Vascular risk factors and morphometric data in cervical artery dissection: a case-control study

Arnold, M; Pannier, B; Chabriat, H; Nedeltchev, K; Stapf, C; Buffon, F; Crassard, I; Thomas, F; Guize, L; Baumgartner, R W; Bousser, M G

Vascular risk factors and morphometric data in cervical artery dissection: a case-control study

Abstract

BACKGROUND: Limited knowledge exists on vascular risk factors, body height and weight in patients with spontaneous cervical artery dissection (sCAD). PATIENTS AND METHODS: In this case-control study, major vascular risk factors, body weight, body height and body mass index (BMI) of 239 patients obtained from a prospective hospital-based sCAD registry were compared with 516 age- and sex-matched healthy controls undergoing systematic health examinations in the Clinical and Preventive Investigations Center, Paris. Gender-specific analyses were performed. RESULTS: The mean body height was higher in sCAD patients than in controls (171.3 cm (SD 8.6) vs 167.7 cm (8.9); $p<0.0001$) and sCAD patients had a significantly lower mean body weight (67.5 (12.2) kg vs 69.3 (14.6) kg; $p<0.001$) and mean BMI (22.9 (3.3) kg/m2 vs 24.5 (4.2) kg/m2; $p<0.0001$) than controls. The overall frequency of hypertension, diabetes, current smoking, past smoking and hypercholesterolaemia did not differ significantly between sCAD patients and controls. The mean total plasma cholesterol level was identical in both groups (5.5 mmol/l, SD 1.1). Gender specific subgroup analyses showed similar results for men and women. CONCLUSION: Patients with sCAD had a higher body height and a lower body weight and BMI than controls, while major vascular risk factors were similar in sCAD patients and controls.

JNNP 2008/151324; Version: 3

Vascular Risk Factors and Morphometric Data in Cervical Artery Dissection: A Case-Control Study

Marcel Arnold, MD[1,3], Bruno Pannier, MD[2], Hugues Chabriat, MD[1], Krassen Nedeltchev, MD[3], Christian Stapf, MD[1], Frédérique Buffon, MD[1], Isabelle Crassard, MD[1], Frédéric Thomas, MD[2], Louis Guize, MD[2], Ralf W. Baumgartner, MD[4], Marie-Germaine Bousser, MD[1]

Assistance Publique, Hôpitaux de Paris, Department of Neurology, University Hospitals Lariboisière, Paris[1], and Clinical and Preventive Investigations Center (IPC), Paris[2], and Departments of Neurology, Inselspital, Bern University Hospital, and University of Bern,[3] and University Hospital of Zurich[4], Switzerland

Address:

Marcel Arnold

Service de neurologie

Hôpital Lariboisière

2, rue Ambroise Paré 75475

Paris Cedex 10, France

Phone: +33 1 49 95 25 97

Fax : +33 1 49 95 25 96

E-mail : marcel.arnold@insel.ch

Key words: cervical artery dissection; stroke in young adults; risk factors

Word count: 1479 words

ABSTRACT

Background: Limited knowledge exists on vascular risk factors, body height and weight in patients with spontaneous cervical artery dissection (sCAD).

Patients and methods: In this case-control study, major vascular risk factors, body weight, body height and body mass index (BMI) of 239 patients obtained from a prospective hospital-based sCAD registry were compared with 516 age- and sex-matched healthy controls undergoing systematic health examinations in the Clinical and Preventive Investigations Center, Paris. Gender-specific analyses were performed.

Results: Mean body height was higher in sCAD patients than in controls (171.3 cm (SD 8.6) versus 167.7 cm (SD 8.9); $p < 0.0001$) and sCAD patients had a significantly lower mean body weight (67.5 (SD 12.2) kg versus 69.3 (SD 14.6) kg; $p < 0.001$) and mean BMI (22.9 (SD 3.3) Kg/m^2 versus 24.5 (SD 4.2) Kg/m^2; $p < 0.0001$) than controls. The overall frequency of hypertension, diabetes, current smoking, past smoking, and hypercholesterolemia did not differ significantly between sCAD-patients and controls. Mean total plasma cholesterol level was identical in both groups (5.5 mmol/l, SD 1.1). Gender specific subgroup analyses showed similar results for men and women.

Conclusion: Patients with sCAD had a higher body height and a lower body weight and BMI than controls while major vascular risk factors were similar in sCAD patients and controls.

