Specific TCD applications for vasospasm diagnosis and monitoring after SAH, TBI and tumor resection

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HISTORY OF ANEURYSMS

History of Aneurysm Identification

- The aneurysm originated from the Greek aneurysma where ana meant across and eurys meant broad
- The Alexandrian surgeon Rufus of Ephesus in 177 BC, studied aneurysms
- Galen was probably first to define and describe the entity of aneurysm. Antyllus in the second century AD distinguish between true and false aneurysms
- Arabian surgeon Al-Zahrawi (Abulcasis) (913-1013 AD) performed surgical treatment of aneurysms

Galen of Pergamum (AD 129 – 217)
**Giovanni Battista Morgagni (1682-1771)**

- Giovanni Morgagni of Padua reported an autopsy case and suggested that aneurysms could be the cause of intracranial hemorrhage.

**History of Aneurysms
Clinical Diagnosis**

- The first reports of possible connection between intracranial aneurysms and SAH were by Bonet (1679) and Wiseman (1696).

- John Blackhall of Oxford (1813), the first to describe a ruptured intracranial aneurysm confirmed at autopsy.

**History of Aneurysms
Clinical Diagnosis**

- Lumbar puncture
  - In 1891 Quinke showed blood in the subarachnoid space as a result of SAH.
- Radiography
  - Heuer and Dandy in 1916 showed intracranial aneurysm calcification on plain skull x-rays.
- Angiography
  - In 1926 Egaz Moniz carried out the first cerebral angiogram in dogs and in 1927 in human. In 1933, Moniz reported visualization of cerebral aneurysm.

**Dr. Heinrich Quinke**

- Born in Germany, Quincke was educated in this country under mentors such as von Kölliker, Helmholtz and Virchow.
- Early on he held a chair in medicine but after 30 years he retired to Frankfort-am-main continue his neurologic pursuits.
- Amongst his contributions to the literature were his classic description of angioneurotic edema, the studies of the mechanism of body temperatures. He recognized the syndrome of meningitis serosa and wrote on anosmia, traumatic brain lesions, and on hyperthermia in cord lesions. His introduction of the spinal puncture and procedures earned him a place in the history of medicine.
In 1926 Egas Moniz carried out the first cerebral angiogram in dogs and in 1927 in human. In 1933, Moniz reported visualization of cerebral aneurysm.

In 1949 he received the Nobel Prize, “for his discovery of the therapeutic value of leucotomy in certain psychoses.”

In 1916 Heuer and Dandy at Johns Hopkins reported a case of a 26-year-old telegraph operator with a history of sudden, violent, frontal headache, nausea, and vomiting 4 years before admission in whom complete blindness in the left eye subsequently developed, followed by partial visual disturbance in the right eye.

The x-ray demonstrated “a series of shadows consisting of broad curved lines and plaques.” The patient refused an extensive operation. Eighteen months later he experienced an explosive headache, vomiting, and loss of consciousness and died. At autopsy two giant aneurysms were found.

Ligation of carotid/s

In 1911 H. Cushing described his vascular clips

Walter Dandy of Baltimore, MD, the first to successfully clip an intracranial aneurysm on March 23, 1937

Fedor Serbinenko introduce balloon occlusion in 1971


M. Heuer and W. Dandy

History of Aneurysms
Surgical & Endovascular Management
AN OVERVIEW OF ANEURYSMS

Fedor Serbinenko (1928-2002)

Guglielmi G: Aneurysm coiling

Aneurysm of the terminal ICA segment
Cerebral aneurysms are classified both by size and shape.
Small aneurysms have a diameter of less than 15 mm.
Larger aneurysms include those classified as large (15 to 25 mm.), giant (25 to 50 mm.), and super giant (over 50 mm.).

Saccular aneurysm refers to any aneurysm with a saccular outpouching including berry aneurysms. Saccular aneurysms are the most common form of cerebral aneurysm.
Berry aneurysm, is a type of saccular aneurysm with a neck or stem resembling a berry.
A fusiform aneurysm describes an aneurysm without a stem.
Aneurysms
Classification

- Congenital, Berry-shaped or saccular
- Arteriosclerotic/fusiform
- Dissecting as in fibromuscular dysplasia
- Inflammatory and infectious (mycotic genesis)
- Traumatic
- Neoplastic
- Micro (Charcot-Bouchard)

Most common location of aneurysms

- ACommA (30 - 35%)
- Bifurcation of the ICA and PCommA (30 - 35%)
- Bifurcation of MCA (20%)
- BA bifurcation (5%)
- Remaining posterior circulation arteries (5%)

Aneurysms
Association with particular diseases

- Systemic lupus erythematosus
- Ehler-Danlos syndrome
- Coarctation of aorta
- Polycystic kidney disease
- Fibromuscular dysplasia
- Moya-Moya disease
- Hereditary connective tissue disorder
- Bacterial meningitis

Aneurysms
Risk factors

- More common among tobacco users
- Alcohol use or binge drinking
- Hypertension may be a risk factor
- Increased rates in women using oral contraceptives
- Drug use, particularly stimulants or cocaine
Aneurysms
Risk factors

- Gender
  In most series of aneurysmal SAH there is a striking female preponderance. Adult women are affected by aneurysmal SAH more than men by ratio of 60 to 40

- Genetics
  Family history (up to 11%)

- Geographic factors
  The incidence of SAH higher in Finland, Japan and low in New Zealand and Middle East. It varies significantly from 22-23/100,000 in Finland and Japan to 8-12/100,000 in other regions.

