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ORIGINAL COMMUNICATION

University education and cervical artery dissection

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Abstract

Background and purpose We investigated whether university education is more likely in cervical artery dissection (CeAD)-patients than in age- and sex-matched patients with ischemic stroke (IS) due to other causes (non-CeAD-IS-patients).

Methods Patients from the Cervical Artery Dissection and Ischemic Stroke Patients study with documented self-reported profession before onset of IS due to CeAD ($n = 715$) or non-CeAD causes ($n = 631$) were analyzed. In the reported profession, the absence or presence of university education was assessed. Professions could be rated as academic or non-academic in 518 CeAD and 456 non-CeAD patients. Clinical outcome at 3 months was defined as excellent if modified Rankin Scale was 0–1.

Results University education was more frequent in CeAD-patients (100 of 518, 19.3%) than in non-CeAD-IS-patients (61 of 456, 13.4%, $p = 0.008$). CeAD-patients with and without university education differed significantly with regard to smoking (39 vs. 57%, $p = 0.001$) and excellent outcome (80 vs. 66%, $p = 0.004$). In logistic regression analysis, university education was associated with excellent outcome in CeAD-patients (OR 2.44, 95% CI 1.37–5.38) independent of other outcome predictors such as age (OR 0.97, 95% CI 0.84–0.99), NIHSS (OR 0.80, 95% CI 0.76–0.84) and local signs (OR 2.77, 95% CI 1.37–5.57).

Conclusion We observed a higher rate of university education in patients with CeAD compared with non-CeAD patients in our study population. University education was associated with favorable outcome in CeAD-patients. The mechanism behind this association remains unclear.

Keywords Cervical artery dissection · Ischemic stroke · Young adults · Outcome · University education · Level of education · Socioeconomic status

Introduction

Socioeconomic status (SES) and university education are inversely associated with incidence of stroke and mortality after stroke [1, 2]. Unfavorable socioeconomic conditions even during childhood were statistically related to ischemic stroke risk in adulthood [3, 4].

Cervical artery dissection (CeAD) is a common cause of stroke in younger adults aged 30–50 years [5, 6]. Therefore, the impact of SES and university education might be more relevant in this group of working age than in elderly stroke patients, the vast majority of whom are retired. However, the impact of SES and university education in CeAD is not well established and data are sparse and to some extent conflicting [5, 7, 8]. In Grau et al., CeAD was associated with high SES, while in Guillon et al. higher education was not [9, 10]. Another study on a largely overlapping sample showed that there are more physicians among young stroke patients with CeAD than among non-CeAD stroke patients [11].

Potential reasons for the association between SES and stroke are different distribution of vascular risk factors across the society, different awareness of a healthy lifestyle and different access to medical care, but a clear causality is yet not known [3, 12, 13].

CADISP (Cervical Artery Dissections and Ischemic Stroke Patients) Co-investigators are listed in Acknowledgements.

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However, CeAD is associated with lower rates of vascular risk factors and a healthy lifestyle including physical activity; this lifestyle might, in contrast, increase the risk of CeAD, e.g., due to trauma [5, 14, 15].

Here we aimed to investigate whether (1) an university education is more likely in CeAD-patients than in age- and sex-matched patients with ischemic stroke or TIA (IS) due to other causes (non-CeAD-IS-patients); and (2) whether university education is associated with outcome in CeAD patients.

Methods

Population

The Cervical Artery Dissection and Ischemic Stroke Patients (CADISP) consortium enrolled 762 CeAD-patients with IS and 658 non-CeAD-IS-patients [8, 16]. The latter group suffered ischemic stroke (IS) with a cause other than CeAD and were frequency-matched to CeAD-patients according to age (in 5-year intervals), sex, and center. CADISP enrolled patients across 18 centers in eight countries [8, 16].

Level of education, occupational status and income are common surrogates for SES [17]. In this study, we compare university education vs. non-university education. University education was assessed on the basis of the self-reported profession of the patients. Patients' profession was dichotomized according to whether the current position required a university education, i.e., university education, or not. In 74 cases, information on the profession was missing. In another 372 of 1346 patients, the documented profession did not allow classification into academic vs. non-academic education. Among non-classifiable professions were "housewife" ($n = 42$), "retired" ($n = 38$), or "unemployed" ($n = 29$) at the time of being registered. For this study, the documented profession of each patient was re-evaluated blinded to CeAD status by all participating CADISP centers to minimize misjudgment by the authors with respect to university education due to different training routes and different professional titles in participating CADISP countries. We further exclude CeAD-patients who present only with local signs but without stroke.

