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The potency of curative-intent treatment for advanced thymic carcinoma

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ABSTRACT

Background: Heterogenous clinical or biological features are characteristic of thymic carcinoma. Well-defined clinical entities remain unclear because of rarity. The aim of this study was to clarify disease profiles, outcomes, and prognostic factors for survival among patients diagnosed with thymic carcinoma.
Patients and methods: A retrospective review was conducted of the medical records of 68 thymic carcinoma patients among 187 patients diagnosed with thymic epithelial tumors between 1980 and 2013 in our institution. Clinical demographics, histology, overall survival, and factors expected to predict survival were analyzed. Differences in survival were assessed using Kaplan–Meier analysis and uni- and multivariate Cox proportional hazards regression analyses.
Results: The study included 38 males (55.9%) and 30 females (44.1%). The median age at diagnosis was 63.5 years. The most common subtypes of thymic carcinoma were squamous cell carcinoma (69.1%), neuroendocrine carcinoma (16.2%), and mucoepidermoid carcinoma (5.9%). Masaoka-Koga staging of the 68 patients demonstrated no patients (0%) in Stage I, 3 (4.3%) in Stage II, 14 (20.6%) in Stage III, 12 (17.6%) in Stage IVa, and 39 (57.4%) in Stage IVb. The median survival time for all stages was 36.4 months (95% confidence interval 23.7–56.4); those for stages II, III, IVa, and IVb were: not reached, 65.8, 24.6, and 27.3 months, respectively. The difference by Masaoka-Koga staging was significant ($p = 0.04$). Overall survival rates at 1-, 5-, and 10-year were 76.3%, 36.0%, and 6.2%, respectively. By univariate analyses, the only favorable prognostic factor for overall survival was surgical intervention ($p = 0.03$), and, for Stage IVb, lymphatic metastasis without distant metastasis. However, clinically interesting variants did not differ significantly for predicting survival.
Conclusion: Surgical intervention results in better survival of thymic carcinoma, even in Stage IVb. The survival value of administration of curative-intent radiotherapy, or of identification of "resectability" in Stage IVb patients must continue to be discussed.

1. Introduction

Thymic carcinoma is a rare cancer, as defined through RARECARE supported by the European Commission, accounting for less than 1–4% of thymic epithelial tumors, including thymomas, and having an annual incidence of 0.15 per 100,000 person-years [1]. However, in Far East Asia, patients with thymic carcinoma are more frequently reported. Thymic carcinoma includes heterogeneous clinical manifestations and is distinguished from thymoma based on biological characteristics. However, because of its rarity, precise clinical characteristics and prognostic factors among patients with thymic carcinoma remain uncertain. Thymic carcinoma results in loss of organotypic features; therefore, these patients do not present with immunological paraneoplastic symptoms, such as myasthenia gravis, pure red cell aplasia, or hypogammaglobulinemia [2,3], but rather with symptoms associated

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with tumor extension or metastasis. Therefore, thymic carcinoma is usually diagnosed at an advanced stage and has poor prognosis. Patients in the early stages (Masaoka-Koga Stage I, II, IIa, IIb, or III) usually receive curative-intent surgery or radiotherapy. In contrast, patients with Stage IVb with distant metastasis receive palliative-intent chemotherapy [4]. Precise clinicopathological characteristics remain unclear; however, previously reported investigations revealed that tumor histological grading, resectability, and stage influence the outcomes [5].

There is only a low level of evidence to support use of various treatment modalities, from a few retrospective studies of small groups of treated patients having diverse backgrounds; thus, the optimal therapeutic strategy remains controversial, unlike the situation for thymoma, which at least has been assessed in single-arm prospective studies. Overall, the prognosis and prognostic factors have not been well investigated in thymic carcinoma patients.

The objective of the present study was to retrospectively clarify the clinical characteristics, prognosis, and prognostic factors of patients treated for thymic carcinoma in our institution during a 30-year period.

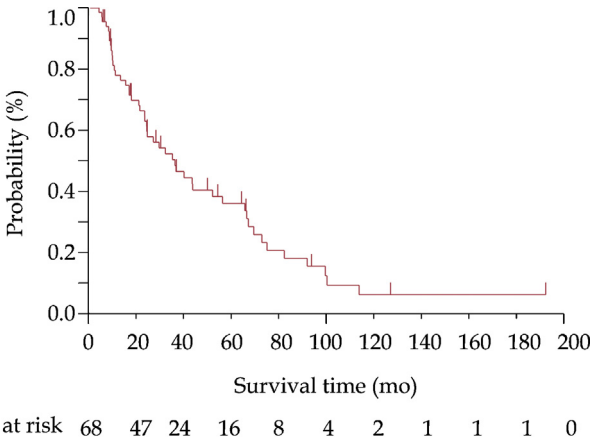

Fig. 1. Median overall survival ($n = 68$) was 36.4 months (95% CI, 23.7–56.4) and 5-year survival rate was 36.0% in all stages; Kaplan–Meier curve.

