Published Ahead of Print on November 22, 2019 as 10.1212/WNL.0000000000008654

ARTICLE

Artery occlusion independently predicts unfavorable outcome in cervical artery dissection

Christopher Traenka, MD, Caspar Grond-Ginsbach, PhD, Barbara Goeggel Simonetti, MD, Tiina M. Metso, MD, PhD, Stéphanie Debette, MD, PhD, Alessandro Pezzini, MD, Manja Kloss, MD, Jennifer J. Majersik, MD, MS, Andrew M. Southerland, MD, MSc, Didier Leys, MD, PhD, Ralf Baumgartner, MD, Valeria Caso, MD, PhD, Yannick Béjot, MD, PhD, Gian Marco De Marchis, MD, MSc, Urs Fischer, MD, Alexandros Polymeris, MD, Hakan Sarikaya, MD, Vincent Thijs, MD, PhD, Bradford B. Worrall, MD, MSc, Anna Bersano, MD, PhD, Tobias Brandt, MD, Henrik Gensicke, MD, Leo H. Bonati, MD, Emmanuel Touzeé, MD, PhD, Juan J. Martin, MD, Hugues Chabriat, MD, PhD, Turgut Tatlisumak, MD, PhD, Marcel Arnold, MD, Stefan T. Engelter, MD,* and Philippe Lyrer, MD,* for the CADISP-Plus Study Group

Correspondence
Dr. Traenka
christopher.traenka@usb.ch

Neurology® 2020;94:1-11. doi:10.1212/WNL.0000000000008654

Abstract

Objective

To assess the impact of dissected artery occlusion (DAO) on functional outcome and complications in patients with cervical artery dissection (CeAD).

Methods

We analyzed combined individual patient data from 3 multicenter cohorts of consecutive patients with CeAD (the Cervical Artery Dissection and Ischemic Stroke Patients [CADISP]–Plus consortium dataset). Patients with data on DAO and functional outcome were included. We compared patients with DAO to those without DAO. Primary outcome was favorable functional outcome (i.e., modified Rankin Scale [mRS] score 0–1) measured 3–6 months from baseline. Secondary outcomes included delayed cerebral ischemia, major hemorrhage, recurrent CeAD, and death. We performed univariate and multivariable binary logistic regression analyses and calculated odds ratios (OR) with 95% confidence intervals (CI), with adjustment for potential confounders.

Results

Of 2,148 patients (median age 45 years [interquartile range (IQR) 38–52], 43.6% women), 728 (33.9%) had DAO. Patients with DAO more frequently presented with cerebral ischemia (84.6% vs 58.5%, $p < 0.001$). Patients with DAO were less likely to have favorable outcome when compared to patients without DAO (mRS 0–1: 59.6% vs 80.1%, $p_{\text{unadjusted}} < 0.001$). After adjustment for age, sex, and initial stroke severity, DAO was independently associated with less favorable outcome (mRS 0–1: OR 0.65, CI 0.50–0.84, $p = 0.001$). Delayed cerebral ischemia occurred more frequently in patients with DAO than in patients without DAO (4.5% vs 2.9%, $p = 0.059$).

Conclusion

DAO independently predicts less favorable functional outcome in patients with CeAD. Further research on vessel patency, collateral status and effects of revascularization therapies particularly in patients with DAO is warranted.

*These authors contributed equally to this work.

From the Department of Neurology and Stroke Center (C.T., G.M.D.M., A. Polymeris, H.G., L.H.B., S.T.E., P.L.), University Hospital Basel and University of Basel; Neurorehabilitation Unit (C.T., H.G., S.T.E.), University of Basel and University Center for Medicine of Aging and Rehabilitation, Felix Platter Hospital, Basel, Switzerland; Departments of Neurology (C.G.-G., M.K.) and Vascular and Endovascular Surgery (C.G.-G.), Heidelberg University Hospital, Germany; Department of Neurology (B.G.S., U.F., H.S., M.A.), University Hospital Bern; Ospedale San Giovanni (B.G.S.), Bellinzona, Switzerland; Department of Neurology (T.M.M., T.T.), Helsinki University Central Hospital, Finland; Department of Neurology (S.D.), Bordeaux University Hospital; Inserm U1219 (S.D.), Bordeaux; University of Bordeaux (S.D.), France; Department of Neurology (S.D.), Boston University School of Medicine, MA; Department of Clinical and Experimental Sciences (A.Pezzini.), Neurology Clinic, University of Brescia, Italy; Department of Neurology (J.J.M.), University of Utah, Salt Lake City; Departments of Neurology and Public Health Sciences (A.M.S., B.B.W.), University of Virginia Health System, Charlottesville; Univ-Lille (D.L.), Inserm U1171, CHU Lille, France; Neuro Center (R.B.), Clinic Hirslanden, Zurich, Switzerland; Stroke Unit and Division of Internal and Cardiovascular Medicine (V.C.), University of Perugia, Italy; Centre Hospitalier Universitaire Dijon Bourgogne (Y.B.), EA7460, Pathophysiology and Epidemiology of Cardio-Cerebro-Vascular Diseases, University of Burgundy, Dijon, France; Department of Neurology (H.S.), University Hospital of Zurich, Switzerland; Stroke Theme (V.T.), Florey Institute of Neuroscience and Mental Health, University of Melbourne, Heidelberg; Department of Neurology (V.T.), Austin Health, Heidelberg, Victoria, Australia; Cerebrovascular Unit Fondazione IRCCS Istituto Neurologico Carlo Besta (A.B.), Milan, Italy; Swiss National Accident Insurance Institution (T.B.), Lucerne, Switzerland; Normandie Université (E.T.), Université Caen Normandie, Inserm U1037, Department of Neurology, CHU Caen Normandie; Department of Neurology (E.T.), CH Sainte-Anne, University Paris Descartes, France; Department of Neurology (J.J.M.), Sanatorio Allende, Cordoba, Argentina; Department of Neurology (H.C.), Lariboisière Hospital, Paris, France; Department of Neurology (T.T.), Sahlgrenska University Hospital; and Department of Clinical Neuroscience Institute for Neuroscience and Physiology (T.T.), Sahlgrenska Academy at University of Gothenburg, Sweden.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Coinvestigators are listed at links.lww.com/WNL/B15.

Glossary

CADISP = Cervical Artery Dissection and Ischemic Stroke Patients; **CeAD** = cervical artery dissection; **CI** = confidence interval; **CIE** = cerebral ischemic events; **DAO** = dissected artery occlusion; **EVT** = endovascular therapy; **ICAD** = internal carotid artery dissection; **IQR** = interquartile range; **mRS** = modified Rankin Scale; **NIHSS** = NIH Stroke Scale; **OR** = odds ratio; **VAD** = vertebral artery dissection.

