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Impact of nutritional therapy during the first wave of the COVID-19 pandemic in intensive care patients: A retrospective observational study

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SUMMARY

Background & aims: The COVID-19 pandemic has caused major organizational challenges to healthcare systems concerning staff, material and bed availability. Nutrition was not a priority in the intensive care unit (ICU) at the beginning of the pandemic with the need for simplified protocols. We aimed to assess the impact of a simplified nutritional protocol for critically ill COVID-19 patients during the pandemic first wave.

Methods: We included all patients with SARS-CoV-2 infections, admitted to the ICU of the Geneva University Hospitals for at least 4 days from March 9 to May 19, 2020. Data on the route and solution of nutritional therapy, prescribed and received volume, calorie and protein intake, amount of insulin, propofol and glucose administered were collected daily during the entire ICU stay. We compared nutritional outcomes between patients admitted to the ICU before and after implementing the simplified nutritional protocol using unpaired t-test.

Results: Out of 119 patients, 48 were hospitalized in the ICU before, 47 across and 24 after the implementation of the nutritional protocol. The mean age was 63.2 (± 12.7) years and 76% were men without significant difference between *before* and *after* group. The nutritional protocol implementation led to an increase in caloric intake (1070 vs. 1357 kcal/day, $p = 0.018$) and in the percentage of days within 80–100% of the energy target (11 vs. 20%, $p = 0.021$). The protein debt decreased significantly from 48 g/day to 37 g/day ($p = 0.015$). No significant difference in the percentage of days within the protein target (80–100%) was observed.

Conclusions: Calorie and protein coverage improved after the implementation of the simplified nutritional protocol in critically ill COVID-19 patients. Further studies are needed to assess the impact of such an approach on patients' clinical outcomes.

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1. Introduction

Since its onset in December 2019, the SARS-CoV-2 infection (Severe Acute Respiratory Syndrome Coronavirus 2) has evolved into a pandemic with fatal outcomes [1].

The pandemic organization of COVID-19 patients in the ICU of the Geneva University hospitals during the 1st wave (129 critically ill COVID-19 patients admitted from March 9 to May 19, 2020) and

their outcomes have been recently reported, with a proportion of 96% of mechanical ventilated patients, a median ventilation time of 12.5 days and a median ICU length of stay (LOS) of 15 days [2]. The clinical characteristics and outcomes of 4244 critically ill COVID-19 patients have been described in a prospective cohort study identifying an overall 90-day mortality of 31% which increased according to the ARDS severity at ICU admission. Mortality was also higher in elderly, immunocompromised, obese (body mass index (BMI) > 30 kg/m²), and diabetic patients, as well as in patients with a short period between first symptoms and ICU admission [3]. COVID-19 patients have also a longer ICU LOS with longer recovery times (slower waking up, longer bed rest and immobilization), which leads to more complications [4].

Malnutrition in the critically ill in general has been associated with higher mortality rate and ICU LOS, disability and post-hospital morbidity [5–9]. Older, sarcopenic COVID-19 patients and patients with pre-existing comorbidities (diabetes, hypertension, obesity etc.) are even at higher malnutrition risk [7,10,11]. The prevalence and the risk of malnutrition in hospitalized COVID-19 patients were recently evaluated [12–15].

For example, in an internal medicine ward a 92% nutritional risk for malnutrition according to the Nutritional Risk Screening 2002 (NRS 2002) score ≥ 3 was observed [13], while the prevalence of malnutrition in hospitalized patients was estimated to be around 38% [12,15], and increased to 52% in the elderly [14]. COVID-19 patients with a good nutritional status (Controlling Nutritional Status score between 5 and 12) developed less adverse outcomes [16]. In addition, COVID-19 patients suffer from reduced oral intake due to dyspnoea, anorexia, anosmia and/or dysgeusia [1,17], and their muscle catabolism increases significantly due to the inflammatory syndrome and the hypermetabolic state [7,18]. In a recent prospective study, it was shown that the coverage of 80–100% of the energy target on day 4 post ICU-admission was associated with a lower ICU mortality [19].

