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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 Comal 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 Comal 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 Comal 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

Capsule Summary

What is already known

Brain computed tomography (CT) is a primary diagnostic approach in patients with acute altered mental status. However, recent studies revealed high rates of negative brain CT findings and issues associated with unnecessary radiation exposure.

What is new in the current study

Considering the neurologic examination findings (presence of focal neurologic deficit and Glasgow Coma Scale) and C-reactive protein results, unnecessary use of brain CT can be reduced.

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INTRODUCTION

Altered mental status (AMS) is one of the most common chief complaints reported in 4% to 10% of emergency department (ED) patients.[1-3] 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.[1,3]

Brain computed tomography (CT), the primary diagnostic tool to identify intracranial pathologies, has been recommended for AMS.[1,3,4] Unfortunately, brain CT has some limitations when used to diagnose non-intracranial pathology-related AMS.[2,5,6]

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 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		P-value
	Done (n = 367)	Not done (n = 141)	
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
Frequent alcohol drinking[a]	35 (9.5)	8 (8.2)	0.273
Glasgow Coma Scale	8.45 ± 3.37	9.47 ± 3.50	0.002
Mental status			0.006
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 ± 3.95	0.016
Heart rate (/min)	88.58 ± 23.97	91.96 ± 22.14	0.214
Respiratory rate (/min)	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 ± 71.73	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 (U/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[b]	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 (1.8)	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)	
Frequent alcohol drinking[a]	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)	
Stupor	30 (20.5)	36 (16.3)	
Semicoma	18 (12.3)	24 (10.9)	
Coma	21 (14.4)	15 (6.8)	
Underlying conditions			
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			
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			
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			
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 (U/L)	296.61 ± 599.37	389.28 ± 865.01	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			
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.

Table 4. Multivariate analysis results

Variable	Adjusted odds ratio	95% Confidence interval	P-value
Focal neurologic deficit	132.6	37.8–464.6	<0.001
Glasgow Coma Scale <9	2.4	1.2–4.8	0.016
C-reactive protein <2	3.9	1.4–10.6	0.008

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).

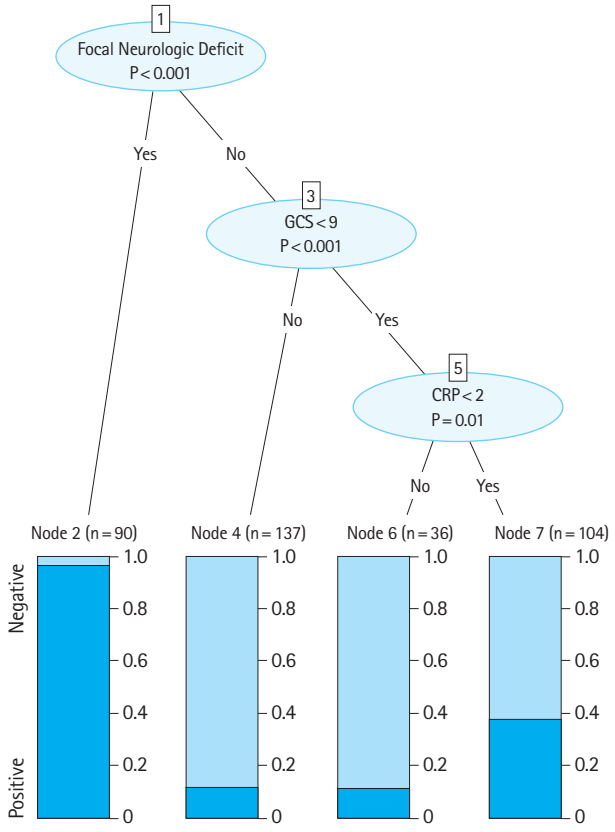

Fig. 1. Conditional inference tree for positive computed tomography (CT) findings. A total of 90 patients had focal neurologic deficit, among whom 87 (96.7%) had positive CT findings (node 2). One hundred and four patients had Glasgow Coma Scale (GCS) scores of <9 and C-reactive protein (CRP) levels of <2 mg/dL; among them, 39 (37.5%) had positive CT findings (node 7). One hundred and thirty-seven patients had GCS scores of ≥9; among them, 16 (11.7%) had positive CT findings (node 4). Among the 36 patients with GCS scores of <9 and CRP levels of ≥2 mg/dL, 4 (11.1%) had positive CT findings (node 6).

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 Brennan[2] 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 pupils, and use of antiplatelet and anticoagulant medications were factors associated with abnormal CT findings. In the present study, the following patient characteristics differed: first, the GCS scores in all patients were <15, and second, trauma patients were excluded. Furthermore, we evaluated laboratory test results that are crucially important for differential diagnosis in the ED, which were not included by Leong et al.[5]

In our analysis, the presence of focal neurologic deficit was a significant factor suggesting positive brain CT findings (Table 4 and Fig. 1). Only three (3.3%) patients with focal neurologic deficit had negative CT findings: two had an acute ischemic lesion on brain magnetic resonance imaging and one hypotension-caused AMS. Only one patient had cerebellar dysfunction, who needed a cerebellar function test requiring cooperation that is typically not possible in patients with AMS, which might affect the results.

Furthermore, changes in the mental status are relatively infrequent in patients with posterior circulation stroke.[14]

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.[4,11,15] 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.[3] Neurologic evaluation may be easier and more accurate in patients with higher GCS scores.

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.[16] 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.[17,18]

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%).[2,5] 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.[1,3] 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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