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Epidemiology, pathophysiology, diagnosis, and management of intracranial artery dissection

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Spontaneous intracranial artery dissection is an uncommon and probably underdiagnosed cause of stroke that is defined by the occurrence of a haematoma in the wall of an intracranial artery. Patients can present with headache, ischaemic stroke, subarachnoid haemorrhage, or symptoms associated with mass effect, mostly on the brainstem. Although intracranial artery dissection is less common than cervical artery dissection in adults of European ethnic origin, intracranial artery dissection is reportedly more common in children and in Asian populations. Risk factors and mechanisms are poorly understood, and diagnosis is challenging because characteristic imaging features can be difficult to detect in view of the small size of intracranial arteries. Therefore, multimodal follow-up imaging is often needed to confirm the diagnosis. Treatment of intracranial artery dissections is empirical in the absence of data from randomised controlled trials. Most patients with subarachnoid haemorrhage undergo surgical or endovascular treatment to prevent rebleeding, whereas patients with intracranial artery dissection and cerebral ischaemia are treated with antithrombotics. Prognosis seems worse in patients with subarachnoid haemorrhage than in those without.

Introduction

Cervicocephalic artery dissection, which corresponds with a haematoma in the wall of a cervical or an intracranial artery, is an important cause of stroke in children and young and middle-aged adults.[1–3] Although dissection of the extracranial cervical arteries has been extensively studied and described,[4–12] less information is available about pure intracranial artery dissection (ie, not including the cervical portion of the artery).[4] Early reports were exclusively based on autopsy series, hence biased towards the most severe cases of intracranial artery dissection.[13,14] Several possible reasons are available for the absence of information about intracranial artery dissections. First, intracranial artery dissection happens less frequently than cervical artery dissection in non-Asian countries, where the largest series of patients who had cervical artery dissection have been reported so far.[9–12] Second, patients who have cervical artery dissection and mainly present with headache, cervical pain, and ischaemic stroke are mostly seen by neurologists, whereas patients with intracranial artery dissection can also develop a subarachnoid haemorrhage and are therefore managed not only by neurologists, but also by neurosurgeons and interventional neuroradiologists, all of whom might have an incomplete picture of the disease. As a result, no consensus is agreed on for the diagnostic criteria and optimum treatment of patients with intracranial artery dissections.

In this Review we provide a comprehensive overview of reported studies into the epidemiology, pathophysiology, diagnosis, management, and outcome of spontaneous intracranial artery dissections, in addition to proposing a consensus statement by a group of international experts from various specialties and countries about the diagnosis and management of intracranial artery dissections.

Epidemiology

The incidence of intracranial artery dissections is unknown, but is probably lower than that of symptomatic cervical artery dissection (2·6–3·0 per 100 000 people per year[15,16]) in populations of European ethnic origin. The proportion of intracranial artery dissections in all cervicocephalic dissections substantially varies between ethnic origin and age groups, and also depends on study recruitment strategies and ascertainment methods used. Recruitment of patients for studies through neurology departments is biased towards those with cervical artery dissection or intracranial artery dissection without subarachnoid haemorrhage, whereas patient recruitment through departments of neurosurgery or interventional neuroradiology is biased towards intracranial artery dissection with subarachnoid haemorrhage. In a series of 195 patients with vertebral artery dissections who were recruited in neurology departments in France and Switzerland, only 11% of dissections were located exclusively in the intracranial portion of the artery.[17] In a Mexican study[18] of 100 patients admitted to a neurology department for vertebral artery dissection with ischaemic stroke and without subarachnoid haemorrhage, 27 (27%) patients had intracranial artery dissection. In studies undertaken in east Asia,[19–23] in which patients were mostly recruited through neurosurgery and interventional neuroradiology departments, intracranial artery dissection

accounted for up to 67–78% of all cervicocephalic artery dissections.[19,20] Most reported series of patients with intracranial artery dissection are from Asia (95% of studies including >40 patients with intracranial artery dissection, and 61% of studies including 20–39 patients with this disorder). Whether this suggests publication bias, differences in disease prevalence across ethnic origin groups, or both, is unclear.

Intracranial artery dissections can also affect children, but a dearth of scientific literature exists about this problem in children, given the rarity of childhood stroke. In a North American single-centre series[24] of

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	N	Country origin (department)	Imaging method	Mean age (range)	Sex	Anatomical location	Presenting symptoms
All types							
Yamaura et al (2000)[23]	357	Japan (neurosurgery survey)	DSA	51 (8–86) years (SAH 53 years, non-SAH 49 years)	Ratio of men to women 2:1; with non-SAH 2·6:1	3% anterior circulation (SAH 2%, non-SAH 5%); 97% posterior circulation (SAH 98%, non-SAH 95%), in VA (261 patients), BA (22 patients), ICA (ten patients), or other artery (29 patients)*	SAH (206 patients [58%]), cerebral ischaemia (112 patients [31%]), headache alone (26 patients [7%]), other (13 patients [4%])
Mizutani (2011)[29]	190	Japan (neurosurgery, radiology)	MRA, DSA, or CTA	49 (0–74) years (SAH 52 [0–65] years, non-SAH 45 [22–47] years)	69% men (SAH 62%, non-SAH 77%)†	14% anterior circulation (SAH 11%, non-SAH 14%); 88% posterior circulation (SAH 89%, non-SAH 86%), VA (155 dissections), PICA (11 dissections), ACA (11 dissections), BA (ten dissections), MCA (eight dissections)†	SAH (108 dissections [52%]), headache, or cerebral ischaemia (98 dissections [48%])†
Ono et al (2013)[30]	143	Japan (neurosurgery)	DSA and CT in all patients, MRI in some patients	51 (7–82) years (SAH 53 [31–83] years, non-SAH 48 [10–74] years)	59% men (SAH 58%, non-SAH 61%)	22% anterior circulation (SAH 15%, non-SAH 32%); 78% posterior circulation (SAH 85%, non-SAH 68%), VA (99 patients; 16 [11%] IADs in the VA were bilateral), ACA (11 patients), MCA (11 patients), ICA (eight patients), BA (seven patients), PICA (five patients), PCoA (one patient), PCA (one patient)	SAH (86 patients [60%]), headache, or cerebral ischaemia (57 patients [40%])
Kwak et al (2011)‡[19]	92	South Korea (radiology)	DSA	51 years§	58% men§	24% anterior circulation (SAH 7%, non-SAH 44%); 76% posterior circulation (SAH 93%, non-SAH 57%)	SAH (25 patients [27%]), SAH and ischaemia (three patients [3%]), infarction (20 patients [22%]), other cerebrovascular symptoms (44 patients [48%])
Metso et al (2007)[31]	45¶	Finland (neurology, neurosurgery)	SAH: DSA (50%) or CTA (50%); non-SAH: MRA (100%), MRI (96%), US (39%), or CTA (9%)	46 (21–67) years (SAH 51 [32–67] years, non-SAH 42 [21–56] years)	58% men (SAH 50%, non-SAH 65%)	16% anterior circulation (SAH 14%, non-SAH 22%); 84% posterior circulation (SAH 86%, non-SAH 78%), VA (28 patients; one [2%] IAD in the VA was bilateral), ICA (five patients), BA (four patients), PICA (three patients), ACA (two patients), SCA (one patient), PCA (one patient), pericallosal artery (one patient)	SAH (22 patients [49%]), headache, or cerebral ischaemia (23 patients [51%])¶
Vertebrobasilar IAD							
Ahn et al (2012)‡[32]	210	South Korea (neurosurgery, radiology)	DSA in all; CTA, MRI, or MRA in some	Median 47 (21–80) years (SAH 45 years, non-SAH 48 years)	61% men	Vertebrobasilar IAD included: 20 (10%) IAD in the VA were bilateral	SAH (48 patients [21%]), non-SAH (182 patients [79%]; ischaemia frequency unknown)
Kim et al (2011)‡[33]	111	South Korea (neurosurgery, radiology)	DSA	45 (24–78) years	63% men	Vertebrobasilar IAD included: BA involved (ten), PICA involved (47), eight (7%) IADs were bilateral	SAH (73 patients [66%]), ischaemia, or headache (38 patients [34%])
Matsukawa et al (2012)‡[34]	103	Japan (neurosurgery)	MRI, MRA, CTA, DSA	53 (IQR 45–66) years (SAH 50 [46–59] years, non-SAH 54 [45–69] years)	69% men (SAH 77%, non-SAH 67%)	Vertebral IAD included: three (3%) IADs were bilateral	SAH (22 patients [21%]), ischaemia, or headache (81 patients [79%])
Kashiwasaki et al (2013)[35]	73	Japan (neurosurgery)	Not specified	52 (SD 9) years	55% men	Vertebral IAD without PICA involvement	SAH (45 patients [62%]), non-SAH (28 patients [38%], asymptomatic, or headache)

