

## Acknowledgments

I would like to express my gratitude to my supervisor Professora Doutora Lina Carvalho for her expertise, understanding and incentive, added considerably to my graduate experience and for providing me the opportunity of growing as a medicine student. I thank her also for the patience and time spent with me.

I would also like to thank to Dr. Vítor Sousa and Dr. Domingos Oliveira for their cooperation in all levels, being always there when I needed some piece of advice. Thanks also to all the other members of the *Instituto de Anatomia Patológica* from *Hospitais da Universidade de Coimbra* for their friendship and patience.

For the *Clínica de Cirurgia Cardiotorácica* from Hospitais da Universidade de Coimbra, my sincere gratitude for the support. All the members of this Service where extremely comprehensive and kind to me, in all senses: thank you them all. A special thanks goes to Dr. Paulo Calvino, my co-supervisor, who allowed the clinical files requisition, this way contributing to my database construction.

For my family, for the unconditional support and belief, even in the worse times, thank you. Thank you mother for making me believe it was possibly!

Finally, I would like to express my gratitude to *Hospitais da Universidade de Coimbra* in general, particularly to *Serviço de Anatomia Patológica* and *Cirurgia Cardiotorácica*.

## **List of Abbreviations**

As – Asymptomatic

C – Cough

CT – Computerized Tomography

CTh – Chemotherapy

D – Dyspnoea

HUC – Hospitais da Universidade de Coimbra

MG – Myasthenia Gravis

MH – Muller Hermelink

MR – Magnetic Resonance

PET – Positron emission tomography

RT – Radiotherapy

SM – Suster-Moran

SS – Systemic Symptoms

T – Thoracic pain

T.pain – Thoracic pain

WHO – World Health Organization

x-Ray – Radiography

# O silêncio clínico dos timomas e a sua classificação histológica

**Base de dados composta por 81 doentes com timoma**

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## **Resumo**

Vários sistemas de classificação têm sido propostos ao longo dos anos para os timomas, sem contudo se revelarem adequados quer para orientar os médicos sobre a sua forma de manifestação clínica, no tratamento e prognóstico, quer para uniformizar a linguagem entre os patologistas.

Foram relacionados 81 casos clínicos de timomas para avaliar a apresentação clínica bem como a interpretação das classificações cirúrgica de Masaoka e histológicas de Muller Hermelink/ OMS 2004 e Suster-Moran.

Da avaliação clínica constatou-se que grande parte dos doentes era assintomático no momento do diagnóstico (31/81) e a “tríade” sintomática (tosse, dispneia e toracalgia) constituía também uma forma comum de apresentação dos timomas.

O estadiamento cirúrgico de Masaoka revelou-se a forma mais simples de prever o prognóstico, se bem que as classificações histológicas, organogénica da OMS 2004 e morfológica de Suster-Moran, mostraram equivalência numérica, remetendo-nos para a primeira, que acompanha a medicina moderna.

**Palavras-chave:** timomas, classificação, sintomatologia, prognóstico.

# **Clinical silence of thymomas encompasses the histological classification**

## **A database with 81 patients suffering from thymoma**

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### **Abstract**

Different histological classifications have been purposed along the years to clarify thymomas. However, none of them could be considered adequate either to elucidate the clinical presentation, treatment and prognosis, or to uniform the language among pathologists.

A serie of 81 clinical files of thymomas were used to evaluate the clinical presentation as well as the surgical classification of Masaoka and histological classifications of Muller Hermelink/ WHO 2004 and Suster-Moran.

A considerable part of the patients were asymptomatic at the time of the diagnosis (31/81) and the symptomatic triad (dyspnoea, cough and thoracic pain) was also a common way of presentation for thymomas.

Surgical staging of Masaoka revealed to be the easier way of gathering the cases and preview the prognosis, while organogenetic classification of WHO 2004 and morphological classification of Suster-Moran were equivalent, reinforcing the actual WHO 2004 to follow modern medicine.

