Observational study to describe precisely headache and associated symptoms in patients with CAD

Phenotype of head pain in patients with cervical artery dissection

Iris Wiederkehr, Christopher Tränka, Stefan Engelter, Till Sprenger

University of Basel, Faculty of Medicine, Department of Neurology, Basel, Switzerland

Summary

Background and objective: Head and neck pain are key presenting symptoms of cervical artery dissection (CAD) and often preceed other clinical signs or symptoms. CAD is a common cause of stroke and therefore it is important to recognise patients at risk. The aim of this study was a precise description of the clinical features of patients with CAD in order to distinguish CAD from primary and other secondary headache aetiologies.

Methods: Medical records of 39 patients previously recruited at the University Hospital of Basel in an observational study (CADISP study) from 2011 to 2015 were reviewed. Telephone interviews were performed to obtain precise descriptions of the clinical features of CAD.

Results: Head and neck pain was present in 34 (87%) patients with CAD. Migraine-like symptoms were reported by 32 (82%) patients and trigeminal-autonomic symptoms (including Horner's syndrome) by 27 (69%) patients. The pain onset was variable, including acute development of pain over seconds to minutes in some patients and subacute onset over hours in others. Dynamics of the pain varied between continuous, fluctuating and recurring. Mean pain intensity rated 6 out of 10 on a visual analogue scale. The pain quality was most commonly described as a pressing (36%) or stabbing (28%) sensation. In contrast to other studies, the pain occured most frequently in the occipital region both in internal carotid artery dissection (ICAD) and vertebral artery dissection (VAD).

Conclusions: In agreement with prior studies, unilateral and ipislateral pain seems to be the key clinical feature in patients with CAD. The pressing or stabbing quality and the frequent occurance of Horner's syndrome seem to be specific and might help to differentiate CAD from migraine as even aura symptoms occur in CAD. The moderate pain intensity might help to differentiate CAD from primary trigeminal autonomic cephalgias such as cluster headache, which are typically characterised by more severe pain.

Key words: cervical artery dissection; internal carotid artery dissection; vertebral artery dissection; headache; head pain; Horner's syndrome; trigeminal-autonomic symptoms; migraine; ischaemic stroke; transient ischaemic attacks

Introduction

Head and neck pain are key presenting symptoms of cervical artery dissection (CAD) [1]. Such pain may occur in isolation or accompanied by other local signs and symptoms such as Horner's Syndrome [2], migraine-like attendant symptoms [3], cranial nerve palsy or ischaemic symptoms (ischaemic stroke or transient ischaemic attacks) [4]. In many cases, the pain precedes other symptoms or clinical signs and may be the only early warning symptom of CAD [5]. The features of such pain tend to mimic other types of headache such as migraine [6]. Therefore, a better understanding of the phenotype of patients with CAD may help in the differential diagnosis, for example, in distinguishing CAD from primary or other secondary headache aetiologies [7]. CAD is a common cause of stroke [7, 8] in young adults [9] and therefore it is important to recognise patients at risk.

In several prior studies, pain due to CAD was described as a steady aching or sharp rather than pulsating pain [1]. However, other authors found pain due to internal carotid artery dissection (ICAD) more often to be of a pulsating quality [5]. Pain occurred in patients with ICAD more often in the ipsilateral anterior region of the head and in patients with vertebral artery dissection (VAD) more often ipsi- or bilaterally in the posterior region of the head and neck [1].

The aim of this study was a precise description of the clinical features of patients with CAD in terms of their headache and associated symptoms.

Methods

Cervical artery dissection patients from the Cervical Artery Dissection and Ischaemic Stroke Patients (CADISP) database of the University Hospital of Basel from 2011 to 2015 were used for this analysis. This observational study was approved by the Ethics Committee as an amendment of the CADISP study and patients had given their written informed consent. The structure and methods of the CADISP study have been described previously [10]. The following variables were included in the analysis: age, gender, date of hospitalisation, presence of stroke or transient ischaemic attack, affected artery. In addition to the information already available in the CADISP study database, telephone interviews were performed to obtain precise descriptions of the clinical features of CAD.