The aetiology of spontaneous cervical artery dissection (sCAD) remains poorly known. Several constitutional and environmental risk factors are thought to be associated with sCAD.[1] A previous case control study showed that hypertension tended to be associated with sCAD.[2] However, knowledge on risk factors in patients with sCAD is sparse and mainly based on case-control studies comparing sCAD patients with non-CAD stroke patients.[3,4,5,6] Furthermore, the relationship between body height, and body weight and sCAD has not been evaluated so far. Therefore we aimed to compare major vascular risk factors and morphometric data of sCAD patients with age- and sex-matched healthy controls.

METHODS

Patients

We analyzed prospectively collected data of consecutive patients presenting with sCAD at the University Hospital, Lariboisière, Paris from December 1996 through December 2005. CAD were categorized as spontaneous when occurring spontaneously or after an effort or minor trauma.[7] In addition to the physical and neurological examinations, all patients underwent routine blood examinations, cervical MRI with fat suppression technique, and MRA or DSA, or both. The definite diagnosis of sCAD was based on cervical MRI and MRA or digital subtraction angiography (DSA), or both.[8,9]

Clinical and imaging findings of some patients have been reported previously.[10,11,12]

Recruitment of Controls and Matching Procedure

Controls were randomly selected from healthy persons undergoing systematic health examinations at Investigations Préventives et Cliniques (IPC) Center, Paris.

The IPC subsidized by the French national health care system, offers all working and retired individuals and their families a free medical examination every 5 years. It performs about

25,000 health examinations per year for people living in the Paris area.[13]Two to 3 healthy controls examined during the same period than the dissection occurred in our patients, were randomly selected and matched to each case for age and sex. Selection of controls proceeded in a blinded fashion.

Morphometric data and vascular risk factors

Pre-admission vascular risk factors and morphometric data of patients were recorded from admission and hospital reports and by a structured interview with the patient or his relatives, if the patient was not able to provide adequate information. Healthy control subjects were investigated at the IPC Center, Paris, by a standardized autoquestionnaire and biological and clinical examinations. The questionnaire included information on body height weight, and body mass index (BMI) was calculated. The following vascular risk factors were assessed: Current and past smoking, hypercholesterolemia, hypertension, and diabetes mellitus. Hypercholesterolemia was defined as a total plasma cholesterol value of >5.2 mmol/l. Cholesterol level was measured under fasting conditions. Hypertension was defined as previous or current antihypertensive medication or a history of hypertension (systolic blood pressure (BP) >160 mm Hg or diastolic BP >95 mm Hg), or both.[14] The previous WHO definition of hypertension was used in this study in order to have a homogeneous definition during the whole observation period.[15] Diabetes mellitus was defined as a preadmission history of diabetes mellitus.

Statistical analyses

Statistical analyses were performed with the SPSS 10.0 for Macintosh program. For differences in categorical variables, $\chi 2$ test was performed. Continuous variables were compared with Mann-Whitney test.

Logistic regression analyses were performed to determine an independent association between sCAD and morphometric data and vascular risk factors. The variables included were sex, age, body height, body weight, BMI, current smoking, past smoking, diabetes, hypertension, hypercholesterolemia and total plasma cholesterol level. 95% Confidence intervals were calculated. After Bonferroni correction for 11 analysed variables, the two-sided significance level was defined as $p = 0.05/11 = 0.0045$.

RESULTS

The study includes 239 patients (50% women) with sCAD and 516 healthy controls.

Of the 239 patients with sCAD, 150 (63%) presented with internal carotid artery dissection (sICAD), 71 (30%) with vertebral artery dissection (sVAD), and 18 (7%) with both, at least one sICAD and sVAD.

The Table summarizes the results of univariate and multiple regression analyses comparing sCAD patients and controls. Mean body height was greater in sCAD patients than controls (171.3 cm (SD 8.6) versus 167.7 cm (SD 8.9); $p < 0.0001$), and mean body weight was lower in patients than in controls (67.5 kg (SD 12.2) versus 69.3 kg (SD 14.6); $p<0.0001$). BMI was lower in patients than in controls (22.9 (SD 3.3) versus 24.5 (SD 4.2); $p < 0.0001$). The overall frequency of the other variables did not differ between patients and controls.

Gender specific subgroup analyses showed similar results. Mean body height was significantly greater [$p < 0.0001$ for women (95% CI 0.843-0.936) and men (95% CI 0.855-0.941)] and mean body weight [p=0.011 for women (95% CI 1.009-1.075); p=0.003 for men (95% CI 1.016-1.080)]. Mean BMI [p=0.005 for women (95% CI 1.038-1.234); p=0.003 for men (95% CI 1.048-1.251)] was significantly lower both in female and male patients than in controls. The other variables did not either differ between female patients and female controls nor between male patients and male controls.

DISCUSSION

We found that patients with sCAD were taller, had a lower body weight and consecutively a lower BMI than healthy controls. This so far unreported association was observed both in men and women. In contrast major vascular risk factors were not associated with sCAD.

