Original article

Evaluation of anorexia and analysis of related factors in patients with COVID-19

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A R T I C L E   I N F O

A B S T R A C T

Objective. – COVID-19 may cause an anorexic situation. This in turn leads to underfeeding, puts the patient in an energy protein malnutrition state, develops the hyperinflammation, weakens the immunity, and makes COVID-19 conditions more dangerous. Meanwhile, the more severe inflammation conditions in the body, the more severe the anorexia, which in turn affect the disease severity. Studies evaluating appetite in COVID-19 patients are very rare; therefore, we evaluated anorexia and analyzed the related factors in patients with COVID-19.

Material and methods. – In this cross sectional study, adult patients' $\geq$18 years old with the positive real-time fluorescence polymerase chain reaction for COVID-19 were included. The patients were classified as mild, moderate, and severe based on the WHO classification. We measured the appetite score, weight, height, body mass index (BMI), depression and anxiety score, at admission for every patient.

Results. – A total of 301 patients participated in the study. The prevalence of admission anorexia was 58%, and this rate was significantly more in the severe group compared to the mild and moderate groups ($P < 0.001$). Comorbidities, depression and anxiety were independently correlated with anorexia risk [(OR = 3.6, 95% CI 1.68–7.70, $P = 0.001$), (OR = 1.23, 95% CI 1.16–1.30, $P < 0001$), and (OR = 1.24, 95% CI 1.17–1.31, $P < 0001$)], respectively. This correlation was adherence to a U-shape association for BMI, which means BMI < 18.5 (OR = 3.35, 95% CI 1.8–10.42, $P < 0001$) and BMI $\geq$30 (OR = 2.45, 95% CI 1.02–6.53, $P = 0.048$) were related to higher risk of anorexia.

Conclusion. – We reported a high prevalence of anorexia (58%) in COVID-19 patients, which was positively correlated with disease severity. Furthermore, any factor worsening inflammatory state, including underweight, obesity, comorbidities, depression and anxiety can exacerbate anorexia in these patients.

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1. Introduction

The current terrible pandemic (COVID-19) created by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) affects a huge number of people, and victims experience from mild to severe degrees of infection [1,2]. The clinical manifestations of this infection have been attributed to the angiotensin-converting enzyme 2 (ACE2) receptor [3]. In addition to the lung alveolar type 2 cells, the mentioned receptor is highly expressed in many tissues, including the gastrointestinal tract [4,5]. This theme explains the extra pulmonary symptoms of COVID-19. In this regard, some epidemiologic studies indicate that there are manifestations such as loss of appetite, diarrhea, nausea, and vomiting in COVID-19 patients [6,7]. Among these gastrointestinal symptoms, loss of appetite has been reported as the most common symptom [8]. Appetite is associated with determinants such as food intake, weight, gender, age, acute illness, history of eating disorders, and psychological, family,

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and social situations. It has long been shown how inflammatory factors can lead to anorexia and reduced food intake, and subsequently predispose a human to malnutrition [9,10]. Meanwhile, the more severe inflammation conditions in the body, the more severe the anorexia, which in turn affect the disease severity. Some factors involved in this process can be older age, obesity, smoking and comorbidities [9–13]. It appears that COVID-19 can cause this scenario by shifting the body to a hyper-inflammatory state, so that the loss of appetite and underfeeding put the patient in an energy protein malnutrition state, which in turn creates a proinflammatory state, weakens the immunity, and makes COVID-19 conditions more dangerous [14]. Recently, numerous studies have evaluated the olfactory and gustatory in COVID-19 patients, which indicate an impairment of these senses under the disease [15,16]. However, the quantitative evaluation of appetite in these patients and its association with the disease severity have been neglected despite its special importance. Thus far, only one study measured appetite in COVID-19 patients using the appetite visual analogue scale (VAS), and found no significant difference between appetite in patients with and without weight loss [17]. The findings of this study indicated that patients with weight loss had more systemic inflammation, impaired renal function and longer disease duration, and only the disease duration was a predictor of weight loss [17]. Whereas, in other medical illnesses, it has been reported that history of decreased eating and low actual eating are associated with the low body mass index (BMI), which in turn is related to a 6-fold increase at a rate of 30-days in-hospital mortality [18]. Moreover, another study on patients admitted to a geriatric acute care ward suggested that inflammation was the underling predictor for poor appetite and food intake, whereas other factors such as infection, chronic inflammatory diseases, age and gender did not show any impact on appetite [10]. Overall, studies on anorexia and its related factors in inflammatory conditions have been rarely conducted in humans, particularly in COVID-19 patients. Therefore, we evaluated anorexia in COVID-19 patients and its relation to disease severity, hypoguesia and hyposmia, BMI, depression, anxiety, age, sex and comorbidity.

