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► To cite this version:

Marie-France Vaillant, Lydiane Agier, Caroline Martineau, Manon Philipponneau, Dorothée Romand, et al.. Food intake and weight loss of surviving inpatients in the course of COVID-19 infection: A longitudinal study of the multicenter NutriCoviD30 cohort. *Nutrition*, 2022, 93, pp.111433. 10.1016/j.nut.2021.111433 . hal-03351419

HAL Id: hal-03351419

<https://normandie-univ.hal.science/hal-03351419>

Submitted on 16 Oct 2023

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Food intake and weight loss of survival inpatients in the course of COVID-19 infection.

A longitudinal study of the multicenter NutriCovid30 cohort

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MF Vaillant had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Concept and design:* Vaillant, Agier, Albaladejo, Lathière, Fontaine. *Acquisition of data :* Vaillant, Martineau, Philipponneau, Romand, Masdoua, Behar, Nessler, Achamrah, Laubé, Lambert, Duquesnoy. *Analysis, or interpretation of data:* Vaillant, Agier, Bosson, Fontaine. *Drafting of the manuscript:* Vaillant, Agier, Lathière, Fontaine. *Critical revision of the manuscript for important intellectual content:* All authors. *Statistical analysis:* Vaillant, Agier, Fontaine. *Administrative, technical, or material support:* Vaillant, Albaladejo, Lathière. *Supervision:*

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Funding source: Nutricia nutrition clinique

Role of the Funding Source: The funding sources had no role in the design and conduct of the study; collection, management, analysis, or interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. All authors received a donation from Nutricia Nutrition clinique for the study. MF Vaillant reported having received support from Fresenius, Nestlé, D Romand from Nutricia, Nestlé, Fresenius, V Masdoua from Nutricia: for congress participations. V Masdoua was employee of Lactalis international (Medical Nutrition) 2017-19, E Fontaine reported having received personal fees for teaching from Baxter, B Braun, Nutricia, Périmètre. No other disclosures were reported.

Acknowledgments: We thank the NutriCoviD30 participants for time and commitment to the study and all following members of participating centers: Reine-Marie Nunzi, Carole Neveu, Coline Quehen, Lise Joly, Clara Meyer, all the dietician team, Stéphanie Schmitt, Aida Mandzo, Cyrielle Clapé (Grenoble), Caroline Gagliotta, Catherine Le Saux, all the dietician team, Monelle Bertrand Patrick Ritz (Toulouse), Aline Auzeric, Estelle Bovier, Marie Dragon, Karin Montagut, Maxime Paturel, Brigitte Boniteau, Mireille Philibert, Didier Barnoud, Cécile Chambrier (Lyon), Coralie Prebet, Edith Marchesi-Samedi, all the dietician teams of Pitié-Sâlpêtrière, Tenon, Saint-Antoine, Marion Thompson, Manuel Sanchez, Agathe Raynaud-Simon, Francisca Joly, Nicole Cournède, Jean-Claude Melchior (Paris),

Mathilde Gâté, Pierre Déchelotte (Rouen), Ronan Thibault (Rennes). Special thanks to Prof. Didier Quilliot and the French Speaking society for Clinical Nutrition and Metabolism (SFNCM) for their scientific contributions. We obtained permission to name them.

Trial Registration: ClinicalTrials.gov Identifier: NCT04365816

Key words: COVID-19; pneumonia; malnutrition; weight loss; food intake

Word counts:

Highlights: 83 words

Abstract: 239 words

Introduction

The sudden onset of the coronavirus SARS-CoV-2 has caused organizational upheavals and challenges in managing the current COVID-19 epidemics worldwide. Nutritional care is one of the key aspects of patients' management in situations of serious infection. In community-acquired pneumonia for instance, malnutrition is known to affect the long term recovery and to increase one- and two-year mortality in survived patients, especially for the elderly¹.

Given the effect of SARS-CoV-2 on patients taste and appetite², as well as on anosmia, ageusia, diarrhea, odynophagia, and anorexia^{3, 4}, COVID-19 patients are particularly at risk of undernutrition. This risk is often heightened by hospitalization^{5, 6}.

Reports of dramatic weight loss during this epidemic outbreak have led the European⁷, American⁸, and French-speaking⁹ learned societies of nutrition to issue expert opinions and recommendations for the nutritional management of patients. Despite this advice, and in the face of the short-term respiratory emergency, nutritional care has received limited attention from clinicians during the initial pandemic wave of the infection.

The aim of this study was to describe the nutritional impact of COVID-19 infection on adult inpatients on the short- to mid-term (up to 30 days after hospital discharge), using food intake and weight measurements. It also aimed to identify factors associated with a decrease in food intake and weight. While SARS-CoV-2 is an emerging and developing disease, this study is expected to improve the understanding of malnutrition in COVID-19 inpatients, and to help clinicians preventing the occurrence and long-term effects of this side effect of the disease.

Methods

Study design

The NutriCoviD30 study was designed as a prospective multicenter cohort of adult inpatients that were hospitalized with a confirmed COVID-19 infection, and who returned home after

hospitalization. Patients were recruited from 11 French university hospitals from May 7 to July 10, 2020, after ethical clearance from the French Committee for the Protection of Persons North West IV.

Patients were called by a nutritionist, medical doctor or dietician, 30 days after hospital discharge. Data was collected in the medical records or during this phone interview, regarding:

1/ prior chronic disease, lifestyle and eating habits before the disease (referred to as t0)

2/ COVID-19 symptoms, hospital stay and nutritional care characteristics during hospitalization (referred to as t1)

3/ World Health Organization (WHO) performance status score, persistence of symptoms and nutritional outcomes one month after hospital discharge (referred to as t2). Appetite assessment can be evaluated with a 10-point visual analogue scale^{10, 11}. Food intake was assessed at t1 and t2 using the 10-point verbal form of the SEFI® scale (Self-Evaluation of Food Intake) scored from 0 (“I eat nothing”) to 10 (“I eat as usual”). This scale has been validated and showed good reliability for the assessment of food and energy intake, and malnutrition among adults^{12, 13, 14}.

Weight assessment was based on patients’ declaration at t0 (considered as the reference weight) and t2. The lowest weight during the acute phase of the disease (reported by the patient or during hospitalization) was used as weight at t1. Weight loss at t1 and t2 were defined in terms of proportion of the reference weight at t0.

Statistical analysis

Quantitative parameters were described by their mean \pm standard deviation, or by their median [25th; 75th] percentiles, depending on the normality of the data. Qualitative parameters were expressed in numbers and percentages. A two-sided $P \leq 0.05$ was considered statistically significant.

SEFI® and weight were compared between two time points, between two groups, and between more than two groups (i) if the variable was normally distributed using Student paired test, Student test, and ANOVA, respectively; (ii) if the variable was not normally distributed using Wilcoxon matched-pairs signed-ranks tests, Wilcoxon signed-ranks tests, and Kruskal-Wallis tests, respectively.

