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Neuroanatomical Predictors of Awakening in Acutely Comatose Patients

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Abstract

Objective—Lateral brain displacement has been associated with loss of consciousness and poor outcome in a range of acute neurologic disorders. We studied the association between lateral brain displacement and awakening from acute coma.

Methods—This prospective observational study included all new onset coma patients admitted to the Neurosciences Critical Care Unit (NCCU) over 12 consecutive months. Head computed tomography (CT) scans were analyzed independently at coma onset, after awakening, and at follow-up. Primary outcome measure was awakening, defined as the ability to follow commands before hospital discharge. Secondary outcome measures were discharge Glasgow Coma Scale (GCS), modified Rankin Scale, Glasgow Outcome Scale, and hospital and NCCU lengths of stay.

Results—Of the 85 patients studied, the mean age was 58 ± 16 years, 51% were female, and 78% had cerebrovascular etiology of coma. Fifty-one percent of patients had midline shift on head CT at coma onset and 43 (51%) patients awakened. In a multivariate analysis, independent predictors of awakening were younger age (odds ratio [OR] = 1.039, 95% confidence interval [CI] = 1.002–1.079, $p = 0.040$), higher GCS score at coma onset (OR = 1.455, 95% CI = 1.157–1.831, $p = 0.001$), nontraumatic coma etiology (OR = 4.464, 95% CI = 1.011–19.608, $p = 0.048$), lesser pineal shift on follow-up CT (OR = 1.316, 95% CI = 1.073–1.615, $p = 0.009$), and reduction or no increase in pineal shift on follow-up CT (OR = 11.628, 95% CI = 2.207–62.500, $p = 0.004$).

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Additional Supporting Information may be found in the online version of this article.

Authorship

R.G.K., M.M.B., J.D., H.A.P., R.D.S., and R.G.G. contributed to study design and interpreted the data. R.G.K. completed the statistical analyses and drafted the manuscript. M.M.B., J.D., and Z.D.C. rated study imaging. R.G.K., M.M.B., J.D., H.A.P., R.D.S., and R.G.G. were involved in acquisition of data. All authors reviewed and revised the manuscript.

Potential Conflicts of Interest

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Interpretation—Reversal and/or limitation of lateral brain displacement are associated with acute awakening in comatose patients. These findings suggest objective parameters to guide prognosis and treatment in patients with acute onset of coma.

The loss of consciousness that accompanies severe brain injury is a major challenge in critical care medicine. The management of the comatose patient demands emergent treatment, but it must also consider prognosis and decisions regarding goals of care. The role of mass effect in loss of consciousness, through lateral displacement of the brain, was characterized in the seminal work of Ropper et al, who found an association between midline shift and onset of coma.¹ In the intervening decades, attempts have been made to predict outcome via an assessment of midline shift or patency of the subarachnoid spaces surrounding the brainstem on head computed tomography (CT) taken at the time of coma onset or hospital admission.^{2–9} This research has focused primarily on unfavorable outcome without considering factors that might predict awakening.^{10–12}

Quantitative thresholds relating midline shift with clinical changes or treatment decisions have been suggested. Ropper's early work found that onset of stupor correlated with shift of the pineal body of 6 mm.¹ Septal shift >5 mm has been used by neurosurgeons as a criterion for evacuation of intracerebral and subdural hematomas.^{13,14} Other midline shift thresholds have been suggested for outcome prediction in brain injury, including >10 mm and >15 mm for poor outcome in traumatic brain injury,^{15,16} and 6 mm for short-term survival in intracerebral hemorrhage (ICH).¹⁷ In contrast, no such threshold has been proposed to predict acute recovery of consciousness in a broad sample of patients with coma from different etiologies. Recently several studies showed that timely therapeutic intervention can reverse brain herniation and that favorable outcome can be achieved in a subset of patients after herniation.^{18–20} Clinical triggers for aggressive intervention with the onset of herniation and coma have been suggested, but objective markers that might guide the intensity and duration of treatment have not been characterized.

We hypothesized that in patients with acute onset of coma, reversal of midline shift and restoration of cistern patency are associated with awakening during the acute hospitalization. Furthermore, we sought to identify clinically relevant thresholds of midline shift for acute emergence from coma.

Patients and Methods

Study Design and Participants

The study is a prospective, observational cohort investigation of patients with coma admitted to the Neurosciences Critical Care Unit (NCCU) of the Johns Hopkins Hospital from May 10, 2010 to May 9, 2011. All NCCU admissions were screened for coma, defined operationally as the failure to follow commands (Glasgow Coma Scale [GCS] motor score [GCS_M] < 6) continuously for 12 hours. Exclusion criteria included unresponsiveness primarily due to sedation, anesthesia, aphasia, or premorbid baseline GCS_M < 6. The study was approved by the hospital's institutional review board.

