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# Predictive value of multiple variable models including nutritional risk score (NRS 2002) on mortality and length of stay of patients with covid-19 infections. The INCOVO study

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SUMMARY

*Background and aims:* This study aimed at evaluating associations between nutritional status and outcomes in patients with Covid-19 and to identify statistical models including nutritional parameters associated with in-hospital mortality and length of stay.

*Methods:* Data of 5707 adult patients hospitalized in the University Hospital of Lausanne between March 2020 and March 2021 were screened retrospectively 920 patients (35% female) with confirmed Covid-19 and complete data including nutritional risk score (NRS 2002), were included. This cohort was divided into three subgroups: NRS <3: no risk of malnutrition; NRS ≥3 to <5: moderate risk malnutrition; and NRS ≥5: severe risk of malnutrition. The primary outcome was the percentage of in-hospital deaths in the different NRS subgroups. The secondary outcomes were the length of hospital stay (LOS), the percentage of admissions to intensive care units (ICU), and the length of stay in the ICU (ILOS). Logistic regression was performed to identify risk factors associated with in-hospital mortality and hospital stay. Multivariate clinical-biological models were developed to study predictions of mortality and very long length of stay.

*Results:* The mean age of the cohort was 69.7 years. The death rate was 4 times higher in the subgroup with a NRS ≥ 5 (44%), and 3 times higher with a NRS ≥ 3 to <5 (33%) compared to the patients with a NRS<3 (10%) ($p < 0.001$). LOS was significantly higher in the NRS ≥ 5 and NRS ≥ 3 to <5 subgroups (26.0 days; CI [21; 30.9]; and 24.9; CI [22.5; 27.1] respectively) versus 13.4; CI [12; 14.8] for NRS<3 ($p < 0.001$). The mean ILOS was significantly higher in the NRS ≥ 5 (5.9 days; versus 2.8 for NRS ≥ 3 to <5, and 1.58 for NRS<3 ($p < 0.001$)). In logistic regression, NRS ≥ 3 was significantly associated with the risk of mortality (OR: 4.8; CI [3.3; 7.1]; $p < 0.001$) and very long in-hospital stay (>12 days) (OR: 2.5; CI [1.9; 3.3]; $p < 0.001$). Statistical models that included a NRS ≥ 3 and albumin revealed to be strong predictors for mortality and LOS (area under the curve 0.800 and 0.715).

*Conclusion:* NRS was found to be an independent risk factor for in-hospital death and LOS in hospitalized Covid-19 patients. Patients with a NRS ≥ 5 had a significant increase in ILOS and mortality. Statistical models including NRS are strong predictors for an increased risk of death and LOS.

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## 1. Introduction

Infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to the coronavirus disease 2019 (Covid-19) pandemic starting in early 2020 [1,2]. Because of the resulting public health crisis, many studies aimed at identifying risk

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factors predicting severe forms of Covid-19 [3,4]. Many clinical conditions have been considered as risk factors [5–7], or excluded, during the initial phase [8]. Currently, there is a general consensus that the following clinical risk factors tend to be associated with severe courses of Covid-19: age or age >65, male sex, smoking, presence of comorbidities (i.e. diabetes mellitus, hypertension, previous coronary heart disease, and/or chronic obstructive pulmonary disease), and obesity [4,9–11].

Malnutrition is a well-known cause of increased hospital length of stay (LOS) [12,13], mortality [13,14], and it is negatively associated with health care costs [14,15]. In most centers, at least 25% of hospitalized patients present with malnutrition [16,17], and this also includes obese subjects with sarcopenia [18]. Malnutrition rates increase with age [18], as well as in patients with multiple comorbidities [19]. Malnutrition impacts several metabolic systems, and it has been suggested to also be a factor impacting the severity of Covid-19 [20,21]. Based on these observations, and on a growing body of evidence suggesting that malnutrition could impact outcomes in patients with Covid-19, the European Society of Parenteral and Enteral Nutrition (ESPEN) released practical guidance to assist health care professionals in the identification of patients with Covid-19 infection and at risk of malnutrition, and to guide the nutritional management of this population [22]. Among the many tools available for the screening for malnutrition, the Nutritional Risk Score (NRS or NRS-2002) is one of the most commonly used modalities [23–25]. Recent studies showed that NRS correlated well with the hospital length of stay (LOS) and mortality in patients with COVID-19 [22,26–28].

Despite the currently available data, there is an evidence gap regarding the relationship between the severity of the NRS and the outcomes of patients with Covid-19. Moreover, to the best of our knowledge, no studies analyzed the predictive value of multiple variable models that include the NRS for hospital mortality and LOS in patients hospitalized for Covid-19.

To further elucidate the possible relationship between the severity of NRS and clinical outcomes, and to study the predictive value of statistical models that include nutritional parameters on mortality and length of stay of patients with Covid-19, we conducted a retrospective monocentric study in Covid-19 patients hospitalized at the University Hospital of Lausanne (Centre Hospitalier Universitaire Vaudois, CHUV), the tertiary center in the Canton Vaud in Switzerland.