**Key-words:** thymoma, classification, symptoms, prognosis.

## Introduction

Thymomas are considered rare neoplasms arising from thymic epithelium (fourth to fifth decades), without distinction of gender. One third of the patients has no symptoms, one third presents local symptoms and the remaining manifest on autoimmune disease at the time of the diagnosis<sup>1</sup>. Systemic symptoms, such as fever, anorexia, asthenia and weight loss are rare. In fact, thymomas are mostly accidental findings during routine exams such as thoracic x-ray<sup>2</sup> and 15% are linked to *myasthenia gravis*, preferentially in women and associated with types AB, B2 and B3 thymomas<sup>3,4</sup>. Besides being the most frequent anterior mediastinal tumours, thymomas are reported as rare, below 1% of all adult cancers, with an incidence rate of 1-5/million population/year<sup>3</sup>. The majority of these thymic tumours are benign, as that the integrity of the thymic capsule is maintained; malignant thymomas are defined as a neoplasm born in thymic epithelium that has later invaded the capsule of the organ; metastatic presentation is not common<sup>1</sup>, and lungs (as other thoracic organs) and the liver are the most common hosts for metastases. The histological classification of primary thymic epithelial neoplasms has been changing due to the wide variety of morphologic appearances that these tumours can display<sup>5</sup>. Various classification schemes have been applied through the years<sup>6</sup>, as those of Masaoka (1981)<sup>7</sup>, Muller Hermelink (1989)<sup>8,9</sup>, Suster-Moran (1999)<sup>10,11,12</sup> and the actual WHO (2004)<sup>13,14,15,16</sup> classifications, and there is still a lack of randomized clinical trials evaluating the prognosis of patients with thymomas and the effects of various treatment modalities<sup>17</sup>. The contemporaneous WHO 2004 classification has a straight correspondence with Muller Hermelink's: WHO type A corresponds to medullary thymoma (spindle cell thymoma); type AB to mixed thymoma; type B1 to predominantly cortical thymoma (lymphocyte-rich thymoma); type B2 to cortical thymoma; and type B3 to well-differentiated thymic carcinoma (squamous thymoma)<sup>3</sup>. The importance of the histopathologic subtype as an independent prognostic factor has varied in different studies<sup>17,18</sup>, mostly due to a lack of concordance among pathologists by the use

of a single classification scheme. The main purpose of the international classification introduced by WHO in 2004 was to provide a universal formula that would facilitate comparison among various terms from the already existing classifications<sup>17, 19</sup>. However, it was not totally well succeeded, since today it still remains a source of discrepancy among different centres<sup>20, 21</sup>. The thymus is a complex and in many ways mysterious organ. As much remains to be learned about its development, structure and function, many observers have suggested that reproducible cytoarchitectural classification is impossible. This is not comfortable for pathologists, who both want to understand tumour morphology and improve the contribution to patient management<sup>22</sup>.

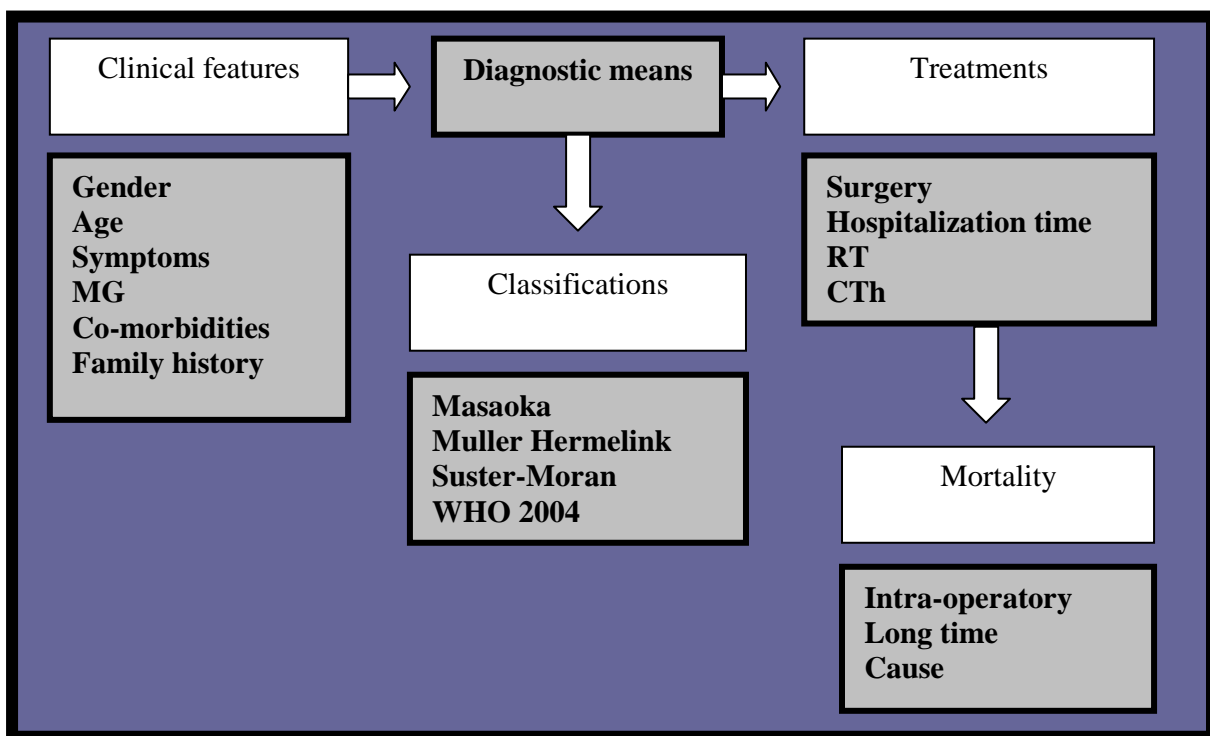
It was our objective to compare the available clinical data with the outcome of patients submitted to thymomas resection after the WHO 2004 classification and characterize the commonest way of clinical presentation of thymomas. This strategy might anticipate the diagnosis, as well as determine if clinical outcome is enough to encourage the universal use of a single classification system. Meanwhile, as adjuvant therapies came out of patient clinical files, a brief consideration will also be made.