2. Material/patients

The current cross sectional study was conducted from April 2020 to December 2020 in a university hospital. The study was approved by the Ethics Committee of the university. Adult 18 years and older patients with positive real-time fluorescence polymerase chain reaction (RT-PCR) for COVID-19 were included in the study. Exclusion criteria were critical patients, lack of weight and height information, corticosteroid consumption, pills affecting the appetite, eating disorders, and history of depressive/anxiety disorder.

Patients were classified as mild, moderate, and severe based on the WHO classification [19].

Mild patients were defined as symptomatic patients meeting the case definition for COVID-19 without the evidence of viral pneumonia or hypoxia. Moderate patients had clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) but no signs of severe pneumonia, including $SpO_2 \geq 90\%$ on room air. Severe were defined as presence of clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) plus one of the:

- respiratory rate > 30 breaths/min;
- severe respiratory distress;
- $SpO_2 < 90\%$ on room air.

Critically patients defined as cases with respiratory failure, shock, or multiorgan dysfunction that should be treated in ICU were excluded, since their response to questionnaires were invalid or impossible.

We measured the appetite score, weight, height, BMI, depression and anxiety score, at admission for every patients.

To assess anorexia, the visual analogue scale (VAS) was performed for all patients on the day of admission. VAS is an applied simple tool, and the subject is asked to rate and mark his/her anorexia on a 0 to 10 analogue rating scale. There is no defined cutoff value on the VAS to diagnose anorexia. We defined a VAS score < 5 cm as indicative of anorexia [20,21]. Anorexia was measured every day in hospitalized patients. In outpatient cases, it was measured at the first visit in the clinic of the hospital, and thereafter by telephone call daily to record the scores.

Weight was measured without shoes while wearing light clothes using SECA digital scales with a precision of 0.1 kg. Height was measured barefoot using a meter attached to the wall with a precision of 1 cm. BMI was calculated as the weight in kilograms divided by the height in meters squared.

Depression and anxiety on the day of admission were measured by the Hospital Anxiety and Depression Scale (HADS), which was a self-report instrument designed to measure the two related negative emotional states, namely depression and anxiety [22]. It consisted of 14 items comprising 2 subscales (depression and anxiety) of 7 items. Each item was rated on a 4-point Likert scale ranging from 0–3, with a score range of 0–21 for both subscales and higher scores indicated a greater anxiety and depression state.

3. Statistical analysis

Data analysis was conducted by the SPSS 21 software for Windows. P values equal to or less than 0.05 were considered the level of significance. Kolmogorov-smirnov (K-S) test was conducted to examine the distribution normality of the variables. Continuous variables were regarded as means ± standard deviation (SD) or medians and interquartile ranges (IQR). Categorical data were presented as proportions (number and percentage). To find the difference between the three groups of COVID-19 concerning normal and abnormal distributed variables, ANOVA and Kruskal Wallis tests were used, respectively. In cases where reporting the difference between the two groups was needed, T test was used. Results were reported as the mean ± standard deviation for parametric tests as well as the median $(Q_1 - Q_3)$ for nonparametric tests. X^2 test was used to report the difference in categorical variables. Logistic regression analysis was used to assess the relationship between related variables as covariates and anorexia as the dependent variable. The VAS score for anorexia at admission was changed to a dichotomous variable with the cutoff point of 5 based on its median, and VAS score < 5 cm as indicative of anorexia. The covariates associated with anorexia in univariate regression were retained in the final model or multiple logistic regression. There was no correlation between these covariates, including age, obesity, being underweight, depression score and anxiety score.

4. Results

A total of 301 patients were included in the study. Table 1 presents the basal characteristics of the patients. Among the participants, 102 (34%) were with mild, 92 (31%) with moderate, and 107 (35%) with severe disease symptoms.