## 2. Material and methods

### 2.1. Ethics approval

The study (Impact of Nutritional Status on COVID-19 infection Outcomes, INCOVO) was approved by the ethics committee of the Canton of Vaud (CER-VD, Switzerland) under the protocol number 2020-01772.

### 2.2. Study design

This is a retrospective study of data extracted from the electronic medical records (EMR) of patients hospitalized at the CHUV between March 2020 and March 2021, with a principal diagnosis of SARS-CoV-2 infection. Of 5707 screened patients, 4787 were excluded due to an age <18 years, a negative RT-PCR for SARS-CoV-2, or for missing data. Ultimately, 920 patients were included in the final analysis (Fig. 1).

### 2.3. Data extraction

The extracted data include:

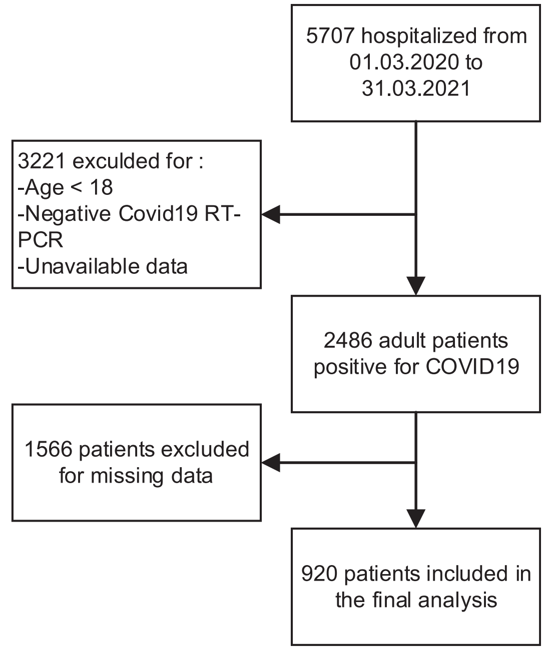


**Fig. 1.** Study flowchart.

- Demographic data: age, sex.
- Anthropometric data: weight, height, and body mass index (BMI) at admission; weight loss during hospitalization.
- Comorbidities: including hypertension, diabetes mellitus, chronic pulmonary disease, chronic liver disease, and history of smoking.
- Baseline laboratory data: C-reactive protein (CRP), albumin, complete blood count, liver enzymes.
- The NRS at admission.

The NRS is a nutritional risk score that uses a numerical scale to evaluate the risk of developing malnutrition. At the University Hospital Lausanne, it is usually used for all patients within the first 3 days after admission. This score includes the current BMI, the recent percentage of weight loss during the last three months, the decrease in patient eating capacities, the age of the patient, and comorbidities [23]. The nutritional status and the listed parameters of the hospitalized patients with Covid-19 infections were followed longitudinally during the hospitalization until discharge or death, and documented in the EMR based on established and validated institutional protocols.

We consider patients with a NRS ≥3 to <5 to be at moderate risk of malnutrition, and patients with a NRS ≥5 at severe risk for malnutrition.

### 2.4. Outcomes

The primary outcome of the study was the rate of in-hospital death secondary to Covid-19. The secondary outcomes included the rate of admissions to the intensive care units (ICU), the length of in-hospital stay (LOS), the ICU admission rate, and the length of stay in the ICU (ILOS).

### 2.5. Statistical analysis

#### 2.5.1. Descriptive analysis of the study cohort

Baseline anthropometric, nutritional, biological, and medical history data of the study cohort have been characterized.

#### 2.5.2. Subgroup analysis

The patient population was divided into three subgroups based on the NRS: NRS <3 (low nutritional risk), a NRS ≥3 to <5 (moderate nutritional risk), and a NRS ≥5 (severe nutritional risk). Subsequently, a comparative analysis of the general characteristics of the three subgroups has been performed, followed by a comparison of the primary and secondary outcomes between the three subgroups.

#### 2.5.3. Univariate and multivariate analysis

In order to identify risk factors associated with in-hospital mortality, a logistic regression was performed. For missing data imputation, K-nearest neighbor (KNN) was implemented. Furthermore, using significantly associated variables identified by univariate analysis, we developed multivariate clinical-biological models to study the prediction of mortality and very long in-hospital stay >12 days.

- **Model 1:** Age, NRS, obesity, smoking, chronic liver disease and/or pulmonary diseases.
- **Model 2:** The variable of model 1 plus diabetes mellitus, hypertension, and sex.
- **Model 3:** The variables of model 2 plus albumin.

Categorical data are expressed as absolute and relative frequencies of the whole cohort, whereas continuous data are expressed as mean and 95% confidence interval (CI). Continuous variables with normal distribution based on the Shapiro–Wilk test were compared with Student's t-test, and with ANOVA for multiple comparisons. A Mann–Whitney or a Kruskal–Wallis test were applied when distributions departed from normality. Discrete variables were compared using the Chi-square test. All tests were performed with R software version 1.4.1106.

