TCD and Brain Death/Total Cerebral Circulatory Arrest

Alexander Razumovsky, PhD, FAHA

Presented for 40th American Society of Neuroimaging Annual Meeting

Cerebral Ischemia Duration

CEREBRAL CIRCULATORY ARREST

- CPP = MAP – ICP
- Normal ICP = 8-12 mmHg
- ICP↑ = DAP
- ICP↑↑ > SAP --- Cerebral perfusion will cease
- CBF↓ = ICP↑ > 35 mmHg – 45 mmHg
  Stop CBF > 50 mmHg

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.)
TCD AND CIRCULATORY ARREST

• CORRELATION BETWEEN CPP AND TCD WAVEFORM
• SPECIFIC TCD PATTERN FOR CEREBRAL CIRCULATION ARREST
• SENSITIVITY 96.5%, SPECIFICITY 100%
• ADDITIONAL TOOL FOR THE ASSESSMENT OF BRAIN DEATH

HISTORICAL BACKGROUND

Andreas Vesalius (1514-1564)

• Madrid, 1565
• Anatomist
• At autopsy: thorax opened → heart beating!
• Forced to leave Spain

Little bit more history…

• Mollaret et Goulon “Le Coma Depasse”
• Harvard Medical School Ad Hoc Committee
• Royal Medical Colleges Conference in UK
• Presidential commission for ethical problems in 1981
• American Academy of Neurology in 1995
Little bit more history…

• The Uniform Determination of Death Act was adopted as part of the President's Commission report in 1981
• The Uniform Determination of Death Act provided the legal articulation of the whole-brain criterion of death as "irreversible cessation of all functions of the brain, including the brainstem"

BRAIN DEATH: Definition

• An individual is dead if he/she has sustained either:
  (1) irreversible cessation of circulatory and respiratory functions, or
  (2) irreversible cessation of all functions of the entire brain, including the brainstem.

Brain Death

• CLINICAL CRITERIA: COMA, APNOEA, ABSENSE OF BRAINSTEM REFLEXES
• CONFIRMATORY TESTS: ANGIOGRAPHY, EEG, PET, TCD

However...

• Several case reports of brain dead patients maintained for weeks even years in one case
Brain Death Mimics Must Be Excluded

- Deep Hypothermia
- Acute poisoning
- Acute metabolic encephalopathies
- Locked-in syndrome
- Guillain-Barre syndrome

A Case Meeting Clinical Brain Death Criteria with Residual Cerebral Perfusion
Ala et al, AJNR, 2006

- A 49-year-old man presented to our institution following cardiac arrest after a seizure. He was resuscitated in the field, with the total duration of asystole estimated to be 5 min. Results of urine toxicology and alcohol screens were negative. His CSF analysis was non-diagnostic. EEG on day 1 and 3 showed low amplitude delta slowing w/o focality, paroxysmal activity, or interval change. A head MRI on day 2 showed bilateral basal ganglionic and medial temporal lobe lesions consistent with a hypoxic-ischemic injury. He never awakened; and after an initial recovery of brain stem reflexes and respiratory effort, during the following days, he progressively lost neurologic function.

- On day 5, a brain death examination was performed. His pupils were nonreactive at 4-mm diameter, and there were no corneal, cough, or gag reflexes and no ocular reflexes to either head movement or to 50 mL of ice water in each ear. He had no respiratory effort during an apnea test with a PaCO₂ of 72 mm Hg. No movements were elicited by nail-bed pressure, sternal rubbing, or supraorbital pressure. The examination was recorded as being consistent with clinical brain death.

- Five hours later, a nurse reported that sternal rubbing would elicit movements of the arms, legs, head, and back. Upon the request of the organ donation personnel, a cerebral perfusion scintigraphy single-photon emission CT (SPECT) scan was ordered to confirm brain death, consistent with the policies of our institution. The CBF study unexpectedly demonstrated prominent hemispheric perfusion, and organ donation plans were suspended.

A Case Meeting Clinical Brain Death Criteria with Residual Cerebral Perfusion
Ala et al, AJNR, 2006

- On day 6, his examination continued to show no brain stem function. During several sternal rubs, the patient’s head turned to the left and his left arm rose slightly off the bed, flexed at the elbow approximately 15°, and tremored for several seconds. No other movements were observed. No further CBF, EEG, or head imaging studies were performed upon the request of the patient’s family. Later that day the patient’s heart was noted to be in asystole. Permission for autopsy was not obtained.

- With the exception of the CBF study, the patient’s examination on day 5 was consistent with many accepted criteria for the clinical diagnosis of brain death—for example, those defined by the AAN. Coma, absence of brain stem reflexes, and apnea were documented, and the required prerequisites were satisfied, including neuroimaging evidence of an acute-central nervous system catastrophe, the exclusion of complicating medical conditions, and a core temperature of 32°C.

