Predictors of abnormal brain computed tomography findings in patients with acute altered mental status in the emergency department

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Objective  Brain computed tomography (CT) is commonly performed to diagnose acute altered mental status (AMS), a critically important symptom in many serious diseases. However, negative CT results are common, which result in unnecessary CT use. Therefore, this study aimed to determine the clinical factors associated with positive CT findings.

Methods  Patients with acute AMS selected from an emergency department–based registry were retrospectively evaluated. Patients with non-traumatic and noncommunicable diseases on initial presentation and with Glasgow Coma Scale scores of <15 were included in the study.

Results  Among the 367 brain CT results of patients with AMS during the study period, 146 (39.8%) were positive. In a multivariate analysis, the presence of focal neurologic deficit (odds ratio [OR], 132.6; 95% confidence interval [CI], 37.8 to 464.6), C-reactive protein level <2 mg/dL (OR, 3.9; 95% CI, 1.4 to 10.6), and Glasgow Coma Scale score <9 (OR, 2.4; 95% CI, 1.2 to 4.8) were significantly associated with positive brain CT results.

Conclusion  The presence of focal neurologic deficit, initial Glasgow Coma Scale score of <9, and initial C-reactive protein levels of <2 mg/dL can facilitate the selection of brain CT to diagnose patients with acute AMS in the emergency department.

Keywords  Unconsciousness; Tomography, X-Ray computed; Diagnosis; Risk factors
INTRODUCTION

Altered mental status (AMS) is one of the most common chief complaints reported in 4% to 10% of emergency department (ED) patients. A wide range of clinical conditions can cause acute AMS, either direct central nervous system (CNS) pathologies such as stroke, seizure, and encephalitis or non-CNS-origin such as sepsis, metabolic imbalance, cardiogenic shock, and intoxication. Moreover, history taking in patients with AMS is, due to their condition, problematic. Thus, determining the exact etiology in patients with AMS is challenging for emergency physicians.

Brain computed tomography (CT), the primary diagnostic tool to identify intracranial pathologies, has been recommended for AMS. Unfortunately, brain CT has some limitations when used to diagnose non-intracranial pathology-related AMS.

Studies evaluating the brain CT of patients with AMS without trauma were limited, as most previous studies investigated its effectiveness in patients with traumatic brain injuries. Therefore, this study aimed to evaluate the effectiveness of brain CT in patients with non-traumatic AMS and, consequently, determine the clinical characteristics predictive of positive brain CT findings in these patients.

METHODS

Study setting

This study was conducted at a single urban academic hospital with an annual ED census of 55,000. A retrospective ED-based registry of AMS was reviewed from April to December 2014. Non-trauma patients who had Glasgow Coma Scale (GCS) scores of ≤14 and presented to the ED with noncommunicable disease were enrolled in this study. Those who had previous neurologic deficit (modified Rankin Scale of ≥2), uncomplicated ethanol ingestion, cardiac arrest, aged <18 years, or recovered from mental illness at the time of the initial ED evaluation were excluded.

Basic patient characteristics such as age, sex, medical history and previous medications, initial vital signs, neurologic findings, initial laboratory test results, brain CT findings, and final diagnoses were collected. One senior resident (third or fourth year) or a faculty of emergency medicine performed full neurologic exams in the patients to determine any cranial nerve abnormality, motor weakness, or cerebellar dysfunction. Only brain CT results conducted in the ED were included for evaluation. Brain CT findings, formal reports, and final diagnoses were reviewed by a faculty of emergency medicine. “Positive CT finding” was defined as the presence of abnormal findings suggestive of acute AMS. This study was approved by the institutional review board of the study hospital (16-2015-3), and written informed consents were waived.