Nutritional therapy of critically ill COVID-19 patients is challenging. A recent study reported that nearly 50% of COVID-19 patients admitted to the ICU developed intolerance to enteral nutrition (EN) due to severe gastrointestinal complications such as bowel dysmotility and ischemia, malabsorption, and hepatobiliary complications ileus, or pseudo-obstruction [20–22]. These patients also present a high risk of refeeding syndrome [23], and broncho-aspiration risk, particularly during the transition from the supine to prone position [24]. At the start of the COVID-19 pandemic in February 2020, nutritional support was difficult and not a priority in treating critically ill COVID-19 patients. Furthermore, due to the rapid increase in the number of hospitalised patients, there were logistical difficulties in terms of hospital staff, material availability and risk of contamination, requiring the introduction of simplified nutritional protocols [25,26]. In this context, experts' opinions, including the European Society for Clinical Nutrition and Metabolism (ESPEN) statement, emphasized to put more attention to diagnosis, prevention and treatment of malnutrition as a crucial part of the multidisciplinary management in COVID-19 patients [25–30].

We aimed to assess the impact of a simplified nutritional protocol [25], on nutritional therapy and outcomes during the first wave of the COVID-19 pandemic at the ICU of the Geneva University Hospitals, Switzerland.

2. Materials and methods

2.1. Study design

This retrospective observational study was conducted at the ICU of the Geneva University Hospitals, Switzerland. All patients

admitted to the ICU during the first wave of the COVID-19 pandemic (from March 9 to May 19, 2020) with acute respiratory failure due to SARS-CoV-2 infection were included. Clinical characteristics and outcomes of these patients have previously been reported [2]. The protocol has been approved by the ethics committee (CCER-2020-00917). Patients with an ICU LOS shorter than 4 days were excluded from the analysis as the efficacy of the simplified nutritional protocol could not be assessed during such short stays. Enrolled patients were divided into three groups based on the dates of their stay: (1) before, (2) across and (3) after the implementation of the simplified nutritional protocol (April 6, 2020). Patients whose ICU stay overlapped with the date of implementation of the nutritional protocol (2) are reported here. However, these patients were excluded from the comparison of nutritional therapy because it was not possible to evaluate the effect of the protocol implementation in this group.

2.2. Data collection

Clinical and nutritional data were collected from electronic health records and merged with the dataset created for the previous publication [2]. Daily nutrition data throughout the ICU stay were collected on the type of nutrition therapy (enteral, parenteral or mixed), prescribed and received volume (ml/24 h), calorie intake (kcal/24 h), protein intake (g/24 h), amount of insulin (unit/24 h), propofol infusion (ml/24 h), and glucose infusion (G5%, G10%, G20%) (ml/24 h).

2.3. Description of the nutritional protocol applied

The simplified nutritional protocol has been described recently [25] and is depicted in Fig. 1. Indirect calorimetry measurements were not used to assess energy target during this first wave due to the risk of contagiousness and the lack of resources. Rapid predictive formulas (20 kcal/kg body weight (BW) in the acute phase and 25 kcal/kg BW in the post-acute phase) were used and protein target was calculated as 1.3 g/kg BW/day following the ESPEN guidelines [7]. In patients with functional digestive tract and without other contraindications, early EN was started at day 1 and increased progressively as described in Fig. 1 [25]. In intubated patients, we aimed to cover 80–100% of the energy target from day 4 onwards. If the 80–100% energy target could not be achieved with EN alone by day 4, supplementary parenteral nutrition (SPN) was initiated. In non-intubated patient, EN was increased to a maximum of 1000 kcal/day to decrease the risk of broncho-aspiration. Nutrition therapy was then adapted on a case-by-case basis either by oral feeding, enteral nutrition or parenteral nutrition depending on the clinical state of the patient, with the aim of covering 80–100% of the needs by day 4. In case of electrolytic or metabolic disorders, the nutrition team could be asked for advice. The dietician in charge of the ICU checked regularly the nutritional therapy prescriptions and suggested adaptations, according to the energy and protein target, and digestive tolerance, when necessary.

2.4. Statistical analysis

Categorical data are presented as number of patients and/or percentages when appropriate. Continuous data are expressed as mean with standard deviation (SD). Nutrition therapy in the groups *before* and *after* were compared using unpaired t-test. Given the exploratory nature of the study, we did not apply a correction for multiple testing. As a result, the p-values are reported as indicative of possible effects and hypothesis-generation for future research. Statistical analyses were carried out using the R software, version 4.0.2.

