What is the nutritional status of patients with prolonged disorders of consciousness? a retrospective cross-sectional study

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Abstract

Background: Nutritional status of patients with disorders of consciousness (DoC) is poorly studied. Objectives: To evaluate the relationship between nutritional status (Body Mass Index, daily calories intake) and clinical variables (level of consciousness, time since injury, diagnosis, aetiology and spastic muscle overactivity; SMO,) in inpatients with prolonged DoC or emerging. Our main hypothesizes are: i) patients with lower level of consciousness (UWS) have worse nutritional status compared to patients in minimally conscious state (MCS), ii) SMO could influence nutritional status. Methods and Results: Among the 80 patients included in the study (19 UWS, 47 MCS, 14 emerging MCS; 43±15 yo; 3±4 years post-injury, 35 traumatic aetiology, 34 females), 9% were at risk to be undernourished, with no differences between UWS and MCS. Patients without SMO had a higher BMI compared to patients with severe SMO. Compared to the recommended daily calories intake, patients with the highest BMI received less calories and patients with the lowest BMI received more calories. We observed a negative correlation between SMO (in lower limbs) and BMI. Conclusion: Our study shows that most patients are well nourished, independently from the level of consciousness. SMO may require additional calories in patients' daily needs; however, longitudinal studies are needed to explore the causal relationship between these variables.

Keywords: UWS, MCS, nutrition, spastic muscle overactivity, BMI

Background & Aim

Acquired severe brain injury caused by traumatic brain injury (TBI), anoxic brain injury or stroke, among others (1), can lead to the presence of Disorders of Consciousness (DoC). The term DoC refers to particular clinical conditions, such as coma, unresponsive wakefulness syndrome (UWS) and minimally conscious state (MCS). After a period of coma, when patients open their eyes, they can

evolve into an UWS, previously termed vegetative state, which is characterized by the presence of reflex behaviors only (2). A patient in UWS can subsequently shows minimal but definite and reproducible cognitive mediated behaviors (e.g., visual pursuit, commands following, intentional communication) (3), characterizing the MCS. Patients emerge from the MCS (eMCS) when they recover functional communication and/or objects' use. The current recommended scale to evaluate patients with DoC and eMCS is the Coma Recovery Scale-Revised (CRS-R) (4, 5, 6, 7).

Scientific literature about nutritional status of DoC patients is scarce, while the importance of nutrition during rehabilitation after severe acquired brain injury is critical. One retrospective study was performed in 9 DoC patients and 11 patients who regained consciousness (17 traumatic brain injury, 2 normal pressure hydrocephalus, 1 anoxia) all of them undernourished, with a BMI under 15 and therefore underweighted. The study highlighted that undernourished patients have higher incidence of complications during the rehabilitation period compared to well-nourished patients (8). Moreover, it takes one more year after brain injury for these undernourished patients to reach the same functional status than the well-nourished control group (8). A recent study conducted on a DoC patient associated poor nutrition to an imbalance in morbidity, mortality and quality of life as well as an increase in infectious complications, impaired health and prolonged hospitalization, underlying the effect of a proper nutritional approach in the reduction of the recovery times and the effectiveness of the therapeutic path (9). In addition, we should stress that a proper nutritional therapy relies on an accurate prediction of the basal metabolic rate and the equations used in DoC patients, which were derived from healthy subjects, were not adequate. Since DoC patients may live a long time with the support of nutrition, their nutrition therapy should be individualized and based on indirect calorimetry (IC) measurements (10).

Beside the importance of a good nutritional status, the alteration of the normal metabolic process, such as the metabolic dysfunction, can impede functional recovery following severe acquired brain injury. For instance, significant body hyper-metabolism (as measured with the energy expenditure)

in the intensive care and neurosurgical units were observed with a risk of severe undernourishment despite nutritional support, in the acute phase following a TBI (11, 12). The neurophysiological mechanisms explaining this metabolic dysfunction are not yet understood. If in the acute phase after TBI a significant hyper-metabolism is observed, in the chronic phase weight tend to increase over time. Significant long-term changes can be observed as a consequence of TBI, one of them being obesity, described both as a contributor to TBI and a common outcome (13). Changes in neurocognitive functioning, emotional well-being, sleep/fatigue, pain, motor functioning, balance, and/or seizures can negatively affect weight and participation in weight management behaviors (e.g., physical activity, healthy diet) such as other factors limiting physical functioning (e.g., orthopedic injuries, surgeries) and dietary intake (e.g., medications; dysphagia; hypothalamic disorder compromising endocrine control) thereby affecting weight (14).