Mixed-effect regression modeling was used to study the evolution of SEFI® at t1 and t2, with subjects nested within centers being modeled as random effects. Data from the Parisian hospital centers of Saint-Antoine, Tenon, and Paul Brousse were aggregated due to their small population sizes. Measures at t0 were not included in the model, because they were considered constant among patients and equal to 10, i.e. “I eat as usual”.

Weight loss at t1 and t2 was analyzed similarly (weight loss at t0 was null for all patients), with the following adjustment factors being additionally included in the model: the number of days in intensive care unit (ICU) (coded as “0 days”, “1 to 7 days”, “8 to 15 days”, and “more than 15 days”) and the admission in post-acute rehabilitation (PAR) unit (yes/no), which are expected to efficiently reflect disease severity; and edema status (coded as “appeared”, “disappeared”, or “did not change” since the previous period) which has a direct impact on weight. Adjustment factors were implemented with independent fixed effects at t1 and t2.

Mixed modeling can cope with partly missing data at the individual level. The analyses were ran on 402 (99.7%) patients for SEFI® (including 2 patients with one missing data at t1 or t2); and on 386 (95.8%) patients for weight loss (including 86 patients with one missing data).

The following COVID-19 potentially influential factors were further tested one by one: for their association with SEFI® and with weight loss evolution, pre-existing chronic conditions, clinical signs of the disease, and implementation of nutritional strategies. Alike adjustment factors, they were modeled with an independent fixed effect at t1 and t2. If the factor only

referred to one period (e.g. to the hospitalization period), the model was fitted only over this period, without a subject random effect.

All data were processed and analyzed using Stata v15.1 (Stata Corporation 4905 Lakeway Drive College Station, TX 77845 USA) and R version 3.3.3 (<https://cran.r-project.org/>).

Results

1. Population characteristics

A total of 1584 adult inpatients were screened in COVID-units, 945 were eligible and 403 were finally recruited in the present study. Of those not included, half of them did not answer to our call or message. Other reasons are listed in **Supplementary Figure 1**.

(a) Before the COVID-19 infection (t0)

Patients were on average 62.2 ± 14.2 years old; 63% were males (**Table 1**). Regarding chronic diseases, 80% of them presented with one or more chronic conditions (**Table 2**).

Our study population had an average reference weight (i.e. before the disease) of 83.4 kg ± 17.3 , and an average body mass index (BMI) of $28.8 \text{ kg/m}^2 \pm 5.3$.

Three hundred eleven (80%) patients considered their weight stable prior to the disease.

Under 3% of patients were at risk of malnutrition, based on BMI $< 18.5 \text{ kg/m}^2$ for patients under 70y, and BMI $< 21 \text{ kg/m}^2$ for patients over 70y.

(b) During the hospitalization for COVID-19 infection (t1)

Patients were hospitalized for a median duration of 13 days. A third were admitted in ICU (median duration: 10 days).

Regarding oxygen requirement, 20% of patients did not receive oxygen, 34% had oxygen therapy $\leq 3 \text{ l/min}$, 27% had oxygen therapy $> 3 \text{ l/min}$, and 19% were intubated (**Table 1**). As expected, patients who received **oxygen** during their hospitalization stayed longer in hospital (median duration: 14 days vs. 7, Wilcoxon test p-value < 0.0001 , **Supplementary table 1**).

Patients massively reported COVID-19 symptoms (**Table 2**).

(c) One month after returning home (t2)

Only 5% of patients were still on oxygen therapy one month after hospital discharge. Fatigue persisted in 39% of our patients; other symptoms persisted in 10 to 27% of affected patients. Changes in diet were reported by a third of patients, mainly towards a balanced diet or a diet adapted to COVID-19 symptoms (i.e. split, enriched, or adapted meals to the patient taste modifications).

General recovery was assessed using WHO performance status score. The median score was 1 [0.25 ; 2], corresponding to patients that were restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (**Table 3**).

2. Food intake and weight impact of COVID-19

SEFI® and weight trajectories are illustrated in **Figure 1**. Only 5% of patients neither reported a weight loss $\geq 5\%$ of their reference weight before the disease, nor a food intake decrease greater than 30% of usual food intake during the course of the disease.

At t1, the median [interquartile] SEFI® was 3 [1; 5] (representing a decrease of 70% of patients' usual food intake), and the average weight decreased to 77 kg \pm 16. This represents a weight loss of 6.5 kg \pm 5.4 (maximum of 30kg), and a 7.6% \pm 5.9 decrease compared to the reference weight (maximum of 32%). Based on etiologic and phenotypic diagnosis criteria, i.e. acute disease and weight loss (from the International Global Leadership Initiative on Malnutrition (GLIM)¹⁵ and French Health Authorities guidelines), 67% patients were malnourished (of whom 42% were severely malnourished).

During the recovery phase (t2), 62% patients recovered their initial SEFI® (i.e. a score of 10), and 19% even reported better appetite than before the disease. Yet a quarter of patients were not hungry when lunch or dinnertime came (**Table 3**).

While the majority of patients regained weight during recovery, our population still recorded an average weight loss of 4.2% \pm 5.0 of their reference weight one month after hospital

discharge (i.e. $-3.8 \text{ kg} \pm 4.7$) (**Table 1**), indicating that 41% patients remained malnourished (of whom 25 % were severely malnourished).

Among the 49% patients that did not recover their initial weight, 62% declared they did so voluntarily.

3. Association between potentially influential factors and food intake or weight

Mixed models confirmed a significant difference between t1 and t2 in SEFI®, and in weight loss, after adjusting for patients and recruitment center variability, and the selected set of adjustment factors: SEFI® regression coefficient was 3.4 at t1 and 8.9 at t2; weight loss coefficient was 6.1% at t1 and 3.4% at t2. As per the adjustment factors, the duration of stay in ICU displayed a significant association with a greater weight loss (6.9% at t1 and of 4.3% at t2 for patients who spent more than 15 days in ICU compared those who were not admitted in ICU, both $p < 0.001$); while PAR stay and edema status were in global not further associated with weight loss at t1 and t2 (**Supplementary Table 2**). In our population, age was not associated with differences in weight loss (**Supplementary Table 3**).

We further screened for an additional effect of COVID-19 potentially influential factors, one by one (**Table 2** and **Table 4**). Regarding SEFI®, chronic diseases had no impact at t1 and t2, except for chronic respiratory diseases which were associated with a 0.7 point decrease in SEFI® at t2 ($p = 0.026$).

All the symptoms of COVID-19 were associated with a statistically significant decrease in SEFI® at t1 (of 0.5 to 3.6 points, all $p < 0.045$). The strongest associations were observed for anorexia and fatigue (**Table 2**). Difficulties drinking, food disgust, anorexia, and painful mouth remained associated with a significant decrease in SEFI® at t2, but of lower magnitude compared to t1 (0.5 to 0.8 points, all $p < 0.025$).

Regarding weight loss, only fatigue ($p = 0.003$), anorexia ($p = 0.006$), and food disgust ($p = 0.013$) were significantly associated with a weight loss at t1 (with, respectively, a 2.3%,

1.8% and 1.3% greater weight loss compared to those who did not display such symptoms).