Incidence

- Incidence of brain aneurysms in general population is 1% - 5%

- Frequency of brain aneurysms ranged from 0.2% - 9.9%

- As many as 400,000 people in the USA may have a brain aneurysm

Aneurysm Growth Occurs at Region of Low Wall Shear Stress.
Patient-Specific Correlation of Hemodynamics and Growth in a Longitudinal Study
Boussel et al., Stroke, 2008

- Evolution of intracranial aneurysmal disease is known to be related to hemodynamic forces acting on the vessel wall. Low wall shear stress (WSS) has been reported to have a negative effect on endothelial cells normal physiology and may be an important contributor to local remodeling of the arterial wall and to aneurysm growth and rupture.

- Seven patient-specific models of intracranial aneurysms were constructed using MR angiography, data acquired at two different time points.

- Mean WSSTA values obtained for the areas with a displacement smaller and greater than 0.3 mm were 2.55±3.6 and 0.76±1.5 Pa, respectively (P<0.001). A linear correlation analysis demonstrated a significant relationship between WSSTA and surface displacement (P<0.001).

- These results indicate that aneurysm growth is likely to occur in regions where the endothelial layer lining the vessel wall is exposed to abnormally low wall shear stress.

Determination of wall tension...
Isaksen et al, Stroke, 2008

- The reported results, where areas with high wall tension corresponded to the usual rupture sites, support clinical experience suggesting that the shape of the aneurysm is an important factor with regard to its rupture risk.
# Aneurysmal SAH

## Epidemiology

- Approximately 5% - 10% of all strokes
- Incidence averages 11 per 100,000 (range 6-16 per 100,000)
- Adults of all ages
- Incidence not declining

## Etiology

<table>
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<tr>
<th>Cause</th>
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<td>Aneurysm</td>
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<tr>
<td>Hypertension</td>
<td>15%</td>
</tr>
<tr>
<td>AVM</td>
<td>6%</td>
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<tr>
<td>Other</td>
<td>28%</td>
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Aneurysmal SAH – Presentation

- Sudden, severe headache.
- The hallmark of aneurysmal SAH-headache is that it develops within seconds.
- It is critical to inquire on how quickly the headache developed.
- Even a careful history cannot distinguish between headache secondary to aneurysm rupture and other more common and benign forms of headache.

Congenital aneurysms

- The circle of Willis has been dissected, and three berry aneurysms are seen. Multiple aneurysms are seen in about 20-30% of cases of berry aneurysm. Such aneurysms are “congenital” in the sense that the defect in the arterial wall is present from birth, but the actual aneurysm takes years to develop, so that rupture is

Ruptured berry aneurysm in the circle of Willis

SAH Diagnosis

- Non-contrast CT scan confirms subarachnoid blood in 98% of patients if performed within the first 12 hours after onset.
- Distribution of blood on CT provides information on the origin of the SAH.
The Fisher Scale

- The Fisher scale, a way of grouping subarachnoid haemorrhage CT scans into four groups according to the amount of blood, and is useful in predicting cerebral vasospasm.
- Group 1: No blood detected
- Group 2: Diffuse thin (<1mm) SAH with no clots.
- Group 3: Localised clots and / or layers of blood >1 mm in thickness
- Group 4: Intracerebral or intraventricular blood (+/- SAH)

Hunt & Hess Scale

describes the severity of subarachnoid haemorrhage, and is used as a predictor of survival.

- Grade 1
  - asymptomatic or minimal headache and slight neck stiffness
  - 70% survival
- Grade 2
  - moderate to severe headache; neck stiffness; no neurologic deficit except cranial nerve palsy
  - 60% survival
- Grade 3
  - drowsy; minimal neurologic deficit
  - 50% survival
- Grade 4
  - stuporous; moderate to severe hemiparesis; possibly early decerebrate rigidity and vegetative disturbances
  - 20% survival
- Grade 5
  - deep coma; decerebrate rigidity; moribund
  - 10% survival

SAH CT-Scan

- Fisher Grade 3

The WFNS grading system

uses the Glasgow Coma Scale and presence of focal neurological deficits

- GCS 15; No deficit
- GCS 13-14; No deficit
- GCS 13-14; No deficit
- GCS 7-12; may be a neurological deficit
- GCS <7; may be a neurological deficit
SAH Diagnosis - MRI

- In the acute phase, MRI with FLAIR demonstrates SAH as reliably as CT
- MRI is superior to CT in evaluating extravasated blood after a few days (up to 6 weeks) and it is a useful tool in patients referred in a delayed fashion if the original diagnosis is in question

SAH Diagnosis – Lumbar puncture

- Necessary in patients with suggestive history but negative CT
- Preferably done after 6 or better 12 hours to allow for xanthochromia
- Xanthochromia persists for at least 2 weeks after SAH

Pathophysiological Alterations following Aneurysmal SAH

- Intracerebral & Intraventricular Hemorrhage
- Hydrocephalus
- Cerebral edema
- Seizures & Seizure-like Activity
- Alteration in Respiratory Function
- Effect on the Heart
- Fluid and Electrolyte Disturbance
- Cerebral ischemia
Vasospasm and Cerebral Ischemia

- Although there are medical therapies for vasospasm after SAH, early detection of vasospasm and initiation of aggressive medical therapy is of utmost importance to avoid delayed neurological ischemia, morbidity, and mortality.

Cerebral Vasospasm

- Some substances (numerous neurotransmitters, blood constituents or breakdown products, and autocoinds) released at the time of SAH acts on smooth muscle wall to cause vasoconstriction.

- Morphological changes of the arterial wall consistent with vasonecrosis or vasculopathy.

