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Thymoma: Results of treatment and role of radiotherapy

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ABSTRACT

Purpose: The aim of this study is to assess results of treatment, factors influencing prognosis with regard to causes of failure and treatment tolerance in patients with thymoma.
Material and methods: Between 1966 and 2006, 63 patients with thymoma had been treated at the Centre of Oncology in Krakow. Patients were treated by means of different treatment modalities: surgery followed by radiotherapy (52%), radiotherapy alone (13%), chemoradiotherapy alone (15%), surgery followed by chemoradiotherapy (5%), surgery alone (5%) and others.
Results: The 10-year locoregional recurrence-free survival (LRRFS) was 79%, disease free survival (DFS) was 57% and overall survival (OS) was 57%. Masaoka stage was the only independent prognostic factor for LRRFS. Masaoka stage and method of radiotherapy delivery (higher photon energies), were independent prognostic factors for OS. For DFS, the independent prognostic factors were age, type of treatment (favoured surgery followed by radiotherapy or chemoradiotherapy), Masaoka stage and year of start of treatment. Most common reactions were lung fibrosis in 36% of patients (mainly asymptomatic in most patients), pneumonitis (9%) and oesophagitis (4%).
Conclusions: Surgery combined with radiotherapy and chemoradiotherapy and modern radiotherapy techniques are correlated with improvement of survival in patients with early stage thymoma.

1. Introduction

Thymomas, which originate from epithelial cells of the thymus, are the most common tumours of the anterosuperior mediastinum and represent about 20–30% of all malignant mediastinal tumours.[1,2] These tumours are rare neoplasms; the age-standardized incidence rates range from 0.1 to 0.5 per 100 000 population annually in different countries.[3] Data regarding incidence of thymomas in Poland are not available.

Usually thymomas are asymptomatic (the tumour is detected by incidental chest X-rays) or associated with symptoms such as myasthenia gravis. The Masaoka classification has been the most widely used staging system.[4,5]

Due to the low incidence of these tumours (which precludes large randomized trials), little is known about optimal evidence-based therapy of thymomas.

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Table 1 – Characteristics of patients.

Characteristics	*n*	%
Age		
Median	43	
Range	17–74	
Gender		
Female	32	51%
Male	31	49%
Symptoms before treatment		
Absent	18	29%
Present	45	71%
Stage (Masaoka)		
I	8	13%
IIa	4	6%
IIb	6	10%
IIIa	18	29%
IIIb	19	30%
IVa	4	6%
IVb	2	3%
Not applicable	2	3%
Type of treatment		
Surgery followed by radiotherapy	33	52%
Radiotherapy alone	8	13%
Chemotherapy	2	3%
Chemoradiotherapy	9	14%
Palliative care	1	2%
Surgery	3	5%
Surgery followed by chemoradiotherapy	5	8%
Surgery followed by chemotherapy	2	3%
Completeness of operation		
R0	16	37%
R1	4	9%
R2	14	33%
Not applicable	9	29%

Surgery still remains the principal method of treatment of resectable thymomas, whereas adjuvant or neoadjuvant radiotherapy plays an important role in subtotally resected and unresectable cases.[1,6,7] In advanced cases (Masaoka stages III and IV) or in patients with recurrence after the treatment, chemotherapy can prolong survival and offers palliation. Advanced thymomas should be treated by a multidisciplinary team including surgeons, and medical and radiation oncologists.[8]

The aim of this study is to assess the results of treatment in patients with thymoma, factors influencing prognosis with regard to causes of failure and treatment tolerance.

2. Materials and methods

Retrospective analysis was performed in a group of 63 patients with thymoma, who had been treated at the Centre of Oncology in Krakow between 1966 and 2006. Characteristics of patients are shown in Table 1. Median age was 43 years, 31 patients were males, 32 were females. About 70% of patients were in stages III and IV. The majority (71%) of patients presented symptoms preceding diagnosis of thymomas; the most common were chest pain with dyspnoea, flu-like symptoms and myasthenia gravis. In all cases diagnosis was confirmed by histology.

Patients were treated using different treatment modalities: surgery followed by radiotherapy (52%), radiotherapy alone (13%), chemoradiotherapy alone (15%), surgery followed by chemoradiotherapy (5%), surgery alone (5%) and others.

Median radiation dose was 4600 cGy (range 3000–7000) in 23 fractions (median). Radiotherapy was delivered by linear accelerator (37 pts), cobalt (18 pts) and ortovoltage (1 pts) because of development of methods of radiotherapy delivery technologies during the 40 years of this retrospective analysis.

Indications for irradiation in our hospital were: subtotally resected, all Masaoka stages II and III in adjuvant setting, and unresectable thymoma.

Techniques of radiation delivery have changed during the 40 years of this analysis. Irradiated volume included whole thymus, tumour bed, mediastinum. Two antero-posterior field techniques were used in the first phase of treatment. Dose to the spinal cord was limited to 45 Gy using two or three oblique fields in the second phase. The majority (60%) of patients treated with chemotherapy received anthracycline- and cisplatin-based regimens. All of them were treated in the adjuvant setting.

In the radiochemotherapy subgroup patients subsequently received nitrogranulogen (3 patients) or anthracycline-based chemotherapy (6 patients).

2.1. *Statistical methods*

The main endpoints of the analysis were locoregional recurrence-free survival (LRRFS), disease-free survival (DFS) and overall survival (OS) rates.

Survival was measured from the date of diagnosis to the date of death or last follow-up.

Locoregional recurrence-free survival was measured from the date of treatment to the date of locoregional recurrence or death or last follow-up in the subgroup of patients after complete resection (confirmed in imaging studies) and patients treated with other modalities with complete response.

Time to progression was measured from the date of the end of treatment to the date of local or distant progression. Local failure was defined as failure occurring inside the mediastinum (and/or with invasive growth into neighbouring organs) and distant failure as any site of failure outside the mediastinum.

Kaplan–Meier method was used to calculate survival rates. Univariate and multivariate analyses of prognostic factors were performed using log rank and Cox's proportional hazard method. In analyses of prognostic factors, clinical factors (sex, age, stage, grade, histological type, symptoms, etc.) and treatment factors (method of resection, completeness, radiation dose, total treatment time, year of start of treatment) were compared. *P*-Values of less than 0.05 were considered to indicate statistical significance.

3. Results

3.1. *Survival*

During a median follow-up of 90 months (range 3–361), we observed 22 cancer-related deaths and 11 patients died from