## 3. Results

### 3.1. General characteristics of the study cohort

The mean age of the population was 69.7; CI [68.7; 70.7] years with a mean BMI of 27.4 kg/m$^2$; CI [27; 27.8].

Within the cohort, 20.4% had chronic liver disease, 9.1% chronic pulmonary disease, 42.2% hypertension, 27% diabetes mellitus, and 4.9% were active smokers (Table 1).

Two hundred thirty eight patients (25.9%) died during the hospitalization. The mean LOS was 20.5 days; CI [19.1; 22.0], and overall 20% of the patients spent at least one night in the ICU (Table 1).

### 3.2. NRS-based subgroup analysis

#### 3.2.1. Comparison of baseline characteristics

Five hundred and sixty two patients (61%) were at risk of malnutrition (NRS ≥ 3); 15% were at risk of severe malnutrition (NRS ≥ 5), and 46% had a moderate risk of malnutrition (NRS ≥ 3 to <5). Chronic liver disease and chronic pulmonary disorders were twice as prevalent in patients in the NRS ≥ 5 category compared to patients without risk for malnutrition (NRS < 3).

Compared to the NRS < 3 subgroup, the NRS ≥ 3 to <5 and NRS ≥ 5 subgroups had a significantly increased CRP levels of 73.7; CI [66.4–81.0] mg/l versus 81.7; CI [76.0–87.4] and 95.3; CI [83.3–107.0] mg/l ($p = 0.002$); significantly increased leucocyte counts of 7.4; CI [7.1–7.7] g/l versus 8.20; CI [7.8–8.5] g/l and 10.6; CI [7.8–13.5] g/l ($p < 0.001$); and a significantly decreased albumin of 34.6; CI [33.9–35.3] g/l versus 32.7; CI [32.1–33.2] g/l and 31.1; CI [30.3–32.0] g/l ($p < 0.001$) (Table 2).

**Table 1**
Characteristics of the study cohort.

| | N = 920 |
|---|---|
| | Mean [95% CI] |
| Age (years) | 69.7 [68.7; 70.7] |
| Admission BMI (kg/m$^2$) | 27.4 [27; 27.8] |
| Percentage of weight Loss | −3.25 [-3.86; −2.63] |
| Smokers n (%) | 45 (4.9) |
| Chronic liver disease n (%) | 187 (20.4) |
| Hypertension n (%) | 388 (42.2) |
| Chronic pulmonary disease n (%) | 83.7 (9.1) |
| Diabetes mellitus n (%) | 284 (27.0) |
| C-reactive protein (mg/l) | 81 [76.7; 85.2] |
| Albumin (g/l) | 33 [32.6; 33.2] |
| Leucocytes (G/l) | 8,27 [7.8; 8.7] |
| Platelet count (G/l) | 258 [251; 265] |
| GGT (IU/l) | 122 [110; 133] |
| ALAT (IU/l) | 51 [46; 56] |
| Death rate n (%) | 238 (25.9%) |
| ICU admission rate n (%) | 190 (20.7%) |
| Length of stay (days) | 20.56 [19.1; 22.0] |

BMI = body mass index; GGT = gamma-glutamyl transferase; ALAT = alanine transaminase; ICU: intensive care unit.

#### 3.2.2. NRS and mortality

Compared to patients with a NRS<3, the death rate was increased in patients with a NRS ≥ 3 to <5 and NRS ≥ 5 with frequencies of 10.3% versus 33.3% and 43.9% respectively ($p < 0.001$). The vast majority of fatal outcomes (84.5%) occurred in the subgroups with a high risk of malnutrition (NRS ≥ 3 to <5 and NRS ≥ 5) (Fig. 2, Table 3).

#### 3.2.3. NRS and hospital length of stay

Compared to patients with a NRS<3, the mean LOS was significantly higher in subjects with a NRS ≥ 3 to <5 and NRS ≥ 5 with 13.4; CI [12, 14.8] days versus 24.9; CI [22.5, 27.1] days and 26; CI [21, 30.9] days respectively ($p < 0.001$) (Table 3).

#### 3.2.4. NRS and ICU admission rate

There were no significant differences in ICU admission rates between patients with a NRS ≥5 (23%) and the NRS ≥ 3 to <5 subgroup (21%) compared to the NRS<3 group (18%) ($p = 0.51$) (Table 3, Fig. 3).

#### 3.2.5. NRS and ICU length of stay

Compared to patients with a NRS <3, the mean ILOS was significantly increased in the NRS ≥ 3 to <5 and NRS ≥ 5 subgroups with 1.58; CI [1.0; 2.16], versus 2.84; CI [2.03; 3.6], and 5.9; CI [3.1; 8.6] respectively ($p < 0.001$) (Table 3, Fig. 4).

