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Recanalization of cervicocephalic artery dissection

Smit D. Patel, Rafique Haynes, Ilene Staff¹, Ajay Tunguturi, Sedeek Elmoursi, Amre Nouh

Abstract:

BACKGROUND AND PURPOSE: While there exists a substantial literature on the risk factors and clinical manifestations of cervical artery dissection (CeAD) including carotid and vertebral artery, little is known about postdissection recanalization. The goal of our study was to provide a descriptive analysis of CeAD and recanalization after dissection with neuroimaging follow up.

METHODS: We retrospectively analyzed 51 consecutive patients with confirmed diagnoses of CeAD based on neuroimaging. Demographic data, risk factors, and dissection characteristics were recorded. Neuroimaging studies were performed at 0, 3, 6, and >6 months.

RESULTS: Among 51 cases, the mean age of dissection (mean \pm standard error) was 49.4 ± 1.92 years, and female comprised 58.8% of the patients. Extent of stenosis was 100% dissection in 37.3%, 51%–99% in 41.2%, and <51% in 21.5%. The most common presenting symptoms were headache (54.9%), neck pain (49.0%), and dizziness/gait imbalance (39.2%). The most common associated risk factors were recent history of trauma to the head and neck (41.2%) and hypertension (41.2%). In follow-up imaging, overall, 47.1% (24/51) had complete recanalization (CR), while 35.3% (18/51) did not; in the former group, 75% (18/24) recanalized completely during the first 6 months following symptom onset. A majority (84.3%) of the patients were discharged home, 15.7% were discharged to a facility, and no mortality was reported. Interestingly, location, type-/nature of dissection, and treatment did not statistically appear to influence the likelihood of recanalization.

CONCLUSIONS: The recanalization of CeAD occurs mainly within the first 6 months after symptom onset, following which healing slows down. The study did not find an association between location, pattern, or nature of dissection on artery recanalization.

Keywords:

Anticoagulants, antiplatelets, carotid artery dissection, dissection, ischemic stroke, recanalization, recurrent stroke, vertebral artery dissection

Introduction

Cervical artery dissection (CeAD) occurs from a tear or separation of the vessel wall layers, allowing blood to collect between layers leading to blood stasis and, subsequently, the formation of intramural hematoma in the false lumen, which in turn results in stenosis or occlusion of the true arterial lumen. This can result in ischemic stroke from artery-to-artery embolization,

hypoperfusion, or a combination of both mechanisms, although the former is the more common reason.^[1,2]

CeAD is the most common cause of stroke in the young and middle-aged, contributing to up to 20% of the events in these age groups,^[3] although it can be seen at any age, with an annual incidence rate of 2.6–2.9/100,000 was reported.^[3] Undoubtedly, the true incidence is likely underestimated, as many cases with dissections are often missed due to inadequate imaging in cases of minor injuries or the absence of clinical symptoms.

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Departments of Neurology
and ¹Research, Hartford
Hospital, Hartford,
Connecticut, USA

Address for correspondence:

Dr. Smit D. Patel,
University of Connecticut/
Hartford Hospital, 80
Seymour Street, Hartford,
Connecticut 06106, USA.
E-mail: drsmitpatel1988@
gmail.com

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Recanalization of the dissected artery is very important to prevent ischemic stroke, including recurrent strokes. Overall, there has been an increasing number of reported patients with dissection in recent years, reflecting both a growing familiarity with this clinical entity and an advance in neuroimaging, including conventional, magnetic resonance, and computed tomography angiography.^[4] Serial neuroimaging can show recanalization or normalization of the vessels and helps guide medical management. Regardless, there is a lack of contemporary data pertaining to CeAD risk factors, patterns, and details regarding progression to recanalization. The primary aim of our study is to assess the timing of recanalization with an overall descriptive analysis of the recanalized population.

Methods

This is a retrospective observational study of patients who presented to our comprehensive stroke center between August 16, 2016, and March 15, 2019, and were found to have a CeAD. Asymptomatic and symptomatic CeAD was defined using the International Classification of Diseases (ICD)-9 and ICD-10 codes that included carotid artery (ICD 9-44321 and ICD 10-I77.71) and vertebral artery (ICD 9-443.24 and ICD 10-I77.74). A total of 125 unique patients were identified using the ICD-9 and ICD-10 codes, from which 51 patients met the study inclusion criteria.

