51 Cervicocephalic Arterial Dissections

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Overview

Cervicocephalic arterial dissections are a major cause of stroke in children and young adults, and an occasional source of stroke in the elderly. In cervicocerebral dissections, blood erupts into the arterial wall, forming an intramural hematoma. When the dissection is situated in the subintimal or the inner medial planes, the intramural hematoma causes the inner vessel wall to bulge inward, narrowing the vessel lumen. When the dissection is in the outer media or subadventitia, the intramural hematoma displaces the external vessel wall outward, creating a dissecting aneurysm. If the dissection cavity is in communication with the main arterial lumen, thromboplastin and other highly thrombogenic elements in the exposed vessel wall provoke vigorous clot formation, with resulting additional lumen compromise and frequent artery–artery embolization. Cervicocerebral dissections are a natural consequence of major penetrating or non-penetrating trauma to the head and neck. In addition, dissections occur with remarkable frequency without any identifiable mechanical provocation or following only minor trauma.

Cervicocerebral dissection was first described in 1915. Hart and Easton's seminal review in 1983[1] clarified the clinical and pathophysiological features of cervicocerebral dissection and laid the foundation for modern investigation. Pathological cases dominated the early literature, providing an unduly dismal picture of the natural history. More recent studies have capitalized on progress in the diagnosis of dissection due to advances in vascular imaging. Diagnostic milestones included delineation of the appearance of dissections on arteriography,[2] ultrasound,[3,4] and magnetic resonance imaging (MRI).[5,6] In the 1980s and 1990s, prospective observation of large-scale single-center and multicenter cohorts clarified the frequency of late stroke and recurrent dissection.[7–10]

Epidemiology

The observed incidence of spontaneous dissection is 2.6 to 2.9 cases per 100 000 individuals across all age groups.[11,12] The true incidence is likely higher as many dissections remain asymptomatic and elude medical surveillance. In a population-based registry, cervical carotid dissections accounted for 2.5% of all first ischemic strokes,[13] and in several registries dissections account for 6% to 25% of ischemic stroke in young adults.[14,15] Spontaneous dissections most commonly affect those between 30 and 50 years old, with more than 70% of patients younger than 50.[16] There is no predilection for gender or ethnic differences. Extracranial internal carotid artery dissections account for 66% of reported cases, extracranial vertebral artery dissections 18%, intracranial internal carotid and middle cerebral artery dissections 6%, intracranial vertebral artery dissections 5%, and basilar artery dissections 4%.[16] Among blunt trauma patients, traumatic carotid dissections occur with an incidence of about one per thousand.[17]

Etiology

Spontaneous dissection likely results from the interaction of intrinsic factors, such as an underlying arteriopathy, and extrinsic factors, including minor trauma. A presumed vasculopathy is thought to explain the association of spontaneous dissection with various connective tissue disorders. Fibromuscular dysplasia is by far the most common, recognized in up to 20% of dissections.[16] Other associated disorders include Marfan's syndrome,[18,19] Ehlers–Danlos syndrome type IV,[20] osteogenesis imperfecta,[18] cystic medial necrosis,[8] reticular fiber deficiency,[21] accumulation of mucopolysaccharides,[22] pseudoxanthoma elasticum,[18] homocystinuria,[18] autosomal dominant polycystic kidney disease,[18] α_1-antitrypsin deficiency,[23] and various collagen disorders. An association with congenital heart disease and lentiginosis implicates a neural crest disorder affecting the muscular arteries of the head and neck.[24,25] A genetic basis has been suggested by the occurrence of familial aggregations of spontaneous dissections and an association with cerebral aneurysms.[7,26,27] Dermal connective tissue abnormalities have recently been reported and correlated with the risk of recurrent dissection.[28] A functional arteriopathy is suggested by the recent demonstration of impaired endothelium-dependent vasodilation in patients with spontaneous cervical artery dissection.[29] Potential risk factors associated with dissection include oral contraceptive use,[30] hypertension,[31] migraine,[32–34] recent infection,[35] smoking,[16] and redundancy of vessels.[36] Physical activities associated with dissection include skating,[37] tennis,[38,39] swimming,[40,41] scuba diving,[42–44] dancing,[45] yoga,[38] vigorous exercise,[38] trampoline use,[46] and amusement park rides.[47–49] Seasonal variation in the incidence rates of dissection have also been demonstrated, and may possibly be related to infection or other environmental factors.[50]

Pathophysiology and pathogenesis

Dissections are characterized by separation of the arterial wall layers with formation of a false lumen due to hemorrhage. The hemorrhage may be

secondary to an intimal tear or result from rupture of the vasa vasorum.[16,51] Subintimal dissections, accounting for 80%, cause expansion of the arterial wall with resultant luminal stenosis or occlusion. Subadventitial dissections may lead to the formation of a dissecting aneurysm. The formation of dissecting aneurysms may be associated with severity of the underlying arteriopathy.[52] If the intramural hematoma dissects back into the original arterial lumen, a double lumen may form.

Mechanical factors appear to influence the location of arterial dissections. Extracranial dissections of the internal carotid artery appear most frequently 2 cm or more distal to the carotid bifurcation, well beyond the typical site of atherosclerotic lesions. Intracranial carotid dissections are most frequent in the supraclinoid segment. Vertebral artery dissections most commonly affect the V3 or V1 segments (Figure 51.1), likely due to maximal torsion at the C1 to C2 level. Multiple simultaneous dissections frequently affect the extracranial vessels, with bilateral lesions in 20% of carotid dissections and 50% of vertebral dissections, and concomitant carotid/vertebral involvement in 6% of all cases.[16,53,54] Chiropractic manipulation is a frequently reported antecedent of dissection. Other reported precipitating activities include minor sports injuries, childbirth, sexual intercourse, coughing, and sneezing.