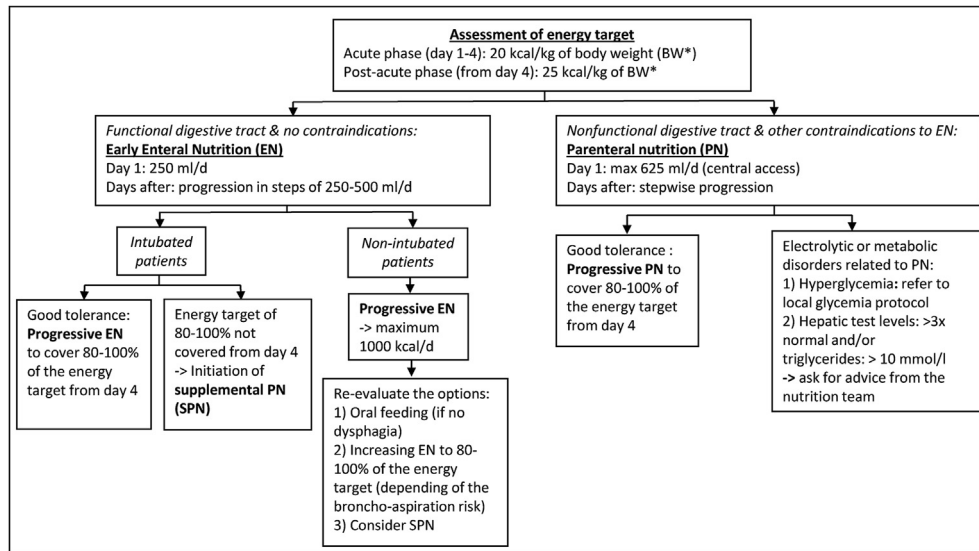


Fig. 1. Flowchart of the simplified nutritional protocol, adapted from de Watteville et al. [25]. *Assessment of energy target: use of actual body weight (BW) if the body mass index (BMI) ≤ 25 kg/m², or the ideal BW (BMI = 22.5 kg/m²) if BMI > 25 kg/m².

3. Results

A total of 129 patients were admitted in the ICU with a confirmed SARS-CoV-2 infection during the first wave of the COVID-19 pandemic (March 9 to May 19, 2020). Ten patients were excluded due to an ICU stay shorter than 4 days. The remaining 119

patients were divided into 3 groups: patients who stayed in the ICU *before* (n = 48), *across* (n = 47) and *after* (n = 24) the introduction of the simplified nutritional protocol (Table 1). The following analyzes only describe the two groups *before* and *after*. The overall mean age was 63.6 (± 12.7) years with a majority of men (76%) and no statistical differences between the *before* and *after* group (p = 0.263).

Table 1
Patient characteristics.