Inclusion and exclusion criteria

Inclusion criteria were included age ≥ 18 presenting with intracranial or extracranial dissection and had follow-up imaging. We included both spontaneous and secondary/traumatic (triggered dissection) dissection patients. Exclusion criteria included patients with missing follow-up imaging, chronic dissection, noncompliance to antiplatelets or anticoagulants agents, absence of dissection on initial imaging, or dissection involving large vessels.

Study variables

The risk factors for CeAD were defined as follows: recent history of trauma to the head and neck, migraine, hypertension, diabetes, hyperlipidemia, atrial fibrillation, hypercoagulable condition, connective tissue disease (CTD), alcohol abuse, and smoking status, drug abuse, and prior history of stroke. The location of the dissection was defined by the standard anatomic categories. The carotid extracranial segments were cervical, petrous, cavernous, and intradural segments supraclinoid and terminal carotid. The vertebral extradural segments were V1, V2, V3, and the intradural V4 segment from the dura to the basilar artery. Baseline characteristics variables are described as per Table 1.

Table 1: Baseline characteristics of cervical artery dissection (n=51)

Variables	Total, n (%)
Age (years; mean \pm SE)	49.4 \pm 1.92
Sex	
Male	21 (41.2)
Female	30 (58.8)
Dissected vessels	
Carotid	20 (39.2)
Vertebral	29 (56.9)
Both	2 (3.9)
Dissection location	
Extradural dissection	39 (76.5)
Intradural dissection	3 (5.9)
Both	9 (17.6)
Nature of dissection	
Spontaneous	37 (72.5)
Traumatic	14 (27.5)
Type of dissection	
100% stenotic dissection	19 (37.3)
51%-99% stenotic dissection	21 (41.2)
<51% stenotic dissection	11 (21.5)
Average duration imaging follow-up (months), (median, IQR)	4.0 (3.0-6.0)
Type of stroke	
Ischemic stroke	21 (41.2)
SAH	2 (3.9)
IPH	3 (5.9)
Recurrent stroke after dissection	2 (3.9)
Hospital disposition	
Home	43 (84.3)
Facility	8 (15.7)
Mortality	0
Symptomatic presentation	
Headache	28 (54.9)
Neck pain	25 (49.0)
Gait imbalance/dizziness	20 (39.2)
Paresthesia	8 (15.7)
Hemiparesis	6 (11.8)
Vision changes	6 (11.8)
Unconsciousness	4 (7.8)
Aphasia	4 (7.8)
Horner syndrome	4 (7.8)
Asymptomatic	1 (2.0)
Associated comorbidities/risk factors	
Recent history of trauma to the head and neck	21 (41.2)
Hypertension	21 (41.2)
Hyperlipidemia	15 (29.4)
Fibromuscular dysplasia	8 (15.7)
Migraine	7 (13.7)
Diabetes	3 (5.9)
Atrial fibrillation	2 (3.9)
Hypercoagulable condition	1 (2.0)
Prior history of stroke	7 (13.7)
Substance use	
Active alcohol use	9 (17.7)
Active smoker	10 (19.6)

Contd...

Table 1: Contd...

Variables	Total, n (%)
Active drug abuse	1 (2.0)
Treatments of dissection	
Medical treatment	
Anti-platelets	40 (78.4)
Anti-coagulants	8 (15.7)
Both	3 (5.9)
Surgical treatment	
Endovascular procedures (stents and angioplasty)	3
Follow-up neuroimaging	
No recanalization	18 (35.3)
Partial recanalization	9 (17.6)
Complete recanalization	24 (47.1)

SAH: Subarachnoid hemorrhage, IPH: Intraparenchymal hemorrhage, IQR: Interquartile range, SE: Standard error

Recanalization definition

Baseline and follow-up imaging of our study patient's dissection was reviewed by experienced vascular neurologists. The choice of the initial and subsequent imaging was at the discretion of the treating stroke attending. If follow-up imaging showed normal findings (i.e., complete recanalization [CR]) or two subsequent imaging showed no recanalization from index imaging, then no further examinations were performed.