(Table 1 continues on next page)

	N	Country origin (department)	Imaging method	Mean age (range)	Sex	Anatomical location	Presenting symptoms
(Continued from previous page)							
Takemoto et al (2005)[36]	62	Japan (neurosurgery)	DSA, MRI	51 (38–62) years (SAH 57 [54–62] years, non-SAH 48 [38–61] years)‖	86% men (SAH 80%, non-SAH 89%)‖	Vertebral IAD	SAH (five patients [8%]), headache (eight patients [13%]), cerebral ischaemia (49 patients [79%])
Shin et al (2014)[37]	60	South Korea and USA (neurology, neurosurgery)	DSA, MRA, CTA	48 (SD 19) years	86% men	Vertebral IAD	SAH (six patients [10%]), headache (ten patients [17%]), cerebral ischaemia (44 patients [73%])
Nakazawa et al (2011)[38]	47	Japan (neurosurgery)	DSA, MRA, CTA	53 (34–70) years (SAH 53 [34–70] years, non-SAH 52 [39–64] years)	66% men (SAH 58%, non-SAH 81%)	Vertebral IAD	SAH (31 patients [66%]), headache (ten patients [23%]), asymptomatic (four patients [9%]), other (two patients [4%])
Jin et al (2009)‡[39]	42	South Korea (neurology, radiology)	DSA in all; CTA or MRA in some	47 (25–73) years (SAH 47 [25–63] years, non-SAH 47 [36–73] years)	62% men (SAH 66%, non-SAH 54%)	Vertebrobasilar IAD: VA (41 patients), BA (one patient)	SAH (29 patients [69%]), cerebral ischaemia (three patients [7%]), headache or neckpain (eight patients [19%]), asymptomatic (two patients [5%])
Zhao et al (2014)‡[40]	97	China (neurosurgery)	DSA	Median 46 (27–80) years	64% men	Vertebral IAD	SAH (57 patients [59%]), symptomatic or unruptured artery (40 patients [41%])
Vertebrobasilar IAD with SAH							
Nakajima et al (2010)[22]	109	Japan (neurology, neurosurgery)	DSA, MRA, CTA	Not reported	Not reported	Vertebrobasilar IAD included	SAH (109 patients [100%])
Zhao et al (2013)‡[41]	57	China (neurology, neurosurgery)	Not reported	Median 48 (27–69) years	51% men	Vertebral IAD included	SAH (57 patients [100%])
Vertebrobasilar IAD without SAH							
Kim et al (2011)‡[21]	191	South Korea (neurosurgery, radiology)	DSA (92%), MRA (79%), CTA (44%)	49 (21–78) years	67% men	Vertebrobasilar IAD included: BA (15 patients), PICA (51 patients); 15 (8%) IADs were bilateral	Cerebral ischaemia (110 patients [58%]), headache alone (81 patients [42%])
Kai et al (2011)[42]	100	Japan (neurology, neurosurgery)	MRI	61 (33–83) years	72% men	Vertebral IAD without SAH	Cerebral ischaemia (30 patients [30%]), headache alone (66 patients [66%]), mass effect (four patients [4%])
Matsukawa et al (2014)‡[43]	77	Japan (neurosurgery)	MRI or MRA (99%), CTA (60%), or DSA (23%)	56 (SD 14) years	70% men	Vertebrobasilar IAD included: BA involved (eight patients), PICA involved (20 patients)	Cerebral ischaemia (33 patients [43%]), headache or neck pain (27 patients]35%]), asymptomatic (17 patients [22%])

N=number of patients. SAH=subarachnoid haemorrhage. VA=vertebral artery. BA=basilar artery. ICA=internal carotid artery. MRA=MR angiography. DSA=digital subtraction angiography. CTA=CT angiography. PICA=posterior inferior cerebellar artery. ACA=anterior cerebral artery. MCA=middle cerebral artery. IAD=intracranial artery dissection. PCoA=posterior communicating artery. PCA=posterior cerebral artery. SCA=superior cerebellar artery. US=ultrasound. *Information about IAD site is missing in 29 patients and there are discrepancies between text and tables. †Numbers and percentages of dissected arteries (206) are presented, not numbers and percentages of patients (190 patients). ‡These series partly overlap. §Numbers and percentages only reported all patients with intracranial and extracranial dissection (133 patients), and not for subgroup of patients with IAD (92 patients). ¶103 patients in total were included in the study, but only 45 patients had pure IAD (the remaining 58 patients had cervical artery dissection with intracranial extension). ‖Numbers and percentages reported only for 14 patients with aneurysm and surgical treatment.

***Table 1*: Clinical and radiological characteristics of patients with IAD in reported series including more than 40 patients**

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263 consecutive patients with cervicocephalic dissections, 18 (7%) occurred in children, of which 11 (61%) were intracranial. Similar proportions were noted in other studies,[24–28] including in non-Asian populations.

In most series, intracranial artery dissections affect the posterior circulation more frequently than the anterior circulation (76–93%; table 1; appendix). By contrast, cervical artery dissections and saccular intracranial aneurysms most commonly affect the anterior blood circulation.[16,44] The relative frequency of intracranial artery dissections in the different intracranial segments varies between studies (table 1; appendix), but in most series the vertebral artery (intradural portion [V4 segment]) is the most common site. Bilateral intracranial artery dissection seems to happen less often than bilateral cervical artery dissection does (<11% in most intracranial artery dissection series[21,30,32,34] *vs* 15% in cervical artery dissection series[11,17,45]), with bilateral intracranial artery dissection mostly reported in the V4 segment.

As stated in initial reports by neurologists, paediatric intracranial artery dissection occurs mostly in the anterior circulation, by contrast with adults, in whom it mostly affects posterior circulation.[24–26,28] However, these reports are probably biased towards cases without subarachnoid haemorrhage. Nowadays, reports by interventional neuroradiologists frequently note posterior circulation involvement in children with

intracranial artery dissection, a location probably more prone to present with subarachnoid haemorrhage than the anterior circulation.[27]

In a study that recruited patients with intracranial artery dissection through both neurosurgery and neurology departments during the same period, investigators reported that the proportion of people with pure intracranial artery dissection (ie, without dissection of the cervical portion of the artery) leading to subarachnoid haemorrhage was 54%.[31] Subarachnoid haemorrhage from intracranial artery dissection is much less common than subarachnoid haemorrhage from ruptured intracranial saccular aneurysms. Autopsy series from Japan[46,47] have reported that between 4·5% and 10·5% of fatal non-traumatic cases of subarachnoid haemorrhage had ruptured intracranial artery dissection. In a study[48] combining data from interventional neuroradiology and neurosurgery departments in two hospitals during 6 years, a total of 756 (568 ruptured [75%] and 188 unruptured [25%]) saccular aneurysms, and 14 (1·8%) symptomatic, intradural, dissecting vertebral aneurysms were treated. Similarly, in the multicentre aneurIST study,[49] 17 intracranial artery dissections among 1834 ruptured and unruptured aneurysms (1·5%) were reported in 1135 patients.

