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Abstract

Rationale: The prevalence of malnutrition and the provided nutritional therapy were evaluated in all the patients with SARS-CoV-2 infection (COVID-19) hospitalized in a 3rd level hospital in Italy.

Methods: A one-day audit was carried out recording: age, measured or estimated body weight (BW) and height, body mass index (BMI,Kg/m^2), 30-day weight loss (WL), comorbidities, serum albumin and C-reactive protein (CRP: nv<0.5 mg/dL), hospital diet (HD) intake, oral nutritional supplements (ONS), enteral (EN) and parenteral nutrition (PN). Modified NRS-2002 tool and GLIM criteria were used for nutritional risk screening and for the diagnosis of malnutrition, respectively.

Results: A total of 268 patients was evaluated; intermediate care units (IMCUs,61%), sub-intensive care units (SICUs,8%), intensive care units (ICUs,17%) and rehabilitation units (RUs,14%): BMI: <18.5, 9% (higher in RUs, p=0.008) and ≥30, 13% (higher in ICUs,p=0.012); WL≥5%, 52% (higher in ICUs and RUs,p=0.001); CRP >0.5: 78% (higher in ICUs and lower in RUs,p<0.001);Nutritional risk and malnutrition were present in 77% (higher in ICUs and RUs,p<0.001) and 50% (higher in ICUs,p=0.0792) of the patients, respectively. HD intake ≤50%, 39% (higher in IMCUs and ICUs,p<0.001); ONS, EN and PN were prescribed to 6%, 13% and 5%, respectively. Median energy and protein intake/kg BW were 25 kcal and 1.1 g (both lower in ICUs,p<0.05) respectively.

Conclusions: Almost all the patients were at nutritional risk, and one-half of them was malnourished. The frequency of nutritional risk, malnutrition, disease/inflammation burden and decrease intake of HD differed among the intensity of care settings, where the patients were managed according to the severity of the disease. The patient energy and protein intake were at the lowest limit or below the recommended amounts, indicating the need for actions to improve the nutritional care practice.

Keywords

SARS-CoV-2, COVID-19, malnutrition, nutritional therapy, NRS-2002, GLIM, epidemiology

Introduction

The novel coronavirus SARS-CoV-2 disease (COVID-19) is the current challenging pandemic arisen in Wuhan, China, in December 2019[1]. COVID-19 primarily involves the respiratory tract, but it may progress to multi-organ failure and threat the patient's survival[2]. The clinical spectrum of COVID-19 ranges from asymptomatic infection to mild upper respiratory tract infection, and severe pneumonia with acute respiratory distress syndrome (ARDS)[1,2]. Older age and the presence of comorbidities, diabetes, cardiovascular diseases and obesity, have been reported to be risk factors for progression of pulmonary disease as well as for death[3,4].

Patients affected by COVID-19 can be at risk of malnutrition because of reduced food intake, inflammation-related catabolism, reduced mobility due to prolonged hospital stay as well as older age and comorbidities [5]. The European Society for Clinical Nutrition and Metabolism (ESPEN) timely devised expert statements and practical guidance for the nutritional management of patients with COVID-19[5]. These guidelines recommend that nutritional intervention and therapy be considered as an integral part of the approach to these patients. Indeed, as for any acute and chronic disease, optimal nutritional care associated to life-support therapy has potential to improve the outcome of patients affected by this life-threatening disease, including better and shorter recovery from the acute phase. However, up to now none of the papers reporting epidemiology, clinical features and outcome of COVID-19 cohorts has described the patient nutritional status and nutritional therapy [1,3,6], excepting the observation of a poorer prognosis in patients with high body mass index[7].

In order to know the prevalence of malnutrition as well as the provided nutritional therapy[8], we carried out a one-day audit therapy in all the COVID-19 adults hospitalized in a third level hospital in Italy.

Material and Methods

Study design and patient cohort

On April 2020, a one-day clinical audit of nutritional status and nutritional therapy was performed on all the adult patients (age ≥18 years) hospitalized in the clinical settings designated for the treatment of COVID-19 in the Sant'Orsola University Hospital of Bologna, Italy. There were no exclusion criteria.

Hospital settings for COVID-19 and management of the nutritional care

The Sant'Orsola University Hospital of Bologna is the main tertiary hospital of the Emilia-Romagna region. This Northern-Italian region was one of the most affected in Italy by the COVID-19 pandemic, with around 15.000 cases at the end of March. In the wake of this outbreak, many hospital units have been converted into COVID-19 units, categorized in four levels of intensity of care: intermediate care units (IMCUs), sub-intensive care units (SICUs), intensive care units (ICUs) and rehabilitation units (RUs).

The Sant'Orsola Hospital is a 1400 bed hospital. The nutritional care [8] is based on clinical procedures and recommendations edited by the Clinical Nutrition Unit and approved by the Clinical Governance Unit. The health-care professionals of any hospital units are required to provide the nutritional therapy to the individual patient, according to those procedures and recommendations. Case-by-case clinical nutrition consultancy is provided by the Clinical Nutrition Unit at the request of the doctors in charge of the patient.