4.1. Anorexia

Based on the VAS score, the prevalence of admission anorexia (VAS score < 5 cm) was 58%, and this rate was significantly higher in the severe group than in the mild and moderate groups (Table 1).

Table 1
Demographic and clinical characteristics of the overall population and stratified by the disease severity.

Variable	Overall ($n = 301$)	Disease Severity			P value
		Mild ($n = 102$)	Moderate ($n = 92$)	Severe ($n = 107$)	
Age, years	61 ± 12.8	58.7 ± 11.7^{a}	60.9 ± 13.2	63.2 ± 2^{a}	0.03*
Sex					0.84**
Male	121 (40)	43 (42.2)	35 (38)	43 (40.2)	
Female	180 (60)	59 (57.8)	57 (62)	64 (59.8)	
BMI (Kg/m^2)	23.5 ± 4.6	22.5 ± 3.3	23.9 ± 4.9	24 ± 5.2	<0.001*
BMI					<0.001**
Normal	207 (68.8)	85 (83.3)	64 (69.6)	58 (54.2)	
Underweight	24 (8)	4 (3.9)^{a}	4 (4.3)^{b}	16 (15)^{a,b}	
Overweight	32 (10.6)	8 (7.8)	11 (12)	13 (12.1)	
Obese	38 (12.6)	5 (4.9)^{a}	13 (14.1)	20 (18.7)^{a}	
Comorbidity	63 (20.9)	13 (12.7)^{a}	19 (20.7)	31 (29)^{a}	0.01**
Smoking	22 (7.3)	9 (8.8)	6 (6.5)	7 (6.5)	0.77
Admission Anorexia	175 (58)	40 (23)^{a,c}	56 (32)^{b,c}	79 (45)^{a,b}	<0.001**
Admission VAS Score	4 (3–6)	5 (3–6)^{a}	4 (3–6)^{b}	3 (2–5)^{a,b}	<0.001***
Admission hypogeusia/Hyposmia	127 (42.3)	34 (33.7)	40 (43.5)	53 (49.5)	0.06**
Depression Score	5 (3–12)	4 (3–6)^{a}	4 (3–15)	7 (7–14)^{a}	0.04***
Anxiety Score	5 (3–12)	3 (3–5)^{a}	3 (2–6)^{b}	13 (5–17)^{a,b}	<0.001***

BMI, Body Mass Index; VAS Score, Visual Analogue Score.

[a] Values with similar superscript letters are significantly different.

[b] Values with similar superscript letters are significantly different.

[c] Values with similar superscript letters are significantly different.

* Kruskal Wallis test (median, IQ).

** X^2 test (n, %).

*** ANOVA (mean, SD).

Median duration of anorexia was 14 (12–16) days in the severe group, which was significantly longer than that of the moderate (10 (10–12), $P = <0.001$) and mild (10 (9–10), $P = <0.001$) groups.

4.2. Age and anorexia

The participants' mean age was 61 ± 12.8 years. The patients' mean age was significantly more in the severe group than in the mild group (Table 1). The mean age was significantly more in patients with anorexia than in patients without anorexia (59.3 ± 11.9 vs. 62.5 ± 13.4, $P = 0.03$). Results of the logistic regression analysis showed a week correlation between age and anorexia. This correlation disappeared after adjustment by covariates (Table 2).

4.3. BMI and anorexia

Mean BMI was 23.5 ± 4.6 in the whole population. On admission, 8% of patients were underweight with BMI lower than 18.5 kg/m^2, and 12.6% were obese with the BMI equal to and more than 30 kg/m^2. Both underweight and obese patients had significantly involved more in the severe type of disease than normal and overweight patients (Table 1).

Results of the logistic regression analysis showed that both obesity and underweight increased the risk of anorexia by 2 and 2.8 times, respectively. This value was increased to 2.45 and 3.3 folds after adjustment by covariates (Table 2).

4.4. Comorbidity and anorexia

In total, 63 (20.9%) patients had comorbidity, which was significantly more in the severe group than in the two other groups (Table 1). Chronic obstructive pulmonary disease was observed in 15, 9 and 4 patients in severe, moderate and mild COVID patients, respectively. Hypertension and cardiovascular disease were observed in 16, 10 and 9 patients in severe, moderate and mild covid patients, respectively. Type 2 diabetes was observed in 14, 13 and 3 patients in severe, moderate and mild COVID patients, respectively.