None were significantly associated with weight loss at t2.

Among the chronic diseases, diabetes was significantly associated with a 1.8% ($p=0.004$) and 1.5% ($p=0.026$) increased weight loss at t1 and t2, respectively; hypertension was associated with a 1.4% increased weight loss at t2 ($p=0.018$). Overweight (BMI between 25 to 30 kg/m²) and obesity (BMI>30 kg/m²) were associated with a greater weight loss compared to patients with a normal BMI (18.5 to 25 kg/m²), of respectively 1.6% and 2.2% at t1, and 1.7% and 3.7% at t2 (all $p<0.020$).

4. Nutritional strategies during the COVID-19 infection and recovery phase

In terms of nutritional strategies, half of the population took oral nutritional supplements (ONS) during their hospitalization, for a median of 8 days, and 14 units in total; and 30% of the patients were prescribed ONS after returning home, for a median 60 units in total. During their hospitalization, 61% of patients received adapted meals (i.e. different from the standard meal, corresponding to enriched meals or texture-modified food) and 49% received snacks. Nutritional care data during hospitalization and the recovery phase does not include artificial nutrition due to their non-exhaustive collection in several centers.

Using mixed models (**Table 3 and 4**), none of these strategies were found to be significantly associated with SEFI® or weight loss, except for advices given by a nutritionist that were associated at t1 with a 1.2% increased weight loss ($p=0.007$), and ONS that were associated with a 1.6% weight gain at t2 for patients who were prescribed ONS at home ($p=0.001$).

Despite the fact that there was no interventional group, we compared patients who received, or not, ONS during their hospitalization (**Table 5**). The 196 patients who were prescribed ONS had lost more weight at t1 than the 189 patients who did not receive ONS ($p\text{-value}<0.001$). However, they recovered better at hospital discharge and at 1 month from hospital

discharge (p-value = 0.0005 and 0.009, respectively). Note that the two groups did not differ in terms of sex ratio, pre-disease weight, or SEFI® at t1, whereas the ONS group was older.

Discussion

In our population of 403 inpatients who survived the COVID-19 infection, 67% suffered from malnutrition (defined by a weight loss greater than 5% within the past 6 months in a population of infected patients). Other studies^{11, 16} using the same malnutrition definition reported an overall prevalence of malnutrition of 31% and 42.1%, respectively. Another study⁶ reported 52.7% malnutrition based on Mini Nutritional Assessment score. These differences result in great part from differences in the study populations, typically in terms of gravity of the disease. For instance, 3% of the 156 inpatients were admitted in ICU in Di Filippo and al. study¹¹, 16% of the 114 inpatients in Bedock and al. study¹⁶, while it affected 30% of the 403 inpatients in the present study (data not available in Li and al.⁶).

As previously reported^{17,18}, we found that anorexia, fever, dyspnea and fatigue were the most prevalent clinical features of COVID-19. Fatigue, anorexia and food disgust were major aggravating factors for weight loss in the acute phase of the disease, along with chronic diabetes, overweight, and obesity. Unsurprisingly, we found that the more severe the disease (as reflected by the number of days spent in ICU), the greater the weight loss.

Distinguishing our work from previous studies, we aimed to understand the recovery process, to investigate breaks on regaining weight and on recovering a normal food intake, as well as to assess the impact of nutritional strategies. The observed decrease in food intake is likely an immediate consequence of the infection-related anorexia and food disgust, it was transient; unlike the COVID-19 impact on weight.

As a matter of fact, 41% of our patients still suffered from malnutrition one month after returning home. This suggests that rapid weight loss is a major side effect which likely predominantly affects muscle mass. Interestingly, a substantial proportion of our patients

voluntarily did not aim to recover their initial weight. These were predominantly patients with overweight or obesity, who were happy with their weight loss. This observation highlights the risk for patients with obesity and sarcopenia, as warned by Barazzoni and al.¹⁹, to be more conscious of public health messages regarding the benefits of losing weight, than of the importance of preserving their muscle mass and function. In line with the European Society for Clinical Nutrition and Metabolism (ESPEN) and the European Association for the Study of Obesity (EASO)¹⁹, and the European Society of Endocrinology²⁰, this leads us to call for particular attention to this population. Adults with diabetes should also benefit from an acute surveillance, as they tend to lose more weight than other patients²¹.

The benefit of nutritional strategies during hospitalization (encouragement to eat, fortified food, etc.) is likely biased by the fact that nutritional supports were predominantly given to the patients most affected by the disease (i.e. those who had the greatest drop in appetite and weight). For instance, patients receiving ONS had lost more weight than patients without ONS.

Disentangling this confounding effect from the effect of a nutritional strategy would have required an intensive follow-up of patients during the acute phase (i.e. routine measures of weight and energy intake), which was not possible during the first epidemic wave when health professionals were overloaded. Consequently, the results at t1 should be interpreted with great caution.

On the contrary, the results obtained during the recovery phase are probably not affected by this confounding effect (all patients were in recovery during this period). Interestingly, ONS were significantly associated with a weight gain at t2. This observation is in favor of guidelines for COVID-19²² stating that meals and snacks should be adapted to patients' dis gusts and capabilities²³ and combined with resisted physical exercise²⁴. This is also in

agreement with Caccialanza and al.²⁵ who recommended two or three bottles of ONS for non-critically ill patients as a systematic prescription for patients with nutritional risk. Note however, that this study was not randomized. Consequently, further interventional studies are needed to confirm our results.

Strengths and Limitations

The strength of the NutriCoviD30 study design lies in collecting repeated SEFI® and body weight measures during the course of the COVID-19 infection, i.e. before the disease, during the hospitalization and 1 month after hospital discharge. When analyzing food intake and weight loss trajectories using linear mixed models, individual characteristics affecting the measure (eg. educational status) are accounted for by the individual random effect, as long as they do not differentially impact the three periods.

There are however several limitations to our study. First, our population consisted only of inpatients survivors. This excludes the most severe inpatients who were still hospitalized or in PAR units at the time of the study, and the less severe patients who did not require to be hospitalized.

A second limitation relates to weight measurements. Its assessment was not complete. At the highest, 98 patients did not provide a weight measure at t2, because of no bathroom scale at home, or because they refused to weigh themselves. Additionally, weighting accuracy depends on the scales tuning, which is expectedly equally affected by positive and negative calibration fluctuations. Hence, weights are measured with a between-person random error, resulting in unbiased estimates of the average weight²⁶. Yet, the variance is inflated, which can lower statistical power in mixed models. Finally, the consistency observed between weight measurements (**Supplementary Table 4**) gives us confidence in the data and analyses we reported.

The use of SEFI® relies on declarative assessment which is less precise than a professional evaluation or measuring energy intake. Yet, our interest lies in the SEFI® trajectories, and was investigated using models that account for inter-individuals differences and focuses on intra individual variations between measures. For people with moderate cognitive decline (3%, **Table 2**), a relative helped to answer the questionnaire during the interview.

