Neuroimaging of headaches attributed to cranial and/or cervical vascular disorders

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ABSTRACT
Secondary headaches comprise approximately 10% of all headache cases. They often have a serious underlying condition that needs prompt and thorough examination, which almost always includes neuroimaging. Each imaging modality serves a different purpose, and various diagnostic methods can be utilized in the diagnostics of headaches attributed to cranial and cerebral vascular disorders which vary in both etiology and manifestation. This literature review aims to summarise and present the role of neuroimaging in the evaluation of patients with the conditions above.

INTRODUCTION
Headache is a recurrent or persistent pain of the head (1). It has a lifelong prevalence of 66-96% and the current prevalence of 46% (1, 2) and is a common presenting complaint in the emergency department, responsible for approximately 2% of all visits (3). Headaches are divided into primary (with no underlying cause) and secondary (caused by another condition) (4). Primary headaches are more common – they comprise 90% of all cases (5). Although rare, secondary headaches are often life-threatening and require immediate action (6). However, diagnosis more often than not requires imaging evaluation of the head. This article aims to present different aspects of secondary headaches attributed to cranial or cervical vascular disorders with a particular focus on neuroimaging of the underlying condition.

REVIEW OF LITERATURE
Headache attributed to a cerebral ischemic event Ischemic stroke is an episode of neurological dysfunction which lasts more than 24 hours and is caused by focal cerebral, spinal or retinal infarction (7). It is a common neurological disorder with an incidence ranging from 95 to 290 per 100 000 inhabitants in Europe (8). Observational studies indicate that 8%–64% of patients report a headache at the onset of an acute ischemic stroke (9). Generally, the stroke associated headache is not severe but continuous and manifests as bilateral tension-type head pain. (10). Basilar strokes are associated with headaches more often than carotid strokes while lacunar strokes are generally not accompanied by headaches at all (9). A small number of migraine patients infrequently suffer from migrainous strokes with an incidence of 0,8 per 100 000 inhabitants (11).

Headache at stroke onset is predictive of a headache development at six months post-stroke (12). Persistent headaches attributed to past ischemic events have been estimated to occur in 10% of post-stroke patients. A post-stroke headache is predominantly characterized as a tension-type headache with a pressing quality (13).

In the setting of an acute stroke, neuroimaging is performed to exclude possible hemorrhages, to assess the degree of brain injury, and to identify the vascular lesion responsible for the ischemic deficit (14).

Non-contrast computed tomography (CT) scans are the first modality of choice in case of acute ischemic stroke because of their wide availability and rapidity of imaging (15). Non-contrast CT scans are useful in detecting large ischemic strokes after 6 to 8 hours from onset. Non-contrast CT has an overall sensitivity of 57-71% to detect an acute ischemic stroke in the first 24
hours but only 12% in the first 3 hours (16, 17). Early non-contrast CT findings include hypoattenuation in the territory of the middle cerebral artery, hypodensity of the lentiform nucleus, cortical sulcal effacement, focal parenchymal hypoattenuation, loss of the insular ribbon or obscuration of the Sylvian fissure, hyperattenuation of large vessels, loss of gray and white matter differentiation in the basal ganglia (14).

Alberta Stroke Program Early CT Score (ASPECTS) method assists in evaluating early ischemic changes in CT scans. ASPECTS is a scoring system of 10 points and can be applied only to the territory of the middle cerebral artery (18, 19).

CT angiography (CTA) provides the means to rapidly and noninvasively evaluate the intracranial and extracranial vasculature in stroke patients, thus providing valuable information about the presence of vessel occlusion or stenosis (20). CTA has a sensitivity of 92-100% and specificity of 82-100% for the detection of intracranial large vessel occlusion and stenosis (21). A noninvasive intracranial vascular study is a must before endovascular therapy (15, 20).

Magnetic Resonance Imaging (MRI) is superior to CT in detecting hyperacute stroke (14). Fluid attenuation inversion recovery (FLAIR) and T2 weighted (T2W) sequences become positive within the first 3 to 8 hours after an acute arterial occlusion. The MRI signs of acute ischemic stroke include increased brain signal intensity, swollen cortical gyri, and increased signal intensity in the lumen of vessels (16). Diffusion-weighted imaging (DWI) is a form of MRI that is capable of detecting brain tissue damage within the first 3 to 30 minutes of ischemia, making it the most sensitive early neuroimaging technique in the setting of an acute ischemic stroke (Figure 1) (23).

A transient ischemic attack is a temporary episode (less than 24 hours in duration) of neurological dysfunction caused by focal brain, spinal, or retinal ischemia without any evidence of acute infarction (7). Headache is rarely a prominent symptom of a transient ischemic attack – its frequency varies between 16 and 36% (24). In the case of transient ischemic attack, head CT or MRI must be performed to exclude infarction. DWI can be used to distinguishing brain, spinal, or retinal ischemia from an acute infarction (25).

**HEADACHE ATTRIBUTED TO NON-TRAUMATIC INTRACRANIAL HEMORRHAGE**

Headache attributed to non-traumatic intracerebral hemorrhage (ICH)

Intracerebral hemorrhage (ICH) is defined as haemorrhage into the brain parenchyma and occurs with the incidence of approximately 25 cases for every 100 000 inhabitants annually (26). Non-traumatic or spontaneous ICH is caused by a variety of aetiologies, the most common reasons being hypertensive or amyloid angiopathy (27). Headache is one of the most prevalent symptoms of ICH (28). The manifestation of the headache does not depend on the cause and is usually gradual (29); however, it may also manifest as a thunderclap headache (30). Other common symptoms include nausea, vomiting, focal neurological deficit symptoms, deteriorating consciousness, etc. (31).