- Mechanical compression may also result in vessels constriction.

Vasospasm mechanisms

Blood breakdown products:

- ApolipoproteinE genotype
  - Immunomodulatory, neurotoxic, oxidative effects
  - APOE4 less effective than APOE3 in suppressing neurotoxicity

- Endothelin1 release from CSF leukocytes
  - Potent vasoconstrictor
  - Synergistic effect in vasoconstriction between APOE and Endothelin1
Double-hit model of delayed ischemic neurological deficits after SAH based on Dreier et al. The two hits on the brain parenchyma consist of acutely triggered microvascular spasm in response to spreading depolarizations, superimposed on chronic vasospasm.

Early Brain Injury

Sehba F, 2011

Mechanisms of Early Brain Injury after SAH

- Mechanical
  - Constriction
  - Mediated in various ways
- Physiological
  - TID: 
  - OPC: 
  - Mild autoregulation

- Molecular
  - Vasodilators, antifibrin
  - ET-1 release
  - Dilation status
  - Platelets
  - Calcium homeostasis
  - Platelet aggregation
- Cell death
  - Necrosis
  - Apoptosis

Clinical Features of Symptomatic Vasospasm

- Variable clinical course
- Usually peaks at 7-10 days following SAH
- Usually gradually evolves with waxing and waning symptoms
- New HA, seizures, or decreased alertness
- New focal neurological signs - MCA/ACA/border zone
Cerebral Vasospasm and Delayed Ischemic Deficit
Dorsch et al., 1994

- Literature review of more than 30,000 cases
- Angiographic vasospasm occurred in 43.3% (range 19% - 97%)
- DID occurred in 32.3% (range 5%-90%)
- Outcome of DID:
  - Death in 30.3%
  - Permanent deficit in 34%
  - Good outcome in 35.7%

A clinical review of cerebral vasospasm and delayed ischaemia following aneurysm rupture
Dorsch N, 2011

- Online and physical searches have been made of the relevant literature.
- The incidence of delayed ischemic deficit (DID) or symptomatic vasospasm reported in 1994 was 32.5% in over 30,000 reported cases. In recent years, 1994-2009, it was 6,775/23,806, or 28.5%.
- Many of the recent reports did not specify whether a calcium antagonist was used routinely, and when this was stated (usually nimodipine or nicardipine), DID was noted in 22.0% of 10,739 reported patients.
- The outcome of DID in the earlier survey was a death rate of 31.6%, with favorable outcomes in 36.2%. In recent reports, though with fewer than 1,000 patients, the outcome is possibly better, with death in 25.6% and good outcome in 54.1%.
- It thus appears likely that delayed vasospasm is still common but less so, and that the overall outcome has improved. This may be due to the more widespread use of calcium antagonists and more effective fluid management.

Cerebral Vasospasm
Clinical Significance

- Cerebral vasospasm constitutes a major complication of SAH
- The presence of vasospasm has been correlated with a 1.5 to 3-fold increase in mortality in the first 2 weeks after SAH
- DID occur during a period ranging from 4 to 12 days, but early (3d) or late manifestations (≤ 3 wk) may be observed

SAH Management
Macdonald, Neurosurg Rev, 2006

- Vasospasm Diagnosis
  - Change in clinical status
  - 4-vessel angiography
  - CTA; Sensitivity 100%, Specificity 92%
    - Proximal arteries: internal carotid, basilar and first segments of ACA and MCA
    - Less useful for distal vessels and for differentiating mild and moderate spasm
  - MRA; Sensitivity 46%, Specificity 70%
    - Related to movement and time required for study
  - TCD; Sensitivity 50% - 60%, Specificity 90% (? ? ?)
  - PtcO2 / CBF / microdialysis
  - Glutamate, glycerol lactate / pyruvate
  - CBF < 15 mL / 100 gm / min
SAH Outcome

- 30-day mortality rate still high
- Many patients die before or shortly after reaching medical attention
- Large percentage of survivors suffers from cognitive sequelae even after “successful” treatment.

Management of complications

- Angiographic VSP is more common (occurring in about two thirds of patients) than is symptomatic vasospasm (with clinical evidence of cerebral ischemia)
- TCD is performed daily to monitor for VSP, which is defined as a mean CBV of more than 100 cm/sec in a major vessel. TCD has a sensitivity that is similar to that of cerebral angiography for the detection of narrowed vessels, particularly in the MCA and ICA
- Once symptomatic VSP is evident (with focal neurologic signs), patients are treated with hypervolemia and induced hypertension
- Patients whose condition does not improve with medical therapy undergo emergency cerebral angiography and transluminal angioplasty or vasodilator infusion when focal vessel narrowing is evident

Prevention of Vasospasm and DID

Naval, CCM, 2006

HHH Therapy:
1. Hypertensive – MAP = 100 to 120 mm Hg
2. Hypervolemic – CVP = 8 to 12 mm Hg
3. Hemodilution – Hct = 30%

- Prevention is controversial
- Statins-protection
- Mg++ -need further studies

Clazosentan to Overcome Neurological Ischemia and Infarction Occurring After Subarachnoid Hemorrhage (CONSCIOUS-1)

Randomized, Double-Blind, Placebo-Controlled Phase 2 Dose-Finding Trial

MacDonald et al., Stroke, 2008

Occurrence of moderate or severe VSP measured by DSA at day 9 ± 2 postaneurysm rupture
• Dr. L. MacDonald presented (CONSCIOUS 1, 2 and 3). C-2 led to a non-significant reduction in mortality/vasospasm-related morbidity but was not associated with an improvement in GOSE (Glasgow Outcome Score Extended). C-3 trial was stopped due to the lack of efficacy data from the Phase 3 clinical study CONSCIOUS-2

