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REVIEW ARTICLE

Association between cervicocerebral artery dissection and tortuosity – a review on quantitative and qualitative assessment

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Abstract

Cervicocerebral artery dissection stands out as a significant contributor to ischemic stroke in young adults. Several studies have shown that arterial tortuosity is associated with dissection. We searched Pubmed and Embase to identify studies on the association between arterial tortuosity and cervicocerebral artery dissection, and to perform a review on the epidemiology of cervicocerebral artery tortuosity and dissection, pathophysiology, measurement of vessels tortuosity, strength of association between tortuosity and dissection, clinical manifestation and management strategies. The prevalence of tortuosity in dissected cervical arteries was reported to be around 22%-65% while it is only around 8%-22% in non-dissected arteries. In tortuous cervical arteries elastin and tunica media degradation, increased wall stiffness, changes in hemodynamics as well as arterial wall inflammation might be associated with dissection. Arterial tortuosity index and vertebrobasilar artery deviation is used to measure the level of vessel tortuosity. Studies have shown an independent association between these two measurements and cervicocerebral artery dissection. Different anatomical variants of tortuosity such as loops, coils and kinks may have a different level of association with cervicocerebral artery dissection. Symptomatic patients with extracranial cervical artery dissection are often treated with anticoagulant or antiplatelet agents, while patients with intracranial arterial dissection were often treated with antiplatelets only due to concerns of developing subarachnoid hemorrhage. Patients with recurrent ischemia, compromised cerebral blood flow or contraindications for antithrombotic agents are usually treated with open surgery or endovascular technique. Those with subarachnoid hemorrhage and intracranial artery dissection are often managed with surgical intervention due to high risk of re-hemorrhage.

Keywords Cervicocerebral artery · Tortuosity · Dissection · Association · Quantitative assessment · Qualitative assessment

Introduction

Cervicocerebral artery dissection is increasingly acknowledged as a significant risk factor for ischemic stroke in young adults [19, 35]. Dissection may occur spontaneously or after an injury [13, 29, 70]. However, the etiology of dissection is still a matter of debate [57, 65]. Among the proposed etiologies is arteriopathy, possibly stemming from an underlying connective tissue disorder that compromises the strength of the arterial wall. Patients with connective tissue diseases often have known genetic mutation and show higher arterial tortuosity compared to general population [9, 77]. In addition, a higher tortuosity index can be a predictor for arterial dissection and overall outcomes in these patients [55]. Despite this associations, only a minority of dissection cases present with overt connective tissue disorders [20]. Nonetheless, even in the absence of identifiable disorders, weakened vascular structures may manifest as increased tortuosity under hemodynamic stress [36].

Some researchers speculate that tortuosity could be a primary indicator of subclinical connective tissue weakness and have conducted qualitative and quantitative investigations into its association with dissection. Therefore, a comprehensive review was undertaken to gain deeper insights into the relationship between cervical artery tortuosity and dissection.

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Epidemiology

The categorization of morphological anomalies of the carotid and vertebral arteries has not been standardized. Reported studies have used multiple terms that may indicate the same pathophysiological process. Weibel and Fields are the first who categorized anomalies of the internal carotid artery into three distinct types: tortuosity, characterized by elongation and a rippled appearance forming a C- or S-shape; kinking, denoting an acute angle within the artery; and coiling, wherein the artery elongates into an exaggerated S-shaped curve or circular configuration [25]. Others have been using tortuosity to describe different anatomical variants of carotid arteries such as kinking, coiling, loop or elongation [45, 68]. Given the variability in definitions, it has been challenging to quantify the prevalence of morphological anomalies in cervical carotid and vertebral arteries. In addition, studies evaluating carotid cervical artery morphology are highly heterogeneous. One population-based study has shown that the prevalence of carotid artery morphological anomalies (kinking, coiling or tortuosity) is 25.9%. Among the studied population 14% were found to have kinking, 11.4% coiling and 8.9% tortuosity [61]. The latest population-based study which focused on carotid artery kinking and coiling found that 9.94% of subjects had kinking or coiling of the extracranial internal carotid artery. The prevalence notably increased at both ends of the age spectrum (≤ 20 and > 60 years old) [23].

