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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). |
| **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. |
| **MFVMCA** | | | | **PI < 0.6 / PI > 1.1** | | | | **MFVMCA** | | | | | | | | **PI > 1.1** | | | | | **MFVMCA** | | | | | **PI > 1.1** | | |
| Good | Lower: 5  Normal: 1  Higher: 2 | | | | 5 | | | | Lower: 6  Normal: 2  Higher: 0 | | | | | | | | 0 | | | | | Lower: 3  Normal: 5  Higher: 0 | | | | | 1 | | |
| Poor | Lower: 8  Normal: 0  Higher: 0 | | | | 7 | | | | Lower: 8  Normal: 1  Higher: 0 | | | | | | | | 0 | | | | | Lower: 9  Normal: 0  Higher: 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. |
| **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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