1. CR is defined as the complete reopening of injured vessels and/or > 50% recanalization from the index imaging
2. Partial recanalization (PR) is defined as <51% recanalization from index imaging
3. Patients who did not show recanalization after two subsequent imaging follow-ups were defined as non-recanalization (NR)
4. Non-CR includes those that failed to undergo CR (PR + NR).

Statistical analysis

A descriptive analysis was performed for all data patients with recanalization, and those without were compared using an independent group using the Wilcoxon Ranked-Sum test and Student's *t*-test for continuous variables, including age and average duration follow-up. Categorical variables were compared between the two groups of patients using Chi-square tests of proportion when cell frequencies permitted and Fisher's exact test when frequencies were too small. All comparisons were univariate as the small sample size was insufficient for any multivariable analysis. Data analysis performed with the statistical package SPSSv21 (IBM, Armonk, NY, USA) to SAS 9.4.

Ethics committee approval

This study was approved by the Institutional Review Board of our hospital with a total waiver of consent

since this study does not contain direct patients' enrollment.

Results

Baseline characteristics

The average age at dissection was 49.4 years; 58.8% ($n = 30$) were female. Vertebral artery dissection was more frequent than the carotid artery (56.9% vs. 39.2%). The most common presenting symptoms were headache (54.9%), neck pain (49.0%), and dizziness/gait imbalance (39.2%). The most common associated risk factors were recent history of trauma to the head and neck (41.2%), and hypertension (41.2%). About 76.5% dissections were extradural, 5.9% intradural, and 17.6% were located in both intra-and extradural compartments. The average median duration of follow-up of vascular imaging was four months. On review of index imaging, 41.2% ($n = 21$) had an acute ischemic stroke; only three patients were treated with IV-tPA/thrombectomy, whereas 9.8% ($n = 5$) had intracranial hemorrhage. In a follow-up period, overall, 47.1% (24/51 cases) had CR, 35.3% (18/51 cases) did not show CR, while only 17.6% (9/51 cases) reported PR. A total of 75% (18/24 cases) of the CR population showed recanalization within the first 6 months. A majority (84.3%) of patients were discharged home, 15.7% were discharged to a facility, and no mortality was reported [Table 1].

Location of carotid and vertebral artery dissections

Among 43 identified carotid dissections, cervical segments were most often affected (46.5%) followed by petrous segments (18.6%); while among 55 identified vertebral artery dissections, V2 (36.4%) and V3 (34.5%) segments were found to be most often affected [Table 2].

Recanalization population

The univariate analysis of CR vs. non-CR is shown in Table 3. From the total sample ($n = 51$), 47% (24/51) patients had CR, whereas 53% (27/51) with non-CR (35.3% [18/51 cases] NR + 17.7% [9/51 cases] PR). There was no mean age difference between CR versus non-CR (~47 vs. ~51 years; $P = 0.32$). There was also no sex difference observed between the two groups. CR has a median duration of follow-up 4.5 versus 3.0 months ($P = 0.04$). Interestingly, location, nature of dissection, and treatment do not show statistically significant differences in the extent of recanalization between these groups [Table 3].

Discussion

In our study, we found that the most common presenting symptoms for CeAD were headache and neck pain. One may hypothesize that outward dissection and

aneurysmal dilatation may cause local symptoms from compression of adjacent nerves and activation of nociceptors from distension of the vessel wall due to the hematoma as similarly described in the existing literature.^[5] In our study, the average age of dissection was ~50 years.^[6] Although the influence of sex in CeAD is controversial,^[7-9] nearly 58.8% of our study comprised

female preponderance. There are several genetic and environmental influences that could hypothetically contribute to these sex differences; although further research is necessary to address this question. The majority of dissections in our population were a result of significant head and neck trauma, although generally speaking, most dissections occur spontaneously or even after a minor injury.^[10] In addition to trauma, underlying CTDs lowers the threshold of dissection in the setting of concurrent trauma. The most common CTD is fibromuscular dysplasia, which accounts for 15%–20% of all cases of CAD reported by Jeffrey *et al.*^[11] similar to the results of our study (15.7%). Other factors associated with dissection include hypertension (41.2%), migraine (13.7%), smoking (19.6%), and alcohol abuse (17.7%).^[12] In our study, we noted that the most common complications from dissection are embolic ischemic stroke in 41.2%, followed by intracranial hemorrhage in 9.8%. Subarachnoid hemorrhage is seen more often with intradural compared to extradural CeAD. In our study, no mortality was noted, and the majority (~84%) of the patients were discharged home.^[13] The low mortality rate in our study may, at least in part, be explained by a small sample size. The most