Data collection

The following data were recorded in each patient: age, gender, measured or estimated/referred body weight (BW) and height, body mass index (BMI, kg/m^2), referred BW before the onset of

COVID-19 related symptoms; partial pressure of arterial oxygen ratio (PaO_2/FiO_2), type of O_2-therapy (Low flow nasal cannula, LFNC; high flow nasal cannula, HFNC; non-invasive ventilation, NIV; continuous positive airway pressure, CPAP; endotracheal intubation, ETI; tracheostomy-mechanical ventilation TMV); smoking habits, comorbidities (Cerebrovascular Disease, CeVD; coronary heart disease, CHD; chronic kidney disease, CKD; chronic liver disease, CLD; chronic obstructive pulmonary disease, COPD; heart failure, HF; type 1 and 2 diabetes mellitus, T1 and T2DM), appetite degree (absent, decreased or normal), gastrointestinal symptoms (dysgeusia; dysphagia; nausea; vomiting; diarrhoea; abdominal pain), frailty and disability, serum concentration of albumin, C-reactive protein (CRP); type of prescribed hospital diet (HD) (regular consistency or soft diet), intake of the prescribed HD the day before the audit (estimated as: >75%, 75-51%, 50-25%, <25%), oral nutritional supplements (ONS), enteral (EN), parenteral nutrition (PN); propofol dosage; length of hospital stay (LOHS). The nutritional therapy was prescribed by the doctors responsible for the COVID-19 units.

The day before the audit, the ward nurses received the structured questionnaire for the data collection (supplementary material 1). On the day of the audit, the ward nurses collected patients' BW, height, and the intake of the prescribed HD the day before. Ten physicians (residents or consultants in clinical nutrition) collected all the other data from the patients' records.

The malnutrition risk and the diagnosis of malnutrition were assessed using modified Nutritional Risk Screening 2002 tool (NRS-2002) [9] and modified Global Leadership Initiative on Malnutrition (GLIM) criteria[10], respectively. Modifications were needed because of safety and hygiene reasons, that caused limitations in measuring the nutritional parameters as required by the original NRS-2002 and GLIM. **Tables 1 and 2** describe how the criteria for the NRS-2002 and GLIM assessment were modified to adapt them to the present study.

The energy and the protein content of the HD and snacks were obtained from the hospital menu chart, and those of the ONS, EN and PN were obtained from their nutritional formulation provided by the manufacturer. The patient's basal energy expenditure (BEE) was calculated by the Harris-Benedict equation, including the patient's ideal BW when BMI was ≥30 kg/m^2. The respiratory clinical feature was categorized by FiO_2/PaO_2, according to the Berlin definition of ARDS [11].

Ethics

The audit was agreed upon with the hospital Clinical Governance Unit and was conducted with full regard to the confidentiality of the individual patient and the principles of the Declaration of Helsinki. Patients' informed consent was not required for an audit of existing clinical practice. The collected individual patient data were anonymized.

Statistical analyses

All the data were included in an Electronic Case Report Form (eCRF) and managed using REDCap electronic data capture tool[12]. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Continuous variables were expressed as the median and interquartile range (IQR, 25th – 75th percentiles). Categorical data were expressed as numbers (percentages). For group comparisons of categorical and continuous variables, Chi-square test, Wilcoxon rank-sum test and Spearman's rank-order correlation were used, as appropriate. All statistical tests were two-tailed, and differences were considered significant at p-value ≤0.05. Statistical analysis was performed using Stata/SE (Version 16; Stata Corp, Texas, United States of America) for Windows.

Results

Patient cohort

The audit included 268 patients (**Table 3**): 60.5% in IMCUs, 7.8% in SICUs, 17.2% in ICUs and 14.5% in RUs. The median age (years) was 74 (63-84): 76 (64-86) in IMCUs, 72 (62-79) in SICUs, 67 (61-73) in ICUs and 76 (70-86) in RUs (p=0.0002). More than one-half of patients were males and 70.9% were older than 64 years. Around one-half (43.6%) had ARDS, and 15.0% were on CPAP/NIV, ETI or TMV O_2-therapy. Three-fourths (74.6%) of patients had one or more co-morbidities. Patients in SICUs and in ICUs settings showed the highest percentages of overweight and obesity and the most severe clinical feature, as represented by the lowest percentages of normal PaO_2/FiO_2 ratio and the use of CPAP/NIV and invasive type of O_2-therapy. The median LOHS (days) was 14 (7-27): 10 (4-16) in IMCUs, 15 (8-24) in SICUs, 27 (17-33) in ICUs and 28 (19-35) in RUs (p<0.0001).

Patient nutritional assessment

The BW before admission was known in 125 (46.6%) patients. The one-month weight loss (1-mo WL) (%) was 5.3 (2.5-9.1): 3.8 (0.8-9.6) in IMCUs, 4.7 (2.9-6.3) in SICUs, 6.3 (3.6-9.4) in ICUs and 7.6 (5.9-9.5) in RUs (p=0.0297). The BMI calculation was based on estimated/referred BW and/or height in 43.2% of cases. The BMI (Kg/m^2) was 25.1 (22.0-27.8): 24.5 in IMCUs (21.5-27.3), 26.5 (24.1-29.4) in SICUs, 27.7 (25.1-30.9) in ICUs and 23.4 (20.0-26.7) in RUs (p= 0.0001). HD intake <50% of the prescribed diet was observed in two-thirds of patients (23.5% were on nil per os) and was more frequent in ICUs (p<0.0001) (**Table 4**). The oral intake was positively associated with the degree of appetite, and negatively with the invasiveness of O_2-therapy, the presence of gastrointestinal symptoms and of frailty/disability (**Figure 1**).