## Materials and Methods

### Clinical and Histopathological Registration

The archive of Pathological Anatomy from HUC was used to select 81 cases of thymomas and lymphomas, as well as other mediastinal tumours, which were excluded together with the absence of clinical information.

The 81 clinical cases collected between the years 1993 and 2008 were then registered in a new base (Figure 1) to correlate the clinical presentation, the application of different histopathological classifications, Masaoka surgical staging, and the final outcome.



*Figure 1 – Clinical registration of patients outcome.*



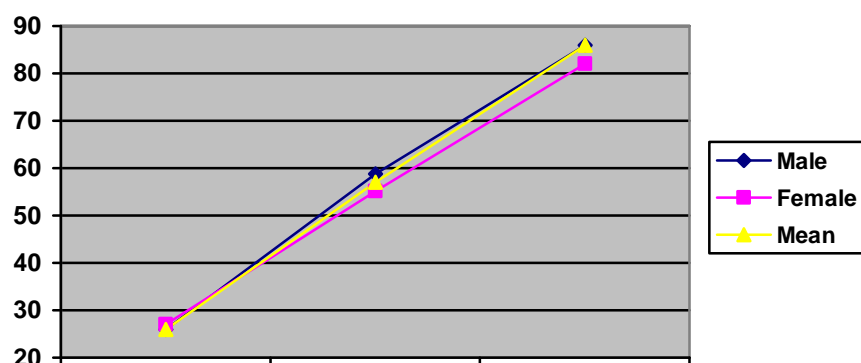
The four most used classifications for thymomas, including Masaoka, Muller Hermelink and Suster-Moran, as well as the actual WHO 2004 classifications are registered in Table I. It is also revealed the parallelism between Muller Hermelink and WHO 2004 classifications.

*Table I – The major classification systems for thymomas and the correlation between Muller Hermelink and WHO 2004 classification systems.*

<b>Masaoka et al.</b> (1981)	<b>Suster-Moran</b> (1999)	<b>Muller Hermelink</b> (1989)	<b>WHO</b> (2004)
<b>Stage I:</b> Encapsulated or minimal capsule invasion	Thymoma – Well differentiated	Medullary thymoma	A
<b>Stage II:</b> Invasion of capsule and/or perithymic fat	Atypical thymoma – Moderately differentiated	Mixed thymoma	AB
<b>Stage III:</b> Gross invasion of adjacent organs	Thymic carcinoma – Undifferentiated	Predominantly cortical thymoma	B1
<b>Stage IV A:</b> Tumoral implants	—	Cortical thymoma	B2
<b>Stage IV B:</b> Metastases	—	Well-differentiated thymic carcinoma	B3
—	—	—	Thymic carcinoma

## Clinical outcomes

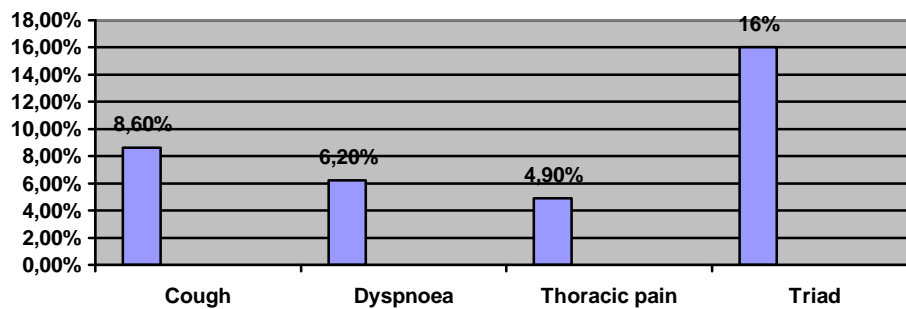
Preference in gender was not sustained, with 42 (52%) thymomas occurring in men and 39 (48%) in women. The mean age of appearance was 57 years, the youngest patient was 26 years-old and the oldest was 86. The mean age among women was 55,2 years-old and 58,8 years-old among men (Figure 2).



