TCD: Critical Tool in Critical Care

Alexander Razumovsky, PhD, FAHA

Presented for 40th American Society of Neuroimaging Annual Meeting

Disclosure

- I have the following financial interest or relationship to disclose:

  A. Razumovsky, PhD, FAHA is FTE for the private practice (Sentient NeuroCare Services, Inc.)

I hope someone is monitoring my brain...

Multimodality monitoring including clinical and laboratory evaluation, imaging, and continuous physiologic data is an important feature of NeuroCritical Care

Multimodality Monitoring

- MAP
- SaO2
- ECG
- Et-CO2
- CVP
- Urine output
- ICP
- CBFV/TCD
- PbO2
- cEEG
- CT/MRI perfusion
Neurocritical care depends, in part, on careful patient monitoring but as yet there are little data on what processes are the most important to monitor, how these should be monitored, and whether monitoring these processes is cost-effective and impacts outcome.

The use of monitoring modalities has become routine despite limited level I evidence to support their use. It is difficult to demonstrate that any single monitor or combination of monitors has a positive effect on outcome, since outcome is influenced by the therapeutic plan driven by monitoring, not by monitoring itself.

Small, randomized studies that focus on intermediate outcomes or biomarker outcomes seem to be a reasonable approach although careful observational studies can also help advance understanding of physiology.

Specific TCD Applications for Neuro-Critical Care

- Vasospasm diagnosis, monitoring and treatment effect evaluation after TBI, SAH, intracranial hemorrhage, tumor resection, etc.
- Acute stroke diagnosis, monitoring and treatment effect evaluation
- PFO screening for cryptogenic stroke and risk assessment
- Emboli and Fat emboli monitoring
- CE/A/CAS effect evaluation
- Neuroradiology test-occlusion (pre, during and post)
- Neuroradiology stenting (pre, during and post)
- Pre- and post-treatment AVM evaluation
- Septic patients evaluation
- Diagnosis and monitoring of intracranial hypertension
- Total cerebral circulation cessation/brain death clinical diagnosis confirmation

Role of TCD: Post SAH vasospasm

- 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.

- 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.

Role of TCD: Post SAH vasospasm
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 w/o 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’s range.

Role of TCD: Post SAH vasospasm

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.

Role of TCD: Post SAH vasospasm

TRAUMATIC BRAIN INJURY

TBI

Civilian
- Every 21 seconds, one person in the US sustains TBI

Battlefield
- Okie, NEJM, 2005: Among surviving soldiers wounded in combat in Iraq and Afghanistan, TBI appears to account for a larger proportion of casualties than it has in other recent U.S. wars. According to the Joint Theater Trauma Registry, 22% had injuries to the head, face, or neck.
TBI PATHOPHYSIOLOGY

Balancing Multisystem Interactions

TBI: Pathophysiology

Primary Injury:
- Contusions/Hemorrhages
- Diffuse Axonal Injury (DAI)

Secondary Injury (Intracranial) occurs hours to weeks/years after injury:
- Blood Flow and Metabolic Changes
- Cerebral Ischemia
- Traumatic Hematomas
- Hydrocephalus
- Cerebral Edema/Increased Intracranial Pressure/Herniation
- PTSD
Clinical Significance

- The reported incidence of traumatic vasospasm ranges from 19%–68%, the true incidence remains unknown due to variability in protocols for its detection (Kramer et al., 2013)
- Extrapolation of current data suggests that as many as 279,000 to 1.2 million patients a year may suffer from post-TBI vasospasm in the USA and 10,800 to 40,000 might experience a resultant clinical decline (W. Rutland-Brown et al, 2006)
- Ischemic symptoms accompanying arterial vasospasm following tSAH are comparable to those found following aneurysmal SAH

POST TBI VASOSPASM

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 posttraumatic cerebral vasospasm occurred in a substantial number of patients with severe neurotrauma, and clinical outcomes were worse for those with this condition