Table 1. Clinical characteristics of patients with acute mental changes

| Characteristics | Brain CT Done (n = 367) | Brain CT Not done (n = 141) | P-value |
|-----------------|-------------------------|-----------------------------|---------|
| **Age (yr)**    | 66.32 ± 15.27           | 63.27 ± 18.21               | 0.079   |
| **Male**        | 195 (52.0)              | 66 (46.8)                   |         |
| **Current-smoker** | 71 (19.3)              | 17 (16.3)                   | 0.317   |
| **Current-smoker** | 35 (9.5)               | 8 (8.2)                     | 0.273   |
| **Glasgow Coma Scale** | 8.45 ± 3.37          | 9.47 ± 3.50                  | 0.002   |
| **Mental status** |                        |                             |         |
| Confusion       | 0 (0)                   | 1 (0.7)                     |         |
| Lethargy        | 223 (60.8)              | 104 (73.8)                  |         |
| Stupor          | 66 (18.0)               | 15 (10.6)                   |         |
| Semicoma        | 42 (11.4)               | 6 (4.3)                     |         |
| Coma            | 36 (9.8)                | 15 (10.6)                   |         |
| **Underlying conditions** |                   |                             |         |
| Hypertension    | 166 (45.2)              | 64 (45.4)                   | 0.981   |
| Diabetes mellitus | 110 (30.0)             | 59 (41.8)                   | 0.015   |
| Malignancy      | 45 (12.3)               | 22 (15.6)                   | 0.342   |
| Chronic liver disease | 35 (9.5)              | 15 (10.6)                   | 0.709   |
| Chronic kidney disease | 26 (7.1)              | 13 (9.2)                    | 0.418   |
| Cerebrovascular disease | 92 (25.1)           | 23 (16.3)                   | 0.029   |
| Parkinson’s disease | 8 (2.2)                | 4 (2.8)                     | 0.746   |
| Dementia        | 42 (11.4)               | 16 (11.3)                   | > 0.990 |
| **Medication** |                        |                             |         |
| Psychotropic    | 39 (10.6)               | 24 (17.0)                   | 0.050   |
| Anticonvulsant  | 21 (5.7)                | 12 (8.51)                   | 0.270   |
| Cardiovascular  | 177 (48.2)              | 68 (48.2)                   | 0.861   |
| Opioid          | 6 (1.6)                 | 5 (3.5)                     | 0.192   |
| Medications for chronic neurologic disorder | 25 (6.8) | 9 (6.8) | 0.892 |
| **Initial vital signs** |                   |                             |         |
| SBP (mmHg)      | 111.67 ± 63.78          | 93.72 ± 61.37               | 0.004   |
| DBP (mmHg)      | 62.90 ± 34.76           | 54.67 ± 39.5                | 0.016   |
| Heart rate (bpm) | 88.58 ± 23.97          | 91.96 ± 22.14               | 0.214   |
| Respiratory rate (bpm) | 16.68 ± 8.39         | 15.66 ± 10.37               | 0.299   |
| Body temperature (°C) | 36.55 ± 1.03          | 36.51 ± 1.04                | 0.106   |
| **Laboratory results** |                   |                             |         |
| WBC (10^3/μL)   | 11.34 ± 8.43           | 11.79 ± 10.34               | 0.707   |
| Hemoglobin (g/dL) | 12.76 ± 2.62          | 12.23 ± 2.73                | 0.045   |
| Sodium (mM/L)   | 137.3 ± 6.18           | 135.9 ± 7.43                | 0.031   |
| Potassium (mM/L) | 4.10 ± 0.84           | 4.25 ± 1.09                 | 0.150   |
| BUN (mg/dL)     | 25.96 ± 21.26          | 26.97 ± 20.46               | 0.629   |
| Creatinine (mg/dL) | 1.82 ± 7.65          | 1.58 ± 1.65                 | 0.717   |
| Glucose (mg/dL) | 174.74 ± 127.03        | 170.97 ± 151.20             | 0.778   |
| AST (IU/L)      | 67.82 ± 170.79         | 82.89 ± 269.83              | 0.454   |
| ALT (IU/L)      | 31.55 ± 77.13          | 36.05 ± 79.17               | 0.539   |
| Total bilirubin (mg/dL) | 1.48 ± 2.24          | 1.54 ± 2.39                 | 0.781   |
| Albumin (g/dL)  | 3.83 ± 2.13            | 3.60 ± 0.63                 | 0.212   |
| Creatine kinase (IU/L) | 353.02 ± 772.33      | 347.09 ± 704.58             | 0.945   |
| C-reactive protein (mg/dL) | 3.21 ± 6.86         | 4.55 ± 8.53                 | 0.098   |
| **Neurologic exam** |                   |                             |         |
| Focal neurologic deficit | 90 (26.3)            | 1 (0.7)                     | < 0.001 |
| Cranial nerve abnormality | 49 (13.4)            | 1 (0.7)                     | < 0.001 |
| Extremity abnormality | 78 (21.3)            | 1 (0.7)                     | < 0.001 |
| Cerebellar abnormality | 1 (0.3)              | 0 (0)                       | > 0.990 |

Values are presented as mean ± standard deviation or number (%). CT, computed tomography; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

a) > 4 days per week. b) Cranial nerve, extremity, and cerebellar abnormality.
Statistical analysis

