Original article

A retrospective analysis of malnutrition risk, nutritional support and outcomes in COVID-19 patients

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S U M M A R Y

Background: The association between obesity and disease severity in COVID-19 has been reported, whilst the impact of undernutrition remains less well-defined. Here we describe nutritional risk profiles of consecutive COVID-19 hospital inpatients, together with clinical outcomes and the impact of nutritional therapy.
Methods: This was a retrospective case—control study of adult inpatients admitted to University College London Hospital between February and July 2020 with PCR-confirmed SARS-CoV-2. Data were extracted from electronic health records and compared to a control group of consecutive patients admitted between March and April 2019. COVID-19 patients were classified as at low, moderate or high nutritional risk according to a local nutritional screening tool on admission. Data relating to demographics, nutritional therapy and clinical outcomes were collected and compared between nutritional risk groups.
Results: A significantly higher proportion of the COVID-19 group were found to be at high nutritional risk (132/381, 34.6% vs. 105/468, 22.4%; p < 0.0001). Within the COVID-19 group, multivariate analysis showed that those at moderate and high nutritional risk had increased odds of having an above-average peak CRP (p = 0.004) and a below-average nadir albumin (p = 0.0002). Inpatient length of stay was on average 5.8 days longer for COVID-19 patients at moderate and high nutritional risk compared to those at low nutritional risk (p = 0.0008). COVID-19 patients at moderate nutritional risk on admission had a higher proportion of ICU admissions (28/89, 31.5% vs. 32/160, 20.0%; p = 0.01). Mortality was significantly worse in COVID-19 patients at high nutritional risk compared to those at low nutritional risk (52/132, 39.4% vs. 24/160, 15.0%; p < 0.0001). Prescription of enteral nutrition in ward-based COVID-19 patients at high nutritional risk was associated with lower inpatient mortality (20/67, 29.9% vs. 22/38, 57.9%; p = 0.009). In crude analysis, the 30-day mortality rate post-discharge was higher in those at moderate and high nutritional risk compared to those at low nutritional risk (13/151, 8.6% vs. 4/136, 2.9%, p < 0.05). Amongst patients at high nutritional risk, nutritional therapy was less common amongst non-white patients compared to white patients (12/29, 41.4% vs. 46/66, 70.0%; p = 0.006).
Conclusion: Patients admitted with COVID-19 were at significant risk of undernutrition, which was associated with adverse clinical outcomes in our study. This risk was reduced by simple nutritional interventions. Mortality amongst patients at high nutritional risk persisted beyond discharge, suggesting close nutritional follow up in the period following hospital admission is warranted.

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1. Introduction

COVID-19 patients requiring hospitalisation are at risk of malnutrition on admission; the average duration of illness prior to hospital admission in the UK is approximately four days and symptoms can include sore throat, diarrhoea, anosmia and anorexia secondary to the acute phase response [1]. Social isolation may also detrimentally affect nutritional intake in the lead up to hospital admission by impacting the quality or quantity of food available and assistance with meal preparation and feeding. In general, patients requiring hospitalisation are likely to be poly-morbid, which in itself is closely linked to malnutrition [2]. Once in hospital there are multiple factors relating to COVID-19 which may further reduce nutritional intake, for example dyspnoea and

prolonged periods of oxygen therapy via face mask or CPAP. In addition, availability of dieticians may be more limited than under usual circumstances and ward staff may be exceptionally busy and therefore unable to provide feeding assistance [15].

This is important because malnutrition is known to adversely affect outcomes in severe illness − in general, 30-day mortality rates have been demonstrated to be significantly higher in non-specifically malnourished and protein deficient patients compared to non-malnourished patients [3]. Severe illness itself can induce a catabolic state which results in the depletion of skeletal muscle and up to 1 kg per day loss in critically ill patients [4]. Nutritional supplementation, however, can reduce skeletal muscle catabolism - reducing the odds of mortality by up to 6.6% for every 10% increase in protein intake [5].

COVID-19-specific studies have observed that patients with higher nutritional risk have worse outcomes; one study of 413 COVID-19 inpatients at Union Hospital in Wuhan, China, demonstrated that a one unit increase in NRS-2002 score was associated with a 1.23 times increase in the risk of mortality [6]. Another study of 139 COVID-19 inpatients demonstrated that those with malnutrition were more likely to be hospitalised longer compared with those of normal nutritional status, by about 11 days on average [7]. A prospective study of 183 COVID-19 patients admitted to ICU in Italy found that 76% survived when calorie adequacy was >80% compared to 33% survival when it was <80% [8]. Furthermore, another Italian study assessing ward-based COVID-19 patients found that deaths in the patients who were meeting their energy and protein needs were reported less frequently than those who were not, with an overall mortality rate of 7.1% vs. 36.8%, n = 94, although this was not adjusted for potential confounding variables [9].

Here, we sought to describe the burden of nutritional risk in COVID-19 inpatients compared to a pre-pandemic control group. We also aimed to correlate nutritional risk with important clinical outcomes in COVID-19, together with the impact of nutritional supplementation. This is one of the largest studies to date regarding nutritional status and outcomes in COVID-19. Furthermore, it provides novel insights into the prescription of nutritional supplements during the COVID-19 pandemic and how this may relate to outcomes when controlled for confounding variables. Finally, it highlights ethnic disparities in the prescription of nutritional supplements in COVID-19 as well as excess post-discharge mortality in undernourished patients which has not previously been demonstrated in the literature.

2. Methods

2.1. Data collection

University College London Hospital (UCLH) is part of a paperless organisation with a single digital platform that collects all clinical data. All data were extracted retrospectively in a de-identified fashion to ensure confidentiality. Data for two groups were extracted: the first was an adult (age ≥18) inpatient group admitted to the hospital for greater than 24 h at any point between February and July 2020 with a PCR-confirmed SARS-CoV-2 admission swab result ("COVID-19 group"). The second was a consecutive adult inpatient control group without COVID-19 who were admitted for any non-elective indication to the hospital for greater than 24 h between March and April 2019 ("control group"). These two months were chosen to make comparisons as relevant as possible since 85% of the COVID-19 group were admitted between March and April 2020, at the height of the pandemic first wave. We used an inclusion criteria of >24 h to capture all patients who should have been nutritionally assessed and considered for nutritional supplementation as per ESPEN guidelines [24].

2.2. Statistical analysis

Statistical analysis was performed with Graphpad Prism 9.0. All t-tests were two-tailed, with statistical significance determined as $p < 0.05$. Multiple logistic regressions were performed to calculate adjusted odds ratios. Two levels of regression were used: level 1 controlled for age, gender and co-morbidities; level 2 controlled for age, gender, co-morbidities and ethnicity.

