Author's response to reviews

Title: Neck Control after Definitive Radiochemotherapy without Planned Neck Dissection in Node-Positive Head and Neck Cancers

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Author's response to reviews: see over
Dear Editor

We are grateful to the reviewers and to you for your helpful comments, and for giving us the opportunity to respond. Please find attached a thoroughly revised manuscript that addresses concerns raised by the reviewers. This manuscript incorporates additional data that continues to support our original conclusions. These together should contribute to enhancing the appeal and relevance of our paper to the readership of BMC Cancer. In the following paragraphs, we address specific points in detail:

Response to the comments from Dr. Pigorsch

1 and 2. “The authors should more explain their background for the asking of this interesting question, there is no clear definition given which lymph nodes were scored as residual or persistent and which as recurrent disease.”
- We agree with your comments and addressed these points by adding the issues about defining complete nodal response and why we included all patients regardless of nodal response in the introduction part. We also described the details of definition of involved lymph node, response criteria, and follow-up policy in the method part. If involved nodes were all disappeared or reduced to <0.5 cm (difficult to measure the correct size), or there was an increase of ≥20% diameter in any node or appearance of new lesion, the decision was simple. However, there were no “strict” size criteria for “residual” nodal disease in our institution, and we included all patients regardless of nodal response.

3 and 4. “The patient characteristics are given only in a table, the methods for the image evaluation are not clear, whether the “recurrent” lymph node patients reached complete remission after radio-chemotherapy or not or whether they had persistent tumor.”
- We originally presented short summary of patient characteristics in the text as we tried not to insert duplicate data in the table and text. In the revised manuscript, we added details of definition of involved lymph node, response criteria, follow-up policy in the methods part based on your comment. Neck nodal recurrence developed in 11 patients. Ten patients underwent salvage neck dissection and seven of ten patients were successfully salvaged. The remained one patient who experienced synchronous mediastinal metastasis received palliative chemotherapy only.

5. “Because there were no definite criteria of complete nodal response, we included all patients treated with definitive radiochemotherapy regardless of nodal response.” This sentence would be helpful in the methods part. PET results are short and not mentioned in the results part.”
- We rewrite the methods section according to your comment and the detailed data of PET scan were also added in the results and discussion section.

6. “They gave not clear their own criteria for classification with an explanation.”
- We addressed this point by mentioning the limitations of our work in the
discussion section. And we added details of definition of involved lymph node, response criteria, follow-up policy in the methods part based on your comment.

7. “The author gave only the topical data and no comparison to their own results of planned neck dissection.”
   - Since our treatment policy was watchful observation and salvage neck dissection, immediate planned neck dissection was not applied. At least two consecutive imaging studies were done before neck dissection, unless there was an evidence of progressive disease.

8. “It is not mentioned that the data are generated by a retrospective analysis.”
   - We added the mentioned that the data area generated by a retrospective analysis in the abstract.

The response to the comments from Dr. Kuhnt

Discretionary Revisions:
1. “Had the administration of chemotherapy (neo, simultaneous, adjuvant) a prognostic influence?”
   - Prognostic impact of chemotherapy was described additionally in the results section and table 2.

Minor Essential Revisions:
1. “It lacks the details of which statistics program was used. There are missing data for the selection of factors in the multivariate analysis.”
   - We addressed this point by describing the details for the program used and the selection factors in the multivariate analysis in the methods section.

Major Compulsory Revisions:
1. “The patient population is not homogeneous. I recommend the work to focus entirely on the SCC H&N”.
   - We agree with your comment that nasopharyngeal carcinoma has a different radiosensitivity compared to non-nasopharyngeal primary. However, neck control (observation or immediate neck dissection) should be the major concern whenever response of lymph node is less than complete response after radio-chemotherapy whether primary is nasopharyngeal or non-nasopharyngeal lesion. Our analysis according to primary site as one of the candidate prognostic factor showed that there was no significant difference in regional recurrence between nasopharyngeal and non-nasopharyngeal primary.

2. “Which staging system was used? (UICC or AJCC). Why seven patients with stage II in classification?”
   - We used 7th edition of AJCC staging system (added in the methods part).
   Nasopharyngeal carcinoma has different staging system (≤6 cm unilateral multiple metastatic lymph nodes above supraclavicular fossa are N1 and cT1-
2N1 is classified as stage II).

3. “The descriptions when a lymph node on CT / MRI or PET-CT was regarded as involved are missing.”
   - We added the details for the definition of involved lymph node, response criteria, and follow-up policy was described in the methods section.

4. “The chemotherapy dosages of the drugs must be described in detail”.
   - Dose schedule for chemotherapy were described in detail in the methods part.

5. “The discussion is a little too insubstantial. What is the role of PET-CT in the response assessment?”
   - PET-CT data in detail were described in results section and role of PET-CT was added in the discussion section. We also discussed of the limitations of this study in the discussion part.

We appreciate all your helpful comments which improve our work.

Respectfully,

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