The serum CRP concentration (mg/dL), was 2.69 (0.72-7.87): 3.01 (0.76-7.57) in IMCUS, 1.48 (0.13-4.35) in SICUs, 10.02 (1.98-15.19) in ICUs and 0.89 (0.25-2.30) in RUs (p=0.0001) (**Table 4**).

Serum albumin (mg/dL) was 29.8 (27.0-33.0): 30.4 (28-33.7) in IMCUs, 30.2 (27-32) in SICUs, 28.2 (25.2-30.1) in ICUs and 29.5 (27.4-32.9) in RUs (p=0.0016). Serum albumin correlated negatively with serum CRP (mg/dL) (r= -0.3854: p<0.0001), positively with daily actual energy intake (kcal/kg BW) (r= 0.2123; p<0.001) and the daily actual protein intake (g/kg BW) (r= 0.2383; p=0.0003).

The nutritional risk screening could be evaluated in the whole cohort, whereas the presence of malnutrition could be assessed in only 151 patients (**Table 4**). Three-fourth of patients were at nutritional risk (modified NRS-2002 score ≥3) with a significantly lower prevalence in IMCUs (67.3%). The modified GLIM diagnosis of malnutrition was observed in one-half of patients, when all the degrees of disease burden/inflammation (CRP cut off >0.5 mg/dL) were considered, (highest prevalence in ICUs and RUs) and in one-third of patients when only moderate or severe burden/inflammation degrees (CPR cut off >5 mg/dL) were included (highest frequency in ICUs). In the 151 patients in whom both nutritional risk and malnutrition were assessed, 25 patients were not at nutritional risk. In this group, malnutrition was diagnosed in only 1 (4%) patient). In the 126 patients who were at nutritional risk, malnutrition was diagnosed in 74 patients (54%) when all the degrees of disease burden/inflammation (CRP cut off >0.5 mg/dL) were considered, and in 44 patients (35%) when only moderate or severe burden/inflammation degrees (CPR cut off >5 mg/dL) were considered. **Figure 2** shows the frequency of nutritional risk and of malnutrition in the 151 patients in whom both were assessed, categorized by the intensity of care settings.

Nutritional therapy

HD was prescribed to 213 (79.5%) patients (regular consistency diet, 105; soft diet, 108), 24 of whom were also receiving medical nutrition therapy. Medical nutrition therapy was given to 63 (23.5%) patients, most of whom were in SICUs or ICUs: ONS in 16, EN in 34 and PN in 13 patients. Around one-half of patients in ICUs were also receiving energy by propofol infusion (**Table 5**).

The median prescribed and actual total energy intake were 143% and 128% of the BEE, respectively, corresponding to 26.7 and 24.8 kcal/Kg BW. The median prescribed and actual protein intake were 1.2 and 1.1 g/Kg BW, respectively. The prescribed quantities did not differ among the setting, whereas the actual intakes were significantly lower in ICUs (actual energy: 103% of the BEE and 20 kcal/kg BW; actual proteins 1.0 g/Kg) (**Table 5**).

Discussion

The results of this cross-sectional study show a very high prevalence of nutritional risk (77.2%) and malnutrition (49.7%) in adult patients hospitalized for COVID-19. When we planned this audit, a PubMed search using the terms “COVID-19 and nutrition” did not find any reference. Recently, a paper from Wuhan has reported the prevalence of malnutrition in older COVID-19 patients (>64 years) assessed by the Mini Nutritional Assessment (MNA) score[13]. However, although MNA is a valuable tool for nutritional risk screening in the elderly, it is not considered a criterion for the diagnosis of malnutrition[10,14]. Therefore, to date, this is the only investigation reporting the prevalence and the causes of both nutritional risk and malnutrition in adult hospitalized COVID-19 patients.

Our results should be evaluated taking in account the limitations due to the modifications of the NRS-2002 [9] and GLIM criteria [10] (**Tables 1 and 2)** made because of safety and hygiene rules to avoid COVID-19 infectiveness of health-care workers. This reduced the chances of contact with the patients for reasons other than life-saving diagnostic and therapeutic interventions. Therefore, estimated/referred BW was used to calculate the BMI in around one-half of the patient cohort, whereas only the one-month non-volitional weight loss could be recorded. A one-day intake of the prescribed HD was used to surrogate the last week’s food intake in comparison with energy requirement and no technique for the body composition assessment was applied, to measure the muscle mass. Indeed, even though the estimation of BW and height is a method used also in the methods of the ESPEN NutritionDay audit [15], it doesn’t allow to evaluate the change in body composition/hydration related to ongoing pathophysiological mechanisms of malnutrition, nor to detect reduced food intake or inflammation-related catabolism, as well as to have a precise calculation of the energy expenditure [16]. Furthermore, older patients or patients in ICUs could have difficulties in recalling data. All these factors could have caused an underestimation of the

