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| --- | --- | --- | --- | --- |
|  | **N** | **Measured Outcome** | **TCD Measurements** | **Comments** |
| **PEDIATRIC PATIENTS** |
| Lovett ME et al., 2018 [1]  | 26 | GOS-E Ped at 3 months* GOS ≤ 4 (good): 13 (50%)
* GOS ≥ 5 (poor): 13 (50%)
 | **Outcome** | **Day 0 (< 24 hrs)** | **Day 2 (72 hrs)** | **Day 4 (120 hrs** | * Poor outcome group had more extreme MFVMCA (> or < 2SDs); good outcome group spent more time with MFVMCA at normative values
* 38% patients in poor group had extreme MFVMCA on day 0 (p = 0.039), and 55% on day 1 (p = 0.023).
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| **MFVMCA (SD)** | **% EFV** | **MFVMCA (SD)** | **% EFV** | **MFVMCA (SD)** | **% EFV** |
| Good | 0.65 | 0% (0/13) | 1.33 | 23% (3/13) | 0.30 | 11% (1/9) |
| Poor | - 0.52 | 38% (5/13) | 2.02 | 60% (6/10) | 1.19 | 57% (4/7) |
| p | - | 0.039 | - | 0.1 | - | 0.11 |
| Lin JJ et al., 2015 [2] | 17 | Pediatric CPC at 3 months* P-CPC 1-2 (good): 8 (47%)
* P-CPC ≥3 (poor): 9 (53%)
 | **Outcome** | **Pre-hypothermia Phase** | **Hypothermia Phase** | **Rewarming Phase** | * Diastolic flow reversal or undetectable flow patterns associated with unfavourable outcomes.
* Normal MFVMCA in the rewarming phase and normal PI in the hypothermia and rewarming phases associated with favourable outcomes.
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| **MFVMCA** |  **PI < 0.6 / PI > 1.1** | **MFVMCA** | **PI > 1.1** | **MFVMCA** | **PI > 1.1** |
| Good | Lower: 5Normal: 1Higher: 2 | 5 | Lower: 6Normal: 2Higher: 0 | 0 | Lower: 3Normal: 5Higher: 0 | 1 |
| Poor | Lower: 8Normal: 0Higher: 0 | 7 | Lower: 8Normal: 1Higher: 0 | 0 | Lower: 9Normal: 0Higher: 0 | 8 |
| p | 0.129 | 0.620 | 0.576 | 0.002 | 0.009 | 0.003 |
| **ADULT PATIENTS** |  |
| Hoedemaekers CW et al., 2017 [3]  | 20 | Survival: S 45%/NS 55% | **Outcome** | **Day 0 (admission)** | **Day 3 (72 hrs)** | No differences between survivors and non-survivors |
| **MFVMCA** | **PI** | **MFVMCA** | **PI** |
| All patients | 26 [18.6-40.4] | - | 63.9 [48.3-73.1] | - |
| Van den Brule J et al, 2017 [4] | 11 | Survival: S 64%/NS 36% | **Outcome** | **Day 0 (admission)** | **Day 3 (72 hrs)** | * MFVMCA similar in S and NS at admission
* MFVMCA in NS increased more significantly compare to S over the time (p=0.001)
* NS had stronger decrease in CVR in NS
 |
| **MFVMCA** | **CVR** | **MFVMCA** | **CVR** |
| All patients | 28.0 [25-39] | 3.91[2.94-5.37](high) | 78 [65-123] | 1.35[0.88-1.81] |
| Heimburger D et al., 2016 [5]  | 51 (82) | CPC at ICU discharge* CPC 1-2 (good): 29 (55%)
* CPC ≥3 (poor): 24 (45%)
 | **Outcome** | **Day 0** | **Day 1** | * No differences in MFVMCA and PI between poor and good outcome patients at 24 and 48 hrs.
* However, for all subjects, MFVMCA significantly higher at 48 h compared with 24 h (45 vs 37 cm/s - p = 0.001).
 |
| **n** | **MFVMCA** | **PI**  | **n** | **MFVMCA** | **PI**  |
| Good | 23 | 38 [35–56] | 0.9 [0.7–1.2] | 19 | 55 [39–64] | 0.8 [0.6–1.1] |
| Poor | 28 | 40 [33–58] | 0.9 [0.7–1.1] | 27 | 42 [38–62] | 0.9 [0.8–1.1] |
| p |  | 0.94 | 0.52 |  | 0.47 | 0.20 |
| Doepp F et al., 2014 [6] | 41 (53) | CPC at ICU discharge* CPC 1-2 (good): 29 (55%)
* CPC ≥3 (poor): 24 (45%)
 | **Outcome** | **< 48 hrs** | **Day 3-5** | **Day 7-10** | * No correlation found between CBF and outcome at either of the 3 defined time points.
* Therapeutic hypothermia did not demonstrate distinct effects on cerebral blood flow.