Statistical analyses were performed using the IBM SPSS Statistics ver. 20 (IBM Corp., Armonk, NY, USA) and R ver. 3.3.1 (R Foundation for Statistical Computing, Vienna, Austria). Categorical variables were recorded as frequency with the corresponding percentage and compared using the chi-square or Fisher's exact test as appropriate. Continuous variables were expressed as the mean ± standard deviation, and Student t-tests were performed. Multivariate logistic models were performed using the forward selection approach, and the results were recorded as adjusted odds ratio (OR) with 95% confidence interval (CI). Conditional Inference Tree Analysis was performed to generate a decision tree to predict positive brain CT results using the R package "Party" ver. 1.0-25.7 8 All statistical tests were two-tailed at 0.05 level of significance.

RESULTS

A total of 508 patients treated during the study period met the eligibility criteria and were enrolled in the registry. Among them, 367 (72.2%) patients had undergone brain CT in the ED. All patients with a focal neurologic deficit underwent brain CT, except one who underwent brain magnetic resonance imaging. Table 1 presents the baseline characteristics of the patients.

A total of 146 patients had positive CT findings: 81 (55.5%) had intracranial hemorrhage, 54 (37.0%) infarction, 10 (6.8%) tumor, and 1 (0.7%) brain swelling. The most common cause was cerebrovascular etiology (122, 83.6%) (Table 2). Table 3 shows the clinical parameters according to brain CT results.

Table 2. Etiologies of acute altered mental status in each group

| Etiology                        | CT negative | CT positive |
|---------------------------------|-------------|-------------|
| Cerebrovascular                 | 5 (2.3)     | 122 (83.6)  |
| CNS infection                   | 4 (1.6)     | 2 (1.4)     |
| CNS tumor                       | 1 (0.5)     | 5 (3.4)     |
| Seizure/postictal confusion     | 29 (13.1)   | 6 (4.1)     |
| Other CNS pathology             | 4 (1.8)     | 1 (0.7)     |
| Sepsis                          | 27 (12.2)   | 5 (3.4)     |
| Hepatic encephalopathy          | 24 (10.9)   | 1 (0.7)     |
| Hypoglycemia                    | 18 (8.1)    | 0 (0)       |
| Other metabolic derangement     | 32 (14.5)   | 2 (1.4)     |
| Cardiovascular                  | 10 (4.5)    | 0 (0)       |
| Hypoxia                         | 6 (2.7)     | 1 (0.7)     |
| Drug intoxication               | 43 (19.5)   | 1 (0.7)     |
| Psychiatric                     | 6 (2.7)     | 0 (0)       |
| Environmental injury            | 10 (4.5)    | 0 (0)       |
| Unknown                         | 2 (0.9)     | 0 (0)       |

Values are presented as number (%).

CT, computed tomography; CNS, central nervous system.

Table 3. Clinical characteristics and univariate analysis according to the result of brain CT

