Cervical Vessels: Non Atherosclerotic Disease

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Non Atherosclerotic Vasculopathies

- These uncommon conditions represent 5% of all ischemic strokes.

- They are relatively more common in children and young adults.

- They include:
  - Dissection
  - Vasculitis
  - Moyamoya
Cervical Artery Dissection (CAD)

- Accounts for 2% of all causes of stroke.
- Represents the leading cause of non-atherosclerotic stroke in young adults: up to 25% of cases.
- Incidence in population based studies: 2.6 to 2.9 new cases per year/100,000 inhabitants.
  
  but

the true incidence is unknown, because of non-ischemic CAD, silent cases of CAD and too few vascular neurologists.
Epidemiology of CAD

- More frequent in **Men**: M:W=1.5:1

- **Median Age** in most studies: 40 years (women are 5 yrs younger), but underdiagnosed in the elderly.

- More frequent in the territory of the Carotid artery: 1 VA : 3 ICA, but in more recent data VA not much < ICA.

- More frequent in the **Extracranial Segment** of the Cervical Vessels with respect to the Intracranial Segment: due to higher mobility of the extracranial segments (traumas).
Sites of CAD

• **Single Vessel Dissection** (80%)
  - ICA involved 3 times more than VA
  - ICA: > 2 cm after the origin
  - VA: V3 or V1 segment (most mobile segments)
  - CCA: rarely involved; think of Aortic Dissection!

• **Multi Vessel Dissection** (<20%)*
  - All combinations

* but many cases may go undetected because of their asymptomatic or oligo-symptomatic presentation and frequently spontaneous recanalization: **31.6% in our series.**
Etiology of CAD

• **Types:**
  - some are *Traumatic*,
  - but *most of them* are *Spontaneous*

• **Predisposing Factors:**
  - FibroMuscular Dysplasia
  - Ehlers Danlos
  - Pseudo-Xantoma Elasticum
  - Marfan’s Syndrome
  - Arteritis  etc.
Pathophysiology of CAD

- Trauma
  - Primary Rupture of the Intima
    - Impaired Vasomotion
      - Mural Hematoma
        - Local Thrombosis
          - Embolisation (more freq)
            - Cerebral Ischemia
  - “Arteriopathy”
    - Primary Rupture of Vasa-vasorum (in the media)
      - Stenosis/Occlusion
        - Hemodynamic failure (rare)
          - Local Symptoms
      - Compression
Vasomotion in Multiple Spontaneous Cervical Artery Dissections

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Aim of the study

- To investigate:
  - spontaneous vasodilation
  - endothelial-dependent vasodilation
  - endothelial-independent vasodilation

in patients with MsCAD
and in a group of healthy subjects

using high-resolution ultrasound.
Final Results

C. Baracchini et al
Stroke 2008;39:1148-1151
Neuropathology of CAD

Mural hematoma:
It is the fulcrum of CAD pathophysiology
It is the cornerstone for the diagnosis of CAD (we can see it in US and MRI).

2 types of CAD

1a Sub-Intimal CAD (more frequent)
1b Sub-Intimal CAD with double lumen (rare)

the hemorrhage can also rupture back through the intima, forming a perfused false lumen
which is separated from a true lumen by a dissecting membrane.

• Stenosis of various degree or Occlusion
• Frequent Ischemic events (TIA or Stroke)
• Silent strokes (DWI changes)

1a
Subintimal hemorrhage (1)
with lumen narrowing.

1b
Formation of a false lumen (2),
dissecting membrane (3),
and true lumen (4).

Courtesy of Prof. E. Bartels
Neuropathology of CAD

2. Sub-Adventitial CAD (rare)
   - Lumen is often normal
   - **Non-ischemic clinical presentation:** usually pain or local symptoms
   - May have normal ultrasound findings

   - These pts usually are not seen by neurologists and do not enter stroke units. Contribute to the % of undiagnosed CAD’s.