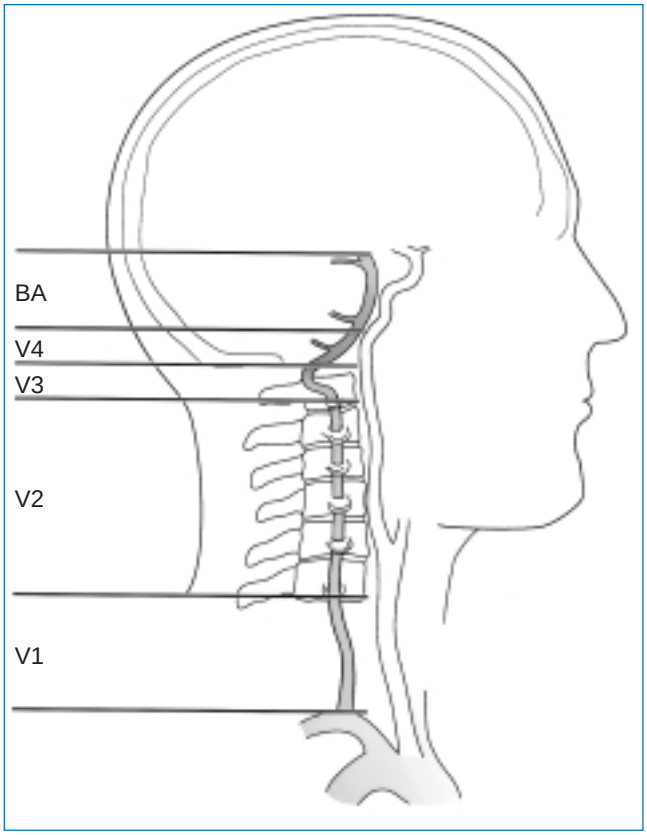


Figure 51.1 Anatomic depiction of the posterior circulation illustrating vertebral artery segments V3 and V1 as common sites of cervicocephalic arterial dissection.

Neurological sequelae may result from the local effects of a dissecting aneurysm or cerebral ischemia due to thromboembolism or hypoperfusion in distal vessels. Dissecting aneurysms may lead to a partial oculosympathetic paresis (Horner's syndrome), lower cranial neuropathies, and, rarely, cervical nerve root involvement, due to local compression or compromise of nutrient vessels supplying these structures.[55] Cerebral ischemia usually results from thromboembolism, promoted by thrombogenic elements at the endothelial surface of the intimal tear. Less commonly, hypoperfusion may result from hemodynamically significant stenoses produced by the inward bulging arterial wall. The predominant role of embolization is reflected in predominance of territorial over watershed infarct topography, frequent visualization of intraluminal thrombus, and occurrence of ischemia in the absence of substantial luminal compromise.[56,57] In the setting of intracranial dissection, the absence of an external elastic lamina and a thin adventitial layer may lead to external rupture of the vessel with subarachnoid hemorrhage.

Genetics

Genetically determined arteriopathies have been suggested as a cause of spontaneous dissections.[7,44,58–60] Genetic markers associated with dissection include defects in fibrillin (Marfan's syndrome), in the *COL1A1* gene that encodes the proα1(I) chains of type I collagen (osteogenesis imperfecta),[44] in the *COL3A1* gene that produces type III procollagen disorders (Ehlers–Danlos type IV), and in the *PKD1* gene (polycystic kidney disease).[58] Familial elastic fiber alterations have also been demonstrated by electron microscopy of skin biopsies.[59]

Clinical features

The clinical presentation of cervicocephalic arterial dissection is highly variable, as some patients remain asymptomatic whereas 5% to 10% suffer disabling strokes. Head and/or neck pain is the most common clinical feature, present in two-thirds of cases,[16,61,62] A partial oculosympathetic paresis (Horner's syndrome) is common in extracranial carotid dissection, reflecting stretching of sympathetic fibers running over the surface of the internal carotid artery with sparing of the external carotid plexus. Other frequent local clinical manifestations include tinnitus, an audible bruit, lower cranial neuropathies,[55] and scalp tenderness. Positive visual phenomena similar to migrainous events are sometimes observed in association with the initial headache.

Ischemic manifestations are usually delayed, typically appearing 1–15 days after inaugural local symptoms.[63] Cerebral ischemia may involve the brain, adjacent nerves, eye, cervical roots, or spinal cord. In reported cases of extracranial internal carotid artery dissection, transient ischemic attacks occur in 30% and cerebral infarcts in 46%.[16] Only a minority of strokes are preceded by transient ischemic attacks. Carotid dissections usually cause infarction in the middle cerebral artery territory, although borderzone

infarcts may result from hypoperfusion. Retinal artery occlusion or ischemic optic neuropathy may also occur.[64–66] Vertebral dissections typically produce lateral medullary infarcts, although other brainstem syndromes and spinal cord ischemia are seen. Intracranial dissections may present with subarachnoid hemorrhage and seizures.

The clinical course of extracranial carotid and vertebral dissections is characterized by complete or excellent recovery in 70% to 85%, major disabling deficits in 10% to 25%, and death in 5% to 10% of cases.[31,67] Prognosis is mainly related to the severity of the presenting infarct. Residual symptoms may include an oculosympathetic paresis or headache. The persistence of a headache may indicate continued vascular abnormalities,[31] although many patients can experience severe headaches that fluctuate for up to 3 months.[61,62] Intracranial dissections frequently have a worse prognosis and an elevated mortality rate due to subarachnoid hemorrhage. Vessels tend to heal with time. Follow-up vascular imaging of extracranial carotid dissections demonstrates that 85% of stenoses, 51% of occlusions, and 43% of aneurysms are improved or returned to normal.[16] The rate or recurrent dissection, in either the initially dissected vessel or another cervicocerebral vessel, is 1% annually.[7,9,10] Risk factors for recurrence include an underlying frank arteriopathy such as fibromuscular dysplasia and a family history of dissection.[7,9] The mean time to recurrence is 4.1 years, ranging from 2 days to 8.6 years.[16]

Classification

Cervicocephalic arterial dissection is traditionally categorized as spontaneous or traumatic. However, minor trauma or intense physical activity precedes 20% to 25% of "spontaneous" dissections, suggesting that this traditional dichotomy masks an underlying spectrum of predisposing mechanical insults.[31] Dissections are further classified as extracranial or intracranial, and according to the specific vessel that is affected.