Procedures

Demographics, premorbid functional status, medical history, and coma onset time and etiology were recorded for all study patients. Hospital course variables included treatment regimens, significant events, physiologic monitoring, and change in mental status. The primary study outcome measure was awakening, defined as the restoration of command following ($GCS_M = 6$). Secondary outcomes were assessed at the time of hospital discharge and included clinical and functional status evaluated by the GCS, modified Rankin Scale (mRS), and Glasgow Outcome Scale; and hospital and NCCU length of stay.

Imaging

Head CT was analyzed at the time of coma onset, awakening, and follow-up. Patients with CT scans available at these study time periods were included in the present analysis. For patients who did not achieve awakening, the scan closest in time to hospital discharge was used as the follow-up CT. For patients who awakened, the CT closest in time following awakening was used, and the patient must have been following commands at the time of the imaging.

CT scans were rated using a standardized instrument by a neuroradiology fellow (Z.D.C.), and by 2 neurologists with training in neurocritical care (M.M.B., J.D.). The neuroradiology rater (Z.D.C.) did not utilize clinical status of study patients for rating. The neurologists who rated the imaging did so as part of an ongoing study of comatose patients, using prospective and predefined criteria, and were not blinded to the patients' clinical state. All 3 (Z.D.C., M.M.B., J.D.) scored the CTs independently and were blinded to each other's scores. Agreement was determined with the unweighted Cohen kappa statistic,²¹ and intraclass correlation coefficients for continuously distributed shift measurements. Measurements of the neuroradiologist were used in the study analysis, which was undertaken after all radiology ratings were completed. Findings of the neurologist raters are presented as Supplementary Tables 1 to 8.

Midline shift at the level of the septum pellucidum and at the pineal gland was measured as described elsewhere.^{1,12,22} All brain displacement measurements were made electronically, on 5mm-thick axial CT slices. Radiologic herniation (defined as subfalcine, central, uncus, or tonsillar), presence of hydrocephalus (with effacement of sulci), presence and location of hemorrhage or infarction, and status of basal cisterns were also recorded. Cisterns were characterized as normal, compressed, or absent, based on Marshall Scale criteria.²³ Changes in midline shift and cistern patency during hospitalization were derived from findings on the coma onset and follow-up CT scans.

Statistical Analysis

For main study analyses, patients were dichotomized into those who achieved awakening versus no awakening. Clinical characteristics and outcome measurements were treated as continuous variables, and dichotomized based on clinically relevant cutpoints.

For brain displacement analyses, midline shift measurements ≥ 3 mm were treated as a binned value of 0. This grouping was chosen based on findings of Ropper¹ that alertness

deteriorates when midline shift is ≥ 3 mm, and is consistent with previous brain displacement categorization.²⁴ Midline shift values >3 mm were included in the analysis as measured. Midline shift observations were considered as dichotomous variables (shift vs no shift) and as continuous variables (magnitude of shift in mm), at the septum pellucidum and at the pineal gland. Extent of shift was also analyzed in bins, with different cutoff values assigned based on predictive value for awakening.

Dichotomous variables were compared with the chi-square test or Fisher exact test where appropriate. The independent samples *t* test (2-tailed) was used to analyze normally distributed continuous variables. For variables with non-normal or categorical distributions, nonparametric tests (Mann–Whitney *U* test, Kruskal–Wallis test, Spearman correlation coefficient) were used. Level of significance was set at $p < 0.05$. Independent predictors of awakening were identified with backward multivariate logistic regression analyses of clinical characteristics, and radiologic findings associated with awakening ($p < 0.05$) in the univariate tests. Key portions of the analysis were repeated in a subset of patients that included only those with an admission GCS total score ≥ 8 (a traditional GCS cutoff for coma). Data were analyzed with SPSS version 20.0 (IBM, Armonk, NY).

Results

Between May 2010 and May 2011, 142 NCCU patients with an acute onset of coma were enrolled, and 85 with available imaging at the 3 specified time points were included in the analysis (Fig). Among the latter, mean age was 58 ± 16 years, 51% were female, 43% were white, and 40% were black or African American (Table 1). Prior to coma onset, 80% of patients had no significant disability (mRS score < 2). Primary coma etiology was cerebrovascular in 78% of cases, with ICH in 52%, subarachnoid hemorrhage in 49%, intraventricular hemorrhage in 47%, and subdural hematoma in 27%. Other coma etiologies were seizures or status epilepticus (26%), tumor (21%), ischemic stroke (20%), and traumatic brain injury (16%). Forty-seven (55%) patients had multiple coma etiologies (Table 2).