#### 3.2.6. Logistic regression analyses

*3.2.6.1. In-hospital mortality.* The association between demographic data, clinical, and biological variables was analyzed for associations with the risk of mortality in patients with Covid-19. A significantly increased risk of mortality was found for an age ≥70 (OR: 5.77; CI [4.05; 8.39]; $p < 0.001$), a history of chronic liver disease (OR: 3.31; CI [2.36; 4.64]; $p < 0.001$), active smoking (OR: 2.91; CI [1.58; 5.35]; $p < 0.001$), an NRS ≥ 3 (OR: 4.83; CI [3.33; 7.16]; $p < 0.001$), and a history of chronic pulmonary disease (OR: 2.62; CI [1.65; 4.14]; $p < 0.001$). We found an inverse association between in-hospital mortality and baseline albumin concentrations ≥32 g/l (OR: 0.37; CI [0.27; 0.50]; $p < 0.001$), and, interestingly, with obesity (BMI ≥30 kg/m$^2$) (OR: 0.7; CI [0.49; 0.98]; $p = 0.004$). Sex, diabetes mellitus, and hypertension were not significantly associated with in-hospital mortality in this cohort.

**Table 2**
Comparison of baseline characteristics between the three subgroups of NRS (NRS <3, NRS ≥3 to <5, and NRS ≥5) (n = 920).

| | NRS < 3 (N = 358) | NRS ≥ 3 to <5 (N = 430) | NRS ≥ 5 (N = 132) | *p* value |
|---|---|---|---|---|
| | Mean [95% CI] | Mean [95% CI] | Mean [95% CI] | |
| Age (years) | 63 [61.3; 64.6] | 73.3 [72.0; 74.7] | 75.8 [73.8; 77.8] | <0.001 |
| Admission BMI (kg/m$^2$) | 28.2 [27.6; 28.7] | 27.3 [26.7; 27.9] | 25.6 [24.5; 26.6] | <0.001 |
| Percentage of weight loss (%) | −0.507 [-1.195; 0.182] | −4.48 [-5.46; −3.49] | −6.68 [-8.6; −4.7] | <0.001 |
| Smoking n (%) | 15 (4.19%) | 22 (5.12%) | 8 (6.06%) | 0.686 |
| Chronic liver disease n (%) | 41 (11.5%) | 115 (26.7%) | 32 (24.2%) | <0.001 |
| Hypertension n (%) | 132 (36.9%) | 202 (47%) | 54 (40.9%) | 0.01 |
| Chronic pulmonary disease n (%) | 25 (6.9%) | 39 (9.07%) | 20 (15.2%) | 0.02 |
| Diabetes mellitus n (%) | 90 (25.1%) | 132 (30.7%) | 27 (20.5%) | 0.04 |
| CRP (mg/l) | 73.7 [66.4; 81] | 81.7 [76; 87.4] | 95.3 [83.3; 107] | 0.002 |
| Albumin (g/l) | 34.6 [33.9; 35.3] | 32.7 [32.1; 33.2] | 31.1 [30.3; 32] | <0.001 |
| Leucocytes (G/l) | 7.4 [7.1; 7.7] | 8.2 [7.8; 8.5] | 10.6 [7.8; 13.5] | <0.001 |
| Platelet count (G/l) | 264 [252; 275] | 255 [245; 265] | 252 [235; 270] | 0.57 |
| GGT (IU/l) | 113 [96; 129] | 126 [108; 144] | 127 [97.5; 157] | 0.74 |
| ALAT (IU/l) | 61 [50.2; 71.5] | 44 [39.4; 49.8] | 49 [35.6; 62.8] | 0.003 |

Results are expressed as mean [95% CI] for continuous data and n (%) for categorical data. p values refer to the one-way ANOVA test (Kruskal–Wallis test) for continuous data and Chi$^2$ or Fisher's exact test for categorical data between the 3 categories of nutritional status.
BMI = body mass index; CRP = C-reactive protein; GGT = gamma-glutamyl transferase; ALAT = alanine transaminase.

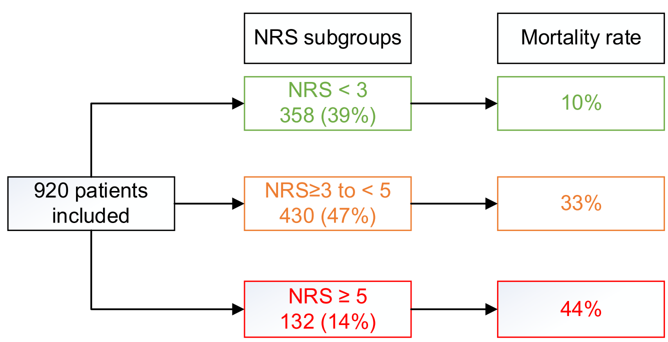


**Fig. 2.** Mortality rate according to the NRS (NRS < 3, NRS ≥ 3 to <5, NRS ≥ 5) (n = 920).

In the multiple variable analysis based on three models of adjustments (see Methods), a NRS ≥3 remained significantly associated with mortality with odds ratios of 2.87; CI [1.92; 4.38] ($p < 0.001$) for model 1, 2.9; CI [1.93; 4.44] ($p < 0.001$) for model 2, and 2.41; CI [1.59; 3.72] ($p < 0.001$) for model 3 (Table 4).