Conclusion

To our knowledge, NutriCoviD30 is the largest multicenter longitudinal cohort studying the nutrition of hospitalized patients with COVID-19 infection to date. Its main interest lies in assessing malnutrition on the mid-term, i.e. including the recovery phase up to 1 month after hospital discharge. This study provides a description of COVID-19 symptoms, and of pre-existing chronic conditions, as well as their potential impact on the patients' food intake and weight loss. It also describes and investigates the nutritional interventions implemented during the infection and recovery phase.

COVID-19 resulted in a substantial weight loss in inpatients, which rapidity infers that it affected the muscle mass much more than the fat mass. Patients only regained half of their weight loss one month after hospital discharge, even though their food intake went back to normal. Malnutrition affected 67% of patients during their hospitalization and persisted for 41% of them one month after hospital discharge. This is partly due to patients not being aware of the severity of muscle wasting during rapid weight loss. The mid- to long-term effects of COVID-19 infection have been widely demonstrated to date; yet, avoiding important weight loss during the acute phase would help limiting these effects. On this goal, nutritional support is needed for COVID-19 inpatients; it should start early in the course of the infection, and should be extended up to the recovery phase. Prevention messages should be delivered regarding the importance of maintaining muscle mass and function.

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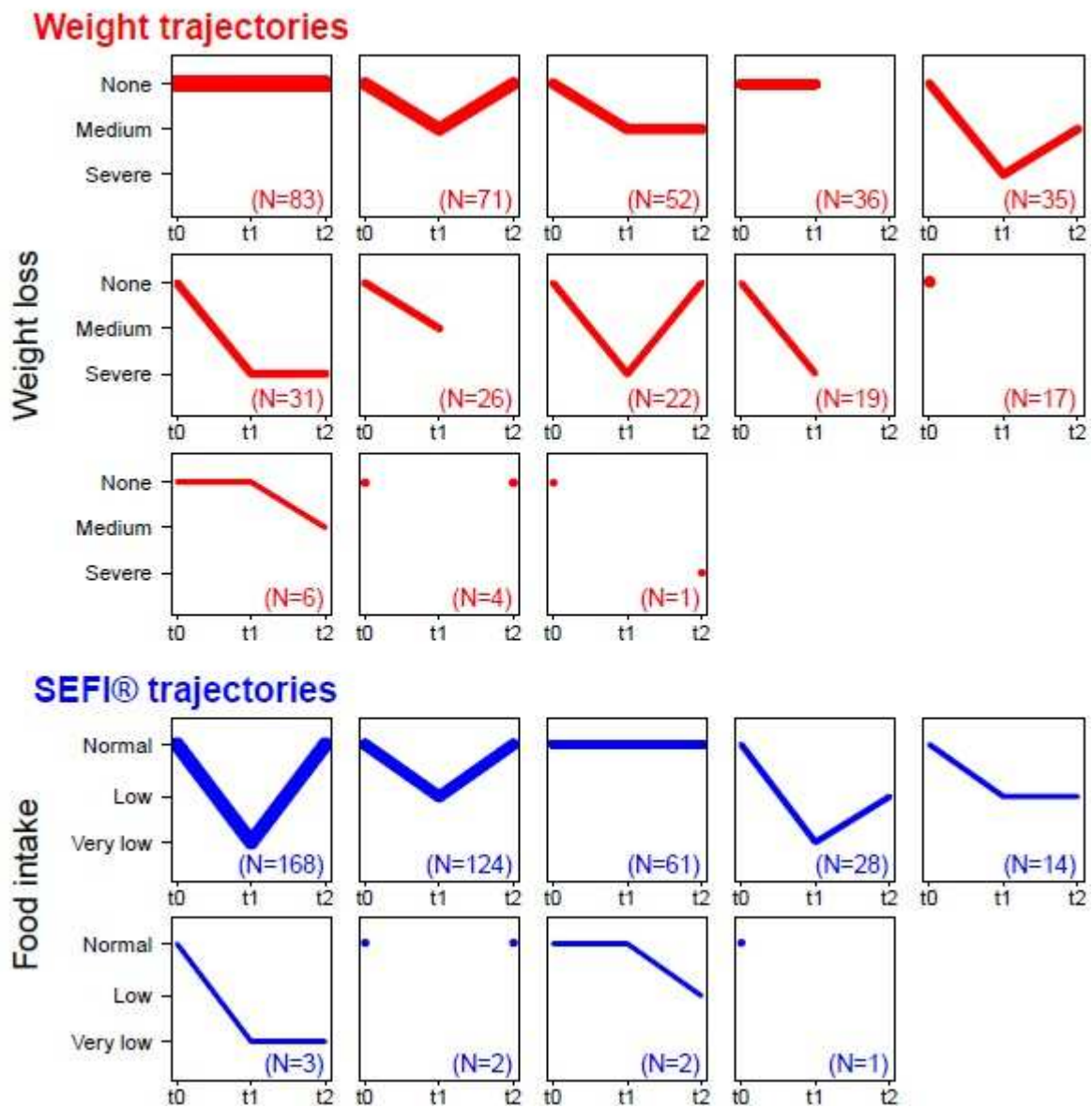
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Figure 1. Weight loss and SEFI® trajectories during the course of COVID-19 infection and recovery period (N=403 patients)



Legend: Weight loss and SEFI® (Self-Evaluation of Food Intake) trajectories at t0 (before the disease), t1 (in the course of COVID-19) and t2 (recovery period at 1 month); incomplete trajectories (i.e. with missing values) are displayed as shorter segments or as dots.

Weight loss values (as a percentage of weight at t0) were grouped into classes: none: <5%, medium: [5%; 10%[, and severe weight loss: ≥10%. Weight loss at t0 was 0 for all patients.

Food intake values were grouped into classes: normal: [0;3[, low: [3;7[, and very low food intake: [7;10]. SEFI at t0 was assumed to be 10 for all patients.

Graphs are ordered by decreasing number of patients per trajectory type.

The thicker and darker the line, the greater the number of patients with this trajectory.

