



Original Contribution

# Metabolic vs structural coma in the ED—an observational study

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## Abstract

**Background:** Patients presenting unconscious may reasonably be categorized as suffering from a metabolic or structural condition.

**Study Objective:** The objective was to investigate if some routinely recorded clinical features may help to distinguish between these 2 main forms of coma in the emergency department (ED).

**Methods:** Adults admitted to an ED in Stockholm between February 2003 and May 2005 with a Glasgow Coma Scale (GCS) score less than 11 were enrolled prospectively. The GCS score was entered into a protocol that was complemented with available data within 1 month.

**Results:** The study population of 875 patients was classified into 2 main groups: one with a metabolic (n = 633; 72%) and one with a structural disorder (n = 242; 28%). Among the clinical features recorded in the ED, 3 were found to be strongly associated with a metabolic disorder, namely, young age, low or normal blood pressure, and absence of focal signs in the neurological examination. Patients younger than 51 years with a systolic blood pressure less than 151 mm Hg who did not display signs of focal pathology had a probability of 96% for having a metabolic coma. The mean GCS score on admission was identical in the groups. Hospital mortality was 14% in the metabolic and 56% in the structural group.

**Conclusions:** These findings indicate that unconscious young adults who present without a traumatic incident with a low or normal blood pressure and without signs of focal pathology most probably suffer from a metabolic disorder, wherefore computed tomography of the brain may be postponed and often avoided.

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## 1. Introduction

The unconscious patient represents a clinical challenge in the emergency department (ED), and approximately 1% of admissions to medical EDs consist of unresponsive persons

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[1,2]. Patients presenting with coma of unknown etiology constitute a high-risk group, and the timing of diagnostic procedures and specific therapy is therefore crucial for their outcome [3-6]. The possible underlying coma etiology in each case may reasonably be acutely classified as either a metabolic or a structural condition, thereby facilitating the choice of interventions with the highest priority, such as, for example, computed tomography scanning of the brain (CT scan), administration of an antidote, or lumbar puncture followed by antibiotic treatment [7,8]. The number of previously published studies of patients presenting with coma to the ED is surprisingly limited [2-6]. According to the study by Levy et al [3], approximately one-third of the patients who present comatose to the nontraumatic ED have an underlying structural etiology. The aims of the present study were to investigate the relative distribution of metabolic vs structural etiologies among nontraumatic patients presenting with impaired consciousness and to examine if some routinely recorded clinical features in the ED may help to correctly distinguish between metabolic and structural coma.

## 2. Materials and methods

Adults admitted consecutively to the nonsurgical ED at either of 2 major teaching hospitals in Stockholm between February 2003 and May 2005 with a Glasgow Coma Scale (GCS) (Table 1) score less than 11 were prospectively enrolled [9]. The reduction in GCS score was required to have been present for at least 30 minutes before inclusion. On admission to the ED, the GCS score was determined by specially trained study nurses and entered into a study protocol together with patient identification data. Each study protocol was complemented with pertinent data from the medical record within 1 month by one of the authors. A GCS score less than 11 was chosen as an inclusion criterion because it implies that the patient is completely unable to communicate. The total patient population enrolled in the present study is identical to that of 2 recently published investigations [4,5]. All available clinical and laboratory data and, in several instances, autopsy findings were reviewed

retrospectively to establish the cause of impaired consciousness in the ED. The different coma etiologies were classified into 2 main groups, metabolic or structural coma, as described by Plum and Posner [6]. Available CT scan results were reevaluated in a blinded fashion by a consultant neuroradiologist. Coma etiologies classified into the structural group were cerebral infarction, intracranial hemorrhage, intracranial tumor, and intracranial infection (meningitis or encephalitis). The remaining occurring coma etiologies were accordingly classified into the metabolic group and constituted poisoning, epilepsy (status epilepticus, seizures, or postictal state), circulatory failure (post-cardiac arrest or circulatory shock), metabolic disorder (hypo/hyperglycemia, hyponatremia, hypothermia, or hepatic failure), extracranial infection, and respiratory insufficiency. Patients were excluded from this study if the explanation to their impaired consciousness on admission was still not clear at hospital discharge or was of a psychogenic nature. In addition, patients with more than 1 plausible coma etiology were excluded. A positive focal neurological sign in the ED was deemed present when (a) the responsible emergency physician on duty had made a written note in the medical record concerning the findings of a neurological examination and (b) the pupils of the patient were of different size without any obvious explanation, the Babinski reflex was present on one or both sides, or there was a clear asymmetry regarding motor responses to painful stimulation or responses to examination of tendon reflexes. The study was approved by the local ethics committee in Stockholm.

