Peer Review File

Reviewer A

Comment 1: A survival prediction model is different from a staging model. In addition to predicting survival, staging models (TNM, EACCD, etc.) are also concerned with stratifying patients into stages/risk groups (usually with explicit grouping rules). Therefore, in this report, the authors actually established a prediction model instead of a staging model. The authors may need to make some related changes on terminology.

Reply 1: Thank you for your valuable advice. In this study, we established a model mostly used to predict DFS. Prediction model is indeed more suitable compared with staging model. Relevant changes have been made according to your comment.

Changes in the text: see Page 3, line 30-33 and Page 5, line 73-74

Comment 2: The authors did not validate the model. The lack of external validation reduces the reproducibility and reliability of proposed model and should be acknowledged in the limitation section.

Reply 2: This is indeed a limitation of this study. To validate the model, the 660 patients should be randomly divided into 2 groups, one for making the model, the other one for validating the model. However, for the accuracy of the statistical model, we chose to use all of the data to make the model. More data of patients (after 2005) is being collected. Relevant verification work will be carried out in the future research.

Changes in the text: see Page 13, line 265-266

Comment 3: The authors used a rather obsolete dataset (2000-2005). Reasons should be given for making this decision (The major reason is the 15 year follow up).

Reply 3: For thyroid cancer is a tumor with excellent prognosis, short time follow-up is not enough to obtain effective statistics. A minimum of 15 years of follow-up is sufficient. Relevant explanations have been added to the manuscript.

Changes in the text: see Page 6, line 92-93

Comment 4: Regarding English, the manuscript contains a large number of errors in grammar and structure. These should be fixed.

Reply 4: Many grammar and structure errors have been corrected.

Reviewer B

Comment 1: Please include references for rationale for the need to have a separate system for Chinse population, for example if there are observed differences in the behaviors or PTC in this particular population. the existing system is broad and applicable in most cases.

Reply 1: Thank you for your valuable advice. East Asia has the highest rates of thyroid cancer. The incidence of thyroid cancer in China is higher than that in western country. Even Asian immigrants in Western countries have higher rates of disease than natives. The difference may be related to race. Relevant clinical studies and predictive models have been carried out in many Asia countries such as Korea. In addition, the therapy of thyroid cancer in China was different from western. Thyroid lobectomy is more common in China, and isotopic therapy is less common. But in western countries, total thyroidectomy and isotope therapy are more common. Prognosis is bound to vary due to differences in morbidity and treatment modalities for Chinse population. Relevant references and explanations have been added to the manuscript.

References:

1. Shah BR, Griffiths R, Hall SF. Thyroid cancer incidence among Asian immigrants to Ontario, Canada: A population-based cohort study. CANCER-AM CANCER SOC. 2017 2017-09-01;123(17):3320-5.

2. Lee KE, Park YJ, Cho B, Hwang Y, Choi JY, Kim SJ, et al. Protocol of a Thyroid Cancer Longitudinal Study (T-CALOS): a prospective, clinical and epidemiological study in Korea. BMJ OPEN. 2015 2015-01-05;5(1):e7234.

Changes in the text: see Page 5, line 74-83

Comment 2: Mention of patients who were treated with RAIA is brief. could be another factor to look at such as in patients who received RAI vs who didn't. I am not sure what defines advanced cancer (for example, metastatic outside the neck? or locally extensive)

Reply 2: It is a pity that detailed isotope therapy data are not available in this study. Because isotope therapy is not available at our center, related data are incomplete and unreliable. And advanced cancer usually means invasive tumors, numerous lymph node metastases, or distant metastases. Relevant explanations have been added to the manuscript.

Changes in the text: see Page 6, line 108-109 and see Page 14, line 280-284

Reviewer C

Comment 1: The authors state elevated Tg without structural target did not constitute an adverse event. Does this mean it was not counted as a recurrence? This

would constitute an indeterminate response in which disease status is uncertain.

Reply 1: Thank you for your valuable advice. In this study, the diagnosis of recurrence was confirmed by pathology like reoperation or needle biopsy. Elevated Tg alone was not the basis for the diagnosis of recurrence. For 161 of the 660 PTC patients had received total thyroidectomy, and fewer of them received isotope therapy. In this case, elevated Tg doesn't always make sense. It prompted us to make a more comprehensive examination like ultrasound, CT, MRI and PET/CT.

Comment 2: Can the authors discuss further the large proportion of patients who underwent lobectomy and central neck dissection? What patients/tumor characteristics were eligible for this treatment? And how was biochemical data followed (if at all) after this surgical approach?

Reply 2: Lobectomy plus central neck dissection is the most common operation in east China. According to *Chinese Guidelines for Thyroid Cancer Diagnosis and Treatment*, T1 and T2 tumor Confined to unilateral lobes, lobectomy was recommended. Total thyroidectomy was performed in T3 and T4 tumor. For some patients with high risk factors, total thyroidectomy is also feasible. These risk factors include multifocal cancer, lymph node metastasis, distant metastasis, family history, and early exposure to ionizing radiation. Total thyroidectomy is also feasible in some cases where postoperative radionuclide therapy is considered necessary. Central neck dissection was performed in cN1 and most of cN0 patients. TSH suppressive therapy was the main treatment after operative. The goal of TSH suppressive therapy is determined by risk grade. For example, 0.5~2 mU/L for low-risk PTC patients after lobectomy. Detailed explanations have been added to the manuscript.
Changes in the text: see Page 6, line 97-110

Comment 3: The numbers would also suggest there were patients who underwent lobectomy, central neck dissection, and lateral neck dissection. Is this the case? This is an unconventional treatment decision that should be further explained.

Reply 3: There were 166 patients received lobectomy, central neck dissection, and lateral neck dissection, but not total thyroidectomy. The principle of lobectomy and central neck dissection is the same as before. Lateral neck dissection was performed in cN1b patients. Total thyroidectomy is optional but not required in patients with lateral neck lymph node metastasis according to *Chinese Guidelines for Thyroid Cancer Diagnosis and Treatment*.

Comment 4: In general, establishing a normogram requires that the treatment rendered is standardized. I think additional explanation of how surgical decision

making was performed is needed to see what patient/tumor characteristics led to which surgical approaches since there seem to be a number of patients who had locoregional metastatic disease but only underwent lobectomy.

Reply 4: Because the data is 15-20 years old and the understanding and treatment of thyroid cancer has changed a lot over the years. There were some differences in operative plan. This is an unavoidable limitation. At most time, the selection of surgical methods follows the principles described above. Total thyroidectomy is optional but not required in patients with locoregional metastatic disease. More detailed explanations have been added to the manuscript

Changes in the text: see Page 14, line 267-280

Comment 5: How many patients received RAI? What dose?

Reply 5: It is a pity that detailed isotope therapy data are not available in this study. Because isotope therapy is not available at our center, related data are incomplete and unreliable. Relevant explanations have been added to the limitation section.

Changes in the text: Page 14, line 280-284

Comment 6: What is meant by surgical residue? Positive margins? Or residual disease? And, if residual disease, how was this distinguished from recurrence?

Reply 6: Surgical residue means residual disease. Surgical residue is usually caused by a tumor that invades vital organs like larynx, trachea and common carotid artery. It was not identified as recurrence if residual disease did not progress on imaging after isotope therapy or radiation therapy in this study.

Comment 7: Suggest a thorough review for spelling and grammar.

Reply 7: Many grammar and structure errors have been corrected.