Reviewer’s report

Title: Is there only one cachexia? Evaluation of routine laboratory parameters in patients with different diseases that can cause cachexia

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Reviewer: Gabi Drochioiu

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Referee report

MS Title: Is there only one cachexia? Evaluation of routine laboratory parameters in patients with different diseases that can cause cachexia
Authors: T. Letilovic, S. Perkov, Z. F. Mestic and R. Vrhovac

This paper describes an interesting evaluation of some biochemical parameters in patients with various forms of cancer that suffer from cachexia. Results are of real interest and well presented. However, in the present form, this manuscript seems to be only a technical report with little information on the mechanisms and a weak interpretation of results. Discussion is made especially on findings in literature and less on own results. Conclusion is not clear and properly written. It is like a general remark on cachexia and not on specificity of own data.

Therefore, I do not recommend this paper be published in its present form; however, it could be published after major revision, since the manuscript has interesting data on cachexia.

I have a few more specific suggestions that might assist the authors if they choose to revise the manuscript:

First of all, this manuscript seems to be more suitable to be submitted to a medical journal than to Nutrition Journal. However, it could be of interest for nutritionists, if the authors could relate more the topic of their manuscript to the specificity of the journal.

Since cachexia is “common to many patients with chronic diseases such as cancer, acquired immunodeficiency syndrome, congestive heart failure, chronic infections, rheumatoid arthritis and kidney failure”, the title seems to me incorrect. The authors analyze some patients with cancer and not with some other “different diseases”. Therefore, I suggest changing the title accordingly.

The first part of “Discussion”, such as “Chronic illnesses in advanced stages are frequently characterized by reduction in body weight and alterations in body composition, a syndrome known as cachexia [9]. Although it was described centuries ago [10,11], its relation to prognosis and inflammatory response was recognized in past decades. It is estimated that 5 million people in United States of America develop cachexia annually [4]. Development of cachexia in the
The evolution of chronic diseases is related to worse survival [12,13] and it is estimated that cachexia directly leads to 2 million deaths annually [14]. Additionally, cachexia is also related to increased incidence of chemotherapy related toxicities [15] and increased perioperative death and complications [16].

While I don’t contest the results obtained, I am afraid that “looking to cachexia as a single phenomenon, with a single set of defining criteria, is rather arbitrary and unjustified” is not a logical conclusion of this paper. Indeed, I’m having difficulty discerning the main conclusion of this paper, which seems to be that cachexia is not an unique phenomenon. However, experimental data and especially the investigated parameters are not comprehensive enough to picture a real mechanism of cachexia. In addition, it could be of interest to consider the evolution of cachectic symptoms, from the beginning of generating pathologies to the patient extinction. In the incipient stage, the mechanism of cachexia could be unclear and complicated; in the final part the biochemical processes involved could be more evident. References like: Tisdale MJ. Pathogenesis of cancer cachexia. J Supp Oncol 2003;1:159-168; Kotler DP. Cachexia. Ann Intern Med 2000;133:622-634, or Drochioiu G. Med Hypotheses 2008; 70:1167–1173 could clarify some aspects of interest. For example, the last mentioned ref considers a unique biochemical mechanism in cachexia. Could the authors of this manuscript discuss their position vs that in such article or articles? Moreover, they found a decrease in the concentration of hemoglobin and albumin. How could they explain this? Is any explanation in their view? The mentioned article in Med Hypotheses 2008 might enlighten these results. For instance, since cachexia could be related to an increased hydrolysis of proteins due to a decreased pH, the balance between protein synthesis and degradation could be shifted toward degradation, including that of albumin. Because in cancer and other diseases, the respiration is altered, less hemoglobin is necessary. Have the authors other explanations? What is the relationship between inflammation, pH, proteolysis, cachexia? Make some explanation more clear.

Minor revision: typographic mistakes and English. In brief, the manuscript is well written, but there are insignificant mistakes (Results, Patients’ characteristics: loss of body weight in cachectic patients between prespecified groups. Clinical characteristics of patients are shown in Table 1.)

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests: No competing interest.