Patient characteristics	Before protocol implementation (n = 48)	Across protocol implementation (n = 47)	After protocol implementation (n = 24)
Age (years), mean (\pm SD)	61.2 (± 12.1)	65.2 (± 10.2)	65.1 (± 13.5)
Sex, n (%)			
Men	32 (66.7)	38 (80.9)	21 (87.5)
Women	16 (33.3)	9 (19.1)	3 (12.5)
APACHE II score, mean (\pm SD)	21.7 (± 9.5)	20.7 (± 8.6)	21.5 (± 7.6)
Comorbidities ^a , n (%)			
None	11 (22.9)	8 (17.0)	4 (16.7)
Hypertension	23 (47.9)	27 (57.4)	9 (37.5)
Diabetes	11 (22.9)	18 (38.2)	4 (16.6)
Hypercholesterolemia	15 (31.2)	12 (25.5)	7 (29.1)
Heart disease	13 (27.1)	10 (21.3)	6 (25.0)
Smoking	3 (6.2)	9 (19.1)	7 (29.1)
COPD	4 (8.3)	3 (6.4)	2 (8.3)
Stroke	2 (4.2)	4 (8.5)	1 (4.2)
Oncology	2 (4.2)	4 (8.5)	4 (8.3)
Chronic renal failure	4 (8.3)	3 (6.4)	3 (12.5)
Admission weight (kg), mean (\pm SD)	84.9 (± 13.4)	84.4 (± 15.4)	88.1 (± 26.5)
BMI n (%)			
<18.5 kg/m ²	0 (0)	0 (0)	1 (4.2)
18.5–24.9 kg/m ²	3 (6.2)	8 (17.0)	6 (25.0)
25.0–29.9 kg/m ²	24 (50.0)	20 (42.5)	9 (37.5)
≥ 30.0 kg/m ²	21 (43.8)	19 (40.5)	8 (33.3)
Ventilation, n (%)			
Invasive mechanical ventilation	48 (100.0)	47 (100.0)	24 (100.0)
Non-invasive mechanical ventilation	16 (33.3)	23 (48.9)	11 (45.8)
High-flow nasal oxygenation	7 (14.6)	16 (34.0)	7 (29.2)
Acute renal failure with RRT, n (%)	6 (12.5)	6 (12.7)	3 (12.5)
Vasopressor therapy, n (%)	42 (87.5)	44 (93.6)	24 (100.0)
ICU length of stay (days), mean (\pm SD)	11.7 (± 4.4)	22.2 (± 9.1)	18.7 (± 7.9)
Hospital length of stay (days), mean (\pm SD)	22.3 (± 10.3)	38.1 (± 15.1)	36.3 (± 16.8)
Discharge alive from ICU, n (%)	39 (81.2)	38 (80.9)	20 (83.3)

(APACHE II = Acute Physiology And Chronic Health Evaluation II; COPD=Chronic Obstructive Pulmonary Disease; BMI=Body Mass Index; ICU = Intensive Care Unit; RRT = Renal Replacement Therapy).

^a Patients could present with more than one comorbid condition, thus the percentages can add to more than 100%, or similar.

We observed a high prevalence of comorbidities: obesity (40%), hypertension (49.6%), diabetes (27.7%) and smoking (16%). Only the smoking rate differed significantly between the two groups ($p = 0.013$). The average ICU LOS for patients hospitalized in the *before* group was of 11.7 (± 4.4) days and of 18.7 (± 7.9) days in the *after* group ($p < 0.001$).

In the comparison of the 48 patients before and the 24 patients after the implementation of the simplified nutritional protocol (Table 2), the percentage of days within the energy target (80–100%) increased significantly from 11.0% (± 15.2) to 20.3% (± 16.7) ($p = 0.021$). The total calories provided increased significantly from 1070.1 kcal/day (± 505.5) to 1357.0 kcal/day (± 396.7) after the protocol implementation ($p = 0.018$). The best amount of calories in relation to BW was 16.7 (± 12.1) kcal/kg BW/day in the *before* group and 19.8 (± 10.3) kcal/kg BW/day in the *after* group, not being statistically significant. Furthermore, after implementing the protocol, the protein debt decreased significantly from 48.5 g/day (± 20.3) to 37.0 g/day (± 14.1) ($p = 0.015$), while the mean daily protein intake increased significantly from 37.0 g/day (± 18.4) to 51.4 g/day (± 17.3) ($p = 0.002$). Energy and protein intake, expressed as the percentage of energy and protein targets per day and by the *before* and *after* group, is shown in Fig. 2.

4. Discussion

SARS-CoV-2 pandemic has caught all the medical system off guard and generated multiple organizational challenges. In this context, a simplified nutritional protocol has been developed to adapt nutritional care to the pandemic context [25]. This study, following the introduction of a simplified nutritional protocol, was carried out on patients admitted to the ICU during the first wave of the COVID-19 pandemic. The results showed that the percentage of days in the energy target (80–100%), and total daily calories and protein intakes increased significantly after the introduction of the simplified nutrition protocol. Furthermore, the protein debt decreased significantly. The percentage of days above or below the energy and protein targets remained however stable between the *before* and *after* group. Albeit borderline significant, we also found a decrease in energy debt after the protocol implementation.