| Characteristics | CT findings | P-value |
|-----------------|-------------|---------|
|                 | Positive (n= 146) | Negative (n= 221) |
| Age (yr)        | 65.93±15.48 | 66.58±15.16 | 0.689 |
| Male            | 79 (54.1)   | 116 (52.5)  | 0.761 |
| Current-smoker  | 30 (20.5)   | 41 (18.6)   | 0.761 |
| Frequent alcohol drinkinga | 18 (12.3)   | 17 (7.7)    | 0.198 |
| GCS             | 7.82±3.31   | 8.86±3.17   | 0.003 |
| Initial GCS < 9 | 84 (57.5)   | 99 (44.8)   | 0.017 |
| Mental status   |             | 0.032     |
| Confusion       | 0 (0)       | 0 (0)      |
| Lethargy        | 77 (52.8)   | 146 (66.1)  | 0.136 |
| Stupor          | 30 (20.5)   | 36 (16.3)   | 0.136 |
| Semicoma        | 18 (12.3)   | 24 (10.9)   | 0.115 |
| Coma            | 21 (14.4)   | 15 (6.8)    | 0.004 |
| Underlying conditions     |             | 0.104     |
| Hypertension     | 66 (45.2)   | 100 (45.2)  | 0.924 |
| Diabetes mellitus | 30 (20.5)   | 80 (36.1)   | 0.002 |
| Malignancy       | 15 (10.3)   | 30 (13.6)   | 0.002 |
| Chronic liver disease | 6 (4.1)    | 29 (13.1)   | 0.004 |
| Chronic kidney disease | 5 (3.4)    | 21 (9.5)    | 0.029 |
| Cerebrovascular disease | 43 (29.5)  | 49 (22.2)   | 0.096 |
| Parkinson's disease | 1 (0.7)    | 7 (3.2)     | 0.115 |
| Dementia        | 8 (5.5)     | 34 (15.4)   | 0.004 |
| Medication      |             | 0.136     |
| Psychotropic    | 7 (4.8)     | 32 (14.5)   | 0.004 |
| Anticonvulsant  | 5 (3.4)     | 16 (7.2)    | 0.136 |
| Cardiovascular  | 71 (48.6)   | 106 (48.0)  | 0.699 |
| Opioid          | 2 (1.4)     | 4 (1.8)     | 0.766 |
| Medications for chronic neurologic disorder | 6 (4.1) | 19 (8.6) | 0.104 |
| Initial vital sign |             | 0.235     |
| SBP (mmHg)      | 117.02±70.20 | 108.14±59.06 | 0.208 |
| DBP (mmHg)      | 64.90±37.74 | 61.58±32.66 | 0.385 |
| Heart rate (min) | 83.40±23.00 | 91.83±24.04 | 0.003 |
| Respiratory rate (min) | 16.03±8.56 | 17.10±8.27 | 0.235 |
| Body temperature (°C) | 36.40±0.83 | 36.64±1.13 | 0.060 |
| Lab results     |             | 0.235     |
| WBC (10^3/μL) | 11.90±8.82 | 10.96±8.17 | 0.337 |
| Hemoglobin (g/dL) | 13.30±2.48 | 12.41±2.66 | 0.607 |
| Sodium (mM/L) | 137.78±4.38 | 136.9±7.12 | 0.187 |
| Potassium (mM/L) | 3.90±0.71 | 4.24±0.78 | < 0.001 |
| BUN (mg/dL) | 22.78±18.84 | 28.07±22.51 | 0.020 |
| Creatinine (mg/dL) | 1.24±1.43 | 2.19±9.78 | 0.248 |
| Glucose (mg/dL) | 169.29±56.11 | 178.35±157.39 | 0.434 |
| AST (IU/L) | 44.62±51.64 | 83.14±214.88 | 0.011 |
| ALT (IU/L) | 25.09±45.21 | 35.77±84.57 | 0.118 |
| Total bilirubin (mg/dL) | 1.23±1.00 | 1.64±2.76 | 0.047 |
| Albumin (g/dL) | 4.14±3.28 | 3.62±0.62 | 0.021 |
| Creatine kinase (UI/L) | 296.61±599.37 | 388.28±665.01 | 0.294 |
| CRP (mg/dL) | 1.40±3.41 | 4.41±8.17 | < 0.001 |
| C-reactive protein < 2 mg/dL | 125 (85.6) | 151 (68.3) | < 0.001 |
| Neurologic exam |             | 0.235     |
| Focal neurologic deficit | 87 (59.6) | 3 (1.4) | < 0.001 |
| Cranial nerve abnormality | 47 (32.2) | 2 (0.9) | < 0.001 |
| Extremity abnormality | 76 (52.1) | 2 (0.9) | < 0.001 |
| Cerebellar abnormality | 1 (0.7) | 0 (0) | 0.398 |

Values are presented as mean ± standard deviation or number (%). CT, computed tomography; GCS, Glasgow Coma Scale; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase. a > 4 days per week.
Brain CT for acute altered mentality

In the multivariate analysis, the presence of focal neurologic deficit (OR, 132.6; 95% CI, 37.8 to 464.6), C-reactive protein (CRP) of < 2 mg/dL (OR, 3.9; 95% CI, 1.4 to 10.6), and GCS score of < 9 (OR, 2.4; 95% CI, 1.2 to 4.8) were significantly associated with positive brain CT results (Table 4).

To generate the decision tree in the Conditional Inference Tree Analysis, the presence of focal neurologic deficit was the primary predictive factor (96.7%) of positive CT result. In patients without focal neurologic deficit, 39 (37.5%) with positive CT scans had GCS scores of < 9 and CRP levels of < 2 mg/dL. Sixteen patients (11.7%) showed GCS scores of ≥ 9, and 4 (11.1%) had GCS scores of < 9 and CRP levels of ≥ 2 mg/dL. The accuracy of the decision tree was 0.8311 (95% CI, 0.7887 to 0.868; P < 0.001) (Fig. 1).

