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CLINICAL RESEARCH

Measures of Malnutrition in Patients with COVID-19

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ABSTRACT

BACKGROUND

No data relating to disease course of COVID-19 and screening of malnutrition in Germany are available yet.

MATERIALS AND METHOD

We evaluated 78 COVID-19 patients, 37 men and 41 women, 65 years + 17 years old admitted from February 2020 to May 2020 to our tertiary hospital.

RESULTS

48.6% of the patients with COVID-19 were multimorbid with >2 chronic diseases. Screening of malnutrition according to NRS 2002 and GLIM consensus showed that the majority (87.3%) of patients were normal weight, overweight or obese without significant weight loss. 38 patients had mild disease (group I, WHO score 3 or 4), 18 patients' severe disease (group II, WHO score 5-7) and 22 died associated with COVID-19 (group III, WHO score 8). The proportion of male patients significantly increased from 36.8% in mild to 63.1% in severe COVID-19. Patients in group III were significantly older. Nutritional laboratory marker in malnutrition at admission such as protein, albumin and haemoglobin were significantly decreased, and CRP significantly increased in severe COVID-19. At follow-up, protein and albumin significantly improved, especially in those patients successfully treated at the intensive care unit (group II). In contrast, this was not the case in patients who died associated with COVID-19 (group III). Here, the nutritional status even worsened at follow-up.

CONCLUSION

Conventional screening of malnutrition is not helpful in COVID-19. However, beside older age and male sex, the course of COVID-19 was affected by low levels of albumin, protein and hemoglobulin suggesting the effect of malnutrition.

KEYWORDS

COVID-19; Coronavirus; SARS-CoV-2; Albumin; Obesity; Malnutrition

1. INTRODUCTION

Beginning in December 2019 in Wuhan, the 2019 novel coronavirus (SARS-CoV-2) has caused pandemic disease (COVID-19). Since February 2021, almost 2.3 million people are infected with SARS-CoV-2 in Germany leading to an overall mortality rate of 2.6% [1]. This mortality rate is similar in the largest German province North Rhine-Westphalia (2.3%) and in Krefeld (1.6%) the largest city in the lower Rhine region close to the city of Heinsberg, the first COVID-19 hot spot in Germany [2]. Previous studies suggest that age, smoking status, maximum body temperature, respiratory failure, C-reactive protein, serum albumin, obesity, and malnutrition are prognostic markers in severe diseases and COVID-19 [3-7]. However, data derived in German populations are not available yet. We, therefore, report on 78 COVID-19 patients hospitalized consecutively at the HELIOS Clinic in Krefeld, the tertiary hospital in the lower Rhine region.

2. MATERIALS AND METHOD

COVID-19 was confirmed by history of epidemiological exposure and/or clinical symptoms and/or typical pulmonary imaging changes together with detection of SARS-CoV-2 by real-time PCR in respiratory specimens in all patients. The patients were cared and stratified according to WHO R&D Blueprint Ordinal Scale for Clinical Improvement [8]. Patients with mild disease (group I, score 3 or 4) were cared for in the isolation ward, patients with severe disease (group II, score 5-7) in the intensive care unit. Patients were evaluated according to their nutritional status according to GLIM consensus [9] including nutritional risk screening (NRS 2002), [10], diagnostic assessment (low non-volitional weight loss, low BMI, phenotypic criterion: Reduced food intake or assimilation, etiologic criterion: disease burden, inflammatory condition). Criteria for malnutrition diagnosis were at least 1 phenotypic and 1 etiologic criterion. Overweight was defined as a body mass index (BMI) > 25, obesity as a BMI >30. Underweight was defined as BMI of <20 if <70 years, or <22 if >70 years. Multimorbid patients were defined as having at least 2 chronic diseases [11,12]. Patients with mild COVID-19 disease received additional oral nutritional supplementation (ONS) according to the recommendation by ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection [13,14]. Patients with severe disease were treated by jejunal tube feeding within 48 hours, supplementary parenteral nutrition (SPN), and total parenteral nutrition (TPN) were started within 3 days to 7 days. Patient files were documented electronically by MEDICO® (Cerner Health Services Deutschland GmbH, Cunoweg 1,65510 Idstein). Data are presented as mean + SD and range. Statistical analysis was performed by One Way ANOVA. Level of significance was set at $p < 0.05$. The retrospective study was approved by the local ethical committee, June 25th, 2020, IRB ethical code number Fr-20-01.

