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### Comments on Pérez-Bárcena et al.: A randomized trial of intravenous glutamine supplementation in trauma ICU patients

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A reply to these comments can be found at doi:[10.1007/s00134-014-3420-7](https://doi.org/10.1007/s00134-014-3420-7).

Dear Editor,

We read the article entitled “A randomized trial of intravenous glutamine supplementation in trauma ICU patients” with great interest [1]. Although Pérez-Bárcena et al.’s study was very well designed, the results were not surprising to us.

Although the authors discussed timing, the effect of dosing, duration of the treatment and route (enteral and/or parenteral) of glutamine administration, we also would like to discuss the complex interdependent effects of pharmac nutrients, which also needs to be underlined. The metabolic pathways of glutamine and

arginine are interdependent. Glutamine supplementation increases systemic arginine concentrations via an interorgan pathway involving intestinal conversion of glutamine to citrulline and renal conversion of citrulline to arginine or via providing nitrogen for arginine synthesis [2]. The higher mortality associated with high dose glutamine may also be explained by increased arginine levels—and higher mortality as a consequence—as seen in previous arginine supplementation studies [3, 4]. We wonder if the researchers still have the serum samples of the patients to measure arginine levels.

We would like to point out that in future studies with glutamine in critically ill patients, one must follow immune functions as well as related molecules such as arginine.

In addition, we would like to mention another issue in the manuscript. In the discussion part of the article, it is stated that low plasma glutamine levels were associated with mortality and the authors also pointed out that they determined high mortality with low plasma glutamine levels at day 6. However, Table 5 shows that the duration of the mechanical ventilation and ICU length of stay is increased in the group with low glutamine levels, whereas there was no statistical significance in either hospital ( $p = 0.932$ ) or ICU mortality

( $p = 0.934$ ) contrary to the authors’ statement.

### References

1. Pérez-Bárcena J, Marsé P, Zabalegui-Pérez A, Corral E, Herrán-Monge R, Gero-Escapa M, Cervera M, Llompарт-Pou JA, Ayestarán I, Raurich JM, Oliver A, Buño A, García de Lorenzo A, Guiem Frontera G (2014) A randomized trial of intravenous glutamine supplementation in trauma ICU patients. *Intensive Care Med* 2014(40):539–547. doi: [10.1007/s00134-014-3230-y](https://doi.org/10.1007/s00134-014-3230-y)
2. Vermeulen MA, van de Poll MC, Ligthart-Melis GC, Dejong CH, van den Tol MP, Boelens PG, van Leeuwen PA (2007) Specific amino acids in the critically ill patient-exogenous glutamine/arginine: a common denominator? *Crit Care Med* 35:S568–S576
3. Bertolini G, Iapichino G, Radrizzani D (2003) Early enteral immunonutrition in patients with severe sepsis: results of an interim analysis of a randomized multicentre clinical trial. *Intensive Care Med* 29:834–840
4. Kalil AC, Danner RL (2006) L-Arginine supplementation in sepsis: beneficial or harmful? *Curr Opin Crit Care* 12(30):3–308

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