2.3. Nutritional screening tool

The Nutritional Screening Tool (NST) is local scoring system which has been used at UCLH and other London hospitals since 2001. The total score ranges from 0 to 22 based on five assessment points (Table 1). A score of 0−2 is considered normal and therefore low nutritional risk. A score of 3−6 is considered moderate nutritional risk, whilst a score of 7+ is considered high nutritional risk. The NST has previously been internally validated against the Malnutrition Universal Screening Tool (MUST) for detecting patients at high nutritional risk (NST score 7+) on a sample of 125 inpatients. It was found to have an excellent discriminative value, area under ROC curve = 0.883 (95% CI 0.844−0.922, $p < 0.001$), high specificity at 92.5% (95% CI 87.1−96.2%) and sensitivity of 77.4% (95% CI 70.5−83.3%).

2.4. Clinical data

All NST scores and BMI scores were defined as admission scores calculated during the first 48 h of the inpatient stay. Average weight loss during the admission was calculated by subtracting discharge weight (the final weight recorded during an admission) from admission weight (weight recorded during the first 48 h of an admission). All patients with weight gain >10 kg during their admission were excluded from analysis in both COVID-19 and control groups due to the likelihood of oedema. Data relating to supplemental nutritional support were also collected, specifically if patients were prescribed oral nutritional supplements (ONS), nasogastric feed (NGF) or parenteral nutrition (PN). Results for C-reactive Protein (CRP) and albumin were collected to include the peak and nadir values during the admission. Peak and nadir interleukins (IL-1, IL-6, IL-10) were recorded in a small number of patients. Length of stay (LOS) was recorded in days. ICU admission was defined as any stay on ICU >24 h during the patient's admission, and inpatient mortality was defined as death due to any cause during the hospital admission. Post-discharge mortality within 30 days was evaluated by checking records on NHS Spine (a central healthcare database in England) which was accessed in July 2020.

2.5. Ethnicity data

Ethnicity was classified according to the subgroups defined in Table 2, as per our local classification system. Patients were excluded from analysis involving ethnicity if it was recorded as "Not yet asked", "Not stated" or "Refused to give".

3. Results

3.1. Patient demographics

As shown in Table 3, the COVID-19 group was older than the control group (mean difference 3.1 years, 95% CI 0.8−5.3 years, $p = 0.008$). There was a significantly higher proportion of males admitted with COVID-19 and they were more likely to be of a non-white ethnicity. The COVID-19 group also contained a higher proportion of former smokers but significantly less current smokers

Table 1
Nutritional screening tool (NST).

Appetite	
Normal for patient	0
Reduced	3
Minimal	5
Neurological Status	
Fully oriented	0
Confused	3
Unconscious	5
Physical Appearance	
Appears appropriate weight	0
Appears thin	2
Appears emaciated	4
Weight Loss	
No weight loss	0
Gradual over months	2
Rapid over weeks	5
Unable to score	2
Intake	
Manages most of three meals a day	0
Poor intake leaving > half of meals offered	3
Total Score	/22

Table 2
Ethnicity classification.

"White"	"Non-White"
White British	**Asian**
White Irish	Asian Indian
Other White Background	Asian Bangladeshi
	Asian Pakistani
	Other Asian Background
	Black
	Black African
	Black Caribbean
	Other Black Background
	Mixed/Other
	Mixed White and Asian
	Mixed White and Black African
	Mixed White and Black Caribbean
	Other Mixed Background
	Other Ethnic Group

Table 3
Comparison of demographics and co-morbidities between the COVID-19 and control groups.

Demographic	COVID-19	Control	Sig.
Age	**n = 517**	**n = 550**	
Mean	63.9	60.8	<0.01
Gender	**n = 517**	**n = 550**	
Female	190 (36.8%)	274 (49.8%)	<0.0001
Male	327 (63.2%)	276 (50.2%)	<0.0001
Ethnicity	**n = 456**	**n = 438**	
White	268 (58.8%)	306 (69.9%)	<0.001
Non-white	188 (41.2%)	132 (30.1%)	<0.001
Smoking Status	**n = 450**	**n = 210**	
Never	249 (55.3%)	99 (47.1%)	Not sig.
Current	34 (7.6%)	50 (23.8%)	<0.0001
Former	167 (37.1%)	61 (29.1%)	<0.05
Co-morbidity	**n = 517**	**n = 550**	
AKI/CKD	94 (18.2%)	42 (7.6%)	<0.0001
Cancer	128 (24.8%)	103 (18.7%)	<0.05
Chronic Lung Disease	44 (8.5%)	34 (6.2%)	Not sig.
Dementia	52 (10.0%)	26 (4.7%)	<0.001
Diabetes	127 (24.6%)	61 (11.1%)	<0.0001
Hypertension	220 (42.6%)	103 (18.7%)	<0.0001

than in the control group. The COVID-19 group was overall more comorbid than the control group, with a significantly higher prevalence of all recorded comorbidities (with the exception of chronic lung disease).

3.2. Nutritional data & outcomes

3.2.1. Admission NST score
As shown in Table 4, significantly more patients were classed as being at high nutritional risk (NST 7+) in the COVID-19 group than in the control group. The odds ratio of being at high nutritional risk on admission for COVID-19 compared to control was 1.98 (95% CI 1.46 to 2.67, p < 0.0001). A significantly higher mean admission NST were observed in the COVID-19 group (mean NST 5.1 vs 3.5; difference 1.6 (95% CI 2.3 to 1.0, p = <0.0001).

3.2.2. Admission weight, BMI & weight loss
The COVID-19 group was significantly heavier on average with an admission weight of 77.4 kg vs 73.0 kg (mean difference 4.4 kg,

95% CI 1.62—6.84 kg, p = 0.002). However, there was no significant difference between the admission BMI of the two groups (26.7 vs 26.1, p = 0.35, n = 668). There was a higher proportion of patients in the obese category (BMI 30+) in the COVID-19 group (27.6% vs 22.2%) although this was not significant (OR 1.33; p = 0.12; 95% CI 0.94 to 1.92). In patients who had both an admission weight and a discharge weight recorded, the COVID-19 group (n = 130) experienced significantly more weight loss than the control group (n = 141) during the admission (3.9 kg vs 1.5 kg, difference between the means 2.4 kg; 95% CI 1.1 kg—3.7 kg, p = 0.0004). Represented as a percentage of admission body weight, this was 5.1% vs. 2.1% weight loss for the COVID-19 and control groups respectively.

3.2.3. Outcomes
When analysed by NST subgroup, mortality rates were significantly greater in patients at high nutritional risk (NST 7+) compared to those at moderate risk (NST 3—6) in both the COVID-19 and control cohorts (Fig. 1). Furthermore, both inpatient mortality and ICU admission in the COVID-19 group were significantly greater than in the control group (OR 9.3, 95% CI 5.7 to 15.1, p < 0.0001 and OR 3.4, 95% CI 2.3 to 5.1, p < 0.0001 respectively).