Diagnosis

The clinical history is fundamental to the diagnosis of dissection. Although minor headache is a frequent accompaniment of cerebral ischemia, heralding head pain and any neck pain should prompt the clinician to consider the possibility of dissection. Dissection should also be considered whenever a young patient or an older patient without typical stroke risk factors presents with signs and symptoms of cerebral ischemia. Furthermore, dissection should always be in the differential diagnosis of a lateral medullary syndrome.

Blood work should include a prothrombin time, partial thromboplastin time and platelet count to screen for a coagulopathy. Screening blood studies for vasculitis should be obtained. More detailed testing for heritable causes of vasculopathy should be individualized based on the clinical and family history. In intracranial dissections, examination of cerebrospinal fluid may be necessary to exclude the possibility of subarachnoid hemorrhage.

Vascular imaging is essential to establish the diagnosis of dissection and to guide treatment decisions at follow-up. Conventional angiography is the most definitive diagnostic study, demonstrating the luminal contour altered by the enlarged arterial wall (Figure 51.2). Angiographic findings include a string sign, gradually tapering stenosis or occlusion, intimal flap, dissecting aneurysm, distal pouch, and underlying arteriopathy such as fibromuscular dysplasia. Extracranial carotid dissections typically arise 2 cm or more distal to the carotid bifurcation and extend to the skull base. Luminal stenoses appear irregular, tapered, or eccentric. Distal branch occlusions may also be visualized. It is imperative that all four cervical vessels are studied, as multivessel dissection may be asymptomatic.[54] The recent development of 3D angiography promises further detail of the anatomic abnormalities associated with dissection.[68]

Non-invasive diagnosis of dissections is increasingly routine, employing MRI and magnetic resonance angiography (MRA), computed tomographic angiography (CTA), and ultrasonography. MRI/MRA simultaneously exhibits luminal abnormalities, arterial wall expansion, intramural hematoma, and the relationship of the diseased vessel with surrounding structures. An eccentric or circumferential rim of hyperintensity surrounding the hypointense vessel lumen forms a pathognomonic MRI crescent sign (Figure 51.3).[69–71] The hyperintensity may vary with age of the lesion, reflecting methemoglobin content of the intramural hematoma. Specificity limitations of MRI may be due to slow flow within the venous plexus surrounding the vertebral artery or surrounding fat that mimics an intramural hematoma. The intramural hematoma may act as a splint and produce a "straight artery sign" on MRA.[72] Examination of the

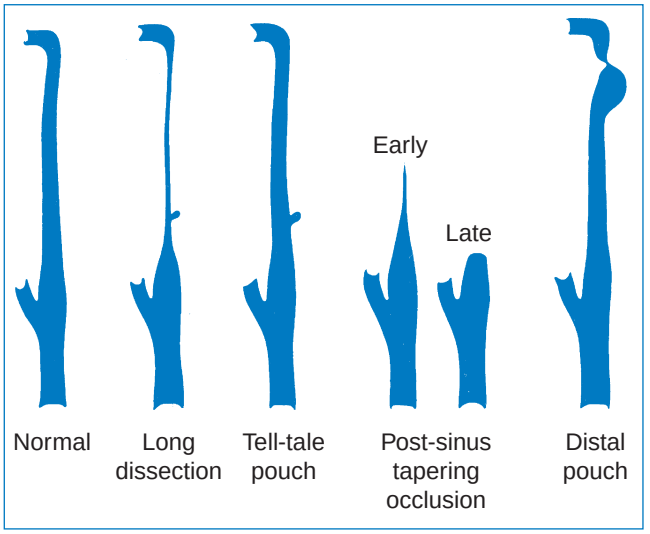


Figure 51.2 Angiographic silhouettes of various dissection patterns (Reproduced with permission, Fisher CM, et al. Can J Neurol Sci 1978;5:9).

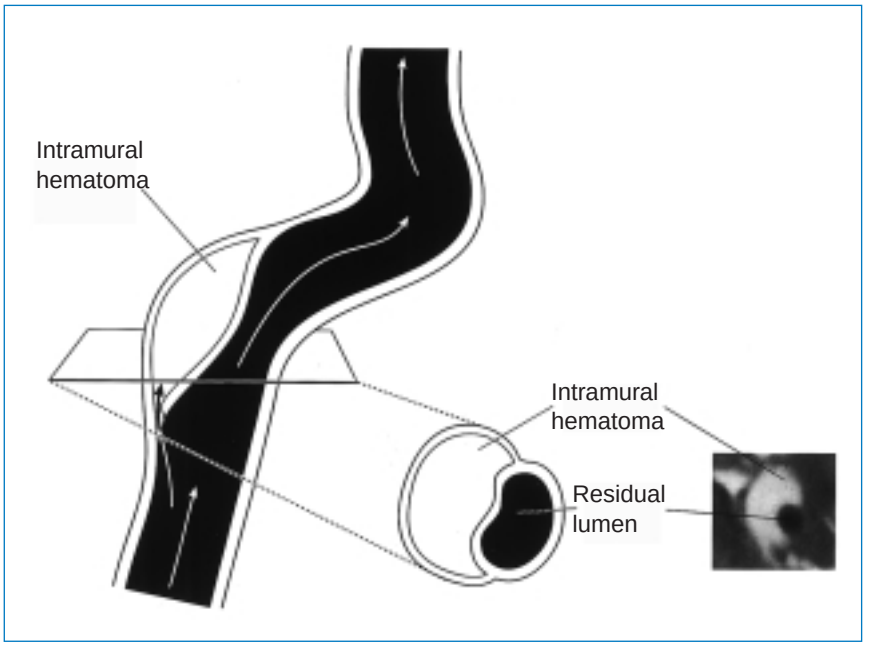


Figure 51.3 Pathognomonic MRI crescent sign of dissection (right), resulting from expansion of intramural hematoma.