### 2.1. Statistics

Univariate and multiple logistic regression analyses were performed to find important relationships between clinical variables (eg, age, blood pressure, body temperature) and their relation to the binary outcome (the 2 main coma etiologies). The results of these findings were reported by means of odds ratios (ORs) and their corresponding 95% confidence intervals (CIs). Hosmer-Lemeshow test and receiver operating characteristics curve were used to determine goodness of fit for the model. When important variables were identified and adjusted for, the next step was to find a clinically applicable and powerful model for predictions to use as a tool in the ED (ie, a model that is powerful enough by means of clinical expertise, predictions accuracy, and goodness-of-fit statistics). The continuous variables in the model were categorized (eg, systolic blood pressure >150 mm Hg and age >50 years) for simpler classification.

## 3. Results

A total of 938 patients were enrolled during the inclusion period. Sixty-three patients (6.7%) were excluded for the

**Table 1** Glasgow Coma Scale

Eye opening	Best verbal response	Best motor response
1 = none	1 = none	1 = none
2 = to pain	2 = incomprehensible	2 = extending
3 = to speech	3 = inappropriate	3 = flexing
4 = spontaneous	4 = confused	4 = withdrawing
	5 = adequate	5 = localizing
		6 = obeying commands

A score less than 11 (inclusion criterion) implies that the patient is unable to communicate.

following reasons: 41 because their coma etiology was still not clear at hospital discharge, 14 because they had more than 1 explanation to the coma, and 8 because their unconsciousness was shown to have been of a psychogenic nature. Among the excluded patients with more than 1 coma etiology, there were 3 with poisoning and a traumatic subdural hematoma. The remaining 875 patients had a mean age of 59 years (15-98), and 464 (53%) were male. Among this final study population, 633 patients (72.3%) were classified into the metabolic coma group and 242 (27.7%) into the structural group. The most common causes of unconsciousness in the metabolic group were poisoning and epilepsy, whereas stroke (cerebral infarction or intracranial hemorrhage) constituted the most frequent coma etiology in the structural group (Table 2).

Table 3 presents a comparison of age and sex distribution, clinical features in the ED, acutely performed interventions, frequency of intensive care treatment during the hospital course, and outcome between patients with a metabolic and those with a structural underlying coma etiology. There was no difference in the frequency of intensive care treatment between the groups. An acute CT scan was performed in 24% of the patients who were later shown to have a metabolic disturbance compared with 90% of the patients in the structural coma group. In the metabolic group, 7 (5%) of the performed CT scan results were not entirely normal. Four of these were evaluated as smaller unspecified changes without clinical significance, 2 as acute global ischemia due to metabolic disorders, and 1 as multiple old infarctions. In the structural group, 182 (84%) of the performed CT scans showed pathological findings. The patients with a structural origin of the coma had a much higher hospital mortality rate: 56% (n = 135) vs 14% (n = 89).

**Table 2** The study population (n = 875) divided into cases with metabolic or structural coma and into the different subclasses of coma etiologies (diagnoses)

Metabolic coma	n (%)	Structural coma	n (%)
	633 (72.3)		242 (27.7)
Poisoning	342 (54)	Cerebral infarction	104 (43)
Epilepsy	116 (18.3)	Intracranial hemorrhage	104 (43)
Extracranial infection	39 (6.2)	Intracranial tumor	17 (7)
Cardiac arrest	42 (6.6)	Intracranial infection	17 (7)
Circulatory shock	17 (2.7)		
Respiratory failure	33 (5.2)		
Hypoglycemia	17 (2.7)		
Hyperglycemia	8 (1.3)		
Hyponatremia	9 (1.4)		
Hepatic failure	8 (1.3)		
Hypothermia	2 (0.3)		

**Table 3** A comparison of clinical features recorded in the ED, acutely performed interventions, frequency of ICU treatment, and outcome between patients with a metabolic coma and patients with a structural underlying etiology

Clinical observations	Metabolic coma n = 633	Structural coma n = 242
Age, mean (y)	53.7 (SD: 20.1)	72.5 (SD: 14.8)
Sex, male	353 (55.8%)	110 (45.5%)
GCS score, mean	5.9 (SD: 2.4)	6.1 (SD: 2.4)
Systolic blood pressure, mean (mm Hg)	126 (SD: 36)	164 (SD: 41)
Clinical signs of focal pathology	88/358 <sup>a</sup> (24.6%)	178/223 <sup>b</sup> (79.8%)
Orotracheally intubated	98 (15.5%)	48 (19.8%)
Acutely performed CT scan	151 (23.9%)	217 (89.7%)
Pathological findings on CT scan	7 (4.6%)	182 (83.9%)
ICU treatment	186 (29.4%)	72 (29.8%)
Hospital mortality	89 (14.1%)	135 (55.8%)

<sup>a</sup> In 358 of 633 patients, notes regarding focal neurological signs were made in the medical records.