Admission anorexia was seen more in patients with comorbidity than in those without comorbidity (35 vs. 28 patient, $P = 0.01$). Results of the logistic regression analysis indicated that the presence of comorbidity increased risk of anorexia by 3.2 times. This value was increased to 3.6 times after adjustment by covariates (Table 2).

4.5. Depression and anorexia

The median admission depression score based on HADS was 5 (3–12) in the whole population. This score was significantly more in the severe group than in the mild group (Table 1).

Results of the Pearson correlation showed no relation between depression and anxiety scores ($r = 0.03$, $P = 0.49$).

Results of the univariate logistic regression analysis showed that each point increase in depression score was associated with a 16% increase in the risk for anorexia. This value was increased by 23% in the multivariate logistic regression model (Table 2).

4.6. Anxiety and anorexia

The median admission anxiety score based on HADS was 5 (3–12) in the whole population. This score was significantly more in the severe group than in the mild and moderate groups (Table 1).

Results of the univariate logistic regression analysis showed that with each point increase in the anxiety score, the risk for anorexia increases by approximately 17%. This value is increased by 24% in the multivariate logistic regression model (Table 2).

4.7. Hypoguesia/hyposmia and anorexia

In total, 42.3% ($n = 127$) of patients had taste/smell impairment on admission. Based on the disease severity, the rate of hypogeusia/hyposmia had a trend to be more in the severe COVID group, but it was not significant ($P = 0.06$) (Table 1). The median duration of Hypoguesia/Hyposmia was 10 (9–10), 10 (9–10) and 14 (12–16) in mild, moderate, and severe groups, respectively. This was significantly more in the severe group than in the two other groups ($P < 0.001$).

Table 2
Binary logistic regression analysis for factors associated with anorexia.

Variable	OR	CI	*P* value	Adjusted OR	CI	*P* value
BMI						
<18.5	2.86	1.13–7.19	0.02	3.35	1.8–10.42	<0001
≥30	2.02	1.04–4.12	0.05	2.45	1.02–6.53	0.048
Comorbidity	3.25	1.76–6.0	<0001	3.6	1.68–7.70	0.001
Depression Score	1.16	1.10–1.21	<0001	1.23	1.16–1.30	<0001
Anxiety Score	1.17	1.11–1.22	<0001	1.24	1.17–1.31	<0001
Age	1.02	1.00–1.03	0.03	1.00	0.98–1.03	0.67
Hypoguesia/Hyposmia	1.37	0.86–2.17	0.97	–	–	–
Smoking	1.04	0.41–2.65	0.92	–	–	–
Sex	0.96	0.68–1.53	0.87	–	–	–

BMI: Body Mass Index.

There was no correlation between taste/smell impairment and admission anorexia analyzed with the logistic regression analysis (OR = 1.37, CI: 0.86–2.17, *P* = 0.17).

4.8. Smoking and anorexia

In total, 7.3% (*n* = 22) of the patients were smoker with no difference in terms of type of disease (Table 1). There was no difference in the rate of admission anorexia between non-smokers 9 (7.1%) and smokers 13 (7.4%) (*P* = 0.92). Logistic regression analysis did not show any correlation between smoking and anorexia (Table 2).

4.9. Sex and anorexia

Sixty percent of the patients were female. There was no difference in the sex involvement between subtypes of disease (Table 1). There was no difference in the rate of the admission anorexia according to their sex (41% male vs. 59% female. *P* = 0.87). Logistic regression analysis did not show any correlation between sex and anorexia (Table 2).