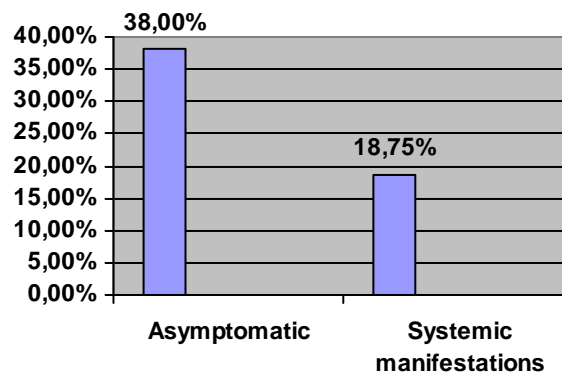
*Figure 2 – Prevalence in age by gender.*

Relatively to the symptomatic way of presentation, the commonest manifestation was MG and, among the 19 patients identified, 12 were women (63%) and 7 were men (37%). Thoracic pain (17 patients, 21%) was followed by cough and dyspnoea (16 patients each, 20% of the cases). As a single symptom, cough occurred in 7 patients (8,6%), dyspnoea in 5 (6,2%) and thoracic pain in 4 (4,9%). This triad together (cough, dyspnoea and thoracic pain) appeared in 13 patients (16%) (Figure 3); 31 patients were asymptomatic (38%), while systemic manifestations (fever, anorexia, asthenia and weight loss) occurred in 15 patients (18,75%) (Figure 4). From the total 19 (23,4%) patients with MG in the database, 7 (8,6%) presented with the classic myasthenia symptoms (dysphagia, diplopia, eyelid drop, diminished muscular strength and asthenia), all of them already with the neurologic diagnosis established at the time of the thymoma occurrence.

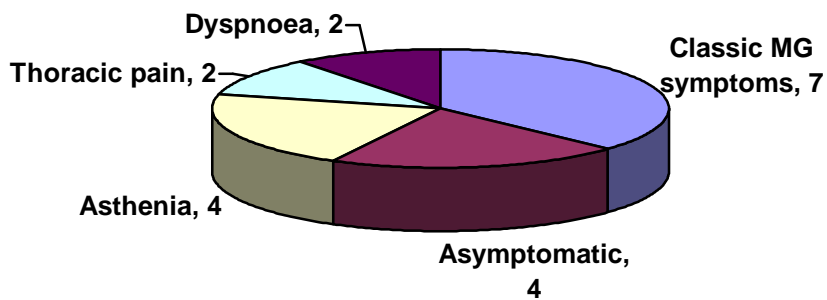
The myasthenic patients who didn't present with these characteristic symptoms were either asymptomatic or asthenic (4 cases each) or had dyspnoea and thoracic pain (2 cases each), as shown in Figure 5. Other symptoms included cyanosis, lipothymia, superior vena cava syndrome and pulmonary acute edema, one case for each. Non related symptoms, such as back pain, were also a way to diagnosis once it led to a causal study.



*Figure 3 – Prevalence of the major symptoms isolated (cough, dyspnoea and thoracic pain) and the symptomatic triad (cough + dyspnoea + thoracic pain) at the time of presentation.*

