Reviewer’s report

Title: Prognostic factors associated with the survival of oropharyngeal carcinoma in Taiwanese community

Version: 1 Date: 12 December 2006

Reviewer: Chris Terhaard

Reviewer’s report:

General

In the review the following points were considered:

1. The question posted by the authors is new, but not well defined. In general oropharyngeal carcinomas are confined to the oropharynx region. That means tonsil, soft palate, base of the tongue, but not the oral cavity. In this study the oral cavity and oropharynx tumours and even hypopharyngeal tumours were included. The second point is the term carcinoma. In the study also lymphomas are included and besides squamous cell carcinoma adenocarcinoma is also included.

2. I do not think the methods are appropriate because the oropharynx, also the hypopharynx and oral cavity are included. All kind of histology: lymphomas, adenocarcinomas, squamous cell carcinomas are included.

3. Are the data sound and well controlled? The most important prognostic factor stage is not included. It is a very large dataset starting with 10,245 persons; 459 patients are excluded. However, in 7% of the included patients no histological conformation of the diagnosis was available. So this 7% should be excluded. If I understand the authors well, the Hakka and Hokkien and Taiwanese aborigines are separately situated. However as stated on page 7 in Hakka regions 25% of the people is not Hakka and in Hokkien regions 15% is not Hokkien. This means that in the table 1 not all the people named aboriginals, Hakka and Hokkien are really aboriginal, Hakka or Hokkien.

4. In general the manuscript adheres the relevant standards for reporting and data deposition, although more details about the uni- and multi-variate analysis could be given.

5. In the discussion again is said that the study goes about oropharyngeal carcinoma subjects. However, it concerns patients with oropharyngeal, hypopharyngeal and oral cavity tumours. Not only carcinomas but also lymphomas. In the discussion many possible prognostic factors that explain the difference between the Hakka and the Taiwanese aborigines and Hokkien are named. However all these factors like cytokine gene polymorphisms are not studied in this manuscript. Also no information is available about the betel-quid chewing habits. In the results no correlation between histology and therapy is given. I suppose that chemotherapy alone was reserved for lymphomas and this explains the better survival in the aborigines for chemotherapy alone compared to radiation alone or surgery plus radiotherapy or radiotherapy and chemotherapy. In squamous cell carcinoma and adenocarcinoma chemotherapy only is a palliative treatment, and prognosis should be comparable with supportive care only. Also not explained in the discussion is the interesting finding that supportive care therapy has the same death hazard as surgery alone and even better than radiotherapy plus chemotherapy in the aborigines.

6. In the summary on page 20, regarded as conclusion, explanation of the better survival of the Hakka group is given, however not based on the data of this study.

7. The title speaks only about oropharyngeal carcinoma. As stated before, there was a wider inclusion in this study.

8. Abstract tells what has been found.

9. In general the writing is acceptable, however for example on page 12, line 15, “lip sites were protective”. I do not understand the word protective. I think the authors mean a better prognosis.

10. My suggestion should be a major compulsory revision based on a selection of patients with histological confirmation of the primary tumour, selection of only those patients with a carcinoma, excluding the lymphomas and the adenocarcinomas. Adding stage to the multi-variety analysis is very important since the treatment would also depend on the stage. I should advise as next step not to accept or reject the manuscript until the authors have responded to the major compulsory revisions.

11. Statistical review: I suggest, that an expert will also review this. There are some questions about the multi-variante analysis.

12. More detailed comments:

Title: this study also involves oral cavity tumours, some hypoharyngeal tumours and lymphomas.

13. Background page 4 and 5:
The same comment about oropharyngeal, oral cavity tumours and hypopharyngeal tumours.

14. Page 6
If we start with 10,245 patients and we exclude 459 patients, 9,786 patients remain. However, 93% of the patients were diagnosed with histological confirmation. My suggestion is to exclude the 7% that did not have a histological confirmation.

15. On page 7 it is not clear or the stratification between Hakka, Hokkien and Taiwanese aborigines is just only based on regions, so not on an exact definition of ethnicity, merely a difference in regions where people live. This may influence the results.

16. On page 8 the choice of therapy is not very detailed analysed. There may be a large difference between chemotherapy used, kind of radiation schedules used, kind of surgery etc.

17. On page 8 the hypopharyngeal tumours were included. This is a quite different group with in general a very bad prognosis compared to oropharyngeal tumours.

18. Page 10: what do you mean by oropharyngeal carcinoma survival rates, disease free survival rates?

19. Page 12 is showing that the survival rates in 1990-1994 are decreased comparing to former years. Do you find any reason for this in your multi-variate analysis?

20. On page 13 it is said that for the aborigines the mortality rates were best with chemotherapy alone. Since we know that chemotherapy alone is only palliative in squamous cell carcinoma and adenocarcinoma this means that chemotherapy alone is only given to the lymphoma patients? The difference in treatment as published on page 13 may be caused by histology and stage. So the multi-variate analysis should include stage, because stage may explain not only the treatment given, but also the results. If people from Taiwanese aborigines have higher stages, this could explain differences in treatment and in outcome.

21. On page 14, 15 and 16 many reasons to explain the difference found in the study are given, however all those prognostic factors are not analysed in this study. The most important is the betel-quid chewing habits, but also these habits are not scored in this study.

22. Page 19, line 15
Surgical therapy alone cannot give a protective effect. I think the authors mean: has a prognostic favourable effect, namely based on patient selection.

23. Page 20
Therapy with chemotherapy alone or radiotherapy alone might indicate that patients have advanced stage, however chemotherapy alone might also be given to lymphomas, giving a good prognosis.

24. Table 3, results of multi-variate analysis
It is not clear why chemotherapy alone is taken as the standard comparing to all other treatments, it looks more logic to take surgery alone.

25. Table 2, adjusted hazard ratio should be based on an analysis using all relevant factors, also including stage.

28. In the figures, number of days is taken for the X-axis, mostly months or years are used.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
see above (2,3,5,10,14)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
see above

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Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes

Declaration of competing interests:
Declaration of competing interests: I declare that I have no competing interest in relation to this paper.