Cervical artery dissection (CeAD) is a major cause of ischemic stroke in young adults.[1] Mural hematoma in the cervical portion of the internal carotid or vertebral artery is a hallmark of CeAD. Its enlargement or local thrombosis at the site of dissection can lead to dissected artery occlusion (DAO), which was found in about one-third of patients with CeAD in prior studies.[2–5] In contrast to the reported prognostic significance of Horner syndrome or pulsatile tinnitus as local signs of CeAD,[5,6] little is known about the prognostic importance of DAO in CeAD. One observational study suggests worse outcome for patients with CeAD with DAO of the internal carotid artery compared to patients with artery occlusion due to atherothrombotic disease.[7] Another study identified DAO as a determinant of delayed stroke in patients with CeAD.[8] However, due to scarcity of comparisons of patients with CeAD with DAO vs those without DAO, it remains to be shown whether DAO independently determines outcome in CeAD.

In this study, we aimed to determine the effect of DAO on functional outcome in patients with CeAD based on analyses of the dataset of the Cervical Artery Dissection and Ischemic Stroke Patients (CADISP)–Plus consortium.[9,10]

Methods

Study population and data collection

The present study is based on data derived from the dataset of the multicenter CADISP-Plus consortium. This dataset currently comprises individual patient data of 2,526 patients with CeAD from 3 large clinical CeAD patient cohorts: (1) the CADISP-1 clinical study (n = 983), which recruited predominantly in European countries[11]; the CADISP-2 cohort (US centers, n = 411 patients); and the Paris-Lariboisière/Zurich/Bern CeAD registry (n = 1,132 patients). In the current study, only data from patients with data on outcome and presence or absence of DAO at baseline were included. The structure and methods of the CADISP-Plus consortium have been described in prior research.[10–12] In brief, patients with CeAD were evaluated and included in the cohorts at neurology departments mostly of tertiary care centers. Iatrogenic dissections were excluded and patients were evaluated according to standardized protocols.[9,12] In a previous study, meta-analyses of separate data of these 3 cohorts showed homogeneity of patient characteristics across cohorts, allowing pooling of data for further individual patient data analyses.[10] All sites contributing data to these clinical CeAD patient cohorts applied the same widely accepted diagnostic CeAD criteria and definitions of key variables described in prior research.[10,12] In brief, diagnostic criteria of CeAD were as follows (at least one): presence of a mural hematoma, aneurysmal dilation, long tapering stenosis, intimal flap, double lumen, or occlusion situated >2 cm above the carotid bifurcation revealing an aneurysmal dilation or a long tapering stenosis after recanalization.[1,11] These criteria were applied for diagnosis of internal carotid artery dissection (ICAD) or vertebral artery dissection (VAD) if suitable and had to be visualized by CT, MRI, or digital subtraction angiography.[12]

Study variables and patient clinical and radiologic characteristics

For the present study, the following data were derived from the CADISP-Plus dataset: (1) demographic data (age, sex); (2) site of dissection (internal carotid artery or vertebral artery); (3) baseline clinical symptoms (cerebral ischemic events [CIE], i.e., TIA or ischemic stroke, including stroke severity as measured by the NIH Stroke Scale [NIHSS]; Horner syndrome; pulsatile tinnitus; cervical pain; or headache); (4) presence or absence of putative CeAD risk factors (preceding mechanical trigger event); (5) history of migraine; and (6) vascular risk factors (hypertension, hypercholesterolemia, or diabetes). The definitions of these variables were described previously.[10–12] Presence or absence of DAO (in ICAD or VAD) at first imaging assessment was determined by individual site investigators and was derived from the CADISP-Plus database for the present analysis. No central adjudication of these findings was performed. All patients with CeAD included in the CADISP-Plus database had imaging-confirmed CeAD; however, there were no standardized (timing or modality) vessel imaging protocols to identify DAO. Performance of acute recanalization therapy (i.e., IV thrombolysis or endovascular therapy [EVT]; i.e., intra-arterial thrombolysis, mechanical thrombectomy, or stenting) as well as choice of antithrombotic therapy (i.e., antiplatelets or anticoagulants) were left to the discretion of the treating physicians and were derived from the database for the present analysis.

Outcome

Functional outcome was assessed between 3 and 6 months during outpatient visit or telephone interview using the modified Rankin Scale (mRS). In the present study, favorable outcome was defined as an mRS score of 0 or 1 (primary outcome) as done in prior research.[5] Data on (1) occurrence of CIE during follow-up, (2) recurrent CeAD, (3) major

hemorrhage (intracranial or extracranial), and (4) death during follow-up were recorded (secondary outcomes).

Statistical analyses

We compared patients with CeAD with DAO at baseline to those without. We compared baseline characteristics and clinical data between both groups using the χ^2 test or the Fisher exact test if appropriate for categorical variables and the Mann-Whitney test for continuous variables.

Primary outcome analyses

To assess the impact of DAO on functional outcome, we first performed univariate binary logistic regression analyses. Based on results from the comparisons of baseline characteristics and prior research on known predictors of outcome,[13,14] we performed multivariable binary logistic regression analyses including the following covariates and favorable outcome (i.e., mRS 0–1) as outcome measures: age, sex, stroke severity as measured by the NIHSS (in patients with CIE), and presence of DAO.

In secondary analyses, we included the following additional covariates in the primary multivariable logistic regression model: occurrence of (1) CIE, (2) recurrent CeAD, or (3) major intracranial or extracranial hemorrhage during follow-up.

In a third step, we performed the following sensitivity analyses using favorable outcome as outcome measure: (1) multivariable logistic regression as performed in the primary outcome analyses separately in patients with ICAD or VAD; (2) including presence of Horner syndrome and tinnitus, both known to predict favorable outcome in patients with CeAD,[5,6] in our primary multivariable logistic regression model in patients with ICAD; and (3) separate multivariable logistic regression analyses including age, sex, and DAO as covariates in patients with (1) no signs of cerebral ischemia, (2) TIA, or (3) ischemic stroke at baseline.

All statistical analyses were performed using SPSS version 25 (IBM; Armonk, NY). A p value <0.05 was considered statistically significant in all analyses.

Data availability

Datasets generated or analyzed during the current study are available from the corresponding author on reasonable request.[12] In each such case, compliance of data sharing with individual processes of patient consenting in participating centers will be reviewed.

Standard protocol approvals, registration, and patient consents

Protocols for the included clinical CeAD patient cohorts were approved by local authorities and ethics committees of all participating centers. Data collection and data analyses were conducted according to national rules of approval and informed consent of the included patients.

Results

Study population and baseline characteristics

Of the 2,526 patients with CeAD in the CADISP-Plus dataset, we included 2,148 patients with CeAD (85%) in whom data on functional outcome and presence or absence of DAO were available. Median age of the study population was 45 years (interquartile range [IQR] 38–52) and 43.6% of the population was women. DAO at first assessment was present in 728/2,148 patients (33.9%). In both groups, the majority of patients had ICAD (66.1% in patients with DAO and 63.5% in patients without DAO).

