

## Nutrition Status Affects COVID-19 Patient Outcomes

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Is there any relation between nutrition status and the coronavirus 2019 (COVID-19) disease? This terrible pandemic has generated a massive amount of publications in a very short time, and the first meta-analysis already appears as “Epub.”<sup>1</sup> Several characteristics have been identified as risk factors of an evolution toward a severe form of the disease. These include hypertension, diabetes, cardiovascular disease, obesity, respiratory diseases, smoking, older age, higher Sequential Organ Failure Assessment score, and a series of laboratory findings, such as D-dimers, procalcitonin, lactate dehydrogenase, leukopenia, and lymphopenia.<sup>1,2</sup> Except for obesity, there has been no mention of any nutrition-related item until the study by Zhao et al.<sup>3</sup> The authors analyzed the nutrition characteristics of 371 patients admitted for confirmed COVID-19, of which 67 were critically ill.<sup>3</sup> They show that 2 characteristics that directly affect their metabolism and immune response are present in the COVID-19 patients at a disproportionate frequency. In addition to the inflammation, the patients present with an unusually high incidence of loss of appetite during the days preceding their admission and some with diarrhea, resulting in a significant reduction of their food intake, as reported with the nutrition risk screening (NRS) score. Does the finding of reduced food intake matter? Certainly, it does, as it is associated with a significantly increased mortality rate already reported in large international populations. The international nutritionDay questionnaire, a prevalence survey including 153,470 patients, shows a sextuple mortality rate in patients with reduced food intake.<sup>4</sup>

The authors used the NRS score to evaluate their patients, as recommended by the Chinese and European societies of clinical nutrition.<sup>5</sup> The NRS score has the enormous advantage of being easy to collect while not requiring any laboratory determination. The score ranges from 0 to 7, assessing nutrition (maximum, 3 points), severity of illness (maximum, 3 points), and age (maximum, 1 point). The nutrition part reports on weight loss, body mass index (BMI), and food ingestion during the last days. Two cutoffs have been validated that should trigger a nutrition intervention: NRS score  $\geq 3$  for inpatients and  $\geq 5$  for critically ill patients.<sup>5</sup> Zhao et al collected NRS scores for 371 of 413 patients: 92% of patients were at risk of hospital malnutrition ( $\geq 3$  points), whereas 16% presented with a very high risk ( $\geq 5$  points), a proportion that increased to

62% in the critically ill. Only 4% of patients with NRS scores 3–4 died. The mortality rate of the entire cohort was 9%, and in patients with NRS scores  $\geq 5$ , the mortality rate was 43%.

Before the actual pandemic, the high NRS score ( $\geq 5$ ) was shown to be able to identify the patients with higher mortality, as in a Lausanne intensive care unit (ICU) cohort of persistently critically ill patients—in these patients nutrition, therapy requires fine-tuning.<sup>6</sup> Zhao et al confirm the importance of this threshold in COVID-19 patients.

Screening and scoring is a good start and reflects good care! But screening is only the first step of nutrition therapy! Only 25% of the 371 patients received a form of nutrition support, and 121 (33%) patients received probiotics as treatment for diarrhea. Feeding was defined as a delivery  $> 10$  kcal/kg/d. The proportion of fed patients was lowest (20%) in the “severe” patients and a little higher (46%) in the critically ill! Among the latter, enteral nutrition (EN) was attempted; 31% received parenteral nutrition (PN), and 8% received a combination of EN and PN. This means that 54% of the critically ill patients were not fed. This is likely to have contributed to the mortality rate, as 62% of the patients had high NRS scores on admission. The authors humbly recognize that were not able to do better. But these findings might well be universal.

Could it have been different? Could a higher proportion of patients have been fed, probably contributing to mortality reduction? The answer is “potentially yes,” as the nutrition therapy could have been more efficient. In the nutritionDay survey, not being fed on the study day was associated with an 8-fold increase in mortality.<sup>4</sup> The

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presence of standard operating procedures (SOPs) might have made a difference. In chaos conditions with limited human and material resources, procedures must be simple. One of the important aims of SOPs is exactly that—to define how to proceed when everything is too much and good, willing caregivers lack training.