The performance of the three models were compared based on ROC analysis (Receiver Operating Characteristics with Area under the Curve (AUC)). Model 3 showed the highest accuracy with an AUC of 0.8 versus 0.771 for model 1, and 0.776 for model 2 (Fig. 5 a).

*3.2.6.2. Very long in-hospital stay (>12 days).* Next, we investigated potential associations between demographic, clinical, and biological variables, as well as the total LOS for more than 12 days, which was considered as a very long hospitalization.

A significantly increased risk of very long LOS in the hospital was found for an age ≥70 (OR: 1.50; CI [1.16; 1.96]; $p < 0.001$), a history of chronic liver disease (OR: 1.95; CI [1.39; 2.77]; $p < 0.001$), active smoking (OR: 2.34; CI [1.21; 4.90]; $p = 0.02$), and a NRS ≥3 (OR: 2.52; CI [1.92; 3.31]; $p < 0.001$). Additionally, we found an inverse association between very long LOS and a baseline albumin of ≥32 g/l (OR: 0.31; CI [0.22; 0.41]; $p < 0.001$). However, obesity, sex, hypertension, diabetes mellitus, and chronic pulmonary diseases did not show a significant association with very long LOS in this cohort. In the multiple variable analysis based on three models of adjustment, a NRS ≥3 remained significantly associated with very long LOS odds ratios of 2.52; CI [1.92; 3.31] ($p < 0.001$) for model 1, 2.37; CI [1.77; 3.19] ($p < 0.001$) for model 2, and 1.94; CI [1.42; 2.65] ($p < 0.001$) for model 3. The performance of the three models to predict very long LOS were compared based on ROC analysis, model 3 showing the highest accuracy with an AUC of 0.723 versus 0.662 for model 1, and 0.773 for model 2 (Table 5, Fig. 5 b).

## 4. Discussion

Infections with SARS-CoV-2 leading to Covid-19 have led to a pandemic that has resulted in multiple challenges and threats to health care and economic systems [2]. Not surprisingly, the presence of comorbidities was rapidly recognized as a major modifier of outcomes [4]. Among others, obesity has a negative impact on the course of Covid-19 and its outcomes [4]. In contrast, the risk or presence of malnutrition, including sarcopenic obesity, on outcomes in patients with Covid-19 have attracted less attention [29,30]. Of note, patients with Covid-19 are particularly vulnerable for developing further weight loss because of the frequent presence of dysgeusia, anosmia, and dyspnea that can further aggravate the anorexia associated with the disease [31]. Furthermore, the viral infection can be associated with a major increase in cytokine

**Table 3**
Mortality, ICU admission rate, length of stay according to NRS categories (NRS < 3, NRS ≥ 3 to <5, and NRS ≥ 5).

| | NRS < 3 | NRS ≥ 3 to <5 | NRS ≥ 5 | *p* value |
|---|---|---|---|---|
| | N = 358 | N = 430 | N = 132 | |
| Death rate % | 37 (10.3%) | 143 (33.3%) | 58 (44%) | <0.001 |
| LOS (days) | 13.4 [12; 14.8] | 24.9 [22.5; 27.1] | 26 [21; 30.9] | <0.001 |
| ICU admission rate n (%) | 68 (18%) | 91 (21%) | 31 (23%) | 0.51 |
| ILOS (days) | 1.58 [1.0; 2.16] | 2.84 [2.03; 3.6] | 5.9 [3.1; 8.6] | 0.001 |

LOS = Length of stay; ILOS = ICU length of stay; ICU: intensive care unit; NRS: nutritional risk score.
Results are expressed as mean [95% CI] for continuous data and n (%) for categorical data. p values refer to the one-way ANOVA test (Kruskal–Wallis test) for continuous data and Chi$^2$ or Fisher's exact test for categorical data between the 3 categories of nutritional status.

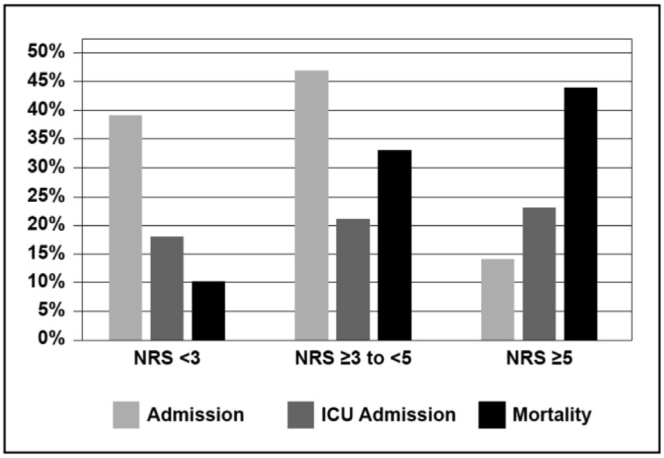


**Fig. 3.** Hospital admission rate, ICU admission rate, and in-hospital mortality according to NRS (NRS < 3, NRS ≥ 3 to <5, NRS ≥ 5) (n = 920).

secretion (or a cytokine storm), which result in a hypercatabolic state [22,31]. In aggregate, it appears that malnutrition may be an important contributing factor worsening outcomes and increasing mortality in patients with Covid-19 [26].