Local signs were defined as Horner's syndrome and/or pulsatile tinnitus and/or cranial nerve palsy. Body Mass Index was calculated according to the formula: weight (kg)/height^2 (m^2). Smoking was defined as never smoker and current smoker or former smoker. Severe trauma was defined as a trauma that prompted the patient to visit a doctor before onset of CeAD/non-CeAD Stroke. All other reported traumas were classified as mild. Outcome at 3 months was defined as excellent if the modified Rankin Scale (mRS) was 0–1.

Statistical analysis

CeAD-patients and non-CeAD-IS-patients were compared according to the baseline and clinical parameters with respect to university education. Normally distributed data were presented as mean and standard deviation (SD), non-normally distributed data as median and interquartile range. For categorical variables, counts and percentages were given. Data were compared with Student's t test, Mann–Whitney U test, or Fisher's exact test where appropriate (Table 1). Multivariable analysis was used to analyze predictors for university education. In the regression analysis, all significant parameters of the univariate analysis in Table 1 were included (Table 2). Logistic regression analysis was used to analyze predictors of excellent outcome in CeAD-patients after adjustment for age, sex, university education, NIHSS, local signs, and smoker (Table 3). Crude odds ratios (OR) with 95% confidence intervals (95% CI) and OR adjusted to potential confounders were calculated. A two-sided p value of < 0.05 was considered as statistically significant. Statistical analysis was performed with the Statistical Package for the Social Sciences, SPSS (SPSS Inc., 23.0 for Windows).

Ethics

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

Results

Statement of university education was available in 518 CeAD-patients and in 456 non-CeAD-IS-patients. Sensitivity analysis showed comparable results in demographic and baseline data between patients in whom statement of profession was available ($n = 974$) and in patients in whom statement of profession was not available ($n = 425$) (data not shown).

In the regression analysis, there was a non-significant association between CeAD and university education (OR 1.38, 95% CI 0.97–1.96, $p = 0.078$) adjusted to smoking (Table 2).

University education was more frequent in the CeAD group (100 of 518, 19.3%) than in the reference group (61 of 456, 13.4%, $p = 0.008$). The rate of university education in contributing countries ranged between 13.9 and 23.5%. CeAD-patients with and without university education

Table 1 CeAD patients' and non-CeAD patients' characteristics according to university education

	CeAD patients $n = 518$			Non-CeAD patients $n = 456$		p
	University education $n = 100$ (19.3%)	No university education $n = 418$ (80.7%)		University education $N = 61$ (13.4%)	No university education $n = 395$ (86.6%)	
Age	42 (12.2)	43 (9.2)	0.106	38 (10.5)	43.8 (9.7)	0.001
Male sex	40 (40%)	184 (44%)	0.270	42 (69%)	249 (63%)	0.400
Delay in admission to hospital (days)	3 (0, 7)	2 (0, 7)	0.380	0.73 (0, 1)	1.43 (0, 1)	0.68
NIHSS admission	2 (0, 6)	2 (0, 7)	0.831	2 (1, 5)	3 (1, 7)	0.15
Stroke	81 (81%)	352 (84.2%)	0.467	61 (100%)	395 (100%)	
TIA	19 (19%)	66 (15.8%)	0.360	n.a.	n.a.	
Local signs	28 (28%)	105 (25%)	0.325	n.a.	n.a.	
Hypertension	17 (17%)	96 (23%)	0.109	14 (23%)	138 (35%)	0.035
Trauma-mild	37 (37%)	155 (37%)	0.531	6 (9.8%)	41 (10.4%)	1.00
BMI	23.6 (3.4)	24.5 (3.9)	0.149	24.9 (3.5)	25.2 (4.8)	0.99
Migraine	41 (41%)	151 (36%)	0.219	16 (26%)	99 (25%)	0.87
Hyperlipidemia	18 (18%)	79 (19%)	0.520	6 (10%)	122 (31%)	0.001
Diabetes	2 (2%)	8 (2%)	0.577	5 (8%)	28 (7%)	0.641
Smoking	39 (39%)	238 (57%)	0.001	26 (43%)	280 (71%)	0.001
Excellent outcome	80 (80%)	276 (66%)	0.004	44 (72%)	266 (65%)	0.201

Numbers are counts and percentages or median and interquartile range

NIHSS National Institute of Health Stroke Scale, *TIA* transient ischemic attack, *BMI* Body Mass Index