Patients were categorised as having either ICAD or VAD, as we expected the dissection type to predict the

Table 1: Clinical characteristics of head and neck pain in 34 patients with ICAD or VAD.

		CAD (n = 39)		ICAD (n = 28)		VAD (n = 11)	
		No.	%	No.	%	No.	%
Head and or neck pain		34	87	26	93	8	73
	Head pain only	12	35	10	38	2	25
	Neck pain only	4	12	1	4	3	38
	Head and neck pain	18	53	15	58	3	38
Onset	Seconds	7	21	3	12	4	50
	Minutes	16	47	12	46	4	50
	Hours	11	32	11	42	0	0
Duration	1–60 minutes	1	3	0	0	1	13
	1–24 hours	4	12	1	4	3	38
	1–7 days	14	41	13	50	1	13
	1–4 weeks	14	41	12	46	2	25
	Persistent	1	3	0	0	1	13
Dynamics	Continuous	12	35	8	31	4	50
	Undulating	11	32	10	38	1	13
	Recurrent	11	32	8	31	3	38
Frequency	With accompagnying symptoms	34	100	26	100	8	100
	First symptom	23	68	17	65	6	75
	Unknown	2	6	2	8	0	0
Quality*		**47**		**39**		**12**	
	Pressing	17	36	14	36	3	25
	Stabbing	13	28	10	26	3	25
	Pulsating	7	15	5	13	2	17
	Burning	1	2	4	10	1	8
	Pulling	5	11	2	5	3	25
	Explosive	1	2	1	3	0	0
	Electifiying	1	2	1	3	0	0
	Toothache like	1	2	1	3	0	0
	Unknown	1	2	1	3	0	0
Localisation head pain*		**56**		**51**		**5**	
	Frontal	8	14	8	16	0	0
	Periorbital	6	11	5	10	1	20
	Maxillary region	3	5	3	6	0	0
	Mandibular region	2	4	2	4	0	0
	Auricular	6	11	6	12	0	0
	Temporal	7	13	6	12	1	20
	Parietal	6	11	6	12	0	0
	Occipital	18	32	15	29	3	60
Localisation neck pain*		**28**		**21**		**6**	
	Posterior neck region	17	61	10	48	6	100
	Lateral neck region	7	25	7	33	0	0
	anterior neck region	4	14	4	19	0	0
Laterality of head pain		**30**		**25**		**5**	
	Unilateral	20	67	17	68	3	60
	Ipsilateral	19	95	16**	64	3	60
	Unknown	1	5	0	0	0	0
	Bilateral	10	33	8	32	2	40
Laterality of neck pain		**22**		**16**		**6**	
	Unilateral	16	73	11	69	5	83
	Ipsilateral	16	100	11	100	5	100
	Bilateral	6	27	5	31	0	0
Pain scale	Mean VAS	6		6		5	
	Maximal VAS	7		7		7	

CAD = cervical artery dissection, ICAD = internal carotid artery dissection, VAD = vertebral artery dissection, VAS = visual analogue scale.
* For quality and localisation multiple specifications were possible and taken in account.
** 1 out of 17 presented with change from ipsi- to contralateral.

pain phenotype. The presence of headache or neck pain accompanying the dissection, as well as cranial autonomic symptoms, migraine-associated symptoms and premonitory symptoms were noted.

We determined the onset, duration, dynamic, quality, severity (using a visual analogue scale [VAS]) and localisation of the pain. As well as the laterality, patients were specifically asked about the precise localisation of the head and neck pain. Head pain was classified as frontal, temporal, parietal, occipital, periorbital, auricular or facial. Facial pain was further subdivided into pain in the maxillary or mandibular divisions of the trigeminal nerve. Neck pain was precisely defined as any pain below the occiput and the chin and above the shoulder region and, moreover, was subdivided into anterior, lateral and posterior regions.