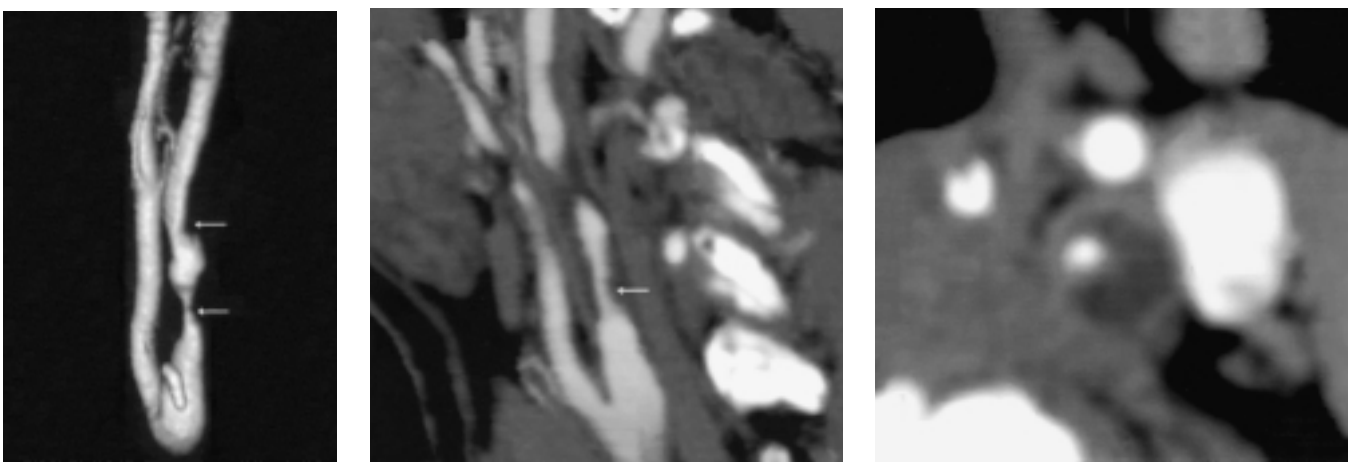
MRA source images is important to assess luminal compromise and document an intimal flap. Difficulties with turbulence and bony artifacts[70,73,74] may be overcome with contrast-enhanced MRA.

The recent development of helical CT and CTA allows for non-invasive evaluation of the cervical vessels without flow phenomena disturbances.[71] This advantage over MRA may be used to detect small, residual lumens and to detail the three-dimensional anatomy of dissections (Figure 51.4). Preliminary studies of CTA in the diagnosis and follow-up of dissection await further validation.[75,76] CTA offers an alternative imaging modality for unstable patients and those with MRI contraindications.

Carotid duplex and transcranial Doppler ultrasonography (TCD) may be used as screening methods, to confirm the diagnosis of dissection, or to monitor therapy.[77,78] Carotid duplex detects abnormalities in 68% to 95% of cases, but has difficulty in distinguishing dissection from atherosclerosis.[4,79] Carotid duplex may demonstrate intramural thrombus, an intimal flap, or double lumen, but is less reliable in detecting dissecting aneurysms.[31] TCD submandibular insonations may be employed to study the high cervical region missed by carotid duplex, and standard TCD to evaluate collateral flow patterns and embolic phenomena.

Plain films are especially informative in the setting of trauma. Cervical views may reveal subluxation or joint instability associated with vertebral dissection.

Histopathological specimens of the dissected vessel are rarely obtained, with most previous descriptions



(a) (b) (c)

Figure 51.4 CTA demonstration of extracranial carotid dissection. (a) 3D volume-rendered view, (b) sagittal maximum-intensity projection, (c) axial maximum-intensity projection.

based on autopsy studies. Pathological examination may reveal intramural hemorrhage, with disruption of the subintimal plane and less frequent separation of the media and adventitia. Extracranial carotid dissections frequently extend distally to the skull base. Specimens may exhibit proliferation of fibrous tissue, smooth muscle cell hyperplasia, and destruction of the elastic lamina, characteristic of fibromuscular dysplasia. Abnormalities in collagen may also be detected. Generalized ultrastructural defects in connective tissue may be confirmed by histopathological examination of skin biopsy.[28]

Differential diagnosis

The clinical presentation of dissection may be similar to migraines, cluster headaches, paroxysmal hemicrania, or Raeder's paratrigeminal neuralgia.[80] Migraine symptoms may be difficult to distinguish from dissection and the two conditions may present simultaneously, but migraines typically produce headaches that are more short-lived and neurological symptoms with a characteristic march.[81–83] Cluster headaches share with dissection severe unilateral facial pain and ipsilateral Horner's syndrome, but typically cluster attacks subside after 30 minutes and no focal deficits occur.[84] Herpes zoster ophthalmicus may also mimic dissection due to severe unilateral pain and blurred vision that predates the dermatological manifestations.[85] Lateral medullary stroke due to other causes, lower cranial neuropathies, or isolated Horner's syndromes may confuse the diagnosis as well.

