TRANSCRANIAL DOPPLER ULTRASOUND IN EXTRACORPOREAL MEMBRANE OXYGENATION

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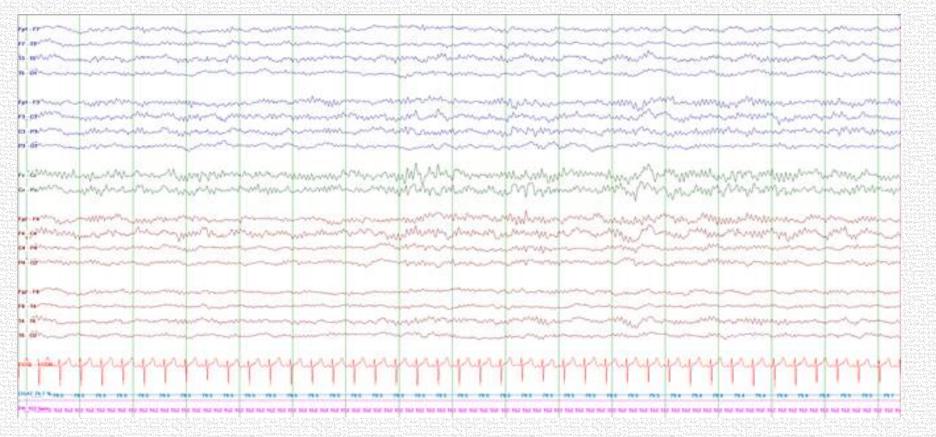
Case I

- 6 yr. old male no significant past medical history, admitted to PICU with decompensated shock; excessive heat exposure- Temp 107° F
 - Generalized Tonic Clonic Seizure
 - Altered Mental Status
 - Negative Head CT
- Severe hypotension in the face of three vasoactive agents
 - VA ECMO via neck cannulation through right carotid artery
 - CRRT initiated as evidence of AKI/failure

Case I

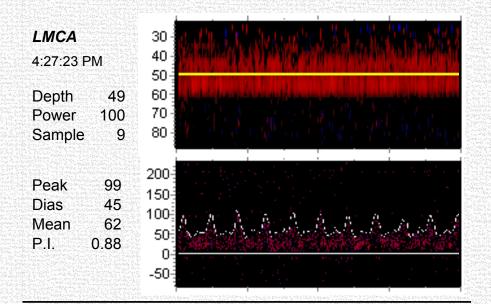
Neurologic monitoring

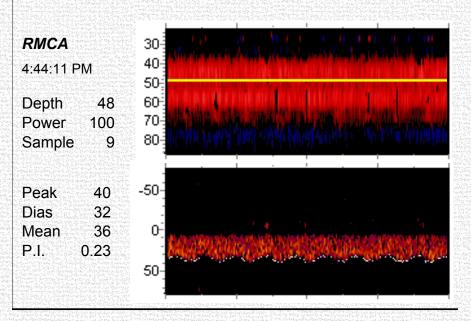
 cEEG: started day of cannulation with relatively nl EEG pattern with continuity and bilateral sleep spindles – indicative of intact corticothalamic function



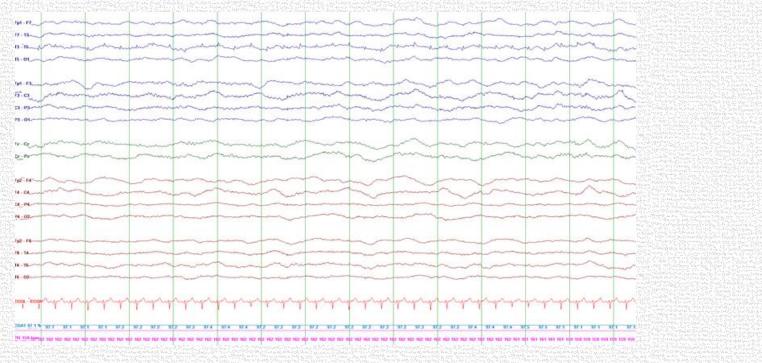
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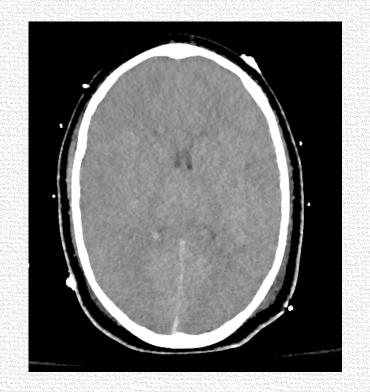
- TCD obtained within an hour of EEG
 - Pulsatile flow throughout the left MCA region; dampened waveforms over right MCA region with decreased mean flow velocities and low PI





