

## Peer Review File

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### Reviewer A

**Comment 1:** As most total thyroidectomy patients are expected to undergo I131 postoperatively as one of the reasons of performing complete thyroidectomy is to facilitate the conduct and efficacy of I131. I am surprised at the no different CSS between total (most with I131) vs non-total (most without I131) thyroidectomy arms, whereas I131 significantly enhance CSS of non-total thyroidectomy subset if I131 is given.

**Reply 1:** We sincerely appreciate the reviewer's insightful observation regarding the relationship between total thyroidectomy, radioactive iodine (I131) therapy, and cancer-specific survival (CSS) in our study. Indeed, as the reviewer correctly points out, most patients who undergo total thyroidectomy are expected to receive I131 postoperatively. This approach is based on the rationale that complete thyroid removal facilitates more effective I131 uptake and treatment. However, our study results reveal a more complex picture that warrants careful interpretation:

1. Regarding patients who underwent total thyroidectomy, our results demonstrate: Before and after propensity score matching (PSM), there were no significant differences in overall survival (OS) and cancer-specific survival (CSS) between the two groups. Post-PSM landmark analysis revealed that beyond 90 months, the total thyroidectomy (TT) group showed a trend towards superior CSS compared to the non-total thyroidectomy (Non-TT) group ( $P=0.06$ ). Although the survival curve for the TT group appeared more favorable after 90 months, the P-value exceeded 0.05, precluding a definitive conclusion of statistical significance. Therefore, we maintain that there were no statistically significant differences in OS and CSS between the two groups.
2. Theoretically, patients who underwent total thyroidectomy typically present with more advanced disease stages and more severe conditions.

Conversely, patients who did not undergo total thyroidectomy often exhibit less pronounced local invasion of surrounding tissues and are generally diagnosed at earlier clinical stages. Notably, even with postoperative I131 treatment, patients who underwent total thyroidectomy did not demonstrate a significantly enhanced survival benefit.

In conclusion, it is important to recognize that multiple factors influence OS and CSS, including tumor stage, surgical approach, administration of I131 treatment, iodine uptake capacity, and tumor characteristics. These results highlight the importance of considering individual patient characteristics and tumor biology in treatment decision-making, rather than relying solely on standardized approaches based on surgical extent. Further research is needed to elucidate the optimal treatment strategies for different subgroups of patients with this condition.

**Changes in the text 1:** We have elaborated on this issue and provided an in-depth analysis in the discussion section of our manuscript (see Page 14, line 374-381).

**Comment 2:** How many patients with total thyroidectomy actually have received postoperative I131 therapy?

**Reply 2:** Thank you for this important question. We appreciate the opportunity to provide more detailed information about the postoperative radioactive iodine (I131) therapy in patients who underwent total thyroidectomy. Prior to propensity score matching (PSM) analysis, among the 2,271 patients who underwent total thyroidectomy:

1,394 patients (61.4%) received I131 therapy

116 patients (5.1%) underwent beam radiation, radioactive implants, or other forms of radiation therapy

761 patients (33.5%) either did not receive I131 therapy or had unknown I131 treatment status

This distribution highlights that while the majority of patients who underwent total thyroidectomy did receive postoperative I131 therapy as expected, a substantial proportion did not or had unclear treatment status. This variability in I131 administration within the total thyroidectomy group is an important factor to consider when interpreting our results.

The reasons for non-administration of I131 in some total thyroidectomy patients may include factors such as individual patient characteristics, tumor features, or institutional practices. This heterogeneity in postoperative management underscores the complexity of treatment decisions in unilateral T3/T4 follicular thyroid cancer and may contribute to the nuanced survival outcomes observed in our study.

**Changes in the text 2:** We have addressed this significant data point in our Results section. (see Page 11, line 285-287).

**Comment 3:** We appreciate the reviewer's insightful question regarding the efficacy of I131 lobar ablation after hemithyroidectomy compared to its conventional use following total thyroidectomy. This is indeed an important consideration in evaluating the overall effectiveness of different treatment approaches.

Unfortunately, we must acknowledge a limitation in our data source that prevents us from directly addressing this question. Our study utilized data from the Surveillance, Epidemiology, and End Results (SEER) database. After thorough examination of the available fields, we have confirmed that the Radiation recode section of the SEER database does not contain any information regarding I131 dosage or the number of therapy sessions.

This limitation in the SEER database means we are unable to provide specific data on how many patients in the non-total thyroidectomy group required two or more radioactive-iodine therapy sessions to achieve satisfactory lobar ablation.

We recognize that this information would be valuable for a more comprehensive understanding of treatment efficacy and patient outcomes.

While we cannot provide the requested specific data, we acknowledge that this is an important aspect of treatment that warrants further investigation. Future studies with more detailed treatment records could potentially address this question and provide valuable insights into the comparative efficacy of I131 therapy following different surgical approaches.

We appreciate the reviewer bringing this point to our attention, as it highlights an area for potential improvement in data collection and analysis in future research on thyroid cancer treatments.

**Changes in the text 3:** We provide a detailed explanation of this matter in the Discussion section (see Page 17, line 460-461).

### **Reviewer B**

**Comment:** This retrospective study aimed to evaluate the long-term survival outcomes of total thyroidectomy and radioactive iodine therapy in unilateral T3 or T4 FTC using propensity score-matched analysis. The article is very written and the sample of patients very large. Results are very interesting.

**Reply:** We sincerely thank you for your thoughtful review of our manuscript. We are grateful for your positive feedback and appreciate the time you've taken to evaluate our work.

We are pleased that you found our article to be well-written and that you recognized the significance of our large patient sample. As you noted, we utilized a substantial dataset to ensure the robustness of our findings, which we believe adds considerable strength to our study.

Your positive evaluation motivates us to continue our research efforts in this field. We hope that our findings will be valuable to clinicians and researchers alike, potentially influencing treatment decisions and future studies in thyroid cancer management.

Once again, we thank you for your encouraging review and for acknowledging the value of our work. Your feedback is invaluable in the process of refining and disseminating our research.

**Changes in the text:** We have not made any modifications to the manuscript in response to this comment, as the reviewer's feedback was entirely positive and did not suggest any necessary revisions. We appreciate the reviewer's thorough evaluation and supportive comments regarding our study's methodology and findings.