The relationship between taller stature and lower weight and sCAD is difficult to explain. Potential explanations include redundancies of cervical arteries[3] in taller subjects or mechanical factors such as increased neck mobility in taller subjects with a longer neck. However, this hypothesis cannot be proved by our data because the length of the neck was not measured, and no imaging was performed in controls. Genetic factors such as more frequent abnormalities of the connective tissue in taller subjects might be another explanation. Patients with Marfan's syndrome are known to be taller than the normal population.[16] However, in our sCAD patients only two women suffered from connective tissue disorders.

Interestingly, the literature on height and the risk of stroke in the general population is controversial. Herbert et al. observed no association between height and the risk of stroke.[17] In another study, taller men tended to have a lower risk of stroke.[18]

Although hypertension is a risk factor for stroke and aortic dissection,[19] it is not clear whether individuals with hypertension are at increased risk for sCAD. Pezzini et al. reported a trend towards a higher prevalence of hypertension in sCAD patients compared with matched controls.[3] We observed no significant association between hypertension and CAD in the present study. Further prospective population-based studies and large multicenter studies are needed to determine whether blood pressure is associated with sCAD.

Diabetes, smoking, hypercholesterolemia and total cholesterol levels were not associated with sCAD in the present study using healthy controls. Our results are difficult to compare with previous studies in which patients with ischemic stroke not related to dissection served as

controls.[1,4,5,6] Nevertheless, further large studies with healthy controls are needed to firmly exclude a weak association between sCAD and those vascular risk factors.

Our study has several limitations: Body weight and height were self-reported by patients. However, the validity of self-reported measurements of body weight has been shown.[20] Moreover, there may be a potential selection bias among controls. It may be possible that subjects undergoing systematic volunteer health examination do not represent the general population. However, comparison with French population based studies showed similar frequencies of vascular risk factors and similar morphometric data.[14,21,22] Finally, we analyzed only the main vascular risk factors and other potential risk factors such as ethnicity, C reactive protein, homocysteine, oral contraceptive use and migraine were not investigated.[1,5,23,24,25]

In conclusion, our study showed a significant association between sCAD and increased body height and lower body weight and lower body mass index. Our results support the lack of association between sCAD and major vascular risk factors.

Table. Demographics and potential risk factors in 239 patients with spontaneous cervical artery dissection and in 516 healthy controls

Characteristics	**Patients**	**Controls**	**P – value Univariate (95% CI)**	**P – value multivariate (95% CI)**
Sex, women (%)	119 (50%)	263 (51%)	0.763	
Mean age, years (SD)	44.4 (9.4)	44.4 (9.7)	0.983	0.216 (0.963-1.009)
Mean plasma cholesterol, mmol/l (SD)	5.5 (1.1)	5.5 (1.1)	0.785	
Mean body height (SD)	171.3 (8.6)	167.7 (8.9)	< **0.0001**	< **0.0001 (0.865-0.927)**
Mean body weight (SD)	67.5 (12.2)	69.3 (14.6)	0.312	< **0.0001 (1.025-1.070)**
Mean body mass index (SD)	22.9 (3.3)	24.5 (4.2)	< **0.0001**	< **0.0001 (1.1075-1.215)**
Current smoking	65/238 (27%)	163/516 (31%)	0.235	0.448 (0.760-1.862)
Past smoking	41/238 (17%)	96/516 (19%)	0.648	0.902 (0.611-1.747)
Hypertension	41/239 (17%)	80/516 (16%)	0.565	0.087 (0.365-1.071)
Diabetes mellitus	3/236 (1%)	6/508 (1%)	0.918	0.616 0.124-3.447)
Hypercholesterolemia	122/178 (68%)	332/515 (64%)	0.324	0.240 (0.497-1.191)

P indicates difference between subgroups by χ^2 test, Fisher's exact test or Mann –Whitney test in univariate and multiple regression analysis; CI, confidence interval

Acknowledgments: We thank Pietro Ballinari, PhD, Inselspital, University Hospital Bern, and University of Bern, Switzerland, for statistical analyses.

Competing interests: none

Funding: none

References

1.Rubinstein SM, Peerdeman SM, van Tulder MW, Riphagen J, Haldeman S. A systematic review of the risk factors for cervical artery dissection. Stroke 2005;76:1575-1580.

2.Pezzini A, Caso V, Zanferrari C, et al. Arterial hypertension as risk factor for cervical artery dissection: A case-control study. J Neurol Neurosurg Psychiatry 2006;77:95-97.