Other factors could also influence the nutritional status and the body weight of these patients; one of them being spastic muscle overactivity (SMO). Few articles showed the positive relationship between SMO and energy consumption (15-17). A case report presented a child with mental retardation and severe SMO whose nutrition and caloric intake were carefully managed on the ketogenic diet and whose SMO was treated by the placement of a baclofen pump. The patient was monitored for 9 months after the baclofen pump's placement. Concomitant decrease in SMO (30 to 40%) and weight increase (+20%) were observed. The SMO reduction induced an imbalance in the caloric consumption, allowing for patient's weight gain. In order to control the weight gain, daily caloric intake was reduced from 966 to 866 calories (approximately 10%) resulted in initial weight loss and then subsequent weight stabilization (15). A similar result is reported in a study conducted on 19 children with cerebral palsy (i.e., presence of hemiplegia, diplegia and quadriplegia) who underwent neurosurgical intervention (i.e., selective dorsal rhizotomy) to reduce SMO. The authors found that the children with the greatest degree of SMO pre-operatively tended to gain more weight, and they explained this result by SMO's energy consumption (16). In a study on 6 patients with severe

head injury, the basal metabolic rate of these patients was higher than normal (130 – 135%) and the suggested energy intake was almost 35 kcal/kg/day (17). It has been shown that this high energy need is due to spasticity, agitation and vegetative dysfunctions (8). Additionally, many of the undernourished patients with head injuries had other limb fractures (polytraumatized), and the treatment of these and of associated complications (infections, fever, pressure sores, septicemia) extended even these energy needs (8).

Due to the paucity of articles related to DoC and nutritional status in the literature and because of the importance of a good nutritional status for the recovery trajectory following a brain injury, our aim is to expand the actual knowledge in this field with this first cross-sectional cohort study in patients with prolonged DoC. In particular, we aim to evaluate the relationship between nutritional status and the level of consciousness, as well as the relationship between the nutritional status and the presence and severity of SMO. We hypothesized that UWS patients will have worse nutritional status compared to MCS or EMCS patients, and that higher SMO could be linked to lower BMIs.

Method

Study design and Population

This is a cross-sectional retrospective study conducted on medically stable DoC and eMCS patients admitted to the University Hospital of Liège (Belgium) for one week of multimodal diagnosis and prognosis assessments. These patients come from their rehabilitation center, homes or nursing homes. The objective of this short hospitalization is to provide an accurate diagnosis using repeated behavioral assessments and neuroimaging techniques and give indications on prognosis and potential treatments. Therefore, for the purpose of our study, the inclusion criteria were: 1) diagnosis of UWS, MCS or eMCS based on repeated evaluations with the CRS-R during the one-week hospitalization (4), 2) time since onset of condition more than three months, and 3) minimum age of 16 years old. The absence of the information related to the clinical and nutritional status was an exclusion criterion.

The study was approved by the ethical committee of the University Hospital of Liège (number 2017/297), and written informed consents were obtained from the patients' legal representatives.

Materials

CRS-R

The patient's state of consciousness was assessed by experienced clinicians using the CRS-R. The CRS-R is composed of six subscales that assess the following domains: visual, motor, auditory and verbal functions, as well as communication, and arousal. The total score ranges from 0 to 23 and the diagnosis is made according to the presence/absence of particular behavioral responses (18). The CRS-R with the highest score was taken as the final diagnosis.

MAS

The SMO was assessed only once for each patient with the MAS, a 6-level ordinated scale with documented reliability (18). Higher scores indicate increasing severity of SMO. Assessment of SMO followed scale's guidelines (i.e., patients assessed in a resting position) and included passive flexion and extension of upper and lower extremity joints. The median MAS score of assessable (i.e., without joint total fixation that makes the evaluation impossible) joints of the upper limbs and lower limbs, separately, was used for our analyses. A MAS score of 0 was indicative of no SMO, a score between 1 and 3 was indicative of moderate SMO, and a score of 4 and 5 was indicative of severe SMO.

Criteria for malnutrition and risk to be undernourished based on ESPEN Guidelines on adult enteral nutrition (2006) (21)

- BMI (< 18.5 kg/m²) and kinetic of weight according to the time (weight loss ≥ 5%/1month or ≥ 10%/6 months)
- Blood test results (albumin (<30 g/l), prealbumin (< 0.15g/l), total protein, C-reactive protein)
- Difference between the daily caloric needs and the real intake of calories and proteins which could trigger undernourishment.

Body Mass Index (BMI)

BMI was calculated dividing the body mass expressed in kilos by the square of the body height expressed in meters. Patients were subsequently classified in 4 different categories according to the following criteria: patient whose BMI was under 18.5 kg/m^2 were classified as under-weighted, those with a BMI between 18.5 kg/m^2 to 25 kg/m^2 had a normal weight, those with a BMI between 25 kg/m^2 and 30 kg/m^2 were overweight, and patients with a BMI higher than 30 kg/m^2 were obese. The World Health Organization regards a BMI of less than 18.5 kg/m^2 as underweight, a BMI equal to or greater than 25 kg/m^2 is considered overweight and above 30 kg/m^2 is considered obese.

Daily Caloric Needs (DCN), Real Caloric Intake (RCI)

DCN are based on the theory and are calculated according to the following formula: 30 kcal/calculation weight (CW) to minimize energy intake in case of obese patients and to avoid undernourishment in case of underweight patients (Table 1). The DCN, calculated according to the above-mentioned formula, is the one used for population with an artificial nutrition (19), and there are no existing guidelines for DoC and eMCS patients. The absence of specific guidelines for this population is responsible for a gap, highlighted by clinical observations and a previous study (10) underlying a discrepancy between the estimated DCN and the Real Caloric Intake (RCI). The difference between the estimated DCN and the RCI will be referred as 'difference between calories' (ΔC).

