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ORIGINAL RESEARCH

Treatment and survival analyses of completely resected thymic carcinoma patients

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Purpose: To investigate the impact of chemotherapy and/or radiotherapy on disease-free survival (DFS) and overall survival (OS) rates of patients with thymic carcinoma after complete resection.

Methods: Between 2001 and 2013, 54 patients with complete resection of thymic carcinoma in Hangzhou Cancer Hospital were retrospectively reviewed. The Kaplan–Meier method was used to evaluate the survival rates. The Cox proportional hazard model was used for multivariate analysis.

Results: Among the 54 patients, Masaoka stage I was observed in seven patients, II in 22 patients, and III in 25 patients. Sixteen patients received adjuvant chemotherapy (six with chemotherapy alone and ten with radiotherapy and chemotherapy), 25 patients received adjuvant radiotherapy, and 13 patients did not receive radiotherapy and/or chemotherapy. The 5-year DFS and OS rates for all patients were 63.0% and 73.4%, respectively. Univariate analysis revealed that radiotherapy was significantly associated with DFS and OS (P=0.014 and P=0.029, respectively), while adjuvant chemotherapy was not (P=0.122 and P=0.373, respectively). Multivariate analysis showed that adjuvant radiotherapy increased DFS (P=0.041), but not OS (P=0.051).

Conclusion: Complete resection followed by adjuvant radiotherapy increased disease-free rates of thymic carcinoma patients.

Keywords: thymic carcinoma, complete resection, adjuvant treatment, radiotherapy, chemotherapy, overall survival

Introduction

Thymic carcinoma is a relatively rare mediastinal tumor.[1] Surgery is the standard treatment for early-stage thymic carcinoma, and complete resection is the most important prognostic factor for survival.[2,3] Although chemotherapy and radiation are widely applied in thymic carcinoma, the role of adjuvant chemotherapy and/or radiotherapy after complete resection remains controversial with very few studies.[4–6]

According to the guidelines of the National Comprehensive Cancer Network, systemic chemotherapy was not recommended after complete resection of thymic carcinoma, but radiotherapy was recommended after complete tumor resection in stages II and III of thymic carcinoma; however, the recommended category is low. Studies focusing on adjuvant treatment after resection of thymic carcinoma are lacking now.[5]

In this study, we retrospectively evaluated the prognosis and treatment of patients with completely resected thymic carcinoma and explored the impact of chemotherapy and/or radiotherapy on disease-free survival (DFS) and overall survival (OS) rates of patients with thymic carcinoma after complete resection.

Patients and methods

Methods

Fifty-four patients who had complete resection for thymic carcinoma between January 2001 and December 2013 in Hangzhou Cancer Hospital were included in the study.

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Based on the Masaoka staging system, the stage of thymic carcinoma was classified. Pathologically proven primary type C (WHO histological classification) thymic carcinoma by surgery. All patients underwent complete resection, and pathology proved no positive margins. No patients underwent induction chemotherapy or radiotherapy before surgery. Recurrence or metastases were confirmed using chest computed tomography (CT) as well as ultrasound and/or CT of the abdomen. The study was approved by the Ethics Committee of Hangzhou Cancer Hospital (Hangzhou, People's Republic of China). All patients provided written informed consent for this study.

Follow-up

Surviving patients were followed every 3–6 months for the first 5 years and then annually. The history, physical examination, and chest CT scan were recorded during the follow-up time. Survival case was recorded from the first day of operation to the date of death or last follow-up time. December 2014 was the last censoring date for survival. The median time from surgery to the last censoring date was 72 months, ranging from 25 to 168 months.

Statistical analysis

The survival curves were generated using the Kaplan–Meier method and compared with log-rank test. The Cox proportional hazard model was applied for multivariate analysis. The statistical analysis using the SPSS Version 16 (SPSS Inc., Chicago, IL, USA) was performed.