• Effect of intracisternal magnesium therapy, Dr. Mori et al from Japan. Experimental work in dogs, the reversible effect of intracisternal magnesium MgSO4 therapy required CSF Mg2+ concentration of more than 3 mEq/l, effect was evident for 3 to 6 hrs, therefore continuous or intermittent infusion probably needed to ameliorate vasospasm

• Prolonged release of nicardipine from pellets (NP) that are placed around vessels during surgical clipping presented by Dr. Kasuya (Japan), initially treated 100 pts provided very impressive results, later 136 multicenter trial in Japan was similar to first results. Now the randomized, double-blind trial of 32 pts with severe SAH done in Germany and the incidence of angiographic vasospasm was significantly reduced 73% control vs. 7% in patients with NPs.

• Current medical therapy (nimodipine/nicardipine) or aggressive 3H-therapy will not prevent patients after aSAH to have vasospasm
• Close to 100% of patients after aSAH would have vasospasm demonstrated by cerebral angiography and/or TCD
• No clear predictive value for patients who will have symptomatic vasospasm based on angiography or TCD data developed
• Early brain injury after aSAH emerges as a new recent concept with emphasis on complex pathophysiological mechanisms that are linked to initial bleed. However, it remains unknown whether global ischemia itself or subsequent events are responsible for the detected cell death and neurodegeneration
• Numerous experimental work going on trying to identify therapies for vasospasm prevention/treatment

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Effects of a Single Dose of Dantrolene in Patients With Cerebral Vasospasm After Subarachnoid Hemorrhage
A Prospective Pilot Study
Muechschlegel et al, Stroke, 2011

• Dantrolene is a known ryanodine receptor inhibitor and is already approved by the U.S. FDA for other indications. There is evidence that dantrolene is neuroprotective. Furthermore, in an ex vivo rat model, dantrolene has been shown to inhibit cerebral vasoconstriction alone as well as in combination with nimodipine

• In a prospective, open-label, single-dose ascending safety trial, 5 patients received i/v dantrolene 1.25 mg/kg and the next 5 patients received 2.5 mg/kg over the course of 60 minutes, TCD was performed at 0, 45, 90, and 135 minutes relative to infusion start

• Peak systolic CBFV decreased significantly (~26 cm/s) with a borderline change in mean CBFV in the low-dose group (~16 cm/sec) and peak systolic CBFV in the high-dose group (~26 cm/s).

• In this pilot study, a single dose of i/v dantrolene in cerebral vasospasm after SAH appears feasible while inhibiting vasoconstriction in the low-dose group, but it may lower MAP

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TCD DIAGNOSIS OF VASOSPASM
CBF Measurements

Xe $^{133}$

SPECT

CBF vs. CBFV

- $^{133}$Xe
- Stable xenon-enhanced CT
- MRI
- PET
- SPECT
- The time, expense, and complexity of these techniques still limits its use in routine clinical practice

TCD Diagnosis of Vasospasm

Newell et al., 1993

Diagnosis and Monitoring of Vasospasm: ANGIOGRAPHY

- Degree of angiographic vasospasm does not always correlate with the clinical condition. Some patients remain asymptomatic with severe vasospasm demonstrated by angiography
- Incidence of angiographic vasospasm is nearly twice that of DID
Diagnosis and Monitoring of Vasospasm: TCD

- High CBFV can identify patients at higher risk for developing DID, but also may occur in asymptomatic patients

- Neurologist/Neurointensivist must determine whether the severity and location of the vessel narrowing/high CBFV are appropriate to cause the clinical deficit

Is routine TCD monitoring useful in the management of SAH?

Warlaw et al., Neurosurgery, 1998

- 186 patients after SAH
- Routine TCD examinations made an important positive contribution to the diagnosis of DID in 72% and led to altered management for the benefit of the patient in 43%
- In 9% of pts with recent SAH, it was believed that outcome might have better if the TCD results had been acted upon appropriately

Is routine TCD monitoring useful in the management of SAH?

Warlaw et al., Neurosurgery, 1998

- The TCD results appeared to alter management beneficially in 37% of emergency and 48% of elective patients
- In the patients admitted on an emergency basis this was often because TCD monitoring showed elevated CBFV’s and influenced (delaying or advancing) the timing of surgery or discharge or even led to simple actions such as continuing bet rest or administration of IV fluids for an additional 24 hrs

Transcranial Doppler in cerebral vasospasm

Newell et al., 1990

- MCA CBFV ≥ 120 cm/s 25% narrowing
- MCA CBFV ≥ 140 cm/s 25-50% narrowing
- MCA CBFV ≥ 200 cm/s 50% narrowing
The value of CTA and TCD in triaging suspected cerebral vasospasm in SAH prior to endovascular therapy.

Ionita et al., Neurocrit Care, 2008

- The purpose of this study was to evaluate the degree of agreement between TCD and CTA in diagnosing clinical CVS following SAH, and to define the role of CTA in triaging patients prior to digital subtraction angiography (DSA) and endovascular intervention.

- 55 consecutive patients with aneurysmal SAH who underwent sequential TCD and CTA were analyzed. TCD CVS was defined as anterior circulation peak mean velocity (PMV) >160 cm/s, basilar artery (BA) PMV >90 cm/s, and Lindegaard ratio (LR) >6. CTA CVS was defined as >50% luminal narrowing in the affected vessel. Clinical CVS was defined as the onset of new focal neurological deficit attributed to delayed ischemic injury.