Table 1. Descriptive statistics of NutriCovid30 population (N=403 patients)

	Missing data (%)	N (%), mean (standard deviation) or median [inter quartile range] ^a
POPULATION CHARACTERISTICS		
Sex (% males)	0 (0%)	255 (63%)
Age (years)	0 (0%)	62.2 (14.2) Min: 22 ; Max: 97
Height (m)	0(0%)	1.7 (0.09) Min: 1.45 ; Max: 1.96
One or more chronic conditions	0 (0%)	323 (80%)
Lifestyle	0 (0%)	
Lives with 1 or several relatives		312 (78%)
Lives in a nursing home		9 (2%)
Lives alone		82 (20%)
WEIGHT BEFORE THE COVID-19 INFECTION		
Weight (kg)	10 (2%)	83.4 (17.3) Min: 43 ; Max: 144
Weight considered stable (patient declaration)	14 (3%)	311 (80%)
Pay attention to his/her weight (patient declaration)	2 (0%)	230 (57%)
Reason for paying attention to his/her weight (several possible answers) ^b	2 (1%)	
To lose weight		91 (40%)
To be in good health		56 (25%)
To gain weight		9 (4%)
To stabilize/maintain weight		102 (45%)
BMI (kg/m ²)	10(2%)	28.8 (5.3) Min: 17 ; Max: 49
At risk of malnutrition (BMI <18.5 kg/m ² for patients<70y, or BMI <21 kg/m ² for patients>70y)	10(2%)	11 (2.8%)
BMI <18.5 kg/m ² for patients<70y ^c	7 (7%)	1 (0.3%)
BMI < 21 kg/m ² for patients≥70y ^d	3 (3%)	10 (8.1%)
DIET BEFORE THE COVID-19 INFECTION		
On diet	1 (0%)	168 (42%)
Type of diet (several possible answers) ^e	0 (0%)	
Healthy/organic foods		67 (40%)
Vegetarian/flexitarian		8 (5%)
Restrictive (low-calorie, free from sugar, lactose, fat, salt, fiber or gluten)		82 (49%)
HOSPITAL STAY CHARACTERISTICS		
University hospital center	0 (0%)	403 (100%)
Grenoble		95 (23%)
Lyon		51 (13%)
Paris AP-HP Pitié-Salpêtrière		51 (13%)
Paris AP-HP Bichat		33 (8%)
Paris AP-HP Paul Brousse/St Antoine/Tenon		31 (8%)
Paris AP-HP Beaujon		29 (7%)
Rennes		28 (7%)

	Rouen	25 (6%)
	Toulouse	60 (15%)
Hospitalization duration (days)	0 (0%)	13 [8 ; 20] Min: 1 ; Max: 97
Admission in intensive care unit (ICU)	1 (0%)	122 (30%)
ICU stay duration (days) ^f	3 (2%)	10 [6 ; 20] Min: 1 ; Max: 65
Admission in post-acute and rehabilitation (PAR) unit	13 (3%)	102 (25%)
Maximum ventilatory support level	12 (3%)	
No oxygen		78 (20%)
Oxygen ≤3l/min		134 (34%)
Oxygen >3l/min		106 (27%)
Intubation		73 (19%)
FOOD INTAKE AND WEIGHT DURING HOSPITALIZATION (t1) AND ONE MONTH AFTER HOSPITAL DISCHARGE (t2)		
SEFI® score at t1	3 (1%)	3 [1 ; 5] Min: 0 ; Max: 10
SEFI® score at t2	1 (0%)	10 [8 ; 10] Min: 1 ; Max: 10
Weight at t1 compared to t0 (%)	22 (5%)	-7.6 (5.9) Min: -32 ; Max: +8
Weight at t1 compared to t0 (kg)	22 (5%)	-6.5 (5.4) Min: -30 ; Max: +7
Weight at t1 compared to t0 < -5%	22 (5%)	256 (67%)
Weight at t2 compared to t0 (%)	98 (24%)	-4.2 (5.1) Min: -23 ; Max: +15
Weight at t2 compared to t0 (kg)	98 (24%)	-3.8 (4.7) Min: -25 ; Max: +10
Weight at t2 compared to t0 < -5%	98 (24%)	125 (41%)

^a Amongst non-missing data. N(%) is used for qualitative data; mean (standard deviation) for normally distributed quantitative data (based on data visualization); and median [inter-quartile range] for non-normal quantitative data.

^b Amongst the 230 patients who pay attention to their weight

^c Amongst the 277 patients aged <70y old

^d Amongst the 126 patients aged ≥70y old

^e Amongst the 168 patients who paid attention to their diet

^f Amongst the 122 patients admitted in ICU

BMI: Body Mass Index, SEFI®: Self-Evaluation of Food Intake

Table 2. Association between COVID-19 potentially influential factors and the evolution of SEFI® at t1 and t2, estimated independently for each symptom using linear mixed-effect regression modeling

		SEFI® at t1 ^a		SEFI® at t2 ^a	
	N/nb of non missing data (%)	Coefficient [CI95 %]	P-value	Coefficient [CI95 %]	P-value
COVID-19 SYMPTOMS					
Anorexia / early feeling of fullness / long satiation	314/401 (78%)	-3.6 [-4.2 ; -3.1]	<0.001 **	-0.7 [-1.2 ; -0.2]	0.010 *
Anosmia / agueusia or dysgeusia / change in taste	225/387 (58%)	-1.4 [-1.9 ; -0.9]	<0.001 **	0.1 [-0.4 ; 0.5]	0.801
Nausea / vomiting	133/401 (33%)	-1.1 [-1.6 ; -0.6]	<0.001 **	-0.5 [-0.9 ; 0]	0.067
Difficulties swallowing / pharyngeal or esophageal pain	88/398 (22%)	-0.7 [-1.2 ; -0.1]	0.021 *	-0.3 [-0.9 ; 0.3]	0.307
Painful mouth / white, pasty tongue	146/387 (38%)	-0.9 [-1.4 ; -0.4]	<0.001 **	-0.7 [-1.1 ; -0.2]	0.007 **
Difficulties drinking	76/396 (19%)	-1.6 [-2.2 ; -1]	<0.001 **	-0.8 [-1.4 ; -0.2]	0.006 **
Food disgust	187/397 (47%)	-1.4 [-1.9 ; -1]	<0.001 **	-0.5 [-1 ; -0.1]	0.023 *
Fever	309/395 (78%)	-1.5 [-2 ; -0.9]	<0.001 **	0.5 [-0.1 ; 1]	0.090
Dyspnea / coughing	314/401 (78%)	-0.9 [-1.4 ; -0.3]	0.002 **	0.1 [-0.5 ; 0.6]	0.850
Pain (muscular, cranial, headaches, ...)	249/394 (63%)	-0.8 [-1.2 ; -0.3]	0.002 **	-0.1 [-0.5 ; 0.4]	0.850
Fatigue	352/402 (88%)	-2.1 [-2.8 ; -1.4]	<0.001 **	-0.1 [-0.8 ; 0.6]	0.830
Digestive or transit disorders	287/400 (72%)	-0.5 [-1.1 ; 0.0]	0.044 *	-0.2 [-0.7 ; 0.3]	0.425
PRE-EXISTING CHRONIC DISEASES					
Cognitive disorders	13/403 (3%)	-0.3 [-1.6 ; 1.0]	0.609	-0.8 [-2.1 ; 0.5]	0.212
Chronic respiratory disease (with chronic medication / home oxygen therapy / sleep apnea)	72/403 (18%)	0.1 [-0.5 ; 0.7]	0.648	-0.7 [-1.3 ; -0.1]	0.026 *
Immunodepression / cancer (presently treated)	51/403 (13%)	0.1 [0.6 ; 0.8]	0.869	0.0 [-0.8 ; 0.7]	0.894
Hypertension	169/403 (42%)	0.4 [-0.1 ; 0.9]	0.091	0 [-0.5 ; 0.4]	0.836
Heart Failure	19/403 (5%)	0.7 [-0.4 ; 1.9]	0.191	-1.1 [-2.2 ; 0]	0.054
Diabetes (all types)	92/403 (23%)	0.2 [-0.3 ; 0.8]	0.464	-0.1 [-0.6 ; 0.5]	0.821
Chronic inflammatory Bowel diseases (Crohn's disease...)	5/403 (1%)	0.9 [-1 ; 1.3]	0.378	-0.2 [-2.3 ; 1.9]	0.829
Inflammatory rheumatic diseases (lupus, rheumatoid arthritis...)	17/403 (4%)	0.2 [-0.9 ; 1.4]	0.694	-0.4 [-1.6 ; 0.7]	0.486
BMI before COVID-19 infection					
<18.5 kg/m ²	3/393 (1%)	1.6 [-1.1 ; 4.2]	0.256	0.4 [-2.3 ; 3.1]	0.761
[18.5, 25[kg/m ²	92/393 (23%)	(ref)	(ref)	(ref)	(ref)
[25, 30[kg/m ²	147/393 (37%)	-0.0 [-0.6 ; 0.6]	0.933	0.4 [-0.2 ; 1.0]	0.237
≥30 kg/m ²	151/393 (38%)	-0.3 [-0.9 ; 0.4]	0.412	0.2 [-0.5 ; 0.8]	0.621
NUTRITIONAL STRATEGIES AND DIFFICULTIES					