In adults, a male preponderance was noted in Asian populations with intracranial artery dissection, but not in non-Asian populations. Mean age at occurrence of intracranial artery dissection was 50·4 years (range 47–61 years),[19,21–23,29–43] and patients with intracranial artery dissection with subarachnoid haemorrhage tend to be older than those with intracranial artery dissection without subarachnoid haemorrhage (table 1; appendix). Studies into paediatric intracranial artery dissections have consistently shown a substantial male preponderance, as with cervical artery dissection in children.[26,27]

Pathophysiology

Anatomy of the intracranial carotid and vertebral arteries

The intradural portion of the internal carotid artery starts at the clinoid segment of the artery (C6), from which the ophthalmic artery originates in most patients. The intradural portion of the vertebral artery is called the V4 segment, from which the anterior spinal artery and posterior inferior cerebellar artery originate (figure 1).

By contrast with cervical arteries, intradural arteries are characterised by a well developed internal elastic lamina, a paucity of elastic fibres in the media, little adventitial tissue, and no external elastic lamina.[52,53] These features, and weaker supporting tissues than cervical arteries,[54] probably make intracranial arteries increasingly prone to subadventitial dissection and subsequent subarachnoid haemorrhage.[13,55] In internal carotid arteries, the external elastic lamina is present in the petrous portion (the portion where the internal carotid artery enters the canal in the petrous portion of the temporal bone; C3), but disappears in the horizontal segment of the cavernous portion (C5) when the artery is situated between the layers of the dura mater, forming the cavernous sinus.[56,57] Hence dissections starting in the intrapetrous portion of the internal carotid artery mimic cervical artery dissections, whereas dissections in the intradural portion of the internal carotid artery—ie, starting in C6—can lead to subarachnoid haemorrhage. In vertebral arteries, the reduction of elastic fibres in the tunica media and external elastic lamina is most pronounced in the last 0·5 cm before the intradural portion, but is not complete until 0·5 cm after the point of dural perforation.[55] Sometimes to distinguish between a dissection of the distal extracranial segment (V3) and a dissection in the V4 segment can be challenging due to blood flow changes immediately proximal and distal of the dissection site.

Mechanisms and pathological features

Little is known about the pathophysiology of intracranial artery dissection. Although available neuropathological specimens have generally shown a disruption of the internal elastic lamina and the media,[30,47] whether direct bleeding of vasa vasorum (small blood vessels in the wall of larger blood vessels) in the arterial wall can be the initial event is unclear.[58] Vasa vasorum are not always seen in intracranial arteries and seem to predominate in the tunica adventitia and proximal intracranial arteries.[59]

In a study[30] where tissue samples were obtained by surgery or autopsy at different timepoints after symptom onset, the intramural haemorrhage was replaced by granulation tissue after 14 days from onset, followed by compensatory intimal thickening around the pseudolumen. In samples obtained after more than 30 days from symptom onset, neovascularisation in the thickened

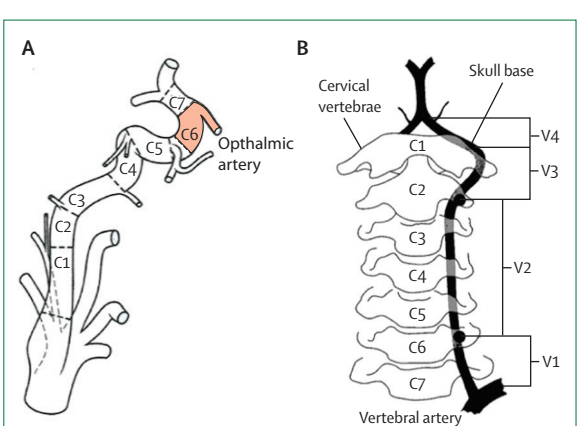

Figure 1: **Anatomy of (A) carotid and (B) vertebral arteries, delineating cervical and intracranial segments**

(A) Segments of the internal carotid artery. The intradural portion starts at the carotid artery segment (C6 [clinoid segment; highlighted in red]), with the ophthalmic artery arising in the intradural portion, except for some anatomical variants. The figure is adapted from Lasjaunias,[59] by permission of *Interventional Neuroradiology*. (B) Segments of the vertebral artery. The figure is reproduced from Khan and colleagues,[51] by permission of *Journal of Neurology, Neurosurgery, and Psychiatry*.

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See Online for appendix

intima was reported, leading to chronic fusiform aneurysm formation,[30] possibly aided by repetitive intramural haemorrhage with the rupture of fragile neovessels.[60]

Different patterns of intimal injury in intracranial artery dissection have been reported. A mural haematoma might be caused by one entrance in the pseudolumen (so-called entry-only lesions) or an entrance and an exit in the pseudolumen (so-called entry-exit lesions). Entry-only lesions can have a higher occurrence of subarachnoid haemorrhage than entry-exit lesions.[61]

The pathophysiological overlap of intracranial artery dissection with giant fusiform aneurysms and blood blister-like aneurysms is controversial, but they should probably be regarded as distinct entities.[62–65] Mycotic or oncological giant fusiform aneurysms are non-dissecting and are caused by the release of proteases by bacteria or tumour cells that break down the vessel wall. Blood blister-like aneurysms located at non-branching sites of intracranial arteries are caused by a degeneration of the internal elastic lamina and media without associated arterial dissection (no mural haematoma or double lumen on pathological examination).[66]

Risk factors and predisposing conditions

Risk factors for intracranial artery dissections are unknown. No comparisons exist between putative risk factors in patients with intracranial artery dissection and healthy controls. In the few studies that included both patients with cervical artery dissection and those with intracranial artery dissection, distribution of vascular risk factors did not differ between the two groups,[31] except for one study[37] showing a higher prevalence of hypertension in patients with intracranial artery dissection. However, this finding[37] might be accounted for by the older age of patients with intracranial artery dissection than control participants in that study (mean age 48 years *vs* 37 years).

Whether cervicocerebral trauma is a risk factor for intracranial artery dissection, as it is for cervical artery dissection,[67] is unclear. In two studies[25,37] that compared patients with cervical artery dissection and patients with intracranial artery dissection, a history of minor trauma was more often present in patients with cervical artery dissection, both in children and adults. In our experience, sudden physical movements that lead to a sudden stretch of the arteries are sometimes reported before the event, but this association has not been systematically analysed in large patient series. Some instances of intracranial artery dissection in children, in our experience, have been associated with intracranial or systemic infections.

Differences in prevalence and characteristics of intracranial artery dissections between ethnic origins, and the more frequent occurrence of intracranial artery dissection in children than in adults, suggest that genetic risk factors could contribute to the occurrence of intracranial artery dissection. However, genetic contribution to intracranial artery dissections has so far not been explored. Exceptionally, intracranial artery dissection might be a complication of rare monogenic disorders of connective tissue, such as Loeys-Dietz syndrome.[68,69] Whether carotid and vertebral artery dissections noted in patients with vascular Ehlers-Danlos syndrome include intracranial artery dissections is not detailed in reported large series.[70,71] Isolated cases of suspected intracranial artery dissections have been noted in patients with Marfan's syndrome.[72]

Patients with fibromuscular dysplasia (a non-atherosclerotic, non-inflammatory vascular disease that mainly affects the renal and cervical arteries) have an increased risk of cervical artery dissection and intracranial aneurysms; whether these patients also have an increased prevalence of intracranial artery dissection is unknown.[73–75] Only isolated instances of intracranial artery dissection and fibromuscular dysplasia have been reported,[76,77] and patients with fibromuscular dysplasia were excluded from many reported series of patients with intracranial artery dissection. Overlap between intracranial artery dissection and segmental arterial mediolysis (a rare arterial disease that presents with life-threatening haemorrhages through ruptured aneurysms in the abdominal cavity), the retroperitoneum, and more seldom the base of the brain, is unclear.[78,79]

Clinical presentation and radiological features

Clinical presentation of intracranial artery dissections is not specific. The two main manifestations are subarachnoid haemorrhage and cerebral ischaemia.[31] In most reported series (table 1), intracranial artery dissections with subarachnoid haemorrhage represent 50–60% of all intracranial artery dissections. Subarachnoid haemorrhage occurs if the arterial wall of an intracranial artery dissection in the intradural portion ruptures. Between 30% and 78% of patients with intracranial artery dissection present with cerebral ischaemia (ischaemic stroke or transient ischaemic attack), without subarachnoid haemorrhage. No specific pattern of brain infarction emerged from our Review, and underlying stroke mechanisms could be either haemodynamic, thromboembolic, or due to occlusion of a perforating artery by the mural haematoma. Rarely, both subarachnoid haemorrhage and ischaemic stroke can be present in combination.[17] About 80% of patients with intracranial artery dissection have prodromal headache, before a subarachnoid haemorrhage or cerebral ischaemia, with subarachnoid haemorrhage occurring within 3 days after onset of headache in 96% of patients.[29,47,80] Onset of prodromal headache was described as sudden in only a few patients (in 13% of patients with intracranial artery dissection without subarachnoid haemorrhage and in 17% with intracranial artery dissection with subarachnoid haemorrhage).[29]

Other uncommon manifestations of intracranial artery dissections include isolated headache and symptoms associated with mass effect, which mostly affects the brainstem or cranial nerves (table 1; appendix). Rarely,

intracerebral haemorrhage has been noted in patients with intracranial artery dissection and, in our experience, even sometimes without subarachnoid haemorrhage.