![Diagram of pseudoaneurysm](image)

**Pseudoaneurysm (5) in the case of a subadventitial hemorrhage**

*Courtesy of Prof. E. Bertaux*
Clinical Findings: ICA Dissections

- Ischemic Events: TIA or Ischemic Stroke
- Pain
  - Not specific
  - 1st symptom in 60% of patients; occurs in 75%.
  - Usually occurs a few days before ischemic events (hours to days)
  - Usually cervical, ipsilateral, up to 1 month before stroke or TIA.
  - Sometimes throbbing headache, sharp pain in neck, jaw, pharinx or face.
  - May suggest migraine attack (no history of migraine in these pts).
  - Recurrence: suggests extension or recurrence.
- Local Symptoms
  - Horner’s syndrome
  - Cranial nerve palsies (especially lower cranial nerves)
  - Pulsatile tinnitus
- Silent ICA Dissection
- SAH: rarely in case of intracranial ICAD
Clinical Findings: VA Dissections

• **Ischemic Events:**
  - TIA
  - Ischemic Stroke (lateral medullary syndrome)
  - Cervical spinal cord infarct

• **Pain**
  - Not as frequent as in carotid CAD.
  - Sharp, unbearable, continuous; extended neck pain; posterior neck stiffness.

• **Local Symptoms**
  - Peripheral motor deficit in the upper limb (cervical root compression mainly due to the dissection hematoma)

• **Silent VA Dissection**

• **SAH:** rarely in case of intracranial VAD
Diagnosis of CAD: which diagnostic work-up?

Primum: Non Nocere.....
considering that the Outcome is good in most CAD’s

• **Non-Invasive approach** in all patients:
  • **US + MRI**: show the Intramural Hematoma (only proof of CAD)
  • **MRA**: indirect signs

• **Invasive approach** only in selected patients:
  • Conventional **Angiography**:
    – More dangerous
    – Less Informative (it shows only indirect signs)
Ultrasonography

• **Diagnosis:**
  - It is the first procedure we have to perform to make the diagnosis of CAD, because it is **non-invasive** and **informative**.

• **Monitoring:**
  - useful for non-invasive monitoring of **Vessel Recanalization**
  - Diagnosis of “**Early-Recurrence**”
  - useful for determining the **Duration of Antithrombotic therapy**
  - Diagnosis of “**Late-Recurrence**”
Echographic Signs

• **Occlusion of the artery without any atheroma** this is suggestive of CAD but not typical of CAD.

• **Tapering stenosis** with or without thrombus: “Irregular Stenosis” with Thickened, hypo- or isoechogenic vessel wall.

• **Double Lumen** (rare)
• **Hematoma, often hypoechoic**

• **Intimal Flap** or **Dissecting Membrane**

• **Pseudoaneurysm**: rare finding (6%), because 1. the aneurysms are often located in the depth of the neck and must thus be investigated with low-frequency transducers, 2. it is difficult to reliably distinguish ICA redundancies from an aneurysm.

• **No or mild atherosclerotic changes** (in over 80% of cases)
• **Intraluminal echoes** resulting from the fresh thrombus.
• **Normal Findings**: remember Subadventitial CAD.
ICA Dissection
“irregular stenosis”*
“tapering stenosis”
most frequent finding
(90% of cases)

* N.B. In contrast to Atherosclerotic ICA Disease:
1. begins distal to the carotid bifurcation
2. extends over a longer distance.

Atherosclerotic ICA Stenosis
Thickened and mainly hypoechochogenic vessel wall

- composed of the **hematoma** and **intraluminal thrombus**
- low detection rate (25%), because only the proximal part of the cervical ICA can be studied with high-frequency linear transducers, whereas mural hematomas can be located exclusively in the less accessible distal part of the vessel.
- The presence of an intimal reflex may allow the reliable distinction of the wall hematoma.
“Irregular Stenosis” and Wall Thickening
ICAD Occlusion without any Atheroma but with Atherosclerotic Changes (in < 20% of CAD’s)

Atherosclerotic ICA Occlusion
Intimal flap

- a flat and hyperechogenic structure bordering the presumed intramural hematoma, floating in the lumen or separating the two lumina with different Doppler signals.
- this finding is rare (2%).
Intimal flap  Double Lumen
Hemodynamic Signs

• **Indirect signs of a Distal flow obstruction**
  – High Resistance Flow Pattern: reduced diastolic flow velocity and increased pulsatility of the spectral waveform.

• **Distal stenosis/occlusion**

• **Modification over time** (highly suggestive of CAD)
  – Vessel Recanalization
  – Early Recurrence
  – Late Recurrence
Pitfalls of Ultrasound Diagnosis of Acute ICAD