Potential risk and protective factors, such as physical activity and relaxation, were assessed by using the Global Physical Activity Questionnaire issued by the World Health Organization [11]. Psychological stress factors such as psychosocial stress and depression were measured by using an adapted version of the questionnaire utilised by the interheart study [12]. Any regular intake of analgesics, triptanes and/or oral contraceptives (suspected risk factor for CAD [13, 14]) during the 6 months preceding the event was noted. We recorded a history of migraine, tension-type headache, anxiety, depression, sinusitis, diabetes and smoking. In addition, potential trigger factors (in regard to well-known migraine triggers [15]) for the pain experienced by the patients were noted.

Results

Patients. Out of 70 patients in the CADISP data base, 39 (56%) were interviewed. Thirty-one (44%) were not included because of unwillingness to participate (n = 9), outdated/incorrect contact data (n = 8), language barrier (n = 2) or unavailability at the time of contact (n = 17).

Out of the 39 patients, ICAD was present in 28 (72%) patients and VAD in 11 (28%). In one patient, multiple vessel dissections in both the right and left internal carotid artery were evident. The mean age of patients with ICAD was 48 years and of patients with VAD 46 years. Twenty-four (62%) of the patients were male and 15 (38%) female. Ischaemic stroke following the cervical dissection was seen in 17 (44%) patients, 9 (53%) with ICAD and in 8 (47%) with VAD. Transient ischaemic attacks were seen in six patients (15%), five (83%) of the ICAD-group and one (17%) in the VAD-group.

Head and neck pain characteristics. Head and neck pain was present in 34 (87%) patients (table 1). Eighteen (53%) patients had a combination of head and neck pain. Iso-

lated head pain without neck pain (12, 35%) was more often seen than isolated neck pain (4, 12%). Head pain was unilateral in 20 (67%) patients, for 19 (95%) of whom the pain was ipsilateral. Neck pain was unilateral in 16 (73%), in all cases ipsilateral. Out of the 10 (33%) patients with bilateral head pain and the 6 (27%) patients with bilateral neck pain, 2 stated one side to be more strongly affected, in both cases ipsilateral.

Head pain occurred most frequently in the occipital region in both the ICAD group (15, 29%) and the VAD group (3, 60%). Neck pain was more frequently in the posterior neck region in patients with ICAD and only in the posterior neck region in patients with VAD.

The onset of the pain occurred in seconds in 7 (21%) patients, in minutes in 16 (47%) and gradually over hours in 11 (32%). Patients with ICAD more often reported an onset of the pain in minutes (12, 46%) or hours (11, 42%). Patients with VAD more often reported onset of the pain in seconds (4, 50%) or minutes (4, 50%), but none reported an onset lasting hours. All 34 patients with pain reported other accompanying symptoms, in 23 (68%) patients the pain was the first symptom.

In the majority of the cases the pain lasted 1–7 days (14, 41%) or 1–4 weeks (14, 41%). Twelve patients (35%) had continuous pain, 11 (32%) undulating pain and 11 (32%) had recurring pain. Characteristics of recurrent pain were heterogenous.

The mean *intensity of the pain* associated with CAD was rated 6 out of 10 on a visual analogue scale (VAS) and the mean intensity of the maximal pain experienced was rated as 7 out of 10 on the VAS. Intake of pain medication was noted in 26 cases, which reduced the perceived pain to a mean of 2/10 on the VAS.

Multiple *pain qualities* were reported in 11 (32%) patients (fig. 1). Overall, a pressing (17, 36%) or stabbing (13, 28%) sensation were most common. Seven (15%) patients described a throbbing sensation and of these, four (57%) had a history of migraine. In comparison, 13 (50%) patients without throbbing pain had a history of migraine.

The medical histories, including events preceding the dissections such as infection or trauma, are shown in table 2. Out of the 39 patients, 28 (72%) had a history of headache, of whom 18 (46%) had a history of migraine. None had a history of any other neurological disease or diabetes mellitus. Less than ten percent had a history of anxiety or depression (table 2). Twenty-three (59%) were smokers with a mean of 22.5 pack years.

Table 2: Medical history of 39 patients with CAD.

