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LETTER TO THE EDITORS

Causes of coma and their evolution in the medical intensive care unit

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Dear Sirs,

Epidemiological data regarding the frequency of the different causes of coma and their evolution over time in the ICU are scarce [1–4]. In the 1970s, Plum and Posner [2] described the causes of 500 successive cases of coma. However, since then no specific study focusing on the causes of coma and their evolution over time has been published although the ICU management of brain injuries has progressed tremendously. Some data are available from prospective and retrospective studies assessing coma outcome [3–8], but the different causes of coma were excluded in these studies. These studies, therefore, do not provide a global description of the causes of coma and their evolution. The aim of this study was to describe the causes of coma and their evolution over an 8-year time period in a medical ICU. From January 2001 to December 2008, we retrospectively identified patients who presented with coma in the first 24 h of ICU admission, defined as a Glasgow Coma Scale below 8 in the absence of sedative drugs, and we retrieved their demographic data (supplementary Table). For statistical purposes, four time periods of 2 years each were defined.

A total of 2,189 out of 4,482 patients were evaluated. Baseline characteristics of the patients can be found in the supplementary Table. Detailed causes of coma, initial Glasgow Coma Scale and ICU survival are shown Table 1. The frequency of anoxo-ischemic encephalopathy and shock of any origin increased as the causes of coma over the 8-year time period is shown in Table 2. At the same time, the frequency of the other causes of coma remained stable. Among the 2,189 comatose patients, 1,139 (52%) survived to ICU discharge (Table 1). Survival rates according to each cause of coma are given in the Table 1.

To our knowledge, this is the largest existing cohort that focused on the causes of coma and their evolution. The study population was comparable in age, sex ratio, and the Glasgow Coma Scale score to previously reported populations of comatose patients as in the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT) cohort. SUPPORT, the largest previously available cohort of 596 non-traumatic comatose patients, studied factors such as high risk of death and severe disability [1–8]. However, the SUPPORT cohort excluded drug intoxication and metabolic causes of coma [4]. Plum and Posner [2] found that the most common causes of coma were drug poisons (30%), cerebral hemorrhage including intracerebral, epidural, and subdural hemorrhages (15%), and brainstem infarction (8%). Cardiac arrest represented only 2% in the Plum and Posner cohort. This discrepancy could be somewhat explained by the fact that the Plum and Posner's study was performed in a neurological ICU, whereas our study was performed in a general medical ICU. Moreover, our study was subject to regular updates of the guidelines for cardiac arrest resuscitation which has improved immediate survival over the last 30 years. This hypothesis is corroborated by the findings of the other previous reports [4–8]. The reason for the

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Table 1 Detailed causes of coma

Causes of coma	*n* (%)	Mean GCS at admission	Survival *n* (%)
Anoxo-ischemic encephalopathy	513 (23%)	3 ± 1	103 (20%)
Poisoning and drug overdose	425 (19%)	6 ± 3	395 (93%)
Multiple CNS depressants intake	162 (7%)		
Multiple drug intake	112 (5%)		
Alcohol	40 (2%)		
Benzodiazepines	33 (1,5%)		
Opioids	29 (1.3%)		
Neuroleptics/phenothiazines	10 (0.5%)		
Carbon monoxide poisoning	2 (0.1%)		
Other	37 (2%)		
Cerebrovascular accident	139 (6%)	5 ± 2	45 (32%)
Intracerebral hemorrhage	61 (3%)		
Cerebral infarction	51 (2%)		
Subarachnoid hemorrhage	20 (1%)		
Cerebral thrombophlebitis	4 (0.2%)		
Posterior reversible encephalopathy syndrome	3 (0.1%)		
Central nervous system infection	66 (3%)	8 ± 3	55 (83%)
Bacterial meningitis	31 (1.4%)		
Viral meningo-encephalitis	15 (0.7%)		
Cerebral toxoplasmosis	7 (0.3%)		
Paludism	5 (0.2%)		
Cryptococcus meningitis	2 (0.1%)		
Brain abscess	2 (0.1%)		
Other	3 (0.1%)		
Status epilepticus	147 (7%)	5 ± 3	132 (90%)
Antiepileptic drug withdrawal	30 (1.4%)		
Alcohol withdrawal	14 (0.6%)		
Cerebral tumors	14 (0.6%)		
Pharmoresistant epilepsy	5 (0.2%)		
Sequelae of ischemic stroke	5 (0.2%)		
Other or unknown	39 (1.8%)		
Metabolic brain dysfunction	222 (10%)	7 ± 3	171 (80%)
Hypercapnic encephalopathy	109 (5%)		
Hepatic encephalopathy	17 (0.8%)		
Uremia and dialysis	5 (0.2%)		
Ionic and acid–base disorders			
Hyponatremia	25 (1.1%)		
Hypernatremia	9 (0.4%)		
Hypercalcemia	1 (0.04%)		
Endocrine disorders			
Hypoglycemia	20 (1%)		
Acidocetosis	11 (0.5%)		
Hyperosmolar state	11 (0.5%)		
Adrenal insufficiency	2 (0.1)		
Myxoedema	1 (0.04%)		
Temperature regulation			
Heat stroke	9 (0.4%)		
Hypothermia	2 (0.1%)		