Food supply difficulties related to home confinement	16/401 (4%)	-1.2 [-2.3 ; 0.0]	0.055	-0.4 [-1.6 ; 0.8]	0.512
Incentives to eat, and if needed, help given by caregivers or a relative	132/379 (35%) at t1, 196/398 (49%) at t2	-0.2 [-0.7 ; 0.3]	0.415	-0.1 [-0.6 ; 0.4]	0.640
Advices given by a nutritionist	105/366 (29%) at t1, 93/395 (24%) at t2	-0.2 [-0.8 ; 0.3]	0.378	0.2 [-0.3 ; 0.8]	0.406
Adapted meals during hospitalization ^b	235/387 (61%) at t1	-0.5 [-1.1 ; 0.2]	0.139	/	/
Snacking during hospitalization ^b	189/386 (49%) at t1	0.4 [-0.2 ; 1.0]	0.197	/	/
Oral nutritional supplements, ONS (yes/no, patient declaration)	196/385 (51%) taken at t1, 120/400 (30%) prescribed at t2	-0.4 [-0.9 ; 0.1]	0.104	-0.2 [-0.8 ; 0.3]	0.336
Total ONS (units, patient declaration) ^c	14 [4.5; 22.5] taken at t1, 60 [15;60] prescribed at t2	-0.00 [-0.01 ; 0.02]	0.921	0.00 [-0.01 ; 0.00]	0.248

** p-value<0.01

* p-value<0.05

^a SEFI analyses were performed using a mixed-effect regression model, with an individual random effect nested in a center random effect, and an independent fixed effect at t1 and at t2 for the variable of interest.

^b Variable affecting only the hospitalization period: analysis was performed at t1 only.

^c 60 (15%) missing data at t1, 18 (4%) missing data at t2.

BMI: Body Mass Index, SEFI®: Self-Evaluation of Food Intake

Table 3. Patients characteristics 1 month after hospital discharge (t2)

	Missing data (%)	N (%), mean (standard deviation) or median [IQR] ^a
Oxygen supply	5 (1%)	19 (5%)
WHO performance status	1(0%)	1 [0.25 ; 2] Min: 0 ; Max: 4
PARTIAL PERSISTENCE OF SYMPTOMS OF COVID-19 INFECTION		
Anorexia / early feeling of fullness / long satiation ^b	0(0%)	32 (12%)
Anosmia / ageusia or dysgeusia / change in taste ^b	0(0%)	35 (18%)
Nausea / vomiting ^b	0(0%)	16 (12%)
Difficulties swallowing / pharyngeal or esophageal pain ^b	0(0%)	16 (22%)
Painful mouth / white tongue, pasty ^b	0(0%)	25 (16%)
Difficulties drinking ^b	0(0%)	8 (10%)
Fever ^b	0(0%)	3 (1%)
Dyspnea / coughing ^b	0(0%)	86 (27%)
Pain (muscular, cranial, headaches) ^b	0(0%)	61 (24%)
Fatigue ^b	0(0%)	136 (39%)
DIET AND APPETITE		
Adaptation of diet after COVID-19 infection	4 (1%)	148 (37%)
Type of adaptation ^c	0(0%)	
<i>Diet adaptation due to COVID-19 infection</i>		59 (40%)
<i>Diet alteration due to COVID-19 infection</i>		18 (12%)
<i>Balanced diet</i>		71 (48%)
Feeling more hungry than before the disease	7 (2%)	77 (19%)
Patient quickly satiated, no appetite	6 (1%)	102 (26%)
SEFI® score of 10	1 (0%)	248 (62%)

^a Amongst non-missing data. N(%) is used for qualitative data; mean (standard deviation) for normally distributed quantitative data (based on data visualization); and median [inter-quartile range] for non-normal quantitative data.

^b Amongst patients who had this symptom at t1

^c Amongst the 148 patients who adapted their diet after COVID-19 infection. Diet adaptation is a strategy to fight or a consequence of COVID-19 infection. It consists of split meals, enriched food, or increased protein intake. Diet alteration consists of a decreased food intake due to a loss of appetite, or a loss/change in taste.

WHO: World Health Organization, SEFI®: Self-Evaluation of Food Intake

Table 4. Association between COVID-19 potentially influential factors and the evolution of weight at t1 and t2, estimated independently for each symptom using linear mixed-effect regression modeling