On the other hand, the incidence of cervicocerebral artery dissection is reported to be about 2.6–2.97 per 100,000 patients per year [8, 50]. This is likely an underestimate given that some patients with cervicocerebral artery dissection have no symptoms, subtle symptoms, or an uncertain non-specific onset of symptoms [34, 68]. Reports on the incidence of internal carotid artery (ICA) dissection versus vertebral artery (VA) dissection also differ, although several studies show ICA dissection to be more common than VA dissection [5, 50, 76]. The mean age of occurrence of cervical artery dissection is about 44, with a lower occurrence in patients above 65 [15, 28, 50]. A study from Mexico shows that the mean age of occurrence tends to be younger among the Hispanic population [2]. Most reported cases of intracranial artery dissection come from Asia, suggesting a higher prevalence among the Asian population. It is unclear whether this indicates a publication bias, differences in disease prevalence across ethnic groups, or both [21].

Studies on the prevalence of tortuosity in patients with cervicocerebral artery dissection are scarce. The study conducted by Barbour et al. for instance, comprised 13 patients in the dissected group and 108 in the control group. Among the dissected group, 8 of 13 patients (62%) and 13 of 20 internal carotid arteries (65%) exhibited significant tortuosity. In contrast, the non-dissected group showed significant tortuosity in 20 patients (19%) and 22 vessels (12%) out of 187 [7]. In another study by Kim et al. comparing spontaneous cervical internal carotid artery dissections with age and sex-matched controls, the prevalence of any carotid tortuosity was found to be 53% and 34% in the per-patient analysis of dissected and control groups, respectively. In per-vessel analysis, the prevalence of tortuosity was 39% in the dissected group and 25% in the control group. Loops were observed in 22% of the study group and 8% of controls. Furthermore, a retrojugular course of the internal carotid artery was evident in 23% of dissected patients and 9% of controls in the per-vessel analysis [45]. Saba et al. showed the prevalence of arterial tortuosity was 50.4% in a separate per vessel analysis study [68].

Pathophysiology

Tortuosity is believed to arise from a combination of genetic factors, degenerative vascular diseases, and changes in blood flow and pressure [36, 62, 66] In tortuous cervical arteries there are a few possible mechanisms associated with dissection. Several studies have shown that elastin and tunica media degradation, which reflects degenerative changes in the arterial wall, is associated with vessel tortuosity. That means tortuous arteries have an underlying vessel wall weakness [4, 26, 36, 49]. Increased wall stiffness subsequently causes higher circumferential wall stress which subsequently alters the vessel wall strucutre [12]. In addition, changes in hemodynamics due to tortuous structure might lead to the local disruption of the endothelial integrity [36]. Moreover, widening of the tight junctions, arteriopathy and the subsequent inflammation of the arterial wall accompanying the release of inflammatory agents in response to hemodynamic injury might predispose patients to cervical artery dissection [6, 15, 63, 74]. Genetic factors may mediate these reported associations as well as possible therapeutic targets.

Measurement of tortuosity and its association with dissection

Combined color duplex and doppler sonography is a non-invasive screening tool for cervical artery dissection. The sensitivity of this method is largely contingent on the operator, and its diagnostic efficacy is limited for arteries situated at the skull base or within the transverse foramina. When vertebral or carotid artery dissection is suspected on duplex

ultrasound, MRA or CTA is often required for confirmation. There is no consensus on how to evaluate and measure the degree of tortuosity. Several measurements have been introduced in the literature, such as arterial tortuosity index, vertebrobasilar artery deviation etc., as shown in the summary table.