5. Discussion

The present study was conducted to evaluate anorexia and analyze related factors in patients with COVID-19. The percentages related to the disease severity among all of our patients were 34%, 31%, and 35%, which belonged to mild, moderate, and severe disease, respectively. Totally, the prevalence of admission anorexia was 58%, and this rate was significantly more, with the longest duration in severe COVID-19 patients compared to those with mild and moderate disease. Among the related risk factors in our work, underweight, obesity, comorbidities, depression and anxiety were predisposing factors to be a severe type of COVID-19. Moreover, the mentioned factors were significantly and positively correlated with anorexia risk, which this correlation was adherence to a U-shape association for BMI. To the best of our knowledge, there are only a few studies in which appetite has been estimated in COVID-19 patients as a prevalent manifestation. Furthermore, evaluation of the inflammation related anorexia in other illnesses also accounted for very low consideration. Consistent with our results, some previous studies suggested a percentage from approximately 42 to 60% for anorexia in COVID-19 patients [2,6,23,24]. Although some studies have failed to show that anorexia is significantly more in severe COVID-19 patients [24], there are studies, along with the present work that have shown an increasing trend in anorexia in severe/critical patients than in the moderate ones [23,25]. Nowadays, it is well understood that chronic and acute diseases can initiate anorexia during pathological processes resulting from infection, inflammation, injury, toxins, immunological reactions, malignancy and necrosis [9,11,26]. Inflammatory factors can reach the hypothalamus, and the neural substrates underlying inflammatory anorexia. This can lead to the change in eating behaviors and reduced food intake that subsequently lead to loss of both fat and lean mass, and cachexia appears, which in turn can have devastating effects on the quality of life and survival [26]. In COVID-19 patients, it is well established that inflammatory factors and cytokines determine the disease severity [25,27,28]. Thus, it is obviously clear that anorexia can be more intense and longer in severe COVID-19 patients than that in mild and moderate ones. Moreover, anorexia in these patients can be secondary to infection, dyspnea, dysosmia, dysgeusia, stress, confinement, and organizational problems limiting attendance at meals [4]. Although a review article demonstrates that a meticulous mechanism of anorexia onset in patients with COVID-19 has remained unknown, and gustatory and olfactory impairment may be exacerbate the loss of appetite [29], we did not found any significant correlation between hypogeusia/hyposmia and admission anorexia in our study. A large number of studies thus far showed the high prevalence of obesity, comorbidities, especially hypertension and cardiovascular disease, chronic obstructive pulmonary disease, and type 2 diabetes in severe COVID-19 patients compared to mild to moderate forms of the disease [4,12,30,31]. In this regard, the results of our study are in line with the evidence. Considering any factor weakening the immune system can lead to the severe type of COVID-19, some studies have examined the relationship between COVID-19 and the history of mood disorders [32]. Although this theme still requires further study, Mazza et al., [33] showed that the systemic inflammation in COVID-19 patients was positively associated with the scores of depression and anxiety. In our study, we found the scores of depression and anxiety to be higher in the severe type of COVID-19 than in mild to moderate types. In addition to the mentioned factors, surprisingly, we found that being underweight (BMI < 18.5) was also associated with severe COVID-19. It is explained that malnutrition and underweight, like obesity, put the body in a proinflammatory state, and levels of C-reactive protein (CRP) and other inflammatory markers are higher in these patients than in normal and overweight patients [34,35]. Moreover, by analyzing the factors associated with anorexia, we found that BMI had a U-shaped correlation with anorexia risk, so that both underweight and obesity were associated with lower VAS scores, being representative of severe anorexia. Previously, such an association shape of BMI was observed with the inflammation in hemodialysis patients [35]. In addition, Forli et al., [36] revealed systemic inflammation in underweight patients with advanced pulmonary disease. Therefore, it appears that the found U-shape association of BMI with anorexia in the present study can be justified by considering the inflammatory status of the body. This is also true for comorbidities, depression and anxiety, which, according to what has been mentioned thus far, leads to an inflammatory situation and anorexia. In our study, older patients were more affected by severe COVID-19, being consistent with the results of previous studies [23–25,37]. However, considering the effect of confounding variables, we did not find a significant

correlation between age and anorexia risk in patients with COVID-19. A possible reason for this finding could be that the age difference between our patients was very negligible. In this regard, our results are consistent with those obtained by Kalantar-Zadeh et al., [38] indicating no significant difference in age between different categories of appetite from very good to poor appetite in hemodialysis patients. In addition, we also did not observe a significant effect of sex and smoking on the risk of anorexia. Although some studies have shown that smoking is associated with anorexia [13], the lack of such a relationship in the present study was probably due to the small number of smokers. For the first time in the literature, in addition to the evaluation of anorexia prevalence in various severities of COVID-19 patients, we evaluated some possible factors related to anorexia in these patients. Considering the hyper-inflammatory nature of COVID-19, and given that any factor worsening inflammatory state can exacerbate anorexia, it appears that health care systems should give more attention to eating behaviors and nutritional intake of COVID-19 patients in order to prevent underweight and worsening of the inflammatory state of COVID-19. Psychological counseling should also be used for the mental relaxation of these patients.

