Peer Review File

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Reviewer #A

1. The text should be read and reviewed for grammar and syntax. There are multiple errors which makes it a difficult manuscript to read. This is an interesting concept to explore, in a small sample of patients.

- We thank the reviewer for this comment. We have had the manuscript rewritten by an experienced scientific editor, who has improved the grammar and stylistic expression of the paper.

Abstract

2. Page 1 line 34: should read 'the aim of this study was …" at present the sentence is not complete/ does not make sense.

- Accordingly, we have modified our text as advised 'The aim of this study was to elucidate the pathogenesis of OSA by comparing the clinical, sleep test parameters and MRI findings both before and after HNC treatment with radiation.' (see Page 3, line 5-7).

Introduction

3. Page 2 line 34-38: this is a very long sentence. I suggest breaking it up at line 36.

- Accordingly, we have broken the sentence and modified our text as advised 'Risk factors of OSA in adults include aging, sex difference (men), obesity, menopause, upper airway anatomy and craniofacial abnormalities. Risk factors for OSA in adults include aging, male gender, obesity, menopause, upper airway anatomy, and craniofacial abnormalities. Furthermore, OSA is an independent risk factor for hypertension, stroke, congestive heart failure, and coronary artery disease, and can thus induce significant morbidity and mortality (1-4)' (see Page 5, line 4-7).

4. Page 2 line 39: this is a very confusing sentence. I think you mean "The prevalence of upper airway tumors and cysts among patients complaining of snoring was 0.24 in a multicenter study (5)

- Accordingly, we have modified our text as advised 'The prevalence of upper airway tumors and cysts among patients complaining of snoring was 0.24 % in a multi-center study (5)' (see Page 5, line 8-9).

5. The introduction cites a couple of references for C/RT treatments for HNC, however does not note that this excludes the surgical arm. Many patients would have C/RT as an adjuvant treatment. This should be covered in the background

-Thank you for the comments. The treatment of this study was not an adjuvant treatment, but a definitive treatment. We have modified the text in the background (see from page 5, line 14 to page 6, line 2). We have added 'Definitive' to the text in 'Patients' section (see page 7, line 5). We have

modified the exclusion criteria (see from page 7, line 9 14).

6. You reference Boscolo-Rizzo 2008 (8) several times in relation to QOL. This is a relatively small study (67 patients) written over 10 years ago. I suggest you find a more up to date one.
- Accordingly, we have replaced the reference # 8 from Boscolo-Rizzo 2008 to 'Metreau 2014' (see References #8).

Materials and Methods
7. Page 3 line 29 – 'almost ALL OF THE patients…' please insert key words to make this sentence make sense
- Accordingly, we have modified our text as advised 'Almost all of the patients were treated with a radiation dose of 70 Gy in 35 fractions, except one who underwent IA-CRT with a radiation dose of 60 Gy in 30 fractions.' (see page 7, line 6-8).

8. Page 3 line 31 – please confirm if they 60Gy dose was also 35 fractions, or in fact ?30fractions. also why this was different to all other patients
- We appreciate the reviewer's comment on this point. The 60 Gy dose was also 30 fractions. The reason of different radiation dose was that one patient who was under gone intraarterial concurrent chemoradiotherapy (IA-CRT) with a radiation dose of 60 Gy. We have modified the text (see page 7, line 6-8).

9. Page 3 line 32 – repetition of '1'
- In accordance with the reviewer's comment. We have deleted one (1) (see page 7, line 9).

10. I don't think you note if these are all adult patients
- We thank the reviewer for this comment. We added the text '(1) under 20 years' in exclusion criteria (see page 7, line 9). The numbering was changed accordingly, from '(1) to (2)', '(2) to (3)', '(4) to (5)', and '(5) to (6)' (see from page 7, line 9 to 14).

11. Should an exclusion criteria be RT delivered in the adjuvant setting? This is possibly covered by exclusion criteria (2)
- We appreciate the reviewer's comment on this point. The adjuvant setting was in exclusion criteria '(3)'. We have modified the text as advised '(3) history of surgery for HNC and/or planned adjuvant therapy' (see from page 7, line 11 to 12).

12. Page 4 line 34 – was the blinded single investigator an author? If so add initials here
- We thank the reviewer for this comment. The blinded single investigator was an author, Naoko Sata, M.D., Ph.D. We added her initial '(N. S.)' (see page 10, line 6).