Awakening

Forty-three (51%) patients achieved the primary outcome of awakening during hospitalization. Of clinical characteristics at the time of coma onset, patients with ICH were less likely to awaken (64% no recovery, $p = 0.007$); awakening was less likely in patients with traumatic brain injury, although this was not statistically significant (64% awakening, $p = 0.071$). Patients who awakened had a higher initial GCS total score than those who did not (median = 9, range = 3–13 vs median = 6, range = 3–11, $p = 0.001$). Patients with bilateral fixed pupils at the time of coma onset were less likely to emerge from coma (76% no awakening, $p = 0.002$; Table 3). Forty-two percent of patients underwent cerebrospinal fluid (CSF) drainage. Most patients were treated with hyperosmolar agents, including mannitol (45%) and hypertonic saline (79%). Seventy-eight percent of patients received 2% saline, whereas almost half received 3% and 23.4% infusions. Patients treated with mannitol were less likely to emerge from coma (59% no awakening vs 30% recovery, $p = 0.007$), as were those who received CSF drainage (64% no awakening vs 32% recovery, $p = 0.007$). The use

of hypertonic saline infusion was high in both groups, and therefore was not associated with differences in coma emergence.

Study Imaging

INTER-RATER VARIABILITY—Agreement between CT scan raters (Z.D.C. vs M.M.B., J.D.) for measurements of midline shift was good. The kappa coefficient for recognition of shift at the septum pellucidum was 0.81 (95% confidence interval [CI] = 0.73–0.89), and at the pineal gland was 0.71 (95% CI = 0.59–0.83). Correlation between ratings on extent of shift at the septum was 0.897 ($p < 0.001$) and at the pineal gland was 0.784 ($p < 0.001$).

COMA ONSET NEUROLOGIC AND IMAGING CHARACTERISTICS—At the time of coma onset, median GCS score was 7.0 (range = 3–13). Pupils were fixed bilaterally in 29% of patients, were fixed unilaterally in 5%, and were anisocoric in 29%, of which 44% were unreactive bilaterally. Eleven percent of patients had an absent cough, 18% an absent gag, and 48% of patients had spontaneous respiration. On head CT, 51% of patients had lateral brain displacement (midline shift). Median midline shift at the level of the septum pellucidum was 1.1 mm (range = 0–18.4), and at the pineal gland was 0.0 mm (range = 0–9.1). Basal cisterns were compressed or absent in 60% of patients, radiologic herniation was observed in 51%, and 46% had hydrocephalus (see Table 2).

Coma Onset Displacement and Awakening

Of radiologic characteristics present at the time of coma onset, extent of pineal shift was less pronounced in those patients who awakened (median = 0.0 mm, range = 0.0–9.1 for coma emergence vs median = 0.0 mm, range = 0.0–9.1 for no emergence, $p = 0.047$). Awakening from coma trended toward association with normal cistern patency at coma onset (49% of those who emerged from coma vs 29% of those who did not, $p = 0.066$, see Table 3).

Follow-up Displacement and Awakening

Time elapsed between coma onset CT and follow-up CT was similar for patients who awakened and those who did not (median = 4.0 days, range = 1–51, emergence vs median = 3.0 days, range = 0–48, no emergence, $p = 0.328$). On follow-up CT, degree of septal shift was less marked in those patients who awakened (median septal shift = 0.0 mm, range = 0.0–13.0, coma emergence vs 5.3 mm, range = 0.0–22.8, no emergence, $p = 0.011$). Lateral displacement at the level of the pineal gland also was less in patients who awakened (median pineal shift = 0.0 mm, range = 0.0–7.6, emergence from coma vs 0.0 mm, range = 0.0–13.5, no emergence, $p = 0.001$). Midline shift < 6 mm at the level of the septum and pineal gland was associated with coma emergence (septum, 88% of those who awakened vs 52% of those who did not, $p = 0.020$; pineal gland, 98% of those who awakened vs 76% of those who did not, $p = 0.003$, Table 4). Normal cistern patency on follow-up CT was associated with coma emergence (56% of those who awakened vs 29% of those who did not, $p = 0.011$, Table 5).

Changes in Displacement and Awakening

Over the hospital course, changes in lateral brain displacement were associated with coma emergence. At the pineal gland, patients who awakened were less likely to have any increase in shift (7% recovery vs 33% no recovery, $p = 0.002$, see Table 4). In patients who emerged from coma, basal cisterns more frequently remained normal or returned to full patency (56% in awakening vs 28% in no recovery, $p = 0.014$, see Table 5).

