

Role of diffusion-tensor imaging in post-cardiac arrest patients still comatose 3-days post-resuscitation

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Introduction:

Early prediction of functional recovery of comatose patients after cardiac arrest remains challenging. The American Academy of Neurology (AAN) practice parameters' evidence-based review reported that absent pupillary light response (PLR) or absent corneal reflexes (CR), or extensor posturing or no motor response to pain 3 days after resuscitation are associated with poor long-term outcome¹. Several studies have also shown that large reductions in the apparent diffusion coefficient were predictive of poor outcome^{2, 3}. However, these studies often involved patients who were noticeable improving, or critically ill patients who died within 72 hours of resuscitation. Imaging may be of most benefit to patients who are still comatose at 72 hours. The goal of this study is to investigate whether imaging can be used to predict recovery in these patients.

Methods:

Non-traumatic comatose cardiac arrest survivors who underwent subsequent MRI and who had a Glasgow Coma Scale score ≤ 8 were retrospectively analyzed (N=49). All patients underwent DWI on a 1.5 T scanner. Apparent diffusion coefficient (ADC) maps were calculated from the slope of the linear regression fit of the log of the DWI (b-value=1000 s/mm²) and b₀ (b-value=0 s/mm²) images. Fractional anisotropy values were derived from eigenvalues measured from the diffusion tensor calculated from the DTI dataset⁴. b₀ images were coregistered to the ICBM-452 T1 5th Order Polynomial Warps Atlas using a semiautomated program (MNI Autreg)⁵. Using the ICBM probabilistic atlases⁶, probability masks for the following regions were generated: cerebellum, frontal, insula, occipital, parietal and temporal lobes; caudate, putamen, and thalamus using a threshold of 50%. Median ADC and FA values were measured in those regions as well as in the entire brain. To minimize effects from cerebral spinal fluid, analysis was limited to tissue with ADC values $\leq 1.2 \times 10^{-3}$ mm²/s. Good functional outcome was defined as a 6 month modified Rankin Scale score ≤ 4 . MRI performed within 72 hours of resuscitation (Early) and later than 72hours (Late) were analyzed separately. Differences between patients with good and poor outcomes were compared (Wilcoxon-test for continuous variables and Fisher's Exact test for categorical variables). We also examined differences in ADC and FA values between patients exhibiting clinical indicators of poor outcome: absent PLR, absent CR, or extensor response or no motor response.

Results:

Table 1 shows the patient demographics in the good versus poor outcome groups. Only shockable rhythm was significantly different between the two groups. There were 26 patients imaged within 72 hours and 23 patients imaged more than 72 hours. There were 3 patients in the Early group with good outcome and 2 patients in the Late group with good outcome. For the Early group, there was no significant difference between patients with good or poor outcome. For the Late group, patients with good outcomes compared to those with bad outcomes had significantly higher ADC in the occipital lobe (0.88 [0.81–0.96] vs 0.70 [0.65–0.77] $\times 10^{-3}$ mm²/s, P=0.04), parietal lobe (0.90 [0.83–0.98] vs 0.75 [0.64–0.80] $\times 10^{-3}$ mm²/s, P=0.03), and whole brain ADC (0.85 [0.81–0.90] vs 0.76 [0.68–0.79] $\times 10^{-3}$ mm²/s, P=0.04). There were also differences for the frontal lobe (0.88 [0.84–0.91] vs 0.80 [0.71–0.83] $\times 10^{-3}$ mm²/s, P=0.07), and white matter (0.81 [0.77–0.86] vs 0.71 [0.60–0.76] $\times 10^{-3}$ mm²/s, P=0.07), but these did not reach significance. There was no difference in terms of FA between good and poor outcome groups for both timepoints.