(Table 1)

Procedure

During our one-week program, we daily administered the CRS-R for the assessment of the state of consciousness. The Modified Ashworth Scale (MAS) for the assessment of SMO was administered once. Information about nutritional status was retrieved from patients' medical report such as the type of nutrition and the amount of daily calories needed, as decided by medical doctors of patients'

sending institutions. At the admission to our hospital, blood tests were performed to check values related to total proteins, albumin, prealbumin and c-reactive protein. Similarly, useful information for the calculation of the BMI such as patients' weight and height were also recorded. All the collected data were anonymized, associating an alphanumeric ID to each patient, and registered in an electronic database.

Statistical analysis

The variables used for statistical analyses were the patients' diagnosis (UWS, MCS, EMCS), energy intake, the BMI, the SMO measured in upper and lower limbs (MAS score), the time since injury and the aetiology.

A chi-squared test was conducted in order to compare the risk to be undernourished among patients with different diagnosis (UWS, MCS). The Spearman's rank correlation test assessed the relation between the BMI and upper and lower limbs' SMO. We conducted three one-way ANOVA analyses. The first one compared, separately, the effect of upper and lower limbs' SMO on the BMI in 'no SMO', 'moderate SMO' and 'severe SMO' groups of patients. In order to further explore the possible differences between groups, we conducted an independent samples t-test. The second ANOVA was conducted to compare the effect of upper and lower limbs' SMO, separately, on the, ΔC (difference between the DCN and the RCI). The third ANOVA compared the effect of the BMI on the ΔC in 'underweight', 'normal', 'overweight' and 'obese' groups of patients. In order to further explore the relation among groups, a multiple comparison of means (Tukey test) was conducted, and Bonferroni correction was applied ($p<0.0125$). In order to study which variables influences the BMI, we conducted a linear regression analysis taking into account the daily caloric needs (DCN), the real caloric intake (RCI), the severity of spasticity, time since injury, aetiology and diagnosis.

Results

Population

Among the patients assessed at the University Hospital of Liège between 2014 and 2017, we enrolled 80 patients according to the inclusion and exclusion criteria of our study (Figure 1).

(Figure 1 near here)

Among the patients included in the study (34 women, 43±15 years old; 3±4 years after injury), 35 had a TBI, 25 suffered from anoxic brain injury, 12 suffered from a stroke, 4 presented mixed aetiology, 1 had an intoxication, 1 had a meningitis, 1 suffered from hypoglycemia and 1 suffered from surgical complication. See Table 2 for comprehensive clinical and nutritional information about each patient.

(Table 2 near here)

Concerning the level of consciousness, nineteen patients were diagnosed in UWS (23.75%), 47 patients in a MCS (58.75%) and 14 eMCS (17.5%). Seven patients (9%) were at risk of being undernourished and 73 patients (91%) were well nourished. Among patients at risk to be undernourished, 4 were in UWS and 3 were in MCS. No patients in eMCS were at risk of being undernourished. Among well-nourished patients, 15 were in UWS (79%), 44 in MCS (94%) and 14 patients in eMCS (100%). UWS patients did not have a higher risk to be undernourished compared to MCS patients (X^2= 3.240; p=0.07) (Figure 2).

(Figure 2 near here)

Concerning nutritional variables, 74 patients were fed by enteral nutrition and 6 were fed exclusively orally. Among patients who were fed by enteral nutrition, 70 had a gastrostomy, 2 had a jejunostomy and 2 had a nasogastric tube; furthermore, 3 of them received food also orally. The pattern (bolus/continuous) was selected according to the information in the medical records, without changes in patients' nutritional plan and administration modalities. Protein, albumin, prealbumin and C-reactive protein values were within the norm, indicating patients' good nutritional status and protein intake. All the patients included in the study were stable and the feed was well tolerated. Looking at

the BMI, 9 patients were underweighted (11%), 46 had a normal BMI (57%), 18 patients were over-weighted (23%) and 7 were obese (9%).

Comparison between BMI, ΔC and SMO

Regarding the differences between BMI and the caloric intake, there was a significant effect of the BMI on the ΔC ($F= 8,37$; $p<0.001$; Figure 3). The ΔC was significantly different in the obese group of patients compared to the patients with a normal BMI ($t=3.5$; $p=0.004$) and to the ones who were under-weighted ($t=4.03$; $p<0.001$). Furthermore, there was a significant difference of the ΔC between over-weighted and under-weighted patients ($t=3.5$; $p=0.004$).

(Figure 3 near here)

Regarding the differences between BMI and SMO, there was a significant negative correlation between median SMO measured in lower limbs and BMI ($rho=-0.29$; $p=0.009$). No correlation was found with median SMO in the upper limbs ($rho=-0.19$; $p=0.09$). According to the ANOVA test, this pattern seems to be confirmed when looking at the effect of lower limbs' SMO on the BMI, that was found significant in the three conditions ('no SMO', 'moderate SMO' and 'severe SMO') ($F=7.29$; $p<0.001$). A multiple comparison of means (Tukey contrasts) was conducted to further explore the comparison between variables and Bonferroni correction was applied ($p<0.0166$). A significant difference was found between the BMI of 'no SMO' group of patients and, 'severe SMO' groups ($t=-3.82$; $p=0.0008$) (see Figure 4).

(Figure 4 near here)

Regarding the comparison between caloric intake and SMO, there was no significant effect of the upper ($F= 0.55$; $p=0.57$) and lower ($F=0.61$; $p=0.54$) limbs' SMO on the ΔC.