3.3. COVID-19 nutritional subgroup analysis

3.3.1. Inflammatory response
Within the COVID-19 cohort, significantly higher peak CRP values were observed in the high nutritional risk group compared to those at low nutritional risk, on average 30 mg/L higher (p = 0.03, 95% CI 3—57 mg/L). Significantly lower nadir albumin values in this group were also observed, on average 3 g/L lower (p < 0.0001, 95% CI 5 to 2 g/L) (Fig. 2). Multivariate analysis demonstrated that moderate and high nutritional risk on admission was an independent predictor for an above average CRP and a below average nadir albumin, as demonstrated in Table 5 and Table 6. Interleukins were measured in a small number of patients (n = 44) and there were no statistically significant results at the p < 0.05 level. Nadir IL-1 in NST 0—2 vs. NST 7+ came closest to

Table 4
Comparison of admission NST score, weight, BMI and weight loss between the COVID-19 and control groups.

	COVID-19	Control	Sig.
Admission NST Score	**n = 381**	**n = 468**	
Low Risk 0–2	160 *(42.0%)*	267 *(57.1%)*	<0.0001
Moderate Risk 3–6	89 *(23.4%)*	96 *(20.5%)*	<0.05
High Risk 7+	132 *(34.6%)*	105 *(22.4%)*	<0.0001
Dietician Referral[a]	111 (50.2%)	92 (45.8%)	Not sig.
BMI	**n = 276**	**n = 392**	
Mean (range)	26.7 *(13.2–53.6)*	26.1 *(10.8–62.0)*	Not sig.
Admission Weight	**n = 356**	**n = 451**	
Mean (range)	77.4 kg *(38.0 – 190.0)*	73.0 kg *(32.0 – 160.0)*	<0.01
Weight Loss	**n = 130**	**n = 141**	
Mean (% body weight)	3.9 kg (5.1%)	1.5 kg (2.1%)	<0.001
Outcome	**n = 517**	**n = 550**	
Survived to Discharge	383 (74.1%)	530 (96.4%)	<0.0001
ICU Admission	111 (21.5%)	39 (7.1%)	<0.0001
Died	134 (25.9%)	20 (3.6%)	<0.0001

"N" represents the number of patients for which that variable was recorded.
[a] Dietician referral was only measured for patients at moderate or high nutritional risk.

significance, 0.5 pg/ml vs. 0.1 pg/ml, mean difference 0.4 pg/ml (95% CI -0.09 to 0.88), $p = 0.1$ (Fig. 3).

3.3.2. Length of stay

As shown in Fig. 4, the mean inpatient overall length of stay was 5.8 days longer in patients with NST >2 vs NST 0–2 (20.1 vs. 14.3 days; $p = 0.0008$, 95% CI 2.4–9.2 days). The mean length of ICU-specific stay was five days longer in patients with NST >2, however it did not reach significance when compared to the length of ICU stay for patients at low nutritional risk (17.5 vs. 12.4 days; $p = 0.12$). Multiple logistic regression was performed to control for potential confounding variables that might influence inpatient length of stay (Table 7). The reference level was the mean inpatient length of stay, which was 17 days. NST score >2 was found to be independently associated with nearly double the odds (adjusted OR 1.87, 95% CI 1.13–3.11) of having a longer than average inpatient length of stay ($p = 0.015$).

3.3.3. ICU admission

As shown in Fig. 5, patients at moderate nutritional risk (NST 3–6) were significantly more likely to have an ICU admission than those at low (NST 0–2) or high (NST 7+) nutritional risk (OR 2.05, 95% CI 1.11–3.76, $p = 0.02$). The risk factors for ICU admission, along with their adjusted odds ratios, are displayed in Table 8. Moderate

nutritional risk on admission (NST 3–6) was an independent risk factor for ICU admission, adjusted OR 2.18 (1.18–4.00), $p < 0.05$.

3.3.4. Mortality

3.3.4.1. Inpatient mortality. As shown in Fig. 6, inpatient mortality of those at high nutritional risk (NST 7+) was significantly higher than those at low nutritional risk (NST 0–2) (39.4% vs. 15.0%, OR 3.28, 95% CI 2.02–5.32, $p < 0.0001$). Those at moderate nutritional risk (NST 3–6) did not have significantly increased mortality compared to those at low nutritional risk, OR 1.32 (95% CI 0.67–2.63), $p = 0.42$. The risk factors for inpatient mortality, along with their adjusted odds ratios, are displayed in Table 9. An admission NST score of 7+ was an independent predictor for inpatient mortality, adjusted OR 3.06 (1.71–5.57), $p < 0.0001$.

3.3.4.2. Follow-up mortality. Patients who survived to discharge (n = 287) were followed up for 30-day mortality rates using NHS Spine. 30-day mortality was nearly three times higher in those at moderate and high nutritional risk (NST >2) compared to those at low nutritional risk (NST 0–2). As shown in Fig. 7, this was significant; 8.6% vs. 2.9%, OR 3.20 (95% CI 1.02%–10.07%), $p < 0.05$. In absolute numbers, there were 13 deaths in the NST >2 group and four deaths in the NST 0–2 group. However, when controlled for potential confounding between other variables in a multiple
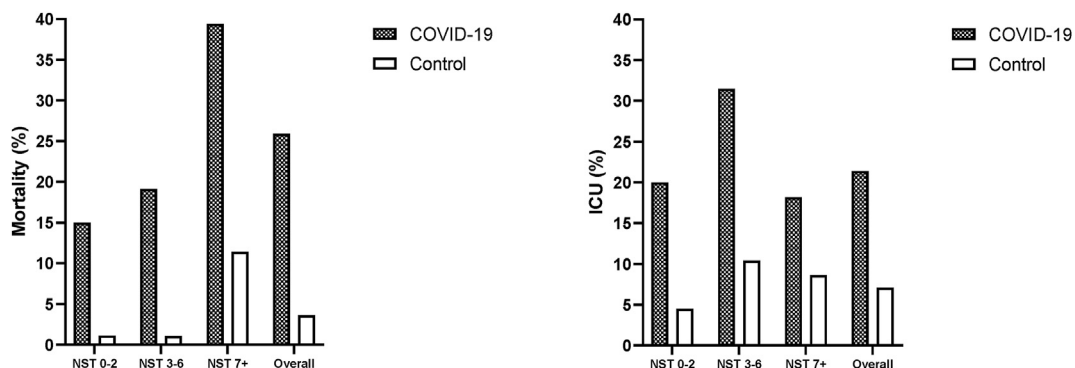

