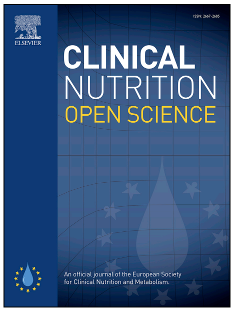
Journal Pre-proof



Is the natural feed the better nutritional therapy in patients with severe acquired brain injury? A retrospective study

Andaloro Adriana, MBiol, Caliri Santina, MBiol, Corallo Francesco, Psy, Placido Bramanti, MD;, Rifici Carmela, MD;, De Cola Maria Cristina, MStat, PhD

PII: S2667-2685(21)00008-5

DOI: https://doi.org/10.1016/j.nutos.2021.02.004

Reference: NUTOS 156

To appear in: *Clinical Nutrition Open Science*

Received Date: 8 September 2020

Revised Date: 4 February 2021

Accepted Date: 12 February 2021

Is the natural feed the better nutritional therapy in patients with severe acquired brain injury? A retrospective study.

Andaloro Adriana, MBiol;[1] Caliri Santina, MBiol;[1*] Corallo Francesco, Psy;[1] Placido Bramanti, MD;[1] Rifici Carmela, MD;[1] and De Cola Maria Cristina, MStat, PhD[1]

[1] IRCCS Centro Neurolesi "Bonino Pulejo", Messina, Italy

*Corresponding Author: Santina Caliri, MBiol

e-mail: santina.caliri@hotmail.it

IRCCS Centro Neurolesi "Bonino-Pulejo",

SS. 113, Contrada Casazza, 98124 Messina, Italy,

Phone: +39-090-60128109.

Abstract

Background. This retrospective study aimed to assess whether the use of natural foods, also in combination with enteral nutrition, improves rehabilitative recovery in patients severe acquired brain injuries.

Methods. 40 severe acquired brain injuries patients (75% males, aged 50.2 ± 16.6) were selected. The study population was divided into three groups based on the type of nutrition administered (enteral, oral, and mixed). Mini Nutritional Assessment and Level of Cognitive Functioning scales were used to assess changes from admission to discharge in each group. Multiple logistic regression model was performed to assess the association between the feeding typology and nutritional recovery.

Results. At admission, about 97.5% of patients were malnourished. We found significant score changes from baseline to follow-up for both test used and in each subgroup, except for the subgroup that includes patients fed with enteral nutrition. There were significant differences in biochemical indicators, including levels of albumin ($p<0.01$) and protein ($p<0.001$), compared to baseline and follow-up. Oral nutrition resulted to be a significant predictor for nutritional improvement.

Conclusions. Nutrition therapy within a multi-disciplinary team may improve both the hospital care and the recovery in severe acquired brain injuries population. Notably, our findings suggest that natural nutrition is superior to enteral nutrition in improving nutritional outcomes, which should be confirmed by further studies.

Keywords: Hospital Malnutrition, Natural Food, Oral nutrition, SABI, MNA.

Number of words: 3843

Introduction

Hospitalization in an intensive care unit for severe acquired brain injury (SABI) often causes protein-energy deficiencies, because of the exhaustion of energetic and plastic substrates. It induces a reduction in lean body mass and an expansion of the extracellular compartment [1], which the long-term can lead to a state of malnutrition. Malnutrition is the multifactorial condition resulting when the body does not get the right amount of nutrients, leading to metabolic alterations and deficiencies in proteins and dietary energy, which affects the correct organ functioning [2]. Thus, malnutrition reduces the immune response, increasing the risk of developing infections [3]. In hospital setting, it has been showed that malnutrition prolongs hospital stay, increasing the risks of unplanned readmission and the risk of death, especially in older adults [4].

Neurological patients have a hypermetabolic and hypercatabolic state with severe nitrogen loss and rapid deterioration of the lean body mass [5]. It can harm the patient's health and affect his rehabilitation recovery [6]. According to the most recent literature, hospital malnutrition prevalence in brain injured patients, neither due to stroke or trauma, is between 1.3% and 73%, depending on criteria used for diagnosis and the presence of comorbidities [7]. In many countries, nutrition screening upon hospital admission is not mandatory, and malnutrition remains under-reported and often poorly documented, although it could allow to timely adopt an appropriated nutritional therapy [8]. Furthermore, patients who do not receive most suitable nutritional cares during the first days of hospitalization are those who will have a worse hospital course, especially if they show symptoms of oropharyngeal dysphagia [9]. Indeed, dysphagia leads to a reduction in effectiveness of swallowing, with a consequently nutritional insufficiency, and it might be the explanation for the reduction in calorie intake [10].