The angiographic findings in dissection must also be distinguished from other conditions. Atherosclerosis, radiation arteriopathy, and congenital hypoplasia of a vessel may produce an angiographic picture similar to the "string sign" of dissection. The presence of a gradually and smoothly tapering lumen leading up to the occlusion is particularly suggestive of dissection rather than alternative etiologies. Luminal stenoses due to dissection may be similar to findings of fibromuscular dysplasia, atherosclerosis, vascular webs, stationary waves, and arteritis.[86]

Treatment

Although the diagnostic literature regarding cervicocephalic arterial dissection has rapidly evolved during the last three decades, only modest progress has been made in treatment. The low incidence of dissection, the low rate of late stroke, the low recurrent dissection rate, and the heterogeneity of the patient population are all important factors hampering development of fully validated treatment strategies.

The infrequency of cervicocephalic dissection limits the treatment experience gained in any one center, and hinders even co-operative, multicenter investigative groups from gathering enough patients to conduct valid randomized, controlled clinical trials. Moreover, many patients already have cerebral infarction at the time of their initial presentation, and the rate of recurrent infarction after the acute period is quite low. For cervical carotid dissections, given the observed annualized late stroke rate of 0.4%,[16] comparing two treatments with an 80% chance of detecting a 50% reduction in events over 3 years would require a sample size of approximately 8000 acute dissection patients. No such trial can practically be mounted due to the infrequency of the condition, the costs that would be incurred, and the generally benign outcome under current modes of management.

Evaluation of therapeutic interventions is also complicated by considerable variability in the clinical spectrum of arterial dissection. Patients with frank underlying arteriopathies may merit more aggressive intervention than patients with subtle, ultrastructural abnormalities, who in turn may best be treated differently than patients with no discernible connective tissue disturbance. The extent or severity of the underlying vasculopathy may be the prime determinant of long-term outcome once the threat of acute cerebral ischemia has passed. Failure to account for the variable risk attributable to the extent of underlying disease in a patient population may bias the interpretation of a study. These differences may explain conflicting results of previous studies that included heterogeneous patient populations.

The factors hindering the development of evidence-based treatments for dissection have simultaneously fostered academic debate. Current treatment recommendations are based on small, uncontrolled series, case reports, and anecdotal experiences. Few studies have directly compared the efficacy of different treatments. Clinicians have relied on general comparisons between outcomes and tailored treatment of individual patients to the clinical findings. In the absence of definitive trial data, treatment frequently rests on reasoned deduction from understanding of the fundamentals of disease pathogenesis and the natural history.

Early reports on the treatment of dissection emphasized aggressive surgical vessel repair at the time of diagnosis. However, increasing recognition of the strong tendency to natural improvement in the vessel wall and the favorable course under medical management have shifted emphasis to medical therapies as the initial treatment of choice in cervical dissections. For those patients with elevated risk of subarachnoid hemorrhage or recurrent ischemia, endovascular techniques have recently provided a less invasive approach for definitive treatment of the arterial lesion.

The medical treatment of dissection must hazard the contradictory pathophysiology of the disease—an intramural hemorrhage constitutes the primary arterial lesion but secondary thromboses produce cerebral ischemia. Antithrombotic therapies are employed to deter thromboembolism but may promote recurrent intramural hemorrhage. As the risk of ischemia declines over time, the risk–benefit ratio of a given therapy will also change.

A general algorithm for treatment is outlined in Table 51.1. The quality of evidence for current therapeutic strategies is restricted to Grade C evidence, consisting of class 4 (non-randomized, historical

Table 51.1 Selected treatment recommendations for acute cervicocephalic arterial dissection

i.a. thrombolysis	Acute cerebral ischemia within 6 h of onset
i.v. thrombolysis	Acute cerebral ischemia within 3 h of onset and no i.a. available
Anticoagulation	Within 1st 3 months of cervical dissection, AND no contraindications
Antiplatelet agents	Delayed presentation without ischemic symptoms
	Contraindications to anticoagulation
	After discontinuation of anticoagulation at 3 months
Angioplasty and stenting	Intracranial dissection with subarachnoid hemorrhage
	Ischemia despite anticoagulation
Surgery	Expanding dissecting aneurysms producing progressive cranial nerve palsies
	Ischemia despite anticoagulation

controls) studies and class 5 (case series, no controls) reports. After the presenting event, most patients do well, either because of or despite treatment.

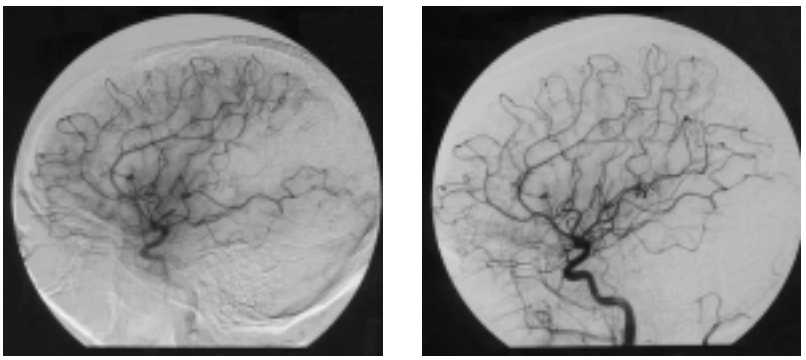
In the dissection patient presenting with acute ischemic stroke, the general principles of management of acute cerebral ischemia fully apply.[87] Blood pressure regulation, fluid management, control of hyperglycemia and other metabolic derangements, and management of airway are critical features of acute management.