- Change in EEG
- · Fixed and dilated pupils, diffuse global cerebral edema
- TCD: occlusion right MCA flow, loss collaterals

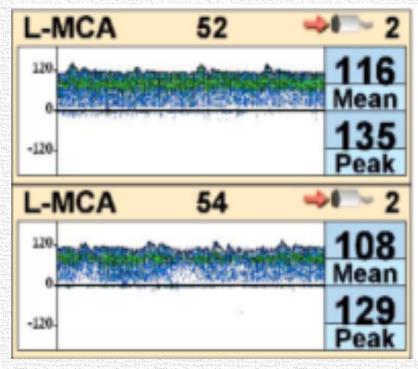


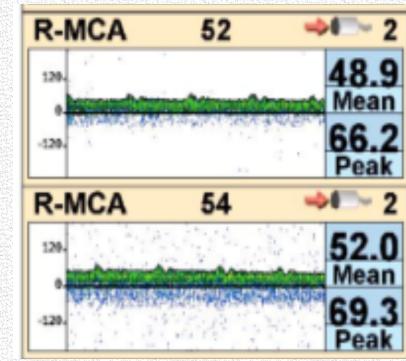


- 12 yr. old female, no past medical hx admitted PICU with Influenza B, fever, metabolic acidosis
 - Myocardial dysfunction: Myocarditis
 - Poor perfusion and hypotension : need vasoactive agent
- Day 2
 - Stable VT progressed to unstable VT: CPR
 - Emergency cannulation to VA ECMO: Femoral cannulation
 - NIRS upper 60's to low 70's

• TCD

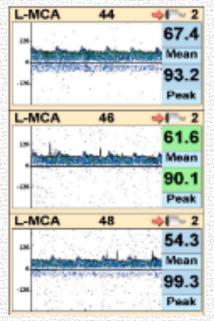
- Day 4 of cannulation: limited right UE movement
- Asymmetry: diminished wave forms, right side diminished velocities





• TCD

- Progressive increase pulsatile flow on serial TCD as improved myocardial output
- Day 8 acute drop in left MCA velocities
- Day 9 acute neurologic changes: fixed dilated left pupil, unresponsive
 - CT showing large left intracerebral hemorrhage

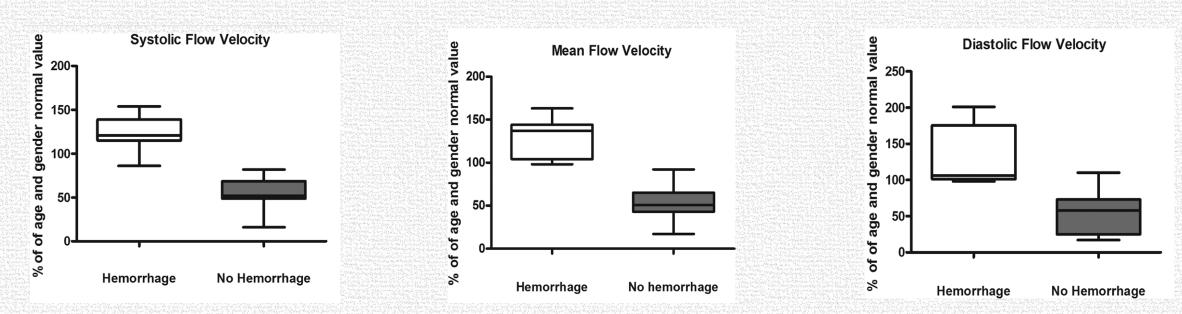




- O'Brien et al 2013
 - Determine impact of ECMO on cerebral blood flow velocities; whether specific changes indicative of acute neurologic insult (ANI) (N=18)
 - · Prospective observational study that compared TCD measurements: Vs, Vm, Vd, PI
 - Reported as % of age and gender normal values; compared children with/without ANI
 - TCDs obtained within 24hrs of cannulation then daily; post cannulation