During the acute phase of brain injury, the use of artificial nutrition might be necessary, often through enteral nutrition, i.e. nose gastric tube (SNG) or percutaneous endoscopic gastrostomy (PEG). The classic approach to enteral nutrition involves the use of industrial formulations, which are not free from side effects, besides to have negative repercussions on the patient's quality of life such as discomfort, limitation of movements, and nutritional restriction [11]. On the contrary, the use of blended foods has both economic and clinical advantages [12]. Indeed, natural feeding reduces diarrhea occurrence, allows to integrate nutrients not present in industrial formulations, facilitating long-term enteral nutrition [13], and offers to familiars the opportunity to prepare meals for their loved ones. However, natural feedings administered to patients with SABI is still an issue little dealt with in the literature [14].

The aim of this study is to retrospectively evaluate the role of natural feed, exclusively administered or in combination with enteral nutrition, in recovering of SABI patients.

Materials and Methods

Study design and settings

A retrospective cohort study evaluated the patients with SABI hospitalized at the neuro-rehabilitation unit of the IRCCS Neurolesi "Bonino-Pulejo" of Messina from January 1, 2018, to December 31, 2019. Usually, patients are followed by a rehabilitation team in collaborations with a skilled nutritionist, and both at admission and at discharge they underwent a clinical assessment, as well as trimestral when hospitalization stay was longer than 90 days.

Study population and data collection

In this study, we selected SABI patients with at least 18 years of age. Exclusion criteria were: hospital death, length to stay in hospital less than 30 days, BMI (Body Mass Index) greater than 23 kg/m2, intestinal malabsorption diseases, and administration of parenteral nutrition. Data were collected in an electronic sheet including age, gender, diagnosis, comorbidities, height and weight, type of feeding, biochemical values (i.e. total proteins and albumin), occurrence of albumin and protein supplements, and pre□and-post scores of both nutritional and cognitive assessment. In absence of at least one assessment (e.g. at baseline or at follow□up) we excluded the patient, whereas in presence of multiple assessments (i.e. long hospitalization stay) we considered the first assessment as baseline (T0) and the closest to the 90th day as follow-up (T1). Patients for whom it was not possible to detect anthropometric parameters were also excluded.

Sixty-three patients were initially screened, and 23 of them were excluded (6 because underwent parental nutrition, 3 were underage, 2 died during the hospitalization, and 12 due to lack of follow-up evaluations or anthropometric parameters). Finally, forty subjects (75% males), with mean age of 50.2 ± 16.6 years and mainly with a diagnosis of stroke (62.5%), were included in the study.

To evaluate whether feeding typology affects nutritional and cognitive recovery, the study population was divided in three groups according to the type of feeding administered during hospitalization. Thus, the first group included patients who underwent enteral nutrition (SNG or PEG), the second group included patients who underwent oral nutrition, and the third group included patients who underwent a mixed nutrition, i.e. the administration of natural foods orally as weaning training during the day, while the administration of formulas for enteral nutrition at night. A more detailed description of the study population is provided in Table 1.

Nutritional and cognitive assessment

Nutritional and cognitive changes during hospitalization were assessed by means of the Mini Nutritional Assessment (MNA) and the Level of Cognitive Functioning (LCF), respectively.

The MNA evaluates the patient's nutritional status, it is specific for elderly (age ≥ 65 years) admitted in hospitals and nursing homes. The MNA is structured in two parts: a screening assessment and a global one, in which anthropometric, medical, lifestyle, dietary, and psychosocial factors are considered. It includes 18 items with a maximum score of 30. Values below 17 indicate default malnutrition, values between 17 and 23.5 indicate risk of malnutrition, while values above 24 indicate normal nutritional status [15]; whereas the LCF allows to evaluate the recovery of consciousness and communication and to monitor patient's cognitive improvements after brain injury. It includes 8 levels scored from 1 to 8 (higher score = better performance) [16].

