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Retrospective Study on Port in Adult Thymoma

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Abstract
Introduction: *Thymoma is a rare neoplasm, and the role of post-operative radiotherapy (PORT) in thymoma is still controversial. We performed an institute based retrospective study to analyze the impact of PORT on overall survival (OS).*
Methods: *We analyzed total 13 patients of thymoma, who were operated outside and come to our institute for PORT during 2010-2018. There were stage I & IIA (3), IIB (7), III (2), IVA (1) patients according to Masoaka –Koga staging system. Surgery done was complete resection (10), partial resection (2), only biopsy (1). Three patients of early I and IIA stage, had not received any RT. Two patients of stage II B with complete resected tumor had refused radiotherapy. Total 8 patients were irradiated with a mean dose of 50.4 Gy (50.4 – 60 Gy). There was 1 patient in PORT and 1 patient in only surgery arm with IIB stage had positive surgical margins. Patients with WHO grade B2 were four, while rest of the nine patients were having grade B3. Three patients were having associated myasthenia gravis two in PORT and 1 in surgery only arm, and were taking treatment for that. Median follow up period was 66 months (1-78 months).*
Result: *Out of 8 patients under PORT, 5 (62.5%) were alive till December 2018, one patient had not completed RT because of acute RT reactions, two patients were dead after RT completion, and cause of death was associate myasthenia gravis in one, while one was died because of thymoma. In surgery alone group, two patients (40%) were alive, one was expired due to cardiac arrest and two patients were dead because of the disease.*
Conclusion: *PORT improved overall survival in patients of thymoma especially in stage II B, III and positive surgical margins.*
Keywords: *Thymoma, PORT, OS.*

Introduction

Thymus, a small lymphatic organ lies in upper chest beneath breast bone. The thymic epithelial tumors (thymoma and thymic carcinoma), a rare neoplasm represent most common anterior mediastinal tumors (50% in adults), grow indolently and rarely spread outside thymus. The incidence of thymic tumors in the USA is 0.13 per

100,000 person-years according to the Surveillance, Epidemiology, and End Results (SEER) database[1]. Approximately 30-45% of thymic tumors may be accompanied with myasthenia gravis (MG)[2], while only 15% of MG patients have thymoma. Primary curative treatment of choice is surgery. Their association with critical mediastinal structure make complete resection difficult. As a result, PORT was used to improve outcome. However, proper indications of PORT has to be define. PORT, according to available data is not beneficial in stage I and II A, while in stage IIB onwards it seems to provide survival benefit as recurrence after resection seen in 10-30% in 10 years.

Material and Methods

Total 13 patients that were included in our study had thymoma histology. Surgery done was median sternotomy with resection of primary that is thymectomy with complete resection (10), partial resection (2), only biopsy (1). They all were referred to our institute for PORT. History and physical examination was done, with especial look for sign and symptoms of myasthenia gravis. They were advised for routine blood investigations, CECT scan thorax. All 8 patients received radiotherapy to median dose of 50.4 Gy (50.4-60 Gy) @ 1.8-2 Gy/#. GTV was defined as surgical bed or residual tumor. CTV was 1 cm around GTV while PTV was 0.5 cm to CTV.

Patient demographic and treatment variables

Relevant data regarding patient age, sex, performance status, surgical margin status, Masoka stage group, WHO grade, associated myasthenia gravis were recorded. Cases were categorized according to the stage for thymic epithelial tumors, stage I (complete encapsulated tumors), IIA (micro invasive tumors into surrounding structures & confined to gland of origin), IIB (macro invasive to capsule and adjacent connective tissue), III (macroscopic invasion to adjacent organ/structure in mediastinum e.g. lungs, sac around heart or large blood vessels), IVA (spread widely around heart and lung), IVB (extension to lymph nodes, metastases).

Statistical Analysis

Chi-square test to calculate patient and treatment related factors between patient who did or did not receive PORT. Primary end point was OS (date of diagnosis to date of death from any cause).

Results

Patient Characteristics

A total of 13 patients with thymoma (n = 13) who met predefined selection criteria were identified. The median age for patients with thymoma was 45 years (range 33–72). The majority of patients presented with WHO grade B3, two patients in each arm were of WHO grade B2. Patient and disease-specific characteristics and comparison of surgery-alone and PORT treatment groups are listed in [Table 1]. The interquartile range for time from surgery to the start of radiation for all patients was 35-42 days. PORT indications included positive margins and stage IIB onwards. Median follow-up was 66 months (range 1–78 months).

Table 1 Patient and disease specific characteristics

	PORT	Surgery alone
Characteristics	No	No
Sex		
Male	5	3
Female	3	2
Age		
20-40	3	1
40-60	4	3
>60	1	1
WHO Performance status		
0-1	7	5
>2	1	0
Surgical margin status		
Negative, R0	4	4
Positive ,NOS	1	1
R1	2	0
R2	1	0
Masoka stage		
I-II A	0	3
IIB	5	2
III-IV	3	0
WHO grade		
A,AB,B1	0	0

B2	2	2
B3	6	3
C	0	0
Associated Myasthenia gravis		
Yes	2	1
No	6	4
Survival (5 year)		
Alive	5	2
Dead	3	3

Discussion

The optimal use of PORT for patients with thymic epithelial neoplasms is unclear, particularly for patients with Masaoka-Koga stage II disease. The 2016 National Comprehensive Cancer Network guidelines acknowledge this controversy and recommend that clinicians should *consider* PORT for completely resected Masaoka-Koga stage II disease.[1] Understandably, there is little current evidence on which to base any strong recommendation for PORT in this setting, and several smaller series have indicated no benefit for PORT in patients with stage II disease.[2,3,4] Two previous SEER database studies lacking data on many important baseline covariates identified longer OS associated with PORT in stage III to IV disease but no corresponding improvement for patients with stage IIB disease.[5,6] NCDB study demonstrates a clear OS advantage for PORT in both stage IIB and stage III thymoma. Smaller NCDB analysis by Boothe et al. that was limited to stage II and III patients also demonstrated improved OS with PORT for patients with thymic epithelial neoplasms.[7] Study of 1263 patients from the International Thymic Malignancies Interest Group database also reported improved OS with PORT for patients with stage II and III thymoma.[8] Although overall their conclusions align well with data from the NCDB, they report an increased magnitude of benefit for PORT among those patients with WHO type B1, B2, and B3 disease. Chinese Alliance for Research in Thymomas (ChART) was searched for patients with stage I to III thymic tumors who underwent surgical resection without neoajuvant therapy between 1994 and 2012, indicates that PORT after incomplete resection could improve OS and DFS for patients with stage I to III thymic tumors. However for those after complete resection, PORT does not seem to have any survival benefit on the whole.[9]

Conclusions

An OS advantage was associated with PORT for patients with Masaoka-Koga stage IIB or stage III disease and positive margins.

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