	CAD (n = 39)	
	No.	%
History of headache	28	72%
Family history of headache	21	54%
Unknown history of headache	3	8%
History of migraine	18	46%
Migraine with aura	4	10%
Migraine without aura	14	36%
Family history of migraine	14	36%
Unknown history of migraine	1	3%
History of neurological disease	0	0%
History of anxiety	2	5%
History of depression	3	8%
History of diabetes mellitus	0	0%
History of sinusitis	17	44%
Smoker	23	59%
Active	11	48%
Previous	11	48%
Unknown	1	4%
Precursor event	38	97%
Previous Infection	8	21%
Previous trauma	7	18%
Oral contraceptive use*	3	20%

CAD = cervical artery dissection
* Only women (n = 15) taken into account

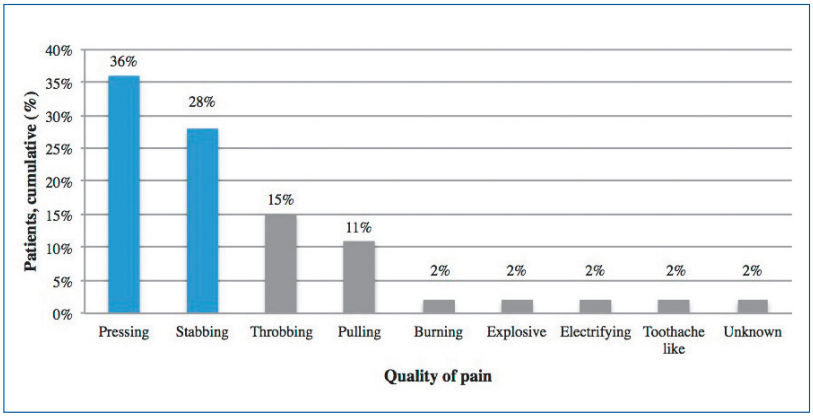

Figure 1: Distribution of pain qualities in 34 patients with CAD and pain as a symptom. CAD = cervical artery dissection. Multiple qualities reported by patients were taken into account and cumulative results are shown in this figure.

For 8 (21%) patients, an infection during the last month preceding the event was noted and 7 (18%) patients had a previous trauma, one of them a severe trauma. Out of the 15 women of this study, 3 (20%) reported regular intake of oral contraceptives during the 6 months prior to the event. Seven (18%) patients reported regular intake of analgesics during the 6 months prior to the event. Only one (3%) patient reported regular intake of triptanes (zolmitriptan).

Among the 34 patients with pain, 25 (74%) had a history of headache. Three (60%) of the five patients without pain had a history of headache.

Accompanying symptoms were present in 38 (97%) patients. One patient with VAD presented with neck pain

only. Trigeminal-autonomic symptoms were reported by 27 (69%) patients (table 3), although these data were available for only 36 (92%) patients, as the others could not recall whether such symptoms were present. Patients with ICAD more often had trigeminal-autonomic symptoms (21 out of 28, 75%) than patients with VAD (6 out of 11, 55%) (table 4). The most common features were partial Horner's syndrome, as miosis was present in 17 (63%) patients and ptosis in 18 (67%) patients. In patients with ICAD, miosis and ptosis were present in 71% of the patients (15 out of 21), whereas in patients with VAD these features were present in only 33–50% of the cases (2 patients with both and one patient with ptosis only, table 4). Two of these three patients with VAD subsequently suffered from an ischaemic event (cerebral infarction in both cases).

Migraine-like symptoms such as nausea, photo- and phonophobia and physical activity-induced aggravation of the pain were frequently reported. At least one of these symptoms was reported by 32 (82%) patients (table 5). Twelve patients (38%) reported (migraine) aura-like symptoms, of which visual disturbance was most common. Out of these patients, six (50%) had an ischaemic event following the dissection, which was similar to the incidence in the patients without aura. A history of migraine was found in 5 (42%) out of these 12 patients, only one previously had migraine with aura. Among these 32 patients, 18 (56%) had a history of migraine, but in comparison none of the 7 patients that did not experience such symptoms had a history of migraine.