Fig. 1. Mortality (%) and ICU admission (%) by NST subgroups in COVID-19 (n = 381) vs. control (n = 486).
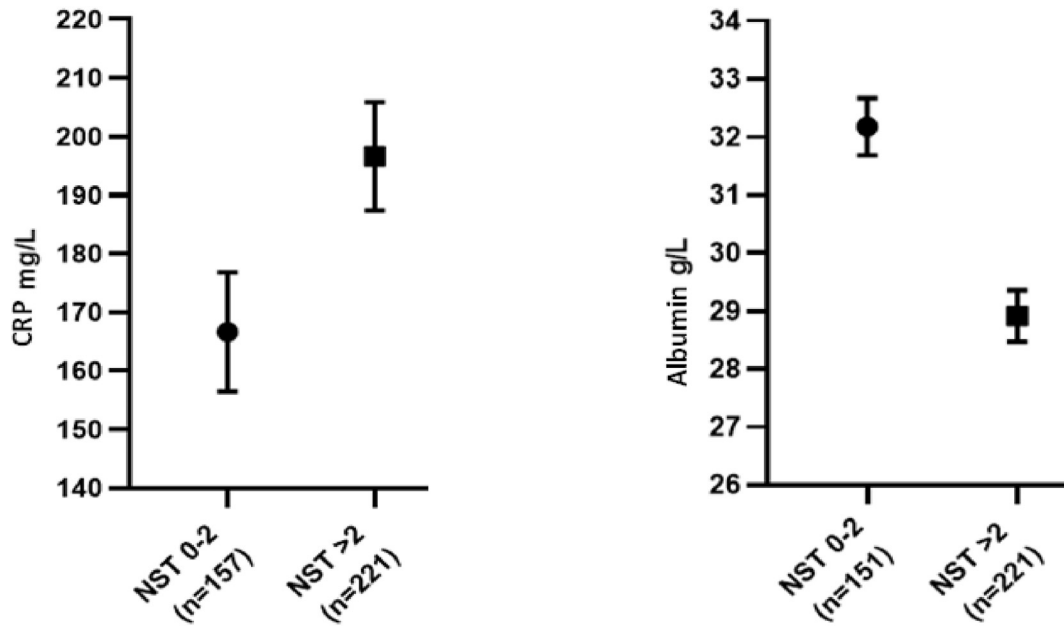
Fig. 2. Peak CRP in mg/L and nadir albumin in g/L across different nutritional risk groups, mean plotted with error bars represent standard error of the mean (SEM).

Table 5
Multivariate analysis showing adjusted odds ratios for predictors of peak CRP >183 (average) (n = 378).

Predictor of Peak CRP Above Average	Adjusted Odds Ratio (95% CI) Regression Level 1	Sig.
Age >70	0.72 (0.47—1.10)	Not sig.
NST >2	1.92 (1.23—3.02)	<0.01
Cancer	1.16 (0.71—1.90)	Not sig.
HTN	1.14 (0.72—1.81)	Not sig.
AKI/CKD	1.34 (0.77—2.30)	Not sig.
Male Gender	1.42 (0.90—2.24)	Not sig.
Dementia	0.36 (0.16—0.77)	<0.05
Diabetes	1.36 (0.83—2.24)	Not sig.
Chronic Lung Disease	0.76 (0.35—1.59)	Not sig.

logistic regression *(Table 10)*, NST >2 was not significant as an independent risk factor for predicting follow-up mortality (p = 0.1).

3.3.5. Nutritional support (excluding ICU)

3.3.5.1. Prevalence of nutritional support. Overall, 40.4% of ward-based COVID-19 inpatients were prescribed some form of nutritional support. The most common form was oral nutritional supplements (ONS) which was prescribed to 38.0% of patients. Nasogastric feeding (NGF) was prescribed to 10.8% of patients and

Table 6
Multivariate analysis showing adjusted odds ratios for predictors of nadir albumin <30 (average) (n = 372).

Predictor of Nadir Albumin Below Average	Adjusted Odds Ratio (95% CI) Regression Level 1	Sig.
Age >70	1.19 (0.72—1.97)ns	Not sig.
NST >2	2.38 (1.52—3.74)	<0.001
Cancer	1.38 (0.84—2.29)	Not sig.
HTN	0.97 (0.60—1.54)	Not sig.
AKI/CKD	1.85 (1.06—3.30)	<0.05
Male Gender	1.64 (1.05—2.58)	<0.05
Dementia	0.43 (0.20—0.89)	<0.05
Diabetes	0.91 (0.55—1.51)	Not sig.
Chronic Lung Disease	0.56 (0.26—1.16)	Not sig.

parenteral nutrition (PN) was prescribed to 1.7%. Table 11 shows a detailed breakdown of the type of nutritional support prescribed in each nutritional risk category.

3.3.5.2. Nutritional support and mortality. As shown in Fig. 8, looking at ward-based COVID-19 patients, there was a significantly lower odds of mortality in patients with high nutritional risk (NST 7+) who were prescribed nutritional support (ONS, NGF or both) compared to those who were not prescribed nutritional support (20/67, 29.9% vs. 22/38, 57.9%; p = 0.009). In the moderate nutritional risk group (NST 3—6) there was no significant difference in mortality with the prescription of nutritional support. In the low nutritional risk group (NST 0—2), there was significantly higher mortality in those who were prescribed nutritional support. Multivariate analysis confirmed that in ward-based patients at high nutritional risk (NST 7+), prescription of nutritional support (ONS ± NGT) was independently associated with significantly lower odds of inpatient mortality (adjusted OR 0.26, 95% CI 0.09—0.69, p < 0.01). The higher odds of mortality in patients at low nutritional risk who were prescribed nutritional support was confirmed not to be significant on multivariate analysis as shown in Table 12.