Arterial Tortuosity Index (ATI)

Measuring arterial tortuosity index (ATI) is a way to describe the level of vessel tortuosity. There are only a few studies which quantitively assessed ATI to investigate the association between cervical arterial tortuosity and dissection. ATI was defined as (actual length of artery/ straight length -1)*100. For the measurement of arterial length, a 3D volume rendered angiogram was used in these studies. Kim et al. conducted a comparative analysis between patients with cervical dissection and age- and sex-matched healthy controls. Despite no variance in vascular risk factors between the two groups, their findings revealed a higher prevalence of tortuosity in cervical arteries among those with cervical artery dissection compared to controls. Their multivariate analysis highlighted the independent association of vascular tortuosity of the vertebral artery with the presence of cervical artery dissection [44] Similarly, Giossi et al. assessed the degree of tortuosity in consecutive patients with spontaneous cervical artery dissection, age- and sex-matched patients with ischemic stroke unrelated to cervical artery dissection, and stroke-free subjects. Their study indicated a higher vertebral Arterial Tortuosity Index (ATI) in patients with cervical artery dissection (median 7.3) compared to non-cervical artery dissection stroke subjects (median 3.4) and stroke-free subjects (median 4.0). Multivariable regression analysis demonstrated an independent association between vertebral ATI and the risk of cervical artery dissection. Moreover, the degree of tortuosity tended to be higher in dissected patients experiencing short-term recurrence compared to those without recurrent events [33] Additionally, Zhang et al. compared 66 patients with cervicocerebral artery dissection with a matched control group, revealing higher internal carotid tortuosity index (25.24 vs. 15.90) and vertebral tortuosity index (11.28 vs 8.38) in the study group compared to controls. They also found independent associations between internal carotid artery tortuosity index, vertebral artery tortuosity index, and Type III carotid siphons with the risk of cervicocerebral artery dissection [79].

Vertebrobasilar artery deviation

Another way of describing vertebral tortuosity level is measuring vertebrobasilar artery deviation which is often assessed with lateral shift of the vertebral artery or vertebrobasilar junction. Kurata et al. evaluated a series of 57 consecutive cases using angiography to examine deviations in the course of affected and contralateral vertebral arteries. They established the midline as a line extending from the septum pellucidum to the anterior median fissure, determined through basiparallel anatomic scanning (BPAS) MR imaging. According to their classification, no deviation was characterized by a sharp angle configuration of the vertebral artery (Type I), mild-to-moderate deviation by an obtuse angle configuration (Type II), and severe deviation by marked deviation to the contralateral side crossing over the midline (Type III). Their findings revealed that the most prevalent pattern of vertebral artery deviation was Type III for the affected side and Type I for the nonaffected side. Interestingly, all Type III dissections occurred proximal to a tortuous portion, whereas the majority of Type I and Type II cases (33 out of 39) were observed near the union of the vertebral artery [48].

Hori et al. classified the deviation of the vertebrobasilar junction into three types: Type 1, where the vertebrobasilar junction is positioned within 2 mm from the midline; Type 2, characterized by a lateral shift of more than 2 mm towards the ipsilateral side of the dominant vertebral artery; and Type 3, indicating a lateral shift of more than 2 mm towards the contralateral side of the dominant vertebral artery. Their findings revealed a higher prevalence of both dominant vertebral artery presence and lateral shift of the vertebrobasilar junction among patients with vertebral artery dissection compared to the control group. Among patients with vertebral artery dissection, the lateral shift of the vertebrobasilar junction was categorized into Type 1 ($n=6$), Type 2 ($n=13$), and Type 3 ($n=17$), while among the controls, it was classified into Type 1 ($n=20$), Type 2 ($n=8$), and Type 3 ($n=7$). Type 3 predominance was noted in patients with vertebral dissection [39] (Table 1).