Cerebral Hemodynamic Changes After Wartime Traumatic Brain Injury
Razumovsky et al, Acta Neurochirurgica, 2013

- 90 patients with moderate to severe TBI were investigated with daily TCD studies and a comprehensive TCD protocol, and published diagnostic criteria for vasospasm and increased ICP were applied
- TCD signs of mild, moderate, and severe vasospasms were observed in 37%, 22%, and 12% of patients, respectively
- TCD signs of intracranial hypertension were recorded in 62.2%
- These findings demonstrate that cerebral arterial vasospasm and intracranial hypertension are frequent and significant complications of combat TBI; therefore, daily TCD monitoring is recommended for their recognition and subsequent management
Comparative Effectiveness of Neuroimaging on the Detection of TBI
DoD Report to Congress in 2011

- MRI, CT, SPECT, PET and TCD
- Relevant team of subjects matter experts were identified and 491 sources were recognized and reviewed
- In this Report only CT and TCD have *high clinical utility* for moderate and severe TBI

* "high clinical utility" indicates that the technique has high clinical applicability for a given severity of TBI

DISCLOSURE: I was not part of subject matter experts

A Review of the Effectiveness of Neuroimaging Modalities for the Detection of Traumatic Brain Injury
Amyot et al, J Neurotrauma, 2015

- CT, MRI, and TCD were determined to be the most useful modalities in the clinical setting, no single imaging modality proved sufficient for all patients due to the heterogeneity of TBI
- TCD is an important tool for monitoring the natural course of TBI, evaluating the effect of medical treatment or intervention, forecasting, and identifying high-risk patients after TBI
- Despite a lack of good prospective data on TCD evaluation and outcome in TBI patients, TCD as a noninvasive, inexpensive, and simple procedure that should be engaged in the daily management of TBI patients

DISCLOSURE: I was one of co-authors of this publication

Transcranial Doppler to Predict Neurologic Outcome after Mild to Moderate TBI
Bouzatt et al, 2016

- A prospective observational study across 17 sites. TCD was performed upon admission in 356 patients with GCS from 9 to 15 with mild lesions on CT. Normal TCD was defined as a PI of less than 1.25 and diastolic CBFV higher than 25 cm/s in the two MCAs. The primary endpoint was secondary neurologic deterioration on day 7
- Results: Twenty patients (6%) developed secondary neurologic deterioration within the first posttraumatic week. TCD thresholds had 80% sensitivity and 79% specificity to predict neurologic worsening. The NPV and PPV of TCD were 96% and 18%, respectively. In patients with mTBI (GCS, 14 to 15), the sensitivity and specificity of TCD were 91% and 80%, respectively. Patients with abnormal TCD on admission (24%, 86 patients) showed a more altered score for the disability rating scale on day 28 compared to those with normal TCD (257 patients).
- Conclusions: TCD measurements upon admission may provide additional information about neurologic outcome after mild to moderate traumatic brain injury. This technique could be useful for in-hospital triage in this context

Role of TCD: Post TBI vasospasm

- The incidence of vasospasm after TBI is similar to that following aneurysmal SAH but seems also could start later (up to 10 days) and be longer
- Because vasospasm is a significant event in a high proportion of patients after TBI, close TCD monitoring is recommended for the treatment of such patients
Role of TCD: Post TBI vasospasm

- Vasospasm following TBI 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
- As TCD-defined vasospasm preceded the neurological deficit in 64%, earlier intervention might reduce the incidence of vasospasm-related stroke in military or civilian hospitals with similar practice patterns

POST-TBI INTRACRANIAL HYPERTENSION

ICP Monitoring Methods

- IV catheter “Gold Standard”
  - Most invasive method
  - High infection rate
  - May be difficult to insert
  - Simultaneous CSF drainage and ICP monitoring not possible
- ED Probe
  - Limited accuracy
  - Relatively delicate
- SA Probe
  - Limited accuracy
  - High failure rate
  - Periodic flushing necessary

