Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Narrative Review

Nutrition risk prevalence and nutrition care recommendations for hospitalized and critically-ill patients with COVID-19

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SUMMARY

Background: Nutritional status is an often-overlooked component in infectious disease severity. Hospitalized or critically ill patients are at higher risk of malnutrition, and rapid assessment and treatment of poor nutritional status can impact clinical outcomes. As it relates to the COVID-19 pandemic, an estimated 5% of these patients require admission to an ICU. Per clinical practice guidelines, nutrition therapy should be a core component of treatment regimens. On account of the urgent need for information relating to the nutritional support of these patients, clinical practice guidance was published based on current critical care guidelines. However, a growing body of literature is now available that may provide further direction for the nutritional status and support in COVID-19 patients. This review, intended for the health care community, provides a heretofore lacking in-depth discussion and summary of the current data on nutrition risk and assessment and clinical practice guidelines for medical nutrition therapy for hospitalized and critically ill patients with COVID-19.

1. Introduction

As of February 14th, 2021, the coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) resulted in 108 million cases and 2.4 million deaths worldwide, with new cases and deaths still being reported [1]. Clinical presentation of COVID-19 at illness onset and over the course of the disease vary from asymptomatic to severe pneumonia with acute respiratory distress syndrome (ARDS), with the most common symptoms being fever, cough, and fatigue [2,3]. Though an individual of any age can contract COVID-19, increasing age and co-morbidities are strong risk factors for severe illness with most patients aged 30–79 years with at least one comorbidity [4,5]. The most commonly reported comorbidities are hypertension, diabetes, and cardiovascular disease (CVD) [3]. Both age and comorbidities are positively associated with disease severity and mortality risk [5]. Overall, approximately 14% of all COVID-19 cases are considered severe and about 5% of all cases and 20% of the hospitalized population require admission to an intensive care unit (ICU) [6].

Multiple chronic diseases or co-morbidities, including diabetes and cardiovascular disease, affect more than 70% of hospitalized adult patients and are often associated with increased risk and prevalence of malnutrition and poorer outcomes [7–9]. The presence of co-morbidities adds complexity to meeting nutritional needs due to the interactions of the diseases, disease state, and nutrition status. In hospitalized patients with co-morbidities, the healthcare team often struggles with prioritizing nutritional management of the primary disease while juggling the underlying nutritional demands of concurrent diseases [8]. Recognizing nutritional risk in these patients is crucial in intervening early to address nutritional needs that may impact outcomes. Similarly, recognizing and treating nutritional risk may play a role in disease severity and outcomes in hospitalized patients with COVID-19 who have multiple co-morbidities. In fact, malnutrition is the leading cause of immunodeficiency and is associated with increased viral infection disease severity, such as in the case of the 1918 influenza pandemic [10,11]. Critically ill hospitalized patients are at higher risk of malnutrition, with 38–78% of patients in the ICU being malnourished; and malnutrition is associated with worse clinical outcomes in the ICU [12]. Despite the obviously

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Abbreviations

ASPEN/SCCM	American Society for Parenteral and Enteral Nutrition/Society of Critical Care Medicine
ARDS	Acute Respiratory Distress Syndrome
BEE	Basal Energy Expenditure
BMI	Body Mass Index
BW	Body Weight
COPD	Chronic Obstructive Pulmonary Disease
COVID-19	Coronavirus Disease 2019
CVD	Cardiovascular Disease
DHA	Docosahexaenoic Acid
HTN	GI Hypertension Gastrointestinal
GLIM	Global Leadership Initiative on Malnutrition
GNRI	Geriatric Nutritional Risk Index
GRV	Gastric Residual Volume
EN	Enteral Nutrition
EPA	Eicosapentaenoic Acid
ESPEN	European Society for Clinical Nutrition and Metabolism
ICU	Intensive Care Unit
IMCU	Intermediate Care Unit
IMV	Invasive Mechanical Ventilation
MNA/MNA-sf	Mini Nutritional Assessment and MNA-short form
MNT	Medical Nutrition Therapy
mNUTRIC	Modified Nutrition Risk in Critically Ill
MUST	Malnutrition Universal Screening Tool
NGT	Nasogastric Tube
NRS-2002	Nutritional Risk Screening 2002
NRI	Nutritional Risk Index
OG	Orogastric
ONS	Oral Nutritional Supplements
PPE	Personal Protective Equipment
PN	Parenteral Nutrition
RU	Rehabilitation Unit
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2

important relationship between nutritional status and clinical outcomes in severely or critically ill COVID-19 patients, the prevalence, severity, and treatment of malnutrition in this population remains to be fully elucidated.

As concluded in a recent scoping review, many gaps exist in the clinical evidence for nutritional management of hospitalized COVID-19 patients [13]. In response to the limited evidence during the rapidly changing circumstances related to COVID-10, many editorials, review articles, and guidance were published using inference to other disease states to guide health care professionals. However, this can be difficult to extrapolate. The phenotype exhibited by acute COVID-19 is unique as characterized by severe hyperglycemia, severe renal failure, increased rate of thrombotic events, and infrastructural problems such as shortage of pumps and lack of protocols. As the scientific literature is rapidly expanding in this population, new data is available that can further guide and improve the nutrition care process and clinical outcomes. The purpose of this review is to summarize recently published evidence and guidance on nutritional status and medical nutrition therapy (MNT) and its relationship to outcomes in hospitalized and critically ill COVID-19 patients following each stage of the nutrition care process.

2. Methods

In order to summarize the current literature, a comprehensive literature search was conducted utilizing available research databases (i.e., PubMed, EBSCO Discovery Service). The following descriptors were used in various combinations: “covid-19”, “sars-cov-2”, “2019-ncov”, “coronavirus”, “covid”, “nutrition”, “nutrition support”, “nutritional care”, “nutritional management”, “nutrition intervention”, “enteral nutrition”, “medical nutrition therapy”, “nutrition assessment”, “diet”, “diagnosis”, “evaluation”, “nutrition screening”, “nutrition monitoring”, “feeding”, “feeds”, “intestinal”, “malnutrition”, “ICU”, and “critical”. This review included pre-prints or publications in English. Relevant articles were then compiled up until the date of manuscript submission (mid-February 2021) for use in this review and duplicates were removed. Due to the evolving nature of COVID-19 and the rapid pace of published literature in this population, articles were not selected on a systematic basis; thus, the reviewed evidence may not be exhaustive.