This study analyzed the relationship between nutritional status as characterized by the NRS and outcomes in 920 patients with Covid-19 in a tertiary center. Other studies explored the nutritional risk profile of Covid-19 patients using different tools to evaluate the nutritional status [13,20,23–27]. Compared to other studies, the study presented here included a significantly larger number of patients (n = 920) and patients with a wide age spectrum (>18 years). Further, to the best of our knowledge, this is the largest European monocentric study to explore the association between NRS and Covid-19 outcomes.

Importantly, the data presented here document an association with the NRS and the rate of inpatient mortality. Overall, 25% (n = 238) of the cohort died, and among them, 84% (n = 201) had a NRS ≥ 3. Among the patients with a fatal outcome, 24% had a NRS > 5 (severe malnutrition), 60% were in the subgroup with a NRS ≥ 3 to <5 (moderate malnutrition), whereas 15.5% had a NRS < 3 (absent risk of malnutrition based on this score). These observations also underscore the utility and validity of the NRS as simple, yet often underused screening tool [26,32,33]. Not unexpectedly, the prevalence of other risk factors for developing severe SARS-CoV-2 pneumonia (older age, chronic liver disease, hypertension, and smoking) was higher in patients at risk of malnutrition. Similarly, patients with a NRS ≥3 had significantly higher inflammatory parameters (CRP, leucocyte count) and lower plasma albumin levels. The latter finding is in line with other studies demonstrating a correlation between albumin levels and the need for ICU admission in patients with severe pneumonia, including Covid-19 pneumonia, and the albumin concentration may also be a predictive factor for the risk of developing a cytokine storm secondary to SARS-CoV-2 infections [28,34,35].

The findings presented here are consistent with previous studies demonstrating an association of the NRS with mortality and LOS [20,27,36,37]. Moreover, the multivariate and univariate analyses did not only confirm that the NRS is highly associated with LOS and death, but also demonstrated that the NRS combined with

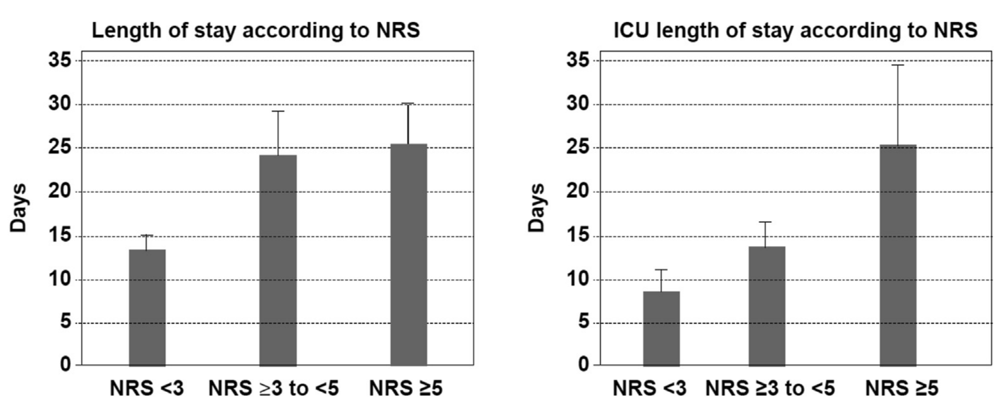


**Fig. 4.** Hospital length of stay and ICU length of stay according to the NRS (NRS < 3, NRS ≥ 3 to <5, NRS ≥ 5) (n = 920).

**Table 4**
Univariate and multiple variable logistic regression evaluating the risk of death according to NRS and other clinical risk factors.