Independent Predictors of Awakening

In a multivariate analysis including follow-up CT findings, independent predictors of awakening were younger age (odds ratio [OR] = 1.039, 95% CI = 1.002–1.079, $p = 0.040$), higher coma onset GCS score (OR = 1.455, 95% CI = 1.157–1.831, $p = 0.001$), nontraumatic coma etiology (OR = 4.464, 95% CI = 1.011–19.608, $p = 0.048$), and lesser pineal shift on follow-up CT (OR = 1.316, 95% CI = 1.073–1.615, $p = 0.009$). In a multivariate analysis including change in displacement during hospitalization, awakening was predicted by younger age (OR = 1.047, 95% CI = 1.007–1.088, $p = 0.021$), higher coma onset GCS score (OR = 1.565, 95% CI = 1.230–1.991, $p < 0.001$), nontraumatic coma etiology (OR = 5.208, 95% CI = 1.129–23.810, $p = 0.034$), and reversal or no increase in pineal shift (OR = 11.628, 95% CI = 2.207–62.500, $p = 0.004$, Table 6).

Subanalysis with Conventional Coma Definition

Key components of the analysis were repeated in a subset of 55 patients with an admission GCS total score ≤ 8 , a conventional definition of severe brain injury²⁵ and coma²⁶ used in previous reports. In summary, main associations between radiologic and clinical factors and awakening identified in the full study population were confirmed in this subset. Greater median midline shift at the level of the pineal gland on follow-up CT ($p = 0.025$), pineal shift ≥ 6 mm on follow-up CT ($p = 0.043$), and increase in pineal displacement during the hospitalization ($p = 0.016$) all were associated with failure to awaken (defined as following commands). Among all patients in this subanalysis, degree of septal shift was not associated with awakening. However, in a subgroup of those patients with any septal displacement identified, greater median septal shift on follow-up CT was associated with failure to awaken ($p = 0.035$). Bilateral fixed pupils at coma onset, and compression of basal cisterns on follow-up CT, also were associated with persisting coma.

Secondary Outcomes

At follow-up (hospital discharge), 53% of patients had moderate to severe disability (mRS = 3–5), and 46% of patients were dead; among survivors, median GCS total score was 9 (range = 3–15). Of those who died, 77% had life supporting measures withdrawn or withheld (Table 7). Patients who awakened during hospitalization were more likely to have a good functional outcome (mRS ≤ 3 ; 7% vs 0%) and were more likely to survive (81% vs 26%) than those who did not recover consciousness, $p < 0.001$. Those who awakened had a longer median intensive care unit (ICU) length of stay (14 days, range = 3–81 vs 6 days, range = 1–33, $p = 0.001$), and a longer median hospital length of stay (23 days, range = 6–103 vs 7 days, range = 1–49, $p < 0.001$, Table 8).

Discussion

The study found that among brain-injured comatose patients, 51% of whom had radiographic evidence of mass effect at the time of coma onset, awakening could be predicted from a smaller extent of lateral brain displacement at coma onset, absolute reversal or limitation of midline shift expansion at the time of follow-up CT, and relative change in shift during hospitalization. At coma onset, smaller incidence and degree of midline shift at the level of the septum pellucidum and the pineal gland were associated with or trended toward association with awakening. On follow-up CT, lesser extent of shift at both the septum and the pineal gland was associated with emergence from the comatose state. Worsening of displacement at the level of the pineal gland, and effacement of basal cisterns, lessened the likelihood of coma emergence. These associations were found in blinded and unblinded ratings of brain imaging.

Reversal and limitation of brain displacement during hospitalization were important factors in predicting awakening. When considered in a multivariate model, independent predictors of awakening included younger age, higher coma onset GCS score, nontraumatic coma etiology, lesser pineal shift on follow-up CT, and reversal or limitation of pineal shift during hospitalization.

In a series of 24 patients, Ropper found an association between mean midline shift 6.8 mm at the level of the pineal gland or 11.1 mm at the septum pellucidum, and onset of stupor and coma.¹ In contrast, our study sought to identify objective radiologic markers for awakening. This included the absolute extent of brain displacement when patients lapsed into coma and when they awakened, as well as relative changes in displacement over time. The study's findings point to 6 mm in midline shift as a potentially useful clinical threshold in this regard. Patients with septal displacement < 6 mm at coma onset were more likely to emerge from coma, as were those with either septal or pineal shift < 6 mm on follow-up CT. In light of these findings, 6 mm of deviation from normal brain symmetry—in cerebral hemispheres and diencephalic structures, and in proximity to brainstem arousal centers—appears to represent a level of unique physiologic importance for consciousness, given typical brain architecture.