prevalence of malnutrition, since it was diagnosed in only 54% of patients who were at nutritional risk. The strength of the study is the observation of a large cohort of patients that was representative of all the clinical features of COVID-19 disease, hospitalized in four levels of intensive care settings in a tertiary university hospital of Northern Italy, one of the most affected areas in Europe. The clinical characteristics of the patient cohort agreed with those reported in the literature: more than one-half were males, two-thirds were older than 64 years, one-half were overweight or obese and each co-morbidity affected at least 20% of the patients. These characteristics were more evident in patients in SICUs or ICUs settings, who were younger (those in ICUs), had greater BMI and the most severe clinical feature, as represented by the lowest PaO_2/FiO_2 ratio, the higher CRP serum concentrations, and the more invasive type of O_2-therapy.

The prevalence of malnutrition as well as its current mechanisms differed among the intensity of care settings, where the patients were managed according to the severity and the stage of the disease. The GLIM guidelines suggest that the serum CRP concentration could be used as a criterion to evaluate the presence and the severity of disease/inflammation burden, but no indications on how to categorize and use it are given[10]. We calculated the prevalence of malnutrition, including either all the categories of disease/inflammation or only the moderate-severe categories. Patients in ICUs showed the highest prevalence (70%) of both nutritional risk and malnutrition. Malnutrition affected one-half of patients in both IMCUs and RUs when all the categories of inflammation/catabolism were considered. When only moderate-severe inflammation/catabolism were included, the prevalence of malnutrition decreased to one-third of patients in IMCUs and to only in 6% of those in RUs. These data are in keeping with the different stage of the disease in patients hospitalized in these two settings: early and acute stage in IMCUs and late and chronic stage in RUs, represented by the higher CRP levels in IMCUs and the longer LOHS in RUs.

The audit of the nutritional therapy showed that both the prescribed and actual nutritional intake were at the lower limit or even below the ESPEN recommended amounts for this patient population, that are 27-30 kcal/kg and 1.0 gr/kg of protein in patients with low-grade disease burden/inflammation, such as those in IMCUs and RUs, and energy 70 to 100% of the BEE and 1.3 g/kg in patients with severe disease burden/inflammation, such as those in SICUs and ICUs[5]. In patients in IMCUs and RUs, both the prescribed and actual energy intake were near to the lowest limit of the range of the ESPEN recommendations, whereas the protein intake was within the range. In patients in ICUs, the actual energy intake was near to the 100% of the BEE, whereas the protein intake appeared below the recommendations. In the whole cohort of patients, the actual oral intake was lower than 75% of the prescribed intake in two-thirds of patients and lower than 50% in 40% of them. As expected, the oral intake was adversely affected by the impairment of appetite, the invasiveness of the O_2-therapy and the presence of frailty/disability. These observations indicate the need to take actions to implement the daily monitoring of the degree of disease/inflammation burden and the oral intake with its causative factors, and to plan tailored nutritional therapy[5,17]. This is highlighted by the data on serum albumin concentration. In COVID-19 patients developing ARDS, decreased serum albumin, and prealbumin concentrations were described [3]. Even though in acute inflammatory stage, serum albumin should be considered a supportive proxy measure of inflammation rather than of nutritional status[10], the positive association we found between serum albumin and protein and energy intake supports the need to provide the recommended amounts[5]. ESPEN guidelines recommend routine assessment of nutritional risk and nutritional status, nutrient intake and inflammation-related catabolism as well as timely and appropriate nutritional therapy in all the hospitalized patients with COVID-19[5]. Body composition assessment and measured energy expenditure are further recommended

for tailored nutritional therapy in critically ill patients on either non-invasive or invasive ventilation [18].

In conclusion, our audit on nutritional assessment and therapy in hospitalized patients with COVID-19 showed that almost all the patients were at nutritional risk whereas one-half of them were malnourished; the frequency of nutritional risk, malnutrition, disease/inflammation burden and decrease intake of HD differed among the intensity of care settings, where the patients were managed according to the severity and the stage of the disease; the prescribed and actual energy and protein intake were at the lowest limit or below the recommended amounts, indicating the need for actions to improve the nutritional care practice for these challenging patients.

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Ethical approval

Being a Clinical Audit approved by the Clinical Governance Unit of the Hospital, submission to the Ethical Committee was not required.

Statement of authorship

LP devised the study protocol, coordinated the study, analysed the results and drafted the manuscript; ASS and FR contributed to data collection and analysis; CB, BB, GB, LB, LL, GAM and AM, FR and ASS carried out the study. All authors contributed to interpretation of data, critically revised, and approved the final version of this manuscript.

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Conflicts of interest

None declared.

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Table 1. Nutritional Risk Screening criteria for nutritional risk assessment. Modification of the NRS-2002[9] to the audit on COVID-19 hospitalized patients.

