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Cervical Artery Dissection (CeAD) in Physicians*Caspar Grond-Ginsbach^a, Christoph Lichy^{a,b}, Stephanie Debette^{c,d}, Didier Leys^d, Alessandro Pezzini^e, Tiina Metso^f, Turgut Tatlisumak^f, Henrik Gensicke^g, Stefan T. Engelter^{g,h}, for the Cervical Artery Dissection and Ischemic Stroke Patients (CADISP)-Study Group*

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The diagnosis of cervical artery dissection (CeAD) in two young colleagues prompted us to search for an association between CeAD and the medical profession. For this analysis we used data from the CADISP (Cervical Artery Dissection and Ischemic Stroke Patients) study [1]. First, we asked whether there were more physicians among CeAD-patients than among a comparison group of age- and sex-matched patients with ischemic stroke (IS) attributable to a cause other than CeAD (non-CeAD IS patients). Second, we evaluated whether characteristics of CeAD differed between physicians and patients with other occupations ('non-physicians').

The CADISP (Cervical Artery Dissection and Ischemic Stroke Patients) consortium enrolled 983 CeAD patients and 658 non-CeAD IS patients [1]. Baseline characteristics, clinical findings, risk factors, treatment, and 3-month outcome data were systematically assessed using a standardized questionnaire, as reported previously [2–4]. For the current study, patients' occupations were dichotomized in 'physicians' and 'non-physicians'. Patients with missing information on occupation were excluded from the analysis.

Among the 1,641 patients from the CADISP database, 828 CeAD patients and 549 non-CeAD IS patients were eligible for analyses. In the CeAD group, 26 patients were physicians (3.1%), compared to three physicians (0.6%) in the non-CeAD IS group ($p = 0.001$).

Compared to non-physicians with CeAD, physicians with CeAD presented less often with stroke (46.2 vs. 65.9%; $p = 0.041$) and more often with neck pain (72.0 vs. 48.8%; $p = 0.025$) or Horner syndrome (52.0 vs. 28.1%; $p = 0.013$). Moreover, physi-

cians were more likely to present with cervical fibromuscular dysplasia and with intracranial aneurysms (table 1). Physicians with IS due to CeAD were more often treated by thrombolysis than non-physicians (33.3 vs. 10.3%; $p = 0.020$). No significant differences were observed in baseline characteristics or risk factors between physicians and non-physicians of the CeAD cohort (table 1).

Our data suggest that (1) there are more physicians among CeAD patients than among non-CeAD IS patients and (2) CeAD with purely local symptoms was more common in physicians than in non-physicians. Moreover, we observed significant differences in the frequency of rare vascular anomalies (fibromuscular dysplasia, intracranial aneurysms) and in acute treatment between physicians and non-physicians. No differences in risk factors were identified to explain these differences. However, the absolute numbers were small and the sample underpowered to reliably detect associations. The BMI of CeAD patients was reportedly lower than that of healthy subjects [3]. Interestingly, in our CeAD cohort, there was a non-significant trend toward a lower BMI among physicians than among non-physicians (table 1: OR 0.88 [0.77–1.02]). Thus, one might speculate whether differences in constitution or life style between physicians and non-physicians might have contributed to our findings.

The observation that CeAD with purely local symptoms was more frequent among physicians than among non-physicians suggests that many CeAD events (in non-physicians) remained undetected. Indeed, it was recently hypothesized that CeAD with mild or transient symptoms may easily remain unrecognized [5].

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Conflicts of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Table 1. Physicians and non-physicians with CeAD

	Non-physicians (n = 802)	Physicians (n = 26)	p*	OR [95% CI]
Demographic characteristics				
Age	43.2±9.5	43.3±8.6	0.968	
Female sex	333 (41.5)	8 (30.8)	0.316	
Presenting symptoms				
Stroke	527 (65.7)	12 (46.2)	0.043	0.44 [0.20–0.97]
Purely local symptoms	177 (22.1)	12 (46.2)	0.007	3.00 [1.35–6.62]
Cervical pain	384 (49.2)	18 (72.0)	0.026	2.77 [1.13–6.76]
Headache	528 (67.7)	16 (64.0)	0.807	0.90 [0.39–2.10]
Horner syndrome	219 (28.1)	13 (52.0)	0.013	2.79 [1.24–6.29]
Vascular imaging				
VAD	306 (38.2)	5 (19.2)	0.059	0.38 [0.14–1.04]
Multiple CeAD	124 (15.5)	5 (15.4)	0.950	1.04 [0.35–3.07]
Occlusive CeAD	269 (33.5)	8 (30.8)	0.728	0.86 [0.37–2.01]
Cervical FMD	31 (5.0)	3 (16.7)	0.031	4.15 [1.13–15.3]
Pseudoaneurysm	99 (12.3)	4 (15.4)	0.652	1.28 [0.43–3.81]
Intracranial aneurysm	16 (2.8)	2 (12.5)	0.025	6.17 [1.25–30.4]
Risk factors				
Arterial hypertension	201 (25.3)	4 (15.4)	0.225	0.51 [0.17–1.52]
Hypercholesterolemia	150 (19.0)	3 (11.5)	0.307	0.52 [0.15–1.81]
Body mass index	24.5±4.0	23.4±2.1	0.084	0.88 [0.77–1.02]
Mechanical trigger event	338 (42.8)	14 (56.0)	0.218	1.66 [0.74–3.73]
For the subgroup of CeAD patients with IS				
n	527	12		
NIHSS on admission	3 [0–25]	9 [0–21]	0.228	1.05 [0.97–1.13]
Delay stroke/hospitalization	0 [0–45]	1 [0–21]	0.796	1.01 [0.93–1.10]
Excellent outcome	313 (62.6)	8 (72.7)	0.450	1.68 [0.44–6.44]
Thrombolysis	54 (10.3)	4 (33.3)	0.020	4.37 [1.27–15.1]