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| **MFVMCA (n)** | **PI (n)** | **MFVMCA (n)** | **PI (n)** | **MFVMCA (n)** | **PI (n)** |
| Good | 45±23 (32) | 1.4 ± 0.5 (32) | 51±18 (26) | 1.2 ± 0.3 (26) | 51±16 (19) | 1.2 ± 0.2 (18) |
| Poor | 53±19 (41) | 1.0 ± 0.4 (41) | 68±23 (26) | 1.2 ± 0.5 (24) | 48±11 (16) | 1.4 ± 0.4 (15) |
| p | 0.06 | 0.01 | 0.01 | 0.36 | 0.60 | 0.12 |
| Bisschops LLA et al., 2012 [7]  | 10 | ICU Survival: S 40% / NS 60% | **Outcome** | **Pre-hypothermia Phase** | **End of hypothermia Phase (72 hrs)** | **Post hypothermia phase** **(108 hrs)** | CBF low after cardiac arrest, gradually increased during 72 hrs cooling period.Temperature by itself probably not a major determinant in regulation of CBF after cardiac arrest.  |
| **MFVMCA (n)** | **PI (n)** | **MFVMCA (n)** | **PI (n)** | **MFVMCA (n)** | **PI (n)** |
| All patients | 26.5[18.7–48.0] | 1.23 [0.94–1.45] | 63.9 [45.6–65.6] | 1.00 [0.88–1.57] | 71.5 [56.0–78.5] | 1.27 [1.15–1.32] |
| Lemiale V et al., 2008 [8] | 18 | Survival at 28 days: S 34% / NS 66% | **Outcome** | **Day 0**  | **Day 1** | **Day 2** | **Day 3** | No significant difference between survivors and non-survivors at any time point (MFV, dFV and PI), except that higher dFV in survivors at 72 hrs (39.6 cm/s versus 29.3 cm/s, *p* = 0.013) |
| **MFVMCA** | **PI** | **MFVMCA** | **PI** | **MFVMCA** | **PI** | **MFVMCA** | **PI** |
| All patients | 27.3[21.5-33.6] | 1.6 [1.3-1.9] | ↑ | ↓ | ↑ | ↓ | 50.5 [36.7– 58.1] | ↓ |
| Wessels T et al., 2006 [9] | 39 | Survival: S 44% / NS 56% | **Outcome** | **Day 0 (+4 hrs)** | **Day 1** | **Day 2** | **Day 3** | Higher PSV and EDV 4, 24 and 72 h after CPR in survivors  |
| **MCA Sys/Dia** | **RI** | **MCA Sys/Dia** | **RI** | **MCA Sys/Dia** | **RI** | **MCA Sys/Dia** | **RI** |
| Survivors | 82/31 | 0.61 | 96/43 | 0.57 | - | - | 101/42 | 0.59 |
| Non-survivors | 67/24 | 0.65 | 77/30 | 0.61 | - | - | 80/36 | 0.58 |
| p | 0.01 | ns | ns | ns | - | - | 0.03 | ns |
| Buunk G et al, 1999 [10] | 30 | CPC* CPC 1-2 (good): 9 (30%)
* CPC ≥3 (poor): 21 (70%)
 | **Outcome** | **T0** **(post-resuscitation)** | **T1** **(6 hrs)** | **T2** **(12 hrs)** | **T3** **(24 hrs)** | NS showed a gradual decrease in PI and an increase in MFVMCA S showed also a gradual but not significant decrease in PI and increase in MFVMCA |
| **MFVMCA** | **PI** | **MFVMCA** | **PI** | **MFVMCA** | **PI** | **MFVMCA** | **PI** |
| Good | 31±11 | 1.38±0.34 | 43±14 | 1.42±0.56 | 43±15 | 1.27±0.45 | 49±20 | 1.16±0.32 |
| Poor | 32±12 | 1.60±0.86 | 52±25 | 1.24±0.49 | 58±22 | 1.05±0.33 | 67±24 | 1.00±0.25 |
| Iida et al., 1997 [11] | 8 | NR | **Outcome** | **T0 (4-12)** | **T1 (12-24)** | **T2 (24-120)** |   |
| **MFVMCA**  | **PI** | **MFVMCA**  | **PI**  | **MFVMCA** | **PI** |
| All patients | 41.5±14.1 | 1.1±0.25 | 70.1±20 | 0.93±0.27 | 117.5±17.3 | 0.57±0.16 |
| Tab. ESM Table 2b. Summary of studies exploring US-TCD prognostic performance |
| CPC: Cerebral Performance Category; CVR: Cerebrovascular Resistance; Dia: Diastolic; SD: standard deviations from previously published normative values for children of similar age and gender; EDV: End Diastolic Velocity;EFV: Extreme flow velocity (=a value greater than or less than two standard deviations from normative); GOS-E: Extended Glasgow Outcome Scale, dFV: Diastolic Flow Velocity; MFVMCA: Mean Flow Velocity Middle Cerebral Artery; NR: not reported; NS: Non-survivors; PI: Pulsatility Index; PSV: Peak Systolic Velocity; RI: Resistivity Index; Sys: Systolic; S: Survivors. |
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4. van den Brule JMD, Vinke E, van Loon LM, et al (2017) Middle cerebral artery flow, the critical closing pressure, and the optimal mean arterial pressure in comatose cardiac arrest survivors—An observational study. Resuscitation 110:85–89. https://doi.org/10.1016/j.resuscitation.2016.10.022

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