Ancillary Testing in Death

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I received research funding for research related to the use of ancillary testing in death by:

- Canadian Institute for Health Research

I have collaborations with:

- Canadian Blood Services
- Trillium Gift of Life
- Transplant Québec
- Canadian National Transplantation Research Program
Learning objectives

- Review the current Canadian recommendations for ancillary testing in death.
- Review the principal challenges associated with ancillary testing in the neurological determination of death.
- Understand the limitations of the current evidence regarding ancillary testing in the neurological determination of death.
Clinical scenario

- ♀48
- Found unresponsive beside 2 empty bottles of nortryptilline
- ROSC 10 minutes CPR
- Usual post CPR care and 3 days clinical observation

Day 4:
- Clinical NDD: consistent with brain death (including apnea test)

Day 5:
- Second clinical exam by independent physician
- Concerns of confounding → CT-angio ordered
Why use ancillary tests for NDD?

- Clinical diagnosis is impossible
  - e.g. Severe facial trauma

- Confounding factor exists
  - e.g. Drug intoxication
Which test should I use?

- Two “Categories” of ancillary tests
  - Brain blood flow (not about “activity”)
    - Conventional 4-vessel angio
    - CT-Angio
    - Nuclear Angio
    - MRI angio...
  - Brain “activity” (so-called neurophysiological tests)
    - EEG
    - Evoked potentials
Practice variations (USA)

Figure 4: Apnea testing: Compliance with American Academy of Neurology guidelines (%)

- Absence of respirations: 87%
- Final pCO2: 87%
- Pre-oxygenation: 76%
- Stop if unstable: 71%
- ABG prior to test: 50%
- Use of supPI O2: 55%
- Hypotension, desat and anhydremia: 49%
- pCO2 rise above baseline: 39%
- Repeat if inconclusive: 16%

Relatively poor compliance with American Academy of Neurology guidelines was seen in the category of apnea testing. Discrepancies occurred in the performance of the testing, the values to be obtained, and the procedures in case of instability or inconclusiveness.

Table 2: Ancillary tests performed and specifics of testing

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<tr>
<th>Tests</th>
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<td>Atropine challenge</td>
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<td>Mean arterial pressure – intracranial pressure for 30 minutes</td>
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</table>
Practice variations (Spain)

- 42 ICUs
- 5% clinical Dx only
- 95% with ancillary test
  - 71% EEG
  - 35% TCD
  - 7.4% Nuclear angio
  - 2.4% CT-Angio
  - 0.5% 4-vessel angio

![Diagram showing practice variations and clinical decision-making processes.]

*Anaesthesia 2015, 70, 1130–1139*
Recommended tests (Canadian consensus)

- Radionuclide angiography
- CT-angio
- Conventional 4-vessel angio
- MR-Angio or Xenon CT
- CT-perfusion
- MR perfusion
- Transcranial Doppler
- EEG
- Evoked potentials

**Brain Blood Flow in the Neurological Determination of Death: Canadian Expert Report**

Sam D. Shemie, Donald Lee, Michael Sharpe, Donatella Tampieri and Bryan Young, on behalf of the Participants in the Expert Consensus Meeting on Brain Blood Flow in the Neurological Determination of Death. Endorsed by the Canadian Critical Care Society
Diagnostic criteria
(In Canada)

Current expert consensus:
- Must show absence of brain blood flow in cerebral hemispheres and posterior fossa structures:
  - basilar
  - middle cerebral
  - anterior cerebral and
  - posterior cerebral arteries
- Intracranial ≠ Intracerebral
- Surface of the brain


Sam D. Shemie, Donald Lee, Michael Sharpe, Donatella Tampieri and Bryan Young, on behalf of the Participants in the Expert Consensus Meeting on Brain Blood Flow in the Neurological Determination of Death. Endorsed by the Canadian Critical Care Society
The ideal test should:

- No false-positives
- Readily available
- Rapid
- Safe
- Portable
- Non-invasive
- Inexpensive
- Independently sufficient to establish brain death
- Not susceptible to external/internal confounding factors
- Standardized in technology, technique, and classification of results
Challenges

1) How accurate are the tests?

2) Are these tests helpful in “isolated brainstem death”?

3) Residual blood flow?
1) Can currently recommended ancillary tests incorrectly classify a patient as brain dead when in fact not brain dead? (False Positive)

2) Can currently recommended ancillary tests incorrectly classify a patient as NOT brain dead when in fact brain dead? (False Negative)
### 4-vessel angio vs clinical Dx

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Chassé et al. Unpublished data
Nuclear scan vs clinical Dx

Chassé & al. Unpublished data
Accuracy

When using ancillary tests, one has to consider that:

- No test has been validated to confirm “not brain dead”
- Should therefore not be used when high suspicion of “not dead”

What they CAN do:

- Support a high clinical suspicion of brain death
- With an increased risk of “false negative”
Isolated brainstem death

- Clinical exam can’t differentiate between “whole brain death” and “isolated brainstem death”

- Situations can occur when “isolated brainstem death” is suspected

  - How to consider those patients with clinical “brainstem death” but presence of blood flow in the anterior circulation after ancillary test?
Isolated brainstem death

- Clinical diagnosis:
  - “Irreversible loss of all brain stem functions”

CMAJ 2006; 174: S1-30

- Determination after ancillary testing
  - “Cases of complete and irreversible loss of brainstem function [...] ancillary testing is performed, brain blood flow to supratentorial regions may be present thus negating the determination of death by neurological criteria”

Brain death is a “concept” and is defined by the medical community:

In all Canadian provinces and territories, the legal definition of brain death is “according to medical standards”.

Is it medical standard to declare “dead” a patient with blood flow in the anterior circulation only?

No test has been validated to confirm “brainstem death”.

CMAJ 2006; 174: S1-30
Residual blood flow?

Every clinician who orders ancillary tests will someday be faced with this dilemma...

- What is “significant blood flow”? 
What would you do?

1. Repeat the test?
2. Do a different test?
3. Declare dead?
Need for more studies

- Future research should:
  - Prospectively validate in human
    - The absence of flow in clinically brain dead patients with no confounding factors
    - Presence of flow in non-brain-dead patients that are neurologically severely injured
  - Application of novel potential ancillary tests should not be used in practice before appropriate validation?
  - Is there a role for more/less ancillary testing?
- Future expert/society consensus (maybe not a matter of scientific research)
  - What is “significant residual blood flow?”
  - What to do with “isolated brainstem death”?
Conclusions

- There are currently no perfect/robust ancillary test for NDD
  - Brain blood flow tests, when used, can “support” brain death in patients with an a priori high suspicion
    - Hence the need to perform an as complete as possible clinical exam
  - Not validated in lower likelihood populations
    - How would the tests perform in deeply comatose non-BD patients?

- Numerous challenges remain
  - Be ready for what you may encounter when ordering one
The “confirmatory” tests do not confirm anything. Brain death is synonymous with a certain clinical state and a certain set of findings (coma, apnea, and no brainstem reflexes in the absence of confounders) and no prototypical neuropathologic substrate exists.

Wijdicks 2010: A case against confirmatory tests

If this is the case, why can’t that “clinical state” be extended to include an accurately validated paraclinic definition?

Thank you!