- **Increased flow velocities in the cervical ICA** may result either from a stenosis or a disease with increased blood flow.
  - **Redundancies of the Cervical ICA** (kinking, coiling, looping) may mimic ≤50% stenosis. Impossible to differentiate whether raised flow velocities in a redundant artery results from the redundancy itself or an additional stenosis. Remember that the high prevalence of redundancies in patients with sICAD is an important cause of false-positive ultrasound findings.
  - **Fibromuscular dysplasia** may narrow the cervical vessel, sometimes with US we see irregular stenoses and aneurysmal dilatations (string of beads) associated with FMD.
  - **ICA vasospasm**: rare etiology of transient ICA stenosis.
  - **Large (>4mm) AVM** of the brain and **Carotid-Cavernous Fistulas** may determine increased flow velocities and also increased vessel diameter in the cervical ICA.
  - **Persistent primitive trigeminal artery** connecting intracranial ICA with the BA, may determine increased blood flow velocity.
  - **Anemia hyperthyreosis**.
Pitfalls of Ultrasound Diagnosis of Acute ICAD

- **Decreased flow velocities in the cervical ICA** may occur in severe stenosis or occlusion of the intracranial ICA or MCA.
  - **Occlusion of the lower carotid siphon**: slow flow velocities without a diastolic component in the cervical ICA, and in most cases reversed flow direction in the ipsilateral OphA.
  - **Severe Intracranial ICA stenosis** or **Occlusion located distal to the origin of the OphA** or **M1 MCA Occlusion**: decreased flow velocities, preserved diastolic component in the ipsilateral cervical ICA, antegrade flow direction in the OphA.

In these cases it is not possible to decide whether the decreased flow velocities in the cervical ICA are due to the intracranial obstruction alone or to the intracranial obstruction and an associated sICAD.
Pitfalls of Ultrasound Diagnosis of Acute ICAD

• **No Doppler signal**: US and angiographic findings observed in Occlusive sICAD are nonspecific: occlusion due to atherosclerosis or dissection?

• **Normal US Findings**: It is mandatory to investigate also the cervical portion of the ICA and the pars petrosa of the ICA, because sICAD may lead to a stenosis with an increased flow velocity in the cervical ICA or in the pars petrosa of the ICA and normal Doppler spectra at the origin.

• In the **distal portion of the cervical ICA**, the distance between the vessel and the ultrasound probe progressively increases. Consequently the examination is performed with low frequency (1.8-3.6 MHz) sector or Doppler probes which have a lower resolution for color Doppler and B-mode imaging compared to linear probes. Thus the wall of the distal cervical ICA usually cannot be assessed with B-mode imaging.
Pitfalls of Ultrasound Diagnosis of Acute VAD

- Difficult to diagnose VAD in most left V0 and V1 segments, and in both V4 segment:
  - Because Linear probes are used to assess the V0, V1, and V2 segments of the right VA, and the V1 and V2 segments of the left VA, whereas the investigation of the V3 may be difficult.
  - Conversely, most left V0 and V1 segments, the V4 segment, and the BA are insonated with sector or Doppler probes. Thus, B-mode and color Doppler imaging will detect wall abnormalities, mainly in the right V0 and V1, both V2, and eventually both V3 segments. Conversely, wall abnormalities in the remaining parts of the VA are rarely depicted.
Pitfalls of Ultrasound Diagnosis of Acute VAD

- Pathological hemodynamic findings are nonspecific: stenosis/occlusion due to atherosclerosis or dissection?
  
  Their location in the V2 or V3 segment, which is rarely affected by atherosclerotic vascular disease, suggests that a dissection might be the underlying cause.
VA Hypoplasia or Dissection?

In Hypoplasia:
- Decreased diastolic velocity
- Small diameter (< 2.0mm)
- Increased diameter in the contralateral VA (exception: primitive Trigeminal Artery)
- Normal Velocity values in the contralateral VA
Pitfalls of Ultrasound Diagnosis of Acute sVAD

- Difficult to differentiate **V4 dissection** from **VA hypoplasia**:
  - In Hypoplastic VA, slow systolic and diastolic flow velocities;
  - Detection of a small vessel diameter in a hypplastic VA.
  - The connection with the BA will be absent in a hypoplastic VA, which ends in the PICA.
  - Preserved diastolic velocities in preocclusional VA.
  - Reversed flow in postocclusional VA in case of VA occlusion located proximal to the origin of the PICA.
Ultrasonography

- **siCAD and carotid territory ischemia**: High sensitivity, but possibility of falsely positive ultrasound findings.
- **siCAD without carotid territory ischemia** (but only headache, neck pain, Horner syndrome or cranial nerve palsy): Sensitivity is about 70%.
- **sVAD**: Sensitivity of US for identifying sVAD is 75-86%.
- Negative predictive value and Specificity for US diagnosis in the latter two cases is unknown.

