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Nutritional Status in Critical Care of COVID-19 Patients

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Nutritional Status in Critical Care of COVID-19 Patients

THESIS

A thesis submitted in partial fulfillment of the
requirements for the degree of Master of Science in Nutrition and Food Systems in the
College of Agriculture, Food and Environment at the University of Kentucky

By

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2022

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ABSTRACT OF THESIS

Nutritional Status in Critical Care of COVID-19 Patients

Critical care nutrition is a poorly researched, and such a sudden pandemic event requiring manipulation of nutritional status via propofol-induced sedation for mechanical ventilation is potentially impactful on patient outcomes. This paper seeks to provide context to the impact of critical care protocols on the nutritional status of obese patients suffering from COVID-19.

KEYWORDS: Nutrition, Critical Care, COVID-19

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Nutritional Status in Critical Care of COVID-19 Patients

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12/09/2022
Date

DEDICATION

To Robin:
I think you may have suffered more than I did through all this. Thank you for giving me the chance.

To Sally:
Your support meant more than you ever knew.

To My Mother:
I Made it.

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Chapter One: Introduction

Background

Overview of COVID-19

Reported in December 2019 in the Wuhan province of China as a pneumonia of unknown etiology, the severe acute respiratory syndrome coronavirus-2, SARS-CoV-2, causing the respiratory disease, COVID-19, has resulted in the greatest public health emergency of the 21st century to date. Globally speaking, males have worse COVID-19 outcomes than females. For instance, as of writing, male patients make up roughly equal numbers of cases compared to female patients, but are make up 55% of hospitalizations, 63% of ICU admissions, and 57% of deaths worldwide at the end of 2021[1]. Discussion of possible causes for the discrepancy between sexes will be discussed in later sections, but there is a clear marked difference in outcomes on sex-determined lines even in wealthier cohorts with greater resources.

Obesity greatly increases risk for adverse outcomes related to COVID-19. Nearly two-thirds of the adult population in the United States is obese. There are sex differences in the prevalence of obesity, with more women having obesity compared to men. Further, susceptibility to SARS-CoV-2 infection and risk for adverse outcomes of COVID-19 is increased by the presence of obesity-related co-morbidities, such as hypertension, of which sex differences also exist. It is not known how the confluence of sex and obesity contribute to greater disease severity in men.

Patients with COVID-19 admitted to critical care, usually with acute respiratory failure, are usually subjected to long periods of mechanical ventilation and receive supplemental nutrition. Critical care nutrition is an important mediator of outcomes. The presence of

obesity presents many challenges to nutrition in a critical care setting. One such challenge is the administration of propofol, an intravenously-administered anesthetic that is delivered in a highly lipophilic emulsion. Effects of increased use of this agent with prolonged mechanical ventilation in patients COVID-19 on critical care nutrition is not well-understood.

1.2 Problem: Whether sex differences in critical nutrition care contributes to adverse outcomes in COVID-19 is not known.

1.3 Hypothesis: We hypothesize that sex differences in critical care nutrition may contribute lower energy intake and poor outcomes in patients with COVID-19 in the ICU at the University of Kentucky.

1.4 Research questions:

1. Do sex differences in prevalence of SARS-CoV-2 diagnosis and COVID-19 ICU admission at UK follow global trends?
2. Is there a difference in energy intake in men versus women in critical care with COVID-19, and is this affected by propofol delivery?

1.5 Impact

The rationale for these studies is that improved information about critical care nutrition management in COVID-19, including sex-based differences, could lead to improved outcomes.

Chapter Two: Literature Review

2.1 COVID-19 and Obesity

Body Mass Index (Kg/M^2)	Interpretation
≤18.49	Underweight
18.5-24.9	Normal Weight
25.0-29.9	Overweight
30.0-34.9	Class I Obesity
>40	Class II Obesity
>50	Class III Obesity

Table 1 Classification of Obesity Using Body-Mass Index

Overweight and obesity are defined as abnormal or excessive fat accumulation (respectively) that present a risk to health. It is usually categorized using Body Mass Index (BMI) calculated from weight divided by height and waist circumference to measure abdominal adiposity, or via Dual Energy X-ray Absorptiometry (DEXA) to analyze body composition. BMI Categorization of individuals broadly falls into 6 major categories indicated in Table 1[2]. As of 1962, approximately 45% of American adults were overweight or obese. By 2018, The prevalence of overweight or obesity in the United States had increased to 73.6%.Obesity is a strong risk factor for risk of hospitalization and needing critical care treatment in persons infected with SARS-CoV-2. The global prevalence of obesity is high, and a recent study demonstrates that even controlled for age, gender, and comorbidities, obesity is independently associated with increased fatality and major adverse cardiac and cerebrovascular events in hospitalized patients with COVID-19 [3]. Obesity also increases susceptibility to Acute Respiratory Distress Syndrome (ARDS), the primary cause of mortality from COVID-19 [4].

A Detroit-based study early in the pandemic found obesity to increase overall mortality by 23%, comparable to hypertension in their study. Additionally, obesity was correlated with a 17% increased rate of admission to the ICU, and a 37% increase in

requiring mechanical ventilation. In comparison, hypertension correlated to a 27% and 29% increased rate respectively [5]. Another study from the same found almost half (47.5%) of patients admitted to the ICU were obese (BMI ≥ 30), and that the distribution was distinctly different from non–SARS-CoV-2 severe acute respiratory syndrome. [6] Further, 68.6% of the ICU patients required mechanical ventilation. The non-COVID-19 patients were distributed approximately the same as the regional prevalence, with patients with a BMI > 30 only making up 25.8% of ICU admissions. A study encompassing all COVID-19 positive patients under care of the U.S. Veterans Health Administration had findings consistent with recent studies linking obesity to increased COVID-19 related hospitalizations, ICU admission, and mortality [7].

2.2 Physiological factors

The association between obesity and adverse outcomes of COVID-19 is likely due to underlying inflammatory and metabolic factors contributing to decreased lung volume/expiratory reserve volume, increased inflammatory cytokines and chemokines, oxidative stress, and development of cardiovascular complications [8]. A combination of physiologic changes (metabolic, immune, and adipose tissue function) associated with

comorbidities and physical features (such as obstructive sleep apnea) lead to adverse clinical manifestations and even impaired vaccine response in persons with obesity.

