatively small number of posterior circulation aneurysms has limited the statistical power for posterior circulation aneurysms. Second, the prevalence of familial preponderance is low in our patient group,

therefore no clear conclusion can be made about the risk factor familial preponderance and preference for a specific location in this patient cohort.

This study was not designed to assess the influence of the studied risk factors on the development of aneurysms or on the risk of rupture of aneurysms. The conclusion that can be drawn from the results is that risk factors as age, gender and no alcohol consumption influence the site of the aneurysm. In other words, aneurysms at different sites differ not only in site but also in risk factors.

The formation of aneurysms is still a largely unknown process. Although this study shows that risk factors differ per aneurysm location, it should be kept in mind that these differences may not be the same for all genetic populations. Patients in our study were Western-European patients, and the results we found may not be the same for Japanese or Finnish patients. However, it seems likely that there are differences in the occurrence of risk factors per aneurysm location for these populations too. Lumping all aneurysms together may not be appropriate in genetic studies, and should therefore be regarded carefully.

List of abbreviations

ACoA = Anterior Communicating Artery

MCA = Middle Cerebral Artery

TCA = T junction of the internal Carotid Artery

PCoA = Posterior Communicating Artery

BA = Basilar Artery

VA = Vertebral Artery

CT = Computed Tomography

SAH = Subarachnoid Haemorrhage

OR = Odds Ratio

CI = Confidence Interval

Disclosure: The authors report no conflicts of interest.

Ethics committee approval: Approval was not applicable as this study used data from existing databases.

Reference List

(1) Feigin VL, Rinkel GJ, Lawes CM, Algra A, Bennett DA, van GJ, Anderson CS. Risk factors for subarachnoid hemorrhage: an updated systematic review of epidemiological studies. *Stroke* 2005;36:2773-2780.

(2) Clarke G, Mendelow AD, Mitchell P. Predicting the risk of rupture of intracranial aneurysms based on anatomical location. *Acta Neurochir (Wien)* 2005;147:259-263.

(3) Unruptured intracranial aneurysms: risk of rupture and risks of surgical intervention. International Study of Unruptured Intracranial Aneurysms Investigators. *N Engl J Med* 1998;339:1725-1733.

(4) Nahed BV, DiLuna ML, Morgan T, Ocal E, Hawkins AA, Ozduman K, Kahle KT, Chamberlain A, Amar AP, Gunel M. Hypertension, age, and location predict rupture of small intracranial aneurysms. *Neurosurgery* 2005;57:676-683.

(5) Rinkel GJ, Djibuti M, Algra A, van GJ. Prevalence and risk of rupture of intracranial aneurysms: a systematic review. *Stroke* 1998;29:251-256.

(6) Suarez JI, Tarr RW, Selman WR. Aneurysmal subarachnoid hemorrhage. *N Engl J Med* 2006;354:387-396.

(7) Wermer MJH, van der Schaaf IC, Algra A, Rinkel GJE. Risk of rupture of unruptured intracranial aneurysms in relation to patient and aneurysm characteristics: an updated meta-analysis. *Stroke* 2007;38:1404-1410.

(8) Ruigrok YM, Rinkel GJ. Genetics of intracranial aneurysms. *Stroke* 2008;39:1049-1055.

(9) Ruigrok YM, Rinkel GJ, Algra A, Raaymakers TW, van GJ. Characteristics of intracranial aneurysms in patients with familial subarachnoid hemorrhage. *Neurology* 2004;62:891-894.

(10) Park SK, Kim JM, Kim JH, Cheong JH, Bak KH, Kim CH. Aneurysmal subarachnoid hemorrhage in young adults: a gender comparison study. *J Clin Neurosci* 2008;15:389-392.