| | Univariate regression | | Multivariate Adjusted OR Model 1 | | Multivariate Adjusted OR Model 2 | | Multivariate Adjusted OR Model 3 | |
|---|---|---|---|---|---|---|---|---|
| | OR [95% CI] | *p* | OR [95% CI] | *p* | OR [95% CI] | *p* | OR [95% CI] | *p* |
| Age > 70 | 5.77 [4.05; 8.39] | <0.001 | 3.61 [2.47; 5.36] | <0.001 | 3.68 [2.51; 5.49] | <0.001 | 3.8 [2.57; 5.71] | <0.001 |
| Obesity [BMI > 30 kg/m$^2$] | 0.7 [0.49; 0.98] | 0.04 | 0.7 [0.48; 1.03] | 0.081 | 0.76 [0.51; 1.14 | 0.19 | 0.97 [0.93; 1] | 0.94 |
| Male sex | 1.2<br>1.3 [0.81; 1.51] | 0.523 | | | 1.19 [0.84; 1.68] | 0.32 | 1.04 [0.73; 1.49] | 0.83 |
| Chronic liver disease | 3.31 [2.36; 4.64] | <0.001 | 2.21 [1.52; 3.21] | <0.001 | 2.29 [1.04; 4.33] | <0.001 | 2.32 [1.56; 3.45] | <0.001 |
| Smoking | 2.91 [1.58; 5.35] | <0.001 | 2.1 [1.03; 4.29] | 0.04 | 2.12 [1.04; 4.33] | 0.037 | 1.99 [0.97; 4.09] | 0.06 |
| Hypertension | 1.19 [0.88; 1.6] | 0.245 | | | 1.02 [0.73; 1.44] | 0.87 | 1.09 [0.77; 1.54] | 0.64 |
| Diabetes mellitus | 1.13 [0.81; 1.57] | 0.437 | | | 0.79 [0.51; 1.14] | 0.26 | 0.84 [0.55; 1.27] | 0.40 |
| NRS ≥ 3 | 4.83 [3.33; 7.16] | <0.001 | 2.87 [1.92; 4.38] | <0.001 | 2.9 [1.93; 4.44] | <0.001 | 2.41 [1.59; 3.72] | <0.001 |
| Chronic pulmonary disease | 2.62 [1.65; 4.14] | <0.001 | 1.86 [1.1; 3.13] | 0.01 | 1.87 [1.1; 3.15] | 0.019 | 1.73 [1; 2.97] | 0.05 |
| Albumin > 34 g/l | 0.37 [0.27; 0.5] | <0.001 | | | | | 0.89 [0.86; 0.93] | <0.001 |

OR = Odds ratio.

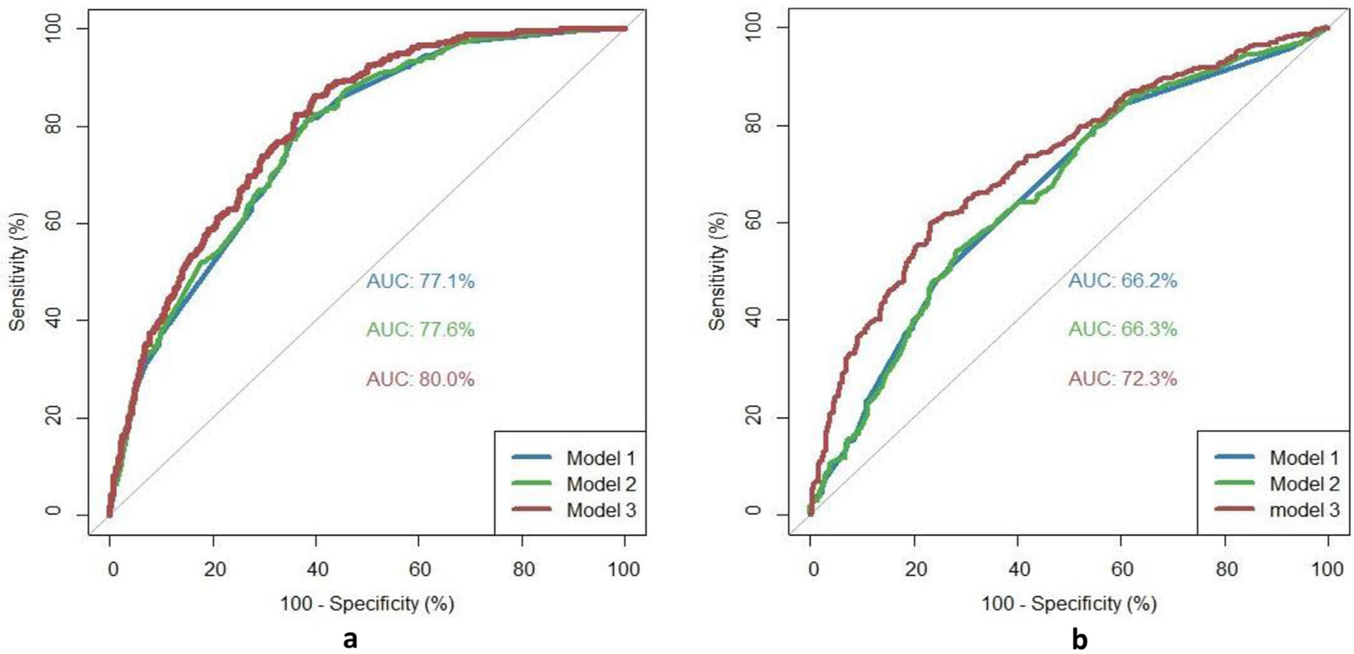


**Fig. 5.** ROC analysis evaluating the predictive value of Statistical models 1, 2 and 3 for mortality (a) and Long hospital stay >12 days (b).