2.1. Baseline characteristics and comorbidities

2.1.1. Presenting characteristics

Mild symptoms associated with COVID-19 include fever, cough, and fatigue, but it is severe symptoms such as pneumonia and ARDS that likely require hospital and ICU admission [2,3]. Based on the studies reviewed in hospitalized and ICU patients, approximately 30–90% of patients presented with fever. Fever is one sign of the body's acute inflammatory response to COVID-19. During the acute phase of the disease, patients with severe symptoms can experience hypermetabolism leading to subsequent nutrition-related outcomes, such as energy deficit and loss of lean body mass [14]. In addition to metabolic derangements, patients commonly experience nutrition impact symptoms such as reduced food intake, nausea and vomiting, and gastrointestinal (GI) intolerance that further exacerbates nutritional risk [15]. Bedock et al., 2020 reported that GI symptoms, anosmia and/or dysgeusia, and anorexia were present in 28%, 36%, and 62.3% of hospitalized COVID-19 patients, respectively [16]. Similarly, Zhao, et al., 2020 reported GI symptoms in 26% and anorexia in 60% of severe and critically ill COVID-19 hospitalized patients [15]. Complications in critical cases can occur from additional organ failures secondary to the inflammatory response. A retrospective, observational study of critically ill COVID-19 patients admitted to three ICUs in China reported the prevalence of several complications during ICU stay including ARDS (88%), acute myocardial injury (54%), acute liver dysfunction (29%), acute kidney injury (41%), secondary infection (65%), shock (67%), embolization/thrombosis (2%) and pneumothorax (5%) [17]. With both age and comorbidities, level of oxygen impairment at admission and markers of inflammation were most strongly associated with critical illness and mortality from COVID-19 [18]. Data from a New York City cohort showed that 23.6% of patients admitted to the hospital with COVID-19 required invasive mechanical ventilation (IMV) [18]. Among critically ill patients, this percentage was higher with 65.4% ($n = 647$) requiring IMV, of which 60.4% ($n = 391$) died. Complications during COVID-19, such

as acute respiratory failure, can lead to longer length of ICU stay exacerbating loss of muscle mass and mobility, malnutrition, and other adverse outcomes [15,19].

2.1.2. Age and comorbidities

Age and comorbidities are strong predictors of hospitalization, critical illness, and mortality in COVID-19 patients [18]. Nursing homes, which typically house a primarily older adult population, only accounted for 3% of total COVID-19 cases as of December 2020. However, these facilities accounted for 40% of COVID-19 related deaths in the United States [20,21]. One such facility based in Seattle, Washington was essentially ground zero for the COVID-19 pandemic in the United States with one of the earliest outbreaks and deaths reported in March 2020 [22]. From this outbreak, 167 cases were confirmed among nursing home residents with a hospitalization rate of 54% [23]. Table 1 summarizes baseline characteristics and comorbidities from studies of hospitalized COVID-19 patients. Overall, the data show that patients are primarily older adults (>50 years) with multiple comorbidities, most commonly hypertension, cancer, chronic obstructive pulmonary disease (COPD), cardiovascular disease, diabetes, and chronic kidney disease. Similarly, a systematic review conducted mostly in Chinese populations during the early months (January 29, 2020, to February 19, 2020) of the COVID-19 pandemic, reported the most common comorbidities included hypertension, cardiovascular diseases, diabetes mellitus, smoking, COPD, malignancy, and chronic kidney disease [24]. Early in the pandemic (March 1, 2020 to April 8, 2020), several hospitals in New York City with a combined 5700 patients hospitalized with COVID-19, reported a mean age of 63 years in a primarily male population (60%) with the most common comorbidities including hypertension (57%), obesity (42%), and diabetes (43%) [4]. This cohort had a median Charlson Comorbidity Score of 4, indicating a high comorbidity burden. In an Italian cohort of 2653 patients who tested positive for COVID-19, after adjusting for age and comorbidities, patients >80 years had a higher risk of hospitalization compared to those aged <50 years [25]. Males had a higher risk of hospitalization (HR 1.4 95% CI 1.2 to 1.6) and more comorbidities than females, according to Charlson Comorbidity Index. Hypertension, cancer, and diabetes were the single most common co-morbidities, and all associated with high (>50%) rates of hospitalization. COPD, chronic kidney disease, and heart failure were most strongly associated with risk of hospitalization. Prevalence of hospitalized older patients with comorbidities diagnosed with COVID-19 are common in countries with a higher older population. However, in Morocco, where the population represents a primarily younger demographic with only 7.4% > 65 years of age, the average age reported in a sample of patients (n = 41) entering a step-down unit from the ICU was 55 years [26]. Diabetes, hypertension, and overweight/obesity represented 43.9%, 34.1%, and 48.9% of comorbidities, respectively. The increased prevalence of chronic disease in this COVID-19 cohort coming from the ICU reflects the increasing number of chronic diseases with 21% of the Moroccan population having at least one chronic disease.

2.1.3. Prevalence of obesity

Obesity is another highly prevalent comorbidity reported in this population and is an important risk factor for malnutrition and critical illness in hospitalized COVID-19 patients. The European Society for Clinical Nutrition and Metabolism (ESPEN) COVID-19 guidance recommends that obese individuals, especially older adults with multiple comorbidities, should be screened for nutritional risk [7]. Obesity was reported in 25%, 30.8%, and 41.7% of hospitalized COVID-19 patients in studies conducted in France, Italy, and the United States, respectively [4,16,19]. These prevalence rates are slightly higher than non-hospitalized general population in France (23%), Italy (20%) and the United States (40%) [27]. Additionally, 2016 data in the general non-hospitalized worldwide population show 39% of adults aged ≥18 years overweight and 13% obese [28]. While age is an important risk factor for disease severity in COVID-19 disease, the presence of obesity could result in more severe disease in younger patients [29]. In a cohort of 265 patients in the United States, there was a significant inverse correlation between age and BMI with patients admitted to the hospital more likely to be obese (P = 0.0002). Prevalence of combined overweight and obesity is even higher ranging from 48 to 70% in hospitalized patients and increases in critically ill patients [15,19]. In China, overweight/obesity (BMI > 24 kg/m^2) was reported in 43% and 49% of severe and critically ill patients, respectively. In an Italian cohort, overweight/obesity was reported in 76.1% of critically ill ICU patients compared to 61.9% in sub-intensive care units (sub-ICU) and 46.1% in intermediate care units (IMCU) [30]. Di Fillipo et al., 2020 reported that overweight or obesity was associated with a 2-fold increased risk of hospitalization compared to normal or underweight [19]. Similarly, compared with normal weight patients, those with obesity had an increased risk of developing a severe COVID-19 case. Severe COVID-19 cases were defined as significantly increased respiration rate of ≥30 times/minute, hypoxia, partial pressure of oxygen/fraction of inspired oxygen ≤300 mmHg or respiratory or other organ failure that required intensive care unit monitoring and treatment, or shock [31]. Abdominal obesity specifically may be a contributing risk factor for critical illness in patients with COVID-19. In a meta-analysis of 6 studies including 560 COVID-19 patients, those in the ICU had higher visceral adipose tissue mass than patients in the general ward (pooled mean difference = 0.46, 95% CI: 0.20, 0.71, P < 0.001) [32]. Patients requiring IMV had higher visceral adipose tissue mass than patients not requiring IMV (pooled mean difference = 0.38, 95% CI: 0.05, 0.71, P = 0.026). A retrospective cohort study of adult patients with COVID-19 hospitalized from the emergency department observed that obesity (≥30 kg/m^2) was associated with an increased risk of death or intubation, as well as increased risk of death in those under IMV in patients aged < 65 years independent of other comorbidities [33]. In a systematic review of data showing the association between obesity and outcomes in COVID-19, a higher mortality rate was observed among obese COVID-19 patients as compared to non-obese COVID-19 patients [34]. More severe outcomes related to COVID-19 in obese/overweight patients could be related to the immune activation as a result of adipose tissue expansion increasing the release of inflammatory proteins which may contribute to the cytokine storm that occurs in critically ill patients [35]. On the other hand, the presence of underweight is low, ranging from 2 to 10% in patients hospitalized with COVID-19 from 6 published studies [15,16,19,26,30,36]. However, underweight (defined by a BMI < 20 kg/m^2) was higher in a Chinese cohort of 523 hospitalized patients with critically ill ICU patients more likely to be underweight (46.9%) compared to critically ill non-ICU patients (22.5%) [37].