Radiological diagnosis of intracranial artery dissection can be a challenge in view of the small size of intracranial arteries and the subtle and non-specific radiological signs, which tend to develop with time. Table 2 lists possible differential diagnoses to consider, along with features in favour of intracranial artery dissection diagnosis.

Pathognomonic radiological findings of intracranial artery dissection include mural haematoma, intimal flap, and double lumen. In one study[81] a dissection flap could be identified on MRI in more than 90% of patients with clinical symptoms and CT angiography findings of a possible intracranial artery dissection. A mural haematoma was identified in more than 50% of these patients. A mural haematoma usually leads to a regular crescent-shaped thickening of the arterial wall with enlargement of the external diameter of the dissected artery and often a reduced and eccentric arterial lumen. On T1-weighted MRI a haematoma is spontaneously hyperintense 48–72 h after onset. Detection of a mural haematoma can be improved by use of high resolution 3 Tesla imaging and three-dimensional acquisition of fat-suppressed sequences with black-blood effect that increase sensitivity and specificity of images (figure 2).[82–84]

Other conditions, such as a partly recanalised thrombus or a haemorrhagic atherosclerotic plaque, might mimic this pattern and decrease specificity of recognition, but these are not associated with a focal enlargement of the external diameter. In our experience, the presence of a mural haematoma is particularly rare in aneurysmal forms of intracranial artery dissections. The presence of an intimal flap, with or without a double lumen, is a subtle sign, which is mainly observed in proximal arterial segments, and is probably best detected by digital subtraction angiography (figure 3).

Intracranial artery dissection can present with aneurysmal dilatation, segmental stenosis, or occlusion, with the distribution of these radiological subtypes widely varying between studies. Some studies[23,29,31,32] reported that aneurysmal dilations were more common in intracranial artery dissection with subarachnoid haemorrhage than in intracranial artery dissection without subarachnoid haemorrhage. Both segmental stenosis and occlusion in subarachnoid haemorrhage are highly suggestive of intracranial artery dissection. However, in intracranial artery dissection without subarachnoid haemorrhage, these findings of segmental stenosis and occlusion are non-specific. Likewise, a fusiform or irregular aneurysmal dilation located at a non-branching site on an artery is very suggestive of intracranial artery dissection if associated with a segmental stenosis, but fusiform or irregular aneurysmal dilations are not specific for intracranial artery dissection in isolation.[85] Additional radiological elements are needed to confirm the diagnosis of intracranial artery dissection, including rapid change in morphology. Whether the shallow and broad-based, blood blister-like intracranial aneurysms at the supraclinoid internal carotid artery are caused by intracranial artery dissections is controversial.[65,86] As a result, some of the criteria used to define intracranial artery dissection in studies included in our Review, such as flame-shaped occlusion or irregular stenosis, are not specific for

	Features that favour intracranial arterial dissection
Atherosclerotic stenosis	Isolated or unusual location of arterial stenosis; absence of other features of atherosclerosis (such as calcifications or plaques in other arteries); serial dynamic physical change of lesion shape (especially improvement of stenosis) on follow-up examinations; of a young age (<65 years) without traditional vascular risk factors
Vasospasm due to subarachnoid haemorrhage	Focal narrowing in intracranial artery seen on the day of onset (vasospasm occurs between 4 days and 3 weeks after subarachnoid haemorrhage)
Reversible cerebral vasoconstriction syndrome	Focal narrowing in one rather than many intracranial arteries; absence of classical triggers for reversible cerebral vasoconstriction syndrome (post-partum period, sympathomimetic or vasoconstrictive drugs); residual stenosis persisting for more than 3 months or serial dynamic physical change of lesion shape on follow-up examinations, especially if developing towards an aneurysm
Vasculitis	Focal narrowing in one rather than many intracranial arteries; absence of diffuse vessel wall inflammatory imaging signs; absence of systemic inflammatory disorder
Fibromuscular dysplasia	Acute symptoms; single so-called pearl-and-string sign and not so-called string-of-beads (medial fibroplasia); long stenosis, string sign, and not focal band-like constriction or tubular stenosis (intimal fibroplasia); dynamic change of lesion shape on follow-up examination
Fusiform aneurysm without dissection	Acute symptoms; mural haematoma, intimal flap, or double lumen; dynamic change of lesion shape on follow-up examination
Dolichoectasia	Acute symptoms; mural haematoma, intimal flap, or double lumen; dynamic change of lesion shape on follow-up examination
Thromboembolic occlusion	Concurrent visualisation of a mural haematoma or subsequent recanalisation showing a long filiform stenosis, a fusiform aneurysm, a pearl-and-string sign, or an intimal flap or a double lumen
Transient cerebral arteriopathy*	Intracranial artery dissection is mainly seen in teenagers; parenchymal infarct often has a large size; arterial lesions are irregular; and an arterial wall haematoma can be seen on T1-weighted fat-saturated sequences
Fenestration (anatomical variant)	Acute symptoms; no distinct adventitial layers (one vessel with two lumina and not two vessels); dynamic change of lesion shape on follow-up examinations

In transient cerebral arteriopathy the infarct is often restricted to the deep territory and associated with a smooth and focal arterial stenosis. All of these conditions can coexist with or might cause intracranial arterial dissection. *Present in children, mainly due to inflammation, parainfectious angiopathy (eg, post-varicella angiopathy), or idiopathic arteriopathy (eg, focal cerebral arteriopathy).

***Table 2*: Differential diagnoses of intracranial artery dissection**

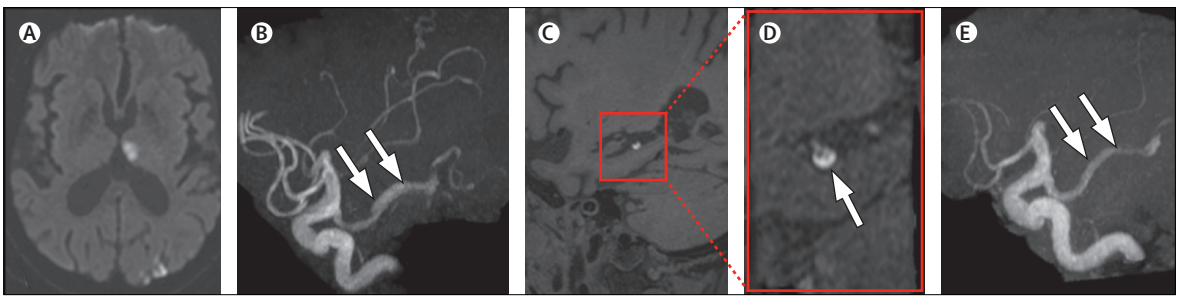

Figure 2: **Example of intracranial artery dissection with mural haematoma changing over time**
(A) Ischaemic stroke in the left occipital lobe and thalamus on diffusion-weighted MRI. (B) Fusiform aneurysmal dilatation of the P2 segment of the left posterior cerebral artery, directly arising from the internal carotid artery on time-of-flight MR angiography (double arrows). (C) Clear hyperintense mural haematoma with eccentric superior lumen of posterior cerebral artery on sagittal cervical and intracranial view of a three-dimensional fat-suppressed T1-weighted sequence, shown on (D), magnified image of C, with arrow. (E) Arrows show normalisation of lumen of the posterior cerebral artery at 3 months follow-up, in MR angiography.