Original NRS-2002 criteria	**Modified criteria for the present study**	**Score in the present study**
Non-volitional weight loss: >5% in 3, 2 or 1 month	One-month weight loss (1mo-WL) calculated using the referred BW before hospitalization (at time of the audit the maximal length of hospital stay was 35 days)	1mo-WL <5%, score 0 1mo-WL ≥5%, score 3
BMI <20.5 or 18.5	Calculated from the measured or estimated/referred patient's BW and height	BMI > 20.5: score 0 BMI 18.5-20.5, score 2 BMI <18.5, score 3
Food intake in the preceding week: <75, 50 or 25% of normal requirement	Actual intake of the prescribed hospital diet (including snacks and ONS) the day before the audit	Actual diet intake as % of the prescribed diet: >75%: score 0 51-75%: score 1 25-50%: score 2 <25%: score 3
Severity of disease COPD Severe pneumonia Intensive care patients (APACHE 10)	Respiratory clinical feature categorized by the PaO_2/FiO_2	PaO_2/FiO_2: ≥300: score 0 200-300 (mild ARDS): score 1 100-200 (moderate ARDS): score 2 <100 (severe ARDS): score 3
Patients age ≥70 years	Unchanged	≥70 years: score 1
Presence of nutritional risk	Total score ≥3	

BMI, body mass index, BW, body weight; ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; ONS, oral nutritional supplement; PaO_2/FiO_2, partial pressure of arterial oxygen ratio

Table 2. Diagnostic criteria for malnutrition. Modification of the Global Leadership Initiative on Malnutrition (GLIM)[10] to the audit on COVID-19 hospitalized patients.

Original phenotypic criteria	**Modified criteria for the present study**	**Presence of the criteria in the present study**
Non-volitional weight loss >5% within past 6 months, or >10% beyond 6 months	One-month weight loss (1mo-WL) calculated using the referred BW before hospitalization (at time of the audit the maximal length of hospital stay was 35 days)	1mo-WL ≥5%
Low BMI <20 kg/m^2 if < 70 years, or <22 kg/m^2 if ≥ 70 years	Unchanged	Unchanged
Reduced muscle mass by validated body composition measuring techniques	Not acquired because of safety and hygiene reasons	Not evaluated
Original aetiologic criteria	**Adapted criteria for the present study**	**Presence of the criteria in the present study**
Reduced food intake or assimilation ≤50% of Energy Requirement > 1 week, or any reduction for >2 weeks, or any chronic gastrointerstinal condition that adversely impacts food assimilation or absorption	Actual intake of the prescribed hospital diet (including snacks and ONS) the day before the audit The GI condition, when present, was acute, therefore it was not considered	Actual diet intake < 50% of the prescribed diet
Disease burden/inflammation	Serum CRP concentration (nv < 0.5 mg/dL)	Serum CRP > 0.5 mg/dL Severity categories: • mild, 0.5-5 mg/dL • moderate, 5-10 mg/dL • severe, >10 mg/dL
Diagnosis of malnutrition	**Presence of at least one phenotypic criterion and one etiologic criterion**	

BMI, body mass index; BW, body weight; ONS, oral nutritional supplement; CRP, C-reactive protein

Table 3. Clinical characteristics of the COVID-19 patient cohort. Data are reported as n. (%)

	Total	**IMCUs**	**SICUs**	**ICUs**	**RUs**	
	n. 268	n. 162	n. 21	n. 46	n. 39	p value
Age (years)						0.001
<55	29 (10.8)	16 (9.9)	3 (14.3)	5 (10.9)	5 (12.8)	
55-64	49 (18.3)	26 (16.1)	3 (14.3)	17 (37)	3 (7.7)	
65-74	63 (23.5)	33 (20.4)	8 (38)	15 (32.6)	7 (18)	
75-84	66 (24.6)	39 (24.1)	6 (28.6)	8 (17.4)	13 (33.3)	
≥85	61 (22.8)	48 (29.6)	1 (4.8)	1 (2.2)	11 (28.2)	
Males	147 (54.9)	81 (50)	12 (57)	31 (67.4)	23 (59)	0.189
Respiratory clinical feature (PaO2/FiO2)						0.010
≥300	150 (56.4)	98 (60.9)	9 (45)	18 (39.1)	25 (64.1)	
200-300 (mild ARDS)	67 (25.2)	40 (24.8)	7 (35)	10 (21.7)	10 (25.6)	
100-200 (moderate ARDS)	34 (12.8)	16 (9.9)	4 (20)	11 (23.9)	3 (7.7)	
<100 (severe ARDS)	15 (5.6)	7 (4.4)	0 (0)	7 (15.2)	1 (2.6)	
O_2 therapy						<0.0001
None	128 (47.7)	87 (53.7)	5 (23.8)	2 (4.4)	34 (87.2)	
LFNC	52 (19.4)	35 (21.6)	9 (42.9)	3 (6.5)	5 (12.8)	
Reservoir mask	41(15.3)	37 (22.8)	2 (9.5)	2 (4.4)	0 (0)	
HFNC	7 (2.6)	3 (1.9)	0 (0)	4 (8.7)	0 (0)	
CPAP/NIV	10 (3.8)	0 (0)	5 (55.6)	5 (10.8)	0 (0)	
ETI	22 (8.2)	0 (0)	0 (0)	22 (47.8)	0 (0)	
TMV	8 (3)	0 (0)	0 (0)	8 (17.4)	0 (0)	
Comorbidity*						