Finally, linear regression's results showed that the variance in the BMI is explained by the cumulative effect of the following (tested) variables: RCI ($F(1,78) =1.41$; $p=0.23$; $R^2 = .0178$), DCN ($F(2,77) =19.19$; $p<0.01$; $R^2 = .3326$), severity of SMO ($F(3,67) =15.70$; $p<0.01$; $R^2 = .3879$) and time since injury ($F(4,66)=16.20$; $p<0.01$; $R^2 = .4955$). The following results were obtained adding the effect of aetiology ($F(5,65)=12.80$; $p<0.01$; $R^2 = .4961$) or diagnosis ($F(6,65)=16.20$; $p<0.01$; $R^2 = .4955$).

Discussion

The aim of this study is to evaluate the relationship between nutritional status and the level of consciousness, as well as the relationship between the nutritional status and the presence and severity of SMO. We hypothesized that UWS patients will have worse nutritional status compared to MCS or EMCS patients, and that higher SMO could be linked to lower BMIs.

This preliminary study shows that (1) the majority of our patients is well-nourished (91%) and only seven patients (9%) were at risk of being undernourished. Among patients at risk of being undernourished, all of them had a DoC and no eMCS patients were at risk of being undernourished. Among DoC patients, there were no differences between UWS and MCS patients (Figure 2);

(2) looking at the BMI, more than a half of our sample (46 patients) have a normal BMI (57%), 18 were over-weighted (23%), 9 patients were underweighted (11%) and 7 were obese (9%); and there is a positive correlation between patients' BMI and the difference between the DCN suggested by the guidelines and the RCI (Figure 3); (3) looking at the relation between BMI and SMO, we found a significant negative correlation between these two variables (Figure 4); furthermore, SMO is not only correlated to the BMI but also plays a causal role in its variance, among other factors.

Our primary observation regarding the proportion of patients being well-nourished is reassuring as only 9% of our sample seems at risk to be undernourished and no difference was found between UWS and MCS patients. A comparison between a previous study and our study results in a higher rate of patients being at risk to be undernourished (41.5% vs 9% observed in our study) who were also under-weighted (41.5% vs 11% observed in our study). This comparison also showed an absence of over-weighted and obese patients. The percentage of normal weighted patients in the two studies was comparable (59% vs 57% observed in our study). The difference observed in the two studies in the risk of being undernourished could be explained by the higher number of under-weighted patients (41.5% vs 11% observed in our study) and the difference in the criteria used to determine the risk of being undernourished, based only on the BMI in the former study. Furthermore, it should be noted that we do not have information on the patients' nutritional status before the injury; therefore, the two

datasets might not be comparable at baseline, which could partially explain such differences, in addition to cultural diversity between Asia (were the above-mentioned study was conducted) and Europe that could have influence the percentage of patients who are underweighted. Regarding the relation between level of consciousness and nutritional status, our study remains the only study conducted so far. Even if we do not observe statistically significant differences in the risk of being undernourished between UWS and MCS patients we can observe a trend (see Figure 2). Studies conducted on larger samples are needed to confirm our results and refuse the hypothesis that there is a link between the level of consciousness and the nutritional status. The hypothesis of a difference in the risk of being undernourished between UWS and MCS patients relies on the so-called self-fulfilling prophecy. According to this idea, our expectations for a bad outcome (i.e., being in a UWS) reduce our investment and actions, and therefore, the poor outcome is more likely to occur. As the author of a recent study explains (22), we may not even be conscious of how our expectation for recovery affects the speed with which we work, the staff we assign to a patient's care, and the medical interventions we offer. The absence of differences between UWS and MCS patients in our sample highlights that the patients with different diagnosis received the same attention and cares.

Regarding the link between BMI and ΔC, the ΔC was significantly higher in the obese group of patients compared to the patients with a normal BMI and to the ones who are underweighted. This result shows that patients who are obese are the ones in which the difference between their DCN and the RCI is higher (-630 kcal). On the other hand, patients whose RCI is superior to the DCN (+106 kcal) are underweighted. Considering that there are no significant differences in the RCI among patients with different diagnosis and aetiology, other factors need to be considered, such as dysfunction of the hypothalamus. Indeed, it is well accepted that the brain, notably the hypothalamus and its complex network, play a crucial role (23). Food intake, beside external factors (e.g., emotions), is influenced by internal factors, such as the 'energy homeostasis' regulatory process that promotes stability in the amount of body energy stored in the form of fat (23). The hypothalamus represents the major center controlling for food intake and body weight; more precisely, the ventromedial

hypothalamic nucleus is the ‘satiety center’, while the lateral hypothalamic area is the ‘hunger center’ (20). More recently, the notion of specific brain’s loci controlling for food intake and body weight has been replaced by the importance of neuronal pathways that generate integrated responses to afferent input related to changing body fuel stores (23). Further investigations including neuroimaging are necessary to study possible hypothalamus dysfunction and the neural pathways involved in energy needs and body weight in DoC patients.

Furthermore, in future studies indirect calorimetry should be used to obtain real measure of energy expenditure instead of doing a DCN estimation, as previously done (10). The big difference in calories observed between the DCN and the RCI in the obese group only could be the result of an overestimation of caloric needs for obese patients, underlying the importance of introducing indirect calorimetry to calculate accurately patients’ daily needs.