Table 1 continued

Causes of coma	*n* (%)	Mean GCS at admission	Survival *n* (%)
Shock	449 (21%)	5 ± 3	94 (20%)
Septic shock	275 (13%)		
Cardiogenic shock	106 (5%)		
Hemorrhage	39 (1.8%)		
Hypovolemic shock	26 (1.2%)		
Other	3 (0.1%)		
Acute respiratory distress	165 (8%)	6 ± 3	105 (64%)
Pneumonia	83 (3.8%)		
Cardiogenic pulmonary edema	29 (1.3%)		
ARDS	22 (1%)		
Other	31 (1.4%)		
Traumatic brain injury	32 (1%)	5 ± 3	20 (63%)
Subdural hematoma	29 (1.3%)		
Other	3 (0.1%)		
Psychogenic coma	7 (0.3%)	6 ± 3	7 (100%)
Miscellanous	19 (1%)		
Unknown cause	5 (0.2%)	6 ± 4	7 (100%)
Total	2,189 (100%)		

ARDS acute respiratory distress syndrome, *CNS* central nervous system, *GCS* Glasgow coma scale

Table 2 Evolution of the causes of coma over time

Causes of coma	Total time period $n = 2{,}189$	Period 1 (2001–2002) $n = 414$	Period 2 (2003–2004) $n = 559$	Period 3 (2005–2006) $n = 649$	Period 4 (2007–2008) n = 567	*p* value
Anoxo-ischemic encephalopathy	513 (23%)	75 (18%)	113 (20%)	168 (26%)	157 (28%)	<0.0001*
Poisoning and drug overdose	425 (19%)	92 (22%)	116 (21%)	128 (20%)	89 (16%)	0.0181
Cerebrovascular accident	139 (6%)	28 (7%)	36 (6%)	45 (7%)	30 (5%)	0.1697
Central nervous system infection	66 (3%)	14 (3%)	17 (3%)	19 (3%)	16 (3%)	0.8524
Status epilepticus	147 (7%)	30 (7%)	44 (8%)	40 (6%)	33 (6%)	0.3421
Metabolic brain dysfunction	222 (10%)	50 (12%)	36 (11%)	51 (8%)	58 (10%)	0.1560
Shock	449 (21%)	74 (18%)	117 (21%)	136 (21%)	122 (22%)	0.0003*
Acute respiratory distress	165 (8%)	37 (9%)	41 (7%)	37 (6%)	50 (9%)	0.4346
Traumatic brain injury	33 (2%)	9 (2%)	6 (1%)	12 (2%)	6 (1%)	0.3916
Psychogenic coma	7 (0.3%)	1 (0.2%)	1 (0.2%)	5 (1%)	0	0.0379
Miscellaneous	19 (1%)	4 (0.01%)	4 (0.01%)	7 (0.01%)	4 (0.01%)	0.7006
Unknown cause	5 (0.2%)	0	0 (0.2%)	2 (0.3%)	2 (0.3%)	0.2615

* According to Bonferroni's correction $p < 0.004$ corresponded to statistical significance

increase in the frequency of shock of any origin over time is unclear. We observed, however, that both the severity of illness and the existence of preexisting chronic diseases increased over time. This could partially explain this evolution. Intracerebral and subarachnoid hemorrhages accounted for only 3 and 2% of the diagnoses, respectively. This proportion is lower than that previously reported [2–4, 7] and can be explained by the case mix. Indeed, whereas Plum and Posner's study was performed in a neurological ICU, we included patients in a medical ICU. Our hospital located in the heart of Paris is a tertiary care center which has a medical and surgical ICU with interventional radiologists on site. The neurological department, which consists of a stroke center, and the neurosurgical department, which is part of the same hospital, are located 6 km away (about 5 min by ambulance). Furthermore, the majority of

our patients are supported by the Service d'Aide Medical d'Urgence (SAMU) which in France provides out-of-hospital advanced medical support by physicians. Thus, it is likely that patients with a high probability of subarachnoid or intracerebral hemorrhage were directly referred to the neurological or neurosurgical ICU. The effect of the recent improvements in the management of cerebrovascular accidents cannot be excluded. The survival rates determined in our study are similar to that reported previously [1, 7] even though it is higher than that reported in the SUPPORT cohort where the main causes of metabolic brain dysfunction were excluded [4, 7].

Coma is a frequent cause for admission to the ICU. Further prospective studies are warranted to promote adequate data for both intensivists and neurologists to help them adapt emergent management.

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Conflicts of interest None.

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