Smoking	14 (5.22)	8 (4.9)	1 (4.8)	3 (6.5)	2 (5.1)	0.978
Overweight and Obesity (BMI≥25)	132 (51)	71 (46.1)	13 (61.9)	35 (76.1)	13 (34.2)	<0.0001
Diabetes	60 (22.4)	31 (19.1)	7 (33.3)	12 (26.1)	10 (25.6)	0.386
Cardiovascular	73 (27.2)	49 (30.3)	5 (23.8)	11 (23.9)	8 (20.5)	0.570
Respiratory	56 (20.9)	32 (19.8)	6 (28.6)	9 (19.6)	9 (23.1)	0.792
Renal	57 (21.3)	33 (20.4)	4 (19.1)	12 (26.1)	8 (20.5)	0.852
Liver	23 (8.6)	17 (10.5)	1 (4.8)	3 (6.5)	2 (5.1)	0.575
Neurological	81 (30.2)	63 (38.9)	3 (14.3)	1 (2.2)	14 (35.9)	<0.0001
Malignancy	56 (20.9)	37 (22.8)	4 (19.1)	4 (8.7)	11 (28.2)	0.121

*Diabetes: T1DM 4,T2DM 56; Obesity (BMI≥30): 35; Respiratory: COPD 48, Asthma 12; Renal: CKD 57 ; Liver: CLD 23; Cardiovascular: CHD 38, CeVD 25, HF 28, Arrhythmias 42

ARDS, Acute respiratory distress syndrome; CeVD, Cerebrovascular Disease; CHD, coronary heart disease; CKD, Chronic kidney disease; CLD, Chronic Liver Disease; COPD, Chronic obstructive pulmonary disease; CPAP, Continuous Positive Airway Pressure; ETI, Endotracheal intubation; HF, Heart failure; HFNC, High flow nasal cannula; ICUs, Intensive care units; LFNC, Low flow nasal cannula; NIV, Non-invasive Ventilation; P/F, PaO2/FiO2; SICUs, Subintensive care units; T1DM, Type 1 Diabetes Mellitus; T2DM, Type 2 Diabetes Mellitus; TMV, Tracheostomy-mechanical ventilation; IMCUs, Intermediate care units; RU, Rehabilitation units

Table 4: Nutritional assessment of COVID-19 patients. Data are reported as n. (%)

	Total	**IMCUs**	**SICUs**	**ICUs**	**RUs**	p-value
1-month weight loss						0.001
patients evaluable (n.)	125	63	17	18	27	
<5%	60 (48)	40 (63.5)	9 (53)	6 (33.3)	5 (18.5)	
≥5%	65 (52)	23 (36.5)	8 (47)	12 (66.7)	22 (81.5)	
BMI (kg/m^2)						0.012
patients evaluable (n.)	259	154	21	46	38	
Underweight (<18.5)	24 (9.3)	15 (9.7)	2 (9.5)	2 (4.5)	5 (13.2)	
Normal weight (18.5 - 24.9)	105 (40.5)	70 (45.5)	6 (28.6)	9 (19.6)	20 (52.6)	
Overweight (25 - 29.9)	95 (36.7)	51 (33.1)	9 (42.9)	23 (50)	12 (31.6)	
Obesity grade I° (30 - 34.9)	25 (9.7)	14 (9.1)	4 (19.1)	7 (15.2)	0 (0)	
Obesity grade II° (35 - 39.9)	9 (3.5)	3 (2)	0 (0)	5 (10.9)	1 (2.6)	
Obesity grade III° (≥40)	1 (0.4)	1 (0.7)	0 (0)	0 (0)	0 (0)	
Hospital diet intake (% of prescribed)						
patients evaluable (n.)	268	162	21	46	39	<0.0001
0%	63 (23.5)	26 (16.1)	1 (4)	36 (78.3)	0 (0)	
0-25%	19 (7.1)	13 (8.1)	2 (10.0)	2 (4.4)	2 (5.1)	
26-50%	22 (8.2)	14 (8.6)	2 (10.0)	3 (6.4)	3 (7.7)	
51-75%	59 (22)	37 (22.8)	8 (38.0)	4 (8.7)	10 (25.6)	
75-100%	105 (39.2)	72 (44.4)	8 (38.0)	1 (2.2)	24 (61.5)	
Disease/Inflammation burden (serum CPR, mg/dL)						<0.0001
patients evaluable (n.)	268	162	21	46	39	
absent (CRP ≤0.5)	59 (22.0)	34 (21.0)	8 (38.1)	3 (6.5)	14 (35.9)	
mild (CRP 0.5 - 5)	113 (42.2)	65 (40.1)	8 (38.1)	16 (34.8)	24 (61.5)	

moderate (CRP 5 - 10)	41 (15.3)	34 (21.0)	2 (9.5)	4 (8.7)	1 (2.6)	
severe (CRP >10)	55 (20.5)	29 (17.9)	3 (14.3)	23 (50.0)	0 (0)	
NRS-2002 score						<0.0001
patients evaluable (n.)	268	162	21	46	39	
<3 (n.)	61 (22,7)	53 (32.7)	3 (14.3)	2 (4.3)	3 (7.7)	
≥3 (n.)	207 (77.2)	109 (67.3)	18 (85.7)	44 (95.7)	36 (92.3)	
GLIM diagnosis of malnutrition						
patients evaluable (n.)	151	82	18	20	31	
considering CRP >0.5 mg/dL	75 (49.7)	41 (50.0)	5 (27.8)	14 (70.0)	15 (48.4)	0.0792
considering CRP >5 mg/dL	45 (29.8)	27 (32.9)	2 (11.1)	14 (70.0)	2 (6.5)	<0.0001