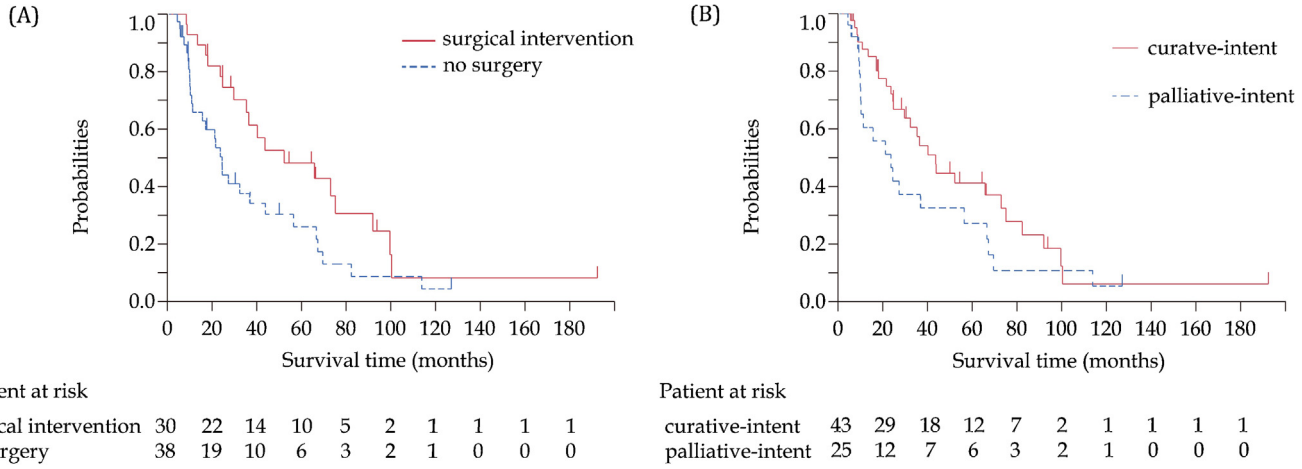

Fig. 2. (A) Survival curves for prognostic category comparing *surgical intervention* ($n = 38$ [solid line]) to *no surgery* ($n = 30$ [dashed line]). Median survival in the *surgical intervention group* was 52.2 months (95% CI, 29.7–92.0), vs. 24.8 months (95% CI, 11.3–43.7) in the *no surgery* group ($p = 0.03$). (B) The treatment-intent did not affect survival ($p = 0.1$).

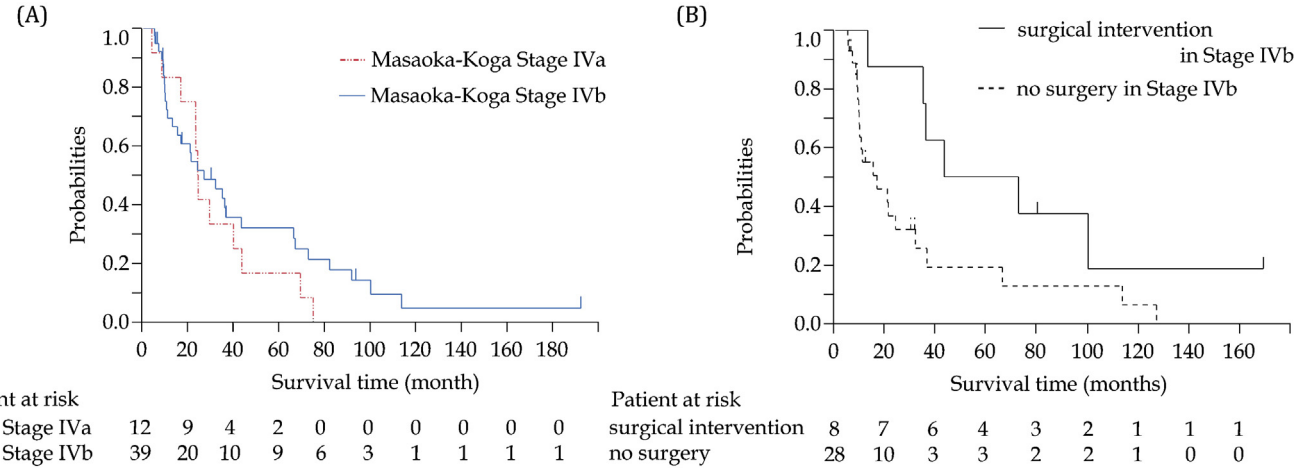

Fig. 3. (A) The median overall survival for Masaoka-Koga Stages IVa and IVb did not differ ($p = 0.8$). (B) When analysis was limited to Stage IVb patients, median survival in the *surgical intervention group* was 58.3 months (95% CI, 13.5–not reached), vs. 17.1 months (95% CI, 9.9–32.4) in the *no surgery* group ($p = 0.03$).