Table 6 shows other accompanying symptoms, which were in total experienced by 29 (74%) patients. Tiredness was reported by 23 patients (79%), dizziness by 16 (55%), neck stiffness by 14 (48%) and disturbed concen-

Table 3: Trigeminal autonomic symptoms in 36 patients with CAD.

	CAD (n = 36)*	
	No.	%
Trigeminal autonomic symptoms	27	69%
Lacrimation	7	26%
Red eye	6	22%
Miosis	17	63%
Ptosis	18	67%
Itchy eye	6	22%
Foreign body in eye	4	15%
Eyelid oedema	2	7%
Rhinorrhoea	3	11%
Occluded nose	6	22%
Facial flush	2	7%
Facial hidrosis	5	19%
Ear pressure	2	7%
Postnasal drip	2	7%

CAD = cervical artery dissection
* Due to lack of recall, data of only 36 patients was obtained

Table 4: Comparison of accompanying symptoms in patients with ICAD and VAD.

	ICAD (n = 28)		VAD (n = 11)	
	No.	%	No.	%
Trigeminal autonomic symptoms	21	75%	6	55%
Miosis	15	71%	2	33%
Ptosis	15	71%	3	50%
Migraine-like symptoms	22	79%	10	91%
Other accompagnying symptoms	19	68%	10	91%

ICAD = internal carotid artery dissection, VAD=vertebral artery dissection. For specific symptoms see table 3a–c.

Table 5: Migraine-like symptoms in 39 patients with CAD.

	CAD (n = 39)	
	No.	%
Migraine like symptoms	32	82%
Nausea	19	59%
Emesis	8	25%
Photophobia	13	41%
Phonophobia	12	38%
Osmophobia	5	16%
Physical activity-induced aggravation	14	44%
Aura-like symptoms	12	38%
Visual	11	92%
Somatosensory	1	8%
Motor	1	8%
Aphasia	1	8%
Agitation	8	25%
Allodynia	6	19%

CAD = cervical artery dissection

Table 6: Other accompanying symptoms in 39 patients with CAD.

	CAD (n = 39)	
	No.	%
Other accompanying symptoms	29	74%
Vertigo	4	14%
Dizziness	16	55%
Tinnitus	7	24%
Tiredness	23	79%
Disturbed concentration	12	41%
Yawning	4	14%
Change in urinary frequency	2	7%
Neck stiffness	14	48%
Depression	4	14%

CAD = cervical artery dissection

tration by 12 (41%). Six (55%) of the patients with VAD reported neck stiffness, compared with only eight (29%) of the patients with ICAD.

Triggers. Of known migraine triggers, sleep deprivation before onset of head or neck pain seemed to be the only frequently occurring factor, reported by 10 out of 34 (29%). patients with pain. In many cases the patients could not recall the presence of such triggers, as listed in table 7.

Table 7: Migraine triggers in 34 patients with CAD and head or neck pain.

	CAD (n = 34)	
	No.	%
Triggers	15	38%
No memory	1	3%
Not asked	5	13%
Alcohol	2	13%
Noise	3	20%
Sharp light	3	20%
Chocolat	0	0%
Caffein withdrawal	1	7%
Nitroglycerin Intake	0	0%
Olfactory stimulus	1	7%
Tactile stimulus	1	7%
Sleep deprevation	10	67%
Oversleeping	1	7%
Altitude	2	13%
Weather condition	3	20%
Menstruation*	2	13%
No memory	1	7%

CAD = cervical artery dissection. * Only women (n = 15) taken into account

Table 8: Psychosocial stress in 39 patients with CAD. Overall and with pain.

	CAD (n = 39)		CAD and pain as a symptom (n = 34)	
	No.	%	No.	%
Any Stress	35	90%	30	88%
Stress at work	32	82%	28	82%
Sometimes	7	22%	5	18%
Often	5	16%	4	14%
Permanently	20	63%	19	68%
Stress at home	17	44%	15	44%
Sometimes	5	29%	4	27%
Often	3	18%	3	20%
Permanently	9	53%	8	53%
Financial stress	3	8%	2	6%
Moderately	0	0%	0	0%
High	3	100%	2	100%

CAD = cervical artery dissection. Using an adapted questionnaire utilized by the interheart study for psychosocial stress measurements in patients with myocardial infarction. Evaluation of psychosocial stress as a risk factor for CAD and factor of aggravation of pain in patients with CAD.