Results

Patient characteristics

Patient characteristics and histological subtypes are listed in Table 1. The median age was 49 years (range, 22–74 years). Squamous cell carcinoma (70.4%) was the most common histological subtype followed by undifferentiated carcinoma and neuroendocrine tumors. Among the 54 patients, five patients had positive mediastinal lymph nodes at surgical resection. Performance score was 0 in 39 patients and 1 for 27.8% patients. Two young males (aged 31 years and 33 years) presented with myasthenia gravis at first diagnosis with elevated AChR-binding antibody levels. The pathology report confirmed no component of thymoma in these two cases.

Table 1 Demographic characteristics of the study population

Characteristics	Number (%)
Sex	
Male	26 (48.1)
Female	28 (51.9)
Age	
Range	22–74
Median	49
<50	29 (53.7)
≥50	25 (46.3)
PS	
0	39 (72.2)
1	15 (27.8)
Myasthenia gravis	
Yes	2 (3.8)
No	52 (96.2)
Masaoka stage	
I	7 (13.0)
II	22 (40.7)
III	25 (46.3)
Histology	
Squamous cell carcinoma	38 (70.4)
Undifferentiated carcinoma	9 (16.7)
Neuroendocrine tumor	4 (7.4)
Others	3 (5.5)
Treatment after resection	
Radiotherapy	25 (46.3)
Chemotherapy	16 (29.6)
Radiotherapy + chemotherapy	10 (18.5)
No	13 (24.6)

Abbreviation: PS, performance score.

Treatment after operation

All 54 patients underwent complete surgical resection. Sixteen patients underwent chemotherapy (six with only chemotherapy and ten with radiotherapy and chemotherapy), 25 patients received radiotherapy, and 13 patients did not receive radiotherapy and/or chemotherapy (Table 1). On day 1, the most common regimen was the combination of cyclophosphamide (400 mg/m^2), adriamycin (40 mg/m^2), and cisplatin (75 mg/m^2) (n=8); the second common regimen was the combination of taxol (175 mg/m^2) and cisplatin (75 mg/m^2) (n=6); and other regimens included docetaxel (75 mg/m^2) and cisplatin (75 mg/m^2) (n=1) as well as vinorelbine (25 mg/m^2) and cisplatin (75 mg/m^2) (n=1). Two-dimensional radiotherapy planning system was used in eleven patients and three-dimensional conformal radiotherapy in 14 patients. The median dose was 54.2 Gy (range, 52–61.2 Gy). There were no differences among age (P=0.47), sex (P=0.52), Masaoka stage (P=0.76), and histology (P=0.31) between the radiotherapy and no-radiotherapy patients.

Factors affecting OS by univariate and multivariate analyses

The 5-year DFS and OS rates for all patients were 63.0% and 73.4%, respectively. The results of univariate analysis for DFS and OS are listed in Table 2. Age, sex, chemotherapy,

Table 2 Univariate analysis of the patient survival according to the clinicopathologic characteristics

Characteristics	5-year DFS rate (%)	*P*-value	5-year OS rate (%)	*P*-value
Sex		0.091		0.157
Male	56.5		70.6	
Female	80.6		81.5	
Age		0.129		0.214
<50	78.5		77.1	
≥50	60.4		67.2	
Histology		0.097		0.412
Squamous cell carcinoma	69.5		77.6	
Others	60.1		65.7	
PS		0.605		0.614
0	79.5		68.5	
I	59.2		82.3	
Myasthenia gravis		0.514		0.512
Yes	66.5		81.5	
No	61.1		64.5	
Adjuvant chemotherapy		0.122		0.373
Yes	56.2		72.9	
No	66.7		73.8	
Adjuvant radiotherapy		0.014		0.029
Yes	77.5		78.6	
No	44.1		66.4	
Masaoka stage		0.102		0.129
I	85.7		85.7	
II	66.0		77.5	
III	53.1		58.3	

Abbreviations: DFS, disease-free survival; OS, overall survival; PS, performance score.