2.1.4. Prevalence of weight loss

While the data show a high prevalence of overweight and obesity in hospitalized patients with COVID-19 upon admission, especially critically ill patients, a significant amount of weight loss is also observed (Table 2). Significant weight loss is used as part of diagnosing moderate to severe malnutrition and is defined by Global Leadership Initiative on Malnutrition (GLIM) as ≥ 5–10% weight loss within the previous 6 months or ≥ 10% beyond 6 months [38,39]. A one-day clinical audit of hospitalized COVID-19 patients in Italy found that 52% of patients experienced ≥5% weight loss within the past month [30]. When broken down by hospital unit, 81.5%, 66.7%, 47%, 36.5% of COVID-19 patients lost

Table 1
Selection of studies reporting baseline comorbidities and characteristics of hospitalized COVID-19 patients.

Patient Population				Baseline Comorbidities									Presenting Characteristics						Reference
Country	Total Subjects, n	Sex, female (%)	Age, median (IQR)	Obesity (%)	HTN (%)	CVD (%)	Diabetes (%)	Renal Disease (%)	Liver Disease (%)	Malignancy (%)	Smokers, ever (%)	COPD (%)	ICU Admission (%)	Fever (%)	Mechanical Ventilation (%)	GI Symptoms (%)	Anosmia, hyposmia, hypogeusia or dysgeusia (%)	Anorexia (%)	
China	523	52.1	52.2 (NA) mean	NR	25	7.3	18	NR	NR	NR	NR	NR	40.3	NR	NR	NR	NR	NR	Li 2020 [37]
China	413	48.6	60.31 (NA) mean	44 (ov/ob)	28	10.7	11.4	2.2	NR	6.5	NR	3.9	NR	82	0.7	26	NR	60	Zhao 2020 [15]
China	182	64.3	68.5 (NA) elderly group	NR	15.9	10.4	28	NR	NR	NR	NR	8.24	NR	NR	NR	NR	NR	NR	Li 2020 [46]
China	123	51.3	68 (56.5−78)	NR	45.5	17.1	21.9	8.1	NR	4	NR	10.5	40.7	61.7	NR	Vomiting: 1.6 Diarrhea: 8.1	NR	NR	Wang 2020 [61]
China	41	73.2	49 [41−58]	NR	15	15	20	NR	2	2	7 (current)	2 (COPD only)	31.7	98	10	NR	NR	NR	Huang 2020 [2]
France	114	39.5	59.9 (NA) mean	25	52.6	20.4	38.6	20.2	NR	8.3	6.7 (current)	7 (COPD)	15.8 (admit FROM ICU)	89.4	NR	28	Anosmia or dysgueusia: 36	62.3	Bedock 2020 [16]
Italy	268	45.1	74 (63−84)	51 (ov/ob)	NR	27.2	22.4	21.3	8.6	20.9	5.2	20.9	17.2	NR	11.2	NR	NR	NR	Pironi 2020 [30]
Italy	156	28.8	61 (53−69)	70.4 (ov/ob)	36	6.6	12.9	3.2	NR	1.3	NR	3.2 (COPD only)	3.2	50	NR	NR	Hyposmia: 37.4 Hypogeusia: 45	NR	di Filippo 2020 [19]
Morocco	41	48.8	55 (NA) mean	48.8 (ov/ob)	34.1	NR	43.9	NR	NR	NR	NR	4.9 (asthma)	75.6 (discharged)	NR	12.2	NR	NR	NR	Haraj 2020 [26]
USA	5700	39.7	63 (52−75)	41.7	56.6	18	33.8	8.5	0.6	6.0	16.6	17.3	22.5	30.7	20.2	NR	NR	NR	Richardson 2020 [4]
France	108	40.7	61.8 (NA) mean	NR	55.6	NR	41.7	NR	NR	NR	NR	NR	13	NR	NR	Diarrhea: 17.8 Nausea/ vomiting: 14.8	Olfactory/ gustatory dysfunction: 12.1	NR	Allard 2020 [53]
China[a]	211	43.6	48.9 (NA) mean	NR	31.1	6.7	20.9	NR	NR	NR	NR	NR	100	NR	NR	NR	NR	NR	Li 2020 [37]
China[a]	136	36.8	69 (57−77)	NR	50	19	41	4	1	6	NR	9 (COPD)	100	91	66	21	NR	NR	Zhang 2020 [17]

Abbreviations: Cardiovascular Disease (CVD), Chronic Obstructive Pulmonary Disease (COPD), Gastrointestinal (GI), Hypertension (HTN), Interquartile Range (IQR), Not Applicable (NA), Not Reported (NR), overweight (ov), obese (ob).

[a] Indicates information reported from ICU-only population.

Table 2
Prevalence of nutritional risk and malnutrition in hospitalized COVID-19 patients.

Population Characteristics			Nutrition Risk Assessment					Malnutrition Diagnosis and Classification			Reference
Country	Hospital Population	Timing	Weight loss	Underweight/ BMI <18.5 kg/ m^2	Albumin, mean (g/ L)	Nutritional Risk	Risk Screening Tool(s)	Malnutrition Diagnosis	Severity	Criteria	
France	Non-Critical (admitted to medical unit from ICU or first line of care to medical unit from ICU or first line treatment)	After transfer from ICU or first line of care to medical unit	≥5% BW: 41.2% >10% BW: 18%	6.2% (BMI<20 kg/ m^2 and age <70 or <18.5 kg/m^2 and age 70)	30.1	NR	NR	42.1%	None: 57.9% Moderate: 23.7 Severe: 18.4	GLIM	Bedock 2020 [16]
China	Critical (ICU)	Upon admission to hospital unit	NR	46.9% (<20.5)	36	None/low: 61.1% Severe: 38.9%	NRS-2002, NUTRIC	NR	NR	NR	Li 2020 [37]
China	Critical (non-ICU)	Upon admission to hospital unit	NR	22.5% (<20.5)	41	NR	NR	NR	NR	NR	Li 2020 [37]
China	Severe	Within 48 h of admission	NR	4%	31.1	None/low: 9% Moderate: 84% Severe: 7%	NRS-2002	NR	NR	NR	Zhao 2020 [15]
China	Critical	Within 48 h of admission	NR	3%	28.4	None/low: 0 Moderate: 38% <Severe: 62%	NRS-2002	NR	NR	NR	Zhao 2020 [15]
Italy	Hospitalized (ICU, sub-ICU, IMCU, RU)	During hospital stay	≥5% BW: 52%	9.3%	29.8	None/low: 22.7% Moderate/ severe: 77.2%	NRS-2002 (adapted for COVID-19)	49.7% (CRP>0.5 mg/ dL)	None: 50.3% Moderate/ severe: 29.8% (CRP>5 mg/ dL)	GLIM (Adapted for COVID-19)	Pironi 2020 [30]
Italy	Critical (ICU)	During hospital stay	≥5% BW: 66.7%	4.5%	28.2	None/low: 4.3% Moderate/ severe: 95.7%	NRS-2002 (adapted for COVID-19)	70% (CRP>0.5 mg/ dL)	None: 30% Moderate/ severe: 70% (CRP>5 mg/ dL)	GLIM (Adapted for COVID-19)	Pironi 2020 [30]
Italy	Critical (sub-ICU)	During hospital stay	≥5% BW: 47%	2%	30.2	None/low: 14.3% Moderate/ severe: 85.7%	NRS-2002 (adapted for COVID-19)	27.8% (CRP>0.5 mg/ dL)	None: 72.2% Moderate/ severe: 11.1% (CRP>5 mg/ dL)	GLIM (Adapted for COVID-19)	Pironi 2020 [30]
Italy	Non-Critical (IMCU)	During hospital stay	≥5% BW: 36.5%	9.7%	30.4	None/low: 32.7% Moderate/ severe: 67.3%	NRS-2002 (adapted for COVID-19)	50% (CRP>0.5 mg/ dL)	None: 50% Moderate/ severe: 32.9% (CRP>5 mg/ dL)	GLIM (Adapted for COVID-20)	Pironi 2020 [30]
Italy	Non-Critical (RU)	During hospital stay	≥5% BW: 81.5%	13.2%	29.5	None/low: 7.7% Moderate/ severe: 92.3%	NRS-2002 (adapted for COVID-19)	48.4% (CRP>0.5 mg/ dL)	None: 51.6% Moderate/ severe: 6.5% (CRP>5 mg/ dL)	GLIM (Adapted for COVID-20)	Pironi 2020 [30]
China	Non-Critical	Upon admission	NR	NR	34.1	Moderate/ severe: 27.5%	MNA	52.7%	NR	MNA	Li 2020 [30]
China	Critical and Non-Critical	Medical records	NR	5%	NR	None/low: 14.9%, 58.9%, 22.7%, 28.4% Moderate/ severe: 85.1%, 41.1%, 77.3%, 71.6%	NRS-2002, MUST, MNA-sf, NRI	NR	NR	NR	Liu 2020 [36]