Risk and protective factors. Psychosocial stress, a potential risk factor as well as aggravating factor of the pain, was assessed as shown in table 8.

Stress was a common factor found in 35 (90%) patients. Thirty-two (91%) patients reported being under stress at work, 20 (57%) patients permanently so. Stress at home was present in 17 (39%), in 9 (26%) patients permanently.

Financial stress was a problem for three (8%) patients. Of the 34 patients with pain as a symptom, stress was reported by 30 (88%) patients. Twenty-eight (93%) patients reported being under stress at work, 19 (63%) patients permanently. Stress at home was present in 15 (50%), in 8 patients (27%) permanently. Financial stress was a problem for 2 (7%) patients. All of the five patients without pain reported to be stressed, but only one (20%) reported to be stressed permanently.

Results on physical activity of the patients are summarised in table 9.

Table 9: Physical activity in 39 patients with CAD.

	CAD (n = 39)	
	No.	%
Physical activity		
Intensive physical activity at work *Average of 3.8 hours per day on 4.5 days per week.*	6	15%
Intensive physical activity at home *Average of 1.4 hours per day on 3.1 days per week.*	17	44%
Moderate physical activity at work *Average of 3 hours per day on 3.4 days per week.*	9	23%
Moderate physical activity at home *Average of 1.6 hours per day on 3.1 days per week.*	27	69%

CAD = cervical artery dissection. Using the GPAQ (Global physical activity questionnaire) issued by the World Health Organization. Evaluation of physical activity as a protection factor for CAD.

Discussion

With 87% of the patients reporting pain as a symptom and 68% of the patients reporting pain as the first symptom, the results of our study are in agreement with prior studies. Accordingly, pain seems to be the key clinical feature in patients with cervical artery dissection [1, 5, 16].

As already established in other studies [5], pain onset and dynamics have to be considered nonspecific, as the pain varies from thunderclap-like pain to progressive pain developing over hours. The pain can be continuous, fluctuating or recurrent. The mean intensity of 7/10 on the VAS is of moderate to high level, which is well in line with migraine-associated pain, more than

a typical tension headache (VAS <5) and less severe than what is seen in cluster headache (VAS >8). (Primary headache syndromes are important differential diagnoses of the head pain [3, 7]).

The duration of the pain varied considerably in our study. Although similar pain durations were found in previous studies [5], pain duration has to be considered with caution as the endpoint of "no pain" strongly depends on the time of treatment. Patients reported that the pain mostly stopped within hours up to two days after hospitalisation and after appropriate treatment of the CAD and the pain. However, the reason for hospitalisation varies from high pain intensity to disabling symptoms due to an ischaemic attack, and therefore not all patients seek help at the same time. Chronic pain following CAD seems to be uncommon as persistent pain occurred in one patient only (with VAD).

The location of the pain is typically unilateral and ipsilateral to the CAD, but nonetheless some patients experienced bilateral pain when only one vessel was dissected. This finding was seen before in other studies [5, 8] and probably has to do with pain processing in the brain and central sensitisation rather than representing a specific pathophysiological feature of dissections. In contrast to other studies, where the pain in patients with ICAD was more frequently frontal and pain in patients with VAD in the occipital region or neck [1], our data showed the highest frequency of head pain both in ICAD and VAD in the occipital region. In accordance with known data [1, 5], if pain was confined to the neck, the origin was more likely to be a VAD and if pain was confined to the head, it was more likely to relate to ICAD. Only pain confined to the neck seems to have reasonable specificity for VAD over ICAD (occurring in 38% in VAD versus 4% in ICAD)

Patients with CAD most frequently experienced pain of a pressing or stabbing quality, which differs from the results of some previous studies [5] that suggested a throbbing quality, a feature often associated with migraine. Interestingly, and against our expectation and the findings of a previous study [1], a history of migraine was not more frequent in patients with throbbing pain than in patients with other pain qualities.