BMI, body mass index; CRP, C-reactive protein; NRS-2002, nutritional risk screening; GLIM, Global Leadership Initiative on Malnutrition; IMCUs, intermediate care units; SICUs, sub-intensive care units; ICUs, intensive care units; RUs, rehabilitation units.

Table 5. Nutritional therapy of COVID-19 patients

	Total	IMCUs	SICUs	ICUs	RUs	
	n. 268	n. 162	n. 21	n. 46	n. 39	p value
Hospital diet (HD)						
n. (%)	205 (76.5)	136 (84)	20 (95)	10 (21.7)	39 (100)	
prescribed energy, kcal/day	1859 (1691-2000)	1876 (1716-2000)	1864 (1800-2000)	1800 (1691-1876)	1800 (1450-1864)	0.0001
actual energy intake, kcal/day	1500 (1268-1867)	1500 (1268-1980)	1500 (1219-2000)	1099 (725-1350)	1450 (1287-1864)	0.0001
prescribed protein, g/day	81.0 (78-90)	84.0 (80-90)	90.0 (81-90)	80.0 (74-81)	80.0 (74-90)	0.0001
actual protein intake, g/day	66.0 (50-90)	67.5 (25-88)	67.5 (56-90)	40.0 (23-56)	74.0 (56-90)	0.0001
Oral nutritional suppl. (ONS)						
n. (%)	16 (6.0)	6 (3.7)	2 (9.5)	1 (2.2)	7 (17.9)	
energy, kcal/day	600 (315-630)	600 (500-600)	465 (330-600)	660	300 (300-792)	0.0055
protein, g/day	12.0 (12.0-18.4)	15.0 (12.0-18.8)	16.0 (12.0-20.0)	20.0	12.0 (12.0-24.0)	0.0062
in addition to HD - n.	14	6	2	0	6	
in addition to EN - n.	0	0	0	0	0	
in addition to PN - n.	1	0	0	1	0	
ONS alone - n.	1	0	0	0	1	
Enteral nutrition (EN)						
n. (%)	34 (12.7)	2 (1.2)	0	32 (69.6)	0	
energy, kcal/day	907 (547-1230)	810 (610-1010)	0	907 (547-1236)	0	0.0001
protein, g/day	40.4 (23-61)	35 (28-42)	0	42 (23-61)	0	0.6969
in addition toHD - n.	8	2	0	6	0	
in addition to ONS - n.	0	0	0	0	0	
in addition to PN - n.	5	0	0	5	0	
EN alone - n.	21	0	0	21	0	

Parenteral nutrition (PN)						
n. (%)	13 (4.8)	2 (1.2)	0	11 (23.9)	0	
energy, kcal/day	1725 (1000-1840)	1228 (955-1500)	0	1795 (1350-2134)	0	0.0001
protein, g/day	56.0 (48.0 - 63.3)	46.0 (40.0 -52.0)	0	60.0 (49.0 - 74.9)	0	0.0001
in addition to HD - n.	2	2	0	0	0	
in addition to ONS - n.	1	0	0	1	0	
in addition to EN - n.	5	0	0	5	0	
PN alone - n.	5	0	0	5	0	
Propofol						
n. (%)	20 (7.5)	0	0	20 (43.5)	0	
energy, kcal/day	110.0 (110.0 - 316.8)	0	0	110.0 (110.0 - 316.8)	0	
Total daily intake						
Prescribed Energy, % BEE	143.8 (125.5-176.7)	146.9 (127.7-176.2)	133.1 (129.8-188.3)	137.4 (83.9-192.4)	144.5 (123.9-161.7)	0.2974
Actual Energy intake, % BEE	124.3 (93.2-149.7)	127.1 (95.9-151.9)	130.6 (94.8-159.0)	103.2 (62.7-140.4)	124.8 (102.3-151.6)	0.0546
Prescribed Energy, kcal/kg	26.7 (24.8-34.5)	26.8 (25.0-34.1)	26.7 (26.5-37.3)	26.5 (17.3-37.8)	28.6 (28.6-33.9)	0.4601
Actual Energy intake, kcal/kg	24.8 (16.7-28.6)	24.9 (18,0-28.6)	26.7 (17.6-29.2)	20.3 (11.4 -27.0)	26.7 (18.6-32.1)	0.0370
Prescribed Protein, g/kg	1.2 (1.0-1.5)	1.2 (1.1-1.5)	1.2 (1.2-1.4)	1.1 (0.8-1.6)	1.2 (1.1-1.5)	0.3073
Actual Protein intake, g/kg	1.1 (0.8-1.3)	1.1 (0.8-1.3)	1.1 (0.8-1.2)	1.0 (0.6-1.2)	1.2 (0.8-1.4)	0.0104

