Author's response to reviews

Title: Prognostic parameters for recurrence of papillary thyroid microcarcinoma

Authors:

Tae Yong Kim (tykim@amc.seoul.kr)
Suck Joon Hong (sjhong2@amc.seoul.kr)
Jung Min Kim (benaiiah@hanmail.net)
Won Gu Kim (blessing19@hanmail.net)
Gyungyub Gong (gygong@amc.seoul.kr)
Jin Sook Ryu (jsryu2@amc.seoul.kr)
Won Bae Kim (kimwb@amc.seoul.kr)
Young Kee Shong (ykshong@amc.seoul.kr)

Version: 3 Date: 14 April 2008

Author's response to reviews:

April 14th, 2008

Dear Editor.

We are grateful for the opportunity to respond to these comments and believe our manuscript has been clearly improved by this revision. We hope that the changes are satisfactory and that the manuscript is now suitable for publication in BMC Cancer.

Kind and helpful comments from the referees are highly appreciated. We have carefully considered each of the issues raised by the two reviewers and have addressed to each concerns in the attached letter and the revised manuscript. We also requested English proofreading to a professional copyediting service. Informed consent was also documented in Patients section and manuscript style (including reference) was also checked according to www.biomecentral.com/info/ifora/medicine_journals.

Revision or Insertions are shown with the following attributes and color: Bold, Red.

Thank you for your kind consideration in advance and I am looking forward to hearing good news.

Sincerely yours,

Young Kee Shong, M.D., Ph.D.
Department of Internal Medicine, Asan Medical Center,
University of Ulsan College of Medicine
388-1 Pungnap-dong, Songpa-gu, Seoul 138-736, Korea
Phone: +82-2-3010-3244, Fax: +82-2-3010-6962, E-mail: ykshong@amc.seoul.kr
[Response to Reviewer 1]

We would like to express out most sincere thanks to the first reviewer for the careful review and helpful comments that have been of paramount assistance in improving the manuscript.

Comment 1] In Table 2, 8 patients had regional (node) recurrence. Which level of regional lymph node was affected in such nodal recurrence? More detailed information about the site of regional node recurrence needs to be described.
: We added the information about the site or regional node recurrence (page 23, table 2 in revised manuscript)

Comment 1] The authors stated that TSH suppression therapy was administered to all patients. In the previous studies, the use of TSH suppression has been considered to decrease the possibility of recurrent disease. Did the authors observed any consideration on TSH suppression therapy?
: TSH suppression have clearly documented role in advanced thyroid cancer, but the role of TSH suppression in low-risk thyroid cancer is somewhat controversial. We think that the role of TSH suppression treatment in PTMC patients (especially for those who received hemithyroidectomy) may need to be clarified in the future study.

Comment 3) Page 8, First paragraph, Line 2-3. Extrathyroid extension was found in 38%. This frequency seemed to be high in microcarcinoma patients. How was "extrathyroid extension" defined? In 2002 AJCC/UICC TNM staging, extrathyroid extension was defined as T3 invasion (minimal extension), T4a invasion (apparently involved adjacent neck structure), or T4b invasion (usually unresectable). The degree of extrathyroid extension in this study should be more clearly mentioned.
: Thank you for your helpful comment. We clarify the degree of extrathyroid extension in result section (page 9, paragraph 1 in revised manuscript).

4) Page 6, Last paragrapgh, Line 5. serum TgAb was positive. This means serum Tg?
: Stimulated Tg level is inaccurate when serum TgAb is positive. Thus, we performed further non-radioiodine imaging to find persistent/recurrent disease when the serum TgAb is positive. We modified description to prevent confusion to readers (page 7, paragraph 1)

5) Major concern is grouping of pNx and pN0 as same group. Such grouping usually seems to be inappropriate, because pNx have possibility of conversion to pN1a or pN1b after central and/or lateral node dissection. If so, the results in this study may alter according to the pN stage conversion. When the authors want to attempt such grouping, N staging should be based on clinical nodal status (cN). Otherwise, pNx category should be separately evaluated or excluded in the statistical analysis.
: We are very grateful for this helpful and kind comment. We performed two
major modification of the manuscript.

First, we separated pNx from pN0 group for statistical analysis (page 11, paragraph 1; page 25 table 3, in revised manuscript). In this study, no patient was recurred in pN0 groups, the odds ratio for pN1a, pN1b over pN0 is indefinite value. Thus, we have to delete the description regarding odds ratio and table 4 in previous manuscript. Furthermore, the significance between gender and clinical recurrence was also disappeared after multivariate analysis and we modified the abstract, result, and discussion sections, accordingly.

Second, we added subgroup analysis of 251 PTMC patients (293 all - 42 pNx) with N0, N1b, and N1b staging to exclude the bias from pNx staging. The N staging was also significant prognostic factor even in PTMC patients who received hemi- or subtotal thyroidectomy. We described these changes in revised manuscript (page 11 paragraph 2 – page 12 paragraph 1; page 27 table 4 in revised manuscript)

[Response to Reviewer 2]
We would like to thank the reviewer for the careful review and insightful comments that have been of great assistance in improving the manuscript.

Comment 1] Abstract: patients with pT3b or pT4 < 10 mm included
- We clarified the subject in background section (page 2, paragraph 1 in revised manuscript)

Comment 2] Abstract: hemithyroidectomy is thyroidectomy and always bilateral, hemithyroidectomy or subtotal thyroidectomy, uni or bilateral
- We deleted the previous definition of bilateral and partial thyroidectomy. Instead we clearly described in detail. “Bilateral thyroidectomy” was changed to “total or near-total thyroidectomy”. “Partial thyroidectomy” was changed to “Hemi- or subtotal thyroidectomy”.

Comment 3] Methods: were LN only operated when they were enlarged or palpable ?, Please confirm that for the central and the lateral neck separately.
- We clarified the indication and number of neck dissection in the revised manuscript (page 6 paragraph 1 in revised manuscript)

Comment 4] local recurrence: remnant ?
- We clarified the definition of recurrence (page 7, paragraph 3, line 1 in revised manuscript)

Comment 5] Results: thyroid bed better than operative bed
- We change the description “thyroid bed” to “operative bed”.

Comment 6] Results, patient 5 and 7 – initial UICC stage? pT3a, b ?
- We added description of initial UICC staging (page 10, paragraph 1, line 13 in revised manuscript)

Comment 7] Discussion, patients without evidence for positive LN in
ultrasonography did not have a neck dissection so the N stage remains unclear.

We added description in discussion section (page 14, paragraph 1 in revised manuscript)

Comment 8] Discussion: must be pT4b (UICC 2002)

pT3 means minimal microscopic extrathyroid extension in UICC 2002 staging. The Prognostic value for pT4a or pT4b is definite as in previous report. However, the meaning of pT3 is quite controversial.

Comment 9] Discussion: There should be said that Korea is a country without a iodine deficiency. Therefore there are many Thyroids with only one nodule and so the excellent Ultrasound findings are possible.

We added the reference and description in the discussion section (page 13, paragraph 1 in revised manuscript)