		Weight at t1 compared to t0 (%) ^a		Weight at t2 compared to t0 (%) ^a	
	N/nb of non missing data (%)	Coefficient [CI95%]	P-value	Coefficient [CI95%]	P-value
COVID-19 SYMPTOMS					
Anorexia / early feeling of fullness / long satiation	314/401 (78%)	-1.8 [-3.1 ; -0.5]	0.006 **	-1.2 [-2.6 ; 0.2]	0.082
Anosmia / agueusia or dysgeusia / change in taste	225/387 (58%)	0.2 [-0.9 ; 1.3]	0.678	0.2 [-1 ; 1.3]	0.768
Nausea / vomiting	133/401 (33%)	-0.4 [-1.6 ; 0.7]	0.431	0.2 [-0.9 ; 1.4]	0.683
Difficulties swallowing / pharyngeal or esophageal pain	88/398 (22%)	-0.8 [-2.1 ; 0.5]	0.221	-0.2 [-1.5 ; 1.2]	0.809
Painful mouth / white, pasty tongue	146/387 (38%)	-0.5 [-1.6 ; 0.6]	0.376	0.4 [-0.8 ; 1.6]	0.511
Difficulties drinking	76/396 (19%)	-0.4 [-1.7 ; 0.9]	0.578	-0.1 [-1.5 ; 1.3]	0.930
Food disgust	187/397 (47%)	-1.3 [-2.4 ; -0.3]	0.013 *	-0.7 [-1.8 ; 0.4]	0.196
Fever	309/395 (78%)	-0.2 [-1.5 ; 1.1]	0.769	-0.1 [-1.5 ; 1.2]	0.863
Dyspnea / coughing	314/401 (78%)	-0.2 [-1.5 ; 1]	0.721	0.0 [-1.3 ; 1.4]	0.948
Pain (muscular, cranial, headaches, ...)	249/394 (63%)	-0.7 [-1.8 ; 0.4]	0.195	-0.3 [-1.5 ; 0.9]	0.608
Fatigue	352/402 (88%)	-2.3 [-3.9 ; -0.8]	0.003 **	-1.0 [-2.7 ; 0.6]	0.227
Digestive or transit disorders	287/400 (72%)	0.3 [-0.9 ; 1.4]	0.661	-0.7 [-2.0 ; 0.5]	0.238
Pre-existing chronic diseases					
Cognitive disorders	13/403 (3%)	-1.8 [-4.7 ; 1.1]	0.223	0.0 [-3.1 ; 3.2]	0.980
Chronic respiratory disease (with chronic medication / home oxygen therapy / sleep apnea)	72/403 (18%)	0.8 [-0.6 ; 2.1]	0.275	0.7 [-0.8 ; 2.1]	0.384
Immunodepression / cancer (presently treated)	51/403 (13%)	-0.9 [-2.5 ; 0.6]	0.235	0.7 [-0.9 ; 2.3]	0.390
Hypertension	169/403 (42%)	-0.4 [-1.5 ; 0.6]	0.446	-1.4 [-2.5 ; -0.2]	0.018 *
Heart Failure	19/403 (5%)	1.0 [-1.4 ; 3.4]	0.405	0.2 [-2.5 ; 2.9]	0.900
Diabetes (all types)	92/403 (23%)	-1.8 [-3.0 ; -0.6]	0.004 **	-1.5 [-2.8 ; -0.2]	0.026 *
Chronic inflammatory bowel diseases (Crohn's disease...)	5/403 (1%)	2.6 [-2.2 ; 7.5]	0.291	3.4 [-1.5 ; 8.3]	0.175
Inflammatory rheumatic diseases (lupus, rheumatoid arthritis...)	17/403 (4%)	0.0 [-2.7 ; 2.7]	0.994	1.6 [-1.3 ; 4.4]	0.275
BMI before COVID-19 infection (in categories)					
<18.5 kg/m ²	3/393 (1%)	-4.8 [-10.6 ; 1.0]	0.105	-0.5 [-6.3 ; 5.4]	0.879
[18.5, 25[kg/m ²	92/393(23%)	(ref)	(ref)	(ref)	(ref)
[25, 30[kg/m ²	147/393 (37%)	-1.6 [-3.0 ; -0.3]	0.018 *	-1.7 [-3.1 ; -0.3]	0.018 *
≥30 kg/m ²	151/393 (38%)	-2.2 [-3.5 ; -0.9]	0.001 **	-3.7 [-5.1 ; -2.3]	<0.001 **
Nutritional strategies and difficulties					
Food supply difficulties related to home confinement	16/401 (4%)	-1.8 [-4.6 ; 1.0]	0.216	-1.4 [-4.3 ; 1.4]	0.327

Incentives to eat, and if needed, help given by caregivers or a relative	132/379 (35%) at t1, 196/398 (49%) at t2	-0.5 [-1.3 ; 0.4]	0.270	-0.1 [-0.9 ; 0.7]	0.839
Advices given by a nutritionist	105/366 (29%) at t1, 93/395 (24%) at t2	-1.2 [-2.1 ; -0.3]	0.007**	-0.5 [-1.5 ; 0.5]	0.307
Adapted meals during hospitalization ^b	235/387 (61%) at t1	-0.7 [-1.9 ; 0.5]	0.239	/	/
Snacking during hospitalization ^b	189/386 (49%) at t1	-1.0 [-2.1 ; 0.1]	0.087	/	/
Oral nutritional supplements (yes/no, patient declaration)	196/385 (51%) taken at t1, 120/400 (30%) prescribed at t2	-0.6 [-1.5 ; 0.2]	0.150	1.6 [0.6 ; 2.5]	0.001**
Total ONS ^c (units, patient declaration)	14 [4.5; 22.5] taken at t1, 60 [15;60] prescribed at t2	-0.01 [-0.04 ; 0.01]	0.325	0.02 [0.01 ; 0.04]	0.001**

** p-value<0.01

* p-value<0.05

a Weight analyses were performed using a mixed-effect regression model, with an individual random effect nested in a center random effect, and an independent fixed effect at t1 and at t2 for the variable of interest and for the adjustment factors (the number of days in intensive care, admission to post-acute and rehabilitation and the edema status).

^b Variable affecting only the hospitalization period: analysis was performed at t1 only.

^c 60 (15%) missing data at t1, 18 (4%) missing data at t2.

BMI: Body Mass Index, ONS: Oral Nutritional Supplements

Table 5: Comparison between patients who received or not oral nutritional supplements (ONS) during their hospitalization

	Patients who received ONS at t1 (N=196) N(%),mean (standard deviation) or median [IQR] ^a	Patients who did not received ONS at t1 (N=189) N(%),mean (standard deviation) or median [IQR] ^a	P-value of the equality test
Age (years)	63.6 (1.0)	60.4 (1.0)	0.023 * (Student t-test)
Sex (% males)	122 (62%)	124 (66%)	0.492 (proportion test)
Weight before COVID-19 (kg)	83.1 (1.2)	84.3 (1.3)	0.510 (Student t-test)
Weight at t1 compared to t0 (%)	-8.6 (0.4)	-6.5 (0.4)	<0.001 ** (Student t-test)
Weight recovery between during the hospitalization and at hospital discharge (kg)	0.6 (0.2)	-0.6 (0.3)	0.005 ** (Student t-test)
Weight recovery between t1 and t2, compared to t0 (%)	4.3 (0.4)	3.1 (0.3)	0.009 ** (Student t-test)
SEFI® at t1	2.5 [1 ;5]	3 [1 ;5]	0.303 (Wilcoxon test)

** p-value<0.01

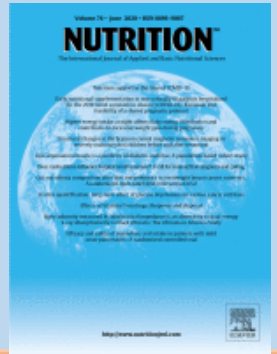
* p-value<0.05

^a Amongst non-missing data. N(%) is used for qualitative data; mean (standard deviation) for normally distributed quantitative data (based on data visualization); and median [inter-quartile range] for non-normal quantitative data.