Typical morphology of TCD wave-form

- MCA (M1 and M2 segm)
- ICA (C1, C3 and C4 segm)
- ACA (A1 segm)
- PCA (P1, P2 segm)
- VA's and BA

- OA
  - High peripheral resistance/High PI
  - resistance/Low PI
TCD wave-form changes with development of intracranial hypertension
Moreno et al, 2000; Blerer et al, 2004; et al, 2005; Splavski et al, 2007; Melo et al, 2011; de Riva et al, 2012 and many, many others

Patient with GSW
Trend shows almost direct inverse relationship between CBFV and PI but epidural ICP values normal
Razumovsky et al, Neurosurgery, 2011

TCD and ICP
- Numerous data shows a highly significant correlation between TCD measured PI and ICP independent of intracranial pathology
- In patients with suspected increase in ICP or where an increased ICP has to be excluded, PI may be of guidance and repeated PI measurements might prove a useful tool in Emergency Room, Neurointensive care or out-patient settings

TCD PI in the management of TBI
- PI measurements permit the early identification of patients with low CPP/high ICP and great risk of cerebral ischemia
- In emergency situations it can be used alone when ICP monitoring is contraindicated or not readily available
Role of TCD: Intracranial hypertension evaluation

- TCD wave-form changes indicates abnormally high ICP, especially after 20 mm Hg
- TCD changes may alarm Neuro-ICU personnel and may indicate malfunctioning of ICP probe
- Abnormally globally decreased pattern of the CBFV’s in parallel with increased PI’s indicate onset of diffuse intracranial hypertension
- Sudden onset of asymmetrical CBFV’s and PI’s changes may indicate potential mid-line shift
- TCD quantitative and qualitative analysis must be taken into account for evaluation of intracranial hypertension, however, MAP, PaCO2 and cardiac output must be within the normal limits

Non-Invasive ICP monitoring would enable

- Triage at the point of contact
  - Battlefield, football field, ambulance, ER…
- In-time and evidence-based application of therapy
  - Titrate therapy to ICP targets
- Long-term monitoring
  - Without the risk of infection or damage to vital brain structures
- Expansion of patient pool for which monitoring might be beneficial
  - Mild and moderate TBI, migraines, pediatric patients,…

Role of TCD: Traumatic Brain Injury

- CBFV’s often increased in patients with TBI due to the posttraumatic vasospasm
- TCD waveform changes can signal significant ICP changes
- TCD is valid in predicting the patient’s outcome

PFO DIAGNOSIS: CONTRAST TCD OR CONTRAST TTE/TEE?
A MULTICENTER TRIAL ON PATENT FORAMEN OVALE (PFO) DETECTION: TRANSCRANIAL DOPPLER (TCD) VS TRANSESOPHAGEAL ECHO (TEE). TCD BETTER THAN TEE?

Vavlitou et al, 2010

- One hundred ICU patients
- The prevalence of PFO detected with TEE was 28% and with TCD 48%. There was no PFO detected with TEE and missed by TCD. TCD was more sensitive than TEE in detecting PFO of grade I (7 with TEE, 17 with TCD) and II (6 with TEE, 16 with TCD), while for grade III the two techniques had equal sensitivity (15 with TEE, 15 with TCD)
- The prevalence of PFO detected by TCD is very high in mechanically ventilated ICU patients and this may have important clinical implications. TCD is more sensitive than TEE in detecting a small PFO.

