Antioxidative amino acids in early enteral versus parenteral nutrition following major rectal surgery

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the treatment-dose heparin for primary prevention, 60% of the experts responded considered multimodal thromboprophylaxis to include mechanical methods. As a result, the dose should be determined based on the risk-benefit balance. Several clinical trials comparing different doses of heparins are planned or initiated (https://clinicaltrials.gov/ct2/results?cond=COVID-19&term=low-molecular-weight-heparin&cntry=&state=&city=&dist=). Until we achieve definitive results, we agree with the many societies that state that the standard prophylaxis dose should be used. In addition to ISTH, World Health Organization, National Institute of Health, all recommend standard prophylactic dose heparin. Recently, Klok et al (6) reported the crude cumulative frequency of the thrombosis was 57% (95% CI, 47–67%), even though the patients received pharmacological thromboprophylaxis. Although it is understandable to think that a higher dose of anticoagulation is necessary, the use of higher doses of anticoagulation does not appear to decrease all-cause mortality (hazard ratio, 0.79, 95% CI, 0.35–1.8).

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Antioxidative Amino Acids in Early Enteral Versus Parenteral Nutrition Following Major Rectal Surgery

To the Editor:

Following major rectal surgery, postoperative ileus is common and few patients reach nutritional goals in the first days after surgery. A previous trial randomized patients to receive supplementary early enteral versus parenteral nutrition after major rectal surgery. Enteral nutrition was superior, as patients experienced less postoperative ileus and anastomotic leakage when compared with patients receiving parenteral nutrition (1).

To study the underlying mechanisms, we previously published a substudy in *Critical Care Medicine* on plasma concentrations of conditionally essential amino acids in patients randomized to early enteral versus parenteral nutrition (2). Postoperative plasma concentrations of glutamine and arginine were lower in patients receiving enteral nutrition, while better clinical outcomes were observed when compared with patients receiving parenteral nutrition (2). Consequently, other mechanisms were postulated to have played a role in the beneficial effects of enteral nutrition. Here, we present additional analyses of plasma concentrations of antioxidative amino acids that were previously unavailable.

This was a substudy of a prospective, single-center, randomized controlled trial including 123 patients undergoing surgical resection of primary locally advanced or recurrent rectal carcinoma. The aim was to investigate whether the route of supplementary nutrition early after major rectal surgery affected postoperative plasma concentrations of antioxidative amino acids (taurine, hydroxyproline, glutamic acid, glycine, and N-acetylcysteine). Furthermore, amino acid concentrations were studied in relation to clinical outcomes. For additional information on methodology, see the Methods section in our previous publication (2).

Baseline characteristics were similar between groups (2). No differences were seen between groups in rate of advancement in oral diet. Since exact nutritional value of oral intake could not be registered, cumulative intake of amino acids via artificial route was calculated over the first 5 postoperative days (PODs).

Cumulative intake of total amino acids ($p = 0.037$), glycine ($p < 0.001$), and glutamine ($p < 0.001$) was higher in the parenteral group, while cumulative intake of cysteine was higher in the enteral group ($p < 0.001$). Cumulative intake of proline was similar between groups ($p = 0.278$).

N-acetylcysteine was not detectable in any blood sample. At baseline, plasma concentrations of all amino acids were comparable between groups (**Table 1**). Glycine concentrations were lower in the enteral group on POD 1 ($p = 0.003$) and POD 5 ($p = 0.005$) when compared with the parenteral group. No other differences between groups were observed. Taurine concentrations on POD 1 correlated with occurrence of anastomotic leakage ($r = 0.211$; $p = 0.024$). Proline concentrations on POD 1

TABLE 1. Plasma Amino Acid Concentrations (μmol/L) After Major Rectal Surgery

Amino Acid	Day	Early Enteral Nutrition ($n = 56$)	Early Parenteral Nutrition ($n = 61$)	p	Effect Size (95% CI)
Taurine	0	44.50 (33.00–56.00)	48.00 (35.00–60.50)	0.555	−0.09 (−0.46 to 0.27)
	1	33.00 (21.50–40.75)	35.00 (28.50–44.00)	0.138	−0.34 (−0.70 to 0.03)
	5	29.00 (19.75–38.00)	32.50 (23.00–45.75)	0.108	−0.35 (−0.72 to 0.02)
Glutamic acid	0	35.50 (27.25–42.75)	33.00 (26.00–45.00)	0.950	−0.08 (−0.45 to 0.28)
	1	30.50 (21.75–35.00)	30.00 (22.00–39.00)	0.913	0.05 (−0.32 to 0.42)
	5	32.50 (25.00–43.25)	37.50 (28.50–51.75)	0.062	−0.34 (−0.70 to 0.04)
Glycine	0	172.00 (143.50–221.25)	172.00 (144.00–202.00)	0.787	−0.10 (−0.46 to 0.26)
	1	142.50 (117.00–176.25)	170.00 (140.50–197.50)	**0.003**	−0.55 (−0.91 to −0.17)
	5	133.50 (113.25–182.50)	170.00 (142.00–209.75)	**0.005**	−0.58 (−0.95 to −0.20)
Hydroxyproline	0	5.00 (4.00–8.00)	5.00 (3.00–7.00)	0.115	0.37 (0.00–0.73)
	1	2.00 (1.00–3.25)	2.00 (0.00–3.00)	0.268	0.20 (−0.17 to 0.57)
	5	2.00 (1.00–4.00)	2.50 (1.00–4.00)	0.860	0.08 (−0.28 to 0.45)

Values are presented as median (interquartile range). Boldface entries are statistically significant values.

($r = –0.246$; $p = 0.008$) correlated with occurrence of early ileus. No other significant correlations were found. Multivariable regression analysis revealed no significant correlations between any plasma amino acid concentration and clinical outcomes.

In conclusion, postoperative amino acid plasma concentrations were lower or similar in the enteral group, while a better clinical outcome was observed when compared with the parenteral group. However, plasma concentrations were not directly associated with clinical outcomes. As such, we postulate that changes in amino acid concentrations may be considered as an epiphenomenon to a diseased state, rather than a valid contributor to impaired surgical convalescence (3). Other studies are needed to explain the beneficial effect of enteral nutrition following major rectal surgery.

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A Centrally Acting Antihypertensive, Clonidine, Sedates Patients Presenting With Acute Respiratory Distress Syndrome Evoked by Severe Acute Respiratory Syndrome-Coronavirus 2

To the Editor:

The severe acute respiratory syndrome-coronarovirus 2 pandemics overwhelmed the critical care units (CCUs) in Alsace, France. The disease evokes acute respiratory