Different anatomical variations of arterial tortuosity

Seldom studies evaluated the association between dissection and different anatomical variation of carotid artery vessel tortuosity. Saba et al. categorized tortuosity as elongation, kinking, or coiling. The findings of their study revealed a statistically significant correlation between internal carotid artery dissection and kinking as well as coiling, whereas no statistically significant difference was observed with arterial vessel elongation. Moreover, internal carotid artery dissection was more frequently observed on the left side compared to the right. These results were further validated using both carotid arteries of the same patient as the dependent parameter, for kinking, coiling, and elongation. In another study conducted by Kim et al., anatomical variations of vessels such as loops, coils, and kinks were examined. On per-vessel analysis, there was no significant difference in the prevalence of loops, coils, or kinks [44].

Table 1 Summary table of studies

Author and publication year	Study subjects (size)	Control subjects (size)	Subjects matched ?	Artery studied for tortuosity	Compared measurement	Calculation or measurement of tortuosity	Imaging tool used
Kim et al. 2016	Cervical artery dissected patients (75)	Healthy patients without cervical artery dissection (75)	Yes	Vertebral artery and carotid artery	Vertebral artery tortuosity index (VTI) and carotid artery tortuosity index (CTI)	Tortuosity index = (Actual/straight length -1)*100	3D contrast enhanced MRA
Giossi et al. 2017	Spontaneous cervical artery dissected patients (102)	Ischemic stroke patients without cervical artery dissection (102); Stroke free patients without cervical artery dissection (102)	Yes	Vertebral artery	Vertebral artery tortuosity index	Tortuosity index = (Actual/straight length -1)*100	3D volume-rendered angiogram created from contrast-enhanced MRA
Zhang et al. 2021	Spontaneous cervical artery dissected patients (66)	Patients without cervical artery dissection (66)	Yes	Vertebral artery and carotid artery	Vertebral artery tortuosity index (VTI) and carotid artery tortuosity index (CTI)	Tortuosity index = (Actual/straight length -1)*100	CTA/MRA/angiogram
Barbour et al. 1994	Spontaneous carotid artery dissected patients (13)	Patients without carotid artery dissection (108)	No	Internal carotid artery	Prevalence of tortuosity	Kinks: a sharp bend in the vessel with an angle < 90° Coils: a 360° turn in the vessel Loops: a C- or S-shaped deformity with two turns in the vessel with angles < 90°	Percutaneous transfemoral cerebral arteriograms
Kim et al. 2018	Spontaneous internal carotid artery dissected patients (83)	Patients without internal carotid artery dissection (83)	Yes	Internal carotid artery	Prevalence of tortuosity	Kinks: a sharp bend in the vessel with an angle < 90° Coils: a 360° turn in the vessel Loops: a C- or S-shaped deformity with two turns in the vessel with angles < 90°	Cervical CTA

Table 1 (continued)

Author and publication year	Study subjects (size)	Control subjects (size)	Subjects matched ?	Artery studied for tortuosity	Compared measurement	Calculation or measurement of tortuosity	Imaging tool used
Kurata et al. 2012	Vertebral artery dissected patients (57)	NA	NA	Vertebral artery	Vertebral artery deviation type I, type II and type III	Type I: no deviation Type II: with mild-to-moderate deviation but not over the midline Type III: featuring marked deviation to the contralateral side over the midline	Angiography
Hori el al. 2020	Vertebral artery dissected patients (43)	Patients without vertebral artery dissection (63)	Yes	Vertebral artery	Deviation of vertebrobasilar junction	Type I: vertebrobasilar junction within 2 mm from the midline Type II: > 2 mm-lateral shift of vertebrobasilar junction to the ipsilateral side of the dominant VA Type III: > 2 mm-lateral shift of vertebrobasilar junction to the contralateral side of the dominant VA	Cervical MRA

Table 1 (continued)