Statistical Analysis

Data were analyzed using the R version 3.5.0, considering a $p<0.05$ as statistically significant. Because of the small subgroup dimensions, non-parametric analysis was performed. Thus, we used the Wilcoxon signed-rank test to compare each group between baseline and follow-up (intra-group analysis), whereas comparisons between groups was made by mean of the Kruskal–Wallis test. We also used the Chi-squared test or, when opportune the Fisher's exact test, to compare proportions. To assess the association between the feeding typology and nutritional recovery, we performed a multiple logistic regressions adjusting for some characteristics (i.e. gender, age, diagnosis, albumin and protein supplement), considering the categorical variable 'MNA improved' (1= yes; 0= no) coded according to the T0-T1 change of the patient's nutritional status (e.g. "yes" indicates a change from "malnutrition" to "risk of malnutrition" or to "normal nutritional status"). We applied a backward elimination stepwise procedure for the choice of the best predictive variables according to the Akaike information criterion (AIC). Finally, the analysis of covariance (ANCOVA) was performed to assess whether the improvement of the nutritional status influenced the cognitive functioning, independently from the score difference at baseline.

Notably, the model had the LCF score at T1 as dependent variable, the variable ‘MNA improved’ as independent variable, and the LCF score at T0 as covariate. We performed ANOVA to verify whether the model was significantly different from the one fitted with the interaction term “MNA improved*LCF score at T0.

Results

Patient characteristics at baseline

About 97.5% of patients were malnourished at admission. No significant differences at baseline among patients in different nutritional settings emerged (Table 1). However, the proportion of patients fed with oral nutrition who needed albumin supplement was significantly lower than whom fed with enteral or mixed method ($p < 0.01$).

Comparison of clinical outcomes between baseline and follow-up

Both MNA and LCF scores changed significantly from baseline to follow-up ($p < 0.001$ and $p < 0.01$, respectively). We observed also a change in BMI median scores, although it did not reach the significance ($p = 0.06$). Performing the intra-group analysis in different subgroups according to nutritional settings, we also considered the subgroup of patients progressed from enteral to oral nutrition during the hospitalization. Results showed a significant improvement in both MNA and LCF scores between T0 and T1 in each subgroup, except in the one including patients fed with enteral nutrition (Table 2).

Comparison of biochemical indicators between baseline and follow-up

There were significant differences in biochemical indicators, including albumin ($p < 0.01$) and protein ($p < 0.001$) levels, from baseline and follow-up. We observed significant changes also within subgroups, especially concerning the one including patients fed with oral nutrition (Table 3).

Analysis of Covariance on changes in cognitive functioning

Since the interaction term "MNA improved*LCF score at T0" was no significant, it was not considered in the ANCOVA models fitting. Results reported in Table 4 show that the nutritional improvement had a significant effect on LCF change ($F = 10.5$; $p < 0.01$), increasing of about 0.99 points its score.

Risk and protective factors for nutritional improvement

The backward elimination stepwise procedure identified the logistic model including as predictors age and type of feedings. However, only oral nutrition resulted to be a significant predictor for nutritional improvement, as reported in Table 5.

Discussion

SABI is a damage to the brain, occurring from traumatic or non-traumatic causes (mainly stroke), and often resulting in deterioration of physical, cognitive, emotional or independent functioning. Since the brain is involved in the process of regulating metabolic activity, metabolic alterations as hormonal changes and inflammatory response occur frequently in SABI patients. Therefore, these patients suffer from severe metabolic disorders, which alter the nutritional balance (i.e. insufficient intake and excessive consumption of nutrients), increase their inflammatory state, and leading to a deficient state of malnutrition [17]. According to recent literature, our sample showed a high percentage of malnourished patients on admission (97,5%), many of whom underwent an artificial feeding.

The most common form of hospital malnutrition involves nutritional deficits, loss of body mass (fat and lean), alteration of blood test values and cognitive deficits [18]. The study of Maruyama et al. [19] showed that the presence of malnutrition increases the incidence of mortality in all pathologies, with greater effect in stroke patients during the rehabilitation phase rather than in the acute phase. Indeed, malnutrition affects the functional status, undermining the patient's recovery [20]. Thus, early in-hospital nutrition plays a fundamental role in rehabilitation recovery of these patients in order to avoid complications due to the impairment of organ functions, as well as to the worsening of the patient's immunological status [21-22] Moreover, the hyper-metabolism condition can complicate the initial patient's stabilization at admission, and prolong the rehabilitation period [17].