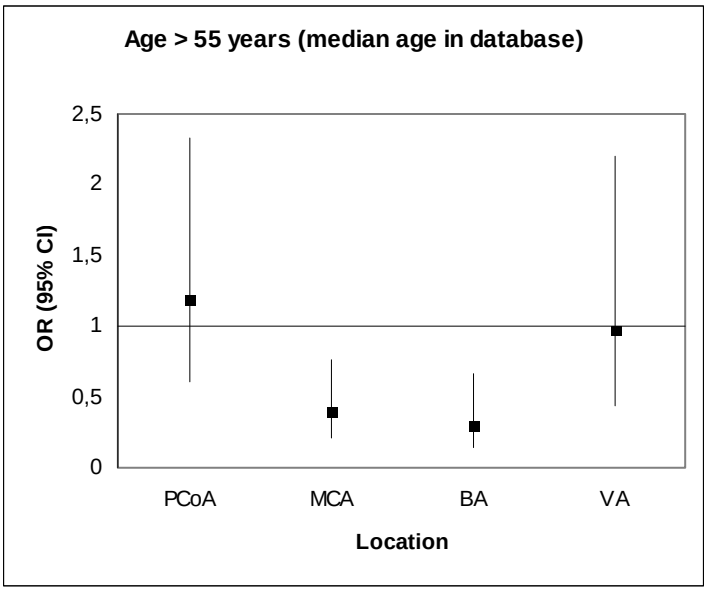
(11) Greebe P, Bromberg JE, Rinkel GJ, Algra A, van GJ. Family history of subarachnoid haemorrhage: supplemental value of scrutinizing all relatives. *J Neurol Neurosurg Psychiatry* 1997;62:273-275.

Figure legend

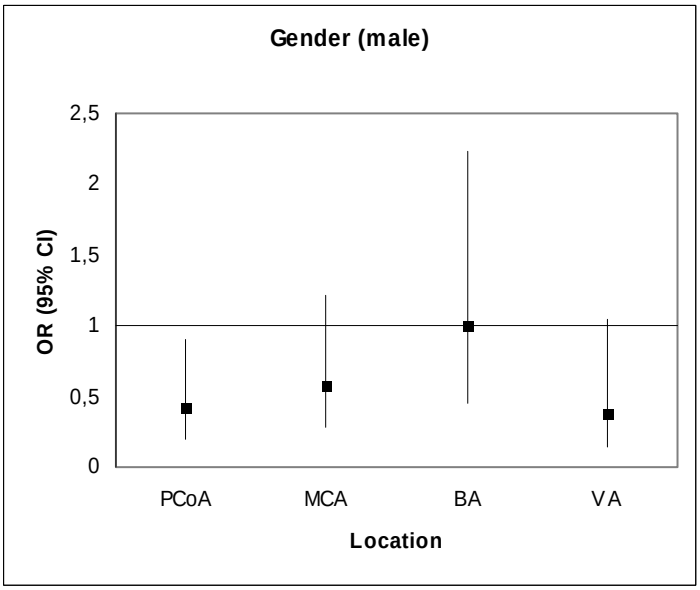
Figure 1 (A-F): Results univariate analyses showing OR and corresponding 95% CI for different locations with the ACoA as reference.

Figure 1

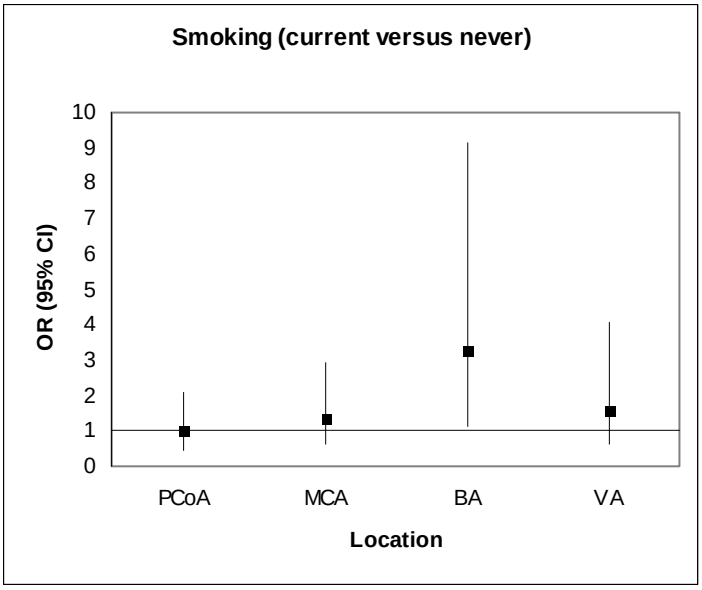
A)


Age > 55 years (median age in database)
OR (95% CI)
2,5
2
1,5
1
0,5
0
PCoA
MCA
BA
VA
Location