Abbreviations: BEE, basal energy expenditure; EN, enteral nutrition; ICUs, intensive care units; IMCUs, intermediate care units; ON, oral nutrition; ONS, oral nutritional supplements; PN, parenteral nutrition; SICUs, Sub-intensive care units;

Figure 1. Prevalence of nutritional risk and of malnutrition in 151 COVID-19 patients, assessed by adapted NSR-2002 tool [9] and GLIM malnutrition criteria [10]. GLIM CRP>0.5, inclusion of all the degree of disease/inflammation burden; GLIM CRP>5, inclusion of only the moderate and severe degrees of disease/inflammation burden. IMCUs. intermediate care units; SICUs, sub-intensive care units; ICUs, intensive care units, RUs,rehabilitation units.

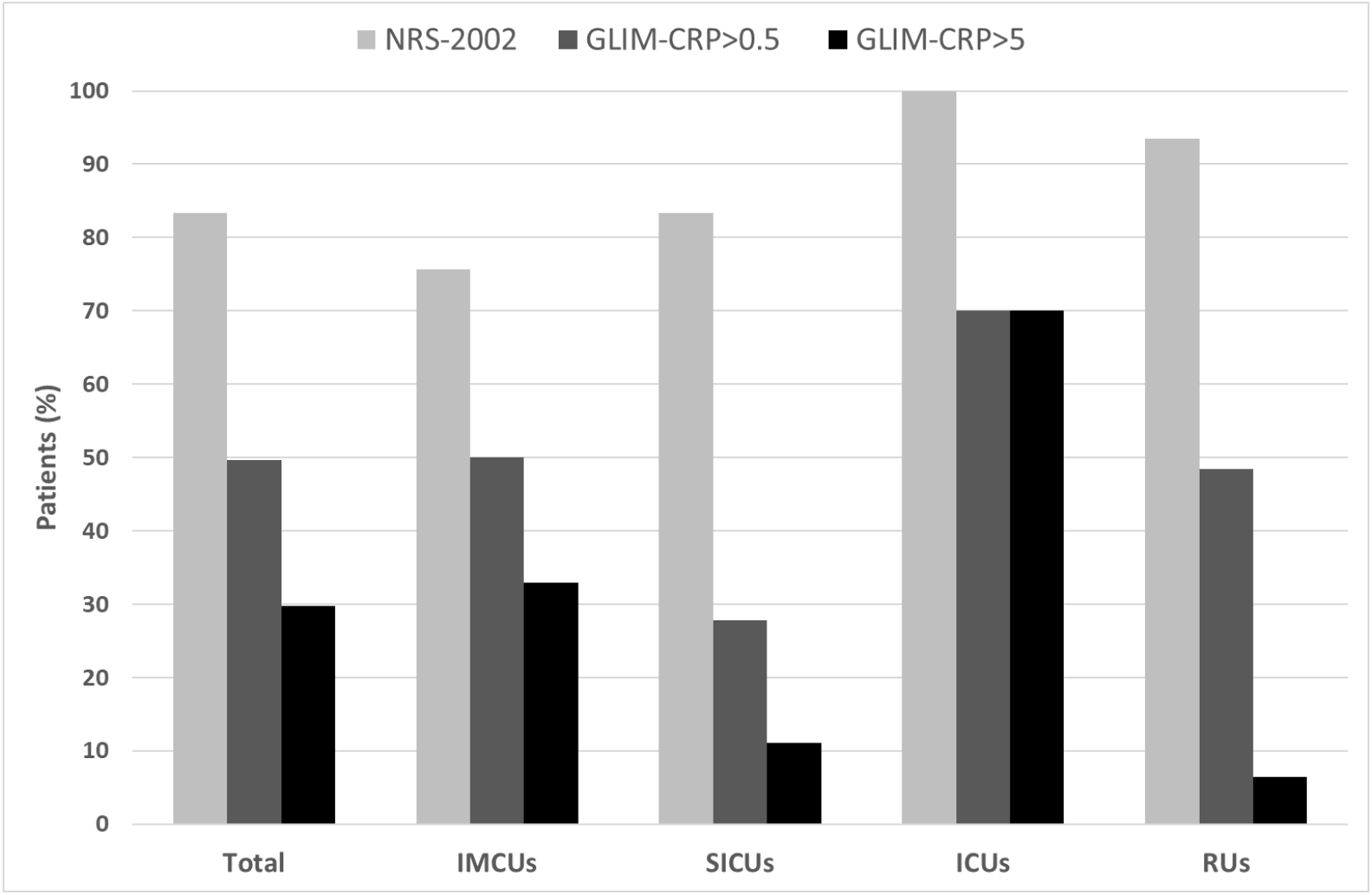

Figure 2. Hospital diet intake (% of the prescribed diet) in 268 patients with COVID-19, according to appetite degree, type of O_2-therapy and presence of frailty/disability and gastrointestinal (GI) symptoms. LFN, low flow nasal cannula; HFNC, high flow nasal cannula; NIV, non-invasive ventilation; CPAP, continuous positive airway pressure; ETI, endotracheal intubation; TMV, tracheostomy-mechanical ventilation.