Since clinical presentation is not sufficient for the differentiation between ischemic and hemorrhagic focal neurological symptom origins, imaging modalities are imperative. The gold standard for acute hemorrhage detection is non-contrast CT or gradient recalled echo (GE) and T2*-susceptibility-weighted MRI (31, 32). CT scan findings assist with clinical decisions by evaluating hematoma volume and predicting the upcoming 30-day mortality (34). Contrast-enhanced CT and CTA may be useful in assessing the risk of hematoma expansion by detecting focal areas of contrast within the hematoma (known as the spot sign) (35–37) or a large number of cerebral microbleeds (38).

In the setting of ICH, CT is inferior to other imaging modalities, such as MRI and angiography, especially sometime after the onset. Nonetheless, as mentioned previously in this review, in emergency diagnostics, CT is the preferred imaging modality for its availability, cost-effectiveness, and rapidity. CT angiography/venography (CTA/CTV), and contrast-enhanced MRI or MR angiography/venography (MRA/MRV) are informative when there is suspicion of an underlying structural lesion (39). Detected hyperin-
tense lesions in DWI indicate acute or subacute ICH (Figure 2) (40). MRI and MRA are far more sensitive when diagnosing older hemorrhages, secondary (primarily structural) causes, such as arteriovenous malformations, tumors, and cerebral venous thrombosis (27, 31, 32, 40).

Headache attributed to non-traumatic subarachnoid hemorrhage (SAH)

1% of all emergency room visitors suffering from headaches are diagnosed with subarachnoid hemorrhage (SAH) (3). SAH is defined as hemorrhaging into the cerebrospinal fluid (CSF) due to cortical meningeal vessel rupture and occurs in approximately 8 out of 100,000 people per year (42). Multiple underlying conditions may be responsible for the development of SAH: various vascular disorders, traumas, blood dyscrasias, etc. (43) Common SAH manifestations include a sudden severe thunderclap headache which can be the only manifestation of the condition (43, 44). Additional symptoms involve changes in consciousness, neurological deficits, seizures, vomiting, and neck stiffness (46). Due to its high prevalence, neuroimaging in the setting of SAH is a widely researched topic. However, currently, there is a significant disparity in opinions concerning the diagnostic protocols (47).

The most common clinical practice is to perform a non-contrast CT scan, followed by lumbar puncture (LP) if the head CT scan is non-diagnostic (48). This protocol is still considered to have the highest sensitivity, while MRI/MRA and CT/CTA are alternative imaging modality protocols, useful in cases where CT/LP is contraindicated or hazardous (49). Furthermore, CT has lower sensitivity when diagnosing SAH in the posterior fossa, in patients without focal neurological abnormalities, and cases of small hemorrhaging volumes (50). Current data suggest that MRI FLAIR sequence is more sensitive than or equal to CT when detecting acute or subacute SAH (42, 50–52) and additional scanning protocols may be useful when diagnosing an underlying condition (54). Nonetheless, negative MRI would still require a follow-up LP (55).

LP is an invasive procedure, which prompts an effort to find a similar or even more sensitive diagnostic tool. It has been hypothesized that CTA could replace LP in the SAH diagnostics as a non-invasive and thus safer procedure with relatively high sensitivity (42). However, data from the recent studies suggest that it would not be an optimal approach seeing as asymptomatic aneurysms could be unnecessarily diagnosed and the imaging modality comes with unwarranted radiation exposure as well as considerable expenses (41, 55, 56). On the other hand, modern third-generation cranial CT scans performed within the first 6 hours of headache onset and evaluated by a qualified radiologist have incredibly high specificity and sensitivity (100% each), which warrants the elimination of a follow-up tool altogether (58–60). This suggests that improved CT scanning protocols negate LP necessity and dangers, which occur due to having a higher probability of complications than of diagnosis (61–63). However, the 6-hour CT diagnostic sensitivity applies only to the patients that have no focal neurological abnormalities or changes in consciousness (64) and CT sensitivity drops to 50% at seven days. Meanwhile, LP is diagnostic from 12 hours post-ictus and up to two weeks after the onset (65).

Once a diagnosis has been established, further imaging modalities are required to determine the cause.

HEADACHE ATTRIBUTED TO NON-TRAUMATIC ACUTE SUBDURAL HEMORRHAGE (ASDH)

Acute subdural hemorrhage (ASDH) is defined as acute bleeding between the dura and arachnoid membranes usually due to damage to the bridging veins (66). Spontaneous ASDH is less common than traumatic subdural hemorrhages, however, it is more dangerous due to higher mortality (67). Non-traumatic ASDH may be caused by multiple conditions, such as impaired hemostasis, cerebral aneurysms, ruptured cortical artery, arteriovenous malformations, neoplasms, hypertensive cerebral hemorrhage, intracranial hypotension, Cerebral Amyloid Angiopathy (CAA), and acquired immune deficiency syndrome (68). The headache manifests suddenly in accordance with the site of hemorrhaging and peaks in seconds or minutes, typically just before the focal neurological symptoms (30).

Non-contrast CT is integral in both initial clinical decision making and as a follow up (67). The
main feature of ASDH as seen on a CT scan is usually a hyperdense and sometimes mixed appearance of the subdural space (69). MRI is more sensitive when diagnosing extremely thin, hemispheric or tentorial subdural hemorrhages (70). Imaging parameters, evaluated in the setting of ASDH are age or thickness of the hemorrhage, midline shift, presence of blood in the basal cisterns, ventricle obstruction. Additionally, underlying conditions may be visualized using CT, MRI, CTA, MRA and other imaging modalities (66). For example, vascular imaging of the head is advisable in patients with spontaneous ASDH without coagulopathy, due to the possibility of a ruptured cranial aneurysm (71–76).

Persistent headache following non-traumatic ICH, SAH, ASDH
Headaches that persist more than three months after a non-traumatic intracranial hemorrhage have no specific imaging characteristics and thus are not described in this review.