In the Lausanne COVID-19 cohort of 117 critically ill patients (unpublished data), the median NRS was 5 points, and the median score for food intake component was 2 (of a maximum 3), contributing heavily to the NRS (in addition to critical illness [2-3 points]), whereas in the Wuhan cohort, weight loss or low BMI were rare (unpublished data). But the majority of Lausanne patients were fed by enteral route, which initiated within 24 hours, nearly straight after intubation; ICU mortality was 13%. Why were they fed despite the fact that an important proportion of physicians and nurses were not ICU trained? Because there are SOPs that were used to orient the untrained ICU personnel during the crisis. In the SOPs, intubation translates into initiating EN right away in the absence of severe shock or other major instability. *How much?*: 20 kcal/kg to be increased over 3 days. *Which product?*: The standard high-protein with fiber product—there is only 1 available. *Micronutrients?*: One multivitamin and multitrace element vial + 100-mg thiamin per day for 6 days. Simple.

There are many contributors to mortality. Malnutrition is one of them, and refeeding syndrome is another—the patients were exposed to both. There are of course epidemiological factors explaining the higher mortality in Wuhan compared with European settings. Wuhan medical teams were discovering the disease and the treatments to apply, whereas we were 2–3 months later taking advantage of this very recent knowledge to orient the treatments. But nutrition matters and is cornerstone to an adequate immune response. Interestingly, the procalcitonin value was significantly correlated with the NRS score. As is the rule in COVID-19 patients, inflammation was present, but it was not massive (median C-reactive protein, 69 mg/L) in the critically ill; but serum prealbumin level, as a visceral marker and an acute phase protein, was deeply depressed (median, 0.10 mg/L; normal, 0.2–0.4 g/L), reflecting a devastating, ongoing catabolic process.

The relation between malnutrition (acute or chronic) and infection is complex<sup>7</sup> but has repeatedly been shown to be a reality, being long recognized at the level of the World Health Organization. It is important to note that

acute, recent underfeeding seemed to matter most, as the medical history does not show any chronic malnutrition. But 60% of patients had not been able to eat normally in the last days before admission in the Wuhan COVID-19 cohort. No chronic malnutrition was responsible for the disease, but acute underfeeding did compromise the immune defenses and contributed to rapid loss of lean body mass, which we know is linked to immunity and outcome. Acute underfeeding (a few days) has a direct impact on the inflammatory response and on the cellular immunity and can be counteracted by individualized feeding using a combination of EN and PN.<sup>8</sup>

With the *retroscope*, it is easy to be critical, but handling chaos is a challenge, and the authors did their best. Everything is more difficult with an overwhelming number of admissions. An SOP that provides a systematic feeding strategy may help reduce the phenomenon and its devastating consequences. As we are all worried about potential second waves of the pandemic, it is important to learn from this experience and to take advantage of a little “pandemic break” to create nutrition SOPs that promote nutrition therapy.

## References

1. Zheng Z, Peng F, Xu B, et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. *J Infect.* Published online April 23, 2020. <https://doi.org/10.1016/j.jinf.2020.04.021>
2. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan. *Lancet.* 2020;395:1054-1062.
3. Zhao X, Li Y, Ge Y, et al. Evaluation of nutrition risk and its association with mortality risk in severely and critically ill COVID-19 patients. *JPEN J Parenter Enteral Nutr.* Accepted manuscript. Published online July 1, 2020. <https://doi.org/10.1002/jpen.1953>. [Correction added on September 12, 2020 after first online publication: Reference 3 was revised.]
4. Hiesmayr M, Tarantino S, Moick S, et al. Hospital malnutrition, a call for political action: a public health and nutrition day perspective. *J Clin Med.* 2019;8(12):2048.
5. Singer P, Reintam-Blaser A, Berger MM, et al. ESPEN guidelines: nutrition in the ICU. *Clin Nutr.* 2019;38(1):48-79.
6. Viana MV, Pantet O, Bagnoud G. Metabolic and nutritional characteristics of long-stay critically ill patients. *J Clin Med.* 2019;8.7:985.
7. Schaible U. E., Kaufmann S. H. Malnutrition and infection: complex mechanisms and global impacts. *PLoS Med.* 2007;4(5):e115.
8. Berger MM, Pantet O, Jacquelin-Ravel N. Supplemental parenteral nutrition improves immunity with unchanged carbohydrate and protein metabolism in critically ill patients: The SPN2 randomized tracer study. *Clin Nutr.* 2019;38(5):2408-2416.