When patients present within the first hours of onset of ischemia, consideration should be given to cerebral thrombolysis. Thrombolysis in the setting of dissection is, at least theoretically, of increased risk. In addition to the usual risk of intracerebral hemorrhage associated with cerebral thrombolysis, the dissection patient is at risk for recurrent hemorrhage into the vessel wall and extension of dissection. Extension of aortic dissection is a well-documented complication of thrombolytic therapy, and in the rare patient aortic dissection may be linked to cervicocerebral dissection.[88,89] Whether systemic, intravenous thrombolysis in practice substantially increases the risk of dissection recurrence or extension is a question that only large treatment series can resolve. Such prospective studies need to be planned in a formal manner.

Initial experience with systemic, intravenous thrombolysis in cervicocephalic dissection is promising, but not unmixed. It is important to note that dissection patients were included in the pivotal National Institute of Neurologic Disease and Stroke trials that demonstrated the efficacy of intravenous tissue plasminogen activator (tPA) begun within 3 hours of symptom onset.[90] However, only a small number of dissection patients were enrolled, and the experience in this subset has not been separately reported. Several case series of intravenous tPA in the setting of dissection have been reported.[91–93] Jacobs and colleagues treated eight patients with cervical internal carotid or vertebral artery dissection with intravenous tPA, 0.9 mg/kg over 60 minutes.[92] Five patients made a full and one a partial functional recovery, with two deaths from large hemispheric infarction and no occurrence of intracerebral hemorrhage. The fatal outcomes occurred in the two patients with the most severe neurological deficits at presentation. The possible impact of thrombolysis on the intramural hematoma remains unclear in this small series of patients lacking pre-and post-treatment detailed vascular imaging. However, three of six surviving patients failed to show complete resolution of vascular stenosis or occlusion on follow-up ultrasonography. Derex and colleagues treated 11 internal carotid artery dissection patients with intravenous tPA at 0.8 mg/kg infused over 90 minutes within 7 hours of symptom onset.[91] No death was observed and three patients had good functional outcome. However, following treatment 88% of patients demonstrated occlusion of the internal carotid artery, higher than the 20% of natural history studies, suggesting dissection extension in some cases.

Intra-arterial thrombolysis has potential advantages over intravenous administration for the treatment of ischemia due to dissection. Intra-arterial thrombolysis allows for selective catheterization of the occluded vessel, distal to the dissection site, and delivery of a smaller total dose of lytic agent (Figure 51.5). These features may diminish the risk of further hemorrhage into the dissection by limiting the systemic exposure of the thrombolytic agent.[16] Selective catheterization may also improve thrombolytic recanalization rates. Recent reports of intra-arterial thrombolysis in the setting of dissection have demonstrated the feasibility of this technique without an increased complication rate.[53,94,95] In our series of four carotid and vertebral dissection patients treated with intra-arterial urokinase, recanalization of target vessels and excellent long-term functional outcome was achieved in all. Urokinase is no longer available for use in the USA, but intra-arterial tPA has shown comparable results to urokinase in other cerebrovascular settings. Thrombolysis should be employed cautiously, if at all, in intracranial dissections, due to the increased risk of subarachnoid hemorrhage. Thrombolysis in dissection may be complicated by the possibility of earlier asymptomatic emboli prior to the acute stroke presentation,[96] although this possibility is not specific to dissection and may be addressed through adherence to current neuroimaging guidelines for thrombolysis. The safety of both intravenous and intra-arterial thrombolysis in dissection requires further investigation.

Until more information regarding the safety of thrombolysis for dissection-related ischemia is avail-



(a) (b)

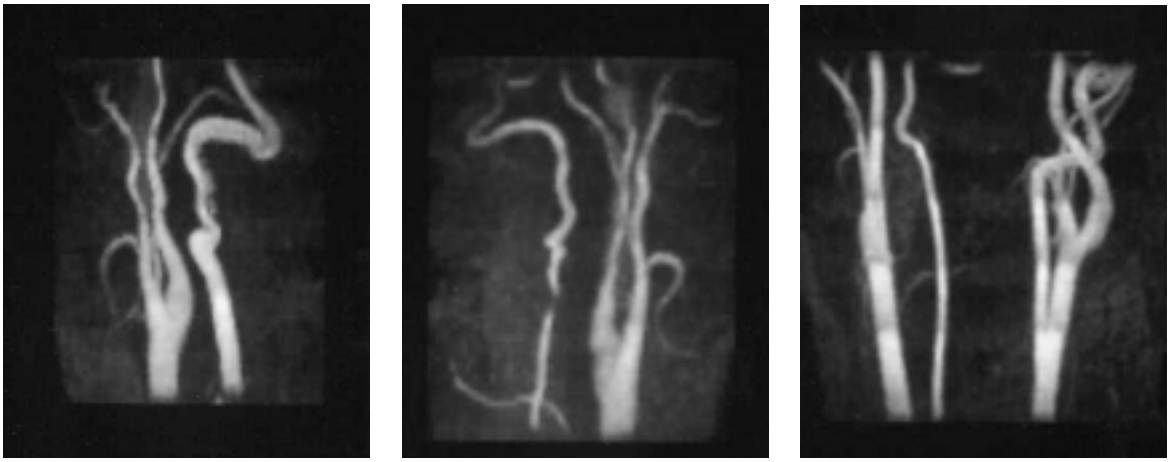
Figure 51.5 Intra-arterial thrombolysis of left middle cerebral artery branch occlusion. (a) Pre-thrombolysis, (b) post-thrombolysis recanalization of branch occlusion.

able, no evidence-based recommendations can be made specific to dissection. For the moment, we favor intra-arterial thrombolysis for select cases of carotid and vertebral artery dissection, employing superselective catheterization and direct delivery of drug onto a distal thrombus, to minimize the risk of provoking dissection recurrence or extension. We pursue i.a. therapy if the patient presents within 6 hours of ischemia onset and no contraindications are present.[53,97] At facilities where acute endovascular intervention is not available, intravenous thrombolysis is a reasonable strategy in patients with potentially disabling neurological deficits presenting within 3 hours of symptom onset. If undertaken, treatment should follow national guidelines for the use of intravenous tPA.[98]