- Thirteen patients (24%) had clinical CVS and 42 patients (76%) were asymptomatic. All patients with clinical CVS had also radiological evidence of CVS (agreement 100%). In 35 patients without clinical CVS, both tests agreed for absence of CVS in 28 cases (agreement 83%). The remaining 7 asymptomatic patients had radiological CVS only, in disagreement with clinical absence of CVS (17%).

- Clinical evaluation and TCD can reliably diagnose CVS in symptomatic patients and PMV >180 cm/s, or can rule out CVS in asymptomatic patients with PMV <140 cm/s. In this category of patients, adding a CTA to clinical evaluation and TCD may not be warranted.

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TCD Criteria for diagnosis of MCA vasospasm

<table>
<thead>
<tr>
<th>Mean CBFV (cm/s)</th>
<th>MCA/ICA ratio (Lindergaard Ratio)</th>
<th>Interpretation</th>
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<tbody>
<tr>
<td>&lt;100</td>
<td>&lt; 3</td>
<td>Nonspecific</td>
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<tr>
<td>100-140</td>
<td>3-6</td>
<td>Mild</td>
</tr>
<tr>
<td>140-200</td>
<td>3-6</td>
<td>Moderate</td>
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<tr>
<td>&gt;200</td>
<td>&gt;6</td>
<td>Severe</td>
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TCD and posterior circulation vasospasm

TCD and angiography

Sloan et al., 1994

- VA
  - Sensitivity: 44%
  - Specificity: 88%
  - PP Value: 54%

- BA
  - Sensitivity: 77%
  - Specificity: 79%
  - PP Value: 62%

Basilar artery vasospasm and delayed posterior circulation ischemia after aneurysmal subarachnoid hemorrhage

Sviri et al., Stroke, 2004

- Patients with very high BA CBFV (>115 cm/s) had a 50% chance of developing delayed BS ischemia. BA-VS was found at a higher rate in patients who experienced reduced rCBF in the cerebellum (56.3%), thalamic nuclei (68.4%), and occipital lobe (81.8%). Although patients with delayed BS hypoperfusion did not present with a higher clinical grade, their clinical outcome was significantly worse (Glasgow Outcome Score after 30 days 2.48+/−1.16 versus 3.3+/−1.27; P=0.001)

- These findings suggest for the first time that BA-VS after aneurysmal SAH is associated with hypoperfusion to BS and other posterior circulation territories

- The risk for delayed BS ischemia increased significantly when TCD BA-FVs were >115 cm/s

TCD Grading Criteria for BA vasospasm

Sviri et al, 2006

- 123 pts, SAH, angiography, BA and extracranial VA TCD within 4 hrs before the DSA
- CBFV ratio between the BA and extracranial VA strongly correlated with the degree of BA narrowing (r=0.86, p<0.0001)
- A ratio higher than 2 associated with 73% sensitivity and 80% sensitivity for BA vasospasm
- A ratio higher than 2.5 with BA CBFV 85 cm/sec was associated with 86% sensitivity and 96% specificity for BA narrowing more than 25%
- A ratio higher than 3.0 with BA CBFV Higher than 85 cm/sec was associated with 92% sensitivity and 97% specificity for BA narrowing more than 50%

Prediction of symptomatic vasospasm after SAH with TCD

- An early CBFV increase (Seiler et al., 1988)
- A rapid CBFV increase in the first 6 days (Grote et al., 1988)
- A CBFV increase of at least 50 cm/sec during 24 hours (Grosset et al., 1993)
- A CBFV increase of 50 cm/sec during 48 hours (Wardlow et al., 1998)
- Relative changes in CBFV's (two or threefold CBFV increase) in patients with aneurysmal SAH correlated better with clinically significant vasospasm than absolute CBFV's (Naval et al, 2005)
TCD for diagnosis of cerebral vasospasm after SAH: mean blood flow velocity ratio of the ipsilateral and contralateral MCA

Nakae et al, 2011

- Retrospective study, 142 pts, 1262 TCD tests, DID defined as neurological deficit or CT evidence of infarct cause by vasospasm (?)
- The threshold value that best discriminated between pts with and w/o DID was I/C mCBFV of 1.5
- I/C mCBFV ratio demonstrated a more significant correlation to DID than the absolute m CBFV

TCD changes after vasospasm

Early Onset Abnormal TCD changes after vasospasm

Unilateral TCD changes after vasospasm
Unilateral TCD changes after vasospasm

Spectral Display, Indices

Pulsatility Indices

TCD Wave-Form
Cerebral vasospasm evaluated by TCD at different intracranial pressures

- 76 patients with SAH
- MAP
- ICP
- PaCO₂
- TCD
  - CBFV
  - RI

Klinghofer et al., 1991

- Evaluation of the interdependence of the patient’s clinical grade, VSP, ICP and TCD parameters

SAH Pt 1

- There was no case in which both high ICP and high CBFV were observed simultaneously
- During the time course of vasospasm, an increase in the resistance index above values of 0.6 with a simultaneous CBFV decrease, indicates a rise in ICP rather than a reduction in VSP
- With a pronounced increase in ICP, evaluation of severity and time course of VSP by TCD based solely upon the mean CBFV can lead to a false-negative results