- O'brien et al 2013
 - No ANI
 - · Relatively little day to day variability
 - CBFV in MCAs significantly reduced:
 - Vs 54% ± 3% predicted, Vm 52% ± 4% predicted
 - Flow velocities improved post cannulation but remained below age/gender norms
 - No statistical difference Vd
 - Location of cannulation
 - No impact on Vs or Vm
 - No significant right /left difference

- O'brien et al 2013
 - Those with ANI (N=4)
 - · All velocities elevated
 - Vs 123% ± 8% predicted, Vm 127% ± 9% predicted, Vd 130% ± 18% predicted
 - Supranormal CBFV noted 2-6 days prior to clinical findings; PI elevation 2-5 days
 - Lindegaard < 3: suggestive of hyperemia



- O'brien et al 2019
 - Prospective multicenter study (N=52)
 - Further understand expected measured TCD variables during VA ECMO; differences in those developing ANI
 - Similar study protocol to prior discussed
 - Velocities recorded as absolute values vs % of normal values; matched to critically ill, mechanically ventilated sedated children
 - ANI defined as development of electrographic seizures or radiographically confirmed diffuse cerebral ischemia or intracerebral hemorrhage

O'Brian NF, Buttram SD, Lovett ME et al. Cerebrovascular Physiology During Pediatric Extracorporeal Membrane Oxygenation: A Multicenter Study Using Transcranial Doppler Ultrasound. Pediatr Crit Care Med 2019; 20:178-186

Age

≤ 10 d

11-90 d

3–11.9 mo

1–2.9 yr

3–6.9 yr

7–9.9 yr

≥ 10 yr

TABLE 3. Mean (sp) Flow Velocities (cm/s) and Pulsatility Index in the Middle Cerebral Artery in a Cross-sectional Study of Children On Extracorporeal Membrane Oxygenation

Middle Cerebral Artery, Mean (sp)^a

Mean Flow Velocity

31 (8)

47 (4)

50(14)

48 (13)

54 (18)

63(11)

39(17)

Diastolic Flow Velocity

22 (7)

31 (17)

32 (13)

31 (12)

37 (17)

46 (12)

27 (14)

Pulsatility Index

0.87 (0.51)

0.85 (0.31)

1.02 (0.43)

1.19 (9.62)

0.89 (0.41)

0.71 (0.32)

1.06 (0.51)

Who Did Not Suffer Acute Neurologic Injury (n = 44)

6

11

9

5

4

2

7

Systolic Flow Velocity

47 (35)

67 (34)

82 (24)

84 (22)

82 (23

92 (16)

64 (23)

aValues represent means (sp) from days 1-9 of extracorporeal membrane oxygenation support.

O'brien (

No ANI

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 - 11/:
 - 7/5

• Differ

- Vs
- No Vd difference

Age	Number	MCA in mechanically ventilated, sedated child
Systolic flow velocity		
< 90 days	31	73 (21)
3-12 months	25	103 (24)
13-35 months	19	113 (32)
3-4 years	13	125 (28)
5-10 years (female)	12	87 (28)
5-10 years (male)	13	106 (26)
11-17 years (female)	12	115 (45)
11-17 years (male)	15	96 (25)
Mean flow velocity		
< 90 days	31	38 (14)
3-12 months	25	58 (15)
13-35 months	19	66 (21)
3-4 years	-13	75 (25)
5-10 years (female)	12	52 (18)
5-10 years (male)	13	62 (13)
11-17 years (female)	12	61 (21)
11-17 years (male)	15	58 (14)