No definitive data are extant to guide the employment of anticoagulation and antiplatelet therapy in the cervical dissection patient. We favor acute anticoagulation if the patient has local signs only, transient ischemic attack, or a small infarct. We employ only antiplatelet therapy early if the infarct is moderate to large. The rationale for this approach is based on Grade C quality evidence from the literature. No controlled trials have been performed to establish the benefit of anticoagulation. Multiple case series have suggested at least no major adverse effect. While the use of anticoagulation may seem contraindicated in a disorder defined by hemorrhage into the arterial wall, most cerebral injury appears to result from secondary thrombotic and embolic complications of dissection. Anticoagulation may prevent occlusion of a stenotic vessel and minimize distal embolization. Extension of an intramural hematoma in the presence of anticoagulation is rare.[1,99] Conversely, there have been several reports of neurological deterioration without anticoagulation.[4,99] Anticoagulation has been demonstrated to reduce the frequency of artery-to-artery microemboli arising from a dissection.[100] Acute anticoagulation may employ either low molecular weight heparin administered subcutaneously at arterial disease dose, or intravenous unfractionated heparin. Possible low molecular weight heparin regimens include enoxaparin at 1 mg/kg bid or dalteparin at 100 units/kg bid. Intravenous unfractionated heparin should be dose adjusted to achieve a goal partial thromboplastin time of 45 to 60 seconds.[101] Transition to warfarin can proceed over the next 5 days in patients who are clinically stable. Anticoagulation is generally avoided in the setting of intracranial dissection due to the risk of subarachnoid hemorrhage. Some have recommended that anticoagulation may be employed if computed tomography and lumbar puncture studies are negative.[86]

Early antiplatelet therapy may be used for patients with contraindications to anticoagulation. There is scant Grade C evidence regarding the efficacy of this treatment. One study demonstrated similar stroke recurrence rates for aspirin versus anticoagulation in patients presenting with ischemic symptoms.[102] Antiplatelet therapy may also be used when an individual presents weeks or months after experiencing non-ischemic symptoms. Most reports have employed aspirin at various doses on a daily basis, whereas there are no data regarding other antiplatelet agents such as ticlopidine, clopidogrel, dipyridamole, or combinations of these agents.

There are no concrete data regarding optimal duration of antithrombotic therapy. We allow the time course of healing of the vessel wall to guide the duration of initial anticoagulation. Serial ultrasound studies show that the median time to resolution of carotid dissections is 6 weeks, most arteries recover by 3 months, and vessels that fail to reconstitute a normal lumen by 6 months are highly unlikely to recover thereafter.[16] After 3 months, repeat imaging is recommended to assess recanalization and healing of the arterial dissection (Figure 51.6).[16,69] MRI and MRA, CTA, ultrasonography, or conventional angiography may be used. Further treatment at 3 months is tailored to the vascular findings (Table 51.2). If the dissection has resolved with recanalization and restoration of smooth luminal contour, anticoagulation may be discontinued and antiplatelet therapy initiated for an additional 3 months or no additional antithrombotics begun. If 3-month imaging reveals persistent luminal irregularities, long-term antiplatelet therapy is recommended. If the vessel is occluded, yet the origin and terminus of the occluded segment are smooth, anticoagulation may be switched to antiplatelet therapy. For severe luminal stenosis or irregularities persisting at 3 months, anticoagulation should be continued for an additional 3 months and imaging then repeated. The persistence of a dissecting aneurysm after several months is associated with the continued risk of



(a) (b) (c)

Figure 51.6 Serial MRA of simultaneous, spontaneous four-vessel dissection. (a) Left carotid and vertebral dissections, (b) right carotid and vertebral dissections, (c) resolution of vascular abnormalities at 3 months.

thromboembolism and anticoagulation is advised with repeat imaging at regular intervals.

Although the majority of patients are treated medically (see overview, Table 51.3), selected patients with progressive or recurrent ischemia may require non-thrombolytic endovascular therapy or surgery. Non-thrombolytic endovascular techniques for the treatment of dissection include angioplasty, stent placement, embolization with various materials, and combinations of these interventions. The role of non-thrombolytic endovascular therapy is yet to be fully defined, as no trials have assessed these techniques in comparison with medical or established surgical procedures. The limited experience with endovascular procedures in the setting of dissection has been described in case reports and case series.[95,103–108] The number of reports has recently accelerated, mostly describing the treatment of traumatic dissections with aneurysm formation. The technical details of these non-thrombolytic endovascular approaches have been well detailed.[105]

The most common indication for endovascular therapy is in intracranial vertebral artery dissection, to minimize the risk of first or recurrent subarachnoid hemorrhage. Rebleeding occurs in about one-quarter of patients with intracranial vertebral artery dissection and an initial subarachnoid hemorrhage, if the dissecting aneurysm is not directly addressed. The fusiform morphology of most dissecting aneurysms precludes surgical clipping of an aneurysm neck. Endovascular intervention may also be employed to deter thromboembolic or hemodynamic ischemia when medical therapy is failing. Early endovascular treatment series focused on embolization of dissecting aneurysms or parent vessel sacrifice with detachable balloons or coils, to decrease the risk of continued distal embolization.[106,109] Endovascular occlusion of the dissected vessel reduces the risk of further thromboembolic complications, but may not be feasible in all patients due to hemodynamic dependence. Test occlusion helps prognosticate if an individual will tolerate parent vessel sacrifice, although occlusion of non-dominant vertebral arteries may not require this precautionary step.