Author and publication year	Study subjects (size)	Control subjects (size)	Subjects matched ?	Artery studied for tortuosity	Compared measurement	Calculation or measurement of tortuosity	Imaging tool used
Saba et al. 2015	Traumatic internal carotid artery dissected patients (64); Spontaneous internal carotid artery dissected patients (60)	NA	NA	Internal carotid artery	Anatomic variations of internal carotid artery: no anomaly, elongation, kinking and coiling	Elongation: presence of abnormal vessel length without kinking or coiling with S- or C-shaped tortuosity or ondulation in the course of the ICA Kinking: a variant of coiling (less pronounced or Z shape), where it is visible in an acute angulation with 60° or less Coiling: presence of elongation or redundancy of the ICA in a restricted space, and an exaggerated S-shaped curve or a circular (or double circular) configuration	Cervical CTA and MRI
Wei et al. 2016	Chidren with dissected arterties (22)	Healthy children (13)	No	Verterbral artery, internal carotid artery, basilar artery and M1 segment of middle cerebral artery	Tortuosity score	Tortuostiy score = Path length of artery/ shortest distance of artery	MRA

Arterial tortuosity in children

A study conducted by Wei et al. centered on arterial tortuosity and the pathogenesis of stroke among patients under the age of 18. Tortuosity was assessed individually for each cervical artery by dividing the path length by the Euclidean (shortest) distance between its end points. The findings revealed that tortuosity was elevated in cases of extracranial cervical dissection. However, there was no discernible difference in tortuosity between traumatic and spontaneous dissections [75].

Clinical manifestations and management

Dissected cervicocerebral arteries often form pseudoaneurysm, intraluminal hematoma or thromboembolism which can result in ischemic stroke or transient ischemic attacks [11, 16, 43, 50, 51, 59, 74]. However, in most cases, patients are asymptomatic or have local symptoms which can differ depending on the location of dissection in cervical arteries. Common local symptoms include headache, neck pain, cervical and cranial neuropathy, pulsatile tinnitus, or Horner's syndrome [18, 31, 51, 54, 71]. Neck pain is common in extracranial vertebral artery dissection [18]. Cervical neuropathy and Horner's syndrome are often seen with carotid artery dissection [18, 51, 71]. Stroke symptoms are generally more severe in carotid artery dissections, whereas subarachnoid hemorrhages (SAH) are more frequently associated with dissections in the intracranial portion of the vertebral artery [17, 21]. In rare cases extracranial carotid artery dissection can cause tongue swelling, vocal cord paralysis, difficulty with swallowing, homonymous hemianopsia or hallucinations [40, 56, 67, 72]. Dissection in the intracranial portion of cervical artery may result in subarachnoid hemorrhage, and this may happen in combination with ischemic stroke. Urgent intervention is often utilized in these situations [3, 21].

At present, there is no absolute consensus on how to treat patients with cervicocerebral artery dissection. However, all symptomatic patients are often placed on antithrombotic medication, either antiplatelet or anticoagulation, to prevent stroke and long-term neurological complications. Extension of intramural hematoma is rare, but still possible, during antithrombotic therapy, hence, the approach may vary for extracranial versus intracranial dissections. Limited available evidence suggests no significant difference in efficacy between anticoagulation and antiplatelet treatment for preventing ischemic stroke in cases of extracranial dissection. Trials such as the Cervical Artery Dissection in Stroke Study (CADISS) or TREAT-CAD trial did not establish superiority of one over the other among anticoagulant and antiplatelet agents [30, 52]. Meta-analyses of non-randomized studies also found no disparities in outcome or complication rates between anticoagulation and antiplatelet therapy [14, 42]. For patients who have ischemic neurologic symptoms caused by intracranial arterial dissection, studies have indicated that antiplatelet therapy might be preferred over anticoagulation due to the potential risk of developing subarachnoid hemorrhage [22].

Most studies debate that the candidates for procedural therapy include those who have recurrent ischemia despite medical treatment and those with significantly compromised cerebral blood flow (narrow vessel lumen) as well as patients with contraindications to anticoagulants or antiplatelets [16, 32, 53]. It is important to note that that all patients, including those who receive surgical or endovascular interventions, receive medical therapy in line with international treatment guidelines [10].