However, our study had certain limitations. It was better to use different validated appetite tools and evaluate the relationship between the VAS score and self-reports of food intake, because food intake is the major criterion measure of anorexia.

6. Conclusion

This study was conducted to evaluate the anorexia and analysis of related factors in patients with COVID-19. We reported a high prevalence of anorexia (58%) in COVID-19 patients that was positively correlated with the disease severity. Furthermore, any factor worsening inflammatory state such as underweight, obesity, comorbidities, depression and anxiety can exacerbate anorexia in these patients. It is recommended that eating behaviors and nutritional intake be considered in order to prevent underweight and worsening of COVID-19 patients' inflammatory state. It is also important to reduce the patients' fear in order to reduce anxiety/depression and consequently anorexia.

Human and animal rights

The authors declare that the work described has not involved experimentation on humans or animals.

Informed consent and patient details

The authors declare that they obtained a written informed consent from the patients and/or volunteers included in the article and that this report does not contain any personal information that could lead to their identification.

Disclosure of interest

The authors declare that they have no competing interest.

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Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by S.S, Z.V, M.K, M.V and E.S. The first draft of the manuscript was written by Z.V and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.nupar.2021.08.001.

References

[1] Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727–33.

[2] Zhao X, Li Y, Ge Y, et al. Evaluation of nutrition risk and its association with mortality risk in severely and critically ill COVID-19 patients. JPEN J Parenter Enteral Nutr 2020, http://dx.doi.org/10.1002/jpen.1953 [Online ahead of print].

[3] Wiersinga WJ, Rhodes A, Cheng AC, et al. Pathophysiology, transmission, diagnosis, and treatment of Coronavirus disease 2019 (COVID-19) a review. JAMA 2020, http://dx.doi.org/10.1001/jama.2020.12839 [Online ahead of print].

[4] Thibault R, Seguin P, Tamion F, et al. Nutrition of the COVID-19 patient in the intensive care unit (ICU): a practical guidance. Crit Care 2020;24(1):447.

[5] Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet 2020;395:1417–8.

[6] Lechien JR, Chiesa-Estomba CM, Place S, et al. Clinical and epidemiological characteristics of 1420 European patients with mild-to-moderate coronavirus disease 2019. J Intern Med 2020;288(3):335–44.

[7] Cholankeril G, Podboy A, Aivaliotis VI, et al. High prevalence of concurrent gastrointestinal manifestations in patients with severe acute respiratory syndrome coronavirus 2: early experience from california. Gastroenterology 2020;159(2):775–7.

[8] Luo S, Zhang X, Xu H. Don't overlook digestive symptoms in patients with 2019 novel coronavirus disease (COVID-19). Clin Gastroenterol Hepatol 2020;18(7):1636–7.

[9] Lennie TA. Anorexia in response to acute illness. Heart Lung 1999;28(6):386–401.

[10] Sieske L, Janssen G, Babel N, Westhoff TH, Wirth R, Pourhassan M. Inflammation, appetite and food intake in older hospitalized patients. Nutrients 2019;11(9):1986.

[11] Plata-Salamán CR. Anorexia during acute and chronic disease. Nutrition 1996;12:69–78.

[12] Zhou Y, Yang Q, Chi J, et al. Comorbidities and the risk of severe or fatal outcomes associated with coronavirus disease 2019: a systematic review and meta-analysis. Int J Infect Dis 2020;99:47–56.

[13] Chiolero A, Faeh D, Paccaud F, et al. Consequences of smoking for body weight, body fat distribution, and insulin resistance. Am J Clin Nutr 2008;87(4):801–9.

[14] Caccialanza R, Laviano A, Lobascio F, et al. Early nutritional supplementation in non-critically ill patients hospitalized for the 2019 novel coronavirus disease (COVID-19): rationale and feasibility of a shared pragmatic protocol. Nutrition 2020;74:110835.

[15] Mullol J, Alobid I, Mariño-Sánchez F, et al. The loss of smell and taste in the COVID-19 outbreak: a tale of many countries. Curr Allergy Asthma Rep 2020;20(10):61.

[16] Qiu C, Cui C, Hautefort C, et al. Olfactory and gustatory dysfunction as an early identifier of covid-19 in adults and children: an international multicenter study. Otolaryngol Head Neck Surg 2020;163(4):714–21.

