

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Features and Trends of Thyroid Cancer in Patients with Thyroidectomies in Beijing, China between 1994 and 2015 – a Retrospective Study
<b>AUTHORS</b>	Zhao, Ling; Pang, Ping; Zang, Li; Luo, Yukun; Wang, Fulin; Yang, Guoqing; Du, Jin; Wang, Xianling; Lyu, Zhaohui; Dou, Jingtao; Yiming, Mu

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Quan-Yang Duh University of California, San Francisco
<b>REVIEW RETURNED</b>	18-Apr-2018

<b>GENERAL COMMENTS</b>	<p>Summary</p> <p>This is a retrospective review of a single institution experience. From 1994 to 2015, of the 10,798 patients who underwent thyroidectomies 5235 had thyroid cancer. They found the proportion of cancer increased (in two-year increments over 22 years, 17 to 70%), PTC went from 65% to 98%. Rate of microPTC also increased from 13% to 51% and size of cancer decreased from 2.3 to 1.2 cm. They also found the risk of LNM is higher with male sex, tumor size &gt; 1 cm and age &lt;45.</p> <p>Comments</p> <ol style="list-style-type: none"><li>1. This is a very large series over a long time showing trends in Beijing that parallel what has been found elsewhere in the world.</li><li>2. Page 5 line 5. "...as a result of improved diagnosis of thyroid cancer...". Do you have preop versus postop diagnosis to see how many were incidental cancers found only on pathology? Another potential explanation for the increasing rate of mPTC could be more meticulous examination of pathology specimen.</li><li>3. Page 4 line 26. Clinically relevant PTC (crPTC) was defined only by size &gt; 1 cm. By this definition, if a patient had a 0.9 cm PTC, but clinically detectable bulky nodes, would this cancer be clinically relevant?</li><li>4. To interpret the data on LNM, please describe in Method Section when lymph node dissection was indicated and how many of the 5235 patients had lymph node dissection. For example, routine central neck node dissection when preoperative diagnosis was cancer (including lobectomy or total thyroidectomy), or not. During this 22-year period was there a change in whether prophylactic node dissection was done? For example, perhaps in earlier years routine node dissection (therapeutic and prophylactic) was done, but in later years only therapeutic dissection was done, etc.</li><li>5. Page 7 line 30. Please comment on whether the thyroid cancer patients in Beijing is representative of all China and whether there are data on this.</li></ol> <p>Minor comments</p> <ol style="list-style-type: none"><li>1. Page 5 line 35, change "unnecessarily" to "not necessarily".</li></ol>
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	<p>2. Figure 1. What is “Permillage”?</p> <p>3. Page 6 line 47. Please check the annual thyroid cancer diagnosis in the world. I believe it is much higher.</p> <p>4. Page 7 3rd paragraph, Use “neck ultrasonography” instead of “head and neck ultrasonography”.</p>
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<b>REVIEWER</b>	Tae Yong Kim Asan Medical Center, Republic of Korea
<b>REVIEW RETURNED</b>	30-Apr-2018

<b>GENERAL COMMENTS</b>	<p>Ling Z et al analyzed 10,798 patients treated by thyroidectomy from 1994 to 2015 and showed that small papillary thyroid carcinoma increased, while neck node metastasis decreased. Thyroid also suggested that tumor size more than 1 cm, gender, age can be risk factors for regional lymph node metastasis.</p> <p>The manuscript is well written, but I am afraid that there are many errors in English grammars such as “Also increased in the number of cases of the ....” in introduction line 18. I recommend the authors to receive professional English proofreading service.</p> <p>I have other minor comments to improve this manuscript</p> <p>The authors used “year – month” format for tables and figures to show time trends such as “10.1-11.12”, ‘2010.1-2011.12’, but simply ‘10-11’ would be sufficient and more easily readable.</p> <p>In figure 2, authors drew the total average percentage on the right side of each figure. These made confusion to authors that there are sudden changes in trends recently. Just delete the column showing average percent to prevent this confusion.</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

- Page 5 line 5. “...as a result of improved diagnosis of thyroid cancer...”. Do you have preop versus postop diagnosis to see how many were incidental cancers found only on pathology?

Response: We agree with the reviewer on the importance of this. Due to the long temporal coverage of this study, the relevant information was incomplete, thus we couldn't provide the stats on the incidental cancers found on pathology.

- Another potential explanation for the increasing rate of mPTC could be more meticulous examination of pathology specimen.

Response: We agree with the reviewer on this and have added this comment in the revised manuscript. (Line 22, Page 8)

- Page 4 line 26. Clinically relevant PTC (crPTC) was defined only by size > 1 cm. By this definition, if a patient had a 0.9 cm PTC, but clinically detectable bulky nodes, would this cancer be clinically relevant?

Response: We understand this was an arbitrary classification for clinical work. PTC smaller than 1 cm does not necessarily mean lack of clinical relevance, it may affect the clinical management as previously suggested by American Thyroid Association in 2015.

- To interpret the data on LNM, please describe in Method Section when lymph node dissection was indicated how many of the 5235 patients had lymph node dissection. For example, routine central

neck node dissection when preoperative diagnosis was cancer (including lobectomy or total thyroidectomy), or not. During this 22-year period was there a change in whether prophylactic node dissection was done? For example, perhaps in earlier years routine node dissection (therapeutic and prophylactic) was done, but in later years only therapeutic dissection was done, etc.

Response: We are grateful to the reviewer for this suggestion and have made relevant changes to the manuscript. The decision-making of lymph node dissection has been included in the Method Section (Line 2, Page 6). The number of cases with LNM has now been indicated (Line 24, Page 8).

- Page 7 line 30. Please comment on whether the thyroid cancer patients in Beijing is representative of all China and whether there are data on this.

Response: The thyroid cancer patients in our hospital generally represent the population of patients in China. Roughly 20% of these patients were locals in Beijing, while the remaining 80% came from other parts of the country. However, bias might exist in these 80% of the patients because they were usually referred to our hospital while the local hospitals couldn't not make definite diagnosis.

- 1. Page 5 line 35, change “unnecessarily” to “not necessarily”.

Response: We thank the reviewer for the suggestion and have made the change accordingly.

- Figure 1. What is “Permillage”?

Response: Permillage means the proportion per thousand, and this definition has been included in Figure 1 legend.

- Page 6 line 47. Please check the annual thyroid cancer diagnosis in the world. I believe it is much higher.

Response: This was spot-on, the statistics in the world and in the United States were mixed-up, appropriate change has been made in the revised manuscript.

- 4. Page 7 3rd paragraph, Use “neck ultrasonography” instead of “head and neck ultrasonography”.

Response: the change has been made accordingly.

Reviewer: 2

- The manuscript is well written, but I am afraid that there are many errors in English grammars such as “Also increased in the number of cases of the ....” in introduction line 18. I recommend the authors to receive professional English proofreading service.

Response: The manuscript has been proofread by Medjaden Bioscience Limited.

- The authors used “year – month” format for tables and figures to show time trends such as “10.1-11.12”, ‘2010.1-2011.12’, but simply ‘10-11’ would be sufficient and more easily readable.

Response: We highly appreciate the reviewer’s suggestion, and have made the appropriate changes accordingly.

- In figure 2, authors drew the total average percentage on the right side of each figure. These made confusion to authors that there are sudden changes in trends recently. Just delete the column showing average percent to prevent this confusion.

Response: We have made appropriate changes to all the panels accordingly in Figure 2.