Table 2 (*continued*)

Population Characteristics			Nutrition Risk Assessment					Malnutrition Diagnosis and Classification			Reference
Country	Hospital Population	Timing	Weight loss	Underweight/ BMI <18.5 kg/ m^2	Albumin, mean (g/ L)	Nutritional Risk	Risk Screening Tool(s)	Malnutrition Diagnosis	Severity	Criteria	
China	Critical (ICU)	Medical records	NR	NR	NR	None/low: 39% Severe: 61%	MUST	NR	NR	NR	Zhang 2020 [17]
Italy	Non-Critical (Admitted to ED and hospitalized, includes ICU)	At admission to emergency department	≥5% BW:31% >10% BW: 9.6%	1.9%	NR	82.8%	MNA	64.3%	NR	MNA	Di Fillipo 2020 [19]
Morroco	Admitted to endocrin ology unit from the ICU	At admission to endocrinology unit from ICU	≥5% BW: 44% >10% BW: 15%	7.31%	NR	None/low: 19.5% Moderate/ severe: 65.9%	MNA	14.6%	NR	MNA	Haraj 2020 [26]
France	Hospitalized non-severe	During hospital stay	≥5% BW within 1 month: 33.8% >10% BW within 6 months: 9%	1.4% (≤21 kg/ m^2 if age ≥ 70 years)	31.9	Absent: 20% Moderate: 53.8% Severe: 26.2%	NRI	33.8%	Absent: 66.2% Moderate: 25.7% Severe: 8.1%	Severe: BMI ≤ 17 kg/m^2 (or ≤ 18.5 kg/m^2 ≥ 70 years) and/or weight loss > 10% (1 month) and/or > 15% (6 months). Moderate malnutrition: BMI 17.0–18.5 kg/m^2 (or 18.5 –21.0 kg/m^2 ≥ 70 years) and/ or weight loss 5–10% (1 month) and/or 10–15% (6 months).	Allard 2020 [53]
France	Hospitalized severe	During hospital stay	≥5% BW within 1 month: 44.1% >10% BW within 6 months: 13.8%	11.5% (≤21 kg/m^2 if age ≥ 70 years)	29	Absent: 6.1% Moderate: 39.4% Severe: 54.5%	NRI	50%	Absent: 50% Moderate: 32.4% Severe: 17.6	Severe: BMI ≤ 17 kg/m^2 (or ≤ 18.5 kg/m^2 ≥ 70 years) and/or weight loss > 10% (1 month) and/or > 15% (6 months). Moderate: BMI 17.0–18.5 kg/ m^2 (or 18.5–21.0 kg/m^2 ≥ 70 years) and/or weight loss 5 –10% (1 month) and/or 10 –15% (6 months).	Allard 2020 [53]

Abbreviations: Body Weight (BW), Emergency Department (ED), Global Leadership Initiative on Malnutrition (GLIM), Not Reported (NR), Nutritional Risk Screening 2002 (NRS-2002), Mini Nutritional Assessment (MNA), MNA-short form (MNA-sf), Malnutrition Universal Screening Tool (MUST), Nutritional Risk Index (NRI), modified Nutrition Risk in the Critically ill (mNUTRIC), Rehab Unit (RU), Intermediate Care Unit (IMCU), Sub Intensive Care Unit (sub-ICU), Intensive Care Unit (ICU).

≥5% initial body weight within the past month in the rehabilitation unit (RU), ICU, sub-ICU, and IMCU, respectively. These data indicate that more prevalent weight loss is dependent upon the disease severity prevalent in the unit and length of hospital stay. Other studies report a high prevalence of weight loss over the course of hospitalization with 31–44% of hospitalized patients experiencing ≥5% weight loss and 9.6–18% experiencing ≥10% weight loss [16,19]. According to ESPEN, weight loss in the presence of chronic disease-related malnutrition occurring at the same time as inflammation is synonymous with cachexia [40]. Cachexia is characterized by metabolic abnormalities due to underlying disease that results in muscle loss with or without loss of fat mass recognized as weight loss in adults. According to the 2008 definition of cachexia by the Society of Cachexia and Wasting Disorders, patients with weight loss ≥5% of total body weight along with reported impaired functional status, loss of appetite, and inflammation meet the definition of cachexia [41]. Hospitalized COVID-19 patients experience many of the factors that define cachexia, including significant weight loss, impaired functional status, loss of appetite, and inflammation [14–16,26]. A recent review of three papers including 589 patients reports 37% of hospitalized COVID-19 patients had cachexia which was correlated with elevated C-reactive protein, impaired renal function, and longer duration of illness [42]. Underweight status (defined as < 18 kg/m^2) was reported in only 4% of patients from 7 studies including 6661 patients indicating that initial weight status in this population alone may be insufficient; thus, monitoring of weight loss is important to identify nutritional risk. Cachexia caused by COVID-19 may contribute to the worse outcomes reported in the older demographic of patients who are already at risk of age-related muscle loss [38].