**Table 5**
Univariate and multiple variable logistic regression evaluating the risk of long hospital stay >12 days, according to NRS and other clinical risk factors.

| | Univariate regression | | Multivariate Adjusted OR Model 1 | | Multivariate Adjusted OR Model 2 | | Multivariate Adjusted OR Model 3 | |
|---|---|---|---|---|---|---|---|---|
| | OR [95% CI] | *p* | OR [95% CI] | *p* | OR [95% CI] | *p* | OR [95% CI] | *p* |
| Age > 70 | 1.5 [1.16; 1.96] | <0.001 | 0.96 [0.71; 1.28] | 0.78 | 0.95 [0.36; 1.28] | 0.75 | 0.91 [0.66; 1.23] | 0.55 |
| Obesity (BMI > 30 kg/m$^2$) | 0.86 [0.65; 1.15] | 0.67 | 0.90 [0.68; 1.20] | 0.77 | 0.96 [0.70; 1.31] | 0.81 | 0.94 [0.68; 1.30] | 0.73 |
| Male sex | 1.12 [0.85; 1.47] | 0.43 | | | 1.02 [0.77; 1.36] | 0.85 | 0.87 [0.64; 1.17] | 0.36 |
| Chronic liver disease | 1.95 [1.39; 2.77] | <0.001 | 1.74 [1.22; 2.48] | 0.002 | 1.7 [1.18; 2.44] | 0.004 | 1.68 [1.15; 2.46] | 0.007 |
| Smoking | 2.34 [1.21; 4.90] | 0.02 | 1.88 [0.96; 3.82] | 0.06 | 1.87 [0.96; 3.80] | 0.07 | 1.76 [0.88; 3.68] | 0.11 |
| Hypertension | 1.07 [0.82; 1.39] | 0.62 | | | 1.04 [0.78; 1.38] | 0.76 | 1.05 [0.78; 1.41] | 0.72 |
| Diabetes mellitus | 1.30 [0.96; 1.74] | 0.08 | | | 1.1 [0.78; 1.53] | 0.56 | 1.15 [0.81; 1.63] | 0.42 |
| NRS ≥ 3 | 2.52 [1.92; 3.31] | <0.001 | 2.37 [1.77; 3.19] | <0.001 | 2.36 [1.76; 3.19] | <0.001 | 1.94 [1.42; 2.65] | <0.001 |
| Chronic pulmonary disease | 1.35 [0.85; 2.17] | 0.21 | 1.24 [0.76; 2.04] | 0.37 | 1.23 [0.75; 2.02] | 0.4 | 1.15 [0.69; 1.93] | 0.57 |
| Albumin > 34 g/l | 0.31 [0.22; 0.41] | <0.001 | | | | | 0.87 [0.84; 0.90] | <0.001 |

OR = Odds ratio.

other risk factors in three statistical models was highly accurate in the prediction of mortality and very long in-hospital stay in patients with Covid-19. To the best of our knowledge this is the first study to identify such a strong statistical model to predict severe outcomes of Covid 19.

The observation presented here emphasizes that the nutritional status is a major risk factor for compromised outcomes in patients with Covid-19 disease. Hence, it is of clinical importance to evaluate the nutritional status of all patients requiring hospitalization for Covid-19 disease. Whether or not nutritional intervention will positively impact outcomes should be evaluated in prospective studies.

Despite the relatively large cohort included in the study presented here, and the fact that it is the largest monocentric study addressing this problem, the study has several limitations. First, the design study is retrospective and the observed associations do not necessarily prove causality. Secondly, the effects of nutritional support and interventions on the outcomes could not be investigated in this retrospective analysis; the findings do, however, provide a rationale to investigate their potential impact in a prospective manner in the future. Thirdly, there may be an inherent bias because the cohort consists of patients hospitalized in a tertiary university center, and that these patients tend to be more severely affected. Fourth, our univariate regression analysis identified obesity as a protective factor for death in our inpatient cohort which could be due to a selection bias, because patients with obesity being are less likely to be screened for the risk of malnutrition. However another explanation for this phenomenon could be the *obesity paradox*, which consists of a protective effect of overweight/obesity in certain conditions associated with ICU admissions, especially the acute respiratory distress syndrome [4,38,39]. Finally, even though the use of the NRS has been recommended in this institution a decade ago, and is used consistently in many departments, it has not been implemented in all service, and only 25% of the identified Covid-19 patients have been formally evaluated with this score, a fact that may also have resulted in selection bias.

## 5. Conclusion

Despite these limitations, the study demonstrates that the nutritional risk, as determined by the NRS is strongly related to in-hospital mortality, LOS, ICU admission rate, and ILOS. Importantly, combined with traditional risk factors, it identified patients with Covid-19 who tend to have unfavorable outcomes. These results not only demonstrate the impact of the nutritional status on outcomes, but also underscore the necessity for prompt evaluation, and nutritional support and intervention in patients with Covid-19.

## Author's contributions

Conceptualization: MB, PK, PMV, GF.
Methodology: MB, PK, PMV, GF.
Formal analysis: MB, PK, PMV, GF.
Writing - original draft preparation: GF, MB, PK.
Writing - review and editing: GF, MB, PK, GF.
All authors contributed to the article and have approved the submitted version.

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## Declaration of competing interest

The authors declare no conflict of interest.

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