DISCUSSION

Acute AMS caused by intracranial pathology usually requires immediate diagnosis and intervention. Brain CT is regarded as one of the essential approaches to manage AMS.4 With technical advancements over the past decade, utilization of brain CT in the ED has continuously increased.9 However, increased rates of CT use can expose patients to excessive levels of radiation and society to higher medical costs. One retrospective study that reviewed brain CT utilization in a single ED found that the rate of brain CT use had increased by 60% over a 7-year period; however, the diagnostic yield for intracranial hemorrhage had remained constant at approximately 3%.10

Therefore, several guidelines for brain CT have been developed, but are mostly relevant to traumatic brain injuries.11-13 Moreover, studies on patients with AMS using brain CT were limited. Hardy and Brennan2 evaluated the brain CT of elderly patients (aged > 70 years) with acute confusion, noting that positive findings were detected in only 14%. Partel et al.6 evaluated the brain CT data of poisoned patients with AMS, determining that no cases had abnormal CT findings and that brain CT was performed at a higher rate for these patients nonetheless.

Leong et al.5 evaluated 382 brain CT scans performed on patients with AMS over the course of 11 months at a single ED. They reported that diastolic blood pressure of > 80 mmHg, GCS score of < 15, focal weakness, increasing plantar response, dilated pup-
Furthermore, changes in the mental status are relatively infrequent in patients with posterior circulation stroke. Based on our results, initial GCS scores of <9 and CRP levels of <2 mg/dL were also correlated with positive brain CT findings (Table 4 and Fig. 1). Traditionally, brain imaging studies have been recommended for patients with low GCS scores, a protocol supported by our results. Neurologic evaluation findings in patients with lower GCS scores (<9) might be more limited and less accurate than those in patients with higher GCS scores, simply due to poor cooperation. CRP is a pentraxin released by the liver during the phase response of acute inflammatory reaction. Although every inflammatory condition can increase the CRP level, its high elevation is thought to be suggestive of infection. Patients with severe sepsis and septic shock had higher CRP levels than those with noninfectious systemic inflammatory response syndrome. In our study, lower CRP levels (<2 mg/dL) were associated with positive CT results (Table 3 and Fig. 1). Most patients with positive CT results (93.2%) have CNS pathology (cerebrovascular, CNS infection, CNS tumor, seizure/postictal confusion, and other CNS pathologies) (Table 2). CRP level can be also elevated in many CNS pathologies, such as ischemic stroke and brain hemorrhage. However, in these conditions, increased CRP levels occur several hours after the brain injury; therefore, routine evaluation of CPR levels is not recommended as an initial assessment, and these can affect our results.

Based on the Conditional Inference Tree Analysis results, we suggest the following protocol: if the patient has focal neurologic deficit, brain CT should be performed (CT positivity rate, 96.7%); if the patient has no focal neurologic deficit and if the initial GCS score is <9 and CRP is <2 mg/dL, brain CT can be helpful (CT positivity rate, 37.5%); and if GCS score is ≥9 or <9 and CRP ≥2 mg/dL, brain CT might not be helpful (CT positivity rate, 11.7% and 11.1%, respectively) (Fig. 1). For the generalization of these results, an external validation study should be conducted.

More than 70% of patients included in the present study underwent brain CT, which is higher compared to relevant previous reports. This could have been influenced by the facts that cases of alcohol ingestion or of AMS in previously neurologically impaired patients were excluded from our study. The rate of positive findings on brain CT was 39.8%, which is not much lower than that of the previous studies (14%, 45%). Regional and cultural factors, which should be noted here, can also affect the pattern of brain CT utilization.

The present study has several limitations. First, its design is retrospective. Patients without brain CT were excluded from the analysis, although if they had been included and had undergone brain CT, abnormal lesions might have also been found, which could have affected the results. The neurologic status of these patients changes easily, even in those with only minor medical conditions. Moreover, in the retrospective setting, degrees of AMS are often difficult to understand, and, therefore, evaluate. Finally, the study lacks an ordering protocol for brain CT; instead, CT scans were conducted based on the attending physician’s decision, which could have resulted in a selection bias. Large-scale prospective multicenter studies will overcome these limitations.

In conclusion, positive findings were detected in 39.8% of patients with acute AMS who underwent brain CT in the ED. Initial GCS scores of <9, CRP levels of <2 mg/dL, and presence of focal neurologic deficit were significantly associated with positive brain CT findings.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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