Klinghofer et al., 1991

Day 1
Rt MCA (M1 segm); 60 cm/s
Lt MCA (M1 segm); 64 cm/s

Day 3
Rt MCA; 100 cm/s
Lt MCA; 110 cm/s
SAH Pt 1

Day 8
Rt MCA (M1 segm); 212 cm/s
Lt MCA (M1 segm); 230 cm/s

Day 15
Rt MCA; 308 cm/s
Lt MCA; 121 cm/s

SAH Pt 2

Day 5
Lt MCA; 125 cm/s
Rt MCA; 88 cm/s

Day 6
Lt MCA; 38 cm/s
Rt MCA; 118 cm/s

SAH Pt 3

Day 7
Lt MCA; 139 cm/s
Rt MCA; 148 cm/s

Day 4
Rt MCA; 38 cm/s
Lt MCA; 43 cm/s
SAH. Pt 3

Day 5
Rt MCA: 131 cm/s
Lt MCA: 158 cm/s

SAH & ICP

- We are judging qualitative TCD wave form morphology changes.
- These changes usually will be obvious after ICP will be more 30 mm Hg.
- However, one condition must be fulfills if you would be using TCD wave from changes to predict intracranial hypertension: MAP, cardiac output and PaCO2 are normal and not different significantly compared to the previous day.

Effect of age on MCA and ICA CBFV
Torbev at el, Stroke, 2011

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<th>≥68 (n=34)</th>
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<td>Range</td>
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<td>IC A CBFV (cm/s)</td>
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- Effect of age on MCA and ICA CBFV
Torbev at el, Stroke, 2011

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<tr>
<th>Symptomatic Vasospasm n(%)</th>
<th>&lt;68 (n=47)</th>
<th>≥68 (n=34)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to symptomatic vasospasm</td>
<td>Median (cm/s)</td>
<td>Range</td>
<td></td>
</tr>
<tr>
<td>MCA CBFV ± 1 day at VSP</td>
<td>92</td>
<td>243</td>
<td>0.009</td>
</tr>
<tr>
<td>ICA CBFV ± 1 day at VSP</td>
<td>10(53%)</td>
<td>5(33%)</td>
<td>0.079</td>
</tr>
<tr>
<td>TCD VSP</td>
<td>42%</td>
<td>23%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Radiological VSP n(%)</td>
<td>10(53%)</td>
<td>5(33%)</td>
<td>0.1</td>
</tr>
</tbody>
</table>

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Role of TCD: SAH

- Elevated CBFV’s in asymptomatic patients warrant meticulous observation in some closely supervised setting until CBFV’s begin trend downward.
- Elevated CBFV’s in a particular vascular territory can focus subsequent neurologic examinations to detect subtle changes earlier in their clinical course.

Factors influencing interpretation

- Patient age
- The presence of moderate to severe anemia (Hct <27)
- Impaired CBF autoregulation (passive CBFV variation with MAP changes)
- Hyperemia induced by triple-H therapy

Role of TCD: SAH

- In symptomatic patients, elevated CBFV’s most likely represent significant vessel narrowing and may obviate the need for cerebral angiography. At this point, triple-H therapy can be initiated or advanced.
- Asymptomatic patients without elevated CBFV’s probably can avoid additional angiography. However, we need to consider patient’s age because elderly patient’s could develop vasospasm in normal or slightly abnormal CBFV range.
Guidelines for the Management of Aneurysmal SAH

Stroke Council, AHA, 1994

• Summary and Recommendations:
  1. SAH is a medical emergency...
  2. CT scanning for suspected SAH is strongly recommended...
  3. Selective cerebral angiography to document...
  4. TCD is recommended for the diagnosis and monitoring of vasospasm, although the cerebral angiography may be required for definitive diagnosis

TCD MONITORING OF VASOSPASM

McGirt et al, 2003

• Objective was to examine the impact of TCD vasospasm monitoring on clinical decision-making following SAH

• The records of 50 randomly selected patients undergoing serial TCD monitoring following SAH were reviewed. Dates and results of TCDs and cerebral angiograms, the use of hypertensive hemodilution (HH) therapy, and the development of new neurological deficits were recorded. The independent effects of TCD-defined vasospasm and new neurological deficits on patient management were determined with multiple logistical regression. Results were validated in a second randomly selected, 50 patient cohort.

Transcranial Doppler monitoring and clinical decision-making after subarachnoid hemorrhage

McGirt et al, 2003

• Mild or moderate TCD-defined vasospasm developed in 76% of patients 5.8 +/- 0.5 days after SAH; 38% developed severe TCD-defined vasospasm after 7.9 +/- 0.7 days. Focal neurological deficits occurred in 50% after 5.7 +/- 0.6 days with TCD abnormalities preceding the deficit by 2.5 +/- 0.7 days in 64%

• TCD-defined vasospasm did not independently influence the use of HH therapy or angiography with both decisions associated with the development of new neurological deficits

• As TCD-defined vasospasm preceded the neurological deficit in 64%, earlier intervention might reduce the incidence of vasospasm-related stroke in institutions with similar practice patterns

Transcranial Doppler monitoring and clinical decision-making after subarachnoid hemorrhage

McGirt et al, 2003

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18 (9.9%) patients demonstrated biphasic CBFV’s profile

1st CBFV’s peak (134 ± 11 cm/s) occurred on post-SAH day 6 ± 1.
2nd CBFV’s peak (148 ± 12 cm/s) occurred on post-SAH day 13 ± 1

Although the 2nd CBFV’s peak is usually not associated with a worsening of symptoms, these patients were more likely to exhibit clinical symptoms during the 1st CBFV peak.
Elevated Transcranial Doppler Ultrasound Velocities Following Therapeutic Arterial Dilation

- Elevated TCD CBFV's seen after balloon angioplasty are commonly interpreted as evidence of residual or recurrent stenosis but may conceivably arise from hyperemia and require different clinical management.
- Four cases of abnormally elevated mean CBFV's obtained after therapeutic arterial dilation with either balloon angioplasty or intra-arterial administration of papaverine are described. In each case, cerebral angiography revealed a dilated vessel, suggesting that hyperemia and impaired autoregulation were the cause of the high CBFV's.
- These examples suggest that high TCD CBFV's after vessel dilation may be produced by unpredictable amounts of vessel narrowing and flow alteration. Although a normalizing CBFV after angioplasty suggests effective vessel dilation, high CBFV's may be due partly to hyperemia, and deserve treatment as brain injury, not recurrent stenosis.