<sup>b</sup> In 223 of 242 patients, notes regarding focal neurological signs were made in the medical records.

Sex and age were known in all patients already in the ED. The blood pressure on admission was not noted in the medical record in 22 patients (2.5%). A written statement in the medical record concerning result of a neurological examination in the ED was missing in a part of the study population. In the metabolic coma group, observations regarding presence of focal neurological signs were noted for 358 patients (57%), whereas 223 such notes were made in the structural group (92%). Eighty-eight patients in the metabolic group showed at least 1 positive focal sign (88/358 = 25%). The dominant underlying coma etiology among these 88 patients was epilepsy, n = 50 (57%), followed by poisoning, n = 13 (15%). The other metabolic diagnoses were evenly distributed among the remaining 25 patients. In the structural group, 178 patients (178/223 = 80%) displayed at least 1 positive focal sign in the ED (Table 3).

Among all the clinical variables that were recorded in the ED, the following were statistically investigated regarding their prediction of a metabolic or structural underlying condition (ORs, expressed as crude numbers, and their 95% CIs): age, sex, GCS score, result of neurological examination, blood pressure, heart rate, respiratory rate, body temperature, pH, PaO<sub>2</sub>, PaCO<sub>2</sub>, serum potassium, serum sodium, serum glucose, and serum creatinine. Age, sex, blood pressure, and result of neurological examination were found to be significantly different between patients in the metabolic group and those in the structural coma group. After adjusting for pertinent variables such as age and blood pressure, and categorization for age and blood

**Table 4** Odds ratios for prediction of a metabolic coma for some clinical features recorded in the ED

Clinical features	OR	95% CI
Age $\leq$ 50 y	4.0	(2.15-7.33)
Blood pressure, systolic $\leq$ 150 mm Hg	3.0	(1.96-4.59)
Focal sign, negative	8.0	(5.2-12.4)
Male sex	1.54	(1.01-2.37)

pressure (ie, systolic blood pressure  $>$ 150 mm Hg and age  $>$ 50 years), multiple logistic regression analyses were performed. The following parameters were found significant: age, blood pressure, focal neurological signs, and sex (Table 4).

To find a predictive and clinically useful combination of parameters, probability tests were performed. The combined findings for age, blood pressure, and result of neurological examination were shown to be highly predictive of either a metabolic or a structural coma. In this final predictive model, 569 out of the total 875 patients fulfilled the 3 variables included; that is, a written statement regarding result of a neurological examination in the ED was noted in the medical record, as were the blood pressure on admission and the age of the patient. Sex as a variable did not add anything to this statistic model and was therefore excluded. The probability for a patient with the combination of age less than or equal to 50 years, systolic blood pressure less than or equal to 150 mm Hg, and negative focal neurological signs of having a metabolic coma was 96.1%. The probability for a patient with the combination age greater than 50 years, systolic blood pressure greater than 150 mm Hg, and positive focal signs for having a structural coma was 79.8% (Table 5).

**Table 5** Prediction of the 2 main forms of coma, metabolic or structural, based on 3 clinical features easily recorded in the emergency department

Probability for	Patients $\leq$ 50 y and systolic blood pressure $\leq$ 150 mm Hg and no focal neurological sign	Patients $>$ 50 y and systolic blood pressure $>$ 150 mm Hg and focal neurological sign
Metabolic coma	<b>0.96</b>	<b>0.20</b>
	95% CI (0.80-0.99)	95% CI (0.03-0.67)
Structural coma	<b>0.04</b>	<b>0.80</b>
	95% CI (0.01-0.20)	95% CI (0.33-0.97)

The statistical calculations are based on the 569 patients who had full data recorded in their medical records. Goodness of fit was ascertained with Hosmer-Lemeshow test ( $P = .90$ ) and receiver operating characteristics curve with an area under curve of 0.84. Prediction accuracy was 80.9% for metabolic origin and 75.2% for structural origin.