HEADACHE ATTRIBUTED TO UNRUPTURED VASCULAR MALFORMATION

HEADACHE ATTRIBUTED TO UNRUPTURED SACULAR ANEURYSM
An unruptured intracranial saccular aneurysm is a protrusion from a cerebral artery that consists of a damaged or absent tunica media and an internal elastic lamina (77). It occurs in 1-2% of the population (78). Sometimes unruptured intracranial aneurysms manifest as a thunderclap headache, loss of visual acuity or palsy of the 3rd cranial nerve but usually, they are asymptomatic (64, 77). Therefore, an unruptured aneurysm is often an incidental radiological finding. Aneurysms of 3 mm or larger can be identified on CT (79), but CTA is frequently required to clarify the diagnosis. CTA has specificity rates of 96–98% (90–94% for aneurysms smaller than 3 mm and up to 100% for aneurysms larger than 4 mm) and sensitivity rates of 96–98% for the detection of an intracranial unruptured saccular aneurysm (79, 80). The majority of saccular aneurysms are found around the anterior and posterior communicating arteries, the bifurcation of the middle cerebral artery, the internal carotid artery, the basilar artery, the superior cerebellar artery and the posterior inferior cerebellar artery (64, 76). Just like CT, MRI has a somewhat limited role in detecting an unruptured saccular aneurysm. However, three-dimensional time-of-flight MRA with volume rendering at 3.0 Tesla has a sensitivity of 99% and specificity of 97% which is irrespective of aneurysm size (81, 82).

Digital subtraction angiography is indicated in the case of negative CTA/MRA or before surgical or endovascular treatment to evaluate adjacent structures and blood flow patterns (Figure 3) (84).

HEADACHE ATTRIBUTED TO ARTERIOVENOUS MALFORMATION
Arteriovenous malformation (AVM) is a congenital disorder of the brain or spinal cord characterized by an abnormal tangle of arteries and veins with varying amounts of fistulas (85). Brain AVMs have a prevalence of 18 per 100 000 inhabitants (86). Presenting symptoms of AVM are intracranial bleeding, headache, seizures, and focal neurological deficits (85). Signs of AVM on non-contrast CT include a usually hyperdense nidus with enlarged draining veins in the periphery of the brain parenchyma. CTA may improve the sensitivity of CT to identify brain AVMs. (87). Signs of AVM on MRI include the nidus, feeding arteries, and draining veins that demonstrate flow void and can be seen on conventional sequences (65), while MRA may help confirm the more subtle AVMs (Figure 4) (88). The diagnosis of AVM is confirmed by cerebral angiography (87).

HEADACHE ATTRIBUTED TO DURAL ARTERIOVENOUS FISTULA
Dural arteriovenous fistula (DAVF) is an abnormal connection between meningeal arteries and dural venous sinuses or subarachnoid veins (89). It has a detection rate of 0.16–0.29 per 100 000 inhabitants each year (90). DAVF frequently presents as painful pulsatile tinnitus or a headache with other symptoms of intracranial hypertension (91). A diagnostic evaluation usually starts with head non-contrast CT or MRI (92). CTA and MRA characterize the feeding arteries, early dural sinus opacification, and prominent draining veins (89). The diagnosis is confirmed with digital subtraction angiography which remains
the gold standard in the case of DAVFs (64, 93). Headache attributed to cavernous angioma
Cavernous angioma occurs in 0.4 – 0.8% of the population and is described as a vascular malfor-
mation of the brain and spinal cord characterized by a lack of tight junctions between the lining
endothelial cells of pathologically dilated blood vessels and slow blood flow within the patholog-
ical structure (94). Some cavernous angiomas may trigger cluster headache-like, SUNCT-like
(short-lasting unilateral neuralgiform headache with conjunctival injection and tearing) or mi-
graine-like attacks. The location of the headache typically coincides with the site of the cavernous
angioma (30). The primary imaging modality for cavernous angiomas is MRI. The most common
finding is a reticulated lesion with mixed signal intensities (Figure 5) (95).

HEADACHE ATTRIBUTED TO ENCEPH-
ALOTRIGEMINAL OR LEPTOMENINGE-
AL ANGIOMATOSIS (STURGE-WEBER
SYNDROME)
Encephalotrigeminal or leptomeningeal angio-
matosis (Sturge-Weber syndrome) is a congeni-
tal vascular disorder characterized by a capillary
or capillary-venous malformation of the face,
brain, and eye (96). It occurs in approximately 1
in every 20 000 – 50 000 newborns (97). Enceph-
alo trigeminal or leptomeningeal angiomatosis
may cause migraine attacks with long motor
auras (30). Other symptoms include port wine
stain on the face, seizures, hemiparesis, visual
disorders, behavioral problems, and mental re-
tardation (98). The primary neuroimaging tech-
nique for the diagnosis of this disorder is brain
MRI with gadolinium contrast (96). Pia and cor-
tical enhancement are usual signs of Sturge-We-
ber syndrome on MRI (99). CT is less useful but
may detect brain calcification and atrophy (98).
Angiography can reveal the lack of superficial
cortical veins and tortuous veins near the vein
of Galen (98). Positron Emission Tomography
(PET) or Single Photon Emission Computed
Tomography (SPECT) are rarely used in diag-
nosing Sturge-Weber syndrome, but abnormal
glucose metabolism and cerebral perfusion may
be detected before the presence of clinical symp-
toms (Figure 6) (98).

HEADACHE ATTRIBUTED TO ARTERITIS
The current gold standard for diagnosing vari-
ous forms of arteritis is a vessel biopsy. Howev-
er, neuroimaging plays a major role in screening
and with increasing improvements may rival the
sensitivity and specificity even of the aforemen-
tioned invasive procedure.