Pain can be the only symptom of CAD [5]. Nevertheless, all of the 34 patients in our cohort with pain also reported accompanying symptoms. As in other studies [17], a (partial) Horner's syndrome was the most common feature in the group with trigeminal-autonomic symptoms. It was found mostly in patients with ICAD, but there were also three patients with VAD who had miosis and ptosis.

We found it especially noteworthy that migraine-like symptoms occurred commonly, in 82% of the patients, which makes it more difficult to differentiate pain due to CAD from pain experienced during a migraine. Only 56% of the patients with migraine-like symptoms had a history of migraine, but there was no history of migraine in patients without migraine-like symptoms. Another remarkable finding was the presence of aura in 12 patients (38%). The mechanism by which aura symptoms in migraine sufferers (or stroke patients) develops is complex. A long-accepted dogma is that cerebral hypoperfusion and cortical spreading depression lead to aura symptoms in migraines. Cortical spreading depression can also occur in stroke [18]. Our data could not prove a relevant connection between ischaemic events and aura symptoms experienced by the patients, as in the groups with and without aura, the number of ischaemic events was the same.

In this study, a history of migraine was found in 46%, a higher number than in other studies [19, 20] and the general population, which may be taken as support for the view that migraine is a risk factors for CAD [14]. The association of migraine in CAD and its positive correlation with cerebral infarction is controversial, as several studies have suggested such an association, but others failed to confirm this [6]. In our study, of those with a history of migraine, 56% had an ischaemic event following the CAD and 48% of the patients that had no history of migraine also had an ischaemic event.

On the subject of ischaemic events following CAD, which was the case in 50% of patients, one could argue that VADs are more prone to cause ischaemic events than ICAD as ischaemia occurred in 82% of the patients with VAD and in only 39% of the patients with ICAD.

As for risk factors such as psychosocial stress, we conclude from our results that patients with CAD have high levels of stress, more so at work than at home. In comparison with data from the interheart study [12] in healthy subjects (n = 13648), stress levels of patients with CAD seem to be higher than those of the general population. In our study, 82% of the patients reported stress at work compared with 17% of the healthy subjects of the interheart study. We also conclude that stress is aggravates the pain, as permanent stress was reported more frequently in patients with pain than in patients without.

Study limitations. It has to be noted that this was a retrospective study and hence recall bias may affect the results. We tried to limit the analysis to patients in whom dissection occurred less than 5 years ago, and patients were phenotyped by a trained rater instead of just by means of a patient self-report questionnaire. Still, we cannot exclude that the prevalence of symptoms is over- or underestimated in our study owing to the time delay between symptoms and interview.

We grouped patients into ICAD and VAD. However, the VAD group turned out to be relatively small; hence, results of the VAD group may not entirely reflect the phenotype in a larger population. The same limitations apply to all comparisons between the relatively small group of patients without pain and patients with pain.

Authors' contribution

IW did the literature search, created the case report form, conducted the interviews with the patients, wrote the draft and prepared the tables and figures. TS initiated and supervised the project, made critical revisions to the case report form and the draft. SE is PI of the CADISP study in Basel, he made critical revisions to the case report form and the draft. CT was of assistance during the conduction of the interviews and allocation of further medical records.

Disclosure statement

Sources of support: CADISP database of the University Hospital of Basel.

There is no conflict of interest of the main author. Co-author Prof. Dr. med. Till Sprenger has received research support from: SNF, Novartis, Grünenthal and Swiss MS Society. His employer and previous employer have received compensation for speaking/consulting from: Sanofi, Genzyme, Novartis, ATI, ElectroCore, Mitsubishi Pharma, Actelion, Teva, Biogen Idec.