3. RESULTS

We analyzed 78 COVID-19 patients (37 men and 41 women) admitted consecutively to our tertiary hospital from February to May 2020. Overall, the mean age of the patients was 65 years + 17 years with a range 22 years - 92 years. There was no significant difference between men (63 years + 14 years, 29 years - 89 years) and women (67 years + 19 years, 22 years - 92 years), table 1.

38 patients, 14 men and 24 women had a mild disease (group I), [7] and could be discharged from the isolation ward at follow-up (table 1). 18 patients, 12 men and 6 women showed severe disease (group II) and were treated in the intensive care unit and survived (table 1). 22 patients, 11 men and 11 women died associated with COVID-19 (group III), (table 1). The proportion of men in group II was 63.1% and significantly higher compared to group I (36.8%) but not to group III (50.0%). Patients in group III were significantly older compared to group I and to group II. C-reactive protein (CRP) was significantly lower in group I compared to group II and group III, table 1.

Table 1: Patients characteristics at admission to the hospital, mean + SD, range.

Parameter	Overall	Group I	Group II	Group III	Significance
Number	78	38	18	22	
Age (Years)	65 ± 17 22-92	60 ± 19 22-92	62 ± 12 43-85	75 ± 10 49-89	Group I *vs.* II, p >0.05 Group I *vs.* III, p = 0.02 Group II *vs.* III, p = 0.001
Sex (m/f)	37/41	14/24	12/6	11/11	Group I *vs.* II, p = 0.035 Group I *vs.* III, p >0.05 Group II *vs.* III, p >0.05
CRP (mg/dl)	78.0 ± 80.5 0.6-333	47.46 ± 63.65 0.9-323	116.25 ± 87.21 1.6-327	99.88 ± 84.19 22.1-333	Group I *vs.* II, p = 0.028 Group I *vs.* III, p = 0.032 Group II *vs.* III, p >0.05
Haemoglobin	12.33 ± 2.3 5.4-16.6	12.88 ± 2.12 5.4-16.6	9.74 ± 1.73 6.7-11.7	12.63 ± 2.00 8.9-15.8	Group I *vs.* II p = 0.01 Group I *vs.* III, p >0.05 Group II *vs.* III, p >0.05

The majority (>80%) of the patients with COVID-19 had at least one chronic disease such as diabetes mellitus, chronic lung (Pulmonary hypertony, COPD, bronchial asthma), cardiovascular (Cardiovascular hypertension, arrythmias, chronic heart failure, coronary heart disease, endocarditis, arteriosclerosis), renal (Renal failure), cerebral (Dementia, cerebral insult, Alzheimer disease) and/or malignant (Pancreatic, gastric, hepatic, breast cancer) disease (table 2). 32 patients (41%) suffered from 2 patients and 6 patients (7.6%) from three chronic diseases. There was no difference between patients with mild (Group I), severe COVID-19 or fatal COVID-19 (Group III). Similar, the blood types were equally distributed among the groups (group I: ARh + n = 5, 0Rh + n = 3, BRh + n = 1/group II: ARh + n = 2, 0Rh + n = 7, ABRh + n = 1, BRh + n = 4/group III: ARh + n = 4, 0Rh + n = 4, ABRh + n = 1, BRh + n = 1, ABRh - n = 1, 0Rh - n = 1/ group X: ARh + n = 1, 0Rh + n = 1) and not significantly different.

Nutritional risk screening according to NRS 2002 [10] and GLIM consensus [11] showed three patients (3.8%) who were underweight at admission and had a BMI of 18.6, 18.8, and 21.1, respectively. Seven patients (8.9%) reported relevant weight loss [10]. Overall, the mean BMI was 27.4 + 4.6 (18.6 - 38.7). There was no significant

difference between men (27.5 + 4.3, 18.6 - 36.2) and women (27.5 + 4.9, 18.8 - 38.7). 28 patients (36%) were overweight, and 18 patients (23%) were obese. Again, no significant differences between men (overweight 14/38%, obese 9 /24%) and women (overweight 14/34%, obese 9/22%) or between group I - group III could be detected (table 2).