3.3.6. Ethnicity review

In patients at high nutritional risk (NST 7+) outside of ICU, non-white patients were significantly less likely to be prescribed nutritional support (ONS ± NGF) than white patients, OR 0.30 (95% CI 0.13—0.71), p = 0.006 (Fig. 9). In patients at moderate or high nutritional risk (NST >2), non-white patients were also significantly less likely to be prescribed nutritional support OR 0.47 (95% CI 0.24—0.95), p = 0.03. They were also less likely to be referred to a dietician, however this did not meet statistical significance, OR 0.59 (95% CI 0.29—1.19), p = 0.1. There were no significant differences between these two groups in terms of age (non-white 72.2 years, white 76.2 years, p = 0.2) or dementia (non-white 28.8%, white 21.4%, p = 0.4). Mortality was higher in the non-white group, however it did not meet statistical significance (44.8% vs 40.9% - OR 1.17, 95% CI 0.50—2.83, p = 0.7).
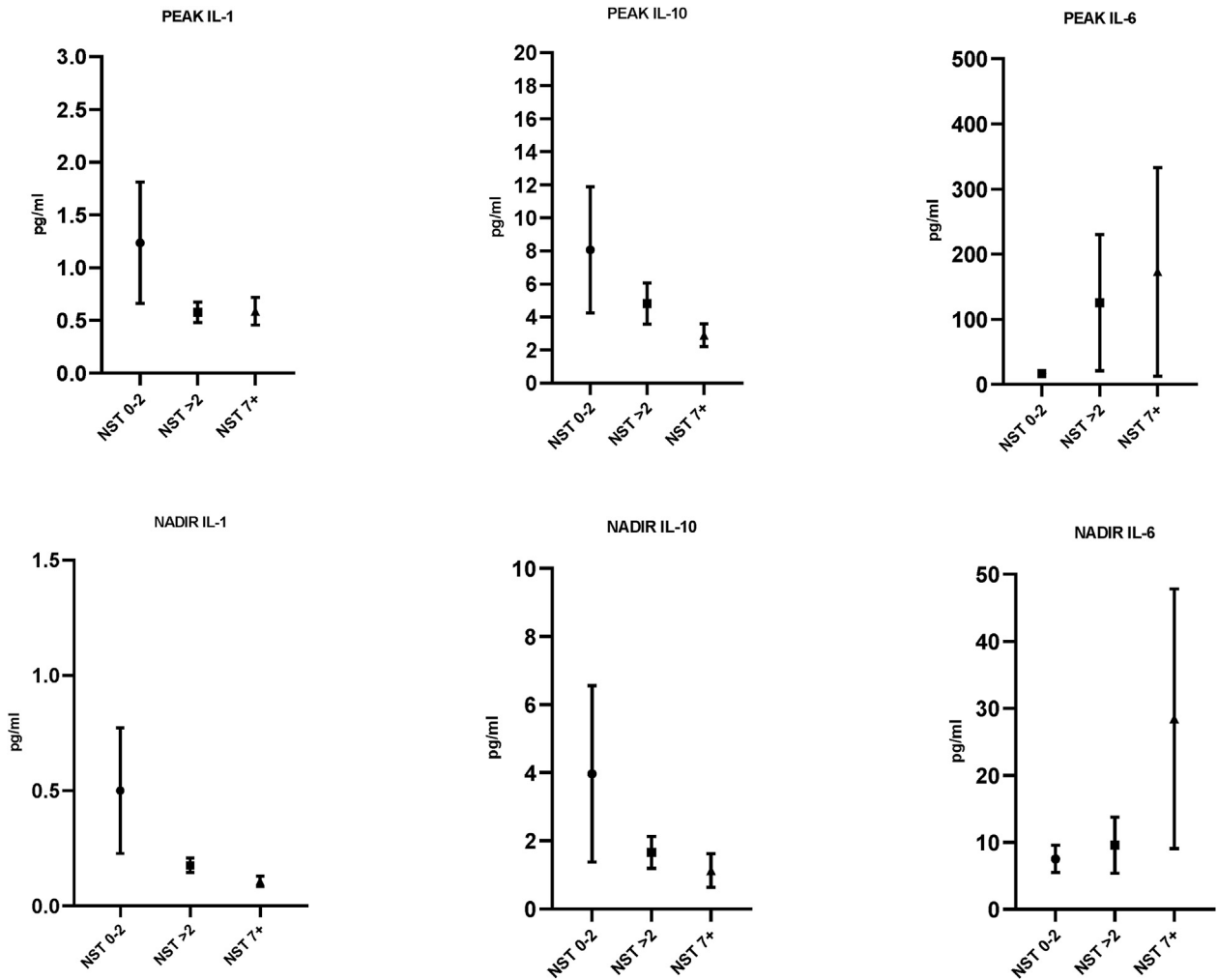
Fig. 3. Mean IL-1, IL-10 & IL-6 peaks and nadirs plotted by nutritional risk groups (n = 15, 29, 19 respectively for NST 0–2, NST >2 & NST 7+). Error bars represent standard error of the mean (SEM).
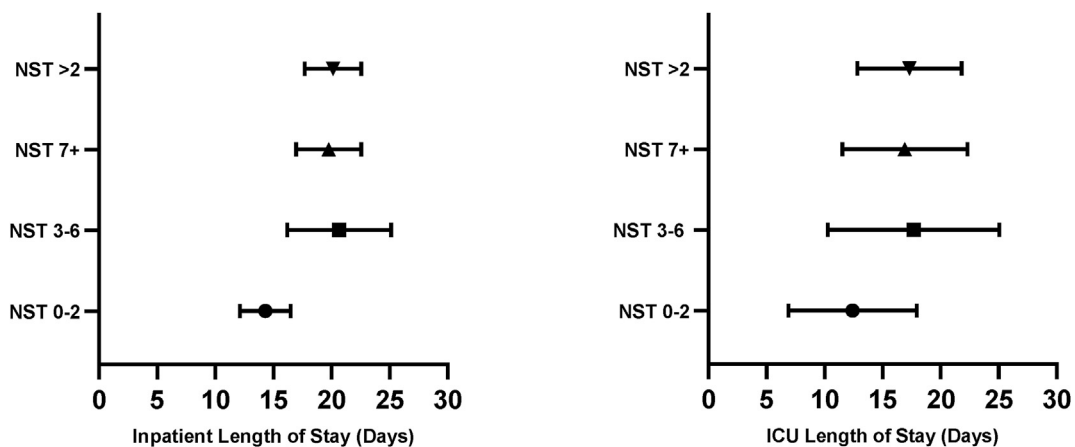

Fig. 4. Inpatient length of stay and ICU length of stay by nutritional status. Means are plotted with lines representing 95% confidence intervals.

4. Discussion

Our data showed that patients with COVID-19 were at significantly higher risk of undernutrition on admission to hospital than a pre-pandemic control group. Moderate and high nutritional risk in COVID-19 was associated with universally worse outcomes including greater inflammatory response, longer length of stay, higher inpatient mortality and higher follow-up mortality. Multivariate analysis showed that nutritional supplementation in patients at high nutritional risk was associated with lower inpatient

Table 7
Multivariate analysis showing adjusted odds ratios for predictors of inpatient length of stay greater than average (>16 days), (n = 381).

| Predictor of Inpatient Length of Stay >16 Days	Adjusted Odds Ratio (95% CI) Regression Level 1	Sig.
Age >70	1.27 (0.72—2.25)	Not sig.
NST >2	1.87 (1.13—3.11)	<0.05
Cancer	1.83 (1.07—3.16)	<0.05
HTN	0.88 (0.53—1.46)	Not sig.
AKI/CKD	1.32 (0.72—2.40)	Not sig.
ICU Admission	6.79 (3.82—12.40)	<0.0001
Male Gender	1.62 (0.99—2.70)	Not sig.
Dementia	2.10 (0.99—4.48)	Not sig.
Diabetes	1.05 (0.60—1.82)	Not sig.
Chronic Lung Disease	1.11 (0.50—2.37)	Not sig.
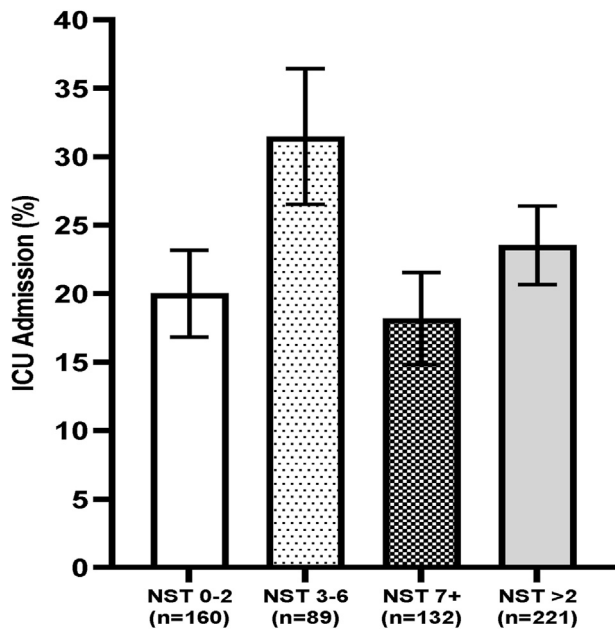
Fig. 5. Graph comparing ICU admission rates across different nutritional risk categories. Means are plotted with error bars representing standard error of the mean (SEM).