CIE at baseline were more frequent in patients with DAO than in patients without DAO (84.6% vs 58.5%, $p_{\text{unadjusted}} < 0.001$). Patients with DAO and ischemic stroke were also more severely affected than patients without DAO with ischemic stroke, as measured by the NIHSS (median NIHSS score [IQR] 4 [1–12] vs 1 [0–4], $p_{\text{unadjusted}} < 0.001$). Likewise, patients with DAO received acute recanalization therapies more frequently than did patients without DAO (16.5% vs 5.4%, $p_{\text{unadjusted}} < 0.001$). In turn, local signs (i.e., Horner syndrome, tinnitus, cervical pain) were significantly more common in patients without DAO (table 1). Vascular risk factors were equally common in both groups (table 1).

Outcome analyses

Primary and secondary analyses

Patients with DAO were less likely to have a favorable outcome when compared to patients without DAO (mRS 0–1 in 59.6% vs 80.1% of patients, $p_{\text{unadjusted}} < 0.001$, odds ratio [OR] [95% confidence interval (CI)] 0.36 [0.30–0.45]). In turn, the rate of CEI during follow-up time was higher in patients with DAO (4.5% vs 2.9%); however, this difference was not statistically significant ($p_{\text{unadjusted}} = 0.059$). In multivariable regression analysis including age, sex, and NIHSS score at baseline, DAO was independently associated with less favorable functional outcome ($\text{OR}_{\text{adjusted}}$ [95% CI] 0.65 [0.50–0.84], $p_{\text{adjusted}} = 0.001$). This association did not change in secondary multivariable regression analyses including the aforementioned covariates as well as CEI, hemorrhage, and recurrent CeAD during follow-up ($\text{OR}_{\text{adjusted}}$ [95% CI] 0.66 [0.50–0.88], 0.70 [0.52–0.94], $p_{\text{adjusted}} = 0.002$, tables 2 and 3).

Sensitivity analyses

We investigated the association of DAO and functional outcome separately for patients with ICAD and patients with VAD (excluding patients with multiple dissections; table 4). Favorable outcome was less frequent in patients with DAO with ICAD (patients with DAO 53.6% vs patients without DAO 80.3%, $p_{\text{unadjusted}} < 0.001$) or VAD (patients with DAO 68.8% vs patients without DAO 78.9%, $p_{\text{unadjusted}} < 0.001$). In multivariable regression analyses (including the same covariates integrated in the primary analyses), DAO was independently associated with less favorable outcome in

Table 1 Patient baseline characteristics and comparisons of patients with or without occlusion of the dissected artery

	All patients (n = 2,148)	Occlusion (n = 728)	No occlusion (n = 1,420)	p Value$_{unadjusted}$	OR$_{crude}$ (95% CI)
Sex, female, n (%)	936 (43.6)	289 (39.7)	647 (45.6)	0.009	0.79 (0.66–0.94)
Age, y, median (IQR)	45 (38–52)	46 (39–52)	45 (38–52)	0.019	NA
Internal carotid artery dissection, n (%)[a]	1,382 (64.3)	481 (66.1)	901 (63.5)	0.23	1.12 (0.93–1.35)
Vertebral artery dissection, n (%)[a]	860 (40)	275 (37.8)	585 (41.2)	0.125	0.87 (0.72–1.04)
CIE at baseline, n (%)	1,446 (67.3)	616 (84.6)	830 (58.5)	<0.001	3.91 (3.12–4.91)
NIHSS score at admission, median (IQR)	2 (0–7)	4 (1–12)	1 (0–4)	<0.001	NA
Horner syndrome, n (%)[b]	553/1,364 (40.5)	147/474 (31)	406/890 (45.6)	<0.001	0.54 (0.42–0.68)
Tinnitus, n (%)	162/2,122 (7.6)	35/719 (4.9)	127/1,403 (9.1)	0.001	0.51 (0.35–0.76)
Cervical pain, n (%)	1,030/2,120 (48.6)	314/719 (43.7)	716/1,401 (51.1)	0.001	0.74 (0.62–0.89)
Headache, n (%)	1,430/2,121 (67.4)	470/719 (65.4)	960/1,402 (68.5)	0.149	0.87 (0.72–1.05)
Mechanical trigger event, n (%)	741/2,130 (34.8)	229/722 (31.7)	512/1,408 (36.4)	0.033	0.81 (0.67–0.98)
Migraine, n (%)	677/2,127 (31.8)	203/724 (28)	474/1,403 (33.8)	0.007	0.76 (0.63–0.93)
Hypertension, n (%)	69/2,128 (3.2)	200/723 (27.7)	351/1,402 (25)	0.19	1.15 (0.94–1.40)
Hypercholesterolemia, n (%)	603/1997 (30.2)	220/684 (32.2)	383/1,313 (29.2)	0.167	1.15 (0.94–1.41)
Diabetes, n (%)	551/2,125 (25.9)	24/723 (3.3)	45/1,405 (3.2)	0.886	1.04 (0.63–1.72)
Acute recanalization therapy, n (%)	178/1927 (9.2)	109/660 (16.5)	69/1,267 (5.4)	<0.001	3.44 (2.49–4.72)
Secondary prophylaxis, antiplatelets, n (%)	765/2,117 (36.1)	262/720 (36.4)	503/1,397 (36)	0.862	1.02 (0.84–1.23)
Secondary prophylaxis, anticoagulants, n (%)	1,255/2,117 (59.3)	439/720 (61)	816/1,397 (58.4)	0.256	1.11 (0.93–1.34)

Abbreviations: CI = confidence interval; CIE = cerebral ischemic event; IQR = interquartile range; NA = not applicable; NIHSS = NIH Stroke Scale; OR = odds ratio.
[a] Numbers for internal carotid and vertebral artery dissection include patients presenting with multiple artery dissection.
[b] In patients with internal carotid artery dissection. Data may not be available for all patients, thus total numbers of patients for each variable may vary.

patients with ICAD ($OR_{adjusted}$ [95% CI] 0.53 [0.37–0.75], $p_{adjusted}$ = 0.001). In patients with VAD, however, this association could not be confirmed ($OR_{adjusted}$ [95% CI] 0.99 [0.65–1.50], $p_{adjusted}$ = 0.956).

In prior research, Horner syndrome and tinnitus have been shown to predict favorable outcome in patients with CeAD and ICAD. Thus we included these variables in our multivariable regression model using favorable outcome (mRS 0–1) as outcome measure (table 5). In patients with ICAD, Horner syndrome was independently associated with a more favorable outcome ($OR_{adjusted}$ [95% CI] 1.46 [1.01–2.10], $p_{adjusted}$ = 0.043). A nonsignificant association in the same direction (statistically nonsignificant) was seen for presence of tinnitus at baseline ($OR_{adjusted}$ [95% CI] 1.81 [0.84–3.88], p = 0.13). In this model (in patients with ICAD and including Horner syndrome and tinnitus as covariates), DAO remained independently associated with less favorable outcome.