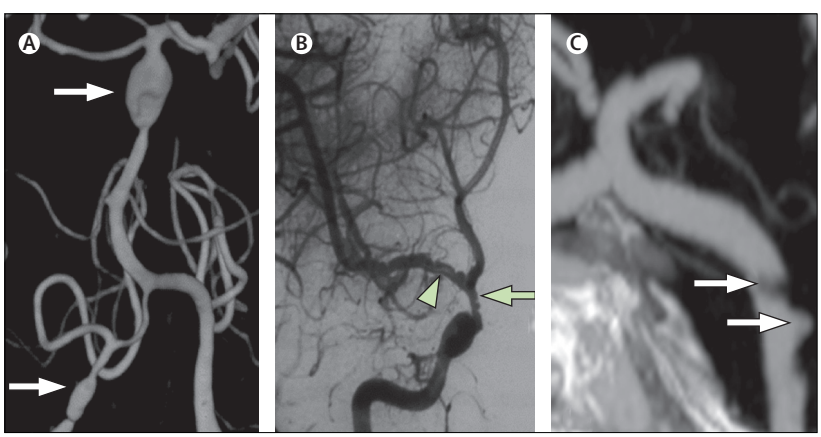

Figure 3: **Detection of intracranial artery dissection with different imaging modalities**
(A) Three-dimensional digital subtraction angiography (DSA) of a patient with subarachnoid haemorrhage. Arrows point to two typical intracranial arterial dissections of the right vertebral artery (bottom arrow) and the basilar artery (top arrow) with associated stenosis and aneurysmal dilatation. (B) DSA of right internal carotid artery with dissecting aneurysm and irregular stenosis resulting in a so-called pearl-and-string sign (arrow). Arrow head points to intimal flap visible in the M1 segment of the right, middle cerebral artery. (C) CT angiography of basilar artery showing dissecting aneurysm (bottom arrow) and intimal flap (top arrow).

intracranial artery dissections (appendix). These non-specific criteria are an important limitation of most studies.

On the basis of a multidisciplinary expert consensus we have compiled terminology standards and grading of imaging diagnostic criteria for the diagnosis of intracranial artery dissection (panel).

To detect a mural haematoma of the arterial wall, high resolution 3 Tesla MRI that includes three-dimensional fat-suppressed T1-weighted images with black-blood effect is regarded as optimum imaging method. Imaging of the arterial lumen to detect an occlusion, stenosis, aneurysm, or intimal flap, with or without double lumen, can be done with CT angiography or MR angiography. Digital subtraction angiography is the gold standard for luminal imaging but, because of its invasive nature this method, is mainly used if CT or MR imaging is inconclusive, if patients present with subarachnoid haemorrhage, or if surgical or endovascular treatment is being considered.

The definite diagnosis of intracranial artery dissection often needs the combination of arterial wall and lumen imaging, and also the comparison between baseline and follow-up imaging (figure 2).

Management and outcome

Treatment options

Optimum treatment for patients with intracranial artery dissections is unknown. No randomised trials exist and only observational studies with small sample sizes are available, thus providing a very low level of evidence.

Patients with intracranial artery dissection with subarachnoid haemorrhage are usually treated with surgical or endovascular procedures because up to 40% of patients have rebleeding within the first days after the event.[30,87] If patients are in very poor clinical health or the proposed treatment has an unacceptably high risk of complications, a decision can be made to withhold surgical or endovascular treatment.

In earlier reported series, patients with intracranial artery dissection without subarachnoid haemorrhage and with aneurysmal dilation were often offered surgical or endovascular treatment because of concern that the dissecting aneurysm would rupture.[21] However, in recent years, most patients with intracranial artery dissection without subarachnoid haemorrhage have been treated medically, and offered acute stroke treatment and long-term prevention of ischaemic stroke. Endovascular treatment is undertaken only in patients with recurrent ischaemic symptoms despite receiving optimum medical treatment. Sometimes, endovascular treatment is undertaken if the dissecting aneurysm has increased in size, to prevent rupture, or more rarely to reduce signs of brainstem compression.[21,35,88,89] In children, the preferred and widespread practice is surgical or endovascular treatment in patients with intracranial artery dissection with subarachnoid haemorrhage and those without subarachnoid haemorrhage and mass-effect, whereas patients with intracranial artery dissection without subarachnoid haemorrhage and cerebral ischaemia tend to be given medical treatment.

Surgical and endovascular treatment

Various surgical and endovascular treatment methods have been proposed for intracranial dissecting aneurysms (figure 4).[22] All treatment methods aim to reduce blood flow in the dissected region. Deconstructive techniques sacrifice the parent artery, whereas reconstructive techniques aim to maintain a parent artery.

Parent artery occlusion is a deconstructive technique in which blood flow into the dissected segment of the artery is stopped by occlusion either surgically or through an endovascular approach. Preferably, the dissected segment is occluded both proximally and distally to prevent rerupture through retrograde filling of a dissecting aneurysm. Parent artery occlusion has a risk of brain infarct in case of insufficient collateral supply. Before permanent occlusion, the collateral supply can be assessed with temporary balloon-occlusion or amobarbital infusion during digital subtraction angiography (with simultaneous monitoring of the patient's neurological function).

Reconstructive techniques, such as selective aneurysmal sac occlusion through clipping (surgical) or coiling (endovascular), are often difficult in intracranial artery dissection given the non-saccular shape of the dissecting aneurysm. In endovascular treatment, stent-assisted coiling can be used. Stenting of the dissected artery without any coiling by flow-diverter stents or conventional close-cell stents has been reported in small series;[85,90,91] however, several days to months can pass before the dissecting aneurysm is thrombosed. Moreover, stenting needs dual antiplatelet treatment for several months after the procedure, thereby exposing patients to an increased risk of haemorrhagic complications.[21,41] Seldom, a bypass surgery between extracranial and intracranial arteries can be considered if the risk of infarction due to parent artery occlusion is unacceptably high and stenting is impossible.[22,42] In very rare instances, mostly in middle-cerebral artery dissections (M2 branches), the dissected segment can be excised and arterial stumps reanastomosed.[92]

As for saccular intracranial aneurysms, endovascular treatment is currently more frequently undertaken than is surgical treatment in most patients with intracranial artery dissection with subarachnoid haemorrhage in scientific literature. A comparison between surgical and endovascular treatment has not been made in a randomised trial.

Some observational studies have reported peri-procedural complications after surgical or endovascular treatment for intracranial artery dissection (table 3; appendix). Recurrent bleeding was reported in 0–11% of patients with intracranial artery dissection with subarachnoid haemorrhage after surgical or endovascular treatment, and after treatment for ischaemia in 0–22% of patients.[19,21–23,29–43] Cranial nerve palsies and spinal cord infarctions were seldom reported.[35,41,93] Overall, of 813 endovascular procedures, 50 (6·2%) cerebral or spinal cord ischaemia, 15 (1·8%) rupture and rebleeding, and seven (0·9%) cases of cranial nerve palsies were reported; of 125 surgical procedures, 23 (18·4%) cerebral or spinal cord ischaemia, one (0·8%) rupture and rebleeding, and one (0·8%) case of cranial nerve palsy were reported. As previously emphasised, these percentages are likely to be an underestimation due to reporting and publication bias.