Patients with absent PLR (N=4) had significantly higher FA in the putamen (0.28 [0.25–0.32] vs 0.24 [0.22–0.26], P=0.04) in early scans but exhibited reduced FA in late scans (0.19 [0.15–0.21] vs 0.23 [0.20–0.25], P=0.02; N=5). There were also significant differences in ADC values for late scans in the regions of frontal lobe (0.66 [0.52–0.77] vs 0.83 [0.76–0.87] $\times 10^{-3}$ mm²/s, P=0.01), temporal lobe (0.74 [0.57–0.80] vs 0.84 [0.78–0.88] $\times 10^{-3}$ mm²/s, P=0.02), white matter (0.52 [0.51–0.65] vs 0.74 [0.69–0.78] $\times 10^{-3}$ mm²/s, P=0.01) and whole brain ADC (0.67 [0.57–0.73] vs 0.78 [0.73–0.80] $\times 10^{-3}$ mm²/s, P=0.03). No significant difference between patients with absent or present PLR existed for early ADC maps. Patients exhibiting absent CR (N=12) had significantly lower ADC values in the occipital lobe (0.68 [0.53–0.75] vs 0.77 [0.70–0.81] $\times 10^{-3}$ mm²/s, P=0.01) for late scans. The 8 patients with absent CR and early MRI exhibited no difference in terms of ADC. Patients with absent CR at early MRI time-points had higher FA in the cerebellum (0.35 [0.29–0.39] vs 0.28 [0.24–0.30], P=0.02), insula (0.22 [0.20–0.25] vs 0.17 [0.15–0.19], P=0.006), occipital lobe (0.28 [0.26–0.33] vs 0.23 [0.21–0.25], P=0.008), parietal lobe (0.25 [0.22–0.29] vs 0.21 [0.20–0.23], P=0.02), putamen (0.28 [0.25–0.33] vs 0.24 [0.22–0.25], P=0.006), temporal lobe (0.27 [0.22–0.31] vs 0.21 [0.19–0.23], P=0.006). For late scans, only the cerebellum (0.29 [0.25–0.35] vs 0.25 [0.24–0.27], P=0.02) and occipital lobe (0.26 [0.24–0.30] vs 0.21 [0.19–0.24], P=0.009) exhibited higher FA values in patients with absent CR. There was no difference in terms of ADC or FA values between patients exhibiting no motor or extensor response and other patients for either early (N=21) or late (N=18) MRI.

Discussion:

Our results suggest that neuroimaging will be useful for assisting management of comatose patients post-cardiac arrest who are still comatose 72 hours post-resuscitation. These patients currently pose a great quandary for clinicians. For these patients, MRI after 72hours may provide critical data to inform the physician on the likelihood of recovery in these patients. Severe injury to the parietal lobe as a predictor of poor outcome can potentially be explained by the parietal lobe's suspected role in consciousness⁷. In addition, FA changes appear to track with clinical indicators of poor outcome. Monitoring FA may therefore be useful for understanding the mechanisms of tissue injury after cardiac arrest. As previously documented^{8–10}, changes in FA are highly dynamic, with both increases and decreases being indicators of tissue injury. It has been suggested that increases in FA are indications of early or ongoing cytotoxic processes. This can perhaps be addressed by serial imaging. Our study is limited by its retrospective nature. There is a need for prospective studies of comatose patients who are neither rapidly improving nor worsening involving serial imaging and neurological exams at pre-specified timepoints to improve management of these patients.

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Table 1: Patient characteristics

	ALL (N=49)	mRS ≤ 4 (N=5)	mRS>4 (N=44)
Age (years)	58 \pm 15	50 \pm 20	59 \pm 15
Female (%)	17 (35%)	2 (40%)	15 (34%)
GCS Admission	4 [3–5]	4 [3–5]	
Hypothermia (%)	9 (18%)	2 (40%)	7 (16%)
Shockable rhythm (%)	17 (35%)	4 (80%)	13 (30%)
GCS Day 3	4 [3–5]	4 [3–7]	4 [3–5]
Absent PLR (%)	9 (18%)	0 (0%)	9 (20%)
Absent CR (%)	20 (41%)	0 (0%)	20 (45%)
No motor or extensor response (%)	39 (80%)	4 (80%)	35 (80%)