HEADACHE ATTRIBUTED TO GIANT
CELL ARTERITIS
Giant cell arteritis (GCA) is a granulomatous
vasculitis of medium and large arteries (100).
This idiopathic and chronic condition occurs
in people older than 50 years with an incidence
ranging from 6.9 to 32.4 per 100 000 inhabit-
ants (101). Headache is a presenting symptom in
two-thirds of GCA patients, but it has no specific
characteristics apart from the occasional com-
plaint of scalp tenderness to touch (102). Other
symptoms of GCA include fever, fatigue, weight
loss, jaw claudication, and vision loss (103).
Temporal artery biopsy is the gold standard for
establishing the diagnosis of GCA. However, it
might not be necessary in case of typical symp-
toms and specific ultrasound or MRI findings
(104). Colour duplex ultrasonography of the
temporal arteries remains an important and
widely available imaging modality of GCA. The
halo sign (dark, hypoechoic circumferential wall
thickening) is highly sensitive and specific to
GCA (102). Meanwhile, MRI and MRA enable
the evaluation of vessel wall inflammation. The
sensitivity and specificity of MRI for GCA ranges
from 68% to 89% and from 73% to 97% respec-
tively (104). MRA can detect an irregular outline
and diameter changes of the arteries wall (101).
In cases of GCA, CT is useful when diagnosing
concentric mural thickening which continues
over long segments and indicates vessel inflam-
mation, while CT angiography is more suitable
in the assessment of stenotic and aneurysmal
lesions of arteries that develop as complications
(105). Further detection of inflammatory chang-
es in the blood vessels can be achieved through
18F-FDG-PET (often combined with CT) based
on the uptake of the radioligand. However, in
comparison to MRI, this diagnostic method has
lower sensitivity and specificity (77% and 66%
accordingly) (106, 108).
HEADACHE ATTRIBUTED TO PRIMARY OR SECONDARY ANGIITIS OF THE CENTRAL NERVOUS SYSTEM (PACNS AND SACNS)

Angiitis of the central nervous system (CNS) refers to a broad spectrum of diseases that result in inflammation and destruction of arteries and veins of the brain, spinal cord, and meninges. Inflammation typically causes medium or small brain blood vessels to become narrowed, occluded, and thrombosed, which results in brain tissue ischemia and necrosis (17). Angiitis of the CNS could be either primary (confined to the CNS) or secondary (part of a multisystem inflammatory disease) (107). PANCS is a rare disease with an incidence of 2.4 per 1 million inhabitants (108). Headache is the dominant symptom of both primary and secondary types of angiitis. Typically it is subacute, insidious, and diffuse but may present in a variety of other characteristics. However, a thunderclap headache should raise suspicion of a reversible cerebral vasoconstriction syndrome which often mimics PACNS (109). Other symptoms of angiitis of the CNS include cognitive impairment, focal deficits, seizures, cranial nerve involvement, myelopathy, and ataxia. Weight loss, fever, or the involvement of visceral organs are usually signs of systemic vasculitis (110). Conventional cerebral angiography is often considered to be the radiological gold standard for the diagnosis of PACNS/SACNS. The typical angiographic finding is defined as beading (alternating areas of stenosis and dilatation) (110). However, some studies have shown that the sensitivity and specificity of cerebral angiography for PACNS might be as low as 70% and 30% respectively (109).

In comparison, MRI has a high sensitivity of 90-100% for diagnosing PACNS but a low specificity. Most common MRI findings, occurring in approximately 53% of patients, are multifocal brain infarcts, while parenchymal hemorrhage, leptomeningeal and parenchymal enhancement are observed less frequently (110, 113, 114). MRA and CTA are less sensitive for angiitis of the CNS than conventional cerebral angiography or MRI. They are useful in evaluating large brain vessels, but angiitis of the CNS typically involves medium and small vessels (107). Brain tissue biopsy of radiographically involved areas remains the gold standard for establishing the diagnosis of PACNS (113).

HEADACHE ATTRIBUTED TO CERVICAL CAROTID OR VERTEBRAL ARTERY DISORDERS

Headache or facial or neck pain associated to cervical carotid or vertebral artery dissection

Cervical artery dissection (CAD) is a tear of the carotid or the vertebral artery wall resulting in the formation of a false lumen and intramural hematoma (114). It has an incidence of 2.6-5 per 100 000 inhabitants per year (8, 117). CAD accounts for 10% to 25% of ischemic strokes in young adults and some cases may also cause a subarachnoid hemorrhage (116). The expanding intramural hematoma of CAD may lead to local compression of adjacent nerves causing pain, lower cranial neuropathies or cervical nerve root damage (116, 119). Headache (with or without the pain of the neck) is the most common and sometimes the only manifestation of CAD occurring in 55-100% of cases (30). Pain is often unilateral (ipsilateral to the dissected artery), sudden, severe, prolonged (up to 3 months after the stabilization of CAD), and associated with Horner’s syndrome, tinnitus or palsy of the 12th cranial nerve (30). In rare cases, the headache may not resolve within three months after the stabilization of CAD and become persistent (30). On the whole, the diagnosis of CAD is based on the detection of loss of integrity of the carotid or the vertebral artery wall. Ultrasound may visualize the lumen, the wall of the artery and the surrounding tissue. The most common findings of ultrasound in the case of CAD include an intramural hematoma, an echogenic intimal flap, floating thrombus within the vascular lumen, and tapering of the arterial lumen (117, 120). Doppler sonography reveals a bidirectional high resistance flow, reduced blood flow velocity or absence of flow, and no flow in the false lumen (119). The sensitivity of ultrasound for CAD is approximately 70% – 86%. Thus other neuroimaging modalities such as MRI/MRA or CTA are needed to establish the diagnosis (45, 122). MRI provides information about the occurrence of intramural hematoma, and MRA evaluates the
vascular lumen (116). The sensitivity and specificity of MRA and CTA for CAD are relatively similar (119, 123). However, CTA is used more often due to its wide availability and fast scanning speed (122). Conventional angiography for CAD is performed only in questionable cases due to its invasiveness and inability to evaluate the arterial wall. Usual signs of conventional angiography of CAD include vessel stenosis or occlusion, false or double lumen, pseudoaneurysm, irregular dilatation and, intimal flap (118). Conventional angiography used to be the gold standard for CAD, but nowadays it is replaced by MRA and CTA due to its high accuracy and wide availability (122).