To the best of our knowledge, this is the first study dealing with natural feeding in recovering of SABI patients. Although there are some differences at baseline in MNA and LCF scores among groups, because of the different impairment of patients in each group, the intra-group analysis findings depict a higher score change magnitude in the oral feed group. Notably, our findings showed an improvement in the nutritional status of all patients receiving an individual nutritional treatment, although it was significant only in patients who underwent natural or mixed nutrition. We also observed a significant improvement, both in nutritional status and in cognitive functioning, in patients passed from artificial to natural oral nutrition during the hospitalization. This important result leaded us to believe that a natural diet conducted within a hospital setting could have the advantage to improve the recovery in patients with SABI, compared to the exclusive use of standard artificial formulations. According to Waitzberg et al., [23], our results highlight the importance of in-hospital nutritional assessment for early detection of malnutrition, together with a prompt nutritional intervention, in particular with oral feeding therapy. Indeed, it is well known that a balanced natural nutrition provides richer food quality than artificial nutrition, allowing better absorption of nutrients. However, neurological conditions of SABI patients usually cause altered levels of consciousness or impaired swallowing mechanisms that necessitate artificial nutritional support. The guidelines of the American Society for Parenteral and Enteral Nutrition (ASPEN) indicate that neurological patients should start nutritional support as soon as possible [24]. Indeed, early nutritional support can provide catabolic calories and other nutrients that the patient needs, maintain the organic functions, reduce infection rates and complications, promote neural function and reduce mortality [22]. Enteral nutrition is considered the best nutritional approach when the gastrointestinal tract is structurally and functionally intact, since its association with the decreasing of T regulatory cells in the lamina propria of the intestinal epithelium, whit a consequent reduction of the inflammatory state [25]. Moreover, enteral nutrition resulted to contribute in maintaining nutrient metabolism in patients with neurologically critical diseases [5]. However, the use of enteral nutrition can produce some adverse risks, as refeeding syndrome, increased volume of gastric residues, diarrhoea and constipation [26]. Notably, diarrhoea exacerbates the microbial gastrointestinal imbalance, increasing the risk of antibiotics need [27]. In his work [28], Savino explains how industrial medical products may not contain the optimal amount of nutrients needed to meet patient needs, especially as concern the quality (presence of branched, essential and non-essential amino acids) and the origin of raw materials.

Although the use of natural foods is not generally recommended because of higher risk of microbial contamination, some studies have shown that the administration of natural foods through enteral nutrition can significantly reduce the occurrence of complications [29]. Indeed, natural feeding allows to integrate nutrients better than industrial formulations and offer to familiars to be more involved in making meals for their relatives; however, could be risky how the familiars prepare the food, e.g. it could be not optimally blended.

The recent literature is lacking in studies conducted on SABI patients undergoing nutritional therapy, especially in studies aimed to compare effects of natural foods versus the ones of enteral or parental nutrition. Schmidt et al. [30], in their study, showed that the use of natural foods can be an effective in the treatment of diarrhoea, by contributing to improve the rehabilitation recovery in neurological patients. However, they administered natural foods (such as milk, meat, and vegetables) only by enteral nutrition. Most recently, Fabiani et al. [31] reported that the administration of natural foods by enteral nutrition significantly reduces the appearance of diarrhoea, but it was observed in patients subjected to cardiac surgery. However, our findings show as the type of nutrition can have a pivotal role in SABI patient's recovery, both from a metabolic and cognitive point of view. Indeed, the oral nutrition seems to have the greatest prognostic capacity for nutritional improvement in SABI patients (Table 5). Thus, the type of nutrition could represent a predictive index of future hospitalizations. Moreover, we found that patients fed with oral nutrition since the beginning of the hospitalization required less albumin supplementation, although both albumin and protein values significantly increased within the normal range during the hospitalization.