We further performed univariate and multivariable (age, sex, DAO as covariates) regression analyses assessing the association of DAO and 3-month outcome (mRS 0–1) in patients with (1) no CIE, (2) TIA only, and (3) ischemic stroke only at baseline. In all separate groups, DAO significantly reduced the likelihood of favorable outcome in both univariable and multivariable analyses (table 6). In patients without CIE at baseline, post hoc analyses triggered by the aforementioned findings revealed a significantly higher number of patients with CIE during follow-up in patients with DAO (8/111; 7.2%) than in patients without DAO (3/574; 0.52%) (OR_{crude} [95% CI] 14.8 [3.9–56.6], p_{crude} < 0.001).

As detailed in table 7, patients with DAO were more likely to have a major hemorrhage during follow-up than were patients without DAO. Triggered by these findings, we further explored the distribution of acute recanalization therapies and secondary prophylaxis (antiplatelet vs anticoagulation) in patients with major hemorrhage (extracranial or intracranial) during follow-up stratified to the presence of DAO (table e-1, doi:10.5061/dryad.q5b3621).

Discussion

Our analyses based on a large compilation of individual patient data derived from CeAD patient cohorts investigating the

Table 2 Predictors of functional outcome (i.e., modified Rankin Scale [mRS] 0–1)

	Univariate analyses (mRS 0–1)		Multivariable analyses (mRS 0–1)	
	p Value	OR (95% CI)	*p* Value	OR (95% CI)
Age	<0.001	0.98 (0.97–0.99)	0.001	0.98 (0.97–0.99)
Sex	0.077	1.19 (0.98–1.45)	0.502	0.91 (0.70–1.18)
NIHSS at admission	<0.001	0.82 (0.80–0.84)	<0.001	0.83 (0.81–0.85)
Dissected artery occlusion	<0.001	0.37 (0.30–0.45)	0.001	0.65 (0.50–0.84)

Abbreviations: CI = confidence interval; NIHSS = NIH Stroke Scale; OR = odds ratio.

impact of DAO on outcome in patients with CeAD revealed the following key findings. First, patients with DAO expectedly differed from patients without DAO, with a higher rate of cerebral ischemic events and a lower rate of local symptoms at baseline. Second, and as a novelty, DAO was an important and independent predictor of unfavorable functional outcome.

DAO is common in patients with CeAD. The frequency of DAO in our study population (i.e., 1/3) is in line with prior research.[3]

In our study population, patients with DAO differed from patients without DAO with regard to presenting symptoms. Most importantly and as to be expected, cerebral ischemia at baseline was more frequent in patients with DAO. Intraluminal growth of the mural hematoma in the dissected artery leads to hemodynamic impairment and can ultimately lead to an occlusion of the affected artery.[15,16] Hemodynamic infarction or local thrombosis with later, secondary embolic infarction into distal arteries may consequently occur[7] and can be expected at a higher frequency than in patients without DAO with CeAD as in the latter cerebral perfusion is at least partially ensured. Thus, stroke mechanisms in patients with CeAD with and without DAO may differ while infarction in the latter is presumed to be due to primary embolism from the site of the dissection.[7,17] Compensatory recruitment of collaterals or favorable baseline collateral status may prevent hemodynamic infarction in case of acute occlusion of cervical arteries. Although there are no reports specifically investigating collateral status in patients with CeAD, one might assume that due to acute rather than gradual, chronic cerebral hypoperfusion, such collaterals are poorly developed and thus lead to a high rate of cerebral ischemia in DAO. Indeed, in a small study investigating recanalization of the dissected artery, presence of collaterals was associated with a higher likelihood of nondisabling ischemic stroke rather than severe disabling ischemic stroke.[18] Likewise, in VAD, the nonaffected contralateral artery might compensate for occlusion in the affected artery, an effect supported by our analyses in which worse outcome in patients with DAO was almost exclusively seen in ICAD rather than VAD. In the present study, patients with DAO with cerebral ischemia at baseline were also more severely affected as measured by a higher median NIHSS score at baseline. This is supported by the aforementioned differences in stroke pathophysiology in patients with vs without DAO with CeAD and data from prior research.[19] One prior study reported significantly larger cortical and subcortical infarcts with global involvement of the middle

Table 3 Multivariable regression analyses on favorable functional outcome including covariates

	Univariate analyses (mRS 0–1)		Multivariable analyses (mRS 0–1)	
	p Value	OR (95% CI)	*p* Value	OR (95% CI)
Age	See table 3		<0.001	0.97 (0.96–0.99)
Sex			0.209	0.83 (0.62–1.11)
NIHSS at admission			<0.001	0.80 (0.78–0.83)
Dissected artery occlusion			0.002	0.66 (0.50–0.88)
CIE during follow-up period	0.007	0.52 (0.32–0.84)	0.002	0.34 (0.17–0.67)
Recurrent CeAD during follow-up period	0.645	1.19 (0.56–2.53)	0.908	1.07 (0.32–3.56)
Major hemorrhage (intracranial or extracranial) during follow-up period	0.028	0.29 (0.1–0.88)	0.41	0.51 (0.10–2.55)

Abbreviations: CI = confidence interval; CeAD = cervical artery dissection; CIE = cerebral ischemic events; IQR = interquartile range; mRS = modified Rankin Scale; NIHSS = NIH Stroke Scale; OR = odds ratio.

Table 4 Sensitivity analyses: Outcome analyses on 3-month outcome in all patients with internal carotid artery dissection (ICAD) and vertebral artery dissection (VAD)

ICAD (total = 1,286 patients[a])	ICAD with occlusion (n = 453)	ICAD without occlusion (n = 833)	*p* Value	OR (95% CI)
Favorable outcome, n (%)	243 (53.6)	728 (80.3)	<0.001	0.29 (0.22–0.37)

	Univariate analyses (mRS 0–1)		Multivariable analyses (mRS 0–1)	
Predictors of outcome, ICAD	*p* Value	OR (95% CI)	*p* Value	OR (95% CI)
Age	0.966	1.00 (0.99–1.01)	0.443	0.99 (0.98 (1.01)
Sex	0.215	1.17 (0.91–1.50)	0.593	0.91 (0.64–1.30)
NIHSS at admission	<0.001	0.82 (0.79–0.84)	<0.001	0.83 (0.80–0.85)
Dissected artery occlusion	<0.001	0.28 (0.22–0.37)	0.001	0.53 (0.37–0.75)

VAD (total = 764 patients[a])	VAD with occlusion (n = 247)	VAD without occlusion (n = 517)	*p* Value	OR (95% CI)
Favorable outcome, n (%)	170 (68.8)	408 (78.9)	0.002	0.59 (0.42–0.83)

