Author's response to reviews

Title: Pancreatic cancer related cachexia: influence on metabolism and correlation to weight loss and pulmonary function

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Author’s response to reviews:

Dear Sir or Madam,

Thank you for your e-mail, which we received on January 16th 2009, regarding your comments on our manuscript mentioned above.

We prepared a revised version of the manuscript including the editorial suggestions and those of the 2 reviewers: all changes are displayed in bold letters and deleted text is marked striked through.

With kind regards,

Marc Martignoni, M.D.
Jeannine Bachmann, M.D.

Response to the Editor’s Comments:

Comment 1: The editor reminded us to make clear that the study was performed with the approval of an ethics committee and in compliance with the Declaration of Helsinki.

The study was performed according to the Declaration of Helsinki. We updated this information.

This study was not approved by an ethics committee, because there were no additional experimental procedures or examinations performed: laboratory parameters are necessary before an operative procedure takes place, and in elderly patients and those with chronic pulmonary diseases, lung function tests
are performed routinely before major abdominal surgery. Data were collected with written informed consent of the patient, but no additional examination or tissue or additional blood sampling was performed.

Thus ethics committee approval for this data acquisition was not necessary.

Comment 2: The editor asked us to confirm that informed consent exists for the patient whose abdominal scan is published in figure 1.

Every patient whose data are presented in this publication gave written informed consent: this also includes their agreement for data acquisition in the follow-up period and for publication of data in an anonymous manner.

Comment 3: The editor asked us to include the Authors' Contributions and Competing Interests sections in the main text of the manuscript and not as additional files.

The sections “authors’ contributions” and “competing interests” were placed at the end of the manuscript instead of in additional files.

Comment 4: The editor asked us to include an Acknowledgements section in the main text of the manuscript, between the Authors’ contributions section and the Reference list, mentioning every person who made substantial contributions to the study’s conception or design, to the acquisition, analysis or interpretation of data, or in drafting the manuscript or revising it critically for important intellectual content, but who does not meet the criteria for authorship. We were also asked to include these contributors’ source(s) of funding, and to acknowledge anyone who contributed materials essential for the study.

Permission to acknowledge should be obtained from all those mentioned in the Acknowledgements.

We were asked to list the source(s) of funding for the study, for each author, and for the manuscript preparation in the acknowledgements section. We were asked to describe the role of the funding body, if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

The part “acknowledgement” has been added.

The “Authors’ contributions” section has been inserted in the main manuscript, after the section “Competing interests”. Every author mentioned fulfils the definition of an author.

We certify that none of the authors has an affiliation with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in the manuscript. The study has not been funded by any organisation.
Comment 5: The editor advised us to copyedit the manuscript to improve the style of written English.

We have now corrected the manuscript with the support of a native English-speaking editor. This person’s name has been added in the Acknowledgments section.

Comment 6: The editor asked us to prepare the abstract according to the guidelines of BMC Cancer.

The abstract was adapted to adhere to the journal's guidelines.

Response to Reviewer “Steven Hochwald”:

Comment 1: The reviewer asked us to change the title, because it has little to do with the results.

We thank you for this advice. We have changed the title to “Pancreatic cancer-related cachexia: influence on metabolism and correlation to weight loss and pulmonary function”.

Comment 2: The reviewer remarked that the abstract is not written properly. He recommended describing the purpose of the study in the Introduction, describing how the study was performed in the Methods, describing the important findings and statistical significance in the Results, and finishing the Conclusions with one to two sentences that correlate with the title.

The abstract has been changed to contain all the required information.

Comment 3: The reviewer asked us to list the duration of symptoms, rather than only describing and defining the symptom “cachexia”.

In our manuscript a patient was defined as cachectic when he had lost 10% of the stable weight. We have now added the time period in which weight loss occurred: these data show a significant difference between patients with and without cachexia.

Comment 4: The reviewer remarked that the performance status is considered to be an important predictor of survival.

The ASA classification data are given in table 1, and show significantly worse values in patients with cachexia. Every patient who underwent operation with curative intention and whose data are presented in this publication has a Karnofsky index of 80 or more; there was no difference between patients with or without cachexia. No other information defining the performance status is available.
Comment 5: The reviewer asked us to perform a multivariate analysis.

We performed Cox regression analysis to show the factors which influence survival: in this analysis, tumour stage and weight loss emerged as independent prognostic factors for survival.

Response to Reviewer “Robert Marsh”:

Comment 1: The reviewer asked us to change the misleading title, because it describes only one facet of the presented data and not the many changes described.

We changed the title to “Pancreatic cancer-related cachexia: influence on metabolism and correlation to weight loss and pulmonary function as mentioned above (comment 1, reviewer “Steven Hochwald”).

Comment 2: The reviewer points out that we have not presented evidence that cachexia per se is responsible for the presented changes and that the changes are not an additional effect of a higher tumour burden or bad biology in patients with cachexia.

The laboratory results of the tumour marker CA19-9, as a marker for tumour load in a patient with pancreatic cancer, do not show a significant difference between patients with and without cachexia; thus we propose that it is not the tumour mass producing the effects of cachexia but the systemic effects of the symptom. The tumour size and grade can only be measured in patients after tumour resection. In resected patients there is no significant difference in tumour size (\(P= 0.270\)) or grade (\(P= 0.166\)) between patients with and without cachexia; this shows that tumour mass and grade are not responsible for the diagnosed differences between the patients. These data have been added to table 1.

Comment 3: The reviewer is in the opinion, that the underlying publication does not present anything new and that we have only presented a textbook chapter on cachexia. He suggested us to present more data on the scientific and biologic basis of cachexia and how their study adds to the understanding of this entity versus the current fairly superficial observation that cachexia is a bad prognostic finding.

Unfortunately, we are not of the same opinion as the reviewer: little is known about the systemic changes and the clinical impact of cachexia in a patient suffering from pancreatic cancer. We tried to present data which shed some light on this symptom, which has such a dramatic effect on survival in these patients. Furthermore we presented data to show that already weight loss exceeding 5% has a clinical impact, but the changes, which are do detect when weight loss is 10% or more, are significantly many more. We are in the opinion that we have presented new data on a symptom many patients with pancreatic cancer are suffering from.