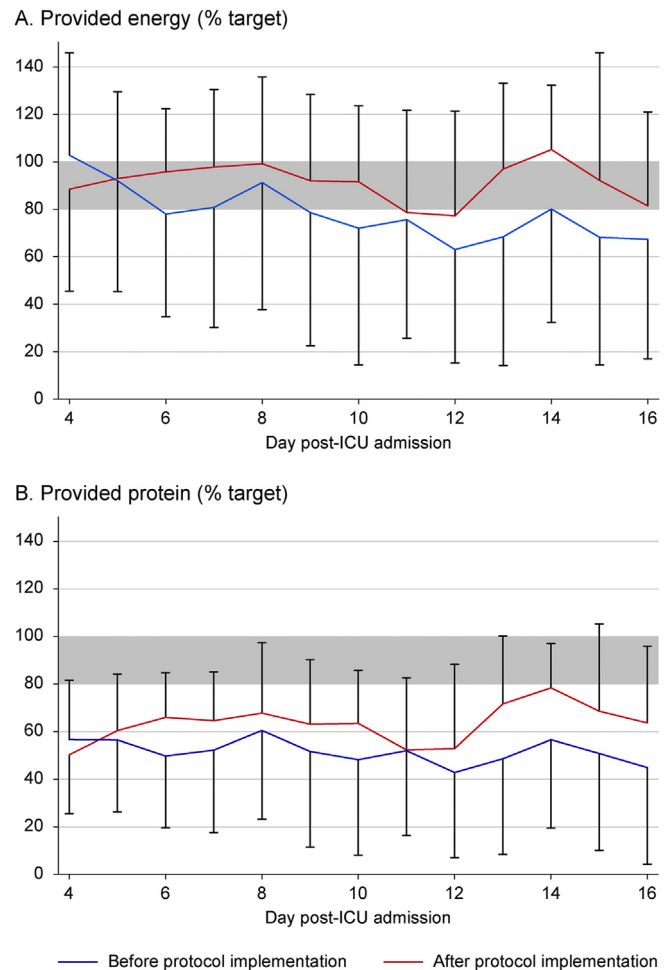


Fig. 2. Mean energy intake (panel A) and protein intake (panel B) expressed in percentage of the target (80–100%) (shaded rectangle) by day post-ICU admission before (blue line) and after (red line) implementing of the simplified nutritional protocol. For readability reasons, the error bars for SD are shown on one side only.

Table 2
Impact of a simplified nutritional protocol on nutritional status of COVID-19 patients in the ICU.

Mean \pm SD	Before protocol implementation (n = 48)	After protocol implementation (n = 24)	p-value for comparison
Percentage of days in the energy target (80–100%)	11.0 (± 15.2)	20.3 (± 16.7)	0.021
Percentage of days below the energy target (80–100%)	53.0 (± 27.5)	40.0 (± 24.0)	0.052
Energy debt, kcal/day	–575.2 (± 524.8)	–342.5 (± 357.6)	0.055
Total calories provided, kcal/day	1070.1 (± 505.5)	1357.0 (± 395.7)	0.018
Calories relative to body weight, kcal/kg BW ^a /day	16.7 (± 12.1)	19.8 (± 10.34)	0.218
Calories by enteral nutrition, kcal/day ^b	1107.4 (± 461.5)	1347.7 (± 397.0)	0.037
Calories by parenteral nutrition, kcal/day ^c	731.1 (± 672.0)	980.6 (± 397.1)	0.561
Calories provided by medication, kcal/day (propofol and glucose)	112.7 (± 92.2)	130.5 (± 84.0)	0.438
Percentage of days in the protein target (80–100%)	15.7 (± 21.8)	13.7 (± 16.9)	0.700
Percentage of days below the protein (80–100%)	81.4 (± 24.0)	80.0 (± 23.3)	0.825
Protein debt, g/day	–48.5 (± 20.3)	–37.0 (± 14.2)	0.015
Proteins provided, g/day	37.0 (± 18.4)	51.4 (± 17.3)	0.002
Proteins relative to body weight, g/kg BW ^a /day	0.58 (± 0.4)	0.7 (± 0.4)	0.152
Insulin infusion, unit/day	24.2 (± 36.1)	25.1 (± 36.8)	0.919

BW = Body Weight.

^a Use of actual BW if body mass index (BMI) ≤ 25 kg/m², or ideal BW (BMI = 22.5 kg/m²) if BMI > 25 kg/m².