2.2. Nutritional screening and nutritional risk in COVID-19

Given the prevalence of weight loss and obesity in the hospitalized COVID-19 patient population, it is critical to identify those patients at nutritional risk for timely implementation of nutrition intervention. However, nutrition risk screening and assessment in hospitalized patients, especially early in the COVID-19 pandemic, posed several challenges as highlighted by Mulherin DW et al., 2020 [43]. Mainly, a limited supply of personal protective equipment (PPE) made it difficult for clinicians including dietitians to the enter rooms of patients in isolation to collect screening and assessment data. Entrance to patient rooms was often limited to one healthcare professional, so dietitians were often reliant on other healthcare providers, or family members, or medical history to collect relevant information. Guidance for nutritional care of the critically ill COVID-19 patient released April 1, 2020 by the Society of Critical Care Medicine (SCCM) and the American Society for Parenteral and Enteral Nutrition (ASPEN) highlights the importance of cluster or bundling care to limit healthcare provider contact [44]. Additionally,

this guidance recommends following PPE recommendations to limit exposure while documenting nutrition assessment findings including how information was obtained. ASPEN/SCCM guidance recommends adhering to institutional guidelines when conducting bedside nutritional assessments while working with available data and collaborating with the care team.

Due to the need for guidance on implementing the nutrition care process in this population, ESPEN also released guidance on the nutritional management of the COVID-19 ICU patient including screening and assessment based on current guidelines, evidence, and best practice applied to similar populations at risk for malnutrition [7]. ESPEN guidance recommends that high-risk COVID-19 hospitalized patients be screened using Nutritional Risk Screening 2002 (NRS-2002) criteria based on the body of evidence supporting its validation and use in general clinical practice and applicability to conditions of malnutrition risk or specific disease states [7]. Those that are considered at high nutrition risk often present with co-morbidities and are typically older adults who may already be experiencing age-related sarcopenia, decreased functional capacity, and other nutritional issues. Recently, several studies evaluated the efficacy of various nutrition risk screening tools in the ICU and hospitalized, elderly COVID-19 population. The modified nutrition risk in critically ill (mNUTRIC) score was found to be a good tool for identifying nutrition risk in a Chinese cohort of COVID-19 patients [17]. In 136 critically ill COVID-19 patients (median age of 69 years) admitted to the ICU, a high nutrition risk (mNUTRIC score > 5) was observed in 61% of patients. Mortality after 28 days in the ICU was higher in patients at high nutritional risk compared to those at lower nutritional risk (adjusted HR = 2.01,95% CI: 1.22–3.32, P = 0.006). Although the prevalence of comorbidities was similar between nutritional risk groups, compared to survivors, non-survivors had significantly more co-morbidities and a higher mNUTRIC score. In a recent systematic review of nutrition risk screen tools in older adults with COVID-19, the NRS-2002, the Mini Nutritional Assessment (MNA), the MNA-short form (MNA-sf), the Malnutrition Universal Screening Tool (MUST), the Nutritional Risk Index (NRI), the Geriatric NRI (GNRI), and mNUTRIC score were assessed in a total of 4 studies [45]. Nutritional risk was highly prevalent regardless of the screening tool utilized with prevalence ranging from 27.5% (MNA) to 100% (GNRI) in patients between aged 65–87 years. The NRS-2002, MNA, MNA-sf, NRI, and MUST all demonstrate high sensitivity, but the MUST demonstrated better specificity while the MNA and MUST demonstrated better criterion validity. The MNA-sf was better at predicting validity for poor appetite and weight loss while the NRS-2002 demonstrated better predictive validity for prolonged hospitalization. The mNUTRIC score, which was developed specifically for ICU patients, demonstrated good predictive validity for ICU-related complications and mortality after 28 days hospitalization. None of the tools were identified as the preferred nutrition risk screening tool for use in the older COVID-19 population. Table 2 summarizes studies reporting prevalence of malnutrition risk using various screening tools in hospitalized COVID-19 patients.

2.2.1. Assessment and prevalence of malnutrition

A review of available data in hospitalized COVID-19 patients showed a high prevalence of malnutrition (14–70%) across studies depending on patient population (Table 2). ESPEN guidance for this patient population does not specify a malnutrition assessment tool but encourages the use of validated tools including Subjective Global Assessment criteria, the MNA criteria validated for geriatric patients, the NUTRIC score criteria for ICU patients, and GLIM (Global Leadership Initiative on Malnutrition). Several studies report the prevalence of malnutrition in hospitalized COVID-19 patients using various diagnostic tools. In a Chinese cohort of hospitalized elderly patients (>65 years) (n = 182), 27.5% were at risk for malnutrition while 52.7% were malnourished according to the MNA tool [46]. Regression analysis revealed that diabetes, low calf circumference, and low albumin were independent risk factors for malnutrition. In a one-day audit of an Italian cohort, 77% of hospitalized elderly patients (>64 years) with COVID-19 (n = 268) were at nutritional risk (modified NRS-2002 score) and 49.7% malnourished (GLIM criteria) with the prevalence higher for both in the ICU compared to the RU [30]. Moderate to severe malnutrition as defined by GLIM criteria and CRP >5 mg/dL, was more prevalent in the ICU (70%) followed by IMCU (32.9%) and sub-ICU (11.1%). Mean weight loss was reported at 5.3% of initial body weight with 52% of patients losing ≥5% BW after one month of hospitalization. Prevalence of malnutrition identified with GLIM criteria was similarly high (42.1%) in patients in a non-intensive medical unit in France (mean age 59.9 years), with 23.7% and 18.4% having moderate and severe malnutrition, respectively [16]. In patients transferred to the ICU, malnutrition was higher (66.7%) with severe malnutrition present in 38.9% of patients. In a cohort of hospitalized ICU COVID-19 patients in Morocco, diagnosed malnutrition and nutritional risk was present in 14.6% and 65.9%, respectively while 69% experienced weight loss and 24% had weight loss greater than 10% [26].

2.2.2. Nutritional risk, malnutrition, and relationship to outcomes

Nutritional risk and malnutrition in hospitalized and ICU patients with COVID-19 is common due to several reasons including hypermetabolism caused by inflammation, reduced food intake, mechanical ventilation, GI intolerance, and other contraindications to nutrition support. Poor nutritional status is linked to worse outcomes in hospitalized COVID-19 patients, including mortality and increased length of stay. In a retrospective study in China, nutritional risk, evaluated by mNUTRIC and NRS-2002 score, was an independent predictor of mortality risk and duration of ICU and hospital length of stay [37]. Average length of stay in the ICU for survivors was 6 days as compared to 13 days for non-survivors. Risk of death in the ICU increased 20% for each point increase in mNUTRIC score. Similarly, high nutritional risk (mNUTRIC) identified at ICU admission was associated with higher 28-day mortality in the ICU compared to those at lower nutritional risk [17]. In another cohort in China, critically ill patients and those with higher NRS-2002 score had a higher risk of mortality and longer stay in hospital [15]. There was a 1.23-fold increase in mortality risk for every 1-unit increase in NRS-2002 (adjusted odds ratio, 2.23; 95% CI, 1.10–4.51; P = 0.026). Using MNA, poor nutritional status was associated with a length of hospital stay >5 days and lymphopenia [26]. Older, hospitalized COVID-19 patients with nutritional risk evaluated by several tools (NRS 2002, MNA-sf, and NRI) had significantly longer lengths of stay, higher hospital expenses, poorer appetite, increased disease severity, and greater weight change compared to patients without nutritional risk [36]. Disease duration was an independent predictor of weight loss in hospitalized and non-hospitalized patients, while length of stay was an independent predictor of weight loss in hospitalized patients [19]. When patients with and without weight loss were compared, those with weight loss had greater systemic inflammation (C-reactive protein levels), worse renal function, and longer length of stay. Longer length of stay in hospitalized and critically ill patients is an indicator of disease severity, including heightened inflammation, with subsequent loss of weight due to increased energy requirements, reduced mobility, and contraindications to meeting nutritional needs. Historically, albumin levels have been used as a biochemical marker of nutrition status. However, a recent publication, approved by ASPEN, argues that albumin is an indicator of inflammation, not malnutrition [47]. Albumin levels decline during the acute phase inflammatory response due to alterations in