One of the main aspects of hospital malnutrition is represented by excessive thinness [32]. Such a condition, demonstrated by a low BMI, was also observed in our sample. Our findings show a mean increase of weight during the hospitalization, with a consequent increase of the BMI. However, the T0-T1 comparison of BMI did not reach the statistical significance. It was probably due to the extreme underweight condition of patients, who were too compromised to reach normal levels.

Our study has some limitations. First, due to the retrospectivity of the study which can lead to information bias. For example, results could be affected by a bias due to different lengths in hospitalization stay. Second, due to the limited number of medical records, the sample could be not large enough to extend correctly results to the SABI patients' population. Third, due to the not completeness of medical records, additional data as biochemical values could reinforce our findings, as well as data concerning patients' calorie and protein intake. We only know that the choice of the necessary calories was made through the Harris-Benedict equation. Further prospective studies are needed to deal with information bias, and to confirm our results by comparing nutritional changes between different feedings during hospitalization.

In conclusion, this study sustains that an ad-hoc nutrition therapy within a multi-disciplinary team may improve both the hospital care and the recovery in SABI population. Results show that natural nutrition is superior to enteral nutrition in improving nutritional outcomes.

Author contributions: CS, CF and MCDC conceptualized the study, PB contributed to study design. CR, CS, and AA collected data. MCDC analyzed data. All authors contributed to data interpretation. AA, CF, MCDC contributed to write the manuscript. All authors revised and approved the final manuscript.

Conflict of Interest: None of the authors have any conflict of interest to report.

References

1. Elia M. Defining, Recognizing, and Reporting Malnutrition. *Int J Low Extrem Wounds*. 2017;16(4):230-237. doi:10.1177/1534734617733902
2. Lean M, Wiseman M. Malnutrition in hospitals. *BMJ*. 2008;336(7639):290. doi:10.1136/bmj.39449.723090.80
3. Corkins MR, Guenter P, DiMaria-Ghalili RA, Jensen GL, Malone A, Miller S, et al. Malnutrition diagnoses in hospitalized patients: United States, 2010. *JPEN J Parenter Enteral Nutr*. 2014;38(2):186-195. doi:10.1177/0148607113512154
4. Leiva Badosa E, Badia Tahull M, Virgili Casas N, Elguezabal Sangrador G, Faz Méndez C, Herrero Meseguer I, et al. Hospital malnutrition screening at admission:

malnutrition increases mortality and length of stay. *Nutr Hosp*. 2017;34(4):907-913. doi:10.20960/nh.657

5. Li X, Yang Y, Ma ZF, Gao S, Ning Y, Zhao L, et al. Enteral combined with parenteral nutrition improves clinical outcomes in patients with traumatic brain injury. *Nutr Neurosci*. 2020;1-7. doi:10.1080/1028415X.2020.1765114
6. Chapple LS, Deane AM, Heyland DK, Lange K, Kranz AJ, Williams LT, et al. Energy and protein deficits throughout hospitalization in patients admitted with a traumatic brain injury. *Clin Nutr*. 2016;35(6):1315-1322. doi:10.1016/j.clnu.2016.02.009
7. Foley NC, Salter KL, Robertson J, Teasell RW, Woodbury MG. Which reported estimate of the prevalence of malnutrition after stroke is valid?. Stroke. 2009;40(3):e66-e74. doi:10.1161/STROKEAHA.108.518910
8. Norman K, Pichard C, Lochs H, Pirlich M. Prognostic impact of disease-related malnutrition. *Clin Nutr*. 2008;27(1):5-15. doi:10.1016/j.clnu.2007.10.007
9. Barker LA, Gout BS, Crowe TC. Hospital malnutrition: prevalence, identification and impact on patients and the healthcare system. *Int J Environ Res Public Health*. 2011;8(2):514-527. doi:10.3390/ijerph8020514
10. Paquereau J, Allart E, Romon M, Rousseaux M. The long-term nutritional status in stroke patients and its predictive factors. *J Stroke Cerebrovasc Dis*. 2014;23(6):1628-1633. doi:10.1016/j.jstrokecerebrovasdis.2014.01.007
11. Ojo O, Brooke J. The Use of Enteral Nutrition in the Management of Stroke. *Nutrients*. 2016;8(12):827. doi:10.3390/nu8120827
12. Regier GK, Lindshield BL, Lilja NK. Nutrient Cost-Effectiveness of Fortified Blended Food Aid Products. Food Nutr Bull. 2019;40(3):326-339. doi: 10.1177/0379572119846331.