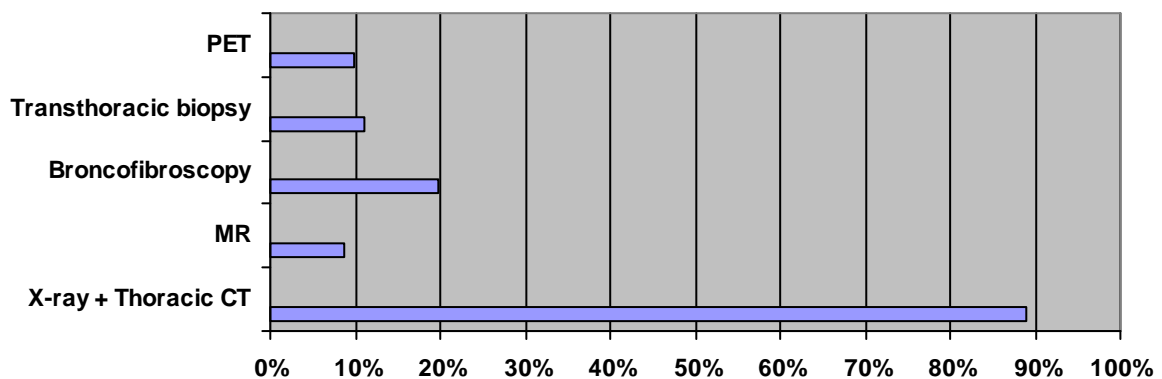


*Figure 4 – Other symptomatic manifestations at the time of diagnosis.*



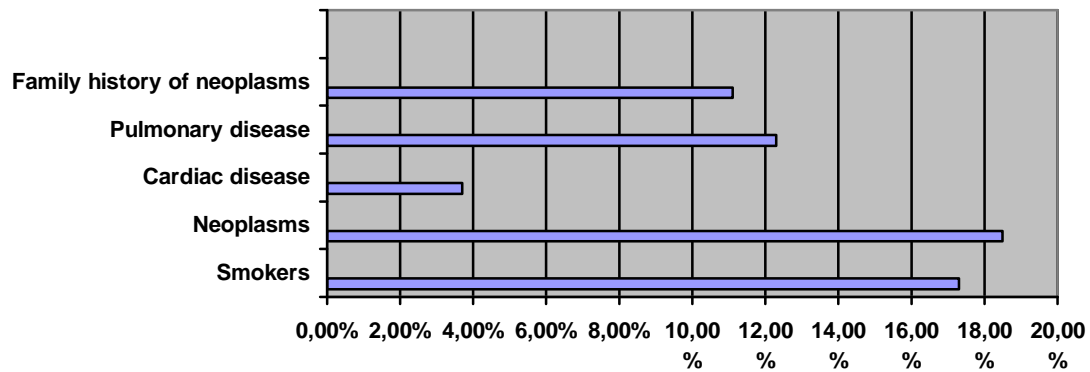
*Figure 5 – Symptoms of presentation among the 19 patients with myasthenia gravis.*

The diagnostic means were mainly thoracic x-ray in association with thoracic CT (89%), 16 patients were submitted to bronchofibroscopy (19,8%), 9 to transthoracic biopsies (11%), 8 to PET (9,9%) and 7 to MR (8,6%) (Figure 6). Other complementary exams included osteoarticular cintigram, transthoracic ultrasound and angio-CT, mostly due to co-morbidities or to locate metastases.



*Figure 6 – Prevalence of diagnostic means.*

The co-morbidities expressed in Figure 7 refer to 14 smokers (17,3%), 15 (18,5%) had already, once in life, had a tumour and 3 (3,7%) had cardiac and 10 (10,2%) pulmonary morbidities; 9 patients (11,1%) had family history of malignant neoplasms.