	Univariate analyses (mRS 0–1)		Multivariable analyses (mRS 0–1)	
Predictors of outcome, VAD	*p* Value	OR (95% CI)	*p* Value	OR (95% CI)
Age	<0.001	0.96 (0.94–0.97)	<0.001	0.96 (0.95–0.98)
Sex	0.27	1.21 (0.87–1.68)	0.787	0.95 (0.63–1.42)
NIHSS at admission	<0.001	0.83 (0.79–0.88)	<0.001	0.83 (0.79–0.88)
Dissected artery occlusion	0.003	0.59 (0.42–0.83)	0.956	0.99 (0.65–1.50)

Abbreviations: CI = confidence interval; mRS = modified Rankin Scale; NIHSS = NIH Stroke Scale; OR = odds ratio.
[a] All analyses performed excluding patients with multiple dissections at baseline.

cerebral artery territory in patients with DAO with CeAD compared to patients with stroke with atherothrombotic occlusion of the cervical ICA.[7] Another study comparing patients with stroke with nondissectional carotid stenosis to those with carotid occlusion also showed significantly more severe stroke in patients with artery occlusion.[20]

Contrary to the frequency of cerebral ischemia in patients with DAO in our population, local signs of CeAD were less frequent in patients with DAO when compared to patients without DAO. Horner syndrome in ICAD is assumed to result from local compression of the sympathetic plexus surrounding the affected artery.[21] In VAD, Horner syndrome is caused by brainstem ischemia.[4] Thus, with DAO being caused by intraluminal expansion of the mural hematoma rather than eccentric expansion, the differences in frequency of Horner syndrome in both groups can be explained in ICAD. While we have not investigated differential features of patients with DAO with ICAD and VAD, in a prior study, also including patients from the CADISP-1 cohort, DAO in VAD was more common in patients with Horner syndrome, which is supported by the different pathophysiology of Horner syndrome

Table 5 Sensitivity analyses: Multivariable regression outcome analyses in patients with internal carotid artery dissection (ICAD) (n = 1,382) including known predictors of favorable outcome

	Univariate analysis (mRS 0–1)		Multivariable analysis (mRS 0–1)	
	p Value	OR (95% CI)	*p* Value	OR (95% CI)
Age	0.949	1.00 (0.99–1.01)	0.343	0.99 (0.98–1.01)
Sex	0.249	1.15 (0.91–1.47)	0.556	0.90 (0.63–1.28)
NIHSS at admission	<0.001	0.82 (0.79–0.84)	<0.001	0.83 (0.81–0.85)
Dissected artery occlusion	<0.001	0.29 (0.23–0.37)	<0.001	0.54 (0.38–0.75)
Horner syndrome at baseline	<0.001	2.92 (2.23–3.82)	0.043	1.46 (1.01–2.10)
Tinnitus at baseline	<0.001	4.11 (2.29–7.37)	0.13	1.81 (0.84–3.88)

Abbreviations: CI = confidence interval; mRS = modified Rankin Scale; NIHSS = NIH Stroke Scale; OR = odds ratio.

Table 6 Sensitivity analyses: Multivariable regression outcome (modified Rankin Scale [mRS] 0–1) analyses in patients with no cerebral ischemia at baseline, TIA at baseline, and ischemic stroke at baseline

		Univariate analysis (mRS 0–1)		Multivariable analysis (mRS 0–1)[a]	
Group	**Outcome predictor**	***p* Value**	**OR (95% CI)**	***p* Value**	**OR (95% CI)**
No CIE at baseline	Occlusion of dissected artery	0.015	0.52 (0.30–0.88)	0.023	0.52 (0.30–0.91)
TIA	Occlusion of dissected artery	<0.001	0.33 (0.20–0.54)	<0.001	0.34 (0.21–0.56)
Ischemic stroke	Occlusion of dissected artery	<0.001	0.53 (0.41–0.69)	<0.001	0.55 (0.42–0.71)

Abbreviations: CI = confidence interval; CIE = cerebral ischemic events; OR = odds ratio.
[a] Adjusted for age and sex.

in ICAD and VAD.[5] Pulsatile tinnitus in CeAD is assumed to occur by local flow acceleration and turbulence at the site of dissection and thus cannot be expected in DAO.[6,22,23] In our sensitivity analyses, we included presence of Horner syndrome and tinnitus at baseline in our multivariable regression model (in patients with ICAD) and confirmed the predictive value of a more favorable outcome in patients with CeAD with these local signs present at baseline.

Most importantly, this study demonstrates that occlusion of the dissected artery independently predicts a less favorable functional outcome in patients with CeAD. In multivariable analyses including known predictors of less favorable outcome in patients with stroke (age, sex, NIHSS), DAO retains its strong, statistically significant predictive value. As shown in a prior study, DAO may be a risk factor for delayed ischemic events in patients with CeAD.[8] Indeed, we identified more ischemic strokes or TIAs during follow-up in patients with DAO at baseline. Likewise, major hemorrhage was more common in patients with DAO during follow-up. We included these covariates as well as occurrence of recurrent CeAD in our multivariable sensitivity analyses, yet DAO remained a strong independent predictor of less favorable functional outcome. Interestingly, in our multivariable sensitivity analyses, we confirmed these results in separate subgroups of patients without (1) any cerebral ischemia at baseline, (2) TIA at baseline, and (3) stroke at baseline. In particular, in those patients without ischemia or TIA at baseline, this is a remarkable finding, suggesting mechanisms of chronic mild cerebral hypoperfusion leading to a less favorable outcome in patients with DAO with CeAD. Our separate analyses of ICAD and VAD might support this theory, as the effect of DAO on outcome seemed to be almost exclusively driven by patients with ICAD in whom crossflow or collateral perfusion might be less effective than the supporting perfusion by a contralateral, nonaffected VAD in the posterior circulation. On the other hand, in post hoc analysis we also identified significantly more CIE during follow-up in this subgroup of patients with DAO (those without CIE at baseline) compared to patients without DAO. Although this might per se be explanatory for a worse functional outcome, numbers of events in these subgroups were very low and thus these findings have to be interpreted very cautiously.

An important strength of our study is the sample size, which minimizes risks of chance findings and allowed us to adjust for potential confounders of outcome in multivariable analyses.

Table 7 Primary and secondary outcomes in patients with or without dissected artery occlusion

	All patients (n = 2,148)	**Occlusion (n = 728)**	**No occlusion (n = 1,420)**	***p* Value$_{unadjusted}$**	**OR (95% CI)$_{unadjusted}$**
Primary outcome					
Favorable outcome (i.e., mRS 0–1)	1,572 (73.2)	434 (59.6)	1,138 (80.1)	<0.001	0.36 (0.30–0.45)
Secondary outcomes[a]					
CIE	72/2098 (3.4)	32/715 (4.5)	40/1,383 (2.9)	0.059	1.57 (0.98–2.53)
Recurrent CeAD	39/2095 (1.9)	14/713 (2)	25/1,382 (1.8)	0.804	1.09 (0.56–2.10)
Major hemorrhage (intracranial or extracranial)	13/1957 (0.7)	8/655 (1.2)	5/1,292 (0.4)	0.038	3.13 (1.02–9.62)
Death	28 (1.3)	15/728 (2.1)	13/1,420 (0.9)	0.027	2.28 (1.08–4.81)

Abbreviations: CeAD = cervical artery dissection; CI = confidence interval; CIE = cerebral ischemic events; mRS = modified Rankin Scale; OR = odds ratio.
Data may not be available for all patients, thus total numbers of patients for each variable may vary. Values are n (%).
[a] During follow-up time.