visceral protein homeostasis regardless of nutritional status. Critical illness with inflammation, such as during severe COVID-19, results in reprioritization of hepatic protein synthesis, lowering albumin levels. Hypoalbuminemia may result in interstitial edema which could lead to poor outcomes such as tissue damage, delayed wound healing, impaired GI function and is commonly associated with post-surgical complications [48,49]. Therefore, albumin is more closely associated with poor outcomes rather than as an indicator of nutrition status [47–49]. Rather albumin can be regarded as an inflammatory marker associated with nutritional risk that must be taken into context during nutrition assessment to identify patients at risk for poor outcomes rather than used to define malnutrition. Consistent with other published literature in hospitalized patients with COVID-19, serum albumin concentrations of ≤35 g/L were associated with decreased survival [37]. Bedock et al., 2020 reported that lower albumin concentrations at admission were associated with a higher risk of ICU transfer independent of age and CRP levels [16]. These findings are consistent with Liu et al., 2020, who observed that a difference of 10 g/L in baseline albumin concentrations was associated with a 5-fold increase in ARDS and a 2-fold increase in mortality [50]. As such, the inflammatory nature of COVID-19 may result in increased prevalence of nutritional risk, especially in high risk elderly patient populations and those with comorbidities. Therefore, albumin levels should be used in the context of the inflammatory nature of COVID-19 to identify those patients who may be most at risk of poor outcomes if nutrition intervention is not provided.

2.3. Nutrition intervention for hospitalized COVID-19 patients

2.3.1. Timing of nutrition intervention

To summarize recent guidance for implementing nutritional intervention in critically ill COVID-19 patients, we reviewed expert COVID-19 guidance (ESPEN, ASPEN/SCCM, etc.) which utilize current guidelines and recommendations, as well as current best practices and published scientific literature. Most expert guidance recommends earlier feeding (within 24–48 h of ICU admission), prioritizing EN versus PN, unless contraindicated [7,44,51,52]. Specifically, ESPEN guidance for COVID-19 ICU patients recommends feeding within 48 h of ICU admission while ASPEN/SCCM recommends EN provided within 24–36 h admission to ICU or within 12 h of intubation and placement on IMV [7,44]. However, nutrition intervention support, regardless of timing, may not be implemented according to the guidelines in this population. Zhao et al., 2020 reported that out of 342 severely and critically ill patients with NRS-2002 score ≥3, only 25% received nutrition support [15]. Among critically ill patients, nutrition support was only provided to 46% of patients with higher nutritional risk. Timing of nutrition support is also a key consideration for proper implementation. A multicenter, retrospective study in China compared early (≤48 h) versus later (>48 h) start of nutrition therapy in COVID-19 survivors and non-survivors in the ICU [37]. Initiation of early nutrition support within 48 h was more prevalent in survivors (81.9%) compared to non-survivors (37.9%). However, after adjusting for variables such as age, gender, BMI, and medical history, there was no difference in risk of hospital death in those who received nutrition support or those who received early versus later nutrition support.

2.3.2. Delivery of nutrition support in Hospital/ICU

Both ASPEN/SSCM and ESPEN highlight nutrition intervention recommendations based on the stage and type of respiratory therapy implemented in COVID-19 patients [7,44]. In non-intubated patients, ESPEN encourages oral feeding over EN or PN, unless contraindications exist. One study reports medical nutrition therapy support, just after implementation of a protocol from the French-speaking Society for Clinical Nutrition and Metabolism (SFNCM) COVID-19 guidance, in patients hospitalized with either severe or non-severe COVID-19 who did not meet criteria for ICU admission [53]. One of the identifiers of severe COVID-19 infection was the need for nasal oxygen flow at or above 6 L per minute. Patients diagnosed with moderate malnutrition or food intake between 50 and 75% usual intake for a week were prescribed two servings of oral nutritional supplements (ONS) in addition to meals plus supplementation with a multivitamin, magnesium, phosphorus, vitamin B9, B1, and D. In patients with severe malnutrition or when food intake was below 50% usual intake, EN was provided or at least three servings of ONS if respiratory status contraindicated EN. Intravenous supplementation of micronutrients was also provided. ONS and EN was prescribed to 82.2% and 8.8% of patients with severe COVID-19 infection, respectively. Less patients with non-severe COVID-19 infection received oral supplements (55.4%) with none receiving EN. The study did not report outcomes related to the nutrition care protocol, but rather evaluated the impact of malnutrition and nutritional risk on outcomes. Nutritional risk was very prevalent (moderate: 49.0%; severe: 35.7%) and associated with severe COVID-19 infection.

COVID-19 patients in the ICU often require invasive or non-invasive ventilation or experience other contraindications to oral feeding which may impact outcomes [7,44]. This is consistent with published papers of hospitalized patients with COVID-19, where reports of oral feeding are generally low (Table 3). Intake of ≤50% of hospital diet was reported in 39% of hospitalized COVID-19 patients with a higher prevalence in ICU (89%) and IMCU (33%) [30]. In general, oral intake was positively associated with degree of appetite (absent, decreased, or normal) and negatively associated with invasiveness of oxygen therapy, GI symptoms, and frailty/disability. Nil per os (nothing by mouth) was reported in 73.8% of ICU patients compared to 23% in the overall hospitalized population. The use of ONS was lower in ICU patients (2.2%) compared to sub-ICU (9.5%), RU (7%), and IMCU (3.7%) patients. The use of EN or PN was highest in the ICU population (69.6% and 23.9%, respectively). A multicenter, retrospective study comparing survivors to non survivors in the ICU observed that initial nutrition therapy with ONS was low in both groups, but higher in survivors (7.8%) compared to non-survivors (4.2%) [37]. A higher percentage of non-survivors also received PN (62.1%) compared to survivors (10.3%), reflecting the increased severity of the disease. Initial nutrition support using EN was also more prevalent in survivors (29.3%) compared to non-survivors (12.6%). Zhao et al., 2020 reports that compared to severely ill patients, a higher proportion of critically ill patients received PN or EN plus PN [15].

2.3.3. Nutrition support during non-invasive ventilation

During non-invasive ventilation, both ASPEN/SCCM and ESPEN recommend PN consideration since airway complications may occur as a result of nasogastric tube (NGT) placement as well as the increased risk of aerosolization putting the healthcare team at risk of virus transmission [7,44]. This delay in EN feeding could lead to inadequate implementation of nutrition intervention, especially during the first 48 h of ICU admission, compromising nutritional status. According to ESPEN, patients receiving flow nasal cannula or high flow nasal cannula support may resume oral feeding unless nutritional needs are unmet, then ONS or EN should be considered [7]. If EN is used to supplement during non-invasive ventilation, then smaller-bore nasoenteric feeding tubes (<12 Fr; primarily used for intestinal feeding) can be considered to improve seal of the mask [44].