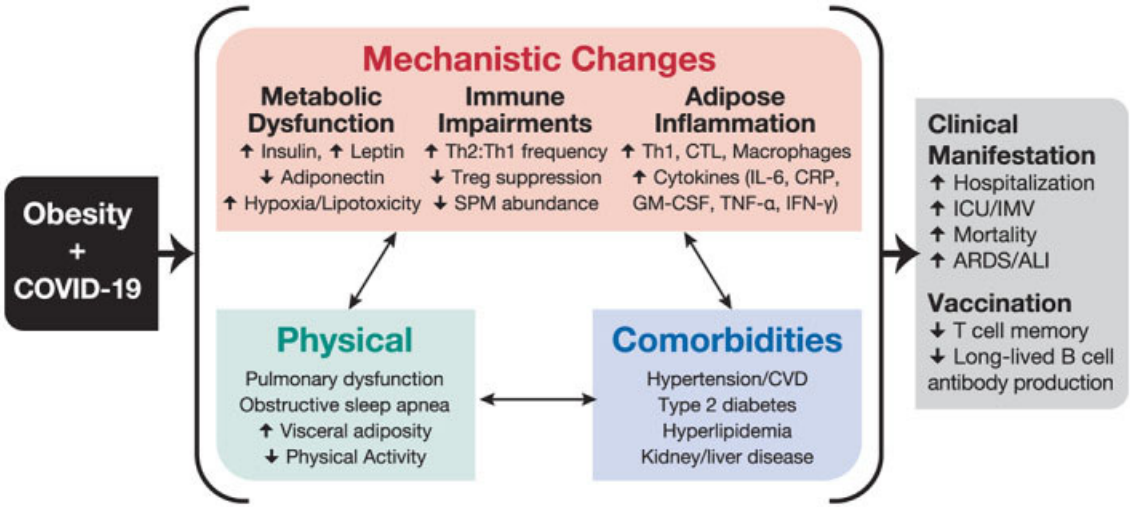

Figure 1. Presumed Mechanistic Behavior of Infection and Immunity.

For example, in an L.A based study in April of 2020[9], obese patients were more than twice as likely to require mechanical ventilation. Elevated levels of Interleukin-6 (IL-6), ferritin, lactate dehydrogenase (LDH) and C-reactive protein (CRP) were found in blood draws from time of admission or day of diagnosis if already admitted and were associated with increased need for mechanical ventilation or intubation. In a study during the same period, obese Chinese patients had similarly elevated levels of CRP and developed more severe symptoms compared to lean patients[10].

In addition to physiological factors, SARS-CoV-2 infections and COVID-19 outcomes appear to unsurprisingly carry a strong socioeconomic status (SES) component, with ethnic minorities bearing the brunt of negative COVID-19 outcomes. Early on, the discrepancies were noted by professional journals such as the Lancet[11], however later

studies[12] have shown disproportionate impact on BIPOC (Black, Indian, People of Color) communities. When controlling for income levels, one study places mortality for black patients at rates 215% of white populations, with Hispanic/Latino populations a close 182% rate.[13] Another study places infection incidence rates for black populations at 1.9% for every 1% of population, and 2.4% for every 1% of Hispanic/Latino population[12].

2.3 Sex differences in COVID-19

One factor leading to the greatest disparities in outcomes for COVID-19 positive patients is biological sex. Early studies from Wuhan noted majority male admittance to ICU and mortality. A clear correlation between male sex and COVID-19 disease severity and mortality has since become evident. In a retrospective cohort study of a 3-month period between April and June of 2020 it was found that among its patients male sex was independently correlated to a 30% higher mortality risk than females, and risk was increased with comorbidities as 79%. [14] An analysis of public patient data in China during the same period placed male mortality rates at approximately 70.3%, 2.4-fold that of women. Further, 37.2% of male patients suffered symptoms described as critical, defined by occurrence of respiratory failure that requires mechanical ventilation, shock, or ICU admission due to combined organ failure.[15] A retrospective case study covering the initial spread of infection in the Lombard Region in Italy found that male patients required ICU admission at 4-fold the rates of female patients and died at almost twice the rate of their female counterparts in the ICU [16].

SARS-CoV-1 and Middle East respiratory syndrome coronavirus (MERS-CoV) had 11% and 34% mortality rates respectively compared to a 4.2-7.3% mortality rate in COVID-19. Both also had slim majority male mortality, but neither had anywhere near the

sex-based variance in mortality or severity despite similar pathologies at play.[15,17] The reason remains unclear, but a combination of physiologic factors likely contributes to sex differences in various aspects of COVID-19 disease course and severity. For example, males tend to have more abdominal adipose tissue, responsible for chronic obesity-induced low-grade inflammation, which is exacerbated by COVID-19-induced inflammatory responses.[18] In addition, the mechanism for SARS-CoV-2 viral entry into cells involves a more robust (compared to previous viruses) exploitation of a protein called angiotensin-converting enzyme 2 (ACE2) compared to SARS-CoV-1, a multifunctional protein best known for its counter-regulatory role as part of the renin-angiotensin system (RAS) in the regulation of blood pressure. As part of the viral mechanism of entry, the normal activity of the RAS is disrupted. One consequence of this is greatly elevated levels of the peptide angiotensin II, which can have diverse adverse effects, such as local (lung, kidney, vessel, heart) inflammation and tissue damage [19]. Modulation of the activity of the RAS by sex hormones contributes to sex differences in development of chronic disease [20] Therefore, it is theorized that pre-menopausal women with estradiol-mediated effects on the RAS, affording some protection from hypertension, may translate into reduced severity of COVID-19 [21]. A study of the protective effects of estrogens on male cardiac tissue identified protein expression profiles with changes in ACE2 and down-regulation of pro-inflammatory and pro-oxidation effectors like LOX-1 and ICAM-1 [22]. These data suggest that discrepancies in COVID-19 mortality between pre-menopausal women and men, that appears to normalize after around age 45, may be related to various cardioprotective effects of sex hormones, including their effects on key mediators of the RAS that overlap with the pathophysiology of COVID-19.

2.4 Critical Care Nutrition

Nutritional care for critical care patients is guided by American Society for Parenteral and Enteral Nutrition (ASPEN) provisions covering a population greater than 18 years of age and a Medica Intensive Care Unit (MICU) or Surgical Intensive Care Unit (SICU) length of stay greater than 2-3 days[23-25], The Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient (2016) covers a broad range of disease states including organ failure (pulmonary, renal, and liver), acute pancreatitis, surgical subsets (trauma, traumatic brain injury [TBI], open abdomen [OA], and burns), sepsis, postoperative major surgery. These guidelines apply to otherwise "normal" adults (healthy weight) in a critical care facility. A different set of guidelines is required for critically ill patients with obesity as their pathophysiology is sufficiently different to require different methodologies and care in the critical care realm. [23] Reasoning for guidelines is multifaceted, mostly based on the provisioning requirements for differing disease states, treatment regimens, developing risk facts, secondary factors affecting nutritional or health status (ICU induced weakness, hospital acquired illnesses, trauma from intubation/mechanical ventilation) or other secondary etiology[24].