Although secondary analyses have to be interpreted cautiously, we were thus able to confirm the main effect of the prognostic importance of DAO in patients with CeAD also in predefined subgroups of patients and thus present a vigorous and comprehensive analysis of this outcome predictor.

We are aware of the following limitations of our study: (1) our analyses are based on data from large CeAD patient cohorts recruited at departments of neurology only, and that are nonrandomized and not monitored; (2) we did not exclude patients with pre-CeAD mRS >1 from the analysis as these data were not collected, but considering that only 26% of patients had a post-CeAD mRS >1, this is unlikely to have jeopardized our key findings; (3) the rate of acute recanalization therapy was lower than would be expected in the current environment of acute recanalization therapies, which might have caused bias towards worse outcome in patients with DAO, who probably would have benefited in particular from EVT; and (4) data on (1) presence vs absence of an occlusion of intracranial arteries downstream of the dissected arteries as well as (2) recanalization, either spontaneously or after acute recanalization therapy, were not available, although we were able to include follow-up data with a high completeness of the collected data.

Knowledge of the course of disease, the extent of expectable functional recovery, as well as risks of recurrences and complications and determining factors of these are crucial for informed, safe, and individualized treatment of patients with CeAD in clinical routine. Our findings emphasize the importance of vascular findings in patients with CeAD. Although there is not yet supporting evidence for superiority of endovascular treatment in patients with CeAD,[24] our findings might support a more rigorous approach in the implementation of EVT in patients with CeAD, in particular those with DAO.

DAO independently predicts unfavorable outcome in patients with CeAD, which may support clinicians in individually tailored decision-making on acute treatment and monitoring. Further research is warranted and should particularly focus on vessel patency status, the effect of collateral status on outcome and treatment effects, as well as best acute recanalization therapies and secondary prophylaxis, in particular in patients with CeAD with DAO.

Study funding

The 3 cohorts of the CADISP-Plus consortium have received funding from the Contrat de Projet Etat-Region 2007, Centre National de Genotypage, Institut Pasteur de Lille, INSERM U744, Emil Aaltonen Foundation, Paavo Ilmari Ahvenainen Foundation, Helsinki University Central Hospital Research Fund, Academy of Finland, Helsinki University Medical Foundation, Päivikki and Sakari Sohlberg Foundation, Aarne Koskelo Foundation, Maire Taponen Foundation, Aarne and Aili Turunen Foundation, Lilly Foundation, Alfred Kordelin Foundation, Finnish Medical Foundation, Orion Farmos Research Foundation, Maud Kuistila Foundation, the Finnish Brain Foundation, Projet Hospitalier de Recherche Clinique Régional, Fondation de France, Génopôle de Lille, Adrinord, EA2691, Institut Pasteur de Lille, Inserm U744, Basel Stroke-Funds, Käthe-Zingg-Schwichtenberg-Fonds of the Swiss Academy of Medical Sciences, the Swiss National Science Foundation (33CM30-124119, 33CM30-140340/1), Swiss Heart Foundation, University of Basel, University Hospital Basel Science Funds (Wissenschaftsfonds), Chair of Excellence grant from the French National Research Agency (Agence Nationale de la Recherche), ARNEVA (Association de Recherche en Neurologie Vasculaire) from Paris-Lariboisiere Hospital, the Leducq Foundation, and the Clinical Investigatorship from FWO Flanders.

Disclosure

C. Traenka has received funding for travel from Bayer, has received a personal scholarship from the University of Basel, and was supported by the Swiss Heart Foundation as well as the Swiss National Science Foundation. C. Grond-Ginsbach and B. Goeggel Simonetti report no disclosures relevant to the manuscript. T. Metso has received funding from the Finnish Medical Foundation, Helsinki University Central Hospital Research Fund, Helsinki University Medical Foundation, Orion Farmos Research Foundation, Päivikki and Sakari Sohlberg Foundation, Maire Taponen Foundation, the Lilly Foundation, Paavo Ilmari Ahvenainen Foundation, Aarne and Aili Turunen Foundation, Aarne Koskelo Foundation, the Maud Kuistila Memorial Foundation, Emil Aaltonen Foundation, Finnish Brain Foundation, and Alfred Kordelin Foundation. S. Debette, A. Pezzini, and M. Kloss report no disclosures relevant to the manuscript. J. Majersik is a member of the editorial board of *Neurology*® (no compensation). A. Southerland is the deputy podcast editor for *Neurology*; and has received a grant from the American Heart Association for a research study of gene expression in cervical artery dissection (AHA 3CRP141400001). Drs. Southerland and Warroll received modest salary support from this grant. D. Leys has participated during the last 5 years with advisory boards, symposia, or trials sponsored by Sanofi-Aventis, BMS, AstraZeneca, Boehringer Ingelheim, Servier, Ebewe, CoLucid Pharm, BrainsGate, PhotoThera, Lundbeck, GSK, Bayer, Pfizer, and Allergan (honoraria paid to Adrinord or research account of the hospital), and served as associate editor of the *Journal of Neurology, Neurosurgery and Psychiatry* (2004–2010) (personal financial compensation). R. Baumgartner reports no disclosures relevant to the manuscript. V. Caso has served as a speaker for Boehringer Ingelheim, Sanofi, and Pfizer. Y. Béjot has received honoraria for or consulting fees from AstraZeneca, Daiichi-Sankyo, Bayer, BMS, Pfizer, Novex Pharma, Medtronic, MSD France, Amgen, and Boehringer-Ingelheim. G. De Marchis has received support from the Swiss National Science Foundation (PBBEP3_139388); Spezialprogramm Nachwuchsförderung Klinische Forschung, University of Basel; Science Funds (Wissenschaftspool) of the University Hospital Basel; Swiss Heart Foundation; Bangerter-Rhyner-Stiftung; Swisslife Jubiläumsstiftung for Medical