Age and body mass index were given as mean value ± standard deviation, stroke severity on admission (assessed by the National Institutes of Health Stroke Scale – NIHSS) and early functional outcome (assessed by the modified Rankin Scale – mRS-3m) were given as median value and [range]. All other variables were given as numbers and (percentages). Purely local symptoms were defined as Horner syndrome, cranial nerve palsy, or tinnitus, in line with prior research [4]; excellent outcome was defined as modified

Rankin Scale 0–1 after three months. Delay stroke/hospitalization was assessed in days.

VAD = Vertebral artery dissection; FMD = fibromuscular dysplasia; IS = ischemic stroke.

* Age and sex of study groups were compared without adjustment; all other items were analyzed between physicians and non-physicians by logistic regression analysis adjusted for age and sex.

Ethics

The CADISP-study protocol (<http://clinicaltrials.gov/ct2/show/NCT00657969>) was approved by relevant local authorities in all participating centers and the study was conducted according to the national rules concerning ethics committee approval and informed consent.

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References

- 1 Debette S, Metso TM, Pezzini A, Engelter ST, Leys D, Lyrer P, Metso AJ, Brandt T, Kloss M, Lichy C, Hausser I, Touzé E, Markus HS, Abboud S, Caso V, Bersano A, Grau A, Altintas A, Amouyel P, Tatlisumak T, Dallongeville J, Grond-Ginsbach C: CADISP-genetics: an international project searching for genetic risk factors of cervical artery dissections. *Int J Stroke* 2009;4:224–230.
- 2 Debette S, Metso T, Pezzini A, Abboud S, Metso A, Leys D, Bersano A, Louillet F, Caso V, Lamy C, Medeiros E, Samson Y, Grond-Ginsbach C, Engelter ST, Thijs V, Beretta S, Béjot Y, Sessa M, Lorenza Muiesan M, Amouyel P, Castellano M, Arveiler D, Tatlisumak T, Dallongeville J; Cervical Artery Dissection and Ischemic Stroke Patients (CADISP) Group: Association of vascular risk factors with cervical artery dissection and ischemic stroke in young adults. *Circulation* 2011;123:1537–1544.
- 3 Engelter ST, Grond-Ginsbach C, Metso TM, Metso AJ, Kloss M, Debette S, Leys D, Grau A, Dallongeville J, Bodenant M, Samson Y, Caso V, Pezzini A, Bonati LH, Thijs V, Gensicke H, Martin JJ, Bersano A, Touzé E, Tatlisumak T, Lyrer PA, Brandt T; Cervical Artery Dissection and Ischemic Stroke Patients Study Group: Cervical Artery Dissection: Trauma and other potential mechanical trigger events. *Neurology* 2013;80:1950–1957.
- 4 Engelter ST, Dallongeville J, Kloss M, Metso TM, Leys D, Brandt T, Samson Y, Caso V, Pezzini A, Sessa M, Beretta S, Debette S, Grond-Ginsbach C, Metso AJ, Thijs V, Lamy C, Medeiros E, Martin JJ, Bersano A, Tatlisumak T, Touzé E, Lyrer PA; Cervical Artery Dissection and Ischaemic Stroke Patients Study Group: Thrombolysis in cervical artery dissection – data from the Cervical Artery Dissection and Ischaemic Stroke Patients (CADISP) database. *Eur J Neurol* 2012;19:1199–1206.
- 5 Grond-Ginsbach C, Metso TM, Metso AJ, Pezzini A, Tatlisumak T, Hakimi M, Grau AJ, Kloss M, Lichy C: Cervical artery dissection goes frequently undiagnosed. *Med Hypotheses* 2013;80:787–790.