13. Brown B, Roehl K, Betz M. Enteral nutrition formula selection: current evidence and implications for practice. *Nutr Clin Pract*. 2015;30(1):72-85. doi:10.1177/0884533614561791
14. Caliri S, Andaloro A, Corallo F, Donato A, Marino S, Mantarro C, et al. Recovery of malnutrition in a patient with severe brain injury outcomes: A case report. *Medicine (Baltimore)*. 2019;98(40):e16755. doi:10.1097/MD.0000000000016755
15. Beck AM, Ovesen L, Osler M. The 'Mini Nutritional Assessment' (MNA) and the 'Determine Your Nutritional Health' Checklist (NSI Checklist) as predictors of morbidity and mortality in an elderly Danish population. *Br J Nutr*. 1999;81(1):31-36.
16. Sander, A. (2002). The Level of Cognitive Functioning Scale. The Center for Outcome Measurement in Brain Injury. http://www.tbims.org/combi/lcfs (accessed June 23, 2020).
17. Cook AM, Peppard A, Magnuson B. Nutrition considerations in traumatic brain injury. *Nutr Clin Pract*. 2008;23(6):608-620. doi:10.1177/0884533608326060
18. Zhao NN, Zeng KX, Wang YL, Sheng PJ, Tang CZ, Xiao P, et al. Research on the nutrition and cognition of high-risk stroke groups in community and the relevant factors. *Eur Rev Med Pharmacol Sci*. 2017;21(23):5408-5414. doi:10.26355/eurrev_201712_13928
19. Maruyama K, Nakagawa N, Koyama S, Maruyama JI, Hasebe N. Malnutrition Increases the Incidence of Death, Cardiovascular Events, and Infections in Patients with Stroke after Rehabilitation. *J Stroke Cerebrovasc Dis*. 2018;27(3):716-723. doi:10.1016/j.jstrokecerebrovasdis.2017.10.002
20. Diekmann R, Wojzischke J. The role of nutrition in geriatric rehabilitation. *Curr Opin Clin Nutr Metab Care*. 2018;21(1):14-18. doi:10.1097/MCO.0000000000000433

21. De Tanti A, Zampolini M, Pregno S; CC3 Group. Recommendations for clinical practice and research in severe brain injury in intensive rehabilitation: the Italian Consensus Conference. Eur J Phys Rehabil Med. 2015;51(1):89-103

22. Wang X, Dong Y, Han X, Qi XQ, Huang CG, Hou LJ. Nutritional support for patients sustaining traumatic brain injury: a systematic review and meta-analysis of prospective studies. PLoS One. 2013;8(3):e58838.

23. Waitzberg DL, De Aguilar-Nascimento JE, Dias MCG, Pinho N, Moura R, Correia MITD. Hospital and homecare malnutrition and nutritional therapy in Brazil. Strategies for alleviating it: a position paper. *Nutr Hosp*. 2017;34(4):969-975. doi:10.20960/nh.1098

24. Mehta NM, Skillman HE, Irving SY, Coss-Bu JA, Vermilyea S, Farrington EA, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Pediatric Critically Ill Patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition. *JPEN J Parenter Enteral Nutr*. 2017;41(5):706-742. doi:10.1177/0148607117711387

25. Schwerd T, Frivolt K, Clavel T, Lagkouvardos I, Katona G, Mayr D, Uhlig HH, Haller D, Koletzko S, Bufler P. Exclusive enteral nutrition in active pediatric Crohn disease: Effects on intestinal microbiota and immune regulation. *J Allergy Clin Immunol*. 2016;138(2):592-596. doi:10.1016/j.jaci.2015.12.1331

26. Lee A, Oliveira Filho RS, Cardenas TC, Ozório GA, Gropp JPL, et al. Quality control of enteral nutrition therapy in cancer patients at nutritional risk. *Nutr Hosp*. 2017;34(2):264-270. doi:10.20960/nh.721

27. Whelan K. Enteral-tube-feeding diarrhoea: manipulating the colonic microbiota with probiotics and prebiotics. *Proc Nutr Soc*. 2007;66(3):299-306. doi:10.1017/S0029665107005551