Table 2 Regression analysis with university education as dependent variable adjusted to CeAD vs. non-CeAD and smoking

	OR	95% CI	p
CeAD vs. non-CeAD	1.38	0.97–1.96	0.078
Smoking	0.41	0.29–0.58	< 0.001

Table 3 Regression analysis with excellent outcome at 3 months (mRS 0–1) as dependent variable in CeAD-patients

	OR	95% CI	p
University education	2.44	1.37–5.38	0.027
Higher age	0.97	0.84–0.99	0.038
Male sex	0.61	0.34–1.10	0.09
NIHSS	0.80	0.76–0.84	< 0.001
Local signs	2.77	1.37–5.57	0.004
Smoking	1.40	0.80–2.47	0.244

All other variables were entered simultaneously as determinants into the logistic regression model

NIHSS National Institute of Health Stroke Scale, *BMI* Body Mass Index

differed significantly in terms of smoking (39 vs. 57%, $p = 0.001$), and excellent outcome (80 vs. 6%, $p = 0.004$) (Table 1).

Logistic regression detected university education as an independent predictor for excellent outcome in CeAD-patients (OR 2.44, 95% CI 1.37–5.38). The association between university education and outcome was independent from other significant outcome predictors such as age (OR 0.97, 95% CI 0.84–0.99), NIHSS (OR 0.80, 95% CI 0.76–0.84), local signs (OR 2.77, 95% CI 1.37–5.57) (Table 3).

Discussion

Our analysis showed an association of CeAD and university education—independent of vascular risk factors. University education was nearly twice as often in the CeAD-patients as in the non-CeAD-IS-patients. However, in the regression analysis, CeAD and university education were not significantly associated when adjusted to smoking. In addition, university education was associated with favorable outcome in CeAD patients.

Although our study does not allow any causality to be inferred, one might speculate that university education might be a surrogate for a more active lifestyle including increased physical activity, which might involve frequent sudden head movements causing distension of the cervical arteries that in turn predispose for CeAD. However, patients with a university education did not report mild trauma more often, and unfortunately, we do not have data on physical activity among our patients. The regression analysis for CeAD showed a non-significant trend between CeAD and university education when adjusted for smoking. This result suggest a more complex relation between CeAD and university education and the need for taking smoking as a confounder for (un-)healthy lifestyle into account. However, the impact of smoking as a well-known risk factor for stroke is most probably more relevant in the non-CeAD-IS-group than in the CeAD group. Thus, the result of this multivariate analysis might be driven by the impact of smoking in patients with strokes caused by other reasons than CeAD.

However, sports and other physical activities may still be the explanatory factors for the association between CeAD and university education. Patients with university education might have better access to medical treatment, and thus even minor symptoms such as headache or neck pain might trigger further diagnostics leading to the diagnosis of CeAD. As a consequence, CeAD might not be more frequent in academics but rather "underdiagnosed" in non-academic persons. Another possible bias might be that patients with university education are underrepresented in the non-CeAD-group, because lower socioeconomic status is associated with increased risk for vascular events. However, due to lack of a control group, we cannot consider with certainty whether the rate of patients with university education is relatively higher in CeAD-patients or relatively lower in non-CeAD-Patients compared with the general population. Both possibilities could provide alternative explanations for our results.

University education turned out to be an independent predictor of excellent outcome after CeAD with an OR of 2.44 after adjustment for potential confounders. In univariate analysis, an additional 14% of academics had a favorable outcome than non-academics (80 vs. 66%). The association of university education and better outcome might be driven—again—by better access to medical treatment and rehabilitation.

Our study has several limitations. In CADISP, data collection did not aim for detailed information with respect to education, profession and other surrogates of SES. Thus, dichotomization according to university education is only a rough classification. CADISP cannot provide data with respect to physical activity, thus all hypotheses about physical activity as an explanatory factor for CeAD are speculative. However, the strengths of this study are the large sample size of CADISP with multinational and multicenter data of CeAD patients and a matched reference group with ischemic stroke of young adults. Since studies of SES and university education and their impact on stroke and especially on CeAD are sparse, our analysis yielded some new findings.

Conclusion

University education was associated with CeAD in ischemic stroke of young adults along with a more favorable outcome in our study population. However, underlying mechanisms are as yet unknown and the impact of socioeconomic factors in CeAD and in ischemic stroke in general requires further investigations.

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Compliance with ethical standards

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

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