The dissociation between clinical brain death and CBF

- On day 6, his examination continued to show no brain stem function. During several sternal rubs, the patient’s head turned to the left and his left arm rose slightly off the bed, flexed at the elbow approximately 15°, and tremored for several seconds. No other movements were observed. No further CBF, EEG, or head imaging studies were performed upon the request of the patient’s family. Later that day the patient’s heart was noted to be in asystole. Permission for autopsy was not obtained.

- With the exception of the CBF study, the patient’s examination on day 5 was consistent with many accepted criteria for the clinical diagnosis of brain death—for example, those defined by the AAN. Coma, absence of brain stem reflexes, and apnea were documented, and the required prerequisites were satisfied, including neuroimaging evidence of an acute-central nervous system catastrophe, the exclusion of complicating medical conditions, and a core temperature of 32°C.
False Positive CTA in Brain Death
Greer et al, Neurocritical Care, 2009

- Ancillary testing is frequently required in the determination of death by brain criteria, particularly in cases in which the clinical examination is drawn into question. Newer tests, such as CTA, have garnered enthusiasm for their ease of performance, but have not been validated as acceptable tests compared with a gold standard.
- A case of a 31-year-old patient who was felt to have cerebral circulatory arrest on CTA, but was subsequently found to have evidence of preserved CBFV on TCD, thus precluding the diagnosis death by brain criteria.
- CTA is not a validated confirmatory test for cerebral circulatory arrest in brain death, and may be falsely positive.
- CTA should be studied further in comparison to validated tests, such as conventional angiography or SPECT, before being accepted as a standard ancillary test in determining death by brain criteria.

Pitfalls in brain death diagnosis: case report.
Ruess et al, 2012

- Although there are distinct guidelines in nearly all countries, a reliable secure assessment of brain death in cases with open head injury can be challenging.
- The authors present a case of a 32-year-old man with severe TBI after intracranial penetration of a grindstone fragment. As the injury led to destruction of nearly the whole greater wing of the right sphenoid bone and parts of the right orbit, the examination of brainstem reflexes and the confirmation of brain death was unfeasible.
- On day 2, all clinical criteria of brain death (coma, absence of brainstem reflexes, apnea) were fulfilled. In addition, there was an extinction of BAEP and cerebral (N20) components of median nerve SSEP, while EEG activity was still present. In the following days, a persisting EEG activity was obtained. Thus, an irreversible loss of whole brain functions could not be proved.

Pitfalls in brain death diagnosis: case report.
Ruess et al, 2012

- Although there are distinct guidelines in nearly all countries, a reliable secure assessment of brain death in cases with open head injury can be challenging.
- The authors present a case of a 32-year-old man with severe TBI. As the injury led to destruction of nearly the whole greater wing of the right sphenoid bone and parts of the right orbit, the examination of brainstem reflexes and the confirmation of brain death was unfeasible.
- On day 2, all clinical criteria of brain death (coma, absence of brainstem reflexes, apnea) were fulfilled. In addition, there was an extinction of BAEP and cerebral (N20) components of median nerve SSEP, while EEG activity was still present. In the following days, a persisting EEG activity was obtained. Thus, an irreversible loss of whole brain functions could not be proved.

Clinical Brain Death with False Positive Radionuclide Cerebral Perfusion Scans
Venkatram S et al, 2015

- Neurological determination of brain death is primarily based on clinical examination; if clinical criteria are met, a definitive confirmatory test is indicated. The apnea test remains the gold standard for confirmation.
- In patients with factors that confound the clinical determination or when apnea tests cannot safely be performed, an ancillary test is required to confirm brain death.
- Radionuclide studies are used most commonly. Two patients with a false positive Radionuclide Cerebral Perfusion
Diagnostic Accuracy of Transcranial Doppler for Brain Death Confirmation: Systematic Review and Meta-Analysis


- Case series studies have generally reported good correlations between TCD confirmation of cerebral circulatory arrest and clinical confirmation of brain death. The purpose of this study is to evaluate the utility of TCD as an ancillary test in brain death confirmation.
- MATERIALS AND METHODS: A systematic review of the literature and a diagnostic test accuracy meta-analysis to compare the sensitivity and specificity of TCD confirmation of cerebral circulatory arrest, by using clinical confirmation of brain death as the criterion standard.
- RESULTS: We identified 22 eligible studies (1671 patients total), dating from 1987 to 2014. Pooled sensitivity and specificity estimates from 12 study protocols that reported data for the calculation of both values were 0.90 (95% CI, 0.87-0.92) and 0.98 (95% CI, 0.96-0.99), respectively.
- CONCLUSIONS: The results of this meta-analysis suggest that TCD is a highly accurate ancillary test for brain death confirmation. However, TCD evaluates cerebral circulatory arrest rather than brain stem function, and this limitation needs to be taken into account when interpreting the results of this meta-analysis.