Medical treatment

Medical treatment of intracranial artery dissection without subarachnoid haemorrhage encompasses both acute stroke treatment (recanalisation) and long-term

Panel: Proposed terminology and grading of imaging diagnostic criteria for intracranial artery dissection

Proposed terminology for imaging diagnostic criteria of intracranial artery dissection

At least one of the three following features should be present when diagnosing an intracranial artery dissection:

- Fusiform or irregular aneurysmal dilation at a non-branching site of an intracranial artery, with at least one of the following criteria
  - Intramural haematoma (hyperintense rim on images with T1-weighted MRI), intimal flap, or double lumen*
  - Rapid change in morphology on repeated imaging (increase or reduction in size, subsequent appearance of stenosis)
  - Association with a focal stenosis (so-called pearl-and-string sign)
- Long filiform or irregular stenosis of an intracranial artery, with at least one of the following criteria:
  - Intramural haematoma (hyperintense rim on images with T1-weighted MRI), intimal flap, or double lumen*
  - Rapid change in morphology on repeated imaging (increase or reduction in size, or subsequent appearance of aneurysmal dilation)
  - Association with a fusiform or irregular aneurysmal dilation (so-called pearl-and-string sign)
- Occlusion of an intracranial artery that recanalises in either a fusiform or irregular aneurysmal dilation at a non-branching site, or a long filiform or irregular stenosis

Proposed grading of imaging diagnostic criteria for evidence of intracranial artery dissection

- Definite intracranial artery dissection
  - Stenosis or occlusion of an intracranial artery secondarily developing towards a fusiform or irregular aneurysmal dilation at a non-branching site
  - Intramural haematoma, intimal flap, or double lumen
  - Pathological confirmation of intracranial artery dissection
- Probable intracranial artery dissection
  - Fusiform or irregular aneurysmal dilation and focal, long filiform, or irregular stenosis (so-called pearl-and-string sign) without subarachnoid haemorrhage, or still present >1 month after subarachnoid haemorrhage
  - Fusiform or irregular aneurysmal dilation at non-branching site with rapid change in morphology (increase or reduction in size, or subsequent appearance of stenosis)
- Possible intracranial artery dissection
  - Fusiform or irregular aneurysmal dilation at non-branching site without change in morphology on repeated imaging within 6–12 months after first imaging
  - Long filiform or irregular stenosis of an intracranial artery, with reduction in size or disappearance over time

*Double lumen should be carefully differentiated from fenestration (which is an anatomical variant)

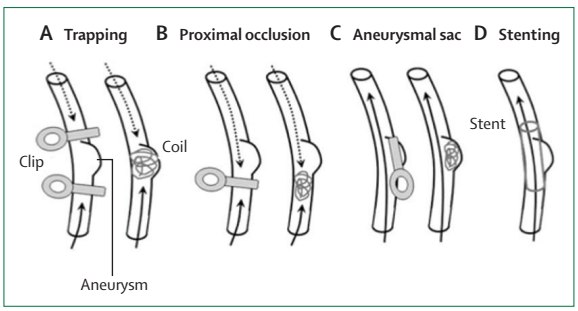

Figure 4: **Four types of surgical and endovascular treatments**
(A) Trapping aims to exclude blood flow from the dissected region and aneurysm. (B) Proximal occlusion reduces blood flow in the dissected region and aneurysm. Both trapping and proximal occlusion can be done by clipping or coiling. (C) Aneurysmal sac occlusion can be done by clipping or stenting and selectively occludes the aneurysm, but does not change blood flow in the vessel. (D) Stenting aims to cover the dissected region and aneurysm, leaving blood flow in the vessel unchanged. Solid arrows represent antegrade blood flow. Dotted arrows represent retrograde blood flow. Figure reproduced from Nakajima and colleagues,[22] by permission of *Acta Neurochirurgica*.

prevention of ischaemic stroke. The safety and effectiveness of intravenous and intra-arterial thrombolysis in patients with intracranial artery dissection without subarachnoid haemorrhage are unknown, because only case reports have been published.[94–97] The choice of antithrombotic treatment (anticoagulants or antiplatelets) in patients with intracranial artery dissection without subarachnoid haemorrhage with cerebral ischaemia has not been assessed in randomised controlled trials or in systematic reviews and meta-analyses of observational data. By assuming that the mechanisms of cerebral ischaemia in intracranial artery dissection resemble those of cerebral ischaemia in cervical artery dissection, examining studies on antithrombotic treatment in cervical artery dissection might be helpful. Results from randomised controlled trials of antithrombotic treatment in cervical artery dissection are also missing. A pilot trial[98] on 250 patients has been completed, showing no difference in efficacy of antiplatelet and anticoagulant drugs at preventing stroke and death in patients with cervical artery dissection, but stroke was rare in both groups. Several meta-analyses[5,99] of observational studies have not shown any significant difference in clinical outcome between patients treated with anticoagulants and those treated with antiplatelets, mostly aspirin. Findings from a meta-analysis[100] using a Bayesian approach suggested a treatment effect in favour of antiplatelet drugs, the advantage of which was less obvious when the analysis was restricted to studies of higher methodological quality. Although no haemorrhagic complication was reported in a small series of patients with intracranial artery dissection without subarachnoid haemorrhage who were treated with anticoagulants,[31] the risk of subarachnoid haemorrhage is greater in intracranial artery dissection than in cervical artery dissection. Several studies reported patients with intracranial artery dissection with initial ischaemic manifestations who then subsequently or concurrently developed subarachnoid haemorrhage, prompting caution.[30]

In patients with intracranial artery dissection without subarachnoid haemorrhage and no signs of cerebral ischaemia, or in rare cases when both subarachnoid haemorrhage and cerebral ischaemia are present, no antithrombotic treatment, but close monitoring has been proposed.[42] Studies investigating the predictors of subarachnoid haemorrhage and cerebral ischaemia in patients with unruptured intracranial artery dissection are warranted to optimise management strategies.

Outcome

Because of treatment and publication biases, little is known about the natural history of intracranial artery dissection. Overall, intracranial artery dissection has a more severe course than cervical artery dissection, with a more ominous outcome in patients with subarachnoid haemorrhage than in those without subarachnoid haemorrhage.[30,101] Table 3 and the appendix summarise outcomes reported in individual studies.

Mortality

Mortality outcome for patients with intracranial artery dissection and subarachnoid haemorrhage ranges between 19% and 50%. In studies including only patients who qualified for endovascular treatment, lower mortality rates (5–9%) were reported, which is not surprising given that these studies excluded the most severe patients from the outset.[35,41] Mortality outcome in patients without subarachnoid haemorrhage is low and similar to that in patients with cervical artery dissection, ranging between none and 3% in reported series.

Recurrent haemorrhagic or ischaemic events

Although recurrences are poorly defined in most studies, overall, recurrent haemorrhagic or ischaemic events seem to follow the pattern of the initial event in more than 90% of patients.[30] In patients with subarachnoid haemorrhage, recurrence of subarachnoid haemorrhage in up to 40% of patients has been reported,[30] with the highest rates being noted in patients treated conservatively.[22] Most haemorrhagic recurrences cluster within the days after the initial event.[22,30] In one study,[30] recurrent subarachnoid haemorrhage occurred more frequently in patients with intracranial artery dissection older than 50 years and less frequently in patients with carotid intracranial artery dissection.

In patients without subarachnoid haemorrhage, recurrence rates of ischaemic stroke ranged between 2% and 14%, with a mean follow-up spanning from 3 months to 8 years. In one study,[42] 38% of patients had recurrent cerebral ischaemia during a mean follow-up of 24 months, but antiplatelet drugs were not prescribed after the initial ischaemic event. Extension of the intracranial artery dissection into the basilar artery and involvement of the posterior inferior cerebellar artery were reported as risk factors for recurrent ischaemic stroke.[43]

Very few patients seem to have different types of events associated with the intracranial artery dissection over time—ie, subarachnoid haemorrhage after initially unruptured, intracranial artery dissection (described between 4 days and 11 days after the initial diagnosis[29,30]) or ischaemic events attributed to residual arterial lesions several months or years after an initial subarachnoid haemorrhage.[30] In some patients, signs of brainstem compression were noted several years after a dissecting aneurysm.[21,30]

Recurrent dissections

Little information is available about the risk of recurrent intracranial artery dissection. One study[29] of 190 patients with regular follow-up imaging after intracranial artery dissection reported recurrent intracranial artery dissection in 18 patients (9%) during a mean follow-up of 3·4 years.[29] Of the recurrent dissections, 12 (67%) occurred within 1 month after the initial event. This rate of recurrent dissections seems in line with the recurrence rate of cervical artery dissection, which is estimated between 0% and 8% in most studies.[7]