Table 2: Location of the cervical artery dissection

	<i>n</i> (%)
Location of carotid artery dissection* (<i>n</i> =43)	
Cervical	20 (46.5)
Petrous	8 (18.6)
Cavernous	7 (16.3)
Clinoid/supraclinoid	6 (14.0)
Terminal segments	2 (4.6)
Location of vertebral artery dissection# (<i>n</i> =55)	
V1	10 (18.2)
V2	20 (36.4)
V3	19 (34.5)
V4	6 (10.9)
Basilar	0

*, #One/>1 location of dissections from carotid artery dissections and vertebral artery dissections

Table 3: Univariate analysis of recanalized cervical artery dissection

Variables	CR (<i>n</i> =24)	Non-CR (PR + NR)			Univariate <i>P</i>
		Non-CR (<i>n</i> =27)	PR (<i>n</i> =9)	NR (<i>n</i> =18)	
Age (years) (mean±SE)	47.3±2.92	51.2±2.53	51.4±4.7	51.0±3.10	0.32
Gender					
Male	41.7	40.7	33.3	44.4	Ref
Female	58.3	59.3	66.7	55.6	0.95
Dissected vessels (%)					
Carotid	45.8	33.3	22.2	38.8	0.97
Vertebral	54.2	59.3	66.7	55.6	0.98
Both	0.0	7.4	11.1	5.6	Ref
Dissection location (%)					
Intradural dissection	8.3	3.7	0	5.6	Ref
Extradural dissection	79.2	74.1	55.6	83.3	0.57
Both	12.5	22.2	44.4	11.1	0.35
Nature of dissection (%)					
Spontaneous	83.3	63.0	77.8	55.6	0.13
Traumatic	16.7	37.0	22.2	44.4	Ref
Imaging follow-up (months), median (IQR)	4.5 (3.0-6.8)	3.0 (2.0-6.0)	4.0 (2.0-6.5)	3.0 (2.0-4.8)	0.04
0-3 months (%)	33.3	59.3	33.3	72.2	0.36
4-6 months (%)	41.7	18.5	44.5	5.6	0.40
>6 months (%)	25.0	22.2	22.2	22.2	Ref
Type of dissection (%)					
100% stenotic dissection	29.2	44.5	44.5	44.4	0.37
51%-99% stenotic dissection	45.8	37.0	33.3	39.0	0.91
<51% stenotic dissection	25.0	18.5	22.2	16.6	Ref
Treatments (%)					
Anti-platelets	83.3	74.1	77.8	72.2	0.44
Anti-coagulants	12.5	18.5	0.0	27.8	0.87
Treated with both agents	4.2	7.4	22.2	0.0	Ref

P-value suggests the results of comparison between CR and non-CR. CR: Complete recanalization, Non-CR: Noncomplete recanalization, PR: Partial recanalization, NR: No recanalization, IQR: Interquartile range, SE: Standard error

common location for carotid dissection was generally beyond or at the carotid bifurcation (46.5%) and in the petrous segment (18.6%), while in posterior circulation most common vertebral segments were V2 (36.4%) and V3 (34.5%), as reported in prior studies.^[14,15] A possible explanation of these findings may be reduced mobility in these segments, making them susceptible to shearing forces on vessel walls layers.