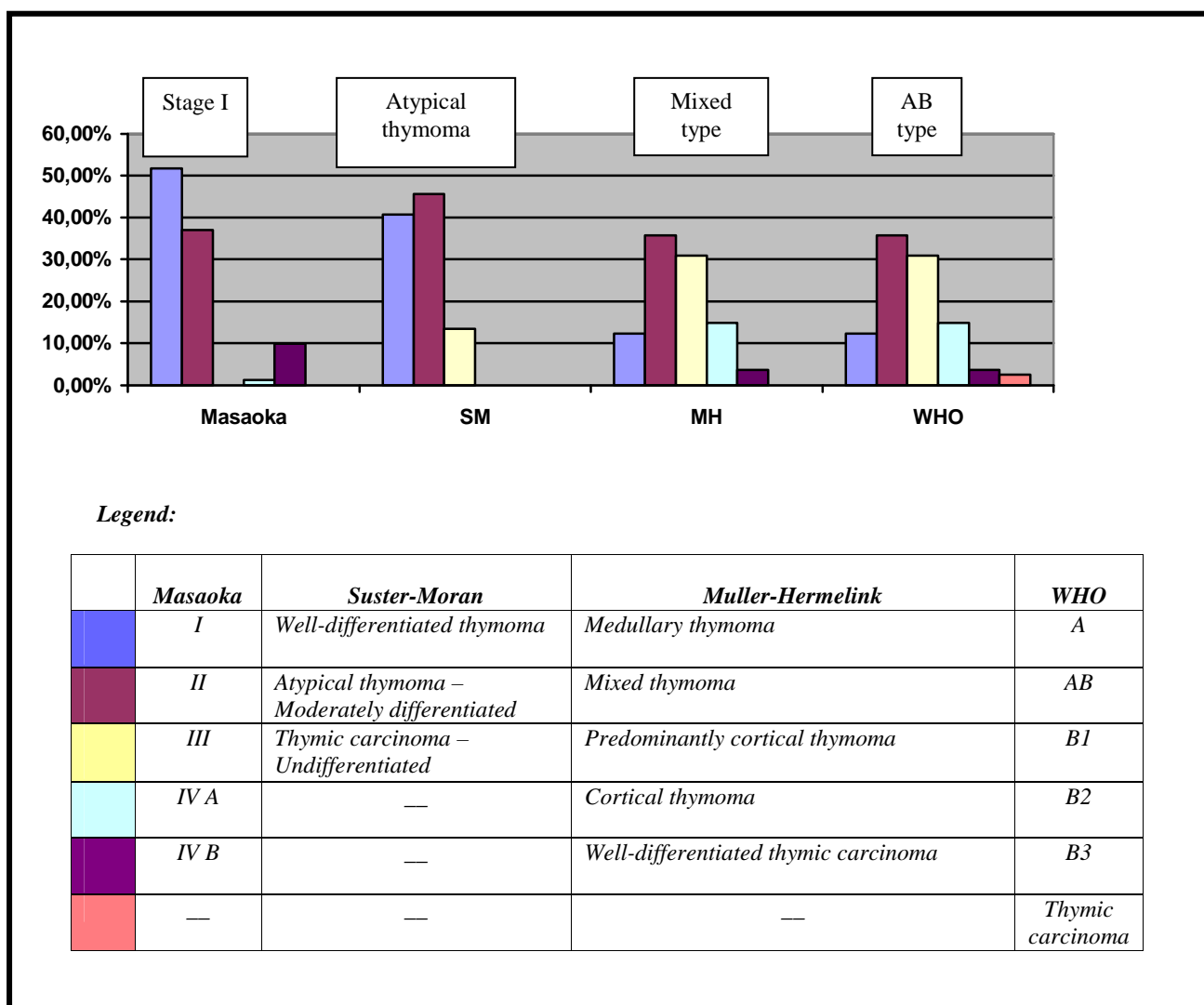


*Figure 7 – Prevalence of co-morbidities.*

The mean hospitalization time was 7,5 days, with a minimum of 1 day and a maximum of 29 days. Only 1 of the 81 patients died during the 5 days of his hospitalization due to pulmonary acute edema as a complication of the surgery. Afterwards, 10 patients (12,3%) were submitted to radiotherapy while only one (1,23%) underwent chemotherapy. The combined scheme (radio+chemo) was applied in 6 patients (7,4%). The radiotherapy schemes comprised 20 to 22 sessions of 180 cGy in a total dosage of 3960 to 5760 cGy of irradiation. The chemotherapy corresponded to 4 to 7 cycles of cisplatin (75mg/m<sup>2</sup>), epirubicin (100mg/m<sup>2</sup>) and etoposide (120mg/m<sup>2</sup>), with no significant toxicity notified and occurred diminishing of the residual tumour after surgery. In one case it was used a combination of octreotidum and prednisolone, as indicated to the pleural lesions of thymomas with somatostatine-positive-receptors<sup>23,24</sup>; the results of such procedure were not conclusive, as the same patient received local irradiation (20 Gy/5Fr) due to dorsolumbar metastases associated with a high risk of fracture.

## Staging and Histopathological Classifications Registration

Relatively to the classification systems (Table II, III and IV), the most frequent was Masaoka I (42 cases – 51,8%), Suster-Moran “atypical thymoma – moderately differentiated” (37 – 45,7%) and WHO 2004 AB type, corresponding to Muller Hermelink “mixed thymoma” type (29 – 35,8%). A general review on these results is presented on Figure 8.



**Figure 8 – Masaoka surgical staging and histopathological correspondence in Muller Hermelink and Suster-Moran classifications.**

Table II – Number of patients and prevalence in Masaoka classification.

Masaoka	Number of patients	Prevalence (%)
<i>I</i>	42	51,8%
<i>II</i>	30	37%
<i>III</i>	0	0
<i>IVA</i>	1	1,23%
<i>IVB</i>	8	9,9%

Table III – Number of patients and prevalence in Suster-Moran classification.