References

1 Silbert PL, Mokri B, Schievink WI. Headache and neck pain in spontaneous internal carotid and vertebral artery dissections. Neurology. 1995;45(8):1517–22.
2 Lyrer PA, Brandt T, Metso TM, Metso AJ, Kloss M, Debette S, et al. Clinical import of Horner syndrome in internal carotid and vertebral artery dissection. Neurology. 2014;82(18):1653–9.
3 Mirza Z, Hayward P, Hulbert D. Spontaneous carotid artery dissection presenting as migraine – a diagnosis not to be missed. Journal of accident & emergency medicine. 1998;15(3):187–9.
4 Debette S, Compter A, Labeyrie MA, Uyttenboogaart M, Metso TM, Majersik JJ, et al. Epidemiology, pathophysiology, diagnosis, and management of intracranial artery dissection. Lancet neurology. 2015;14(6):640–54.
5 Arnold M, Cumurciuc R, Stapf C, Favrole P, Berthet K, Bousser MG. Pain as the only symptom of cervical artery dissection. Journal of neurology, neurosurgery, and psychiatry. 2006;77(9):1021–4.
6 Evers S, Marziniak M. Headache attributed to carotid or vertebral artery pain. Handbook of clinical neurology. 2010;97:541–5.
7 Debette S, Leys D. Cervical-artery dissections: predisposing factors, diagnosis, and outcome. Lancet neurology. 2009;8(7):668–78.
8 Kim YK, Schulman S. Cervical artery dissection: pathology, epidemiology and management. Thrombosis research. 2009;123(6):810–21.
9 Leys D, Bandu L, Henon H, Lucas C, Mounier-Vehier F, Rondepierre P, et al. Clinical outcome in 287 consecutive young adults (15 to 45 years) with ischemic stroke. Neurology. 2002;59(1):26–33.
10 Debette S, Metso TM, Pezzini A, Engelter ST, Leys D, Lyrer P, et al. CADISP-genetics: an International project searching for genetic risk factors of cervical artery dissections. International journal of stroke: official journal of the International Stroke Society. 2009;4(3):224–30.
11 Armstrong T, Bull F. Development of the World Health Organization Global Physical Activity Questionnaire (GPAQ). J Public Health. 2006;14:66–70.
12 Rosengren A, Hawken S, Ounpuu S, Sliwa K, Zubaid M, Almahmeed WA, et al. Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): case-control study. Lancet. 2004;364(9438):953–62.
13 Rubinstein SM, Peerdeman SM, van Tulder MW, Riphagen I, Haldeman S. A systematic review of the risk factors for cervical artery dissection. Stroke; a journal of cerebral circulation. 2005;36(7):1575–80.
14 D'Anglejan-Chatillon J, Ribeiro V, Mas JL, Youl BD, Bousser MG. Migraine – a risk factor for dissection of cervical arteries. Headache. 1989;29(9):560–1.
15 Ward TN. Migraine diagnosis and pathophysiology. Continuum. 2012;18(4):753–63.
16 Lee VH, Brown RD, Jr., Mandrekar JN, Mokri B. Incidence and outcome of cervical artery dissection: a population-based study. Neurology. 2006;67(10):1809–12.
17 Dziewas R, Konrad C, Drager B, Evers S, Besselmann M, Ludemann P, et al. Cervical artery dissection – clinical features, risk factors, therapy and outcome in 126 patients. Journal of neurology. 2003;250(10):1179–84.
18 Dalkara T, Nozari A, Moskowitz MA. Migraine aura pathophysiology: the role of blood vessels and microembolisation. The Lancet Neurology. 2010;9(3):309–17.
19 Lichy C, Metso A, Pezzini A, Leys D, Metso T, Lyrer P, et al. Predictors of delayed stroke in patients with cervical artery dissection. International journal of stroke: official journal of the International Stroke Society. 2015;10(3):360–3.
20 Metso TM, Tatlisumak T, Debette S, Dallongeville J, Engelter ST, Lyrer PA, et al. Migraine in cervical artery dissection and ischemic stroke patients. Neurology. 2012;78(16):1221–8.

Correspondence:
Dr. med. Christopher Traenka
Neurology and Stroke Center
University Hospital of Basel
Petersgrapben 4
CH-4031 Basel
christopher.traenka[at]usb.ch