Cervical MRI and MRA must confirm ultrasound suspicion of sCAD
Cervical MRI
- T1 fat suppression technique -

- Semilunar signal hyperintensity (intramural hematoma)
- Degree of wall expansion
- Surrounding tissues
- Narrowed eccentric hypointensity (lumen)
MRA/Angiography of the Cervical Vessels

Only Indirect Signs

- Stenosis
- Occlusion
- Pseudo-Aneurysm
US Monitoring

- Monitoring of **Vessel Recanalization**
  - Recanalization results from
    - The resorption of the wall hematoma
    - The resolution of the intraluminal thrombus
  
  Useful for determining the **Duration of Antithrombotic therapy**.

- Diagnosis of **CAD Recurrence**: “Early”, “Late”.
Vessel Recanalization in ICAD

Recanalization Rates:
- Stenosis: 63%
- Occlusion: 35%
Vessel Recanalization in VAD

Recanalization Rates
- Stenosis: 50%
- Occlusion: 30%
there are limited and contrasting data regarding CAD recurrence rate (0% ⇒ 8%).

- Bogousslavsky et al 1987
  - 1 recurrent CAD in 30 pts (mean f-up 3.2yrs)
- Schievnik et al 1994
  - 4 recurrent CAD in 200 pts (mean f-up 7.4 yrs)
- Leys et al 1995
  - 3 recurrent CAD in 105 pts (mean f-up 3 yrs)
  - Rate of recurrent stroke: 0.6% per year
- Sturzenegger et al 1996
  - 4 recurrent CAD in 74 pts (mean f-up 34mo)
- Touze et al 2003
  - 4 recurrent CAD (2 with stroke, 2 without stroke) in 459 pts (mean f-up 31mo)
CAD Recurrence: in our center

- Overall, there were 105 dissections (61 carotid, 44 vertebral).
- **Multivessel dissections** were present in 24 (31.6%) patients appearing:
  - either simultaneously (in 4 pts, 5.3%)
  - or within the first week - early recurrence – (in 20 pts, 26.3%).
- During follow-up, recurrent dissection - late recurrence - occurred in 2 (2.7%) patients presenting with headache, neck pain and Horner’s syndrome.
  - In one case it involved a previously dissected carotid artery while under prophylaxis with an anticoagulant.
  - In the second case it involved a previously dissected vertebral artery while the patient was taking aspirin.
- 6 patients had a family history of arterial dissection and a recurrent sCAD was identified in 2 (33.3%) of these patients compared with none of the patients without a family history of sCAD.
Late Recurrence
LATE FOLLOW-UP
CERVICAL VESSEL VASCULITIDES

• They represent a rare, but potentially treatable series of conditions that can lead to stroke through diverse mechanisms.

• The most important ones are Primary Vasculitides, namely:
  • Temporal Arteritis
  • Takayasu Arteritis
Temporal Arteritis

- It is the most common primary vasculitis
- **Age ≥50yrs** at disease onset, in more than 99% of pts
- Symptoms:
  - Headache localized in the temporal region (74%)
  - Swollen, tender and firm temporal arteries, with reduced pulse (64%)
  - Jaw claudication (37%)
  - Eye involvement (32%): AION with blindness
- **ESR is ≥50mm/h** in 85% of pts
- **Temporal Artery Histology**
  is positive in 85% of pts with temporal arteritis: possibility of false negative histology because the inflammation is often segmental: skip lesions.
US Findings in Temporal Arteritis

- **Halo sign:**
  - dark, hypoechoic wall thickening around the lumen of the inflamed temporal artery
  - it represents vessel wall edema.

- **Stenosis**

- **Occlusion**

**Overall Sensitivity:** 88%
**Overall Specificity:** 95%
**Specificity for halo sign:** 99.5%
Temporal Arteritis

- Diagnostic Criteria:
  - 50-50 rule + Halo sign

- Follow-up:
  - Start tapering corticosteroid therapy when Halo sign disappears (usually within 2-3 weeks).
Takayasu Arteritis

- Less frequent than Temporal Arteritis: incidence of 1.2-2.6 cases/million/year.
- Age: **10-40yrs** at disease onset.
- **Females** in >80% of cases
- Symptoms: long prodromal phase of malaise, followed by symptoms of stenosis/occlusion.
- Also named the **Aortic Arch Syndrome**, because it involves the Aorta and its major branches.

Arteries most commonly involved:
- **Subclavian artery** (93%)
- Aorta (65%)
- Carotid arteries (58%)
- Renal arteries (38%)
- Vertebral arteries (32%).
US Findings in Takayasu Arteritis

- **Concentric homogeneous midechoic** thickening of the arterial wall, most frequently seen along the **CCA**.