Suster-Moran	Number of patients	Prevalence (%)
<i>Thymoma (well differentiated)</i> <i>(preservation of organotypical features of differentiation; no cytological evidence of atypia)</i>	33	40,7%
<i>Atypical thymoma (moderately differentiated)</i> <i>(preservation of organotypical features of differentiation; mild to moderate cytological atypia)</i>	37	45,7%
<i>Thymic carcinoma (poorly differentiated)</i> <i>(loss of organotypical features of thymic differentiation; presence of overt cytological evidence of malignancy)</i>	11	13,5%

Table IV – Number of patients and prevalence in Muller Hermelink/ WHO 2004 classifications.

Muller-Hermelink	WHO	Number of patients	Prevalence (%)
<i>Medullary thymoma</i>	<i>A</i>	10	12,3%
<i>Mixed thymoma</i>	<i>AB</i>	29	35,8%
<i>Predominantly cortical thymoma</i>	<i>B1</i>	25	30,9%
<i>Cortical thymoma</i>	<i>B2</i>	12	14,9%
<i>Well-differentiated thymic carcinoma</i>	<i>B3</i>	3	3,7%
—	<i>Thymic carcinoma</i>	2	2,5%

The 19 patients with MG are presented in Figure 9; the commonest type was WHO 2004 AB, corresponding to “Mixed thymoma” (Muller Hermelink), followed by B1 and B2 types.

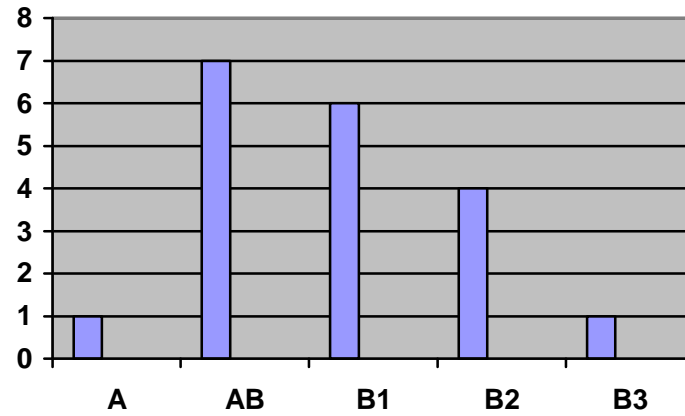


Figure 9 – Prevalence of WHO 2004 classification among the 19 patients with Myasthenia Gravis.

#### Mortality data

There were 7 deaths among the reviewed patients, without relationship to MG or important morbidities; 4 tumours were in Masaoka higher stages. The mortality is listed on Table V.

Table V – Mortality.

Gender	Age	MG	Adjuvant Therapy	Classifications		
				Masaoka	SM	MH/ WHO
Male	54	No	RT+QT	IV B	Thymic carcinoma	B1
Female	68		No	I	Thymoma	AB
Female	67		No	II	Atypical thymoma	B1
Male	39		RT+QT	IV B	Thymic carcinoma	B2
Male	81		RT	II	Thymic carcinoma	B1
Female	35		RT+QT	IV B	Thymic carcinoma	AB
Male	81		RT	II	Thymic carcinoma	B1



## Results

### Clinical correlations

The prevalence of the clinical presentations through the several stages of the different classification systems is presented on Tables VI, VII and VIII. A brief review of these data can be seen on Figures 10, 11 and 12.

Masaoka stage I patients were preferably asymptomatic, stages II and IV B commonly presented with systemic symptoms, while dyspnoea was the main symptom found among stage IV A.

All the histological subtypes of Suster-Moran were mainly asymptomatic at the time of the diagnosis, excluding the Atypical thymoma, which had a similar prevalence both of asymptomatic and triad presentations. The second most frequent way of presentation in all the Suster-Moran stages was through systemic symptoms.

Relatively to Muller Hermelink/ WHO 2004 classifications, Medullary/ type A, Mixed/ AB, Cortical/ B2 thymomas and Thymic carcinoma/ B3 were mainly asymptomatic at the time of the diagnosis. B1 thymoma presented with the classic triad of cough, dyspnoea and thoracic pain. Other thymic carcinomas (linfopitelioma-like) were presented whether by cough, whether by dyspnoea.