Table 2: Characteristics of COVID-19 patients as classified according to the WHO R&D blueprint ordinal scale for clinical improvement [8]. WHO Score (n/m/f)-n (all patients in this group), m (male), f (female). DM: Diabetes Mellitus; OV: Overweight at Admission; OD: Obesity at Admission; BMI: Body Mass Index (kg/m^2); CLD: Chronic Lung Diseases; CVD: Cardiovascular Disease; CND: Chronic Neurological Diseases; CKD: Chronic Kidney Disease; CCD: Chronic Cerebral Disease; MD: Malignant Disease. Mean + SD, range. There were no significant differences between the groups.

WHO Score (n/m/f)	OV OD (n/%)	BMI Range	DM n %	CLD n %	CVD n %	CKD n %	CCD n %	MD n %
Group I Score 3, 4 (n = 38/14/24)	12 (31.6) 10 (26.3)	29.4 ± 5.5 18.6-38.8	8 21.6	3 0.81	17 44.7	2 5.40	1 0.27	7 18.4
Group II Score 5-7 (n = 18/12/6)	8 (42.1) 5 (26.3)	27.6 ± 4.1 18.8-36.0	4 22.2	4 22.2	8 44.4	4 22.2	2 11.1	0
Group III Score 8 (n = 22/11/11)	9 (40.9) 3 (13.6)	27.1 ± 4.0 21.1-36.3	4 18.1	2 0.90	8 36.3	7 87.5	11 50.0	2 0.90

Table 3: Nutritional laboratory markers in malnutrition [4] of Covid-19 patients at admission. Mean + SD, range. Group I, II and II according to WHO R&D Blueprint Ordinal Scale for Clinical Improvement (7). Mean + SD, range.

Parameters	Group I	Group II	Group III	Significance
Protein at Admission	6.20 ± 0.16 4.9-7.7	5.34 ± 0.16 4.4-6.8	5.72 ± 0.36 3.8-7.9	I *vs.* III, p >0.05 II *vs.* III, p >0.05 I *vs.* II, p = 0.014
Protein at Follow up	6.34 ± 0.22 4.8-7.6	6.04 ± 0.22 5.2-7.9	5.24 ± 0.49 2.4-6.4	I *vs.* III, p = 0.037 II *vs.* III, p >0.05 I *vs.* II, p >0.05
Albumin at Admission	3.20 ± 0.22 2.4-4.4	2.4 3± 0.12 1.8-3.9	2.53 ± 0.20 1.3-4.6	I *vs.* III, p = 0.015 II *vs.* III, p >0,05 I *vs.* II, p = 0.002
Albumin at Follow up	3.28 ± 0.22 2.0-3.9	2.87 ± 0.13 1.9-3.7	2.24 ± 0.20 1.2-3.0	I *vs.* III, p = 0.002 II *vs.* III, p = 0.03 I *vs.* II, p >0.05

Table 1 and 3 illustrate the nutritional laboratory markers in malnutrition such as the levels of protein, albumin and hemoglobin. Patients with severe or fatal COVID-19 (group II, III) had significantly lower serum albumin compared to moderate COVID-19 (group I). In addition, serum protein level and hemoglobin at admission were significantly reduced in group II compared to group I. Levels of protein and albumin significantly increased during the hospital stay in group II (table 3). Consequently, the significant difference between both group I and II disappeared at follow-up. However, this was not the case in patients who died associated with COVID-19 (group III) (table 3). Comorbidities, age and sex had no significant effect on the nutritional status of the patients.

4. DISCUSSION

The study shows that patients with normal weight, overweight or obesity predominate in COVID-19. Only three patients with decreased BMI and only seven patients with relevant weight loss at admission could be identified. This finding illustrates that screening and evaluation of malnutrition according to NRS 2002 and GLIM consensus [10,11] at admission to the hospital is not helpful to identify malnutrition as a risk factor for the course of COVID-19 in clinical practice because only few patients will be detected. Malnutrition as a risk factor for the course of COVID-19 has been assumed in some studies and recommendations [13-16]. This is, because the nutritional status has significant impact on the immune system, susceptibility to infections, prognosis of various diseases, complication rates, length of hospital stay and mortality. In this line, Li et al. [15] reported a prevalence of malnutrition in COVID-19 showing a high proportion of 52.7% malnutrition in their COVID-19 patients. However, a relation between malnutrition and severity of disease was not analyzed.