2011 AHA/ASA Metrics for Measuring Quality of Care in Comprehensive Stroke Centers

- Among different measures for Comprehensive Stroke Centers is:

  **Median frequency of noninvasive monitoring for surveillance for vasospasm in patients with aneurysmal SAH during the period between three and 14 days after SAH**
POSTTRAUMATIC VASOSPASM

Post-Traumatic VSP

- Ischemic symptoms caused by cerebral arterial spasm following traumatic SAH are comparable to those found following aneurysmal SAH:
  - appearance of symptoms between Days 4 and 16 after injury, with the peak incidence on Days 9 and 10
  - close correlation between the main site of the subarachnoid blood and the location of severe vasospasm responsible for the symptoms; and a higher incidence of symptoms in patients with massive SAH than those with slight SAH
- Subarachnoid blood plays an important role in the later development of vasospasm, not only following aneurysm rupture but also after head injury. Nevertheless, there is no general agreement that subarachnoid blood in head injury is an important risk factor in the development of vasospasm and ischemic brain damage.

Traumatic Brain Injury & TCD

- Cerebral ischemia due to the post-traumatic vasospasm
- Increased Intracranial Pressure
- Brain Death

Explosion and concussion effect on the water surface
• There is an increasing use of improvised explosive devices (IEDs) in terrorist and insurgent activities. Exposure to blast is becoming more frequent.

• Injuries occur as a direct result of blast wave-induced changes in atmospheric pressure (primary blast injury), from objects put in motion by the blast hitting people (secondary blast injury) and by people being forcefully put in motion by the blast (tertiary blast injury).

• Blast-related injury during war is now very common. A recent study found that 88% of military personnel treated at an echelon II medical unit in Iraq had been injured by IEDs or mortar.

• Many (47%) of these injuries involved the head. Similarly, 97% of the injuries to one Marine unit in Iraq were due to explosions (65% IEDs, 32% mines). The majority of these (53%) involved the head or neck. The authors noted the importance of prompt evaluation of CNS symptoms indicative of concussion. Most (82%) returned to duty following an average of 3 (range=0–30) light duty days.

• The Defense and Veterans Brain Injury Center (DVBIC) has reported that 59% of an "at risk" group of injured soldiers returning from Afghanistan or Iraq to Walter Reed (2003–2004) suffered at least a mild TBI while in combat.

• Further characterization of 433 war fighters revealed that the TBI was moderate or severe in more than half the group. The TBI was due to a closed head injury in 88%. Similarly, a study of patients with explosive injury only to the lower extremities found that 51% (665/1303) had neurological symptoms (e.g., headache, insomnia, psychomotor agitation, vertigo) consistent with TBI. Of these, 36% had EEG alterations during the acute stage (most commonly hypersynchronous, discontinuous, or irregular brain activity). Both neurological and EEG abnormalities persisted into the chronic stage for 30% of this group.
Blast-Related Traumatic Brain Injury: What Is Known? 
Taber et al., 2006

- Both neurological and EEG abnormalities persisted into the chronic stage for 30% of this group. An earlier study found that veterans with post traumatic stress disorder who had been exposed to blast had EEG abnormalities and attentional difficulties consistent with mild TBI.
- The limited clinical evidence to date suggests a similar range of neuropsychiatric impairments as seen with other traumas (e.g., accidents, assaults). In many cases, TBI clearly resulted from secondary and/or tertiary blast injuries. The vulnerability of the human brain to primary blast injury is controversial and an area of active research.

TBI and VSP

- Cerebral posttraumatic VSP (PTV) was first described by Lorn in 1936.
- The incidence of CT documented traumatic SAH has been identified in 4% to 63% of pts after TBI.
- Study from the University of Mississippi Medical Center indicated that traumatic SAH complicate course of TBI in 69% of the patients due to the presence of PTV.

Clinical Significance

- 41% of patients who died from TBI had PTV (MacPherson et al., 1973).
- 24% with massive tSAH developed ischemic symptoms in contrast to 3% of patients with mild tSAH (Taneda et al., 1996).
- Ischemic symptoms accompanying arterial VSP following tSAH are comparable to those found following aneurysmal SAH.