Functional outcome

Functional outcome is not always reported in published series and has been rated on different scales. Overall, more than 79% of patients with intracranial artery dissection and without subarachnoid haemorrhage had a favourable functional outcome (modified Rankin Scale ≤1 or ≤2, or equivalent).[19,21–23,29–43] One study[21] showed that

	N	Treatment	Follow-up time	Deaths during follow-up	Good functional outcome	Recurrences or complications
All types						
Yamaura et al (2000)[23]	357	SAH: 125 (61%) surgical or endovascular treatment, 80 (39%) treated conservatively (no details); non-SAH: 26 (17%) surgical or endovascular treatment, 125 (83%) treated conservatively (no details; one [<1%] not described)	≥3 months	17% (SAH 27%, non-SAH 3%)	75% GOS 5 (SAH 63%, non-SAH 90%)	34 (10%) recurrence (no details on type; SAH: 29 recurrences [14%; no details on type of recurrence]; non-SAH: five recurrences [4%; no details on type of recurrence])
Mizutani (2011)[29]	190	SAH: 71 (71%) surgical treatment, 31 (29%) treated conservatively (no details); non-SAH: mild-volume expansion plus free radical scavengers for infarction (occasionally antiplatelet drugs or anticoagulants for infarction plus stenosis), three (3%) surgical treatment (in patients who had aneurysm extension)	Mean 3·4 years (range 2–20·4 years) in non-SAH	11% (SAH 68%,* non-SAH 2%)	Not reported	18 (10%) recurrence (new IADs, all in different arteries, 12 recurrent IADs occurred within 1 month, six recurrent IADs occurred after >1 year); one (1%) patient had a SAH at day 11 after onset
Ono et al (2013)[30]	143	SAH: 54 (63%) surgical treatment, 32 (37%) treated conservatively (no details); non-SAH: 12 (21%) surgical treatment, 45 (79%) treated conservatively (no details)	Mean 8·2 years (range 1 day–25 years)	18% (SAH 29%, non-SAH none)	69% independent (SAH 55%, non-SAH 90%)	36 (33%) SAH (SAH: 35 patients [41%] rebleeding at mean 4·8 days [range 0–26 days]; non-SAH: one [2%] SAH 4 days after initial ischaemic event), 10 (7%) ischaemic stroke (SAH one [1%] ischaemic stroke at 85 months, non-SAH nine [16%] ischaemic stroke); non-SAH group one (2%) hemifacial spasm at 21 months due to compression by enlarged aneurysm
Kwak et al (2011)†[19]	92	Not reported	Not reported	Not reported	Not reported	Four (4%) SAH (SAH: four [14%] rebleeding)
Metso et al (2007)[31]	45	SAH: 19 (86%) surgical or endovascular treatment (no details), three (14%) treated conservatively (no details); non-SAH: 23 (100%) treated with anticoagulation	Mean 1·3 years (range 1 day–8 years)	16% (SAH 32%, non-SAH none)	58% mRS≤2 (SAH 32%, non-SAH 83%)	No SAH for patients without SAH; not reported for patients with SAH
Vertebrobasilar IAD						
Ahn et al (2012)†[32]	210	SAH: 48 (100%) endovascular treatment; non-SAH: 59 (32%) endovascular treatment	Median 47 months (range 8–105 months)	Not reported	Not reported	No SAH
Kim et al(2011)†[33]	111	Endovascular treatment	Mean 35 months (range 15–84 months)	8%	85% mRS≤2 (SAH 77%, non-SAH 100%)	Six (5%) SAH (SAH: six [8%] rebleeding, of which one [1%] on day of onset, four [5%] 3–4 days after treatment, and one [1%] 15 days after treatment), four 4% unruptured angiographic recurrent dissection in 100 patients with radiological follow-up, seven (10%) ischaemic stroke (SAH: five [11% ischaemic stroke]; non-SAH: two [7%] ischaemic stroke)
Matsukawa et al (2012)†[34]	103	Not reported	Not reported	Not reported	Not reported	Not reported

(Table 3 continues on next page)

	N	Treatment	Follow-up time	Deaths during follow-up	Good functional outcome	Recurrences or complications
(Continued from previous page)						
Kashiwasaki et al (2013)[35]	73	Endovascular treatment	Mean 55·6 months‡ (range 6–145 months)	8% (SAH 13%, non-SAH none)	91% mRS≤2 (SAH 86%, non-SAH 100%)	One (1%) SAH (SAH: one (2%) rebleeding periprocedural), seven (10%) ischaemic stroke (SAH: five [11%] ischaemic stroke; non-SAH: two [7%] ischaemic stroke), two (3%) spinal cord infarction, six (8%) cranial nerve palsy, two (3%) asymptomatic recurrences
Takemoto et al (2005)[36]	62	SAH: five (100%) surgical treatment; non-SAH: nine (16%) surgical treatment, 48 (84%) treatment not specified	Not reported	None§	79% GOS 5§ (SAH 40%, non-SAH 100%)	No SAH; two (14%) cerebral infarction (SAH: one [20%] periprocedural cerebral infarction; non-SAH: one [11%] cerebral infarction 2 weeks after treatment)§
Shin et al (2014)[37]	60	Not reported	3 months	SAH 50%, non-SAH not reported	Favourable outcome (SAH 50%, non-SAH not reported)	Not reported
Nakazawa et al (2011)[38]	47	SAH: 31 (100%) endovascular treatment; non-SAH: four (25%) endovascular treatment, 12 (75%) surgical treatment	Not reported	15% (SAH 23%, non-SAH none)	81% good recovery (SAH 71%, non-SAH 100%)	One (2%) SAH (SAH: one [3%] rebleeding after treatment), two (4%) ischaemic stroke (SAH: two [6%] periprocedural ischaemic stroke)
Jin et al (2009)†[39]	42	Endovascular treatment	Mean 21·1 months (range 1–44 months)	10% (SAH 14%, non-SAH none)	69% GOS 5 (SAH 55%, non-SAH 100%)	Three (7%) SAH (SAH: three [10%] rebleeding after treatment), nine (21%) cerebral infarction (SAH: nine [31%] periprocedural cerebral infarction)
Zhao et al (2014)†[40]	97	Endovascular treatment	Mean 58 months¶ (range 12–132 months)	7%	84% mRS≤1	Three (3%) SAH (SAH: one [2%] rebleeding; non-SAH: two [5%] SAH), seven (7%) angiographic recurrent dissection or aneurysm
Vertebrobasilar intracranial artery dissection with SAH						
Nakajima et al (2010)[22]	109	88 (81%) surgical treatment, 21 (19%) treated conservatively (no details)	Not reported	Not reported	Not reported	Ten (9%) rebleeding (eight [38%] in patients treated conservatively, two [7%] rebleeding after surgery)
Zhao et al (2013)†[41]	57	Endovascular treatment	Mean 62 months (range 12–78 months)	5%	83% mRS≤1	Two (4%) rebleeding after treatment (one not confirmed by imaging), five (9%) angiographic recurrence
Vertebrobasilar intracranial artery dissection without SAH						
Kim et al (2011)†[21]	191	46 (24%) endovascular treatment, 49 (26%) anticoagulants (all with ischaemic events), 48 (25%) antiplatelet drugs, 48 (25%) analgesics only (all without ischaemic events)	Mean 46 months (range 15–102 months‖)	1%	94% mRS≤1	Four (2%) recurrent cerebral ischaemia within 6 months, one (1%) brainstem compression symptoms at 3 years due to compression by enlarged aneurysm
Kai et al (2011)[42]	100	Four (4%) initial surgery or endovascular treatment, five (5%) endovascular treatment during follow-up (due to lesion progression [three], new ischaemia [one], or mass-effect [one patient], despite medical treatment); 91 (91%) treated conservatively (if progressive ischaemia, antiplatelet drugs given [after second ischaemic attack]; if progressive mass-effect, given steroids; if headache only, non-progressive ischaemia, or mass-effect, systolic blood pressure controlled [<140 mm Hg]; if progression despite medical treatment, further surgical or endovascular treatment)	24 months	Not reported	Not reported	No SAH, 38 (38%) recurrent or de-novo cerebral ischaemia (initially headache [18 patients] or ischaemia [20 patients])
Matsukawa et al (2014)†[43]	77	75 (97%) treated conservatively (analgesics and blood pressure control in all; if ischaemic stroke give aspirin [five patients]), two (3%) endovascular treatment due to prominent aneurysmal dilation	Mean 17 months (range 3–38 months)	None	Not reported	Three (4%) cerebral ischaemia, three (4%) vertebrobasilar insufficiency (not specified), 19 (25%) morphological worsening of IAD (ie, aneurysmal enlargement, worsening of stenosis, or occlusion)