The advent of angioplasty and stenting has increasingly obviated the need for parent vessel sacrifice. Angioplasty with or without stenting may eliminate luminal irregularities, obliterate the false lumen, and reconstitute the original lumen of the dissected vessel. Patients who fail antithrombotic therapy may be treated with angioplasty and stenting without sacrifice of the parent vessel.[107] This approach is particularly suitable for patients with hemodynamic compromise who will not tolerate parent vessel sacri-

Table 51.2 Selected treatment recommendations based on vascular findings at 3 months

Vascular findings	Recommended treatment
Resolution with smooth lumen	Discontinue anticoagulation ± start antiplatelet agent × 3 months
Mild luminal irregularity	Discontinue anticoagulation + start chronic antiplatelet therapy
Occlusion with smooth origin and terminus	Discontinue anticoagulation + start antiplatelet agent
Severe luminal stenosis, irregularity	Continue anticoagulation, repeat imaging at 6 months
Dissecting aneurysm	Continue anticoagulation, repeat imaging at regular intervals

Table 51.3 Clinical pearls for cervicocephalic arterial dissection

Clinical features
• Variable symptomatology, typically including head/neck pain and focal deficits • Ischemic manifestations are usually delayed by several days • Prognosis is mainly dependent on the severity of cerebral ischemia • Intracranial dissection has a worse prognosis, related to subarachnoid hemorrhage • Annual recurrence rate is 1% • Risk factors for recurrence include an arteriopathy or family history of dissection
Diagnosis
• Common cause of ischemia in the young patient or those without typical risk factors • Differential diagnoses include migraine, cluster headache, paroxysmal hemicrania, Raeder's paratrigeminal neuralgia, and herpes zoster ophthalmicus • MRI may reveal a pathognomonic crescent sign, illustrating eccentric or circumferential intramural hematoma • Angiographic findings include a string sign, gradually tapering stenosis or occlusion, intimal flap, dissecting aneurysm, distal pouch, or underlying arteriopathy
Treatment
• i.a. thrombolysis, and possibly i.v. thrombolysis, should be considered for acute cerebral ischemia • Antithrombotics are used for chronic management, often warfarin initially, followed by antiplatelet therapy • Anticoagulation is generally avoided for intracranial dissection • Endovascular or surgical approaches are reserved for recurrent ischemia or treatment of symptomatic dissecting aneurysms • Serial imaging studies guide long-term antithrombotic therapy

fice. The use of uncoated stents may require adjunctive techniques, including embolization with coils through the interstices of the stent, to minimize thromboembolic complications. Stent placement and embolization may be used to treat fusiform dissecting aneurysms that are not amenable to surgical clipping. The use of covered stents theoretically reduces associated complications. Although balloon-expandable covered stents have been used, self-expanding stents may be superior as they transmit a measured radial force on the friable arterial wall, adapting to the natural anatomy of the vessel.[108] Further refinements in the non-thrombolytic endovascular treatment of dissection await the anticipated development of covered, self-expanding stents.

These novel endovascular therapies have developed rapidly, and several important treatment issues remain to be clarified. These concerns include the complication rates related to distal migration of a stent, further arterial injury during deployment, stent thrombosis, and delayed intimal hyperplasia. A registry or larger, randomized controlled trials of non-thrombolytic endovascular techniques should address these concerns, as well as long-term safety and efficacy issues.[104] The most dangerous adverse event during angioplasty and stenting is arterial rupture, which mandates immediate surgical intervention. As there is a known risk of thromboembolic complications directly related to endovascular procedures, anticoagulation and sometimes antiplatelet therapy are employed during the procedure. These agents harbor the theoretical risk of enlarging the intramural hematoma. Similar concerns surround the required post-stenting antithrombotic regimens that are used to prevent stent closure. Regimens typically employ aspirin and clopidogrel or ticlopidine for a period of 4 weeks, followed by continued aspirin therapy. The optimal post-stent placement antithrombotic regimen is yet to be established in clinical trials.

Surgery is generally considered only when medical or endovascular options fail. Individuals with progressing symptoms and localized, accessible lesions may benefit from surgical vessel reconstruction or bypass.[16] Expanding dissecting aneurysms producing progressive cranial nerve dysfunction may also require surgery. Resection of the dissecting aneurysm with reconstruction of the parent vessel is the most common intervention.[110] Other surgical revascularization procedures include local bypass, extracranial–intracranial bypass, endarterectomy, thrombectomy, and proximal vessel ligation.[111] Limited data exist regarding surgical efficacy and long-term sequelae. There have been no controlled trials of these interventions. Surgery may also become necessary for subarachnoid hemorrhage related to intracranial dissection. There is no information regarding the frequency and complication rates of vasospasm due to dissection-related subarachnoid hemorrhage. For moderate to large subarachnoid bleeds, use of nimodipine and selective use of hypervolemic hypertensive therapy is appropriate.

General measures to reduce the risk of recurrent cervicocerebral dissection are warranted in all patients. Estrogen-containing compounds should be discontinued, as estrogen has been shown to induce proliferation of intimal and fibromuscular arterial tissue.[16,96] Hypertension should be tightly controlled. All patients should be cautioned to avoid contact sports, chiropractic manipulation, and any other activity that increases the chance of a sudden blow to the head or sudden rotation and flexion–extension of the neck. These precautions are to prevent the possibility of exacerbating the arterial lesion or provoking dissection in other vessels that may harbor an underlying vasculopathy.

Symptomatic treatment of headaches related to dissection may be necessary. Headaches may be treated with acetaminophen, although additional benefit may be achieved with naproxen sodium taken orally, 1200 mg 3 times daily or as needed, or ibuprofen taken orally, 200–400 mg 3 times daily or as needed.

Stroke rehabilitation following dissection follows general treatment principles,[112] with the added caveat of avoidance of excessive neck manipulation.

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