Reply - Letter to the Editor - The usefulness of GLIM criteria to guide nutritional treatment needs further study

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We thank Dr. Catikkas and colleagues for their letter in response to our secondary analysis looking at value of modified GLIM criteria to predict adverse clinical outcome and response to nutritional treatment within the EFFORT patient population [1,2]. While the analysis confirmed the strong prognostic value of the GLIM criteria reported in previous investigations, the results did not confirm the absence of effect of nutritional support in GLIM negative patients. In fact, within the subgroup of patients at nutritional risk with a NRS score ≥3 points, but negative GLIM criteria, nutritional support was associated with a (non-significant) reduction in the risk of adverse outcome (odds ratio 0.95, 95%CI 0.65 to 1.40) and mortality (odds ratio 0.85, 95%CI 0.42 to 1.70). Although these effects were less pronounced compared with GLIM positive patients, interaction analyses did not show evidence for effect modification suggesting that GLIM criteria may not help to separate responders to nutritional therapy from non-responders. Importantly, the limitations of subgroup analyses are well established including the risk for false negative results due to inadequate power, and subgroup analyses should in most cases be viewed as exploratory analyses with later confirmation in prospective trials [3]. Because GLIM was not available at the start of the EFFORT trial, these analyses were not preplanned (including sample size calculation). The lack of significant interaction, however, may be explained by two key factors: low effect size (i.e., how well GLIM separates responders from non-responders) and/or low number of patients.

However, different analyses from the EFFORT trial suggested that several specific patient characteristics and blood markers exist (with significant results in interaction analyses) which may help to predict treatment response and which may thus help to improve GLIM criteria in this regard: inflammation, which is important driver of reduced food intake and muscle catabolism was a strong predictor for a lack of response to nutritional treatment in the EFFORT cohort [4-6]. While patients with low or moderate inflammation and CRP concentrations ≤100 mg/L had a strong benefit from nutritional support, this benefit was not observed in patients with high inflammation [4]. Response to nutritional support was also greater in patients with advanced chronic kidney disease [2] and low hand-grip strength [7], while admission albumin concentrations and different screening tools did not separate responders from non-responders [8,9].

Understanding how to best use individual nutritional support to treat malnutrition remains complex. While GLIM criteria have been proven to have strong prognostic implications, we need to be careful regarding their use for guiding nutritional interventions because GLIM negative patients may still benefit from support. Thus, we may need to better understand different phenotypes of malnutrition to develop more personalized approaches in the future and understand which nutritional intervention for which patient. Secondary analyses of the EFFORT trial and other trials should be considered hypothesis-generating, but, may still help to lead the path towards these important goals [10].

References

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