Author's response to reviews

Title: Health status evaluation in 640 head and neck cancer survivors using EORTC QLQ-C30 and QLQ-H&N35 questionnaires

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Version: 5 Date: 7 February 2011

Author's response to reviews: see over
Reviewer 1:
Major Compulsory Revisions:
The authors used parametric statistical methods like t-Test and ANOVA. Usually Quality of Life data follow non-parametric distribution. The authors should provide additional information in the Statistical Analysis section.
Answer: Thanks for the suggestion. The mean scores and standard deviations of the HR-QoL scales were calculated according to the EORTC QLQ scoring manual. In the manual, the scores of the QoL scales could be converted the continuous form, ranging from 0 to 100. As reported in the cited references, the use of QoL variable in the continuous (numeral) form has been widely accepted. We have re-written the statistic method and re-analyzed our data. As shown in the revised sections of Statistic Analysis, Results and Tables, we used the general linear model multivariate analysis of variance (GLM-MANOVA) to explore the overall effect of the independent variables with the HR-QoL, followed by ANOVA to investigate the association between the significant prognostic factor and each HR-QoL scale.

Minor Essential Revisions:
Answer: Thanks for the suggestion. It was cited in Reference 23.

2) Page 14, Line 4: The term conformal RT should be corrected to conventional RT.
Answer: Thanks for the suggestion. It was corrected.

Reviewer 2:
Minor Compulsory Revisions: The authors confirmed that RT technique is a determining variable affecting xerostomia in HNC survivors - not only reducing the oral symptoms but also the global QoL.
Being the xerostomia usually cited as the most prevalent complications in HNC survivors post RT, it would be interesting clarify this important aspect in the relatively heterogeneous group of HNC patients, considering tumor stage, site and treatment modalities.
Answer: Thanks for the suggestion. In consideration of the heterogeneous component of the study cohort, we have used multiple linear regression model as shown in Table 4 to explore the prognosticators for xerostomia, we observed a significant trend that
survivors with CCI ≥ 1 (β=5.2, p=0.034), tumor sits at nasopharynx (β=-9.1, p=0.034), or treated by 2DRT (β=-12.2, p<0.01) had a higher probability to report a high level of xerostomia. The HR-QoL outcome for HNC survivors at different tumor site, or with different RT techniques was also investigated in details in Table 5 and Table 6, respectively. (Addressed in Result)

Discretionary Revisions: The title could be more associated to the full text (QoL; RT)
Answer: Thanks for the suggestion. The title was changed to “Health-related Quality of life in 640 head and neck cancer survivors after radiotherapy using EORTC QLQ-C30 and QLQ-H&N35 questionnaires”.

Reviewer 3:
Major compulsory revisions:
1. The title does not reflect the content of the paper. The term health status should have been changed by Health-related Quality of life (HRQoL)
Answer: Thanks for the suggestion. The title was changed to: “Health-related Quality of life evaluation in 640 head and neck cancer survivors after radiotherapy using EORTC QLQ-C30 and QLQ-H&N35 questionnaires”.

2. The introduction does not give an adequate introduction to the field. This is readily visible when the publication year of the references is noted. The introduction should be re-written.
Answer: Thanks for the suggestion. We have re-written the Introduction with the associated information updated.

3. How many patients are lost to follow up? How many patients did not agree to participate? How many could not answer intelligibly?
Answer: This study is a cross sectional investigation, analyzing HR-QoL data of HNC patients who were cancer free when their HR-QoL was assessed during the period from January 2005 to December 2008. Concerning the existence of selection bias, we compared the distributions of sociodemographic characteristics (including age, gender, marital status, and education level) between HNC survivors in the study and all other surviving HNC patients (n=221) found in the cancer registry database in the department. No statistically significant differences were found between them. There were 92 patients unwilling to finish the questionnaire. Participants who were not intelligible with the questionnaire were provided with the assistance of a trained interviewer to read them in a dialect they could understand.
4. How were co-morbidities measured/determined?

Answer: The comorbidity status was measured according to the Charlson comorbidity index and determined by review of chart and on the basis of self-report. (Addressed on the METHODS)

5. The results of the EORTC C30 scores in the present publication (e.g. pain/fatigue) should be judged according to exclusion of coincidental differences. One idea could e.g. be to use sum scores. Another possible approach could be to use a MANOVA test with several indexes included simultaneously to the analyses.

Answer: Thanks for the suggestion. As shown in the revised sections of Statistic analysis, Results and Table 3, we have used the general linear model multivariate analysis of variance (GLM-MANOVA) to perform the test of the overall effect of the sociodemographic and clinical variables on the EORTC QLQ-C30 and H&N35 scales, respectively.

6. In particular, the regression analyses with global QoL could have been performed with multiple linear regression showing the relative importance of the different explaining variables.

Answer: Thanks for the suggestion. As shown in the revised sections of Results and Table 4, we have used the multiple linear regression models to overall effect of the sociodemographic and clinical variables specifically on global QoL and xerostomia, separately.

7. Like the introduction, the discussion does not include a discussion to other contemporary research in the field.

Answer: Thanks for the suggestion. We have re-written the Discussion with some of the associated information updated.

8. Why xerostomia is discussed in detail is not well justified.

Answer: As shown in many publications and the Discussion section, xerostomia related symptoms were usually cited as the most prevalent complications in HNC survivors post RT. Patient-reported xerostomia has been found to significantly correlate with mean dose to the parotid glands and the minor salivary glands in the oral cavity. Furthermore, one of the major endpoints in the evolution of modern RT technique is to perform so called “parotid sparing” to reduce xerostomia.

9. One interesting aspect is QoL differences related to site of the tumour. This could have been analysed in more detail.
Answer: Thanks for the suggestion. As shown in the sections of revised Results and Table 5, we have compared the outcome of EORTC QLQ-C30 and H&N35 scales for head and neck cancer survivors at different tumor sites.

10. Table 2 and 3 could be combined to one table.
Answer: Thanks for the suggestion. The Table 2 and 3 were re-organized into Table 6, and the results were written.

11. Table 5 should be changed to be based on linear regression analyses.
Answer: Thanks for the suggestion. It was done as suggested.

Minor revisions:
1. The statistics text about clinically important differences as to QoL scores could be shortened.
Answer: Thanks for the suggestion. With large sample size in the study, we decided to cancel the comparisons of “clinically important differences” to make the interpretation of the results simple and intelligible.