When looking at the relation between SMO and the BMI, we found that the more severe is the SMO in lower limbs, the lower is the BMI. In addition, we found that patients with no SMO have a significant higher BMI compared to patients with severe SMO in lower limbs (but not in upper limbs). Among patients with severe SMO, the majority of them had a normal BMI indicating that SMO, alone, is not causing the patient to be under-weighted, but could be responsible for a lower BMI compared to the weight before the acquired brain injury. Nevertheless, all the patients who were underweighted had severe or moderate SMO. This observation is coherent with the result suggesting that underweighted patients, who also have a higher SMO, are the ones who receive the highest amount of calories compared to what is recommended by the guidelines, showing a possible higher consumption of calories (21). The multiple linear regression confirmed that the severity of SMO, alone, is not responsible for variation in the BMI and that other variables such as caloric intake, time since injury, aetiology and diagnosis may influence the BMI. Therefore, further studies need to be conducted to understand the nature of the link between these variables.

Some caveats need to be taken into account when interpreting these preliminary results. One of the limitations of our study is the design as this is a cross-sectional retrospective exploratory study;

a longitudinal prospective protocol would allow for a better understanding of the cause-effect relationship between patients' weight and nutritional status and other factors. The heterogeneity of our population is an additional limitation as patients had a wide range of time since injury as well as various etiologies, therefore our results cannot be generalized. Another limitation is the single assessment of SMO as it is known that SMO can vary from one day to another and is influenced by external factors such as pain or fatigue. Additional and more objectives measures could provide more robust data, such as a calorimetry, electromyography, blood markers and weight before the acquired brain injury.

However, this needs to be confirmed in prospective studies. Larger prospective multicentric studies should use indirect calorimetry to calculate the energetic needs of DoC and eMCS patients and further investigate the relation between SMO and the BMI. Furthermore, to better understand the role of aetiology, diagnosis and time since injury, larger studies should be conducting in TBI vs. non-TBI patients, with a large sample size allowing to categorize patients also according to DoC diagnosis. Due to the possible role played by TSI in patients' BMI, acute/post-acute and chronic patients should be study independently.

Conclusion

The majority of the patients with DoC and eMCS included in this study was well-nourished and among patients at risk to be undernourished, UWS patients did not have a higher risk compared to MCS patients. Furthermore, our results underline the relation between the BMI and ΔC, which is by itself reassuring. The gap between patients with DoC and eMCS and patients with artificial nutrition, on which guidelines are based, could be smoothed out taking into account other factors like SMO and complications secondary to acquired brain injury. SMO may play a role on the amount of daily calories needed by patients in prolonged DoC and eMCS, which may favor a BMI that falls in the underweight range in particular conditions.

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Disclosure of interest

The authors report there are no competing interests to declare.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

MF, SL, NP, CI, AT planned and designed the study, MF and CM collected the data. CI and AT analyzed the data. CI, MF, AT and CM interpreted the results. CI wrote the paper under AT supervision. All authors critically revised the paper and gave their approval of the final version of the manuscript.

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Words count (max 5000 words): 4810

Tables with captions

Table 1

Body Mass Index (kg/m²)		**Calculation weight (CW)**
Underweight	< 18.5	Calculate the ideal weight to have a BMI = 18.5 kg/m²
Normal	18.5 to < 25	Use the usual weight
Overweight	25 to < 30	Calculate the ideal weight to have a BMI = 25 kg/m²
Obese	>30	Adjusted weight formulas = ideal weight + (0.25 x (usual weight – ideal weight))

Table 1. Parameters to calculate the DCN in patients with artificial nutrition (17).