POST-ENDARTERECTOMY HEADACHE
Carotid endarterectomy is a neurosurgical procedure performed to remove the atherosclerotic plaque from the inside of an artery and reestablish the diameter of the vessel lumen to prevent strokes (125, 126). There are three different types of headaches associated with carotid endarterectomy. The first type of pain is the most common. It occurs within the first few days after surgery as a diffuse and mild headache. The second type resembles a cluster headache occurring once or twice a day for roughly two weeks. The third type of headache is unilateral, pulsating and severe (30). It usually begins three days after surgery due to the hyperperfusion syndrome which has already been described in the previous section (126, 131). Imaging modalities are utilized only when there is suspicion of other conditions or complications of the procedure. Headache attributed to cranial venous disorder

Cerebral venous thrombosis (CVT) is a potentially lethal condition and is most common in adults (with a mean age of 39 years), more so in women than in men (130). The incidence of this condition is 1.3 per 100 000 adults and maybe even higher in developing countries (131). A severe slow-onset diffuse headache is a common manifestation, occurring in more than 90% of cases, and usually accompanied by focal neurological symptoms that are a sign of a brain parenchymal lesion, and/or seizures that occur in 40% of all CVT cases (132, 134). Rarely the headache presents unilaterally, suddenly, thunder-like, or mildly, not unlike a migraine (30).

Although CVT is a rather rare condition, early diagnosis and treatment, which are heavily dependent on the knowledge of neuroimaging methods and signs, are crucial (133). As usual, the primary imaging modality in the emergency department is non-contrast CT, which is often insufficient for diagnosis. However, increased attenuation of the obstructed cortical vein (“cord sign”), dural or the posterior portion of the superior sagittal sinus (“dense triangle sign”) is indicative of CVT (136, 137). Additionally, Hounsfield unit (HU) to hematocrit ratio measurement has been suggested as a rather sensitive diagnostic criterion for CVT. However, further studies are required (136). In contrast-enhanced CT CVT manifests as the “empty delta sign”: a contrast-enhanced wall of the thrombosed posterior superior sagittal sinus (137). Further indirect signs of CVT can be observed in CT scans: dilation of the venous structures, small ventricles, brain parenchymal lesions, falx and tentorium enhancement (138). Unfortunately, neither contrast-enhanced nor non-contrast negative
CT scans can rule out CVT. In cases of CVT, MRI and MRV are the preferred modalities in all stages (133). MRV and CTV are both adequate for assessing changes in the venous system. However, CTV is inferior for the visualization of changes in the brain parenchyma (136, 141, 142). CT is superior to Time-of-Flight MRV when diagnosing partial vessel occlusion (141). MRV as a separate imaging modality is not sufficient. CVT diagnosis requires a full MRI in addition to MRV (141, 144). The signal intensity of the thrombus depends on its age (139), and specific sequences have their advantages: susceptibility weighted or T2*W GE sequences are most beneficial when evaluating the obstruction in an acute setting or of the cortical vein (143). Contrast-enhanced MRV is superior to Time-of-Flight MRV for assessing smaller sinuses or slow blood flow (144). All in all, neither MRI nor CT is sufficient, and CTV or MRV are necessary when clinical suspicion of CVT is high (Figure 7). Catheter angiography is considered to be the most accurate diagnostic tool; however, due to its invasive nature, this method is rarely applied in clinical practice (135, 147).

Another reason for headaches, related to the cranial venous sinuses, is stenting. It is the most common adverse effect of the procedure, which occurs ipsilaterally to the stent and lasts for a few days. The precise frequency is difficult to determine due to many other stent unrelated types of headaches that patients experience following the procedure (146). The aforementioned adverse reaction to the cranial venous sinus stenting needs to be differentiated from other conditions, such as complications or comorbidities. However, neuroimaging has no different role to play in the diagnosis of this type of headache.

HEADACHE ATTRIBUTED TO OTHER ACUTE INTRACRANIAL ARTERIAL DISORDER

INTRACRANIAL ENDARTERIAL PROCEDURE RELATED HEADACHE AND ANGIOGRAPHY HEADACHE

Headaches associated to intracranial end-arterial procedures (IEP) include angioplasty, embolization, stenting, and typically develop within the first week and resolve within a month, while headaches attributed to angiography develop within a day and resolve in 72 hours after the procedure (30). Typically, they are different in types of severity and duration; symptoms may be migraine-like in patients with an underlying migraine. IEP related headaches are typically unilateral (30). However, head imaging is required only when there is suspicion of complications, such as stent thrombosis or stroke.

Headache attributed to RCVS

Reversible cerebral vasospasm syndromes (RCVS) are known as a group of conditions that clinically manifest during physical exertion, sexual activity, Valsalva maneuvers, bathing, or emotional stress as a thunderclap headache due to a reversible multifocal dilation and constriction of the cerebral arteries (29, 149). Although the precise incidence is not known, it is believed that the condition is relatively common (112). RCVS is considered the most common cause of thunderclap headache in patients without an aneurysmal subarachnoidal hemorrhage, and the most common recurrent thunderclap headache (148). The thunderclap headache can be accompanied by nausea, photosensitivity, and focal deficits (151, 152). Additionally, a small percentage of RCVS patients report atypical headaches (151, 152). RCVS can lead to various types of intracranial hemorrhages (convexal subarachnoid, intracerebral, subdural hemorrhages), as well as posterior reversible encephalopathy syndrome (PRES) and ischemic stroke (151).