Our study defined coma as failure to follow commands, or a GCS motor score < 6. This criterion was selected because of the inherent limitation of the verbal component of the GCS for assessing intubated ICU patients, and inter-rater variability calculating the total score. The GCS motor score also has an advantage in simplicity and ease of bedside administration. However, conventionally coma has been defined as a GCS total score 8 in many past reports. A subanalysis was therefore undertaken of patients meeting the traditional definition of coma in the present study. This confirmed main associations for awakening identified in the population of patients who met the motor score criterion, a finding that may aid design of future coma studies.

Possible mechanisms of brain displacement and associated herniation in precipitating coma and affecting outcome are numerous, and include increased intracranial pressure,²⁷ derangement of cerebral autoregulation,^{28,29} reduction in cerebral blood flow,³⁰ and

interruption of synaptic or neurochemical functions in the ascending reticular activating system.³¹ This study's findings could provide a framework for further studying biologic mechanisms associated with the recovery of consciousness. Furthermore, insight into the extent of brain displacement and emergence from coma may help identify clinical therapeutic targets, guide urgency and duration of treatment, and assist in decision making for patients with severe brain injuries who become unconscious.

The comatose state is a dynamic process, and may evolve favorably over time depending on severity. This study's radiologic findings suggest the reversal or mitigation of midline shift, both in the region of the cerebral cortex and the brainstem, is as important of a consideration as initial shift—and arguably more so—for predicting acute awakening in comatose patients.

Limitations

The study did not assess awakening beyond the time of hospital discharge. Because evolution of midline shift was associated with increased emergence from coma during the hospitalization period, and may continue after discharge, evaluation of this effect for longer time periods is warranted. The study was not designed to assess effects of treatments that can alter degree of mass effect, such as hyperosmolar therapy. Patients in this study were subjected to similar therapies when acute brain herniation was suspected. Accordingly, treatment effects in this study population are equivocal. Patients who received mannitol and CSF drainage were less likely to emerge from coma, suggesting greater brain impairment at coma onset in patients given these treatments. Therapeutic effect of hypertonic saline infusion could not be determined between consciousness recovery and nonrecovery groups, because of a practice in our institution of applying these treatments broadly in patients with clinical evidence of herniation. The study does not purport to make conclusions on efficacy of these therapies on midline shift, and coma emergence. The study also was constrained to available brain imaging, excluding from the final analysis some patients who otherwise met inclusion criteria.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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FIGURE 1.

Flow of acutely comatose patients. AED = antiepileptic drug; CT = computed tomography; GCSM = Glasgow Coma Scale motor score; NCCU = Neurosciences Critical Care Unit.

TABLE 1

Demographics and Comorbid Conditions, N = 85

Characteristic	Value
Age, yr	58.0 ± 16.5
Female	43 (51)
Race/ethnicity	
White	37 (43)
Black or African American	34 (40)
Asian	3 (3)
Hispanic or Latino	4 (5)
Hawaiian/other Pacific Islander	0 (0)
American Indian/Alaska Native	0 (0)
Other	6 (7)
Smoke tobacco	21 (28) ^a
Alcohol use	18 (30) ^b
Illicit drugs	7 (13) ^c
Hypertension	49 (58)
Hyperlipidemia	25 (29)
Arrhythmia	13 (15)
Seizures	13 (15)
Ischemic stroke	16 (19)
Diabetes	24 (28)

Data are No. (%) or mean ± standard deviation.

^aData available for 74 patients.^bData available for 59 patients.^cData available for 53 patients.

TABLE 2

Patient Characteristics at Coma Onset, N = 85

Characteristics	Value
Clinical	
Premorbid mRS score	
0 = no symptoms	41 (48)
1 = symptoms, no significant disability	27 (32)
2 = slight disability	5 (6)
3 = moderate disability	6 (7)
4 = moderate severe disability	2 (2)
5 = severe disability	3 (3)
Unknown	1 (1)
Coma etiology	
Traumatic brain injury	14 (16)
Cerebrovascular	
SAH	42 (49)
ICH	44 (52)
IVH	40 (47)
ICH + IVH	31 (36)
SAH + ICH	33 (39)
SAH + IVH	29 (34)
SAH + ICH + IVH	24 (28)
SDH	23 (27)
Ischemic stroke	17 (20)
Tumor, primary or metastatic	18 (21)
Seizures/status epilepticus	22 (26)
Infectious disease	11 (13)
Noninfectious neuroinflammatory	1 (1)
Radiologic	
Coma onset midline shift	43 (51)
Amount septum pellucidum, mm	1.1 [0–18.4]
Amount pineal gland, mm	0 [0–9.1]
Basal cisterns	
Normal	33 (39)
Compressed	39 (46)
Absent	12 (14)
Herniation	43 (51)
Hydrocephalus	
Communicating	10 (12)
Obstructive	27 (32)