Table 2

Patient ID	Age	TSI (yrs)	Aetiology	Diagnosis	Undernourished	BMI	CRS-R TS	SMO (Upper)	SMO (Lower)	General SMO
1	33	14.7	Anoxia	UWS	At risk	Under-w	6	Moderate	Moderate	Moderate
2	47	0.4	Anoxia	UWS	No	Under-w	6	Moderate	Moderate	Moderate
3	71	5	Other	MCS	At risk	Under-w	17	Moderate	Severe	Severe
4	41	4.9	TBI	MCS	No	Under-w	10	Severe	Severe	Severe
5	30	3.3	Anoxia	MCS	At risk	Under-w	12	Severe	Severe	Severe
6	32	1.5	TBI	MCS	No	Under-w	11	Severe	Severe	Severe
7	45	1.6	Anoxia	UWS	No	Under-w	8	Moderate	Severe	Severe
8	35	12	Anoxia	MCS	No	Under-w	9	Severe	Severe	Severe
9	30	1.5	Anoxia	MCS	At risk	Under-w	8	Severe	Severe	Severe
10	54	1.1	Stroke	MCS	No	Over-w	10	Moderate	Moderate	Moderate
11	58	2	Mixed	MCS	No	Over-w	6	Moderate	Moderate	Moderate
12	62	2	Stroke	MCS	No	Over-w	12	Moderate	Moderate	Moderate
13	58	2	Anoxia	UWS	At risk	Over-w	7	Severe	Moderate	Severe
14	37	0.9	TBI	MCS	No	Over-w	14	Severe	Moderate	Severe
15	29	6.5	TBI	EMCS	No	Over-w	19	NA	NA	NA
16	63	2.1	Anoxia	EMCS	No	Over-w	23	NA	NA	NA
17	48	11	Stroke	MCS	No	Over-w	14	No SMO	No SMO	No SMO
18	38	17.8	TBI	EMCS	No	Over-w	21	No SMO	No SMO	No SMO
19	21	0.5	TBI	EMCS	No	Over-w	19	No SMO	No SMO	No SMO
20	40	0.4	Other	EMCS	No	Over-w	22	No SMO	No SMO	No SMO
21	33	1	TBI	UWS	No	Over-w	6	Severe	No SMO	Severe
22	54	0.7	Stroke	MCS	No	Over-w	16	Moderate	Severe	Severe
23	55	4.8	TBI	MCS	No	Over-w	20	Moderate	Severe	Severe
24	78	5.7	TBI	MCS	No	Over-w	20	Severe	Severe	Severe
25	22	2.8	TBI	MCS	No	Over-w	8	Severe	Severe	Severe
26	64	1.1	Stroke	MCS	No	Over-w	12	Severe	Severe	Severe
27	60	0.8	Anoxia	UWS	No	Over-w	6	Severe	Severe	Severe
28	44	0.4	Other	EMCS	No	Obese	15	Severe	Moderate	Severe
29	65	1.1	Stroke	MCS	No	Obese	10	NA	NA	NA
30	50	0.5	Anoxia	UWS	No	Obese	6	Moderate	No SMO	Moderate
31	41	2	Anoxia	UWS	No	Obese	5	Moderate	No SMO	Moderate
32	65	0.4	Anoxia	UWS	No	Obese	6	No SMO	No SMO	No SMO
33	58	3.8	TBI	EMCS	No	Obese	14	Severe	Severe	Severe
34	42	0.6	Stroke	MCS	No	Obese	8	Severe	Severe	Severe
35	60	1.9	Anoxia	MCS	No	Normal	10	Moderate	Moderate	Moderate
36	22	3.3	TBI	MCS	No	Normal	9	Moderate	Moderate	Moderate
37	22	1.2	TBI	MCS	No	Normal	11	Severe	Moderate	Severe
38	49	0.6	TBI	MCS	No	Normal	10	Severe	Moderate	Severe
39	33	11.1	TBI	EMCS	No	Normal	18	Severe	Moderate	Severe
40	34	0.8	Stroke	EMCS	No	Normal	22	Severe	Moderate	Severe
41	55	0.8	Anoxia	MCS	No	Normal	15	Moderate	Moderate	Moderate
42	55	7	Mixed	MCS	No	Normal	13	Moderate	Moderate	Moderate
43	35	1.1	Stroke	UWS	No	Normal	7	Severe	Moderate	Severe

44	31	1	TBI	UWS	No	Normal	7	Severe	Moderate	Severe
45	65	0.7	Stroke	MCS	No	Normal	13	NA	NA	NA
46	42	3.3	TBI	EMCS	No	Normal	20	NA	NA	NA
47	27	0.6	TBI	MCS	No	Normal	7	Moderate	No SMO	Moderate
48	38	14.6	Anoxia	MCS	No	Normal	6	No SMO	No SMO	No SMO
49	67	0.8	Mixed	MCS	No	Normal	7	No SMO	No SMO	No SMO
50	37	5.6	TBI	EMCS	No	Normal	23	No SMO	No SMO	No SMO
51	21	3	Other	MCS	No	Normal	12	Severe	No SMO	Severe
52	42	0.7	Anoxia	MCS	No	Normal	10	Moderate	Severe	Severe
53	60	5.9	TBI	MCS	No	Normal	13	Moderate	Severe	Severe
54	19	1	TBI	MCS	No	Normal	16	Moderate	Severe	Severe
55	61	1	TBI	EMCS	No	Normal	19	Moderate	Severe	Severe
56	61	1	TBI	EMCS	No	Normal	23	Moderate	Severe	Severe
57	62	14.6	Stroke	MCS	No	Normal	17	No SMO	Severe	Severe
58	66	2.5	Stroke	EMCS	No	Normal	19	No SMO	Severe	Severe
59	46	0.4	TBI	MCS	No	Normal	10	Severe	Severe	Severe
60	32	7.1	TBI	MCS	No	Normal	15	Severe	Severe	Severe
61	21	1.4	TBI	MCS	No	Normal	7	Severe	Severe	Severe
62	60	5.4	TBI	MCS	No	Normal	12	Severe	Severe	Severe
63	19	1.2	TBI	MCS	No	Normal	8	Severe	Severe	Severe
64	32	1.6	Mixed	MCS	No	Normal	14	Severe	Severe	Severe
65	46	0.6	Anoxia	MCS	No	Normal	9	Severe	Severe	Severe
66	21	0.7	Anoxia	MCS	No	Normal	11	Severe	Severe	Severe
67	27	0.7	TBI	MCS	No	Normal	14	Severe	Severe	Severe
68	46	3.8	TBI	MCS	No	Normal	11	Severe	Severe	Severe
69	57	1.1	Anoxia	MCS	No	Normal	7	Severe	Severe	Severe
70	20	1.1	TBI	MCS	No	Normal	15	Severe	Severe	Severe
71	49	1.3	TBI	MCS	No	Normal	11	Severe	Severe	Severe
72	28	4.3	TBI	MCS	No	Normal	11	Severe	Severe	Severe
73	22	1	Anoxia	UWS	No	Normal	8	Moderate	Severe	Severe
74	63	0.9	Anoxia	UWS	At risk	Normal	6	Moderate	Severe	Severe
75	40	0.9	Anoxia	UWS	No	Normal	5	Severe	Severe	Severe
76	57	0.4	Anoxia	UWS	At risk	Normal	6	Severe	Severe	Severe
77	34	0.8	TBI	UWS	No	Normal	5	Severe	Severe	Severe
78	42	2.2	Anoxia	UWS	No	Normal	5	Severe	Severe	Severe
79	24	1	TBI	UWS	No	Normal	6	Severe	Severe	Severe
80	23	1.3	Anoxia	UWS	No	Normal	7	Severe	Severe	Severe