N=number of patients. SAH=subarachnoid haemorrhage. GOS 5=Glasgow outcome scale version 5. MCA=middle cerebral artery. mRS=modified Rankin Scale score. *Follow-up only available for 31 patients without surgical treatment. †Series partly overlap. ‡Duration of follow-up was calculated only for 61 survivors not lost during follow-up. §Numbers and percentages only reported for 14 patients with aneurysm and surgical treatment. ¶Duration of follow-up was calculated only for 90 survivors. ‖178 patients.

***Table 3*: Treatment and outcome of patients with intracranial artery dissection in reported series that included more than 40 patients**

being older and basilar artery involvement were independent predictors of unfavourable functional outcome. Between 24% and 86% of patients with vertebral subarachnoid haemorrhage were reported to reach a good functional outcome after treatment, with the highest rates in patients who were preselected for endovascular treatment. Older age and unfavourable Hunt-Hess scale scores at admission to hospital were independent predictors of unfavourable functional outcome.[41]

Recanalisation rates with conservative treatment

The timeframe of changes seen in imaging characteristics in patients with intracranial artery dissection and the rate of recanalisation for conservative treatment are unknown. In patients without subarachnoid haemorrhage, one study[29] reported that major changes in vessel geometry are almost completed within the first 2 months after dissection, with minor changes still happening after 2 months. After a mean follow-up of 15 months, in another study[32] of 114 patients with vertebrobasilar intracranial artery dissection without subarachnoid haemorrhage, the imaging results showed improvement in 66 (58%), no change in 34 (30%), and worsening in 14 (12%) patients. In another independent series of 91 patients who were treated conservatively, partial or complete normalisation was reported in 18 (20%), no change was seen in 70 (77%), and secondary occlusion occurred in three (3%) patients.[42] In patients with intracranial artery dissection and subarachnoid haemorrhage, the natural timecourse of structural arterial changes is unknown, because most patients undergo an operation.[29]

Conclusions and future directions

Intracranial artery dissection is an uncommon and presumably underdiagnosed cause of both ischaemic stroke and subarachnoid haemorrhage. Diagnosis of intracranial artery dissection is often difficult because of non-specific clinical presentation; low sensitivity of radiological methods for pathognomonical signs, such as a mural haematoma, intimal flap, or double lumen, in view of the small size of the arteries; and the dynamic nature of the disease. We propose terminology and grading of imaging diagnostic criteria for intracranial artery dissections (panel). The definite diagnosis of intracranial artery dissection often needs the combination of arterial wall and lumen imaging and also the comparison between baseline and follow-up imaging.

In view of the absence of randomised trials, suggestions for treatment of intracranial artery dissection are general and empirical. Hence, we propose a multidisciplinary expert consensus statement on the management of intracranial artery dissection. In patients with an acute ischaemic stroke suspected to be caused by intracranial artery dissection (diagnosis is seldom definite within the short time window for thrombolysis), intravenous thrombolysis should probably not be withheld in the absence of associated haemorrhage on initial brain imaging. Outside the time window for thrombolysis, before initiation of antithrombotic treatment in patients with intracranial artery dissection and cerebral ischaemia, a lumbar puncture can be done if neuroimaging cannot formally rule out minor subarachnoid haemorrhage. The higher theoretical risk of subarachnoid haemorrhage than cervical artery dissection and the superiority of aspirin over anticoagulants in the acute phase of ischaemic stroke in general[82] are empirical arguments in favour of prescription of aspirin rather than anticoagulants. In case of recurrent thromboembolic events despite aspirin, dual antiplatelet treatment or anticoagulants could be considered. Endovascular or surgical treatment might be an option if additional embolic events happen or if a progressive increase in aneurysmal size is reported, particularly if it causes a mass-effect.

Risk of rebleeding in patients presenting with subarachnoid haemorrhage probably justifies endovascular or surgical intervention in most instances. Treatment indications and options should be discussed in multidisciplinary teams before implementation. Many centres consider endovascular parent artery occlusion as the first treatment choice. Stent placement or stent-assisted coiling or, in some instances, surgical repair or bypass are mostly regarded as a second treatment choice, in case of insufficient collateral blood supply or important side branches stemming from the parent artery.

Despite providing important information about the characteristics, treatment, and outcome of intracranial artery dissections, reported studies have important limitations. First, all studies were retrospective and included quite small cohorts (<400 patients), because of the low frequency of the disease. Second, the definition of intracranial artery dissection was often non-specific

Search strategy and selection criteria

References for this Review were identified through searches of PubMed with the terms "intracranial", "intradural", "intracranial aneurysm", or "intracranial artery diseases" in combination with "dissection", "vertebral artery dissection", "carotid artery, internal, dissection", or "aneurysm, dissecting" between PubMed inception and Dec 1, 2014. We also identified scientific papers by reviewing reference lists of relevant articles and through searches of the authors' personal files. We considered articles published in English, French, German, Dutch, Italian, Turkish, Finnish, Swedish, and Spanish. Abstracts published only at meetings were excluded from our search. Only original articles describing at least one aspect of clinical characteristics and radiological features and outcome, in series of at least 20 patients, were chosen. If several studies into overlapping samples had been reported, only the largest and most recent were included, except if the overlap was only partial or if different parameters were assessed. Autopsy series and papers describing iatrogenic dissections or dissections secondary to penetrating trauma were not included. Additionally, cervical artery dissection with an intracranial extension, intracranial arterial dissection secondary to penetrating trauma, and iatrogenic intracranial arterial dissection are not discussed in this Review.

and varied between studies. Third, recruitment was often biased towards patients seen in specialised departments of neurology, neurosurgery, or interventional neuroradiology. Fourth, most data are derived from Asian populations, restricting the generalisability of findings to populations worldwide. Fifth, follow-up time was very heterogeneous between and within studies, attrition was not well examined or accounted for, and no standard criteria were used for clinical or radiological outcomes (recurrences of ischaemic or haemorrhagic events, recurrent dissections, functional outcome, and measurement of lesion progression). Sixth, some reports of a particular endovascular technique were biased towards patients with less severe disease from the outset, and mortality rates and outcome were sometimes missing; moreover, out of all interventional studies done, publication bias likely favoured studies showing improved clinical outcomes. Finally, data for intracranial artery dissection in children are particularly scarce and, apart from the few studies in children covered in our Review, other information obtained from the scientific literature might not be generalisable to children.

In conclusion, multicentre prospective studies and, ultimately, trials with standardised protocols for diagnosis, imaging, and follow-up of intracranial artery dissection are needed. Future efforts should aim to promote international transdisciplinary collaborations, which will be necessary to gather large enough and representative samples.

Contributors

SD designed the structure of the Review, did the literature search, convened the expert committee, and prepared the first draft and subsequent versions of the Review. AC did the literature search, modified subsequent drafts, and contributed to the preparation of tables and figures. SS did the literature search. M-GB initiated the Review, refined the conception and design, contributed to writing, and critically revised the draft. SD, AC, M-AL, MU, TMM, JJMaj, BG-S, STE, AP, AMS, YB, JWC, AD, GG, SS, PR, HS, JCW, SJ, JJMar, TB, CG-G, AB, ET, PAL, HC, HSM, BBW, SC, RB, CS, TT, MA, and M-GB attended the consensus meeting. All authors revised the draft critically.

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