Table 8
Multivariate analysis showing adjusted odds ratios for predictors of ICU admission (n = 340).

Predictor of ICU Admission	Adjusted Odds Ratio (95% CI) Regression Level 2	Sig.
Asian Ethnicity	2.40 (1.17—4.85)	<0.05
NST 3—6 (Moderate Risk)	2.18 (1.18—4.00)	<0.05
Male Gender	1.99 (1.08—3.78)	<0.05
AKI/CKD	1.84 (0.93—3.58)	Not sig.
Cancer	0.69 (0.33—1.36)	Not sig.
HTN	1.18 (0.64—2.18)	Not sig.
Diabetes	0.75 (0.38—1.44)	Not sig.
Dementia	0.15 (0.01—0.79)	<0.05
Age >70	0.37 (0.19—0.72)	<0.01

Fig. 6. Mean inpatient mortality (%) between different nutritional risk categories (n = 381). Error bars represent standard error of the mean (SEM).

Table 9
Multivariate analysis showing adjusted odds ratios for predictors of inpatient mortality (n = 340).

Predictor of Inpatient Mortality	Adjusted Odds Ratio (95% CI) Regression Level 2	Sig.
Age >70	6.26 (3.24—12.65)	<0.0001
NST 7+	3.06 (1.71—5.57)	<0.0001
NST >2	1.21 (0.53—2.72)	Not sig.
AKI/CKD	1.78 (0.93—3.39)	Not sig.
ICU Admission	3.89 (1.86—8.47)	<0.001
HTN	1.65 (0.91—3.03)	Not sig.
Cancer	2.19 (1.15—4.17)	<0.05
Dementia	0.75 (0.31—1.78)	Not sig.
Diabetes	0.55 (0.27—1.08)	Not sig.
Chronic Lung Disease	1.25 (0.50—3.04)	Not sig.
Male Gender	1.01 (0.55—1.86)	Not sig.
Non-White Ethnicity	1.41 (0.75—2.66)	Not sig.

mortality, yet it was only prescribed for two-thirds of high nutritional risk patients. Concerningly, and despite being disproportionally affected by COVID-19, non-white patients were less likely to be prescribed nutritional support. We have also shown for the first time that there may be excess mortality risk in undernourished patients in the period after discharge with crude analysis showing significantly higher 30-day mortality rates.
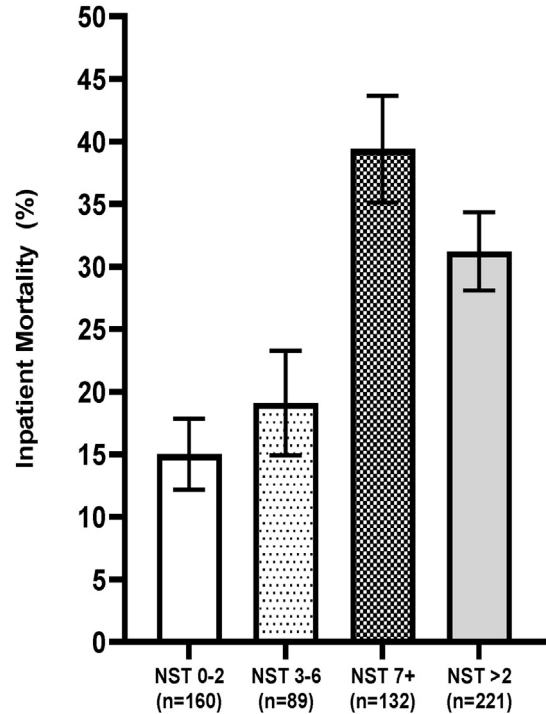
The high nutritional risk in COVID-19 patients is likely multifactorial. Firstly, increasing age is a risk factor for undernutrition — older patients are more likely to have inadequate dietary intake, anorexia from age-related physiological changes and sarcopenia [10]. The presence of multiple co-morbidities increases the risk of cachexia from underlying chronic illness [11]. This baseline undernutrition is accentuated by the acute illness - in the time leading up to hospital admission from the time of infection, these patients are entering a disease-driven catabolic state. The acute phase response increases energy demand whilst suppressing appetite [12]. This is made worse by symptoms such as anosmia and dysgeusia which were reported in a meta-analysis to affect nearly 40% of COVID-19 patients [13] and were associated with decreased oral intake prior to admission [14]. Nutritional intake may be further negatively impacted by pandemic-related societal factors such as food availability, willingness or physical ability to go to shops and reduced access to carers [15].
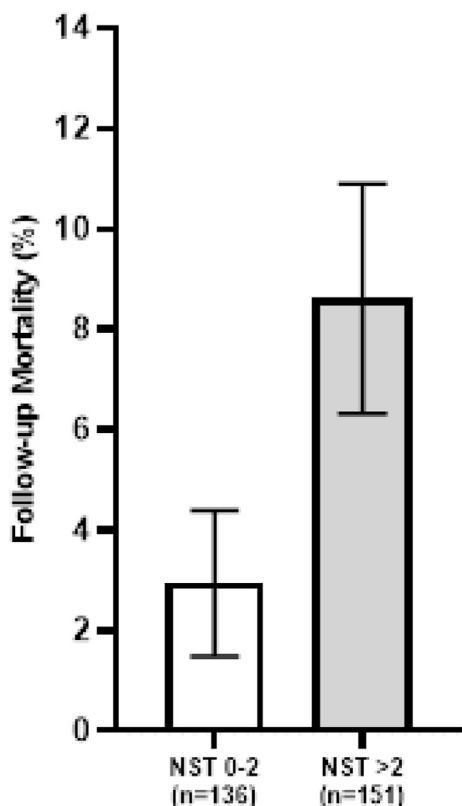
Fig. 7. Mean follow-up mortality (%) in low nutritional risk vs. moderate and high nutritional risk. Error bars represent standard error of the mean (SEM).