The prevention of the complications above requires early diagnosis and management of the RCVS (152–154). Imaging is an indispensable part of the diagnostic workup. However, various means of evaluation can be utilized: angiography, transcranial Doppler sonography, CT or MR angiography. More than a third of initial CT/MRI scans are normal in the presence of cerebral vasospasm (114, 151, 152). Nonetheless, imaging evaluation should begin with non-contrast CT. Convex subarachnoid hemorrhage especially in patients younger than 60 years of age, signs of previous and/or current multifocal infarcts, and typical clinical findings should raise suspicion of RCVS (157, 158). Further assessment requires CT angiography, MR angiography or conven-
tional angiography. CT angiography is less sensitive than conventional angiography; however, it is the setting of proximal branch involvement, CTA detects the segments of vasoconstriction in addition to possible comorbidities or complications (157). MRI is superior to CT when evaluating possible complications and alternative diagnoses, yet remains insufficient for the diagnosis of RCVS (151, 152, 159). Hyperintense vessels along cerebral sulci in T2 FLAIR imaging, while not specific, are indicative of RCVS and higher risk of ischemic stroke and PRES incidence (152, 160, 161). Although MRA is less sensitive than conventional angiography, it is often utilized because of the non-invasive nature (155). MRA is used to assess the extent, distribution, and progression of the arterial constriction and associated complications (160). Even transcranial ultrasound has been utilized. However, this modality cannot exclude the diagnosis or RCVS (161). Conventional cerebral angiography, although invasive, is considered to be the gold standard (151, 157). It has the superior spatial resolution to MRA and CTA and enables the assessment of small and distal cerebral arteries, which is why MRA and CTA sensitivity for RCVS-related arterial stenoses is 80% in comparison to conventional angiography (162, 164). Typical angiography findings in RCVS are segments of arterial constriction and dilatation, known as ‘string of beads’ or ‘sausage on a string’ signs (162).

Certain conditions, especially primary angiitis of the CNS, may manifest similarly to RCVS. Imaging plays a critical role in differentiation (155). Vessel Wall Imaging is an MR technique, useful when differentiating vasculitis from RCVS among other things. RCVS related wall thickening is less often enhanced, unlike in the setting of central nervous system vasculitis (165, 166). Perfusion imaging enables the detection of multifocal hypoperfusion areas, which helps with the evaluation of progression and treatment response in addition to the effects of specific segment stenosis (167, 168).

Persistent RCVS related headaches are longer than three months and persist even after the cerebral arteries normalize (30).

Headache attributed to intracranial artery dissection
Intracranial artery dissection (IAD) is best known for its association with severe subarachnoid hemorrhages that tend to recur (169, 170). Headaches attributed to IAD present unilaterally and suddenly and may progress as subarachnoid hemorrhage or stroke (29, 171). The precise incidence is not known, however, it is believed to be less than 2.6 - 3.0 per 100 000 people (170). Clinical presentation is not specific, and imaging evaluation is not always conclusive. Typical radiological signs include mural hematoma, intimal flap, and a double lumen (170). It is important to note that no modality can detect all of these findings, seeing as CT and MRI visualize the extraluminal, while CT/MR/conventional angiography detects intraluminal changes. In the setting of IAD, a mural hematoma is associated with enlarged external diameter, which is not related to other conditions that can manifest as intramural hematomas as well (170). 2 - 3 days following the onset of the IAD, MRI T1W sequence and exceptionally high-resolution 3 Tesla MRI that includes three-dimensional fat-suppressed T1W images with a black-blood effect can detect the hyperintense hematoma (171). An intimal flap is best observed in digital subtraction angiography (170). Dissection may also be accompanied by aneurysmal dilatation, which indicates a higher risk of subarachnoid hemorrhage, while segmental stenosis and occlusion in subarachnoid haemorrhage is indicative of IAD (172, 174, 175). CTA and MRA are useful when diagnosing intraluminal changes, while digital subtraction angiography is utilized only in cases of negative CT/MRI, before surgical or endovascular treatment, and when patients present with subarachnoid hemorrhage (170). Depending on the findings, a combination of CT/MRI and intraluminal imaging is often required to confirm the diagnosis of IAD.

HEADACHE ATTRIBUTED TO GENETIC VASCULOATHY

HEADACHE ATTRIBUTED TO CADASIL
Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) is a small vessel disease de-
termined by a mutation in the NOTCH3 gene (174). It is considered to be the most frequent of all small vessel diseases and hereditary stroke disorders with a prevalence of approximately 2-5 cases per 100 000 inhabitants (11, 176–179). It manifests by the late middle age most frequently as a migraine with prolonged aura (29, 180). Additional symptoms include transient ischemic attacks and strokes, cognitive impairment, changes in mood and gait, epilepsy, and others (179). Neuroimaging plays a significant role in the diagnosis of CADASIL, even in patients presenting with no symptoms whatsoever (180). Typically, CADASIL is differentiated from other small vessel diseases by detecting early subcortical ischemic changes that progress to involve the anterior temporal poles and less frequently the external capsule or the superior frontal gyrus (182, 183). MRI T2W and FLAIR sequences show the extent and age of the white matter abnormalities that typically progress with years, while the DW sequence enables the quantification of chronic white matter changes (184, 185). Other less prevalent pathological MRI findings, common to CADASIL are CSF filled lacunas, cortical infarctions, and involvement of corpus callosum (182, 185, 186).