Table 3
Summary of published literature reporting nutritional interventions in hospitalized COVID-19 patients.

Patient Population				Nutrition Therapy						Other	Reference
Country	Study Design	Hospital Ward Population	Total Subjects (N)	Any Nutritional Support (%) - NOT hospital diet	No nutritional support (due to contraindications)	ONS (%)	EN (%)	PN (%)	EN + PN (%)	Propofol (%)	
China	Multicenter retrospective observational	Critical (ICU)	211	NR	NR	6.2 (initial therapy mode)	21.8 (initial therapy mode)	33.6 (initial therapy mode)	NR	NR	Li 2020 [37]
China	Retrospective	Non-Critical	73	NR	NR	NR	NR	8.6	NR	NR	Wang 2020 [61]
China	Retrospective	Critical	67	NR	NR	NR	NR	86	NR	NR	Wang 2020 [61]
China	Retrospective, observational	Severe	346	20.3	NR	NR	13	8.1	1	NR	Zhao 2020 [15]
China	Retrospective, observational	Critical	61–66	45.9	NR	NR	23	31.1	8.2	NR	Zhao 2020 [15]
Italy	One-day clinical audit	Hospitalized (ICU, sub-ICU, IMCU, RU)	268	NR	NR	6	12.7	4.8	10.9	0	Pironi 2020 [30]
Italy	One-day clinical audit	Critical (ICU)	46	NR	NR	2.2	69.6	23.9	10.9	43.5	Pironi 2020 [30]
Italy	One-day clinical audit	Critical (sub-ICU)	21	NR	NR	9.5	0	0	0	0	Pironi 2020 [30]
Italy	One-day clinical audit	Non-Critical (IMCU)	162	NR	NR	3.7	1.2	1.2	0	0	Pironi 2020 [30]
Italy	One-day clinical audit	Non-Critical (RU)	39	NR	NR	7	0	0	0	0	Pironi 2020 [30]
China	Retrospective, observational	Critical (ICU)	136	NR	11	NR	57	10	22	NR	Zhang 2020 [17]
France	Retrospective, observational	Non-severe (Hospitalized, not ICU)	74	NR	NR	55.4	0	0	NR	NR	Allard 2020 [53]
France	Retrospective, observational	Severe (Hospitalized, not ICU)	34	NR	NR	82.4	8.8	0	NR	NR	Allard 2020 [53]

Abbreviations: Enteral Nutrition (EN), Parenteral Nutrition (PN), Not Reported (NR), Rehab Unit (RU), Intermediate Care Unit (IMCU), Sub Intensive Care Unit (sub-ICU), Intensive Care Unit (ICU).

2.3.4. Nutrition support during invasive mechanical ventilation

As the disease progresses, intubation and IMV may be required if respiratory status deteriorates. In intubated/ventilated ICU patients, both ASPEN/SCCM and ESPEN recommend EN should be started via NGT or 10–12 Fr orogastric (OG) unless patients are at high risk for aspiration or gastric intolerance is present despite prokinetic treatment, then post-pyloric feeding should be considered [7,44]. ASPEN/SCCM guidance specifically recommends continuous EN delivery rather than bolus feeding to improve GI tolerance and reduce COVID-19 exposure to the healthcare professional team [44]. Checking gastric residual volumes (GRV) during EN is not recommended by ASPEN/SCCM since GRV is an unreliable determinant of delayed gastric emptying and aspiration risk and may unnecessarily expose healthcare workers to COVID-19 while delaying EN implementation. In contrast to ASPEN/SCCM COVID-19 guidance, expert guidance created to guide healthcare providers in Australia and New Zealand recommends monitoring GRV every 8 h even if the patient is fed in the prone position [51]. If GRV >300 mL, then prokinetics should be administered for 24–72 h. If GRV >300 mL persists, then the guidance recommends considering post-pyloric feeding or PN.

2.3.5. Contraindications to nutrition support

Although nutrition support is recommended within the first 12–48 h of ICU admission, contraindications can result in delay of EN and implementation of PN including patients at high nutritional risk with severe GI symptoms, uncontrolled shock requiring increased vasopressor support, and uncontrolled hypoxemia, hypercapnia, or acidosis [7,44]. One study reported a high proportion (66%) of ICU patients with COVID-19 received vasopressor support and 11% did not receive nutrition support due to contraindications [17]. Although these contraindications were not identified, EN intolerance was reported as vomiting/gastric retention (32%), diarrhea (5%), hyperglycemia (63%), and hypoglycemia (3%). Before considering nutrition support, it is recommended to stabilize the patient, provide intravenous fluids as needed, and consider EN trophic feeding including supplementing with PN feeding if malnourished and/or BMI $\leq$25 or $\geq$35 [7]. Once patients are stabilized, trophic EN feeding can be initiated, targeting 30% of energy expenditure as measured by indirect calorimetry.

In the absence of escalating vasopressor support and GI intolerance, ASPEN/SCCM recommends early trophic EN not be contraindicated in COVID-19 patients experiencing sepsis or circulatory shock [44]. In patients who develop refractory hypoxemia, prone positioning can improve oxygenation and bronchial secretion clearance [54]. Behrens et al., 2020 reviews the unique challenges of enteral feeding of the COVID-19 patient in the prone position along with strategies to maximize tolerance and intake. To ensure access, the enteral feeding tube should be placed prior to turning patients to the prone position to avoid any delay in enteral feeding. During rotation between supine and prone position, the feeding tube can be temporarily disconnected and attached to the patient to maintain position and access. Although there are concerns over increased risk of elevated gastric residual volume, emesis, and aspiration which could lead to pneumonia, especially when moving from trophic to full-feeding, the research challenges these risks and demonstrates that enteral feeding during prone positioning does not pose any increased risk of GI or pulmonary complications [54]. In agreement with these recommendations, other guidance, including ASPEN/SCCM and ESPEN, do not consider prone

positioning to be a contraindication for EN feeding [7,44,51,52]. When introducing EN feeding during prone positioning, it is recommended to elevate the bed to a reverse Trendelenburg position (10–25°) [44,54]. When considering tolerance in the prone position, EN should be provided at trophic rates over the first week and slowly progressing to the full rate, with no contraindications for full-rate feeding.