13. There are multiple acronyms which are not written in full, e.g. BRT. While these are commonly used they should be written in their full form the first time they are written. Eg page 3 line 28,
- Accordingly, we have added the full form as ‘bioradiotherapy (BRT)’ (see page 7, line 5).

14. why did you do post test at the 2-month post starting treatment mark? That would bring most patients to about 1 week post-completion of radiation, which is a time where their symptoms from the radiation is at its peak. I would imagine this would replicate symptoms and mask some results. I note you write this as a limitation however you should justify why this time point was considered in the first place.
- We regret this oversight. First, it was incorrectly stated ‘within 2 months after starting treatment’. The post-test was performed ‘2 month after starting treatment’. Seconds, as the reviewer pointed out, it would be appropriate to do post-test in late phase. We had experienced the severe obstructive sleep apnea (OSA) associated with edema in laryngo-hypopharynx after CCRT for advanced laryngeal and hypopharyngeal cancer (Ref.#12 Inoshita 2021). The patient was diagnosed OSA 3.5 years after the end of CCRT treatment, so we evaluated at the end of treatment in this study.
We have modified our text ‘For post-treatment tests, only those who gave consent and had a sleep test during hospitalization were included. Based on our past experience, post-treatment tests were performed 2 months after starting the treatment (12).’ (see page 8, line 16 to page 9, line 2).

Results
15. Page 5 line 25 – you note that 82.3% had OSA, however I thought an inclusion criteria was OSA, why was this number not 100%
- We believe the reviewer is mistaken on this point. The inclusion criteria of this study was undiagnosed-OSA with head and neck cancer which located at nasopharynx, oropharynx, hypopharynx and larynx. We have modified our text ‘The prevalence of OSA in pre-treatment HNC was 81.3 % (26 patients) and the mean AHI was 20.8±19.0 events/hr’ (see page 1, line 7-8).

16. it strikes me that page 5 line 19 ‘declined for personal reasons’ is not sufficiently specific for a scientific paper. It also makes it impossible to determine what level of bias the following results have
- We appreciate the reviewer's comment on this point. There were two main reasons: (1) the first PSG was more painful and discomfort than expected because there were 25 sensors; and (2) severe side effects of radiation therapy, such as sore throat and dermatitis. We have modified the text (see page 11, line 17 to page 12, line 2).

17. Page 5 line 31 – T4N2 – is this clinical or pathological staging? Which system are you using?
- The TNM staging system were clinical. In accordance with the reviewer's comment, we have added ‘c’ before ‘T4N2M0’ (see page 12, line 13).

Discussion

18. Line 29 – I think the statement that RT Induced anatomical and functional changes is very obvious and expected.

- Accordingly, we have deleted the text (see page 14, line 17).

19. Page 7 , paragraph starting line 21 – this is a confusing paragraph with Conclusion

- We are uncertain as to the meaning of the reviewer's comment. The discussion is provided in the paragraph which the reviewer pointed out, and the conclusion is stated separately (see page 19, line 9 to line 15).

Reviewer #B

Interesting article with new clinical information that will change clinical practice

- We wish to express our deep appreciation to the reviewer for the insightful comment.

Reviewer #C

The authors report on a prospective study of patients with HNC and OSA. They show a high incidence of OSA in this special population. The cited literature includes most of the published literature on this topic. The authors defined and applied appropriate inclusion and exclusion criteria. The included number of patients is relatively small but similar to previously published literature.

- We strongly appreciate the reviewer's comment on this point.

Treatment of HNC (RT, CRT, BRT and IA-CRT) as well as diagnosis of OSA (using two different devices/methods) are not completely homogenous which makes the comparability of results difficult and leads to potential bias. The authors comment on this in the discussion. The results of MRI findings are also discussed. Here a correlation of the MRI findings to the severity of OSA, the location of underlying HNC and the dose of applied radiation would be of great interest to the reader.

- We wish to express our deep appreciation to the reviewer for the insightful comment.

Editing by an English native speaker is advisable.

- We thank the reviewer for this comment. We have had the manuscript rewritten by an experienced scientific editor, who has improved the grammar and stylistic expression of the paper.

In conclusion this publication shows a significant burden of disease in a subpopulation that merits attention and thereby confirms prior research.

- We wish to express our deep appreciation to the reviewer.