28. Savino P. Knowledge of Constituent Ingredients in Enteral Nutrition Formulas Can Make a Difference in Patient Response to Enteral Feeding. *Nutr Clin Pract*. 2018;33(1):90-98. doi:10.1177/0884533617724759
29. Sullivan MM, Sorreda-Esguerra P, Santos EE, Platon BG, Castro CG, Idrisalman ER, et al. Bacterial contamination of blenderized whole food and commercial enteral tube feedings in the Philippines. *J Hosp Infect*. 2001;49(4):268-273. doi:10.1053/jhin.2001.1093
30. Schmidt SB, Kulig W, Winter R, Vasold AS, Knoll AE, Rollnik JD. The effect of a natural food based tube feeding in minimizing diarrhea in critically ill neurological patients. *Clin Nutr*. 2019;38(1):332-340. doi:10.1016/j.clnu.2018.01.007
31. Fabiani A, Sanson G, Bottigliengo D, Dreas L, Zanetti M, Lorenzoni G, et al. Impact of a natural versus commercial enteral-feeding on the occurrence of diarrhea in critically ill cardiac surgery patients. A retrospective cohort study. *Int J Nurs Stud*. 2020;108:103605. doi:10.1016/j.ijnurstu.2020.103605
32. Franz K, Otten L, Müller-Werdan U, Doehner W, Norman K. Severe Weight Loss and Its Association with Fatigue in Old Patients at Discharge from a Geriatric Hospital. *Nutrients*. 2019;11(10):2415. doi:10.3390/nu11102415

Table 1. Demographic and clinical description of patients at baseline in different nutritional forms.

Characteristic	All (n = 40)	Nutrition			p-value
		Enteral (n = 14)	Mixed (n = 13)	Oral (n = 13)	
Males	30 (75.0)	11 (78.6)	9 (69.2)	10 (76.9)	0.84
Age (years)	50.2 ± 16.6	49.7 ± 18.8	46.2 ± 12.6	54.6 ± 17.7	0.46
Diagnosis					
Traumatic brain injury	12 (30.0)	5 (35.7)	4 (30.8)	3 (23.1)	
Stroke	25 (62.5)	9 (64.3)	9 (69.2)	7 (53.8)	0.26
Spinal lesion	3 (7.5)	0 (0.0)	0 (0.0)	3 (23.1)	
Comorbidity					
None	11 (27.5)	3 (21.4)	3 (23.1)	5 (38.5)	0.67
Hypertension	10 (25.0)	4 (28.6)	2 (15.4)	4 (30.8)	0.73
Hypertriglyceridemia	1 (2.5)	1 (7.1)	0 (0.0)	0 (0.0)	0.99
Hypercholesterolemia	3 (7.5)	2 (14.3)	0 (0.0)	1 (7.7)	0.76
Diabetes type 2	6 (15.0)	3 (21.4)	2 (15.4)	1 (7.7)	0.86
Cardiopathy	8 (20.0)	2 (14.3)	4 (30.8)	2 (15.4)	0.61
Hypothyroidism	2 (5.0)	0 (0.0)	0 (0.0)	2 (15.4)	0.20
Other	5 (12.5)	1 (7.1)	3 (23.1)	1 (7.7)	0.50
Nutritional status					
Well-nourished	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Risk for malnutrition	1 (2.5)	0 (0.0)	1 (7.7)	0 (0.0)	0.65
Malnourished	39 (97.5)	14 (100.0)	12 (92.3)	13 (100.0)	
Supplement					
None	4 (10.0)	0 (0.0)	1 (7.7)	3 (23.1)	0.13
Protein	22 (55.0)	7 (50.0)	9 (69.2)	6 (46.1)	0.44
Albumin	26 (65.0)	12 (85.7)	10 (76.9)	4 (30.8)	**< 0.01**

Continuous variables were expressed as mean ± standard deviation, whereas categorical variables as frequencies and percentages. Significant differences are in bold.

Table 2. Intra-groups analysis of clinical outcomes in different nutritional subgroups.