Characteristics	Value
Neurologic examination	
GCS total score	7.0 [3–13]
Unilateral fixed pupil	4 (5)
Bilateral fixed pupils	25 (29)
Anisocoria	25 (29)
Unilateral absent corneal reflex	3 (4) ^a
Bilateral absent corneal reflex	10 (13) ^a
Absent cough	9 (11) ^b
Absent gag	13 (18) ^c
Spontaneous respiration	41 (48)

Data are No. (%) or median [range].

^a Available in 75 patients.

^b Available in 78 patients.

^c Available in 73 patients.

GCS = Glasgow Coma Scale; ICH = intracerebral hemorrhage; IVH = intraventricular hemorrhage; mRS = modified Rankin Scale; SAH = subarachnoid hemorrhage; SDH = subdural hematoma.

TABLE 3

Comparison of Patients without and with Awakening from Acute Coma, N = 85

Characteristic	No Awakening, n = 42	Awakening, n = 43	p
Demographics			
Age, yr	59.0 ± 16.5	56.9 ± 16.7	NS
Female	20 (48)	23 (53)	NS
Race/ethnicity			
White	16 (38)	21 (49)	NS
Black or African American	17 (40)	17 (39)	
Asian	2 (5)	1 (2)	
Hispanic or Latino	2 (5)	2 (5)	
Hawaiian/other Pacific Islander	0 (0)	0 (0)	
American Indian/Alaska Native	0 (0)	0 (0)	
Other	4 (9)	2 (5)	
Clinical characteristics			
Premorbid moderate or greater disability, mRS 3	5 (12)	6 (14)	NS
Any premorbid symptoms, mRS > 0	24 (58)	19 (44)	NS
Coma etiology			
Traumatic brain injury	10 (24)	4 (9)	0.071
Cerebrovascular	36 (86)	30 (70)	0.078
SAH	23 (55)	19 (44)	NS
ICH	28 (67)	16 (37)	0.007
IVH	21 (50)	19 (44)	NS
ICH + IVH	20 (48)	13 (30)	0.100
ICH, vs other cerebrovascular	27 (75)	16 (53)	0.066
Ischemic stroke	17 (40)	14 (33)	NS
Subdural hematoma	13 (31)	10 (23)	NS
Tumor or metastatic lesion	6 (14)	12 (28)	NS
Seizures	11 (26)	11 (26)	NS
Infectious disease	7 (17)	4 (9)	NS
TBI or cerebrovascular	38 (90)	32 (74)	0.052
Structural: TBI, cerebrovascular, or tumor	38 (90)	39 (91)	NS
Radiologic characteristics at coma onset			
Coma onset midline shift			
Amount septum pellucidum, mm	3.3 [0.0–17.5]	0.0 [0.0–18.4]	NS
Amount pineal gland, mm	0.0 [0.0–9.1]	0.0 [0.0–9.1]	0.047
Basal cisterns			
Normal	12 (29)	21 (49)	NS
Compressed	22 (54)	17 (39)	

Characteristic	No Awakening, n = 42	Awakening, n = 43	<i>p</i>
Absent	7 (17)	5 (12)	
Basal cisterns normal	12 (29)	21 (49)	0.066
Herniation	26 (62)	17 (39)	0.039
Hydrocephalus	23 (55)	16 (37)	NS
Communicating	6 (14)	4 (9)	NS
Obstructive	16 (38)	11 (26)	
Neurologic examination			
GCS score, total	6 [3–11]	9 [3–13]	0.001
Unilateral fixed pupil	1 (2)	3 (7)	NS
Bilateral fixed pupils	19 (45)	6 (14)	0.002
Anisocoria	14 (33)	11 (26)	NS

Data are mean $\pm$ standard deviation, No. (%), or median [range].

GCS = Glasgow Coma Scale; ICH = intracerebral; IVH = intraventricular hemorrhage; mRS = modified Rankin Scale; NS = not significant, $p > 0.100$; SAH = subarachnoid hemorrhage; TBI = traumatic brain injury.