Potential Pitfalls

Adopted from Walter U et al, Ultraschall in Med, 2016

- Primarily undetectable flow signals must not be interpreted on their own as proof of cerebral circulatory arrest.
- False-negative findings may be obtained in the case of larger skull bone defects, or in infants with a fontanel that is still open.
- Pronounced tachycardia (e.g. tachyarrhythmia, sinus tachycardia > 120/min) may simulate remaining flow due to the overlap of pulse waves.
- Pronounced bradycardia may extend the duration of systolic spikes to more than 200 ms which precludes their use for diagnosing cerebral circulatory arrest according to the guidelines of the German Medical Association.
- Incidentally detected weakly pulsatile intracranial venous flow signals may result in false-negative findings (supposed arterial cerebral blood flow).
- Artifacts or flow changes due to intra-aortic balloon pump (IABP), extracorporeal membrane oxygenation (ECMO), or mechanical ventilation may make it difficult to interpret sonographic findings.
- TCD test must be repeated in 30 minutes to confirm first test results as a cessation of cerebral blood flow.

Doppler and Duplex Sonography for the Diagnosis of the Irreversible Cessation of Brain Function (“Brain Death”): Current Guidelines in Germany and Neighboring Countries

Walter U et al, Ultraschall in Med, 2016

- After EEG, TCD and TCCS are the most commonly used ancillary methods worldwide and regardless of geographical region.
- TCD is even mandatory in 5% of countries but is used optionally in the USA.
- In Germany, TCD is the most frequently used method for determining cerebral circulatory arrest, ahead of CTA and selective DSA.
- TCD of only the bilateral MCAs and the BA is required in Holland, Poland, and Latin America in agreement with the recommendation of a N. American group of experts*; while bilateral examination of the MCA, ICA, and VA is required in Germany, Austria, the Czech Republic, and Japan (with additional examination of the BA being required in the Czech Republic).

TCD wave form progression from intact CBFV to circulatory arrest

Hassler et al., 1988

TCD CBFV changes with ICP changes
Lovrencic-Huzjan, 2012

Transcranial Doppler sonography
Hemodynamic changes in MCA during ICP increase

“TO-AND- FRO”

American Society of Neuroimaging 40th Annual Meeting

TCD wave form progression from intact CBFV to circulatory arrest

American Society of Neuroimaging 40th Annual Meeting
TCD pattern in Brain Death

low CPP = 0

American Society of Neuroimaging
40th Annual Meeting

Brain Death Pattern: Phase I

Low Diastolic CBFV: A rapid sharp peak of the TCD waveform takes place during systole, followed by a rapid decline to EDV to near zero. Anterograde flow is present throughout the entire cardiac cycle, and no evidence of retrograde flow exists. This pattern is associated with increasing ICP and preserved cerebral perfusion and may be reversible. Low EDV corresponds diminished CPP gradient as ICP approaches diastolic blood pressure.

American Society of Neuroimaging
40th Annual Meeting

Brain Death Pattern: Phase II

- **Systolic peak**: Only systolic CBFV is detected. A sharp peak in the waveform which may last through the entire cardiac cycle, is seen. No diastolic blood flow is present. This pattern may be still reversible if it is associated with treatable ICP elevation.

American Society of Neuroimaging
40th Annual Meeting

Brain Death Pattern: Phase III

**Oscillating Blood Flow/To-and-Fro movement**: Anterograde short systolic peaks/spikes alternate with brief, normal or sharply contoured, retrograde EDV. With careful measurements of CBFV in both directions, a net zero velocity may be calculated. This pattern of flow may be reversible if it is associated with reversible ICP elevations. The corresponding angiographic finding is delayed, tapered filling of the basal cerebral arteries.

American Society of Neuroimaging
40th Annual Meeting
Brain Death Pattern: Phase IV

**Short Systolic Spikes:**
The only detectable signals are brief anterograde spikes in the waveform that last for a brief portion of the cardiac cycle (as opposed to systolic peaks, which are longer). These are associated with the absence of cerebral blood flow, as angiography demonstrates cessation of flow in the cavernous or petrous portion of the ICA and stasis of flow in the proximal VB system.

Brain Death Pattern: Phase V

- **Absence of TCD signal:**
  No intracranial TCD signal is detectable. Oscillating blood flow in the extracranial ICA is usually detectable with submandibular insonation. This pattern, or actually absence of any pattern, has been associated with extracranial angiographic arrest of flow in all vessels. Use of the absence of TCD signal to confirm intracranial circulatory arrest should be restricted to patients who previously have had demonstrated TCD waveforms. Otherwise, the absence of TCD signal could be result of a thickened skull and inadequate cranial windows.

**CT-scan in patient with clinical diagnosis of brain death**

**Brain Death. Initial flow images show minimal radiotracer activity in the region of the brain which may represent brain activity versus scalp activity (i/v inj. of TC 99 DTPA)**
TCD study in patient with clinical diagnosis of brain death

TCD pattern in patient with brain stem stroke

Guidelines for the use of TCD as confirmatory test of brain death

- The cause of coma has been established
- Intoxication, hypothermia, severe arterial hypotension, metabolic disorders and others have been excluded
- Clinical evaluation by experienced examiners shows no evidence of cerebral and brainstem function

"The monitors all show that you're dead... but to be sure, we'll need to run some more tests."
Questions?
arazumovsky@sentientmedical.com