Accuracy of transcranial Doppler for the diagnosis of intracardiac right-to-left shunt: a bivariate meta-analysis of prospective studies

Mojadidi et al, JACC Cardiovasc Imaging, 2014

- A systematic review of Medline, the Cochrane Library, and Embase was done to look for all the prospective studies assessing intracardiac RLS using TCD compared with TEE as the reference; both tests were performed with a contrast agent and a maneuver to provoke RLS in all studies
- A total of 27 studies (29 comparisons) with 1,968 patients (mean age 47.8 ± 5.7 years; 51% male) fulfilled the inclusion criteria. The weighted mean sensitivity and specificity for TCD were 97% and 93%, respectively
- TCD is a reliable, noninvasive test with excellent diagnostic accuracies, making it a proficient test for detecting RLS
- If knowledge of the precise anatomy is required, then TEE can be obtained before scheduling a patient for transcatheter PFO closure.

Transcranial Doppler versus transthoracic echocardiography for the detection of patent foramen ovale in patients with cryptogenic cerebral ischemia: A systematic review and diagnostic test accuracy meta-analysis


- OBJECTIVE: PFO can be detected in up to 43% of patients with cryptogenic cerebral ischemia undergoing investigation with TEE. The diagnostic value of TTE in the detection of PFO in patients with cryptogenic ischemic stroke or transient ischemic attack has not been compared with that of TCD using a comprehensive meta-analytical approach
- METHODS: We performed a systematic literature review to identify all prospective observational studies of patients with cryptogenic cerebral ischemia that provided both sensitivity and specificity measures of TTE, TCD, or both compared to the gold standard of TEE
- RESULTS: Our literature search identified 35 eligible studies including 3,067 patients. The pooled sensitivity and specificity for TCD was 96.1% and 92.4%, whereas the respective measures for TTE were 45.1% and 99.6%. TTE was superior in terms of higher positive likelihood ratio values whereas TCD demonstrated lower negative likelihood values compared to TTE. Finally, the area under the summary receiver operating curve (AUC) was significantly greater (p < 0.001) in TCD compared to TTE studies
- INTERPRETATION: TCD is more sensitive but less specific compared to TTE for the detection of PFO in patients with cryptogenic cerebral ischemia. The overall diagnostic value of TCD appears superior, although TTE...

PFO Diagnosis: Contrast-TCD vs. c-TTE or c-TEE?

No such question any more!
**TCD and TEE**

- Bubble-TEE
  - Sedation
  - Not possible to perform in patients with swallowing difficulties
  - Involves many specialists, expensive equipment

- Global Fee $1,400.00

- Bubble-TCD is the cost-effective and minimally invasive compared to bubble-TEE
- Direct demonstration of embolism through a PFO to the cerebral circulation has been demonstrated

- Global Fee $219.00

---

**Consensus Statement**

*Cerebrovasc Dis, 2000*

A 4-level categorization was accepted according microemboli appearance using unilateral MCA monitoring:

1. No occurrence of microemboli
2. 1-10 microemboli
3. >10 microemboli but no curtain
4. curtain or shower where a single microemboli cannot be discriminated within the TCD spectrum

---

**Power M-Mode Transcranial Doppler for Diagnosis of Patent Foramen Ovale and Assessing Transcatheter Closure**

*Spencer at al., 2004*

- To grade RLS, a 6-level logarithmic scale was used for both resting and Valsalva injections as follows:
  - Grade 0 =0 ETs,
  - Grade I = 1-10 ETs,
  - Grade II = 11-30 ETs,
  - Grade III =31-100 ETs,
  - Grade IV = 101-300 ETs,
  - Grade V > 300 ETs.

---

**Factors influencing number of HITs**

- The numbers of HITs represented tracers of the conductance of RLS flow to the anterior circulation of the brain. The conductance takes into account many factors including:
  - The RLS flow distribution to the anterior circulation of the brain,
  - The size of the foramen while open
  - The right-to-left pressure gradient when the foramen is open.
- All HITs must be counted visually.
Differentiation of shunts?