2.3.6. Energy and protein needs

Only one study in Italy reports detailed nutritional intake, including energy and protein, in hospitalized COVID-19 patients, broken down by hospital unit (ICU, sub-ICU, IMCU, RU) and collected during a 1-day audit (Table 3). The hospital diet was prescribed to 79.5% of hospitalized patients with 11.3% of these patients also receiving medical nutrition therapy [30]. Medical nutrition therapy was provided to 23.5% of hospitalized patients with a higher proportion in the ICU and sub-ICU. Medical nutrition therapy was provided by ONS, EN, and PN in 25%, 54%, and 21% of hospitalized patients, respectively, with EN and PN higher in the ICU. The median prescribed total energy intake was 143% of basal energy expenditure (BEE) requirements, corresponding to 26.7 kcal/kg body weight/day, and did not significantly differ by hospital unit. Mean actual total energy intake was 128% BEE (24.8 kcal/kg body weight/day) across all hospital units. Mean actual total energy intake was significantly lower than prescribed energy intake in the ICU (103% of BEE and 20 kcal/kg body weight/day). Although less than the prescribed goal, energy intake was in line with expert recommendations for critically ill COVID-19 patients [7,44]. Specifically, expert guidance for critically ill hospitalized patients recommends slowly progressing to goal calorie intake ranging between 15 and 20 kcal/kg/day, depending on guidance and BMI status [7,44]. ASPEN/SCCM and ESPEN stress the need to begin feeding the patient slowly with hypocaloric or trophic feeding [7,44]. ASPEN/SCCM specifies reaching an energy goal 70–80% caloric requirements (15–20 kcal/kg actual body weight/day) during the first week while ESPEN recommends not exceeding 70% energy requirements in the initial phase of illness progressing to up to 70–80% of energy requirements by day 3. In emergency situations, ESPEN recommends predictive equations with 20 kcal/kg/day used increasing to 50–70% predictive energy needs by day 2 and 100% by day 4 [7]. Pironi et al., 2020 reports mean and prescribed total protein intake as 1.2 and 1.1 g/kg body weight/day, respectively [30]. Although prescribed protein intake did not vary by hospital unit, actual protein intake was lower in the ICU (1 g/kg body weight/day), which is lower than expert recommendations for this population. ASPEN/SCCM recommends a higher protein range to meet goal requirements over the first week (1.2–2.0 g/kg actual body weight/day and 2.0–2.5 g/kg ideal body weight/day for BMI > 30 kg/m^2) while ESPEN recommends 1.3 g/kg/day or 1.3 g/kg adjusted body weight/day (obese individuals) combined with mobilization to maximize muscle maintenance [7,44]. While patients often have higher protein requirements, slow, hypocaloric and moderate protein feeding is recommended in the first week of ICU admission progressing slowly to the goal rate [7,44]. Pironi et al., 2020 reported 43.5% of patients were receiving propofol which should be considered when prescribing medical nutrition therapy [30]. Patients receiving large doses of propofol may have lower energy and fat requirements to prevent overfeeding [44].

2.3.7. Enteral and parenteral formula selection during medical nutrition therapy

In the studies reviewed, evidence for the use of specialized formulas in hospitalized COVID-19 populations are lacking with the type of ONS, EN, or PN formula used as part of medical nutrition therapy not described. A standard, high protein, polymeric isosmotic EN formula is recommended by ASPEN/SCCM with the addition of fiber only after the patient stabilizes in the absence of GI intolerance [44]. Since loss of skeletal muscle mass and function (ICU-acquired weakness) can impact long-term outcomes of ICU survivors, interventions that avoid overfeeding while delivering appropriate energy and adequate protein administration are critical as stated by the ESPEN COVID-19 guidance. This guidance also states that “although definitive guidance cannot be made on additional specific treatments potentially due to lack of high-quality studies, recent evidence seems to indicate potential positive impact of physical activity with supplemental amino acids or their metabolites” [7]. This is based on evidence utilizing essential amino acid supplementation in critically ill [55] or post-ICU patients undergoing physical therapy [56]. ASPEN/SCCM and ESPEN COVID-19 guidance both mention the potential benefits of fish oil in EN and PN formulas in this patient population [7,44]. Fish oil containing eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) may benefit ARDS patients experiencing the cytokine storm through its immunomodulatory effects by improving oxygenation and reducing length of ventilation and hospital stay [57,58]. Therefore, Thibault, et al., 2020 recommends EN formulas enriched with 3.5 g/day of EPA and DHA and intravenous doses of 0.1–0.2 g/kg/day for PN feeding [52]. The use of pure, soy-based lipid emulsions for PN should be limited during the first week in the ICU when the acute inflammatory response is present, opting for less inflammatory oils such as olive oil, MCTs, and fish oil. Triglycerides should be monitored in patients receiving propofol and/or intravenous lipid emulsions. It should be noted that in a subset of COVID-19 patients, elevated triglycerides may be an indicator of hyperinflammation as a secondary response to the cytokine storm (secondary hemophagolymphocytic histiocytosis) [59].

3. Conclusion

Nutritional risk is highly prevalent in hospitalized COVID-19 patients. The etiology of nutrition risk is multi-factorial and is likely due to an older patient population and high prevalence of comorbidities combined with altered energy intake secondary to increased protein and energy needs due to fever, mechanical ventilation, weight and muscle mass loss, and hypermetabolism, and decreased nutrient intake due to reduced appetite, dyspnea, mechanical ventilation, and gastrointestinal intolerance [60]. Therefore, it is agreed upon by most expert guidance that it is imperative to screen and/or assess using validated screening/assessment tools for nutritional risk in hospitalized COVID-19 patients. While oral intake is the preferred route of feeding, contraindications often exist, in which case, EN or PN should be administered soon after ICU admission (within 12–48 h, depending on source of expert guidance) [7,44]. However, according to the literature reviewed, hospitalized patients may not be receiving timely nutrition intervention which may lead to poor outcomes. This may be due to several reasons including difficulty accessing patients to evaluate nutritional risk, contraindications to feeding such as severe gastrointestinal symptoms, uncontrolled shock requiring increased vasopressor support, and uncontrolled hypoxemia, hypercapnia or acidosis. Cluster care is recommended to avoid potential exposure to SARS-CoV-2, and details related to screening for malnutrition may need to come from other healthcare professionals, family, and/or caregivers. If patients are experiencing contraindications to nutrition support such as gastrointestinal intolerance or increased vasopressor support, it's important to prioritize stabilizing the patient while considering enteral trophic feeding or PN. Once the patient is stabilized, trophic EN can be initiated by slowly progressing to goal nutritional requirements. A standard, high protein, polymeric isosmotic EN formula is

recommended by ASPEN/SCCM; however, a higher protein formula might be more appropriate to help meet protein needs in this population. Additionally, formulas enriched with EPA and DHA may benefit critically ill, hospitalized COVID-19 patients through immunomodulatory effects [51,52].

Although clinical evidence is lacking to provide specific recommendations for nutritional management in COVID-19 patients, experience from clinicians and guidelines related to similar disease states may serve as a foundation until more clinical data is available. As more data emerges in this population, specific recommendations and guidelines can be updated. Currently, recent publications demonstrate that severely and critically ill COVID-19 patients, those hospitalized or in an intensive care unit (ICU), are at higher nutritional risk. Increased nutritional risk is associated with poorer clinical outcomes in these populations. Thus, rapid assessment, identification, and treatment of poor nutritional status is essential for improved clinical outcomes in severely and critically ill COVID-19 patients.

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Author contribution

Sara Thomas: Investigation, Writing- Original draft preparation, Review & Editing.

Celeste Alexander: Investigation, Writing- Original draft preparation, Review & Editing.

Bridget A. Cassady: Conceptualization, Funding Acquisition, Project Administration, Writing- Review & Editing.

Declaration of competing interest

Sara Thomas and Bridget Cassady are employees and stockholders of Abbott. At the time this review was conducted, Celeste Alexander was also an intern at Abbott. The authors have no additional conflicts of interest to report.

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