* The echogenicity of the arterial wall thickening is higher than in temporal arteritis, because Takayasu arteritis has a more chronic course.

- **Stenosis or Occlusion of the CCA, ICA.**
- **Stenosis or Occlusion of the Subclavian Artery.**
Subclavian Steal

Hyperemia Test

Cuff Pres > Sys BP

Released Cuff
Traditional Imaging in a case of Takayasu Arteritis

Right Cerebellar Ischemic Stroke
Left Subclavian Occlusion
“Irregular profile” of the descending aorta
Marked stenosis of the right renal artery
MOYAMOYA

- **Non-atherosclerotic, non-inflammatory, non-amyloid intracranial vasculopathy** of unknown etiology.
- It accounts for about **10-20% of ischemic strokes in children**.
- **Sex**: F>M
- **Age**: <10yrs (Children) and 30-50yrs (Young Adults)
- Most frequent in **Orientals** (Japanese), but it can affect any population.
- **Moyamoya disease**: Idiopathic
- **Moyamoya syndrome**: associated with other conditions: Down syndrome, neurocutaneous syndromes such as neurofibromatosis, FMD, congenital cardiopathies, Fanconi disease, vasculitides, childhood brain radiation, Marfan syndrome, sickle cell anemia, etc.
MOYAMOYA

- It is characterized by chronic progressive stenosis or occlusion (due to intimal hyperplasia?) of the distal ICA’s and/or proximal portions of the MCA and/or ACA. It tends to spare the posterior circulation.
- In Moyamoya disease bilateral involvement.
- In Moyamoya syndrome unilateral involvement.
NEURO-RX Findings in MOYAMOYA

Multiple stenoses/occlusions
The arterial obstruction leads to a classic “puff of smoke” appearance on a cerebral angiogram, which is a myriad of tiny (moyamoya in Japanese) vessels – rete mirabilis – that forms in response to the blockage (compensatory effect? Hyperplasia of the embrionic network?).

- Clinical Manifestations: TIA, ischemic stroke, hemorrhagic stroke, seizures, progressive cognitive or learning impairment.

- Treatment:
  - Direct brain bypass procedure (STAMCA bypass): superficial temporal artery (STA) to MCA.
  - Indirect bypass or “onlay” procedure such as enchephaloduro-myo-synangiosis (EDMS), with or without a direct bypass as well.
NEURO-RX Findings in MOYAMOYA

Red arrow: occluded TICA
Blu arrow heads: rete mirabilis
Red circle: “puff of smoke” appearance
Green arrows: collaterals from the pial surface of the brain and the dura
US Findings in MOYAMOYA

- **Cervical Vessel US:**
  - **Increased vascular resistance in the ICA’s:** decrease in end-diastolic flow velocity.
  - **“Internalization” of the ECA’s:** decrease in vascular resistance.
  - **Bottle neck sign:** marked narrowing of the ICA at the proximal portion without atherosclerosis.
  - **Diameter reversal sign:** diameter of ICA < diameter of ECA.
TCD/TCCS Findings in MOYAMOYA

- **Stenosis/Occlusion of TICA and/or M1-MCA, A1-ACA.**

- *3 blood flow velocity patterns* in the proximal and distal segments:
  - **Hi-hi**: Early Stage of Disease; younger pts.
  - **Hi-lo**: Intermediate Stage of Disease; most common pattern.
  - **Lo-lo**: Advanced Stage of Disease; older pts.

- **The presence of MES is associated with disease progression**
  it is a sign of active Moya-moya disease.

- **Vasomotor Reactivity (Diamox-Test): impaired only in advanced stage** ⇒ increased risk of hemodynamic stroke.


Power Doppler evaluation of revascularization in childhood moyamoya

Abstract—Moyamoya disease is generally recognized in young children. One potential treatment is direct extra-intracranial bypass combined with indirect revascularization using encephalo-myo-synangiosis. Standard follow-up to assess neoangiogenesis includes repeat cerebral angiography, which is invasive. The authors studied whether noninvasive power Doppler imaging could evaluate the patency of the bypass and the degree of indirect revascularization. They found that transcranial power Doppler imaging is a valid noninvasive alternative to cerebral angiography.

NEUROLOGY 2005;64:558–560

F. Perren, MD; S. Meairs, MD; P. Schmiedek, MD; M. Hennerici, MD; and P. Horn, MD

Power Doppler Imaging is a non-invasive, no-risk alternative to Cerebral Angiography for post-operative follow-up especially in small children.