Table 2: The table shows individual clinical and nutrition data of patients with DoC and eMCS. For each patient, we indicated age, time since injury (TSI) expressed in years, aetiology (TBI= traumatic brain injury; Other=intoxication, meningitis, hypoglicemia, surgical complication), clinical diagnosis (as assessed with the CRS-R), information related to the risk of being undernourished, BMI (under-w =underweight; over-w =overweight), and the presence of SMO as assessed with MAS (upper limbs, lower limbs and general SMO).

The severity of general SMO is determined by the highest level of SMO measured in upper limbs or lower limbs.

Figures

Figure 1

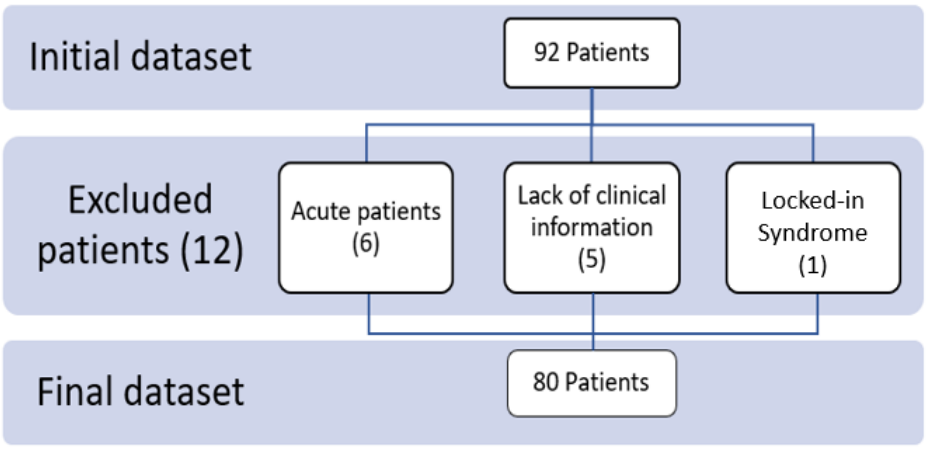

Figure 2

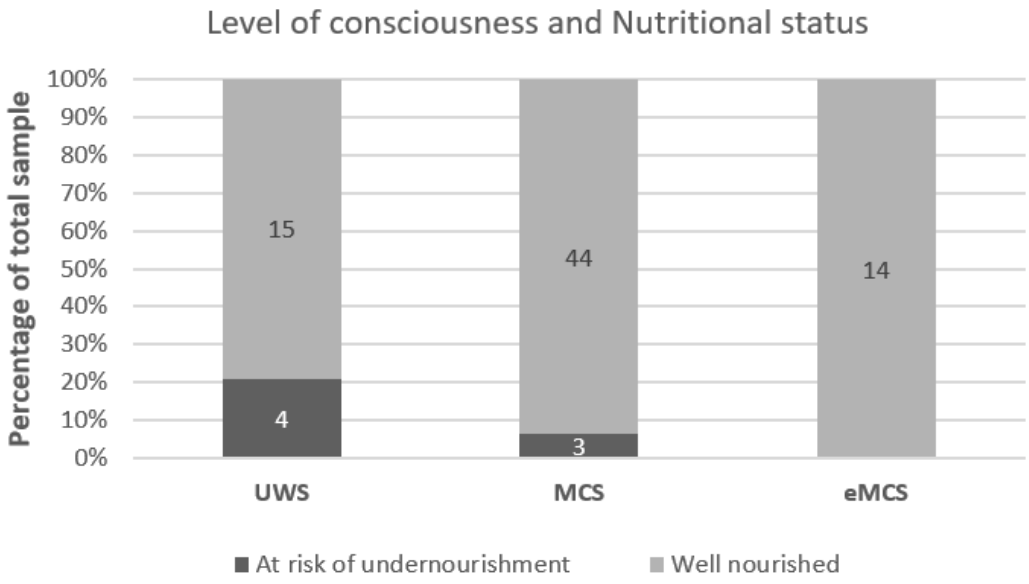

Figure 3

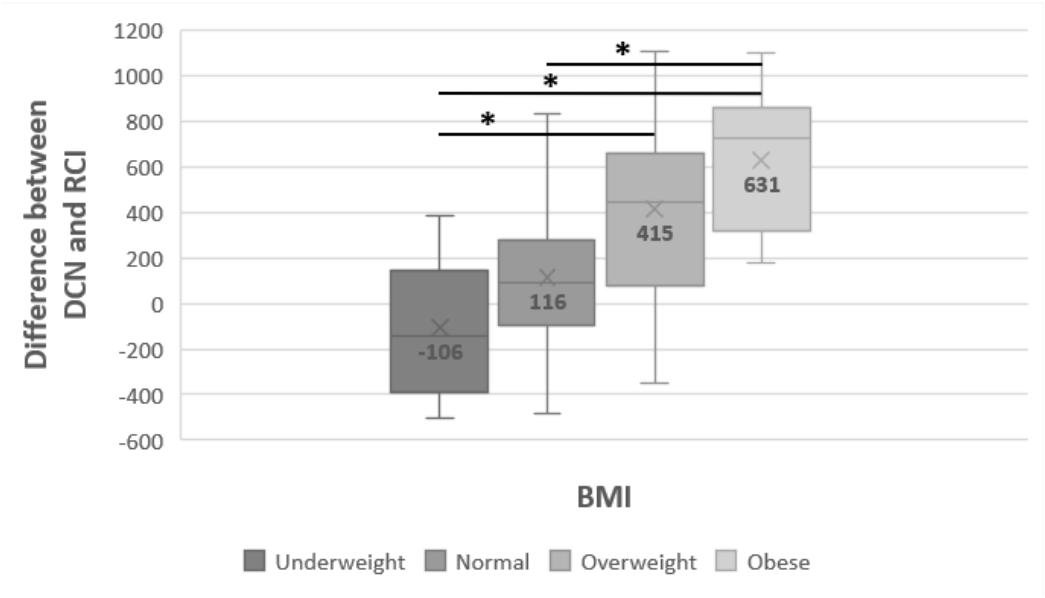

Figure 4

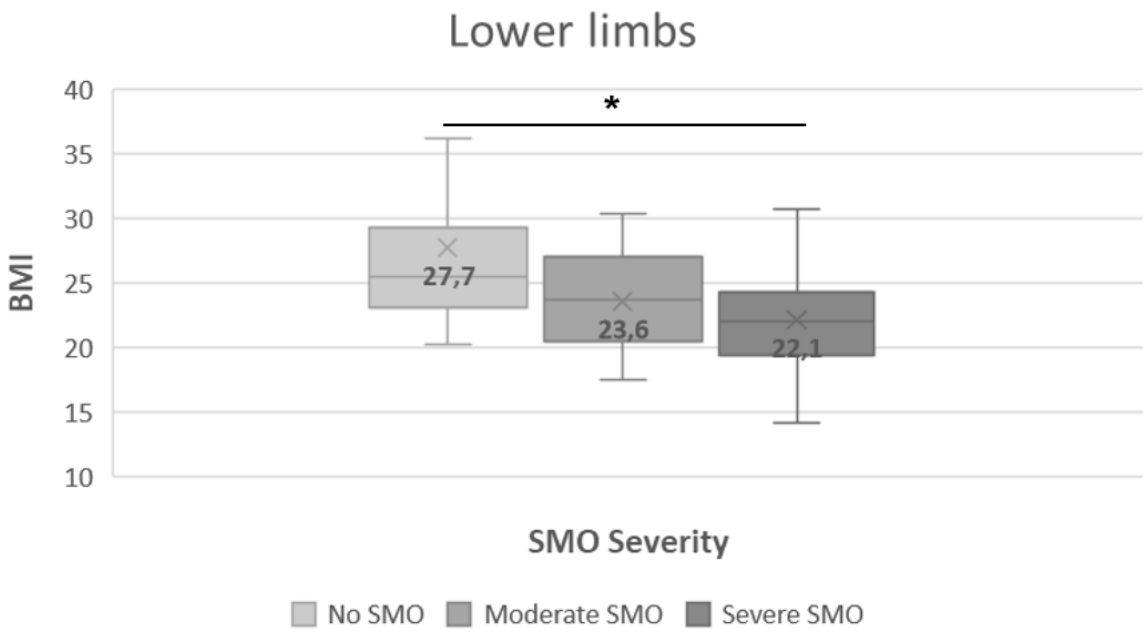

Figure 1. Starting from a database composed of 92 patients, 6 patients were excluded since they were in an acute phase, 5 patients were excluded due to a lack of clinical information and one patient was excluded because they were a locked-in syndrome, therefore not a DoC patient.

Figure 2. The columns in the graph represents the total of our sample categorized according to the level of consciousness. In each column are indicated patients who are well nourished and the ones at risk of undernourishment. The numbers indicate how many patients fall in each category.

Figure 3. The box and whiskers graph shows how the difference between the daily caloric needs (DCN) and the real caloric intake (RCI) varies according to the BMI in the four groups of patients (underweighted, normal, overweighted, and obese). Numbers in bold indicate such difference. Negative results means that patients are receiving more calories than the amount suggested by the guidelines.

Whiskers represent the lowest and the highest observed value and boxes represent the interquartile difference between the 1^{st} and 3^{rd} quartile. The horizontal line in the middle of the bar represents the median and the cross represents the mean. The star * indicates $p<0.0125$, as Bonferroni correction was applied.

Figure 4. The box and whiskers graph shows the variation of the BMI in the three groups of patients with no SMO, moderate SMO and severe SMO. Whiskers represent the lowest and the highest observed value and boxes represent the interquartile difference between the 1^{st} and 3^{rd} quartile. The horizontal line in the middle of the bar represents the median and the cross represents the mean. The star * indicates $p<0.0166$, as Bonferroni correction was applied. Patients with no SMO have a higher BMI compared to patients with severe SMO ($p<0.001$).