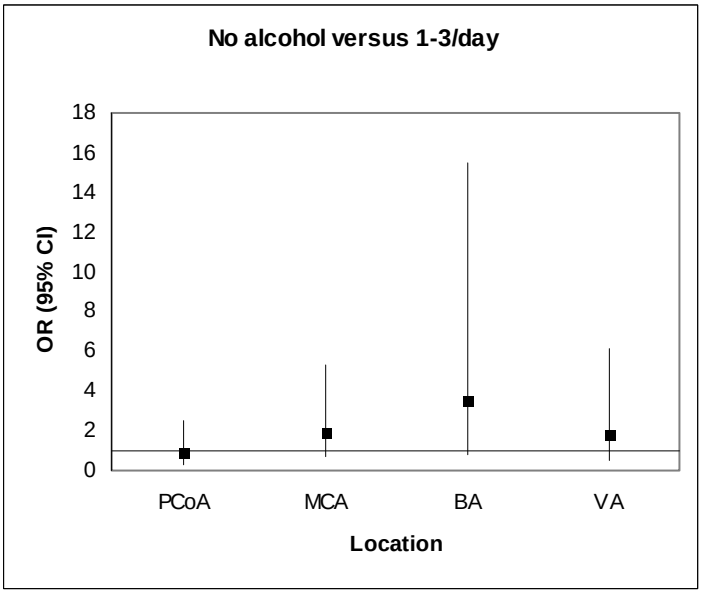
B)


Gender (male)
OR (95% CI)
2,5
2
1,5
1
0,5
0
PCoA
MCA
BA
VA
Location

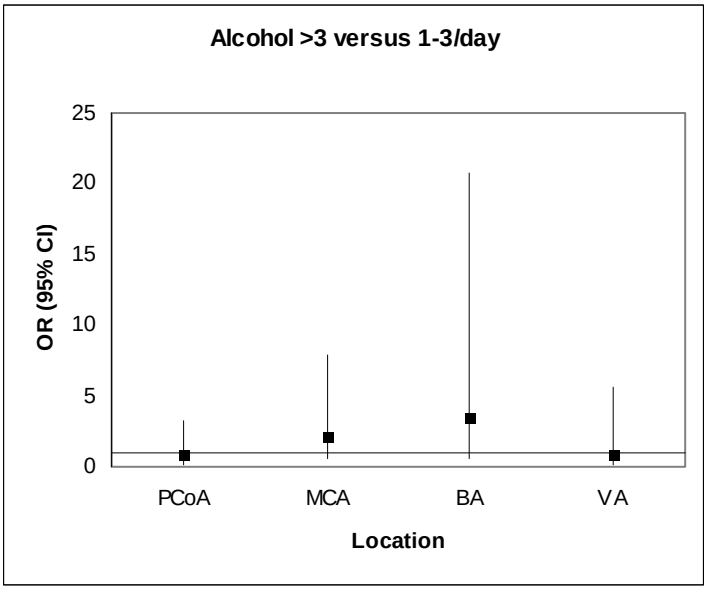
C)


Smoking (current versus never)
OR (95% CI)
10
9
8
7
6
5
4
3
2
1
0
PCoA
MCA
BA
VA
Location

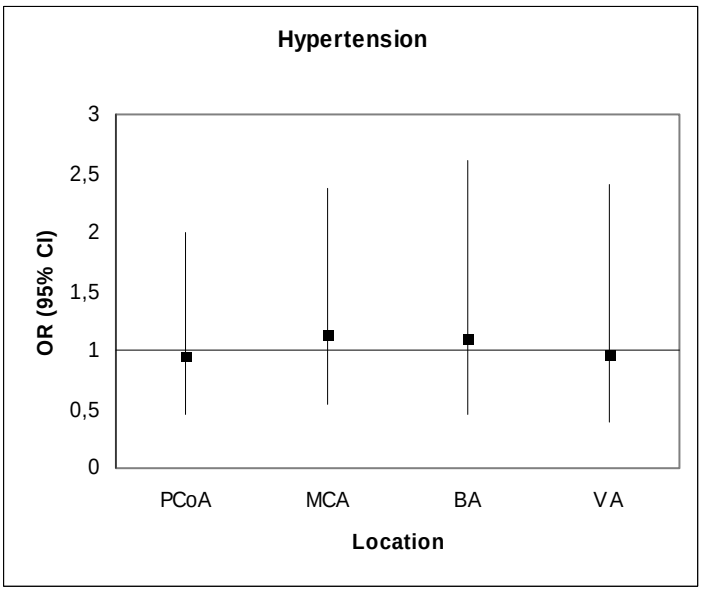
D)


No alcohol versus 1-3/day
OR (95% CI)
18
16
14
12
10
8
6
4
2
0
PCoA
MCA
BA
VA
Location

E)


Alcohol >3 versus 1-3/day
OR (95% CI)
25
20
15
10
5
0
PCoA
MCA
BA
VA
Location

F)


Hypertension
OR (95% CI)
3
2,5
2
1,5
1
0,5
0
PCoA
MCA
BA
VA
Location