Table 10
Multivariate analysis showing adjusted odds ratios for predictors of follow-up mortality (n = 287).

Predictor of Follow-Up Mortality	Adjusted Odds Ratio (95% CI) Regression Level 1	Sig.
Age >70	5.95 (1.51—29.72)	<0.05
Dementia	3.34 (0.77—15.63)	Not sig.
Cancer	6.20 (1.64—26.50)	<0.01
NST >2	2.52 (0.71—10.53)	Not sig.
ICU	0.48 (0.02—3.31)	Not sig.
Diabetes	1.93 (0.46—7.73)	Not sig.
HTN	0.33 (0.08—1.14)	Not sig.
AKI/CKD	0.72 (0.12—3.11)	Not sig.
Chronic Lung Disease	0.68 (0.09—3.15)	Not sig.
Male Gender	2.79 (0.77—13.54)	Not sig.

We found that this nutritionally at-risk cohort of COVID-19 patients experienced a greater inflammatory response — CRP was significantly raised and albumin was significantly suppressed in those at moderate and high nutritional risk compared to those at low nutritional risk. This finding was independent of age and co-morbidities, suggesting that undernutrition is independently associated with a greater inflammatory response in COVID-19. However, it does not define the specific nature of the association. It is possible that patients with more severe disease have a stronger inflammatory response, with subsequent catabolism manifesting as a higher nutritional risk score. However, it is also plausible that malnutrition itself could predispose to immune dysregulation [25], resulting in a maladaptive immune response to acute infection with SARS-CoV-2.

Although raised levels of IL-1 have been associated with severe COVID-19 [16], there was a non-significant trend in our patients at high nutritional risk for a depressed IL-1 response compared to those at low nutritional risk (it must be emphasised that this did not reach statistical significance and numbers were relatively low, n = 44). This is not unexpected as IL-1 activity can be suppressed in malnutrition as demonstrated by both in-vitro and in-vivo studies [17,18], compared to the IL-6 response which is preserved or even up-regulated [19]. Indeed, we noted a non-significant trend for elevated IL-6 response in patients at higher nutritional risk, which would correlate with the significantly higher CRP in this group. Interestingly, there was a non-significant trend towards lower IL-10 levels in patients with higher nutritional risk (p = 0.2). The role of IL-10 in the inflammatory response is complex, however it is generally regarded as having immune-regulatory and anti-inflammatory effects in most circumstances [20]. It has been proposed that alterations in cytokine balance, particularly a higher IL-6:IL10 ratio, can identify patients at risk of impending poor outcomes in COVID-19, as per the Dublin—Boston score [21]. Further work is required to elucidate the interleukin response pattern in malnourished COVID-19 patients, particularly as the IL-inhibitors anakinra (IL-1) and tocilizumab (IL-6) are being used as biologic therapies [22].

We found inpatient length of stay to be on average nearly a week longer in the patients who were at moderate and high nutritional risk on admission. Again, this is likely to be multifactorial with a combination of physical deconditioning and skeletal muscle catabolism as well as more severe illness experienced by these patients. It is in keeping with similar results from other studies where malnutrition increased length of stay by nearly 11 days in patients hospitalised with COVID-19 [7]. This emphasises the importance of rapid nutritional screening, appropriate dietetic intervention, nutritional support where necessary and physical therapy to reduce length of stay at a time when hospital beds are a scarce resource.

High nutritional risk on admission was independently associated with increased risk of inpatient mortality in COVID-19. Despite representing only one third of the COVID-19 cohort, they accounted for nearly two-thirds of the overall mortality. Furthermore, COVID-19 patients with high nutritional risk on admission had a four times higher mortality rate compared to patients at high nutritional risk

Table 11
Nutritional support prescription across all nutritional risk groups for ward-based patients (n = 297).

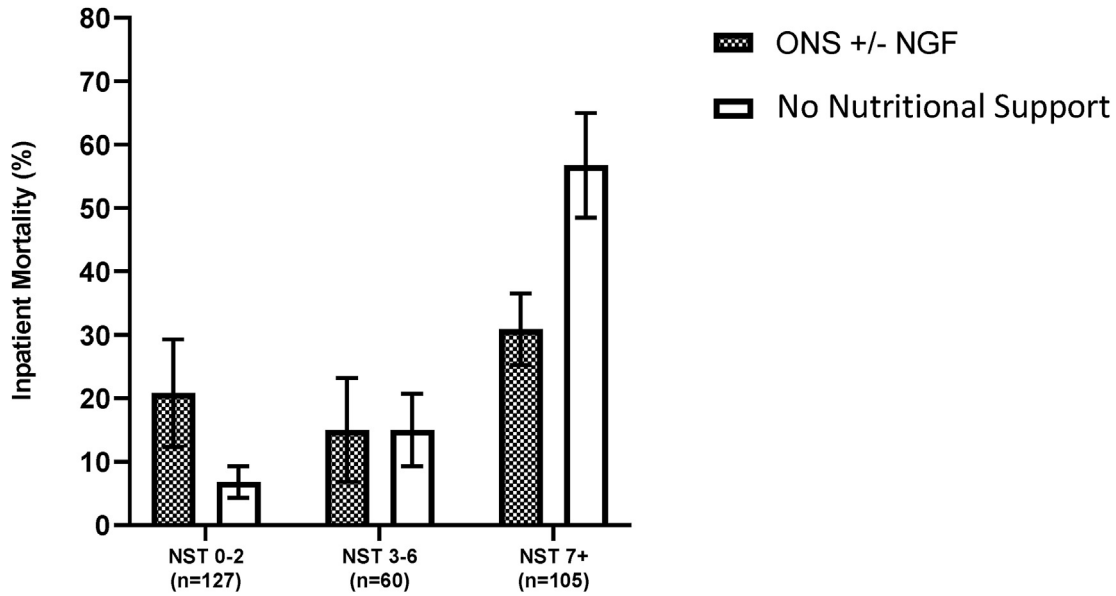|	NST 0—2 (n = 128)	NST 3—6 (n = 61)	NST 7+ (n = 108)
Nutritional Support (%)	n = 27 (21.1%)	n = 23 (37.7%)	n = 70 (64.8%)
ONS alone	18 (14.1%)	19 (31.2%)	47 (43.6%)
NGF alone	1 (0.1%)	1 (1.6%)	5 (4.6%)
PN alone	0	0	0
ONS + NGF	7 (5.4%)	2 (3.3%)	15 (13.9%)
ONS + PN	1 (0.1%)	0	3 (2.8%)
PN + NGF	0	0	0
ONS + PN + NGF	0	1 (1.6%)	0
None	100 (78.7%)	34 (62.3%)	38 (35.2%)

Fig. 8. Mortality between patients prescribed nutritional support (ONS ± NGF) and those not prescribed nutritional support in different nutritional risk groups. Patients on ICU or receiving PN are excluded. Means are plotted with error bars representing standard error of the mean (SEM).