histology, myasthenia gravis, and Masaoka stage showed no significant association with DFS and OS (Table 2), while radiotherapy showed significant association with DFS and OS (*P*=0.014 and *P*=0.029, respectively) (Figures 1 and 2). There were significant differences for DFS among the radiotherapy alone, radiotherapy and chemotherapy, chemotherapy alone,

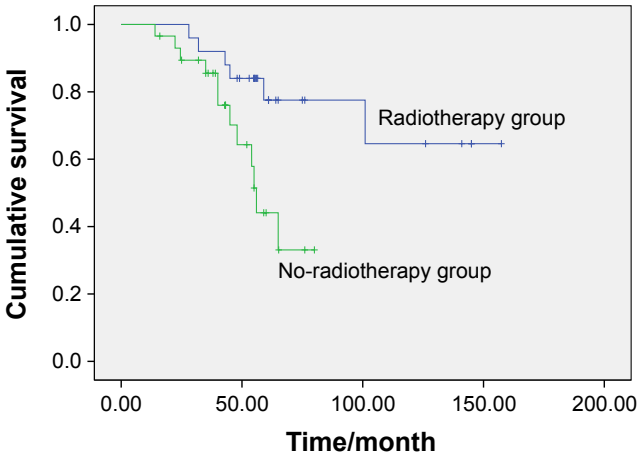

Figure 1 DFS in radiotherapy group and no-radiotherapy treatment group (*P*=0.014).
Abbreviation: DFS, disease-free survival.

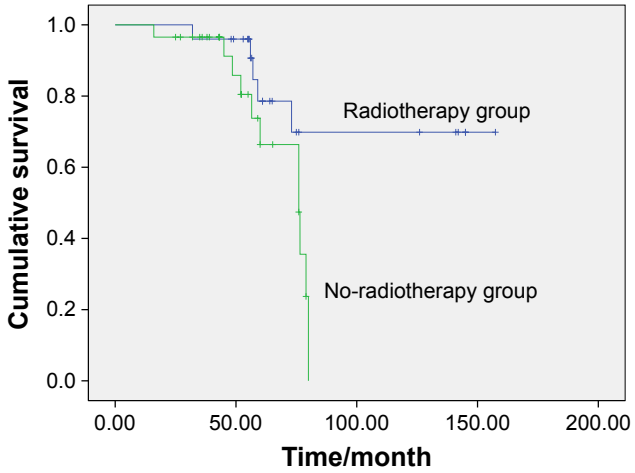

Figure 2 OS in radiotherapy group and no-radiotherapy treatment group (*P*=0.029).
Abbreviation: OS, overall survival.

and no adjuvant treatment patients (*P*=0.013), but not for OS (*P*=0.054) (Figures 3 and 4).

A multivariate Cox regression model showed that adjuvant radiotherapy and stage significantly influenced DFS, but not OS (Table 3).

Discussion

Due to the rarity of thymic tumors, randomized controlled data are lacking, and the available evidence on adjuvant treatment comes from small retrospective studies. Our results suggest that adjuvant radiotherapy after complete resection could impact the DFS rates of thymic carcinoma patients.

The role of postoperative radiation therapy and chemotherapy in reducing the rate of recurrence and increasing the OS remains controversial. A multi-institutional retrospective study[7] demonstrated that adjuvant radiation does not improve the OS rate in patients with completely resected thymic