Research; Swiss Neurologic Society; Fondazione Dr Ettore Balli; De Quervain research grant; Thermo Fisher GmbH; consultant and travel honoraria by Bayer; and speaker honoraria by Medtronic and BMS/Pfizer and is a member of the editorial board of *Stroke*. U. Fischer is a consultant for Medtronic, Stryker, and CSL Behring and has received funding for research projects from Medtronic. A. Polymeris has received funding for travel or speaker honoraria from Bayer, Boehringer Ingelheim, Pfizer Inc., and Medtronic; has served on scientific advisory boards for Shire, Bayer, Pfizer, and Boehringer Ingelheim, and on the editorial board of *Stroke*; is an associate editor of *Acta Neurologica Belgica*; and has received honoraria for being on the steering committee of the AX200 trial (SYGNIS). H. Sarikaya has received funding for travel or speaker honoraria from Bayer, Boehringer Ingelheim, Pfizer Inc., and Medtronic; has served on scientific advisory boards for Shire, Bayer, Pfizer, and Boehringer Ingelheim, and on the editorial board of *Stroke*; is an associate editor of *Acta Neurologica Belgica*; and has received honoraria for being on the steering committee of the AX200 trial (SYGNIS). V. Thijs has received funding for travel or speaker honoraria from Bayer, Boehringer Ingelheim, Pfizer Inc., and Medtronic; has served on scientific advisory boards for Shire, Bayer, Pfizer, and Boehringer Ingelheim, and on the editorial board of *Stroke*; is an associate editor of *Acta Neurologica Belgica*; and has received honoraria for being on the steering committee of the AX200 trial (SYGNIS). B. Worrall is a deputy editor of *Neurology*. A. Bersano has received funding for travel and congress participation from Shire, Boehringer Ingelheim, and Sanofi-Aventis. T. Brandt and H. Gensicke report no disclosures relevant to the manuscript. L. Bonati received grants from the Swiss National Science Foundation, The Swiss Heart Foundation (Berne, Switzerland), and the University of Basel, Switzerland; an unrestricted research grant from AstraZeneca; consultancy or advisory board fees or speaker's honoraria from Amgen, Bayer, Bristol-Myers Squibb, and Claret Medical; and travel grants from Amgen and Bayer. E. Touzé has served on scientific advisory boards for Bayer Schering Pharma, Pfizer, BMS, and Shire; has received speaker honoraria from Boehringer Ingelheim, Bayer Schering Pharma, Pfizer, BMS, and Shire; has received funding for travel from AstraZeneca and BMS; serves as assistant editor for *Stroke*; and has received research support from the French Ministry of Health. J. Martin has served on the editorial board of *The European Neurologic Journal* since May 2009 (no compensation). H. Chabriat is on the scientific advisory boards of Lundbeck and Janssen and is a member of the editorial board for *Cerebrovascular Disease*. T. Tatlisumak has received academic grants from Helsinki University Central Hospital, Sigrid Juselius Foundation, Finnish Academy of Sciences, Sahlgrenska University Hospital, and University of Gothenburg; has/has had research contracts with Boehringer Ingelheim, Bayer, Pfizer, Prtola Pharma, and BrainsGate; and has advisory board activities with Boehringer Ingelheim, Bayer, and Lumosa Pharma. M. Arnold is on advisory boards for Bayer Schering, Boehringer Ingelheim, and Pfizer/BMS; received speaker honoraria from Bayer Schering, Boehringer Ingelheim, and Covidien; received research grants from the Swiss National Science Foundation, the Swiss Heart Foundation, SHIRE Human Genetics, and BRAHMS GmbH; and reports personal fees from speaker honoraria from Bayer, Medtronic, and Covidien, and scientific advisory board honoraria from Bayer, Boehringer Ingelheim, BMS, Pfizer, Covidien, Daiichi-Sankyo, and Nestlé Health Science. S. Engelter has received funding for travel or speaker honoraria from Bayer, Boehringer Ingelheim, and Daiichi-Sankyo; has served on scientific advisory boards for Bayer, Boehringer Ingelheim, BMS/Pfizer, and MindMaze and on the editorial board of *Stroke*; and has received an educational grant from Pfizer and research support from Daiichi-Sankyo, compensation from Stago for educational efforts, and research support from the Science Funds (Wissenschaftsfonds) of the University Hospital Basel, the University Basel, the "Freiwillige Akademische Gesellschaft Basel," the Swiss Heart Foundation, and the Swiss National Science Foundation. P. Lyrer has served on scientific advisory boards for Bayer Schering Pharma and Boehringer Ingelheim; has received funding for travel or speaker honoraria from Bayer Schering Pharma, Boehringer Ingelheim, and Shire plc; serves as coeditor for *Neurologie und Psychiatrie* and on the editorial board of *Swiss Archives of Neurology and Psychiatry*; and has received research support from AstraZeneca, Boehringer Ingelheim, Sanofi-Aventis, PhotoThera, the Swiss National Science Foundation, and the Swiss Heart Foundation. Go to Neurology.org/N for full disclosures.

Publication history

Received by *Neurology* February 2, 2019. Accepted in final form July 8, 2019.

Appendix Authors

Name	Location	Role	Contribution
Christopher Traenka, MD	University Hospital Basel; Felix-Platter Hospital Basel, Switzerland	Author	Designed/conceptualized the study, analyzed/interpreted the data, drafted the manuscript, and collected data
Caspar Grond-Ginsbach, PhD	University Hospital Heidelberg, Germany	Author	Data collection, critical review of the manuscript, editing manuscript for content
Barbara Goeggel Simonetti, MD	University Hospital Bern; Ospedale San Giovanni, Bellinzona, Switzerland	Author	Data collection, critical review of the manuscript, editing manuscript for content
Tiina M. Metso, MD, PhD	Helsinki University Central Hospital, Finland	Author	Data collection, critical review of the manuscript, editing manuscript for content
Stephanie Debette, MD, PhD	Bordeaux University Hospital, France; Boston University School of Medicine, MA	Author	Data collection, critical review of the manuscript, editing manuscript for content

Continued

Appendix *(continued)*

Alessandro Pezzini, MD	Neurology Clinic, University of Brescia, Italy	Author	Data collection, critical review of the manuscript, editing manuscript for content
Manja Kloss, MD	University Hospital Heidelberg, Germany	Author	Data collection, critical review of the manuscript, editing manuscript for content.
Jennifer J. Majersik, MD, MS	University of Utah, Salt Lake City	Author	Data collection, critical review of the manuscript, editing manuscript for content
Andrew M. Southerland, MD, MSc	University of Virginia Health System, Charlottesville	Author	Data collection, critical review of the manuscript, editing manuscript for content
Didier Leys, MD, PhD	University of Lille, France	Author	Data collection, critical review of the manuscript, editing manuscript for content
Ralf Baumgartner, MD	Clinic Hirslanden, Zurich, Switzerland	Author	Data collection, critical review of the manuscript, editing manuscript for content
Valeria Caso, MD, PhD	University of Perugia, Italy	Author	Data collection, critical review of the manuscript, editing manuscript for content
Yannick Béjot, MD, PhD	University of Burgundy, Dijon, France	Author	Data collection, critical review of the manuscript, editing manuscript for content
Gian Marco De Marchis, MD, MSc	University Hospital Basel, Switzerland	Author	Data collection, critical review of the manuscript, editing manuscript for content
Urs Fischer, MD	University Hospital Bern, Switzerland	Author	Data collection, critical review of the manuscript, editing manuscript for content
Alexandros Polymeris, MD	University Hospital Basel, Switzerland	Author	Data collection, critical review of the manuscript, editing manuscript for content
Hakan Sarikaya, MD	University Hospital Bern; University Hospital of Zurich, Switzerland	Author	Data collection, critical review of the manuscript, editing manuscript for content
Vincent Thijs, MD, PhD	University of Melbourne, Heidelberg, Victoria, Australia	Author	Data collection, critical review of the manuscript, editing manuscript for content