Table 12
Multiple logistic regression showing adjusted odds ratios for predictors of inpatient mortality in the NST 7+ group, excluding those on ICU or receiving PN, n = 105.

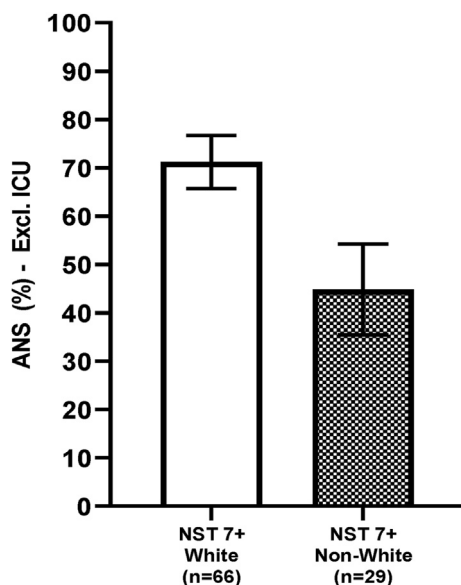| Predictor of Inpatient Mortality	Adjusted Odds Ratio (95% CI) Regression Level 1	Sig.
ONS ± NGF (NST 0—2)	3.20 (0.70—7.58)	Not sig.
ONS ± NGF (NST 7+)	0.26 (0.09—0.69)	<0.01
Age >70	5.77 (1.81—21.15)	<0.01
Cancer	2.41 (0.81—7.49)	Not sig.
AKI/CKD	3.44 (1.13—11.21)	<0.05
HTN	1.617 (0.57—4.61)	Not sig.
Dementia	0.47 (0.14—1.46)	Not sig.
Diabetes	0.76 (0.23—2.45)	Not sig.
Male Gender	1.66 (0.60—4.77)	Not sig.
Chronic Lung Disease	2.21 (0.53—9.58)	Not sig.

Fig. 9. Prescription of nutritional support according to ethnicity in the highest risk nutritional group (NST 7+).

in the control group, highlighting the importance of nutritional status in this disease. Although obesity has been reported as an independent risk factor for disease severity in COVID-19, we did not observe significant differences in mean BMI values between the COVID-19 and control groups. The impact of obesity on COVID-19 outcomes was not the focus of this study.

Despite being extremely vulnerable to COVID-19, those at high nutritional risk were not more likely to be admitted to ICU. This is likely due to poor physiological reserve which could have precluded them from being deemed suitable candidates for aggressive therapy; critically unwell patients with malnutrition are known to have poor outcomes [23], and during a pandemic when ICU beds are extremely limited, they may not have been prioritised for ICU admission. Although moderate nutritional risk on admission was not an independent predictor of inpatient mortality, it was however associated with significantly increased odds of requiring ICU admission. This could be explained by the fact that patients at moderate nutritional risk are likely to be more unwell than those at low nutritional risk, and therefore more likely to require intensive care - yet still having more physiological reserve then those at high nutritional risk, making them generally more suitable ICU candidates.

With regards to follow-up mortality, there were significantly more deaths in the group who were at moderate or high nutritional risk on admission to hospital compared to those at low nutritional risk on admission to hospital. This has not been demonstrated before in the literature for COVID-19. Although statistical significance was achieved in the crude analysis, it was lost in multivariate analysis. However, due to a relatively low number of deaths in the follow-up period it is possible that a larger sample size would have yielded multivariate significance. This is worth further investigation as more attention may need to be placed on the aftercare of undernourished COVID-19 patients in the immediate period post hospital discharge.

We observed that the prescription of oral nutritional supplements and/or nasogastric feeding in the ward-based setting was independently associated with significantly lower mortality in high nutritional risk COVID-19 patients. This group have the most to gain from nutritional support, and this association was not demonstrated in those at moderate or low nutritional risk. Of concern, only two

thirds of our high nutritional risk patients were prescribed some form of nutritional support. This falls short of international guidelines that advise nutritional support should be offered to all patients at risk of malnutrition [24]. This may reflect the pressures on clinical services during the first wave of the pandemic — staff were thinly stretched and under extraordinary workloads and this was compounded by the fact that, at our centre, dieticians were not present on the wards in order to limit staff contact with the SARS-CoV-2 virus. It was found that patients at low nutritional risk who were prescribed oral nutritional supplements and/or nasogastric feeding in fact had significantly higher mortality than those who were not prescribed supplements. This is very unlikely to be the nutritional supplementation increasing their mortality, but rather an observed association which reflects the severity of their underlying illness e.g. dependant on high flow oxygen or CPAP, with nutritional supplementation suggesting they were too unwell to eat normal meals.

Ethnic disparities were also highlighted by our study, with non-white patients at high nutritional risk being significantly less likely to be prescribed nutritional support compared to white patients. They also had fewer referrals made to dieticians, however this was not statistically significant. Further evaluation of this disparity in care is essential going forward. It may relate to a number of factors including cultural perceptions of nutritional supplementation, variations in taste or language barriers.

Limitations of our study included the retrospective design, with inherent risks of missing data points and possible bias. Additionally, this was an association study, limiting assumptions relating to causality between nutritional supplementation and mortality. It is possible that patients receiving nutritional support may have been more likely to also receive other therapeutic interventions, however this is unlikely as during the first wave of the pandemic consensus guidelines on corticosteroids and biologic therapy had not yet been produced. Furthermore, we measured nutritional support via an electronic prescribing and administration system. Therefore even if recorded as prescribed and administered electronically, we cannot guarantee that an oral nutritional supplement was actually consumed by the patient. Finally, although NST 7+ (high nutritional risk) has been internally validated against MUST, low (NST <2) and moderate (NST 3—6) nutritional risk categories have not been validated against internationally recognised scoring systems. Our study was strengthened by the digital collection of consecutive patients which limited data error. Furthermore, only PCR-positive patients were included rather than also including patients in whom a clinical diagnosis was made.

In conclusion, COVID-19 patients were more likely to be older, polymorbid and of non-white ethnic origin. Those at highest nutritional risk experienced more adverse outcomes, however nutritional supplementation was associated with lower inpatient mortality. Follow-up mortality was also higher suggesting the risk of undernutrition in COVID-19 may extend beyond hospital discharge. Taken together, these findings suggest that the identification and treatment of undernutrition in patients with COVID-19 improves clinical outcomes and should not be overlooked in the event of futures waves or pandemics.

5. Statement of authorship

Dr James Bell contributed to study design, database collection, statistical analysis and wrote the manuscript. Dr Nicola Heyer and Dr Alan Greenstein contributed to study design and critical review of the manuscript. Dr Konstantinos Fragkos contributed to study design and statistical analysis. Mr Christopher Baxter-Derrington contributed to database collection. Dr Shameer Mehta devised the project concept, contributed to study design, critical review of the manuscript and was overall project lead.

Financial disclosures

Declaration of competing interest

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