3.Barbour PJ, Castaldo JE, Rae-Grant AD, et al. Internal carotid artery redundancy is significantly associated with dissection. Stroke 1994;25:1201–1206

4.Grau AJ, Brandt T, Buggle F, Orberk E, et al. Association of cervical artery dissection with recent infection. Arch Neurol 1999;56:851–856.

5.Tzourio C, Benslamia L, Guillon B, et al. Migraine and the risk of cervical artery dissection: a case-control study. Neurology. 2002;59:435–437.

6.Guillon B, Berthet K, Benslamia L, Bertrand M, Bousser MG, Tzourio C. Infection and the risk of spontaneous cervical artery dissection: a case-control study. Stroke 2003;34:e79–e81

7.Caso V, Paciaroni M, Bogousslavsky J. Environmental Factors and Cervical Artery Dissection. In: Baumgartner RW, Bogousslavski J, Caso V, Paciaroni M, eds. Cerebral Artery Dissection. Basel: Karger;2005:47-53.

8.Ozdoba C, Sturzenegger M, Schroth G. Internal carotid artery dissection: MR imaging features and clinical-radiologic correlation. Radiology 1996;199:191–198.

9.Provenzale JM, Morgenlander JC, Gress D. Spontaneous vertebral dissection: clinical, conventional angiographic, CT, and MR findings. J Comput Assist Tomogr 1996;20:185-193

10.Arnold M, Kappeler L, Georgiadis D, et al. Gender differences in cervical artery dissection. Neurology 2006;67:1050-102.

11.Arnold M, Bousser MG, Fahrni G, et al.Vertebral artery dissection: presenting findings and predictors of outcome. Stroke 2006; 37:2499-2503.

12.Arnold M, Cumurciuc R, Stapf C, Favrole P, Berthet K, Bousser MG. 2006;67:1050-102. Pain as the only symptom of cervical artery dissection. J Neurol Neurosurg Psychiatry 2006;77:1021-1024.

13. Guize L, Thomas F, Panier B, Bean K, Danchin N, Benetos A. All-cause mortality associated with specific combinations of the metabolic syndrome according to recent definitions. Diabetes Care 2007;30:2381-2387.

14.Marques-Vidal P, Ruidavets JB, Cambou JP, Ferrieres J. Trends in hypertension prevalence and management in Southwestern France, 1985-1996. J Clin Epidemiol 2000;53:1230-1235.

15.Guidelines Subcommittee. World Health Organization-International Society of Hypertension guidelines for the management of hypertension. J Hypertens 1999;17:151-183

16.Erkula G, Jones KB; Sponseller PD, Dietz HC, Dieritz RE. Growth and maturation in Marfan syndrome. Am J Med Genet 2002;10:100-1015

17.Hebert PR, Rich-Edwards JW, Manson JE, et al. Height and incidence of cardiovascular disease in male physicians. Circulation 1993:88:1437-1443.

18.Walker SP, Rimm EB, Ascherio A, Wawachi I, Stampfer MJ, Willet WC. Body size and fat distribution as predictors of stroke among US men. Am J Epidemiol 1996;144:1143-1150.

19.Nienaber CA, Fattori R, Mehta RH, et al, on Behalf of the International Registry of Acute Aortic Dissection. Gender-related differences in acute aortic dissection. Circulation 2004;109:3014-3021.

20.Rimm EB, Stampfer MJ, Colditz GA, et al. Effectiveness of various mailing strategies among nonrespondents in a prospective cohort study. Am J Epidemiol 1990; 131 1068-71.

21.Yarnell JW. The PRIME study: classical risk factors do not explain the severalfold differences in risk of coronary heart disease between France and Northern Ireland. Prospective Epidemiological Study of Myocardial Infarction. QJM 1998;91:667-676.

22.Sykes DH, Arveiler D, Salters CP, et al. Psychosocial risk factors for heart disease in France and Northern Ireland: the Prospective Epidemiological Study of Myocardial Infarction (PRIME). Int J Epidemiol 2002;31:1227–1234.

23.Forster K, Poopert H, Conrad B, Sander D. Elevated inflammatory laboratory parameters in spontaneous cervical artery dissection as compared to traumatic dissection: a retrospective case-control study. J Neurol 2006; 253:741-745.

24.Pezzini A, Del Zotto E, Archetti S, et al. Plasma homocysteine concentration, C677T MTHFR genotype, and 844ins68bp CBS genotype in young adults with spontaneous cervical artery dissection and atherothrombotic stroke. Stroke 2002;33:664–669.

25.d'Anglejan-Chatillon J, Ribeiro V, Mas JL, Youl BD, Bousser MG. Migraine—a risk factor for dissection of cervical arteries. Headache 1989;29:560–561