^b Only for patients under EN (n = 46 in before group and n = 23 in after group).

^c Only for patients under PN (n = 3 in before group and n = 4 in after group).

The daily energy debt, which is still considerable even after the introduction of the nutritional protocol, can be explained by the fact that patients with SARS-CoV-2 often suffer from digestive intolerances [20–22], which lead to a temporary cessation of enteral nutrition. In addition, doctors were concerned about the risk of broncho-aspiration in the prone position or after extubation, which resulted in feeding breaks or periods of undernutrition [24].

The percentage of days in the protein target after the protocol implementation did not increase. This is not very surprising and can be explained by several factors: (1) our simplified nutritional protocol primarily focused on covering energy needs, (2) COVID-19 patients were often given a large amount of propofol for sedation, which is rich in lipids but does not contain protein and thus limited nutritional support, (3) the nutritional composition of the EN and PN formulas available in our ICU during the first wave of COVID-19 did not allow us to meet the protein target when covering the energy target. Nevertheless, we observed a decrease in protein debt and an increase in protein provided per day.

We are aware of the significant difference in LOS in the ICU between the group *before* and *after* the implementation of the protocol and assume that at the beginning of the first wave, all seriously ill COVID-19 patients were mainly admitted to the ICU while awaiting the availability of intermediate care beds. In this context, after the implementation of the protocol, only the most critically ill patients remained in the ICU, which resulted in a longer stay.

Our study has several strengths. First, the simplified nutritional protocol has been carried out by a multidisciplinary team considering the complexity of patient care in a pandemic context and supporting non-ICU trained healthcare providers. In addition to the protocol implementation, close cooperation between the nutrition team and the intensivists enabled an optimized nutrition therapy by regular monitoring and suggestions for nutritional prescriptions.

Second, to the best of our knowledge, it is the first study to evaluate the implementation of such a protocol in patients with severe SARS-CoV-2 infection in the ICU, and to observe an improvement in nutritional management after its implementation.

Some limitations of our study need to be acknowledged. The patient sample is relatively small, which could lead to power issues. Apart from smoking and ICU length of stay, no statistically significant differences in the patient characteristics could be determined between the groups. However this could be explained by the small sample size.

Moreover, it should be noted that this is an exploratory study, which should be repeated in order to obtain generalizable results. The retrospective observational design of the study makes it possible to establish an association between the implemented protocol and the nutritional status of the patients, but does not allow any conclusions to be drawn about a direct effect of the protocol. As mentioned above, it is also possible that due to the ICU and intermediate care units' reorganization, we compared patients with different profiles, namely the most severe patients after implementing the protocol. In addition, due to the risk of contagion and lack of resources, no assessment of energy expenditure by indirect calorimetry was performed during the first wave of the COVID-19 pandemic. Indeed, indirect calorimetry measurements appear to be a priority for patients with long ICU stays [31]. Finally, the available EN formulas did not allow coverage of the protein target. The use of protein enriched formulas is required to optimize protein intake and cover the needs.

Further research and clinical practice should focus on the use of indirect calorimetry measurements to guide nutritional therapy and to a higher protein provision.

5. Conclusion

The implementation of the simplified nutritional protocol has improved nutrition therapy during the first wave of the COVID-19 pandemic. These results made it possible to adapt our simplified nutrition protocol, thereby improving nutrition management for the following waves of COVID-19. Further studies are needed to determine whether the increased calorie and protein intake associated with the implementation of the nutritional protocol has a significant impact on clinical outcomes.

Statement of authorship

Aude de Watteville, Florencia Montalbano & Hannah Wozniak contributed equally to the article: Conceptualization, Methodology, Investigation, Formal analysis, Writing - original draft, Review & editing.

Tinh-Hai Collet & Laurence Genton: Conceptualization, Methodology, Visualization, Writing - review & editing.

Cyril Jaksic: Formal analysis.

Christophe Le Terrier & Jérôme Pugin: Writing - review & editing.

Claudia Heidegger: Conceptualization, Methodology, Formal analysis, Writing - original draft, Review & editing, Supervision, Validation.

All authors read and approved the final manuscript.

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Conflicts of Interest

The authors have no potential conflict of interest to declare.

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