- O'brien et al 2019
 - ANI (N=8)
 - All cerebral edema: 6/8 infants
 - No significant difference when comparing mean velocities with those without injury; no asymmetry
 - PI statistically higher p=0.006
 - 9mo and 10yr
 - Profound alterations in CBFVs day 1 with slow normalization
 - Right/Left asymmetry: 39% 9mo and 35% 10yr old
 - Study conclusions
 - MCA Vs, Vm, PI significantly lower first few days; greater than 30% asymmetry Vs common
 - · Elevated PI in infants may be marker for ANI

- Rilinger et al 2017
 - Characterize changes in TCDV during ECMO; determine if TCD could identify ANI
 - Combined retrospective/prospective study ages 0-18yrs
 - Prospective group: N=17
 - TCD every other day first week of cannulation and once post cannulation: total 5 studies
 - Daily/ qOD EEG, daily head ultrasound where age appropriate, neurologic exam, MRI prior D/C
 - Retrospective group: N=10
 - Medical records: ECMO patients with TCD studies
 - 10/39 (26%) met criteria

Rilinger JF, Smith CM, O.deRegnier RA et al. Transcranial Doppler Identification of Neurologic Injury during Pediatric Extracorporeal Membrane Oxygenation Therapy. J Stroke and Cerebrovascular Dis, Vol26, No10 (Oct), 2017:2336-2345

- Rilinger et al 2017
 - Results
 - TCD velocities/indices reported as means; compared norms healthy and critically ill age matched
 - Predominately VA runs (96%) with 70% neck cannulation
 - No children ages 3yr to 9.9 yrs.
 - Overall findings
 - MCA and ICA velocities lower compared to healthy and critically ill; ACA trended upwards and PCA no difference
 - Neonates: MCA and ACA velocities higher than norms healthy
 - Post cannulation: Vs, Vm, Vd significantly increased compared to cannulation, MCA most significant change
 - Asymmetry: RMCA Vs significantly lower (17% relative difference/p=0.02) PI lower (12%, p=0.003); RPCA significantly greater than left post cannulation

- Rilinger et al 2017
 - No significant association between velocity measurements and ANI
 - Prospective Data: 11/16 pts
 - 69% neurologic insult
 - Global velocity elevation 45% vs 40% in uninjured group
 - Case specific:
 - Pt bilateral strokes and left side seizures: asymmetry and bilateral elevation MCA and ACA
 - Pt right hemorrhagic stroke showed velocity increases all vessels 4 days prior to identified ANI

- Rilinger et al 2017
 - Conclusions
 - Striking age variability with neonates showing higher velocities, lower velocities in children
 - No statistically associated global TCDVs and ANI but based on case analysis regional velocity elevation may be indicator: focal changes may be more clinically useful
 - Suggested focal elevation and significant asymmetry in TCDV predictive of injury

- Salna et al 2019
 - Adult study
 - N=18, 49% via femoral artery/vein cannulation
 - TCD MCAs obtained x 1; median time 6 days
 - Primary interest MCA blood flow while on VA ECMO with neurologic complications secondary

Findings

- No significant difference R/L MCA velocities or PI based on site cannulation although mean flow velocities tended to be higher in the axillary group
- PI significantly lower in axillary group
- No ANI in femoral group; Ischemic stroke x 1 in the axillary group

Salna M, Ikegami H, Willey JZ et al. Transcranial Doppler is effective method in assessing cerebral blood flow patterns during peripheral venoarterial extracorporeal membrane oxygenation. J Card Surg 2019; 34:447-452

Conclusions/Points of Discussion

- What would be expected normal velocities indices in children receiving ECMO?
 - Current studies suggest lower than age/gender norms with exception of neonates
- What degree of asymmetry is expectable?
 - O'brien used >30% but saw higher % without CNS insult
 - MCA Vs and PI with significant asymmetry in Rilinger study but not associated with ANI
- What factors should we be using to suggest pending CNS insult?
 - Acute changes
 - Asymmetry
 - Focal differences

Does cannulation site have any impact on velocities and ANI ?