2.5 Therapeutic goals:

Nutritional therapeutic goals vary from patient to patient, but there are some generalizable evidence-based targets suggested by ASPEN and the Society Critical Care Medicine (SCCM) with the goal of reduced mortality. Of interest in the case of COVID-19 patients, previous guidelines had specific recommendations for ARDS [25], while the most recent suggests simply targeting 12 to 25 kcal/kg and a protein intake of 1.2 to 2.0 g/kg in the first 7-10 days of ICU stay [26]. In the context of glycemic control, ASPEN

defers to SCCM guidelines of insulin therapy to maintain blood glucose levels in the 140 to 180 mg/dL range as it is not atypical for critical care patients (or often, any long-term patient subject to hospitalization) to develop hyperglycemia.[27]

2.6 Nutrition screening.

Dynamic screening for nutritional risk is recommended for critically ill patients. Screening criteria include parameters in flux rather than static: recent weight loss, current BMI, change in treatment regimen, expected alterations in nutritional status, etc. Assessment and subsequent nutritional support objectives should be conducted at the time of admission to the ICU and during the implementation of enteral nutrition, ideally within 24-48 hours. Results from a meta-analysis conducted in ICU patients demonstrated that early enteral nutrition (within 24 h of ICU admission) reduced mortality compared with delayed enteral intake [28]. Tools for nutrition risk screening include the Nutrition Risk Screening Form (NRS 2002) and use of a a Nutrition Risk in Critically Ill (NUTRIC) score (or modified NUTRIC score) is recommended for screening.

Patients may be given a physical exam for assessment of lean muscle mass and body fat on admittance, but generally those outside of the dietetics field are focused on injury, signs suggestive of illness (i.e. lesions and HIV, or yellowing eyes and jaundice/liver dysfunction) and the like. Often, signs of malnutrition must be relatively extreme for an attending clinician to note. The evaluation of malnutrition should be repeated regularly and frequently due to the dynamics of the disease and increased risk of dysphagia in the elderly after pneumonia, and after prolonged respiratory therapy (post-extubation dysphagia) [29].

2.7 Determination of Estimated Energy Requirements (EER).

Determination of energy requirements for patients, be they minorly injured up to critically ill patients with obesity, can be a complicated. The gold standard for determination of energy requirements is indirect calorimetry (IC). IC is highly accurate and, while preferred, potentially cumbersome to utilize and requires trained personnel to apply. IC measures O_2 consumption and CO_2 produced during oxidative phosphorylation as indirect proxies for heat expenditure and generation during substrate oxidation and allows accurate estimation within 1% of the metabolic rate of the subject. It also allows determination of substrate usage for energy production, allowing the healthcare professionals to glean useful knowledge of the metabolic pathways associated with energy production. Utilization of IC has over the decades since its introduction led to the characterization of stress responses to injury and other altered or hypermetabolic states and subsequent design of appropriate nutrient regimens.

Formula Type	BMR Calculation
Harris-Bendict - Male	66.5 + (13.75 * weight in kg) + (5.003 * height in cm) - (6.75 * age)
Harris-Bendict - Female	655.1 + (9.563 * weight in kg) + (1.850 * height in cm) - (4.676 * age)
Mifflin-St Jeor - Male	(10 × weight in kg) + (6.25 × height in cm) - (5 × age in years) + 5
Mifflin-St Jeor - Female	(10 × weight in kg) + (6.25 × height in cm) - (5 × age in years) - 161
Penn. State. University - Original	MSJ(0.96) + Tmax(167) + Ve(31) - 6,212
Penn. State. University - Modified	MSJ(0.71) + Tmax(85) + Ve(64) - 3,085

Table 2. Common formulae for determination of caloric needs.

In an environment where infectious disease concerns reign and exposure is limited, as well as hygienic concerns over the enclosed devices used to measure outputs, the hood or mask required for IC is difficult to utilize. Additionally, it does require the patient to be consume sufficient oxygen without support and intubation or other mechanical ventilation both physically makes it more difficult to apply IC and alters the input and outputs sufficiently to make it useless. As such, falling back on standardized formulae to

calculate EER based on body weight is the norm in an ICU environment. There are various formulas for calculation of basal metabolic rate (BMR), summarized in the table 2. Additionally, the BMR is multiplied by an activity modifier, based on level of physical activity, described in table 3.

These formulae, while fairly accurate in usage on healthy individuals in some BMI ranges, fail to consider the needs of patients with altered energy intake/expenditure, such as in obesity. Patients in critical care have altered metabolic needs and patients in critical care with obesity is even more challenging. Using an expected 25-30 kcal per kg of actual or ideal body weight may lead to either over- or under-feeding. The H-B formula is suitable for healthy individuals but is no more than 65% accurate in critically ill patients and is not validated for BMI > 30. A somewhat uncommon formula, Ireton-Jones, is suitable for use with patients with BMI > 30 but is not validated for any patient requiring mechanical ventilation support. [30] The only predictive formula validated for a theoretical patient with obesity in Critical Care is Penn State University. This is a concern in care of all Critical Care patients, but not all patients are on Total Parenteral Nutrition (TPN). [31]

Activity Level	Activity Modifiers for BMR
Sedentary	BMR x 1.2
Lightly Active	BMR x 1.375
Moderately Active	BMR x 1.55
Very Active	BMR x 1.725
Extremely Active	BMR x 1.9

Table 3 Sex based EER ratios in first 5 days

According to the 2016 ASPEN/SCCM Guidelines, whenever it is impossible to measure VCO2 directly, energy requirement needs should be estimated according to body weight. For non-obese critically ill patients, the recommended amount of energy is 25–30 kcal per day/kg. For overweight and obese critically ill patients, the recommended amount of energy is 21 kcal per day/kg. In ventilator-dependent obese patients, the PSU or HBE equations with actual body weight and a stress factor of 1.1 (if the patient is spontaneously breathing) may be applied. For obese and critically ill patients, if the BMI is 30–50 kg/m2, the recommended energy target is 11–14 kcal/kg per day.

BMI Value [kg/m^2]	kcal/per day/kg Body Mass	Calculation of Ideal Body Mass (Y/N)	Calculation of Actual Body Mass (Y/N)
20–25	25–30	yes	
25–30	21		Yes
30–50	11–14		yes
>50	22–25	yes	

Table 5 Per kilogram estimation of caloric needs in critical care patients

2.8 Critical care challenges with obesity and COVID-19.

Due to the high prevalence of obesity in adults, nutrition support clinicians are encountering greater numbers of obese patients who require nutrition support during hospitalization. Obesity poses a number of challenges to optimal care in critically ill patients.

Typically, 20% of critical care patients present with obesity, somewhat less than the national prevalence [32]. Physical challenges include airway positioning and access. Other challenges include pharmacologic and nutritional support. This has been even more relevant during the COVID-19 crisis, where the number of ICU patients with obesity reaches 43.9% (BMI ≥30 and a further 7.3% with severe obesity (BMI ≥40) [32]

Critically ill COVID-19 patients are at risk for malnutrition resulting from imbalances in energy intake and expenditure which is exacerbated by factors affecting energy consumption and intake. Critically ill patients can experience dramatic alterations in energy consumption due to fever, mechanical ventilation, and exacerbated activity of breathing muscles [33]. Reduced or insufficient energy intake can result from reduced appetite, dyspnea, or intubation, and can further be impaired by adverse effects of SARS-CoV-2 on the GI tract [17]. Further, existing metabolic disturbances or disorders can have adverse effects on nutrient metabolism. Challenges to meeting nutritional goals include: Increased blood sugar and insulin resistance, reduced glucose oxidation, increased glycolysis and gluconeogenesis; impaired protein metabolism (increased protein breakdown, and enhanced synthesis of acute phase proteins, decreased muscle protein synthesis and negative nitrogen balance in the body); and increased fat mobilization.

2.9 Macronutrient considerations

Careful balancing of glucose administration in TPN or of gluconeogenesis via enteral nutrition (EN) is necessary to balance diet induced thermogenesis (DIT) and nitrogen loss in catabolism. This is associated with release of insulin and a cascade of protein-sparing metabolic behaviors that return the body to a level closer to neutral with regard to protein synthesis and anabolic/catabolic phases. Easily oxidizable substrates such as glucose and simple amino acid or glutamine-bearing complexes such as ornithine ketoglutarate added to nutritional intake function as part of a pseudo-sacrificial shield of preferential metabolism and allow protein synthesis to continue without being interrupted by catabolic calls for energy from the muscles. This preserves lean body mass associated with more positive outcomes in patients.

An additional aspect of critical care regarding standardized formula are pharmacological effects introduced and with EN or TPN. Lipid infusions as part of TPN for instance interferes with lung hemodynamics and alters regulation of ventilation/perfusion ratios in the pulmonary system. Elevation of omega-6 PUFA lipid supply shifts metabolic balance and oxidative substrate usage towards b-oxidation. Increased lipid supply also increases synthesis of vasodilating prostaglandins, leading to increased arachidonic acid that eventually overwhelms the speed of prostaglandin synthesis and rebounds to drastically increase in thromboxane and leukotrienes which in turn leads to vasoconstriction. These metabolic alterations lead to worsening gas exchange, leading to further impairment of ventilatory perfusion. In particular, the overabundance of thromboxane and leukotrienes reduce PaO_2 and increase pulmonary vascular resistance. This is controllable in many CC instances, but in subjects with sepsis or ARDS, control is much more difficult and clinically relevant. Further, excess lipid supply leads to negative effects on immune response and down-regulation or alteration of the mononuclear phagocyte system, also known as the reticuloendothelial system, that is a key first line element of immune defense against a range of pathogens. Of import this includes human respiratory viruses such as hRSV and SARS-CoV-2.[8]

Broadly, protein intake monitoring should occur in all patients and especially in critical care patients. Catabolism is common in hospitalized patients in any state and what may be excessive in a health individual may lead to positive outcomes in many cases (burns and wound healing being the classic examples.) Supportive and supplementary protein intake is commonly prescribed for such cases but are again importance in disease states where lung hemodynamics and perfusion alteration are symptomatic of whatever

etiology. Protein administration increases the minute ventilation and respiratory drive more than would be expected for its increase in Resting Energy Expenditure (REE), and branch chain amino acids (BCAAs), a common bolus additive for inflammatory states, further increases the effect. While this may be attenuated by control of PUFA ratios in EN/TPN in other cases, the increased ventilatory drive can be lethally dangerous in patients with ARDS or lack the ability to increase their work of breathing. [25,33]

2.10 Propofol use in obese critical care patients

Propofol (sold predominately under the brand name Diprivan) is an intravenous sedative-hypnotic anesthetic agent commonly used for IV induction of maintenance of general anesthesia, though it is unrelated to other sedative-hypnotic agents. Propofol is useful in critical care as a sedative-hypnotic agent due to its particular GABA receptor binding that allows usage with intravenous pain relief drugs (commonly fentanyl) without additional respiratory depression. Propofol can produce hypercapnia in patients, the persistence of which can depend on volume dosing and rate of administration. This potentially leads to decreases in respiratory rate, minute volume, tidal volume, and functional residual capacity It has a rapid onset, provides rapid recovery after bolus or infusion removal, and has anti-emetic properties. Its highly lipophilic nature allows it to cross the blood-brain barrier leading to said rapid onset. Emergence is also quick, as the drug is redistributed to peripheral tissue and tissues and follow-up metabolic clearance. These characteristics make propofol a common intravenously delivered induction agent in hospitals or ambulatory clinics where it is used as a part of almost every modern Total Intravenous Anesthesia. As a sedative, propofol is preferably delivered on a per kilogram basis using either adjusted body weight or Ideal body Weight (IBW) to avoid supratherapeutic concentrations in cases where patients are excessively outside the

accepted normal range for their height when using actual body weight. This is important to consider because body weight and drug clearance are not linearly correlated.

Due to the lipophilic qualities, propofol administration requires a carrier vehicle of (soybean) oil and (egg) lecithin as a white, stable emulsion for intravenous delivery. Most lipids (and other absorbed nutrients or materials) are delivered to the liver via the hepatic portal vein after enrichment along the tissues of the GI tract. Intravenous administration of this drug and its vehicle maintains a caloric content equivalent to lipids consumed (e.g. 9 kcal/g). As propofol is delivered as an emulsion, it is commonly calculated at 1.1 kcal/mL and 10mg of propofol itself per mL of solution is administered. Dosing recommendations can be somewhat confusing, as both mg/kg/hr and mL/kg/hr are commonly used, sometimes interchangeably, in recommendation guidelines. For patients with obesity, calculations purely focused on weight have multiple issues or concerns. Linear scaling by weight does not take into account issues previously discussed such as the lipophilic nature of the drug causing alteration of pharmacokinetics and therapeutic dosing, as well as altering times for onset and recovery of sedation.

Critically ill patients receive a much larger percentage of their daily energy intake as lipid (<55%) compared to the recommended >35% daily intake for healthy adults aiming to reduce their risk of cardiovascular disease. Some studies indicate that high-doses of long-chain triacylglycerols in critically ill patients lead to poorer outcomes[34]. This becomes concerning in obese patients who may be consuming far greater lipid content as energy from propofol delivery than from dietary sources. Given the metabolic alterations in lipid metabolism during critical illness (where hypertriglyceridemia is observed in a large percentage (45%) of patients requiring multiple days of ICU care), the

contribution of propofol (i.e excess lipids) to energy intake in obese persons could have a negative impact on outcomes. An additional factor is the potential replacement of carbohydrate and protein macronutrients to accommodate the addition calories from propofol delivery.

In a retrospective analysis, the quantity of lipid and the proportion of both energy and lipids in propofol-sedated critically ill adults was determined in two ICU centers (n = 701) for a total of 3,484 propofol days.[35] The energy targets were approximately 1,987 kcal/day, and mean energy intake was approximately 70% of targets. The mean propofol sedation dose was 2,045 $\pm$ 1,650 mg/day an (additional 146 kcal/per day). Fat constituted 17% of total energy. Fat delivery was significantly increased in propofol-sedated patients receiving high-fat formula EN feeds. In survivors, high-fat proportion was associated with prolonged ventilation time. These data indicate that fat content with propofol delivery is greatly increased in critical care. Further, the authors noted that in the early days of ICU stay, fat content from propofol could constitute up to 100% of energy intake in some patients. This study did not determine additional effects in obese patients.

In a study published in the Journal of Parenteral and Enteral Nutrition, medical records from n = 370 patients were retrospectively analyzed for proportion of total daily energy provided as propofol, overall energy balance, hospital mortality, duration of mechanical ventilation and ICU LOS. Patients administered propofol received a greater proportion of their total energy prescription compared with those who were not. Proportion of energy provided as propofol was not significantly associated with outcomes. The authors demonstrated that the proportion of propofol and associated lipid calorie content were greatest in the early days of ICU care (i.e. day 1 and 2), but that 53%

of patients were receiving 80% of EER on day 3. Overfeeding was observed in approximately 1 in 5 patients receiving propofol on day 5. Overall, protein delivery was poor (<1.2 g/kg/day). These data suggest that obese persons receiving propofol during ICU stay may be at risk for either over-feeding or replacement of protein (shown in separate studies to be positively associated with critical care outcomes) with lipid as vehicle for propofol delivery.

Data regarding critical care nutrition and metabolism in patients with COVID-19 is scarce, given the novelty of this disease. Much research has been focused on drug treatments or management of respiratory conditions. Because patients with COVID-19 often require prolonged mechanical ventilation, they might receive large quantities of propofol, which could be of particular concern to the large numbers of patients with COVID-19 who are obese. In a recent prospective observational study, it was reported during the first 10 days, COVID-19 patients received more lipid (propofol sedation) and less protein compared to patients with persistent critical illness, without COVID-19 and prescribed energy targets were below those of the ICU protocol [36].

2.11 Sex differences in critical illness:

2.11.1 Gaps in literature

We have examined factors contributing to outcomes in critically ill patients with COVID-19. Outcomes in COVID-19 are significantly impacted by male sex and presence of comorbidities (especially those related to cardiometabolic risk). Sex differences in critical care demonstrate that females compared to males, may receive less appropriate care for management of ARDS. However, female sex hormones may have protective effects in critical illness states. COVID-19 patients with obesity may have increased challenges with nutrition in a critical care setting, due to the increased delivery of highly

lipophilic propofol with prolonged mechanical ventilation. However, the impact of the quality of nutrition care, and whether there are sex differences in critical care nutrition with COVID-19 contributing to the increased severity of disease in men versus women are unknown.

3. Methodology

3.1 Aggregate data from i2b2.

At the time the data were collected, February 2021, sex differences in COVID-19 diagnosis and outcomes were emergent. To determine whether global trends demonstrating increased severity and outcomes of COVID-19 infection were present in the population served by the University of Kentucky, we collected aggregate data from UKHealthcare. We used the i2b2 patient survey portal to query the following terms: COVID (Diagnostic Code) and with or without Hypertensive Diseases (Diagnostic Code = I10 – I15). We examined the incidence of COVID-19 diagnosis in adults across each BMI category, with or without a diagnosis of hypertensive disorders, and grouped by sex (men or women) – See Figure 2 for an example search.

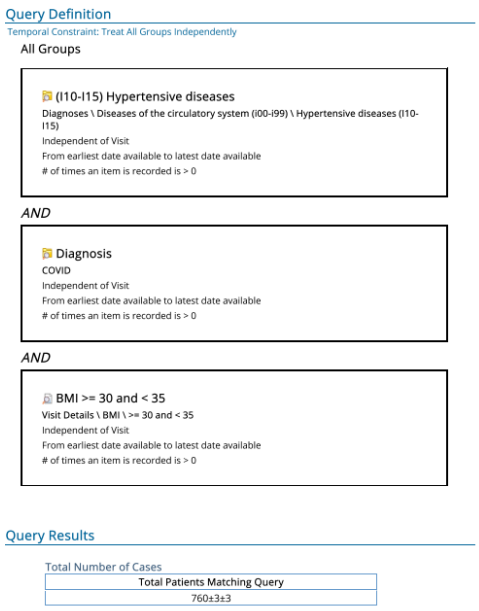

Figure 2 i2b2 portal query

To further confirm global trends of male sex being associated with increased ICU admissions over the course of the pandemic, we again queried i2b2 using the terms for confirmed COVID-19 diagnosis and Acute Respiratory Distress (see figure 3).

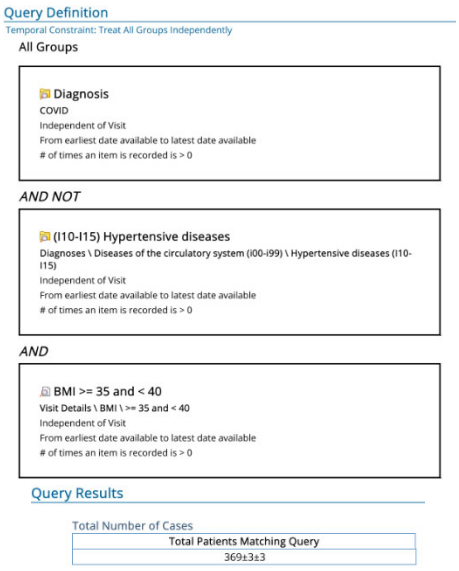

Figure 3 i2b2 portal query with COVID diagnosis

3.2 Clinical cohort.

To determine whether there were sex differences in critical care nutrition, we retrospectively examined a cohort of n=31 men and women admitted to the Medical Intensive Care Unit at UK Chandler Hospital between March 2020 – February 2021. This cohort consisted of men and women who received critical care for acute COVID-19 and were subsequently followed in the post-ICU clinic (PICS) at UK. The patients were originally selected as part of a pilot study to examine pulmonary outcomes in the PICS clinic. Collection of acute data for this study was approved under the University-wide IRB approved COVID-19 Registry and Specimen Biobank. Pertinent clinical data were abstracted from electronic medical records (EMR) via Sunrise Clinical Manager (SCM) and stored in a secure, IRB-approved REDCap database. Data from the pilot cohort, used for clinical nutrition investigation in the current study were obtained via collaboration with Dr. Sturgill, and included demographic variables of: age, sex, race, smoking status, weight and height used for the calculation of BMI; risk factors related to lung outcomes of: chronic and interstitial lung disease, asthma, COPD, pulmonary hypertension, and obstructive sleep apnea. Variables for hospital disease course included: Charleston index and SOFA score (indices of disease severity), length of hospital and ICU stay, and length of mechanical ventilation.

Eligibility criteria for patients admitted for critical care include one or more of the following in patients who were previously admitted to the ICU: > 48 hours of mechanical ventilation, new tracheostomy, > 72 hours septic shock requiring vasopressor, new multi-organ system failure (at least 2 organ systems), ICU-acquired weakness (<48/60 on medical research council-sumscore), delirium or acute respiratory syndrome diagnosed in the ICU, > 48 hours required extracorporeal membrane oxygenation.

3.3 Clinical nutrition data collection.

We collected clinical nutrition data from medical records of n=31 men and women admitted to critical care with COVID-19 who received propofol (for mechanical ventilation) concurrent with enteral nutrition during their ICU stay. Of the n=31 patients whose received enteral nutrition during the acute ICU stay, there were wide variations in the number of enteral nutrition and/or propofol days. Therefore, a 14-day period beginning with admittance or transfer to COVID-19 ICU ward was selected.

For each patient, data was extracted from dietitian *Assessment, Diagnosis, Intervention, Monitoring/Evaluation* (ADIME) notes recorded in SCM at each time of nutrition care assessment. Values for energy recommendations, daily energy intake (as mL of formula delivered), and propofol (as mL delivered in a lipid infusion) were used to calculate energy intake as kcal (including macronutrient breakdown) as well as energy derived from propofol as a lipid infusion.

Energy recommendations from dietitian notes were reported as kcal per kilogram per day, and concurrently reported body mass was used for the calculation of total daily kcal requirements. UKHC utilizes five different EN formulas, and mL/hr bolus from notes was used to determine mL delivered per formula. Daily energy (in kcal) and macronutrient intakes (in grams of protein, carbohydrate, and lipid) were calculated from the volume of formula delivered. This volume was converted into total energy intake by multiplying the volume of formula delivered by the energy content in kcal per mL for

Peptamen VHP	Per mL	Per 250 mL	Per 1000 mL
Kcal	1	250	1000
Novasource Renal	Per mL	Per 250 mL	Per 1000 mL
Kcal	2	500	2000
Diabetisource AC	Per mL	Per 250 mL	Per 1000 mL
Kcal	1.2	300	1200
Replete Liquid	Per mL	Per 250 mL	Per 1000 mL
Kcal	1	250	1000

Table 6 Formulary calorie values by type.

each type of formula used, Table. Daily macronutrient intakes in kcal from formula were similarly calculated on a g/mL basis based on individual formula concentrations.

The amount of propofol each patient received per day was a volume in mL was abstracted from SCM and energy received from propofol, as well as energy from lipids received as part of the propofol delivery, were calculated from the following formulae:

Energy received from propofol (Kcal): energy received from propofol as mL propofol received × 1.1kcal/mL (content reported from the manufacture)

Lipid received from propofol (g): lipids received from propofol as mL propofol received × 0.1222 = total grams lipid from propofol .

As with energy intake and macronutrient values, these values were calculated on a per-day basis, and also averaged over a 14-day period.

4. Results

4.1 Sex differences in COVID-19 diagnosis with or without hypertension.

Aggregate data from UKHealthcare i2b2 patient survey portal was retrieved in February 2021 using the query terms: COVID and with or without Hypertensive Diseases across each BMI category and grouped by sex (men or women). Of the 3437 patients with a SARS-CoV-2 diagnosis, 2091 (60.8%) were women and 1346 (39.2%) were men. Across each BMI category, there were more women compared to men with a SARS-CoV-2 diagnosis. Of the 2971 patients with a SARS-CoV-2 diagnosis and a concomitant diagnosis of hypertensive diseases, 1499 (50.5%) were women and 1472 (49.5%) were men. In patients who also had hypertension, there were more men than women with a SARS-CoV-2 diagnosis in the normal and overweight BMI categories. However, in the obese categories, there were more women than men with SARS-CoV-2 diagnosis and hypertension. These data suggest sex differences in SARS-CoV-2 prevalence are influenced by obesity and hypertension.

Data retrieved from July 2022 using the query terms for confirmed SARS-CoV-2 diagnosis and Acute Respiratory Distress indicate approx. 2120 adults over the age of 18 admitted to UKHealthcare, about 984 (46%) women and 1139 (54%) men. These data indicate more men than women were admitted to critical care with COVID-19 caused by SARS-CoV-2, consistent with literature that men have worse outcomes than women.

4.2 Propofol and critical nutrition care.

Patient characteristics and nutritional info are described in Table B. There were 15 men and 16 women in our cohort. The mean BMI was 35.3 and 35.9 kg/m2 respectively, with no difference between men and women. Similarly, there was no difference in the hospital or ICU length of stay. Energy intake was the lowest in the first 5 days of ICU stay.

Figure 4 demonstrates that EER is the lowest in the first day of ICU stay and increases each day. Although it varied on some days between men and women, there were no significant differences in EER among men and women.

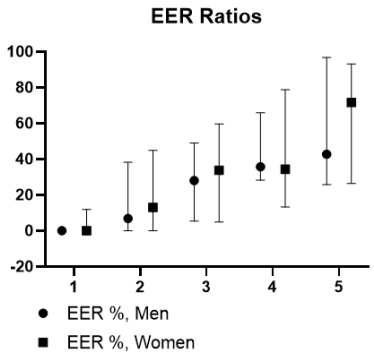

Figure 4 Sex based EER ratios in first 5 days

There were no significant differences in the nutritional parameters. Men and women received similar daily kcal during the 14-day period (998 versus 950 kcal/day), which represented 51.7% and 57.9% EER, respectively. In this period, propofol consisted of 21% of total kcal delivered in men and 17.1% of total kcal delivered in women. Men and women received approximately 46 grams of lipid on days with propofol delivery, which was comprised of 21% of lipid intake of propofol in men and 17.6 % of lipid intake of propofol in women.

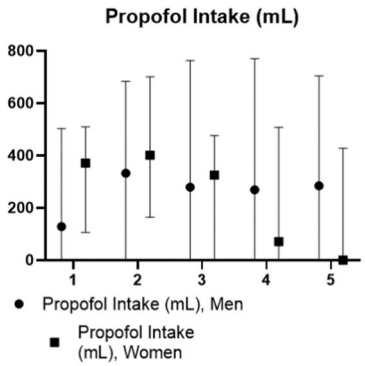

Figure 5 Sex based propofol intake in first 5 days

However, the macronutritional profile varied slightly between men and women. In the same 14-day period, men received 51.8% of total kcals from total lipids derived from propofol and formula, while women received 56.4% of their total kcals from total lipids.

While not significant, the sex-based variation of total proportion of protein and carbohydrates delivered was striking. After controlling for body mass, Men received approximately 60.3 grams of protein daily (17.8% of total kcal intake) while women received 65.9 grams of protein (21.5% of total kcal intake.)

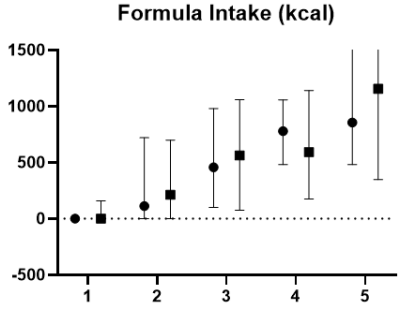

Figure 6 Sex based formula intake in first 5 days

Men received 93 grams of carbohydrate daily (28.1% total kcal) but women received 63.3 grams daily (equating to 19.4% of total kcal.)

Parameter	Male N = 15	Female N = 16
HOSP LOS	30.1 ± 7.2	27.3 ± 10.0
ICU LOS	15.8 ±	14.1 ± 6.9
BMI	37.5 ± 7.0	37.3 ± 9.3
Kcal (daily)	1048 ± 229	973 ± 188.9
% EER received	51.7% ± 18.0	56.4% ± 17.6
P.D	6.5 ± 3.8	6.6 ± 4.3
Avg lipid intake propofol, g	46.4 ± 27.5	48.7 ± 22.0
Avg lipid intake propofol, % of kcal	21.1% ± 16.1	22.1% ± 14.5
formula Lipid % kcal	38.5% ± 4.3	36.7% ± 3.7
Total % diet lipid	51.8%	56.4%
Fed. Avg. PROT (g)	60.3 ± 23.4	64.2 ± 30.9
PROT diet %	23.9% ± 9.3	27.0% ± 12.2
Fed. Avg. CHO (g)	93.0 ± 24.9	80.3 ± 16.6
CHO diet %	35.2% ± 4.3	33.1% ± 4.3

Table 7 Cohort characteristics

5. Discussion

This study examined sex differences in SARS-CoV-2 diagnosis, admittance into critical care, and in critical care nutrition therapy. Using aggregate data from UKHealthcare, we found that between the period April 1, 2020 – February 23, 2021 , there were more women than men with a COVID-19 diagnosis. However, when including hypertension as a comorbidity, more men than women were diagnosed with COVID-19. Further, aggregate data revealed that more men than women were admitted into critical care with COVID-19 for the period described. We examined whether sex differences in critical care nutritional therapy could be a factor contributing to the known increased severity of COVID-19 in men. While there were generally no differences in nutritional parameters in our cohort, we observed a trend of elevated protein intake in women versus men. This was associated with proportionally less propofol intake in women. This suggests that in our cohort, women were able to receive more kcal as nutrition (and specifically protein) than lipid in the form of propofol compared to men. Since both the overall kcal intake and protein intake during critical care are associated with outcomes, our data (while not significant), suggest that better nutrition during acute critical care for COVID might contribute to the better (acute) outcomes in women compared to men.

Since the global outbreak of SARS-CoV-2, numerous data indicate there are significant sex differences in COVID-19 severity and outcomes. Specifically, the number of critical care admissions is greatly increased in men [37,38]. In the current study, we used aggregate data from UKHealthcare to determine whether trends in our region were similar to global trends. We found that a COVID-19 diagnosis in patients with hypertension was more prevalent in men versus women. This is supported by literature

that the presence of comorbidities greatly increases the severity of COVID-19 disease course in men versus women [16]. Our data also indicated that more men than women were admitted into critical care at UK, which is also in agreement with both national and global trends. [1]

Many factors, including physiological, biological, sociocultural, etc, contribute to sex differences in COVID disease severity. These include, for example, the number of ACE2 receptors available for virus binding[22], hormonal factors that may be protective (e.g. estrogen) [39], gender discrepancies in self-care/behavior [13,38]. We wanted to examine the impact of nutrition therapy during critical care. Reasons for this include the well-known associations among critical care nutrition and ICU outcomes [27,40], and because patients with COVID-19 require sustained mechanical ventilation and are given very large amounts of propofol (in a highly calorific lipid emulsion vehicle) beyond the historical uses of this agent. Further, there is a dearth of evidence of sex differences in critical care nutrition therapy (especially with respect to propofol usage). We found amount of propofol used was limited to generally 3 to 5 day (post-surgical) up to a limit of 5 to 10 days in ICU sedation cases. [41]

5.1 Limitations

The limitations of the study I performed for this analysis were somewhat clear at the start time, given the cohort used. Some of the more pertinent issues lay with the data set focusing on COVID-19 patients who 1) were admitted to the ICU 2) survived their infection, 3) consented to the cardiopulmonary study that the data was extracted from, 4) attended the clinic and 5) attended follow-up. This restricts some more obvious

outcomes (e.g. mortality rates) and excludes a number of individuals (the initial cohort was greater than 240, but was cut down once eligibility criteria were applied.

5.2 Future Directions

An obvious direction to this research would be to recruit a broader cohort without some of the defining subject limitations from the study we sourced our own cohort. This cohort was narrowly defined and excluded a number of subjects that may have impacted our findings (e.g. mortality or extremely poor outcome patients that were incapable of attending the cardiopulmonary clinic) in one direction or another. While we may have seen the "healthier" extreme of the UKHC patients, the less healthy extreme would be where we could potentially identify negative impacts of propofol and lipid intake. Additionally, a larger cohort would improve the statistical power and potentially improve any significance that is teetering on the grey area of 0.5 to 0.10.

Additional research that may be of interest to this topic of nutritional status impact on ICU patients is difficult draw back to a wet bench or animal study level. Long-term propofol usage or mechanical ventilation in lab animals is not common, and COVID-19 mouse models are not especially similar physiologically. Inflammatory reactions, mACE2 entry vectors, hormonal impacts, and RAAS alterations have similarities, but appear to be significantly different from humans in some mouse models[42] with neurological impact similarities approaching zero[43]. Longitudinal studies of patients as COVID-19 remains a common viral infection may remain the best plan, with identification of several potential key markers of interest (cytokine markers, lipid panels, etc.) ahead of time and a testing methodology settled before recruitment and patients tracked during their stay rather than long after. Additionally, with a cohort "currently"

admitted, potential errors in I/O and weight tracking could be dealt with as needed and any issues cropping up (e.g., patient inability to handle formula secondary to disease vs alternative reasons) clarified for analyses.

6. Conclusion

Our data shows that the population treated at UK Chandler hospital broadly follows the global trends at the time of collection, with an excess of male patients admitted both to the hospital and ICU and apparent severity (via SOFA score) divided as well. There are clear sex based differences seen in at least the earlier strains of COVID-19. The presumed connection between lipid intake via propofol, limited macronutrient intake, and mechanical ventilation or length of stay was not apparent in the cohort analyzed. Further analysis with an expanded cohort with less stringent inclusion criteria may find some connections that are not clear in these analyses.

While this study may have been unable to identify a connection between COVID-19 patient outcomes and propofol intake, potentially due to limitations with the cohort, COVID-19 continues to both affect people worldwide. Given there are several variant diseases in this family that previously affected global populations to a lesser extent and the potential for further coronavirus outbreaks or mutations, we strongly recommended further research in the topic if propofol and mechanical ventilation requirements continue to be extensive in such a large population.

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Definitions & Formulae

Propofol delivery:

Propofol (mL) is defined as amount in a given 24-hr period was determined by [adding up?] propofol IV indication in I/O portion of patient records and compared to ordered amount in doctors notes.

Propofol Days (P.D) are defined as 24-hr periods where patients received ≥ 100 mL of 1% propofol, equivalent to 1000 mg of active drug.

Total Propofol Intake (TPI) is defined as total received propofol solution in the described 14-day period.

Propofol day averages is defined as TPI ÷ P.D.

Nutrition Delivery:

Formula (mL) is defined as total enteral nutrition delivered in a given 24-hr period as determined from I/O portion of patient records and compared to recommendation in Dietitian ADIME notes

Fed Days (F.D.) are defined as 24-hr periods where patients received ≥ trophic feeding levels (10-20mL/hr) during administration. Cut-off determined by I/O records, not Formula (mL) ÷ 24-hrs.

Total VHP/Total DBS/Total Renal/Total Replete/Total Isosource

Total VHP: Total mL Peptamen Very High Protein formula

Total DBS: Total mL Diabetisource AC formula

Total Renal: Total mL Novasource Renal formula

Total Replete: Total mL Replete Liquid formula

Total Isosource: Total mL IsoSource 1.5 formula

Total formula intake (mL) (TFI): is defined as total received enteral nutrition given in the described 14-day period

Total Daily Avg (ml): Is defined as total formula intake ÷ 14 days

Fed day Avg (ml): is defined as total formula intake ÷ Fed Days

EER (kcal/day): "Estimated energy requirements" as defined by dietitian in ADIME notes

EER Total (kcal over stay) Total energy intake recommendation over the described 14-day period

EER avg (kcal/day): EER Total ÷ 14 days

Protein recommendation (g/day): grams of protein recommended as defined by Dietitian in ADIME notes

Protein recommendation avg (g/day): Total grams of protein recommended ÷ 14-days

Energy received from formula (Kcal): is defined as total kcals derived from enteral nutrition

Total: Sum of VHP + DBS + Renal + Replete + Isosource =

Average: Total energy received from formula ÷ 14-day period

F.D. Average: Total energy received from formula ÷ Fed Days

VHP: [Total mL VHP × 1 kcal/mL] = Total kcal from VHP

DBS: [Total mL DBS × 1.2 kcals/mL] = Total kcal from TBS

Renal: [Total mL Renal × 2 kcal/mL] = Total kcal from Renal

Replete: [Total mL Replete × 1 kcal/mL] = Total kcal from Replete

Isosource: [Total mL Isosource 1.5 × 1.5 kcal/mL] = Total kcal from Isosource

Lipid received from formula (g)

Total: Sum of VHP + DBS + Renal + Replete + Isosource = Total

Average: Total lipid received from formula ÷ 14-day period

F.D. Average: Total lipid received from formula ÷ Fed Days

VHP: [Total mL VHP × 0.038 g/mL] = Total grams lipid from VHP

DBS: [Total mL DBS × 0.059 g/mL] = Total grams lipid from TBS

Renal: [Total mL Renal × 0.1005g/mL] = Total grams lipid from Renal

Replete: [Total mL Replete × 0.034 g/mL] = Total grams lipid from Replete

Isosource: [Total mL Isosource 1.5 × 0.059g/mL] = Total grams lipid from Isosource

Energy received from propofol (Kcal): energy received from propofol as mL propofol received × 1.1kcal/mL

Lipid received from propofol (g): lipids received from propofol as mL propofol received × 0.1222 = total grams lipid from propofol

CHO received from formula (g)

Total: Sum of VHP + DBS + Renal + Replete + Isosource = Total grams carbohydrate received

Average: Total grams carbohydrate received ÷ 14-day period

F.D. Average: Total grams carbohydrate received ÷ Fed Days

VHP: [Total mL VHP × 0.076 g/mL] = Total grams carbohydrate from VHP

DBS: [Total mL DBS × 0.1 g/mL] = Total grams carbohydrate from TBS

Renal: [Total mL Renal × 0.184 g/mL] = Total grams carbohydrate from Renal

Replete: [Total mL Replete × 0.112 g/mL] = Total grams carbohydrate from Replete

Isosource: [Total mL Isosource 1.5 × 0.176 g/mL] = Total grams carbohydrate from Isosource

PROT received from formula (g)

Total: Sum of VHP + DBS + Renal + Replete + Isosource = Total grams protein received

Average: Total grams protein received ÷ 14-day period

F.D. Average: Total grams protein received ÷ Fed Days

VHP: [Total mL VHP × 0.092 g/mL] = Total grams protein from VHP

DBS: [Total mL DBS × 0.015 g/mL] = Total grams protein from TBS

Renal: [Total mL Renal × 0.091 /mL] = Total grams protein from Renal

Replete: [Total mL Replete × 0.064 g/mL] = Total grams protein from Replete

Isosource: [Total mL Isosource 1.5 × 0.068 g/mL] = Total grams protein from Isosource

*Total energy intake (kcal): [*Total energy received from formula + Total energy from propofol = total energy intake in kcals]

Overall avg energy intake (kcal): Total Energy Intake ÷ 14-days

Total lipid intake (kcal): Total lipid received from propofol (g) + Total lipid received from formula (g)

Total % formula (kcal): Total Energy received from formula ÷ total energy intake = proportion of total energy from enteral formula

Total % propofol (kcal): Total energy received from propofol ÷ total energy intake = proportion of total energy from propofol

Total % lipid (in kcal): [Total Lipid received from propofol (g) + Total lipid received formula (g)] × 9 kcal/g lipid ÷ Total Energy intake = Total proportion of energy from lipids

Avg % lipid (in kcal):

Total CHO intake (kcal): [Total grams carbohydrate received from formula × 4kcal/g] = Total kcals received from carbohydrates

Total % CHO (in kcal): Total kcals received from carbohydrates ÷ Total Energy Intake = Proportion of kcal from carbohydrates

Avg % CHO (in kcal): Total CHO kcals ÷ 14-day period

Total PROT intake (kcal): Total protein x 4

Total % PROT (in kcal): Total PROT intake ÷ Total Kcal

Avg % PROT (kcal): Total PROT ÷ 14-day period

Total intake/Total EER ratio: Total Kcal intake ÷ Total EER value

Total Lipid % of kcal: Total Lipid Intake ÷ Total Kcals

EN/IV Nutrient day count: Specifies days when non-propofol NPO nutrition was delivered to patient

Average lipid %: Total Lipid Intake ÷ 14-day period

Propofol Lipid % of kcal: Total lipids (g) from Propofol x 9 ÷ Total kcal received

Formula Lipid % of kcal: Total lipids (g) from formula x 9 ÷ Total kcal received

Vita

Education

B.S. Dietetics, 2020, University of Kentucky, Lexington, KY

M.S Human Nutrition & Food Systems, 2022 (anticipated), University of Kentucky, Lexington, KY

Honors

2020 - 2021 John I. and Patricia J. Buster Fellowship, University of Kentucky

2019 Academic Excellence Scholarship, University of Kentucky

2018 – 2020 Agriculture & Human Environmental Sciences AG & HES Scholarship in Honor of Dr. Marjorie

Stewart, University of Kentucky

Professional Positions

2022 - Laboratory Manager, RAAS Analytical Laboratory, University of Kentucky, Lexington, KY

2020 - Research Assistant, College of Agriculture, Food and Environment, RAAS Analytical Laboratory, University of Kentucky, Lexington, KY

2020-2021 University of Kentucky Assistantship

Publications

Valdez, L.; AlSiraj, Y.; Huang, H.; Bauer, JA.; Radulescu, A.; Davis, D.; Shoemaker, R. Sex differences in cardiometabolic risk factors of obese adolescents. Sept 7 2022;79:AP092.https://doi.org/10.1161/hyp.79.suppl_1.P092

**Winner, Trainee Poster Award Session*