Other imaging modalities are less sensitive when detecting changes, common to CADASIL. In the preliminary stages of the disease, CT imaging may reveal nonspecific periventricular white matter hypodensities. However, the common anterior temporal lobe abnormalities can be diagnosed only in the advanced stages of CADASIL (181). Therefore, CT may indicate the disease. However, MRI is necessary to confirm the diagnosis (Figure 8). Few studies analyze the diagnostic value of FDG-PET and diffusion tensor imaging. However, even those studies suggest that findings are not specific to CADASIL (181). Headache attributed to MELAS Mitochondrial Encephalopathy, Lactic Acidosis and Stroke-like episodes (MELAS) are known as one of the maternally inherited mitochondrial metabolic diseases that often manifest before the fourth decade of life as a multisystemic disorder (186). Certain features of MELAS overlap with CADASIL, but the main symptoms include migraine-like attacks, stroke-like episodes, and encephalopathy often with dementia and/or seizures (187).

The clinical manifestation of MELAS is intricate. Nonetheless, brain imaging visualizes white and grey matter changes that are characteristic and aid the diagnosis of MELAS. In patients, presenting with stroke-like symptoms, infarction simulating lesions are unlike the vascular territories, develop slowly, may change location, and progress into atrophic regions with time (189, 190). Typically, the involvement of parietal and occipital lobes is observed (189). While MRI findings are similar to CADASIL (both conditions are known for the subcortical white matter damage), cortical area involvement with vasogenic edema and mass effect in acute and subacute phases is more indicative of MELAS (190). Seeing as typical radiological findings are brain parenchymal lesions, MRI is the preferred modality (189, 192). Common CT scan findings include bilateral basal ganglia and thalamic calcifications (192). DWI is useful when differentiating cytotoxic from vasogenic edema, the latter usually but not always manifesting in MELAS as elevated ADC and sometimes progressing to cytotoxic (193–198). SPECT findings differ between studies and depend on the acuity of MELAS (198, 200–202). CTA, MRA, and catheter angiography may be utilized to evaluate the obstruction of cerebral arteries and in MELAS; it is common to find the arteries of the seemingly ischemic zones to be patent (201). Other imaging modalities, such as PET, Arterial Spin Labeling, Oxygen Extraction Fraction, Magnetoencephalography, and trancranial ultrasound may be utilized when there are doubts concerning the diagnosis (202–206).

HEADACHE ATTRIBUTED TO MMA

Moyamoya angiopathy (MMA) is described as a chronic progressive disease, defined by an abnormal vasculature at the base of a brain following bilateral stenosis and/or occlusion of the terminal inferior cerebral artery branches (207). This disease is most prevalent in Asia, with 10.4 cases per 100 000 patients in Japan (208). MMA is yet another condition, associated with recurring and migraine-like headaches, which may manifest as a stroke in early childhood or adolescence (30). Neuroimaging enables the confirmation of the
diagnosis. Head CT scan visualizes infraction of both cortical and subcortical areas or parenchymal hemorrhages into the basal ganglia, thalamus, ventricles, however, it does not provide information on the vasculature itself (209–211). MRI is more sensitive than CT when diagnosing MMA and enables the detection of findings that suggest MMA even in asymptomatic cases. Characteristic findings indicative to MMA are the dilatation of leptomeningeal and cortical collateral vessels (known as the “ivy sign”), absent flow voids in the distal portions of inferior and middle cerebral arteries, and absent signal in the basal ganglia (212–216). High-resolution MRI further increases the sensitivity of this modality, by visualizing the narrowing of the outer arterial wall diameter, and long-segment concentric enhancement of the inferior or middle cerebral artery. These findings raise the suspicion of MMA even in the early stages (217–220). Other, MMA common findings observed on MRI are ischemic lesions in deep watershed zones (221), and asymptomatic cerebral microbleeds (223, 224). Noninvasive or catheter angiography is required for the detection of steno-occlusion of the inferior, middle, and/or anterior cerebral artery, and grading, according to Suzuki’s six stages (224). Conventional angiography is performed usually in cases when bypass surgery is being considered (212). Additional studies may be utilized for the evaluation of intracranial hemodynamics: transcranial sonography, perfusion CT, MRI, PET, SPECT, arterial spin labeling, etc. (225–230).

HEADACHE ATTRIBUTED TO CAA
Cerebral Amyloid Angiopathy (CAA) is a small and medium-sized vessel disease that affects the walls of the leptomeninges and cerebral cortex vessels due to the accumulation of amyloid-β (231). The prevalence of the disease increases with age and dementia development: autopsy results observed CAA related changes in up to 60% of dementia patients and 28-38% of nondementia patients (232). Patients suffer from late-onset auras, typically without or with a mild headache as well as other typical CAA dementia symptoms (30). Although definite diagnosis requires validation by pathological brain tissue examination, neuroimaging can detect findings indicative of CAA (233). Lobar hemorrhages, commonly in the temporal and occipital regions, usually visualized by T2*W GE MRI sequences, raise suspicions of CAA in dementia patients (234, 235). Although CAA may be the reason for ICH, it has been concluded that the vast majority of CAA patients do not suffer ICH (235).

In patients over 60, CAA is considered to be the most common cause of convex subarachnoidal hemorrhage (156), which in turn increases the risk of future ICH (236). Another finding, common to small vessel disease, is cerebral microbleeds, which are seen as small hypointense areas on blood-sensitive T2*W GE or susceptibility-weighted MRI sequences (237). Cerebral microbleeds correlate with microvascular leakage and are not specific to any condition. However, lobar cerebral microbleeds are indicative of CAA and increased intracerebral hemorrhage and ischemic stroke risks (237–242). White matter hyperintensity (leukoaraiosis) is a specific diagnostic term, which is used to described low-density areas on CT scans and high signal areas on T2W MRI scans. It has been hypothesized that particular localization (occipital region) of leukoaraiosis may indicate CAA, even though white matter hyperintensity is common in most small vessel disease (243).

Meanwhile, cortical superficial siderosis is identified by specific MRI sequences and occurs more often in CAA patients than in the general population (Figure 9) (245, 246). In addition, cortical superficial siderosis indicates a high risk of recurrent ICH (246). Finally, PET assessment of amyloid deposit localization has diagnostic value and may predict the occurrence of CAA related ICH (247).