	Baseline	**Follow-up**	**p-value**
All (n = 40)			
MNA	8.75 (6.37 – 11.62)	16.25 (12.38 – 19.38)	**< 0.001**
BMI	18.90 (17.57 – 20.55)	19.60 (18.10 – 20.90)	0.06
LCF	3.00 (2.00 – 4.00)	4.50 (3.00 – 6.00)	< **0.01**
Enteral (n = 6)			
MNA	7.75 (5.37 – 9.37)	11.0 (8.75 – 11.75)	0.20
BMI	20.65 (16.57 – 25.18)	20.70 (18.25 – 24.12)	0.99
LCF	2.00 (1.25 – 2.00)	3.00 (2.25 – 3.75)	0.06
Mixed (n = 13)			
MNA	7.00 (5.50 – 9.00)	13.50 (12.50 – 18.00)	< **0.01**
BMI	18.90 (17.70 – 19.40)	18.60 (18.10 – 20.90)	0.52
LCF	2.00 (2.00 – 4.00)	4.00 (3.00 – 4.00)	**0.04**
Oral (n = 13)			
MNA	10.50 (8.50 – 12.00)	18.50 (16.50 – 21.00)	< **0.01**
BMI	18.70 (18.50 – 20.70)	19.70 (18.32 – 20.70)	0.08
LCF	5.00 (4.00 – 6.00)	6.00 (5.00 – 7.00)	< **0.01**
From enteral to oral (n = 8)			
MNA	9.50 (6.62 – 11.87)	18.00 (13.50 – 21.38)	**0.02**
BMI	19.25 (17.27 – 20.50)	19.75 (17.88 – 21.60)	0.24
LCF	2.00 (2.00 – 3.00)	6.00 (4.00 – 6.00)	**0.04**

Legend: LCF = Levels of Cognitive Functioning scale; MNA = Mini Nutritional Assessment; BMI = Body Mass Index. Scores are reported as median (first-third quartile). Significant differences are in bold.

Table 3. Intra-groups analysis of biochemical outcomes in different nutritional subgroups.

	Baseline	Follow-up	p-value
All (n = 40)			
Albumin (g/L)	2.90 (2.30 – 3.42)	3.15 (2.87 – 3.50)	< **0.01**
Protein (g/L)	6.15 (5.77 – 6.60)	6.55 (6.27 – 6.90)	< **0.001**
Enteral (n = 6)			
Albumin (g/L)	2.50 (2.15 – 2.92)	2.50 (2.27 – 2.95)	0.99
Protein (g/L)	6.40 (5.85 – 6.72)	6.80 (6.72 – 8.30)	**0.04**
Mixed (n = 13)			
Albumin (g/L)	2.90 (2.30 – 3.50)	3.10 (3.00 – 3.30)	0.21
Protein (g/L)	6.30 (6.20 – 6.60)	6.70 (6.40 – 6.90)	**0.01**
Oral (n = 13)			
Albumin (g/L)	2.90 (2.50 – 3.30)	3.20 (3.00 – 3.50)	< **0.01**
Protein (g/L)	5.80 (5.60 – 6.00)	6.50 (6.10 – 6.50)	< **0.01**
From enteral to oral (n = 8)			
Albumin (g/L)	3.05 (2.67 – 3.47)	3.35 (3.17 – 3.60)	0.10
Protein (g/L)	6.10 (5.97 – 6.72)	6.50 (6.37 – 6.75)	0.08

Values are reported as median (first-third quartile). Significant differences are in bold.

Table 4. ANCOVA results on patient's cognitive functions.

Coefficients	**Sum Squares**	**Estimate**	**Std. Err.**	**Df**	**F value**	**p value**
LCF (at baseline)	27.48	0.53	0.13	1	15.62	< **0.001**
MNA improved	18.49	0.99	0.30	1	10.51	**0.002**
Residuals	65.08	-	-	37	-	**-**

Df = Degree freedom; LCF = Levels of Cognitive Functioning scale; MNA = Mini Nutritional Assessment. Significance are in bold.

Table 5. Backward Logistic regression: significant predictors of nutritional improvement.

Predictors	OR	Std. Err.	Wald z	[95% Conf. interval]		p-value
Age	1.04	0.02	1.66	0.99	1.10	0.06
Nutrition- Mixed	2.44	1.33	0.67	0.21	60.59	0.50
Nutrition-Oral	16.08	1.27	2.19	1.81	383.15	**0.03**

Pseudo-R^2=0.21; Prob > $\chi^2(3)$ <0.01

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: