COVID-19 LONG HAULERS: NUTRITION IMPLICATIONS AND MANAGEMENT

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OUTLINE

- Malnutrition in COVID-19
  - Causes
  - Prevalence
- Hypermetabolism in COVID-19
- Long term nutrition needs after acute COVID-19
- Nutritionally relevant long term effects of COVID-19
  - Loss of taste and smell
  - Respiratory
  - Dysphagia
  - Endocrine
  - Renal
  - Gastrointestinal
- Case study

ABOUT ME

- Clinical dietitian at University of Maryland Medical Center
- COVID-19
  - Floor COVID patients
  - Worked with patients on "modular unit"
    - Built specifically for stable COVID patients
    - Often stepped down from ICU and stayed until their discharge, typically to a rehabilitation center
    - Many spent months in ICU on ventilators, some on ECMO
    - Tracheostomies common. Ventilator weaning
    - Transition from tube feeding to PO diets

COVID-19

- Caused by novel coronavirus SARS-CoV2
- Symptoms
  - Flu-like
  - Cough, fever, weakness
  - Nausea, vomiting, diarrhea, dysgeusia, hyposmia
- Symptoms range from mild to severe
  - Severe symptoms include acute respiratory distress syndrome (ARDS) and multi-organ failure
- Obesity, hyperlipidemia, diabetes and frailty are risk factors for severe COVID-19

COVID-19

- 20-30% require hospitalization and 5-10% of those patients require ICU admission
- Average length of stay is often limited to <7 days in patients with COVID -19[4]
- Median hospital length of stay ranged from 4 to 53 days or 4 to 21 days
- Of critically ill patients, 47-71% need mechanical ventilation. 4-42% require advanced organ support with mechanical ventilation[5]

MALNUTRITION IN COVID-19

- Malnutrition is prevalent in patients with critical illness and associated with poor outcomes
  - Prevalence 38-78%
  - Outcomes: increased morbidity and mortality, increased healthcare costs
- Inflammation increases protein catabolism, limits protein anabolism, increases resting energy expenditure and promotes anorexia[4]
- COVID-19 patients are at risk for malnutrition
  - Reduced food intake, inflammation related catabolism, reduced mobility, and comorbidities

MALNUTRITION IN COVID-19

- Cross sectional study in a tertiary hospital in Italy
  - Nutrition Risk Screening 2003 Tool (malnutrition risk) and Global Leadership Initiative on Malnutrition GLIM (diagnosis of malnutrition)
  - Among 268 patients, ¾ were at nutritional risk, among those at risk 54% were diagnosed with malnutrition
  - 60.5% were admitted to IMC, 7.8% to SICU, 17.2% to ICU and 14.5% to rehabilitation unit[9]
- Retrospective observational study in France
  - Malnutrition was diagnosed if one parameters was met: body mass index (BMI < 18.5 or <21 if >70 years old, weight loss of 5% in the past month and/or 10% in last 6 months
  - 108 patients, malnutrition was seen in 38.9%
  - 31.4% of population had severe COVID-19 (defined as need for nasal oxygen >6L/min)
  - Excluded ICU patients[8]

MALNUTRITION IN COVID-19

- Severe COVID-19 may cause ARDS and/or multiple organ failure that is associated with cytokine release syndrome
  - Elevated inflammatory response
  - Pro-inflammatory cytokines initiate different signaling pathways on immune and tissue cells resulting in fever, ARDS and potentially multiorgan failure and death in most severe cases[11]
  - Inflammatory response possibly contributes to hypermetabolism that is seen with patients who are critically ill with COVID-19

HYPERMETABOLISM IN COVID-19

- Inflammation likely causes hypermetabolism during critical illness
- Patients with severe cases show an ongoing inflammatory response during the second week of illness and for several weeks or more after
- Prolonged hypermetabolic response likely continues beyond day 7-10

HYPERMETABOLISM AND COVID-19

- Retrospective case series
  - 7 adults requiring mechanical ventilation
    - Did not require renal replacement therapy and/or thoracostomy tubes
  - Measured REE (resting energy expenditure) with IC (indirect calorimetry)
  - Compared REE with predicted REE (using predictive equation, Penn State)
  - Energy needs likely increase after acute phase of critical illness[2]

Table 1. Indirect Calorimetry Results.

Patient #	Age	Body mass index	Measured REE (kcal/d)	Predicted REE (kcal/d)	VCO_2 (mL/min)	VO_2 (mL/min)
1	62	26.6	5186	1733	582	750
2	74	24.6	2845	1296	303	416
3	70	37.5	3052	1865	295	455
4	57	28.1	4044	2108	452	585
5	57	27.4	3952	1955	468	565
6	69	25.1	4282	1617	401	642
7	55	25.2	5414	1753	555	798

REE, resting energy expenditure.

Table 2. Inflammatory Markers.

Patient #	Hospital day (#)	Measured REE (kcal/d)	Measured REE/predicted REE (% predicted)	C-reactive protein (mg/dL)	D-Dimer (ng/mL)
1	8	5186	299	7.11	13,862
2	8	2845	219	0.5	2894
3	22	3052	164	13.36	1160
4	23	4044	192	3.94	980
5	30	3952	202	13.38	2019
6	32	4282	265	14.5	560
7	55	5414	309	12.6	1393

REE, resting energy expenditure.

HYPERMETABOLISM IN COVID-19

- Observational cohort study
  - 22 ICU patients
  - Compared mREE (measured resting energy expenditure) using IC and pREE (predicted REE) using Harris Benedict equation
- 1st week of ICU stay, mREE was between 15 and 20 kcal/kg
- Increasing hypermetabolism and wider variability in mREE was seen post 1st week
  - Measured REE through day 21 of ICU stay
- Mean mREE was 150% pREE in 3rd ICU week[3]

NUTRITION NEEDS AFTER ICU STAY?

- Guidelines exist for nutrition management during critical illness, but none that address nutritional needs after a patient is discharged from ICU
- Goals of nutrition support during critical illness focuses on preventing or delaying malnutrition
- Acute phase or post ICU recovery phase should focus on optimizing energy and protein intake to restore nutrition status

BARRIERS TO NUTRITION INTAKE

- Oral intake is often poor after patients have been discharged from ICU
- Causes
  - Physiological
    - Weakness, fatigue, poor appetite, early satiety, dysgeusia, and pain
  - Psychological
    - Depression, anxiety, delirium

NUTRITION POST ACUTE COVID-19

- Malnutrition is common
- Energy needs are likely high for many weeks after ICU stay
  - Range of 30-35 kcal/kg for calories has been suggested
  - However, high energy intake may not be appropriate for everyone
    - Limited mobility and lower energy expenditure
    - Could tax metabolic systems and increase cardiopulmonary demands
- Protein
  - Muscle loss is common
  - 1.5-2.5g/kg for protein has been suggested
  - Couple with resistance training if able

WHAT CAN WE DO?

- Anabolic steroids
  - Oxadrolone and propranolol
- Nutrition supplements
- Supplemental tube feeds if feasible
- Optimizing nutrition support
- Diet
  - Could following diet high in vegetables, fruits, omega-3 fatty acids prevent severe inflammatory response?
  - No research to indicate certain foods may prevent COVID-19[12]
- Frequent medical nutrition therapy
  - Liberalizing diets, nursing and staff encouragement

LONG TERM NUTRITION EFFECTS OF COVID: LOSS OF TASTE AND SMELL

- Anosmia (acute loss of smell), ageusia (acute loss of taste), dysgeusia (altered taste) all common, particularly among mild cases
- Study of 3,191 patients
  - 15% had anosmia or ageusia in the early stages of COVID
  - Median time of recovery from anosmia and ageusia was 7 days
  - Most patients recovered within 3 weeks[7]

LOSS OF TASTE AND SMELL

- Prevalence
  - Cross-sectional study found gustatory dysfunction was seen in 78.9% patients (more mild cases) and seen in 51.9% in hospitalized (moderate/severe) cases
  - Loss of taste or smell occurred in 79.6%, 14.8%, 3.5% and 2.2% of COVID-19 patients with asymptomatic to mild, moderate, severe and critical illness[7]
- Duration
  - Studies have found that median duration of dysgeusia associated with COVID-19 resolves anywhere from 7.1 to 26 days
  - Other studies have shown that taste changes can occur up to 60 days or longer[10]
- Nutrition effects
  - May hinder PO intake
  - Suggestions
    - Cold vs hot foods, acidic foods, etc

LONG TERM NUTRITION EFFECTS OF COVID: RESPIRATORY

- Long term, patients may have dyspnea, difficulty weaning from ventilators, fibrotic lung damage
- Study showed that of the patients that required tracheostomies, 52% were weaned from ventilator 1 month later in national cohort study from Spain[1]
- Nutrition implications
  - May require tube feeding/nutrition support long term
  - Difficulty breathing hindering PO intake

LONG TERM NUTRITION EFFECTS OF COVID: DYSPHAGIA

- Data on prevalence of dysphagia in COVID-19 patients is not yet known
- In ARDS patients (not COVID), about 1/3 of intubated patients had dysphagia during hospitalization
  - Dysphagia increases risk of aspiration and aspiration pneumonia, delays oral feeding, can contribute to malnutrition and decrease in quality of life
- Post intubation dysphagia is related to the duration of mechanical ventilation
  - In patients intubated for more than 48 hours, the prevalence of dysphagia increases by 56%[5]
- Nutritional implications
  - Decreased PO intake
  - Ways to overcome
    - Nutrition supplements, thickeners, supplemental tube feeds

LONG TERM NUTRITION EFFECTS OF COVID: ENDOCRINE

- Insulin resistance and diabetes
  - Could worsen insulin resistance in patients with pre-existing type 2 diabetes mellitus
  - Diabetic ketoacidosis has been seen in patients without known diabetes mellitus weeks to months after COVID-19 symptoms resolve
- Vitamin D
  - Immobilization, use of steroids and vitamin D deficiency could cause demineralization[1]
  - Vitamin D deficiency seen among our patients, particularly among more severe cases

LONG TERM NUTRITION EFFECTS OF COVID: RENAL

- Severe acute kidney disease requiring renal replacement therapy (RRT) in 20-31% of critically ill patients with COVID-19
- Studies have shown that 27-64% were dialysis dependent by 28 days or ICU discharge[1]
- Nutrition implications
  - Potential for elevated potassium, phosphorous levels and need for alternative tube feeding formula or ONS
  - May need fluid restrictions or diet restrictions

LONG TERM NUTRITION EFFECTS OF COVID: GASTRO-INTESTINAL

- COVID has potential to alter the gut microbiome
  - Increase in risk for opportunistic infectious organisms
- Meta-analysis from China found that 17.6% of COVID patients had gastrointestinal symptoms, anorexia being the most common (26.8%), then diarrhea (12.5%), nausea and vomiting (10.2%) and abdominal pain (9.2%)[1]
- Nutrition Implications
  - Decreased PO intake, intolerance to tube feeding
  - Add soluble fiber (Banatrol, Nutrisource, Metamucil), limit solution or elixir medications

CASE STUDY

- Patient A
- 60 year old male
- PMH: HTN, HLD, DVT
- Admission weight 220lbs, height 67 inches
  - BMI 34.6

ICU COURSE

- 11/6/20-12/29/20 – Extended ICU course at outside hospital, acute respiratory failure due to COVID-19 requiring tracheostomy. PEG tube placement. Discharged to rehab on 12/29/20
- 1/2/21 – Admitted to ICU from rehab for respiratory failure. On mechanical ventilation via tracheostomy. Vent dependent
- ICU course
  - Low vitamin D levels (13). Supplemented with 50,000 units vitamin D weekly
  - On CRRT, eventually transitioned to iHD
  - Required vasopressors
  - Nutrition via PEG tube
    - Tube feeding eventually adjusted to lower volume TwoCal HN due to elevated GRVs (higher than 500ml) and to lower free water volume (often fluid overloaded)
    - By end of ICU stay, tube feeding provided 19 kcal/kg and 1.9g/kg IBW protein

HOSPITAL COURSE AFTER ICU STAY(POST ACUTE PHASE)

- 1/19/21 - Transferred to modular unit
  - Began trach collar trials. Eventually weaned to trach collar and was off mechanical ventilation. Tracheostomy decannulated at end of stay
  - Continued to require iHD
  - Nutrition
    - Tube feeding of TwoCal HN because of hyponatremia continued. Provided 19 kcal/kg and 2.1g/kg IBW protein
    - Eventually passed speech language pathology evaluation for PO diet, but continued to provide overnight tube feeding to supplement PO intake
  - Started on appetite stimulant, Marinol. Added protein supplements. Magic cup patient's preference
  - PO intake improved and tube feeding stopped just prior to discharge
- 1/27/21 - New weight 202lbs (8% wt loss since admission ~3 weeks)
  - Difficult to assess weights due to fluid shifts
- 2/10/21 – discharged to rehab

FOLLOW UP 3 MONTHS LATER

- Patient was discharged to rehab 2/2021 and re-admitted to hospital 5/24/21 with cough, pneumothorax
- Admission weight 170lbs (23% wt loss from UBW of 220lbs in November)
  - Diagnosed with severe malnutrition (use GLIM criteria)
- Patient had PEG tube removed 1 week prior to admission and had improving PO intake over the past several months, but still experienced occasional low appetite
- Off dialysis, but creatinine remained high and had elevated phosphorous levels
- Recommended 1.5g/kg protein, no dietary restrictions to promote PO intake with Magic Cup supplements (preference)
- Patient likely experiencing ongoing hypermetabolism related to COVID-19 infection

CONCLUSION

- Malnutrition in COVID-19 is common, particularly for those who experience severe COVID-19 or ARDS
- COVID-19 also has many long term effects that could affect nutritional status (renal, respiratory, GI)
- Patients recovering from severe COVID-19 likely are hypermetabolic for weeks to months after their illness
- Post ICU recovery phase should focus on restoring nutritional status
  - Ongoing nutrition therapy and individualized interventions key to recovery and improvements in nutritional status

SOURCES

1. Nalbandian, A., Sehgal, K., Gupta, A. *et al.* Post-acute COVID-19 syndrome. *Nat Med* **27,** 601–615 (2021). https://doi.org/10.1038/s41591-021-01283-z
2. Yu P, Cassiere H, et al. Hypermetabolism and Coronavirus Disease 2019. JPEN J Parenter Enteral Nutr. 2020; 44:1234-1236. DOI: 10.1002/jpen.1948
3. Wischmeyer PE; LEEP-COVID Study Group. Persistent hypermetabolism and longitudinal energy expenditure in critically ill patients with COVID-19. Crit Care. 2020 Sep 28;24(1):581. doi: 10.1186/s13054-020-03286-7. PMID: 32988390; PMCID: PMC7521195.
4. Burslem R, Parker A. Medical nutrition therapy for patients with malnutrition post-intensive care unit discharge: A case report of recovery from coronavirus disease 2019 (COVID-19). Nutr Clin Pract. 2021 Aug;36(4):820-827. doi: 10.1002/ncp.10728. Epub 2021 Jul 10. PMID: 34245599.
5. Frajkova Z, Tedla M, Tedlova E, Suchankova M, Geneid A. Postintubation Dysphagia During COVID-19 Outbreak-Contemporary Review. Dysphagia. 2020 Aug;35(4):549-557. doi: 10.1007/s00455-020-10139-6. Epub 2020 May 28. PMID: 32468193; PMCID: PMC7255443.
6. Ochoa JB, Cárdenas D, Goiburu ME, Bermúdez C, Carrasco F, Correia MITD. Lessons Learned in Nutrition Therapy in Patients With Severe COVID-19. JPEN J Parenter Enteral Nutr. 2020 Nov;44(8):1369-1375. doi: 10.1002/jpen.2005. Epub 2020 Sep 24. PMID: 32833241; PMCID: PMC7461365.Lee Y, Min P, Lee S, Kim SW.
7. Prevalence and Duration of Acute Loss of Smell or Taste in COVID-19 Patients. J Korean Med Sci. 2020 May 11;35(18):e174. doi: 10.3346/jkms.2020.35.e174. PMID: 32383370; PMCID: PMC7211515.
8. Allard L, Ouedraogo E, Molleville J, et al. Malnutrition: Percentage and Association with Prognosis in Patients Hospitalized for Coronavirus Disease 2019. Nutrients. 2020;12(12):3679. Published 2020 Nov 28. doi:10.3390/nu12123679
9. Pironi L, Sasdelli AS, Ravaioli F, et al. Malnutrition and nutritional therapy in patients with SARS-CoV-2 disease. Clin Nutr. 2021;40(3):1330-1337. doi:10.1016/j.clnu.2020.08.021
10. Tsuchiya H. Oral Symptoms Associated with COVID-19 and Their Pathogenic Mechanisms: A Literature Review. *Dent J (Basel)*. 2021;9(3):32. Published 2021 Mar 11. doi:10.3390/dj9030032
11. Yang, L., Xie, X., Tu, Z. *et al.* The signal pathways and treatment of cytokine storm in COVID-19. *Sig Transduct Target Ther* **6,** 255 (2021). https://doi.org/10.1038/s41392-021-00679-0
12. Zabetakis I, Lordan R, Norton C, Tsoupras A. COVID-19: The Inflammation Link and the Role of Nutrition in Potential Mitigation. *Nutrients*. 2020;12(5):1466. Published 2020 May 19. doi:10.3390/nu12051466