Various open surgical and endovascular approaches have been outlined for managing carotid and vertebral artery dissections and pseudoaneurysms. The American Heart Association/American Stroke Association (AHA/ASA) recommends surgical repair only for internal carotid artery dissection and not vertebral artery dissection [10]. The AHA/ASA also fails to clarify when exactly medical therapy alone is inadequate and surgical intervention should be considered. For surgical management, the diseased portion of the carotid artery that contains the dissection is either repaired directly, resected, or bypassed. Primary artery repair is performed by removal of the clot (i.e.thromboendarterectomy) and then the artery is repaired with patchplasty using autologous vein (a segment of the patient's own vein, typically saphenous) or a synthetic patch. If the damaged arterial segment is resected, it is replaced with an autologous interposition vein graft or synthetic graft. If there is redundant artery with a loop or kink, primary anastomosis can be employed. Bypass of the diseased segment can also be performed with autologous vein graft or a synthetic tube graft.

Endovascular approaches include angioplasty or stent placement which acts as a scaffold that is used to tack down the intimal flap and to reinforce the cervical arterial wall [27, 46, 58, 64, 69, 73]. Flow diversion has also been used in the management of vertebral and carotid artery dissection [24, 78]. Radial or femoral access can be used with endovascular techniques. Guidewires and catheters are then used to cannulate the carotid or vertebral artery under X ray guidance, and the stent or flow diverter is delivered over the guidewire and into the diseased artery. International guidelines, in particular those from the AHA/ASA, recommend to consider angioplasty and stenting when ischemic neurological symptoms persist despite antithrombotic therapy following acute dissection [10]. Numerous studies have investigated endovascular repair of internal carotid artery dissection and vertebral artery dissection, with successful results regarding safety and

recurrent stroke [1, 37, 38, 41, 58, 64, 69, 73]. Therefore, although the indications for endovascular repair are not entirely specific, these treatments remain options for patients who do not respond to medical therapy and in patients with severe ischemic symptoms who are not candidates for thrombolytics, anticoagulation, or antiplatelet agents. Endovascular techniques can also be used in the treatment of persistent pseudoaneurysms associated with dissection. The tortuosity of the involved cervical artery can make endovascular repair challenging. Some studies have shown that silk flow diverter, straightening with a peripheral micro-guidewire, or distal guiding catheter access can greatly facilitate endovascular therapy through the tortuous vascular anatomy [47, 60, 78]. However, the criteria for open surgical versus endovascular management of tortuous dissected cervical arteries has not been discussed or compared in a head-to-head comparison in the literature. It likely depends on the level of vessel tortuosity and surgeon's experience with either endovascular or open surgical techniques. Further studies with rigorous quantitative assessment on cervical artery tortuosity and dissection may well help to provide insight into these issues.

For intracranial artery dissection and pseudoaneurysm with subarachnoid hemorrhage, aggressive intervention should be pursued to avoid rehemorrhage. This may be accomplished by bypass and occlusion of the dissected segment or by endovascular techniques of vessel sacrifice or flow diversion.

Conclusion

This review is on the qualitative and quantitative evaluation of the association between cervicocerebral artery dissection and arterial tortuosity. However, the methodology and study subjects reported in the literature to date are quite variable without standard techniques of tortuosity documentation. Thus, it was impossible to do a stratified analysis on this topic. The definition of tortuosity is inconsistent between studies which hindered the comparison of data. In addition, studies that explored the quantitative association between cervical artery tortuosity and dissection are scarce. Therefore, future emphasis should be placed on the transition from visual observation-based diagnosis to objective measures of level of vessel tortuosity and well-defined differentiation between cervical vessel anomalies. It is also important to apply common measurement strategies throughout and between studies. Lastly, future studies with well-balanced study and control groups through propensity matching or randomized design can better assess the association between cervicocerebral artery tortuosity and dissection.

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