- So far, no attempt made to differentiate pulmonary shunts from cardiac shunts with pmTCD
- Assumption is that HITS from a pulmonary capillary shunt would fall within grade I and that grades I and II may not be of sufficient conductance to justify closure
- If a pulmonary arteriovenous malformation (AVM) present, then it could be identified and located at catheterization
- Based on Spencer et al. (2004) data initially, patients with any positive grade of conductance were selected for closure. Later, it was realized that crossing the septum with the guide-wire in patients with grade I or II conductance was technically difficult. Thereafter, only patients who had grades higher than grade II were selected for catheterization

Case Report

- This is a 33-year-old-female that had an episode of slurred speech and a moderate headache lasting two minutes in March 2002. She complains of occasional dizziness and had a history of migraine with visual aura since her teenage years. We are asked to evaluate for the presence of a right to left cardiac/pulmonary shunt.
Fat Embolism Syndrome (FES)

- FES syndrome remains a potentially life-threatening complication of long bone fractures. The true incidence is difficult to assess as many cases remain undiagnosed.
- It varies from 0.5% to 30% of fractured patients with higher rates in multiply injured patients and presents a mean mortality rate of 10%.
- Manifests 24-72 hours post injury.
- Cerebral involvement varies from confusion to encephalopathy with coma and seizures. Clinical symptoms and CT are not always diagnostic, while MRI is more sensitive in the detection of a suspected brain embolism.

Epidemiology

- United States
  Frequency is estimated to be 3-4%. Fat embolism is a clinical diagnosis. Many patients are likely to have a missed diagnosis because of subclinical illness or confounding injury or illness.
- Mortality/Morbidity
  The mortality rate of fat embolism is 10-20%. Patients with increased age, multiple underlying medical problems, and/or decreased physiologic reserves have worse outcomes than other patients.

FES and PFO

- The presence or the reopening of a PFO due to pulmonary hypertension is associated with an increased risk for systemic manifestations of FES.
- TCD is the unique standard for evaluation of emboli.
- Bubble-TCD is more accurate for evaluation of PFO compared to bubble-TTE and bubble-TTE.
The use of TCD at hospital admission allows identification of patients with brain hypoperfusion due to the stroke, vasospasm after SAH/TBI 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 represent effective tool to monitor effects of treatment and interventions.

Detect a Change from Baseline/Normal Values Early in the Course of Illness and Before Irreversible Damage Occurs.

Contributes to the pharmacological management, further diagnostic testing and/or interventional treatment.

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 and/or hypoperfusion or hyperperfusion.

Based on high frequency of posttraumatic vasospasm and intracranial hypertension TCD testing must be utilized for management of patients after moderate to severe TBI.

TCD is a Critical Tool in Critical Care

Clinical Value of TCD for Critical Care

TCD is a Critical Tool (Quantitative Biomarker) in Critical Care

MULTIPLE PERSPECTIVES
FUTURE DEVELOPMENTS

New Developments

HeadSense Medical, Ltd, Israel

NeuroChaos Solutions, USA

Changes in the multiscale complexity of the dynamics of CBFV may indicate an abnormal state of the brain.

RapidICP takes TCD to the next level by leveraging advanced waveform analytics and a patient database for machine learning.

TCD Advantages

- Rapid assessment of cerebral vasculature, provides physiological and hemodynamics data
- Quantitative
- Repeatable
- Changes often precede clinical symptoms
- Changes precede angiographic narrowing

From Lundberg ICP:
Computational Physiology and Modeling ICP
From Kashif et al. Sci Transl Med, 2012
**TCD Advantages**

- No contraindications
- Portable
- Non-invasive
- Safe and not painful
- Cost-effective alternative to neuroimaging choices

**TCD “Disadvantages”**

- Operator dependent: *Myth*
- N. American medicine relies on imaging very broadly vs. interpretation: *True*
- Neuroimaging overutilization: *True and need*
- Absence of structured teaching: *True*
- Absence of credentials for sonographers who are doing TCD exams: *work in process*

**Questions?**

arazumovsky@sentientmedical.com