Beside malnutrition, it has been also shown that obesity is associated with poorer immune response and outcomes in patients with respiratory disease [17,18] and COVID-19 [19]. For example, prognostic effects of overweight or obesity in COVID-19 were reported by Cai et al. [6] who showed, similar to our finding, 32.0% overweight and 10.7% obese COVID-19 patients at admission. In this study, overweight patients had 1.84, obese patients 3.40 and obese male 5.66 times greater odds of developing severe COVID-19 when compared to normal weight patients/female after adjusting for other potential risk factors. This is in contrast to our study where the proportion of overweight or obesity was not different between moderate, severe of fatal COVID-19. Unfortunately, parameters of malnutrition were not reported in this study [6].

In our study, the nutritional laboratory markers in malnutrition such as the levels of protein, albumin and hemoglobin at admission were significantly different between the groups. Patients with severe or fatal COVID-19 (group II, III) had significantly lower serum albumin compared to moderate COVID-19 (group I) and serum protein level and hemoglobin at admission were significantly reduced in group II compared to group I. We had no evidence for the influence of large volume intravenous infusions on the values of albumin and protein. In addition, albumin and protein were measured at admission to the hospital before intravenous treatment. These findings suggest that lower serum levels of albumin, protein or hemoglobin are associated with a severe course of COVID-19. This is in agreement with other studies showing that in addition to age, smoking status, maximum body temperature, respiratory failure and C-reactive protein, protein and serum albumin are independent prognostic markers in hospitalized patients with severe diseases [7]. With regard to malnutrition, a recent meta-analysis [20] illustrated that especially BMI, hemoglobin, and total cholesterol were useful markers in older adults. This is, because, in contrast to albumin and protein, they were relatively independent of the state of inflammation and disease severity. In our, study, patients with severe COVID-19 expressed significantly higher levels of CRP. Therefore, the finding of lower levels of albumin and protein as an expression of malnutrition should be interpreted with caution [21]. In addition, our data suggest that lower inflammatory response was correlated with better outcome of COVID-19. However, the problem of cause or effect of malnutrition in COVID-19 remains unclear. We think, that both factors may be responsible for the course of COVID-19.

Another finding of our study points to the prognostic relevance of malnutrition for the course of COVID-19. Our nutritional therapeutic strategies were effective because protein and albumin could be improved, especially

in those patients successfully treated at the intensive care unit (group II, table 3). Consequently, the significant difference between both group I and II disappeared at follow-up. However, this was not the case in patients who died associated with COVID-19 (group III). Here, the nutritional status even worsened at follow-up. The reasons for this discrepancy remain unclear but could be related to the severity of malnutrition at the beginning, assuming that it could not be compensated within the short treatment period.

It is interesting to learn, that, at admission, women represented two third of the COVID-19 patients with mild disease (group I). This is in accordance with Li et al. [15] who also reported 64% female in their analyzed COVID-19 population. However, our study showed, that in severe disease (group II), the male-female ratio was significantly inclined towards male (60%), (table 1). These findings are in line with the daily reporting of the Robert Koch Institute (RKI), demonstrating the slight overbalance of female with COVID-19, but predominance of male among severe course and deaths associated with the disease in Germany [22]. This phenomenon has also reported in other countries where the risk of male to die with COVID-19 is 1.8 to 2.2 times higher compared to female [23]. Interestingly, this phenomenon has been also reported for SARS-CoV-1 or MERS-CoV infection [24,25] and is probably caused by sex chromosome genes and sex hormones, including estrogens, progesterone and androgens, that contribute to the differential regulation of immune responses between the sexes (26). Additionally, the age distribution with an overall mean age of 65 years and the multimorbidity of our COVID-19 patients were in agreement with the literature, suggesting higher susceptibility to the SARS-CoV-2 infection [15], (table 1). Patients who died associated with COVID-19 (group III) were significantly older compared to the other groups. In contrast, the proportion of underlying diseases, especially diabetes mellitus, was not significantly different between the groups (table 1). Similar, blood types as suggested as prognostic factor [27] were not significant different between sex, age or group I - group III.

5. CONCLUSION

In summary, the results of our study suggest that screening tools for malnutrition such as NRS 2002 [10] and GLIM consensus [11] at admission to the hospital are not helpful in COVID-19, because of the high proportion of normal weight, overweight and obesity. However, beside older age and male sex, the course of COVID-19 is affected by low levels of albumin, protein and hemoglobin and high levels of CRP at admission that may be improved by medical and nutritional therapy.

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