

Landscape of Adult Neuropsychological Assessment White Oak Conference

Ralph J. Petrucci, Ed.D.
Psychiatry and Medicine
Neuropsychology
Drexel University College of Medicine
Philadelphia, PA



Disclosure statement

Title- Landscape of Adult Neuropsychological Assessments

I will not discuss off label use of devices
Neuropsychological consultant:

Thoratec Corporation

FDA- Circulator Device and
Neurologic Device Panels

I have no financial investments in devices

Current FDA LVAD approvals #1

Slaughter et al. 3/10

- Pulsatile flow: 4 of 6

	<u>Type</u>	<u>Approval</u>
– HeartMate XVE	LVAD	BTT, DT
– Thoratec PVAD	Bi/Uni	PC*, BTT
– Thoratec IVAD	Bi/Uni	PC, BTT
– Excor	Bi/Uni	
– MEDOS VAD	Bi/Uni	
– CardioWest	TAH	BTT

* post-cardiotomy

Current FDA LVAD approvals #2

Slaughter et al. 3/10

- Continuous flow (Axial): 3 of 5

	<u>Type</u>	<u>Approval</u>
– HeartMate II	LVAD	BTT, DT
– Jarvik 2000	LVAD	IDE*, ongoing BTT
– Heart Assist 5	LVAD	IDE, ongoing BTT
– Incor	LVAD	
– Synergy	LVAD	

* invest. device exemption trial

Current FDA LVAD approvals #3

Slaughter et al. 3/10

- Continuous flow (Centrifugal): 0 of 4

	<u>Type</u>	<u>Approval</u>
– HVAD HeartWare	LVAD	IDE*, ongoing BTT
– DuraHeart	LVAD	IDE, ongoing BTT
– Levacor VAD	LVAD	IDE, ongoing BTT
– EVAHEART	LVAD	IDE for BTT

* invest. device exemption trial

Improving device technology

- Pulsatile

Limited by body size

Pump and drive line durability

Complications with high stroke & infection rates

- Continuous flow

Some pumps are smaller for pediatric application

Pump and drive line durability improving

Complications lower with stroke & infection rates

Trials

REMATCH trial NEJM 2001

- 129 pts Class IV HF randomized
- Neuro Events
 - 3% - OMT
 - 33% - LVAD

INTRPID trial J Am Coll of Card 2007

- 55 pts inotrope dependent non-randomized
- Neuro Events
 - 11% - OMT
 - 62% - LVAD

Exposure

Drexel

- 170 VADS over 2 decades
 - Novacor, AbioMed, AbioCore, Thoratec
- Using NC measures bedside & office
- Training students to use NC tests

Thoratec

- 200 pts in the BTT and DT trials

Early background

2003 - FDA established a Guidance Panel to provide suggestions for Industry and FDA reviewers re: Neurologic and Neurocognitive assessment for VADs

FDA Guidance premise

- Tests to be selected by each medical center
- Did not have to be administered by Neurologist or Neuropsychologist
- Administered pre/post implant intervals
- Purpose for longitudinal information
- Designed for inpatient application

FDA Guidance suggestions

- Cognitive tests not used for VAD selection
- Acknowledge copyright materials
- Involve IRB approval with expedited process
- Establish inter/intra center reliability
- Offer training certification
- Monitor training of additional staff
- Work would be submitted for publication

Neurocognitive assessment

- Administered in less than one hour
- Bedside or office
- Maintain quality control for administration with NC core lab
- Use standardized psychometrics
- Survey 5 cognitive domains:
 - memory, language, processing speed, visual/ spatial perception & abstract/ executive functions

Establish registry

- NHLBI/CMS/FDA- INTERMACS
NC tool –Trail Making B
Liked by Industry, CT surgery and
Cardiology
Poor for adequate cognitive survey
- Pediatric HT Study database (PHTS)
Mechanical support (VADs, ECMO, IABP)
Age appropriate domains: sensory-motor, language,
visual-spatial ability, acad. achievement and
adaptive behavior

Suggestions for Multi-center training

- Identify high, medium & low volume centers
- All centers initially trained together at central location
- Introduce and familiarize measures
- Participants given opportunity to practice
- Provide film of test administration- DVD
- Sites will require retraining due to personnel changes
- Establish core NC lab to monitor, score & maintain quality control

Lessons

Inherent problems with multiple centers

- Programs and staff do not remain stable
- Using other than Neuropsychologists (NP) for reasons of familiarity, inside availability and prompt responding presents issues
- NPs need immediate access to ICUs

Lessons

Inherent problems within centers

- NC exams in ICUs and telemetry units is challenging
- Scheduling out-pt NC revolves around labs, VO_2 , computer and drive line checks, etc.; NC often last in line
- NPs practice structure and billing guidelines may limit involvement

Lessons

Inherent issues with methodology- What is a significant NC decline?

1. Establishing a-priori confidence intervals, p-values and significant sd (1.0, 1.5, or 2.0)
2. Is it a decline of $\geq 20\%$ on tests?
3. Is it a decline of $\geq 20\%$ on 20% of tests?
4. Do you want to use an impairment ratio?

Lessons

Inherent issues with methodology- Sponsor perspective

1. Focus is on product performance therefore the pre- implant cognitive baseline may not be a primary concern for industry
2. Randomized criterion for pt enrollment fraught with challenges and may be ethically untenable
3. If randomization occurs length of blinded period an issue

Lessons

Inherent issues with methodology- NC perspective

1. Pre implant-

When to establishing a baseline?

Start measures within what time period?

Define “too sick” as a reason not to examine.

2. Post implant-

When to start f/u testing? (1 mo, 3 mo, etc.)

What are your intervals?

What is your time tolerance when skipping measures?

Lessons

Inherent issues with methodology- NC perspective

3. Repeated measures, i.e., test-retest & practice effect- use alternative measures
4. Sensitivity to:
 - degenerative disorders (adults)
 - development (children)
5. Few cohort norms available for comparison

Areas where we can move forward

1. Develop standard NC approach for devices.
2. Develop VAD removal, end-of life and palliative care plans.
3. Ethical issues with VAD availability widening and considering VAD self-care requires greater acumen:
 - a. Does everyone get a VAD?
 - b. How do we manage problem pts moving between centers?
 - c. Guidelines for vehicle operation?
 - d. In DT, what happens with dementia onset?

END

Neurocognitive tests

1. Clock drawing
2. WMS III logical memory (LM)
3. WMS III visual reproduction (VR)
4. WAIS-III block design
5. Boston Naming Test (abbreviated)
6. WAIS III digit symbol
7. Trail Making A & B
8. WMS III 30' delay LM & VR

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Continuous flow vs Pulsatile NEJM 2009

- 200 DT pts random 2:1
- Neuro Events
 - Cont Flow 17%
 - Pulsatile 14%

REVIVE-IT Trial (NHLBI) 7/10

RELIANCE Trail