WARTIME TRAUMATIC CEREBRAL VASOSPASM: RECENT REVIEW OF COMBAT CASUALTIES
Armonda et al., Neurosurgery, 2006

- The first study to analyze the effects of blast-related injury on the cerebral vasculature.
- This study showed that TCV occurred in a substantial number of patients with severe neurotrauma, and clinical outcomes were worse for those with this condition.
Clinical Material

- Ninety patients (2 females) aged 18 to 50 years (mean 25.9 years) who had suffered wartime TBI injuries (with Glasgow Coma Scale scores ranging from 3 to 15) were investigated with daily TCD studies.
- A total of 567 TCD studies (mean 6.4 tests/patient, ranged from 1 to 30) were made after admission.
TCD signs of Vasospasm (in %) by type of TBI

<table>
<thead>
<tr>
<th>TBI Type</th>
<th>Post TBI VSP (%)</th>
<th>High ICP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHI</td>
<td>13/14.4</td>
<td>12/13.3</td>
</tr>
<tr>
<td>CHI/IED</td>
<td>12/13.3</td>
<td>9/10</td>
</tr>
<tr>
<td>PHI</td>
<td>21/23.3</td>
<td>16/17.7</td>
</tr>
<tr>
<td>PHI/IED</td>
<td>11/12.2</td>
<td>12/13.3</td>
</tr>
<tr>
<td>Total</td>
<td>57/63.3</td>
<td>49/54.4</td>
</tr>
</tbody>
</table>

TCD signs of VSP & high ICP

Presence of ICH (%)

TCD AND TUMOR RESECTION
The occurrence of vasospasm and delayed cerebral ischemia after resection of intracranial tumor has not received extensive attention clinically, and is often misdiagnosed and improperly treated as surgical brain damage or brain swelling. However, DID from vasospasm after tumor resection is a complication that is being reported in increasing numbers.

Reports are sparse and mainly are case series. Vasospasm was found in 2% to 49% patients. No significant difference among age, sex, surgical approaches, pathological diagnosis, duration of surgery, amount of blood loss and transfusion during surgery were found, but significant difference was seen in cisternal hemorrhage on CT scan and the amount of blood in cerebrospinal fluid.

It is suggested that accumulation of blood in the basal cisterns may have been responsible for this unusual condition, and it is therefore important to consider vasospasm as a probable etiological cause of clinical deterioration in patients undergoing the surgical removal of a cerebral tumor. For this reason, whenever any neurological deterioration occurs in such patients, it is advisable to perform TCD in order to verify the presence of any vasospasm and promptly commence suitable treatment.

Surgery: To decrease the amount of blood in basal cistern by microsurgery


ICU: Differentiation of vasospasm from brain swelling are helpful to confirm the coexistent or causal relation based on neurological assessment, CT, TCD and ICP monitoring both in deciding therapeutic strategy and successfully controlling vasospasm.

ICU: Nimotop played a key role in preventing brain damage from vasospasm and cerebral swelling.
Role of TCD: Tumor Resection

- It is useful to perform TCD test after surgery and perform daily TCD studies when patient is in the ICU.
- The frequency with which TCD should be performed may be guided by patient clinical presentation, knowledge of risk factors for VSP, early clinical course.
- TCD studies should be performed after endovascular treatment to identify patients with recurrent VSP.

Role of TCD: SAH monitoring

- It is useful to perform TCD test on admission (or ASAP after surgery) and perform daily TCD studies when patient is in the ICU.
- The frequency with which TCD should be performed may be guided by patient clinical presentation, knowledge of risk factors for vasospasm, early clinical course.
- TCD studies should be performed after endovascular treatment to identify patients with recurrent vasospasm.

Role of TCD: SAH Monitoring

- The presence and temporal profile of CBFV’s in all available vessels must be detected and serially monitored.
- The pattern of CBFV’s elevation may indicate the need to follow patient carefully for evidence of deficits related to specific vascular territory.
- Waveform appearance either regionally, or globally may be clinically significant.
TCD and SAH

- Currently, the gold standard for vasospasm diagnosis is cerebral angiography, replaceable by CTA, only when angiography is not available. Obviously, it is not feasible to perform such investigation as frequently as bedside clinical assessment.
- Repeated clinical assessments of a patient's neurological status carry the problem of detecting the clinical signs and symptoms of vasospasm, which occur only after vasospasm has already manifested its deleterious effects on the cerebral parenchyma.
- TCD is a relatively new, non-invasive tool, allowing for bedside monitoring to determine CBFV’s indicative of changes in vascular diameter.

TCD can be useful pre-, intra- and post-operatively, while helping to recognize the development of cerebral vasospasm before the onset of its clinical effects.
- Vasospasm following SAH is a very important source of morbidity and mortality. Too often, the first sign is a neurologic deficit, which may be too late to reverse.
- TCD assists in the clinical decision-making regarding further diagnostic evaluation and therapeutic interventions. When performed in isolation, the contribution of TCD to improving patient outcome has not been established. Nevertheless, TCD has become a regularly employed tool in neurocritical care and perioperative settings.

TCD is a Critical Tool in Critical Care

- The value of TCD in clinical practice is well established, especially to measure and grade vasospasm following SAH and TBI.
- Based on AHA Guidelines and many years of clinical practice TCD is a tool employed by the Neurosurgeon, Neurointensivist and Neurologist in the management of vasospasm.
- Based on high frequency of posttraumatic vasospasm and intracranial hypertension TCD testing must be utilized for management of patients after SAH (aneurysm rupture, wartime or civilian TBI, tumor resection).

- The use of TCD at hospital admission allows identification of patients with brain hypoperfusion due to the vasospasm and/or intracranial hypertension. In such high-risk patients, early TCD goal-directed therapy can restore normal cerebral perfusion and might then potentially help in reducing the extent of secondary brain injury.
- TCD could provide information about abnormally high ICP/brain death.
- In the future incorporation of TCD data may facilitate more injury- and time-specific therapies for patients after SAH (aneurysm rupture, wartime or civilian TBI, tumor resection).
Do we know everything about TCD and vasospasm?

- TCD criteria for vasospasm for the young (less than 20-30 yo) and old (more than 68-70 yo) patients?
- CBFV calculation formula that will take into account Hct values
- Cerebral angiography could be negative but TCD could be positive for vasospasm
- TCD prediction for clinical vasospasm