HEADACHE ATTRIBUTED TO RVCLSM
Retinal vasculopathy with cerebral leukoencephalopathy and systemic manifestations (RVCLSM) is a hereditary neurovascular syndrome caused by mutations in the TREX1 gene (248). This condition is best known for retinal vasculopathy, brain dysfunction, in addition to white matter and intracerebral mass lesions on neuroimaging, while systematic manifestations are less frequent (248). The headache is defined as mi-
graine-like episodes, often without aura, with or without other clinical features (30). The diagnosis is based on genetic testing, while characteristic neuroimaging manifestations occur and progress from the fifth decade (249). CT is not sufficient as the disease affects mostly the white matter of the brain and merely focal calcifications can be observed (248). MRI is superior and can detect punctate non-enhancing T2-hyperintense lesions in the periventricular and subcortical white matter, or enhanced punctate lesions either with DWI related restriction or with various rim enhancements (more familiar to the later stages) that are generally associated with edema and mass effect (248). Typical enhanced lesions as seen on an MRI are considered to be the major diagnostic criteria, while the aforementioned non-enhanced MRI and focal calcifications on CT are minor criteria of the RVCLSM (248).

**HEADACHE ATTRIBUTED TO OTHER CHRONIC INTRACRANIAL VASCULOPATHY**

In theory, all intracranial vasculopathy can cause migraine-like attacks. However, this group includes migraine-like headaches with and without aura by any chronic vasculopathy (30). There are no specific neuroimaging indications or findings. Thus the imaging evaluation of these headaches is not discussed in this review.

**HEADACHE ATTRIBUTED TO PITUITARY APOPLEXY**

Pituitary apoplexy (PA) is a potentially life-threatening clinical syndrome that is characterized by the sudden enlargement of the pituitary gland frequently following infarction of a preexisting pituitary adenoma (250). It is a rare condition with an estimated 6.2 cases per 100 000 inhabitants (251). PA often manifests as a sudden and severe thunderclap headache, commonly accompanied by visual disturbances, diplopia, changes in consciousness, less frequently nausea, vomiting, and hypotension (253, 254). Imaging plays a crucial role in the diagnosis of PA. It helps to rule out other conditions, such as subarachnoidal hemorrhage, meningitis, cerebral sinus thrombosis, midbrain infarction, migraine, and aneurysms (250). The measurement of the pituitary mass influences clinical decisions (252). Due to the sudden onset of the condition, the first diagnostic test is usually a non-contrast CT of the head. However, in cases of a negative CT, patients should undergo an MRI scan, seeing as MRI is far more accurate when diagnosing subacute PA (253, 255–257). Two signs of PA can be observed on a CT scan: an interstellar mass (80% of cases) and hemorrhagic components (20-30% of cases) (253, 258). In contrast-enhanced CT certain features of the pituitary tumor may become visible: inhomogeneous enhancement with or without ring enhancement (258). It has been reported that MRI findings are sensitive enough to be comparable to histopathological conclusions (259). T1W sequences are useful for detecting altered signal intensity sella turcica lesions, while T2W images detect hemorrhages (260). T2*W GE imaging increases the sensitivity of blood product detection even further (261). All in all, imaging, especially MRI, plays a crucial role in diagnosis and decision making in the setting of PA (Figure 10).
Figure 1. CT and MRI of an ischemic stroke in the left MCA (a - axial CT showing no features of stroke in the early stages; b-f MRI: b - T1W axial; c - T2W FLAIR axial; d - DW axial; e - ADC axial; f - TOF)
Figure 2. MRI of a non-traumatic haemorrhage at the right cerebellum hemisphere (a - T1W axial; b - T2W FL2d hemo axial; c - T2W coronal (movement artefacts); d - T2W FLAIR axial).
Figure 3. Saccular aneurysm at ACM dex. vessel: a - axial CT; b - CT angiography basic; c - angiography; d - CT angiography 3D reconstruction.
Figure 4. Arteriovenous malformation, MRI (a - T2W FLAIR axial; b - T2W axial; c - T2W fl2d hemo axial; d - T1W sagittal; e - TOF vein; f - TOF arterial).
Figure 5. Cavernoma at the left frontal lobe (a - axial CT; MRI: b - T2W/FLAIR axial; c - T1W axial; d - T2W fl2 hemo axial; e - T2W coronal).
Figure 6. Sturge-Weber syndrome with an acute epidural haematoma at the left frontal lobe as a concomitant pathology (a, b – axial CT; axial MRI: c - T1W; d - T2W fl2d hemo; e - T2W FLAIR).
Figure 7. Multiple different venous sinus thromboses (thrombosis of the superior sagittal sinus: a, b - axial CT; and thrombosis of the left transversal sinus vein MRI: c - T2W coronal; d - T2W FLAIR axial; e – TOF).
Figure 8. CADASIL, MRI (a, b - T2W FLAIR axial; c - T2W coronal).
Figure 9. Cerebral amyloid angiopathy and encephalopathy, MRI (a - e T2W fl2d hemo axial; f - T2W/FLAIR axial).
Figure 10. Pituitary apoplexy, MRI (a - T1W coronal; b - T1W sagittal).

CONCLUSIONS
Headaches attributed to cranial and cerebral vascular disorders vary in etiology, clinical and radiological manifestation. Therefore, a good understanding of the purpose that each imaging modality serves is required. CT imaging is a widely available and a quick diagnostic tool which, unfortunately, is also associated with ionizing radiation. MRI is a sensitive brain parenchymal lesion evaluation tool that does not expose patients to radiation and enables the evaluation of small pathological structures in different sequences. However, MRI scans take longer, are more expensive, and not as widely accessible as CT scanners. Other imaging modalities provide additional information on the intraluminal, metabolic, or perfusion changes in the brain when initial imaging is not sufficient and requires clarification.
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