[17] Filippo LD, Lorenzo RD, D'Amico M, et al. COVID-19 is associated with clinically significant weight loss and risk of malnutrition, independent of hospitalisation: a post-hoc analysis of a prospective cohort study. Clin Nutr 2020;S0261–5614(20):30589–96.

[18] Hiesmayr M, Tarantino S, Moick S, et al. Hospital malnutrition, a call for political action: a public health and nutritionday perspective. J Clin Med 2019;8(12):2048.

[19] World Health, Organization. Clinical management of COVID-19: interim guidance, 27 May 2020. World Health Organization; 2020 [https://apps.who.int/iris/handle/10665/332196].

[20] Zabel R, Ash S, Bauer J, et al. Assessment of subjective appetite sensations in hemodialysis patients. Agreement and feasibility between traditional paper and pen and a novel electronic appetite rating system. Appetite 2009;52:525–7.

[21] Molfino A, Kaysen GA, Chertow GM, et al. Validating appetite assessment tools among patients receiving hemodialysis. J Renal Nutr 2016;26(2):103–10.

[22] Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361–70.

[23] Chen Q, Zheng Z, Zhang C, et al. Clinical characteristics of 145 patients with corona virus disease 2019 (COVID-19) in Taizhou, Zhejiang, China. Infection 2020;48(4):543–51.

[24] Xiong S, Liu L, Lin F, et al. Clinical characteristics of 116 hospitalized patients with COVID-19 in Wuhan, China: a single-centered, retrospective, observational study. BMC Infect Dis 2020;20(1):787.

[25] Ren L, Yao D, Cui Z, et al. Coronavirus disease 2019 patients with different disease severity or age range: A single-center study of clinical features and prognosis. Medicine (Baltimore) 2020;99(49):e22899.

[26] Braun TP, Marks DL. Pathophysiology and treatment of inflammatory anorexia in chronic disease. J Cachexia Sarcopenia Muscle 2010;1(2):135–45.

[27] Hajimohammadebrahim-Ketabforoush M, Shahmohammadi M, Zali A, et al. COVID-19-associated stroke risk: could nutrition and dietary patterns have a contributing role? World J Meta-Anal 2020;8(6):435–45.

[28] Chen G, Wu D, Guo W, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest 2020;130:2620–9.

[29] Su S, Shen J, Zhu L, et al. Involvement of digestive system in COVID-19: manifestations, pathology, management and challenges. Therap Adv Gastroenterol 2020;13 [1756284820934626].

[30] Berger MM. Nutrition Status Affects COVID-19 patient outcomes. JPEN J Parenter Enteral Nutr 2020;44(7):1166–7.

[31] Chow DS, Glavis-Bloom J, Soun JE, et al. Development and external validation of a prognostic tool for COVID-19 critical disease. PLoS One 2020;15(12):e0242953.

[32] Zandifar A, Badrfam R, Yazdani S, et al. Prevalence and severity of depression, anxiety, stress and perceived stress in hospitalized patients with COVID-19. J Diabetes Metab Disord 2020:1–8.

[33] Mazza MG, De Lorenzo R, Conte C, et al. Anxiety and depression in COVID-19 survivors: role of inflammatory and clinical predictors. Brain Behav Immun 2020;89:594–600.

[34] Salahudeen AK, Fleischmann EH, Bower JD, et al. Underweight rather than overweight is associated with higher prevalence of hypertension: BP vs. BMI in haemodialysis population. Nephrol Dial Transplant 2004;19(2):427–32.

[35] Kahraman S, Yilmaz R, Akinci D, et al. U-shaped association of body mass index with inflammation and atherosclerosis in hemodialysis patients. J Ren Nutr 2005;15(4):377–86.

[36] Forli L, Mellbye OJ, Bjortuft O, et al. Systemic inflammation and weight gain in underweight patients with advanced pulmonary disease. Nutrition Research 2005;25:119–31.

[37] Lorenzo RD, Conte C, Lanzani C, et al. Residual clinical damage after COVID-19: a retrospective and prospective observational cohort study. PLoS One 2020;15(10):e0239570.

[38] Kalantar-Zadeh K, Block G, McAllister CJ, et al. Appetite and inflammation, nutrition, anemia, and clinical outcome in hemodialysis patients. Am J Clin Nutr 2004;80(2):299–307.