Peer review file

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Reviewer A

This study aimed to clarify the significance of postoperative radiation therapy for thymoma staged II, III undergoing surgery in prospective analysis. I think these results were very interesting and being value for publication. However, some points need revisions.

1. Why did PORT improve the survival of thymoma Stage III only? The author should add the comment in the discussion.

Reply 1: The authors appreciate the reviewer's insightful comments. We added comment in the revised manuscript (see Page 11, Line 237 - 240).

Changes: It was difficult to explain why PORT improved the survival of thymoma only in stage III. However, stage III thymoma has a greater risk than stage II, thus, PORT could be helpful to patients with stage III thymoma. Nonetheless, there should be further investigation, as this is contested topic.

2. In table 4, among stage III the variable of recurrence did not have the impact on overall survival, however, among stage II, the recurrence did have impact on the overall survival. How did the authors explain the reason?

Reply 2: Among stage III, recurrence also had a positive HR without statistical significance. This may be attributable to the fact that there were less patients in the stage III group than in the stage II group.

Changes: No changes were made.

3. In figure3, C1, The survival curves were cross each other, however, that suggested

the significant difference. Not only me but also the other readers think that it was not correct statistical methods. The authors should explained the methods or the main reason of the result.

Reply 3: Upon reviewing figure 2, we found that there was an error; indeed B-1 and C-1 were the same. We replaced figure 2.

Changes: Figure 2 was replaced.

4. The PORT impact of survival in stage III thymoma in this study. Then, the authors think how much the PORT is recommended based on this result? Is it absolute recommendation or strong recommendation or possible recommendation? The author should describe that in the discussion.

Reply 4: We have modified our text as advised (see Page 12, Line 250 – 253).

Changes: There currently is no consensus on whether PORT has a positive impact on OS or RFS. In this study, the benefit of PORT on OS and RFS in stage III thymoma was shown. However, the study group was relatively small. Therefore, in conclusion, it appears that PORT could improve the RFS and OS in stage III thymoma.

Reviewer B

The authors evaluate the role of postoperative radiotherapy (PORT) for patients with Masaoka-Koga stages II and III thymoma using KART large database. They showed that the PORT group showed significantly better 5-year recurrence free survival (RFS) among stage III patients after propensity score matching analysis. They also showed that PORT was a significant positive prognostic factor in terms of both RFS and overall survival (OS) in patients with stage III thymomas. The treatment strategy for advanced thymoma after resection have still been controversial, thus this manuscript is new and helpful for studying thymoma treatment. In general, this manuscript is logical and interesting, and discussed a hot topic in thymic epithelial tumor. However, the following points should be addressed.

The author should discuss as follows:

Major points

Although the authors described that tumor-node-metastasis (TNM) staging is not useful for thymomas in Introduction section, how was the efficacy of PORT for the patients classified by TNM staging? Especially we wonder whether PORT improved the RFS and OS in patients with pericardial invasion. If the data were available, please show or discuss this issue.

Reply: The authors appreciate the reviewer's insightful comments. However, it is difficult to provide a discussion regarding the TNM staging due to lack of data.

Changes: No changes were made.

We also want to know whether WHO histological subtype would have some influence on indication of PORT. How was the efficacy of PORT for patients with "stage II and B2/B3 thymoma" or "stage III and B2/B3 thymoma"? Establishment of an optimal treatment strategy for patients with Masaoka-Koga stage III disease as well as WHO cell types B2 and B3, is needed to further improve their long-term outcome.

Reply: We have modified out text as advised (see Page 11, Line 240 - 244).

Changes: Meanwhile, the WHO subtype analysis was not considered in the study design. However, additional analysis was performed using the same database. PORT had a positive impact on stage III and WHO B2/B3 thymoma (P=0.056 for RFS and P=0.002 for OS; n=41), but not on stage II and WHO B2/B3 thymoma (P=0.919 for RFS and P=0.228 for OS; n=127). However, further evaluation is warranted.

Reviewer C

The authors performed a retrospective analysis of patients with thymoma, tried to identify the effectiveness of post-operative radiation therapy (PORT) using multicenter

cohort. They concluded that PORT improved the recurrence-free survival and over-all survival in stage III thymoma patients. This article contains appropriate methods of analyses using propensity score matching. However, there are already more reliable reports with regard to effectiveness of PORT for thymoma patients. Furthermore, most serious problem in this study was that main course of which PORT seems to be effective in patients with stage III thymoma might be the post-operative death in patients could not receive PORT in this study. Authors should mention this truth in discussion and abstract sections.

Reply: The authors appreciate the reviewer's insightful comments. Postoperative mortality rate was low in both stage II and III diseases. This study was a multicenter study. This means that the indication of PORT may not have been the same throughout the various institutions. Propensity score matching was performed to revise the confounding factors.

Changes: No changes were made.

Other problems:

1. The authors should show those regimens of post-operative chemotherapy for patients with thymoma.

Reply: Due to the lack of data, further discussion regarding this may not be possible.

Changes: No changes were made.

2. Over all or recurrence free survival rates were quite worse than other study. Authors should show the speculation of those reasons of the worse results.

Reply: The OS of thymoma was different from each study. Also, unlike other tumors, thymoma is a rare disease, and thus, any cohort of thymoma patients may not be a good representative sample. However, the cohort in this study may be the largest cohort in South Korea, from a multicenter database, which means it could be a decent representative cohort of thymoma patients in South Korea.

Changes: No changes were made.

3. Figure 2-C showed that those patients without PORT died of post-operative mortality. Authors should reveal those courses of patients' death within post-operative one year.

Reply: We have modified our text as advised (see Page 8, Line 155 - 157).

Changes: Among stage III thymoma, three patients without PORT died within the postoperative 1 year. The cause of deaths was 1 myocardial infarction, 1 thymoma related death, and 1 unknown cause.

4. Authors should mention that main course of which PORT seems to be effective in patients with stage III thymoma might be the post-operative death in patients could not receive PORT in this study.

Reply: We added comment in the revised manuscript (see Page 11, Line 237 - 240).

Changes: It was difficult to explain why PORT improved the survival of thymoma only in stage III. However, stage III thymoma has a greater risk than stage II, thus, PORT could be helpful to patients with stage III thymoma. Nonetheless, there should be further investigation, as this is contested topic.