TABLE 4

Lateral Brain Displacement and Awakening from Acute Coma, N = 85

Midline Shift	Septum Pellucidum			Pineal Gland		
	No Awakening, n = 42	Awakening, n = 43	p	No Awakening, n = 42	Awakening, n = 43	p
Coma onset CT						
Median shift, mm	3.3 [0.0–17.5]	0.0 [0.0–18.4]	NS	0.0 [0.0–9.1]	0.0 [0.0–9.1]	0.047
Absolute shift, mm						
0.00	20 (48)	28 (65)	NS	31 (74)	39 (91)	NS
+3.10 to +5.99	6 (14)	6 (14)		7 (17)	2 (5)	
+6.00 to 18.99	10 (24)	5 (12)		3 (7)	1 (2)	
9.00	6 (14)	4 (9)		1 (2)	1 (2)	
0.00	20 (48)	28 (65)	NS	31 (74)	39 (91)	NS
+3.10 to +5.99	6 (14)	6 (14)		7 (17)	2 (5)	
+6.00	16 (38)	9 (21)		4 (9)	2 (5)	
+6.00	16 (38)	9 (21)	0.082	6 (14)	2 (5)	NS
Follow-up CT						
Median shift, mm	5.3 [0.0–22.8]	0.0 [0.0–13.0]	0.011	0.0 [0.0–13.5]	0.0 [0.0–7.6]	0.001
Absolute shift, mm						
0.00	18 (43)	27 (63)	0.088	25 (59)	38 (88)	0.012
+3.10 to +5.99	3 (7)	5 (12)		7 (17)	4 (9)	
+6.00 to +8.99	7 (17)	6 (14)		6 (14)	1 (2)	
9.00	14 (33)	5 (12)		4 (9)	0 (0)	
0.00	18 (43)	27 (63)	0.069	25 (59)	38 (88)	0.005
+3.10 to +5.99	3 (7)	5 (12)		7 (17)	4 (9)	
+6.00	21 (50)	11 (26)		10 (24)	1 (2)	
+6.00	20 (48)	5 (12)	0.020	10 (24)	1 (2)	0.003
Displacement						
Median shift, mm	0.0 [–8.3 to +18.8]	0.0 [–7.2 to +8.5]	NS	0.0 [–4.5 to +13.5]	0.0 [–5.0 to +5.0]	0.038
Absolute shift, mm						

Midline Shift	Septum Pellucidum		Pineal Gland	
	No Awakening, n = 42	Awakening, n = 43	No Awakening, n = 42	Awakening, n = 43
				<i>p</i>
-6.00	1 (2)	1 (2)	0 (0)	0 (0)
-5.99 to -3.00	2 (5)	4 (9)	2 (5)	1 (2)
-2.99 to -0.10	7 (17)	3 (7)	3 (7)	2 (5)
0.00	16 (38)	25 (58)	23 (55)	37 (86)
+0.10 to +2.99	4 (9)	5 (12)	3 (7)	1 (2)
+3.00 to +5.99	3 (7)	2 (5)	7 (17)	2 (5)
+6.00	9 (21)	3 (7)	4 (9)	0 (0)
Decrease	10 (24)	8 (19)	5 (12)	3 (7)
No change	16 (38)	25 (58)	23 (55)	37 (86)
Increase	16 (38)	10 (23)	14 (33)	3 (7)
Increase vs other	16 (38)	10 (23)	14 (33)	3 (7)

Data are No. (%) of patients or median [range].

CT = computed tomography; NS = not significant, *p* > 0.100; shift = change between coma onset CT and follow-up CT.

TABLE 5

Basal Cistern Patency and Awakening from Acute Coma, N = 85

Basal Cistern Patency	No Awakening, n = 42	Awakening, n = 43	<i>p</i>
Coma onset CT			
Normal	12 (29)	21 (49)	NS
Compressed	22 (54)	17 (39)	
Absent	7 (17)	5 (12)	
Follow-up CT			
Normal	12 (29)	24 (56)	0.001
Compressed	18 (43)	18 (42)	
Absent	12 (29)	1 (2)	
Normal vs abnormal	12 (29)	24 (56)	0.011
cistern patency			
Normal → normal	7 (17)	19 (44)	0.002
Compressed → normal	5 (12)	5 (12)	
Absent → normal	0 (0)	0 (0)	
Absent → compressed	0 (0)	5 (12)	
Normal → compressed	5 (12)	2 (5)	
Normal → absent	0 (0)	0 (0)	
Compressed → compressed	13 (32)	11 (26)	
Compressed → absent	4 (10)	1 (2)	
Absent → absent	7 (17)	0 (0)	
Unchanged normal	7 (17)	19 (44)	0.006
Improved	5 (12)	10 (23)	
Worsened	9 (22)	3 (7)	
Unchanged effaced	20 (49)	11 (26)	
Normal/improved to normal	12 (29)	24 (56)	
Effaced/worsened to effaced	29 (71)	19 (44)	
Normal or improved	12 (29)	29 (67)	<0.001
Effaced or worsened	29 (69)	19 (44)	

Data are No. (%) of patients.