## 4. Discussion

In this study of 875 unselected patients with impaired consciousness presenting to 2 nonsurgical EDs, approximately three-quarters were suffering from a metabolic condition. In a previous study by Levy et al [3], the corresponding proportion of patients with a metabolic underlying disorder was around two-thirds. However, in that study, poisonings were not included. The other major finding in the present study was that 3 routinely recorded clinical features, namely, age, blood pressure, and findings on neurological examination, were found to be strong determinants of the 2 main coma categories: metabolic and structural. Patients younger than 51 years with a systolic blood pressure less than 151 mm Hg who did not display signs of focal pathology had a statistic probability for having a metabolic coma of 96%. The combination of these 3 clinical features composes a simple decision aid, not described before, which may help emergency physicians to rapidly and more correctly distinguish patients with metabolic conditions from those with a structural coma.

The methods of classifying coma into groups based on related etiologies vary in the literature [7,10,11]. The 2 main groups—metabolic and structural coma—that were used in the present study mainly follows the classification method of Plum and Posner [6] that, in addition to cerebral infarction, intracranial hemorrhage, and intracranial tumor, also includes intracranial infections such as encephalitis as structural conditions. The rationale for this is partly that all these conditions may warrant an acute CT scan and partly that these coma etiologies have a much poorer prognosis than the coma etiologies in the metabolic group [3,5].

The 3 clinical features that were found valuable to distinguish between structural and metabolic coma in this study will hardly surprise the experienced clinician. Firstly, low age is known to be typical for cases of poisoning, which constitute the numerically dominating metabolic subgroup [2,4]. Furthermore, the incidence of stroke increases with increasing age [12,13]. Secondly, high blood pressure is more prevalent in old age and is a risk factor of stroke [14]. Moreover, in situations when the intracranial pressure suddenly rises, as for example after a cerebral hemorrhage, the activity of intravascular baroreceptors will lead to an elevated systemic blood pressure to secure the cerebral blood flow [15]. Thirdly, the presence of focal signs in the neurological examination is usually associated with a structural intracranial lesion, even though they may occur in some metabolic disorders, that is, hypoglycemia, postictal states, hepatic encephalopathy, and some poisonings [6,16-20]. One possible explanation for the occurrence of focal signs in the latter instances is alterations in intracranial pressure due to edema that may develop after circulatory disturbances or metabolic changes in the brain [6].

It is commonly assumed that almost all patients with a structural coma display focal neurological signs, whereas patients with a metabolic coma do not. In the present study, the patients with structural coma, who had a result of a neurological examination noted, displayed positive focal signs in only 80%. The inclusion of the intracranial infections into the structural coma group explains a part of the missing 20%, but also the fact that patients with slowly progressing intracranial diseases or diffuse lesions in the cortex may present unconscious without any sign of focal pathology [6]. The corresponding proportion of patients with positive focal signs in the metabolic group was 25%. Reasons for this surprisingly high proportion, beyond the above-mentioned explanation, may be that more than 10% of a healthy population has an isolated anisocoria and that some of the study patients had neurological sequelae after a previous stroke [6,21]. The most important explanation, however, was probably that notes regarding focal signs were made only in 358 of the 633 patients with metabolic coma; and it is reasonable to assume that a vast majority of the remaining 275 patients did not display any focal neurological sign. If the latter is true, the real proportion of patients in the metabolic group with positive focal signs would have been smaller.

The acute performance of CT scan has more or less become a routine in cases presenting with coma worldwide. When a structural lesion is suspected and an indication for acute neurosurgical or thrombolytic treatment is reasonable, there is no doubt about its indication. However, if the impaired consciousness is due to a metabolic disorder, an emergency CT scan is most often medically unnecessary and resource demanding and carries a risk of delaying important treatment and intensive care unit (ICU) monitoring. In the present observational study, 151 CT scans were acutely performed among the patients in the metabolic group.

#### 4.1. Limitations

The inclusion procedure, including the grading of the coma level, was managed prospectively; but the remainder of the data collection was performed within 1 month of each case. This course of action may have been of some advantage because it implied that the physicians and medical staff who managed the patients were not aware of the study. However, although carefully performed, this investigation carries some of the weaknesses common to all retrospective studies.

#### 5. Conclusion

The findings of this study indicate that unconscious young adults who present to the ED without an obvious traumatic

incident with a low or normal blood pressure and without signs of focal pathology most probably suffer from a metabolic underlying disorder, wherefore CT of the brain may be postponed and often avoided.

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