Appendix *(continued)*

Bradford B. Worrall, MD, MSc	University of Virginia Health System, Charlottesville	Author	Data collection, critical review of the manuscript, editing manuscript for content
Anna Bersano, MD, PhD	Istituto Neurologico Carlo Besta, Milan, Italy	Author	Data collection, critical review of the manuscript, editing manuscript for content
Tobias Brandt, MD	Swiss National Accident Insurance Institution, Lucerne, Switzerland	Author	Data collection, critical review of the manuscript, editing manuscript for content
Henrik Gensicke, MD	University Hospital Basel, Switzerland	Author	Data collection, critical review of the manuscript, editing manuscript for content
Leo H. Bonati, MD	University Hospital Basel, Switzerland	Author	Data collection, critical review of the manuscript, editing manuscript for content
Emmanuel Touzeé, MD, PhD	University Paris Descartes, France	Author	Data collection, critical review of the manuscript, editing manuscript for content
Juan J Martin, MD	Sanatorio Allende, Cordoba, Argentina	Author	Data collection, critical review of the manuscript, editing manuscript for content
Hugues Chabriat, MD, PhD	Lariboisière Hospital, Paris, France	Author	Data collection, critical review of the manuscript, editing manuscript for content
Turgut Tatlisumak, MD, PhD	Sahlgrenska University Hospital, Gothenburg, Sweden	Author	Data collection, critical review of the manuscript, editing manuscript for content
Marcel Arnold, MD	University Hospital Bern, Switzerland	Author	Data collection, critical review of the manuscript, editing manuscript for content
Stefan T. Engelter, MD	University Hospital Basel, Felix-Platter Hospital Basel, Switzerland	Author	Initiated, designed, conceptualized and supervised the study, analyzed/ interpreted the data, revised the manuscript, collected data
Philippe Lyrer, MD	University Hospital Basel, Switzerland	Author	Initiated, designed, conceptualized and supervised the study, analyzed/ interpreted the data, revised the manuscript, and collected data

References

1. Engelter ST, Traenka C, Lyrer P. Dissection of cervical and cerebral arteries. Curr Neurol Neurosci Rep 2017;17:59.
2. Debette S, Grond-Ginsbach C, Bodenant M, et al. Differential features of carotid and vertebral artery dissections: the CADISP study. Neurology 2011;77:1174–1181.
3. Lee VH, Brown RD Jr, Mandrekar JN, Mokri B. Incidence and outcome of cervical artery dissection: a population-based study. Neurology 2006;67:1809–1812.
4. Arnold M, Bousser MG, Fahrni G, et al. Vertebral artery dissection: presenting findings and predictors of outcome.Stroke 2006;37:2499–2503.
5. Lyrer PA, Brandt T, Metso TM, et al. Clinical import of Horner syndrome in internal carotid and vertebral artery dissection. Neurology 2014;82:1653–1659.
6. Kellert L, Kloss M, Pezzini A, et al. Prognostic significance of pulsatile tinnitus in cervical artery dissection. Eur J Neurol 2016;23:1183–1187.
7. Milhaud D, de Freitas GR, van Melle G, Bogousslavsky J. Occlusion due to carotid artery dissection: a more severe disease than previously suggested. Arch Neurol 2002;59:557–561.
8. Lichy C, Metso A, Pezzini A, et al. Predictors of delayed stroke in patients with cervical artery dissection. Int J Stroke 2015;10:360–363.
9. Debette S, Goeggel Simonetti B, Schilling S, et al. Familial occurrence and heritable connective tissue disorders in cervical artery dissection. Neurology 2014;83:2023–2031.
10. Traenka C, Dougoud D, Simonetti BG, et al. Cervical artery dissection in patients >/=60 years: often painless, few mechanical triggers. Neurology 2017;88:1313–1320.
11. Debette S, Leys D. Cervical-artery dissections: predisposing factors, diagnosis, and outcome. Lancet Neurol 2009;8:668–678.
12. Compter A, Schilling S, Vaineau CJ, et al. Determinants and outcome of multiple and early recurrent cervical artery dissections. Neurology 2018;91:e769–e780.
13. Wouters A, Nysten C, Thijs V, Lemmens R. Prediction of outcome in patients with acute ischemic stroke based on initial severity and improvement in the first 24 h. Front Neurol 2018;9:308.
14. Sato S, Toyoda K, Uehara T, et al. Baseline NIH Stroke Scale score predicting outcome in anterior and posterior circulation strokes. Neurology 2008;70:2371–2377.
15. Schievink WI. Spontaneous dissection of the carotid and vertebral arteries. N Engl J Med 2001;344:898–906.
16. Debette S. Pathophysiology and risk factors of cervical artery dissection: what have we learnt from large hospital-based cohorts? Curr Opin Neurol 2014;27:20–28.
17. Bejot Y, Aboa-Eboule C, Debette S, et al. Characteristics and outcomes of patients with multiple cervical artery dissection. Stroke 2014;45:37–41.
18. Caso V, Paciaroni M, Corea F, et al. Recanalization of cervical artery dissection: influencing factors and role in neurological outcome. Cerebrovasc Dis 2004;17:93–97.
19. Weimar C, Kraywinkel K, Hagemeister C, et al. Recurrent stroke after cervical artery dissection. J Neurol Neurosurg Psychiatry 2010;81:869–873.
20. Weimar C, Goertler M, Harms L, Diener HC. Distribution and outcome of symptomatic stenoses and occlusions in patients with acute cerebral ischemia. Arch Neurol 2006;63:1287–1291.
21. Baumgartner RW, Arnold M, Baumgartner I, et al. Carotid dissection with and without ischemic events: local symptoms and cerebral artery findings. Neurology 2001;57:827–832.
22. Baumgartner RW, Bogousslavsky J. Clinical manifestations of carotid dissection. Front Neurol Neurosci 2005;20:70–76.
23. De Ridder D, Menovsky T, Van de Heyning P. An otoneurosurgical approach to non-pulsatile and pulsatile tinnitus. B-ENT 2007;3(suppl 7):79–86.
24. Traenka C, Jung S, Gralla J, et al. Endovascular therapy versus intravenous thrombolysis in cervical artery dissection ischemic stroke: results from the SWISS registry. Eur Stroke J 2018;3:47–56.

Artery occlusion independently predicts unfavorable outcome in cervical artery dissection

Christopher Traenka, Caspar Grond-Ginsbach, Barbara Goeggel Simonetti, et al.

Neurology published online November 22, 2019
DOI 10.1212/WNL.0000000000008654