CT = computed tomography; NS = not significant, $p > 0.100$; patency = change between coma onset CT and follow-up CT.

TABLE 6

Factors Predicting Awakening from Acute Coma, N = 85

Factor	AOR (95% CI)	<i>p</i>
Follow-up CT findings		
Younger age	1.039 (1.002–1.079)	0.040
Higher coma onset GCS	1.455 (1.157–1.831)	0.001
Non-TBI coma etiology	4.464 (1.011–19.608)	0.048
Hydrocephalus		NS
Coma onset pineal shift, extent in mm		NS
Coma onset septal shift, extent in mm		NS
Lesser follow up pineal shift, extent in mm	1.316 (1.073–1.615)	0.009
Lesser follow-up septal shift, extent in mm		NS
Change in CT findings		
Younger age	1.047 (1.007–1.088)	0.021
Higher coma onset GCS	1.565 (1.230–1.991)	<0.001
Non-TBI coma etiology	5.208 (1.129–23.810)	0.034
Hydrocephalus		NS
Coma onset pineal shift, extent in mm		NS
Coma onset septal shift, extent in mm		NS
pineal shift, reduced or no increase	11.628 (2.207–62.500)	0.004
septal shift, reduced or no increase		NS

AOR = adjusted odds ratio; CI = confidence interval; CT = computed tomography; GCS = Glasgow Coma Scale; NS = not significant, $p > 0.100$; TBI = traumatic brain injury; shift = change between coma onset CT and follow-up CT.

TABLE 7

Patient Characteristics at Hospital Discharge, N = 85

Characteristic	Value
Discharge mRS score	
0 = no symptoms	0 (0)
1 = symptoms, no significant disability	1 (1)
2 = slight disability	0 (0)
3 = moderate disability	2 (2)
4 = moderate severe disability	12 (14)
5 = severe disability	31 (36)
6 = dead	39 (46)
Discharge GOS score	
1 = good recovery	1 (1)
2 = moderate disability	2 (3)
3 = severe disability	31 (36)
4 = vegetative state	11 (13)
5 = death	39 (46)
Life-supporting measures withdrawn/withheld	30 (35)
Hospital discharge GCS total score	9 [3–15]
GCS _{Total} , coma onset to hospital discharge	+0.5 [–6 to +12]
NCCU LOS, days	11 [1–81]
Hospital LOS, days	15 [1–103]

Data are No. (%) of patients or median [range].

GCS = Glasgow Coma Scale; GOS = Glasgow Outcome Scale; LOS = length of stay; mRS = modified Rankin Scale; NCCU = Neurosciences Critical Care Unit.

TABLE 8

Awakening from Acute Coma and Outcome at Hospital Discharge, N = 85

Characteristic	No Awakening, n = 42	Awakening, n = 43	<i>p</i>
Discharge mRS			
0 = No symptoms	0 (0)	0 (0)	<0.001
1 = Symptoms, no significant disability	0 (0)	1 (2)	
2 = Slight disability	0 (0)	0 (0)	
3 = Moderate disability	0 (0)	2 (5)	
4 = Moderate severe disability	0 (0)	12 (28)	
5 = Severe disability	11 (26)	20 (46)	
6 = Dead	31 (74)	8 (19)	
Discharge GOS			
1 = Good recovery	0 (0)	1 (2)	<0.001
2 = Moderate disability	0 (0)	3 (7)	
3 = Severe disability	4 (9)	27 (63)	
4 = Vegetative state	7 (17)	4 (9)	
5 = Death	31 (74)	8 (19)	
Life-supporting measures withdrawn/withheld	23 (74)	7 (87)	NS
Discharge GCS score, total	4 [3–12]	13 [3–15]	<0.001
GCS _{Total} , coma onset to hospital discharge	−1 [−6 to +7]	+5 [−5 to +12]	<0.001
NCCU LOS, days	6 [1–33]	14 [3–81]	0.001
Hospital LOS, days	7 [1–49]	23 [6–103]	<0.001

Data are No. (%) of patients or median [range].

GCS = Glasgow Coma Scale; GOS = Glasgow Outcome Scale; LOS = length of stay; mRS = modified Rankin Scale; NCCU = Neurosciences Critical Care Unit; NS = not significant, $p > 0.100$.