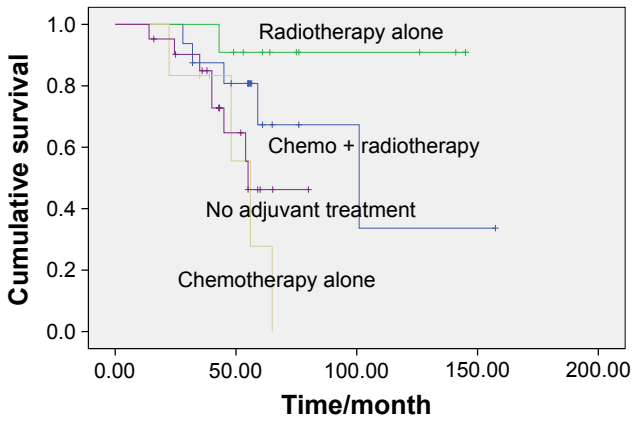

Figure 3 DFS among the radiotherapy alone, radiotherapy and chemotherapy, chemotherapy alone, and no adjuvant treatment group (*P*=0.013).
Abbreviation: DFS, disease-free survival.

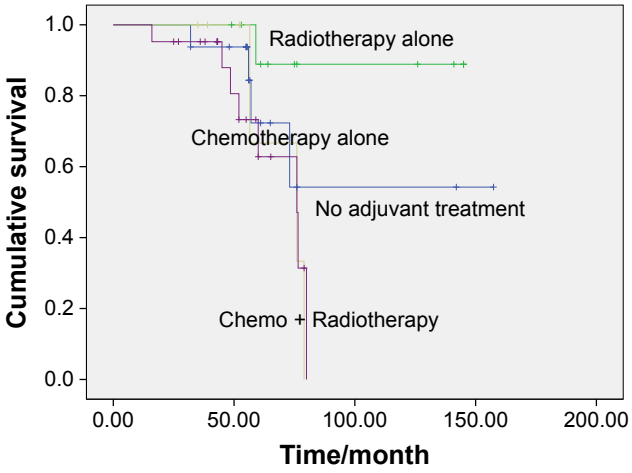

Figure 4 OS among the radiotherapy alone, radiotherapy and chemotherapy, chemotherapy alone, and no adjuvant treatment group (*P*=0.054).
Abbreviation: OS, overall survival.

carcinoma. In contrast, another multi-institutional retrospective study by Omasa et al showed that postoperative radiotherapy increased relapse-free survival for stages II and III thymic carcinoma.[8] Patel et al reported the results of 1,464 patients with thymic carcinoma from centers that participated in the Surveillance, Epidemiology, and End Results program,[9] which indicated that OS significantly improved with radiotherapy, and an improved cause-specific survival trend was observed. In this study, the patients benefited from adjuvant radiotherapy, which is consistent with the findings of Omasa et al.

Adjuvant chemotherapy in some studies showed a benefit of reducing distant metastasis rate and prolonging OS and others did not indicate any role.[5,10–16] Song and Zhang[5] and Sun et al[16] found no DFS and OS differences in completely resected thymic carcinoma patients receiving surgery alone versus surgery plus adjuvant chemotherapy. Our series also revealed that adjuvant chemotherapy showed no significant effect in completely resected thymic carcinoma.

Table 3 Multivariate survival analysis for DFS and OS

Parameters	DFS			OS		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Sex (male vs female)	2.15	0.43–3.21	0.76	4.2	0.35–4.87	0.51
Adjuvant chemotherapy (yes vs no)	1.57	0.21–5.21	0.55	1.21	0.11–1.97	0.54
Adjuvant radiotherapy (yes vs no)	0.67	0.42–0.95	0.041	0.67	0.43–101	0.051
Stage (I + II vs III)	0.47	0.43–0.99	0.042	0.54	0.33–1.88	0.056
Histologic subtype (squamous cell vs other types)	0.45	0.32–5.54	0.24	0.76	0.43–3.98	0.21

Abbreviations: DFS, disease-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval.

Our study is limited by its retrospective nature and with a small number of patients included. However, considering the rarity of the disease, the report of 54 cases is regarded as a relatively large study; our retrospective study may also be meaningful.

Conclusion

In summary, adjuvant radiotherapy after complete resection of thymic carcinoma could increase DFS. Prospective trials are required to further elucidate the effect and survival after adjuvant chemotherapy and radiation.

Disclosure

The authors report no conflicts of interest in this work.

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