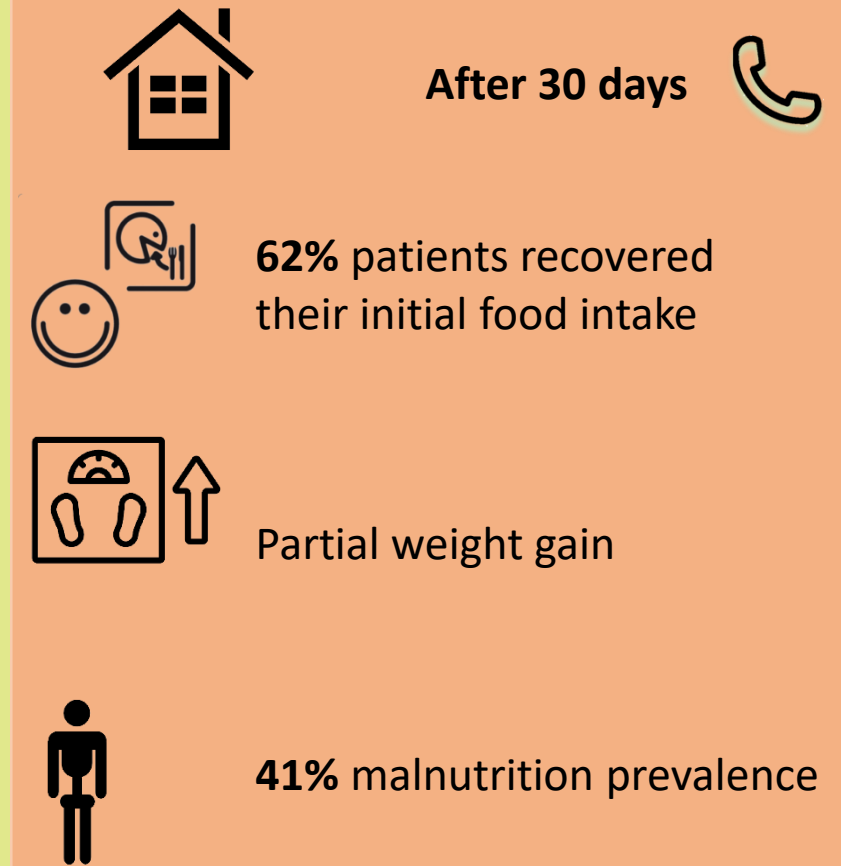
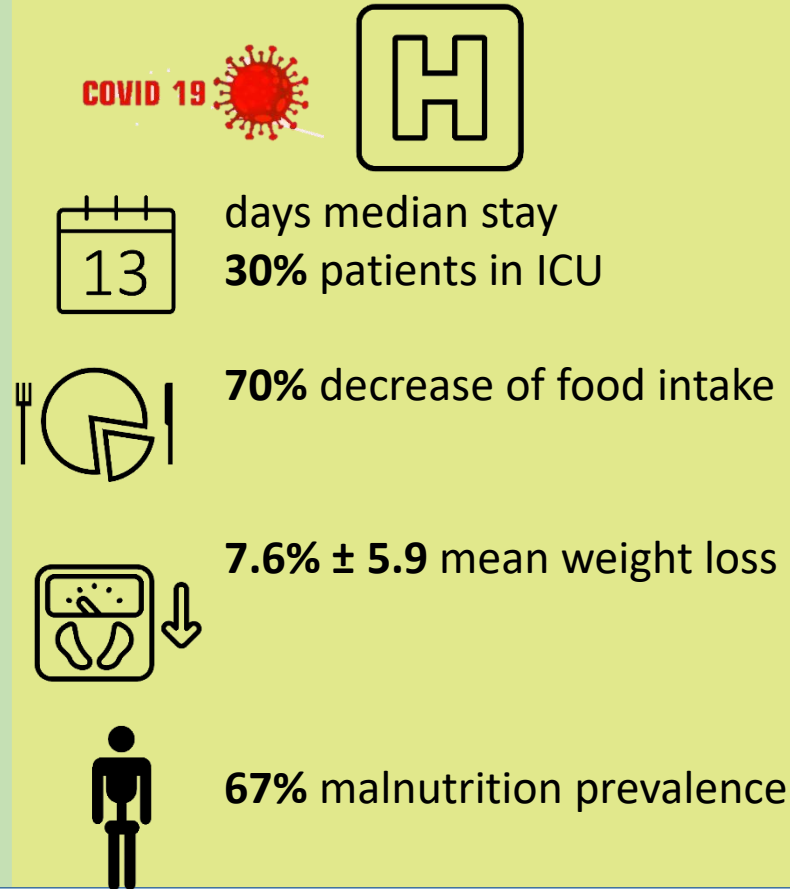
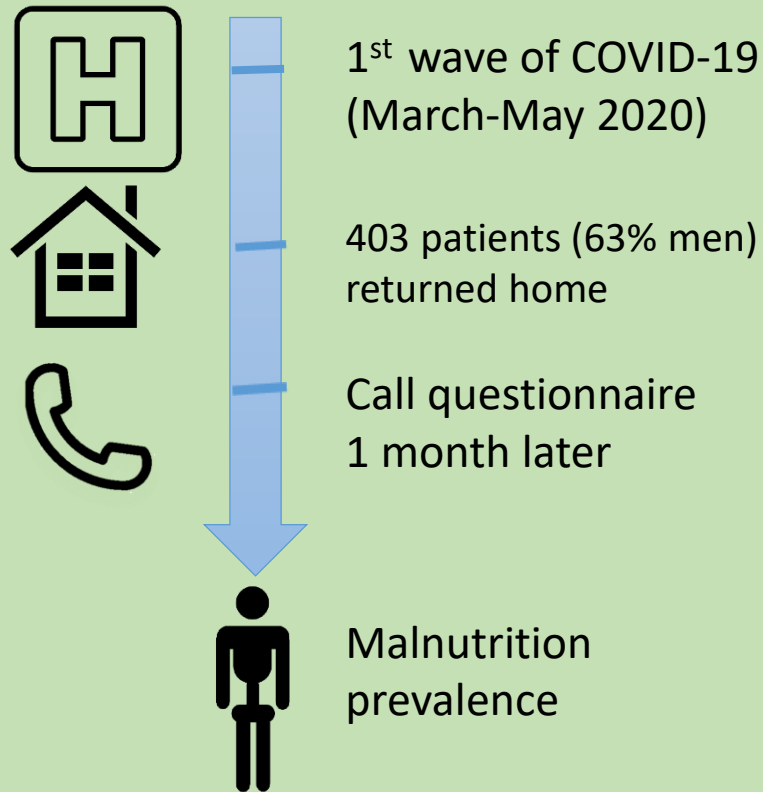
SEFI®: Self-evaluation of food intake scale

Food intake and weight loss of survival inpatients in the course of COVID-19 infection

A longitudinal study of the multicenter NutriCovid30 cohort



Methods and cohort



Conclusion:

High prevalence of malnutrition due to Covid-19 infection and persisting at 1 month. Importance of appropriate nutritional management all along the disease.

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QR CODE