The main aim of the treatment is to prevent recurrent ischemic events following dissection and recanalization of the injured vessels. The majority of our patients treated with anticoagulants (15.7%) or antiplatelets (78.4%) therapy or both (5.9%). Three patients received endovascular treatments (2 received angioplasty only and 1 received stents). From them, two were discharged home, and one was discharged to the facility for rehabilitation therapy. The choice between antiplatelets and anticoagulants therapy should be directed by the clinical experience of the treating physician and by patient preferences, comorbid conditions, and tolerance of these agents. The American heart association recommends treatment with either antiplatelets or anticoagulants therapy for 3–6 months is reasonable for patients with ischemic stroke and extracranial carotid or vertebral arterial dissection (class IIa recommendation) based on published CADISS trial.^[16] However, other factors such as stroke burden, hemorrhagic transformation from stroke, extended intracranial dissections should be considered before augmentation of anticoagulants. Data from randomized controlled trials are missing for treatment for intracranial artery dissections. However, patients with intracranial artery dissection and cerebral ischemia are treated with antiplatelets to avoid hemorrhagic complications.^[17] Angioplasty and/or stenting can be indicated in recurrent ischemic events despite appropriate maximum medical therapy, however efficacy of endovascular procedures is not yet established from randomized trials.^[16]

In our study, 75% of total CR achieved during the first 6 months, similar to findings from other studies, as the majority of vascular healing takes place during this period.^[8,9] Our study reported a median time for CR of 4.5 months versus 3.0 months for non-CR. Nedeltchev *et al.*^[8] showed CR in ~60% of patients (160/268 cases) with carotid artery dissection within the first 6 months. The study by Arauz *et al.*^[9] showed that CR of vertebral artery dissection was achieved in ~63% of patients (39/62 cases) within the first 6 months. These findings support the existing practice at our center of performing follow-up imaging at 3 and 6 months and continuing either antiplatelets or anticoagulants until complete or stagnant healing achieved. Type of imaging modality used and decisions regarding pharmacotherapy depended on the clinical situation, resources and were at

the discretion of the practicing stroke neurologists. Our study showed nonsignificant differences in the rate of recanalization in traumatic dissection (16.7% vs. 37.0%) and spontaneous dissection (83.3% vs. 63.0%) similar findings reported by Ramchand *et al.* study.^[18] Similar to previous studies, our study did not find the effect of treatment types (antiplatelets vs. anticoagulants) on recanalization.^[18,19] There was higher rate of recanalization observed in incomplete stenotic dissection, including 51%–99% stenotic dissection (45.8% vs. 37.0) and <51% stenotic dissection (25.0% vs. 18.5%), while lower rate of recanalization observed in complete stenotic dissection (29.2% vs. 44.5%), although non-statistically difference. Similar findings were observed in a carotid artery dissection study by Nedeltchev *et al.*^[8] However, a vertebral artery dissection study by Arauz *et al.* did not show a significant difference for the influence of the type of dissection on recanalization.^[9] Such differences may be a result of variances in sample-size, recruitment pattern, environmental, and patients level risk factors. Interestingly, our study did not find any significant association of dissection location on the likelihood of recanalization. Further study is warranted to explore possible associations of dissection location on the recanalization that might alter the treatment strategy.

Our study has a few limitations. Types of follow-up neuroimaging, choices of anticoagulants and antiplatelets were at the discretion of stroke neurologist on-call, availability of resources. Another limitation is a small sample size, and we could include only 51 patients after following strict inclusion criteria. Another downside of this study is variability with regards to the timing of initial and follow-up neuroimaging; this was unavoidable as the majority of patients presented with nonspecific symptoms, with an unclear time of onset, while only a small fraction of patients presented with symptoms of stroke or TIA to the emergency room; in the latter scenario, we likely captured them early upon initial imaging. Indeed, many patients with CeAD may present to the outpatient clinic as a headache and neck pain as a presenting symptom that could delay the diagnosis depending on the familiarity of the diagnosis to the treating physician. Finally, we could not control patient compliance with follow-up imaging. In this study, 19% of follow-up imaging was missed on subsequent encounters.

Conclusions

Headache and neck pain are the most common presenting symptoms for CeAD. The most common locations for dissection are cervical and petrous segments in carotid arteries and V2 and V3 segments in vertebral arteries. CR was typically achieved between 4 and 6 months after index imaging. Our study did not find any statistical

association between location, type of dissection, and type of treatments on the extent of recanalization.

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Conflicts of interest

There are no conflicts of interest.

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