*Table VI – Clinical presentation of Masaoka classification.*

Masaoka	As.	SS	Cough	Dyspnoea	T. pain	Triad	MG
<b>I</b>	<b>(20)</b> 48%	(7) 17%	(3) 7,14%	(1) 2,4%	(2) 4,8%	(11) 26,2%	(3) 7,14%
<b>II</b>	(10) 33,3%	<b>(12)</b> 40%	(2) 6,7%	(6) 20%	(1) 3,3%	(5) 16,7%	(3) 10%
<b>III</b>	-	-	-	-	-	-	-
<b>IV A</b>	-	-	-	<b>(1)</b> 100%	-	-	-
<b>IV B</b>	(1) 12,5%	<b>(4)</b> 50%	-	(3) 37,5%	(1) 12,5%	(3) 37,5%	-

(As.) – Asymptomatic; (SS) – Systemic Symptoms; (T.pain) – Thoracic pain; (MG) – Myasthenia Gravis

Table VII – Clinical presentation of Suster-Moran classification.

Suster-Moran	As.	SS	Cough	Dyspnoea	T. pain	Triad	MG
Thymoma	(15) 45,4%	(5) 33,3%	(3) 9,09%	(1) 3,03%	(2) 6,06%	(7) 21,2%	(3) 9,09%
Atypical Thymoma	(11) 29,7%	(10) 27%	-	(8) 21,6%	(1) 2,7%	(11) 29,7%	(3) 8,1%
Thymic carcinoma	(4) 36,4%	(3) 27,3%	(2) 18,2%	(1) 9,1%	(1) 9,1%	(2) 18,2%	-

(As.) – Asymptomatic; (SS) – Systemic Symptoms; (T.pain) – Thoracic pain; (MG) – Myasthenia Gravis

Table VIII – Clinical presentation of Muller Hermelink/ WHO 2004 classifications.

MH/ WHO	As.	SS	Cough	Dyspnoea	T. pain	Triad	MG
Medullary/ A	(4) 40%	(2) 20%	-	(1) 10%	-	(2) 20%	(1) 10%
Mixed/ AB	(11) 36,7%	(3) 10%	(1) 3,3%	(3) 10%	(4) 13,3%	(5) 16,7%	(2) 6,7%
P. Cortical/ B1	(8) 32%	(1) 4%	(2) 8%	(4) 16%	-	(9) 36%	(2) 8%
Cortical/ B2	(5) 45,4%	-	(1) 9,09%	(1) 9,09%	-	(3) 27,3%	(1) 9,09%
T. Carc./ B3	(3) 100%	-	-	-	-	-	-
Others	-	-	(1) 50%	(1) 50%	-	-	-

(As.) – Asymptomatic; (SS) – Systemic Symptoms; (T.pain) – Thoracic pain; (MG) – Myasthenia Gravis

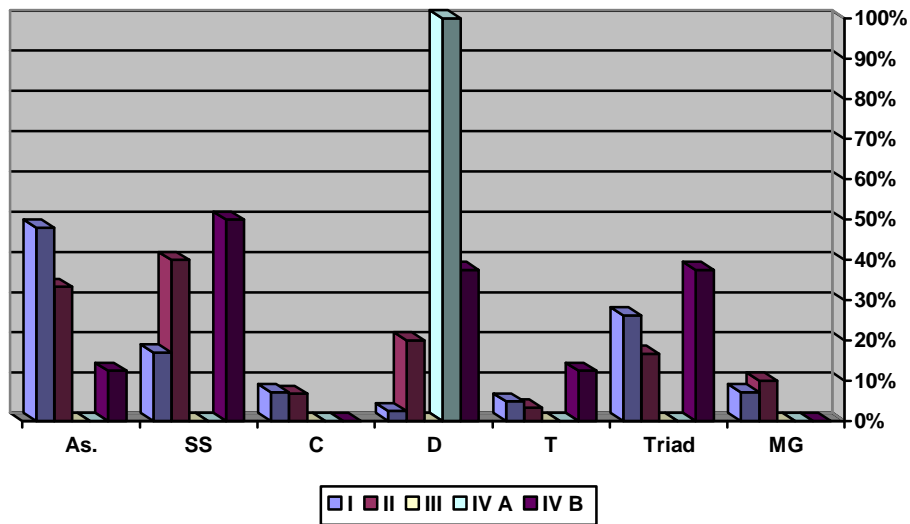


Figure 10 – Clinical presentation in Masaoka classification.

(As.) – Asymptomatic; (SS) – Systemic Symptoms; (C) – Cough; (D) – Dyspnoea; (T) – Thoracic pain;

(MG) – Myasthenia Gravis

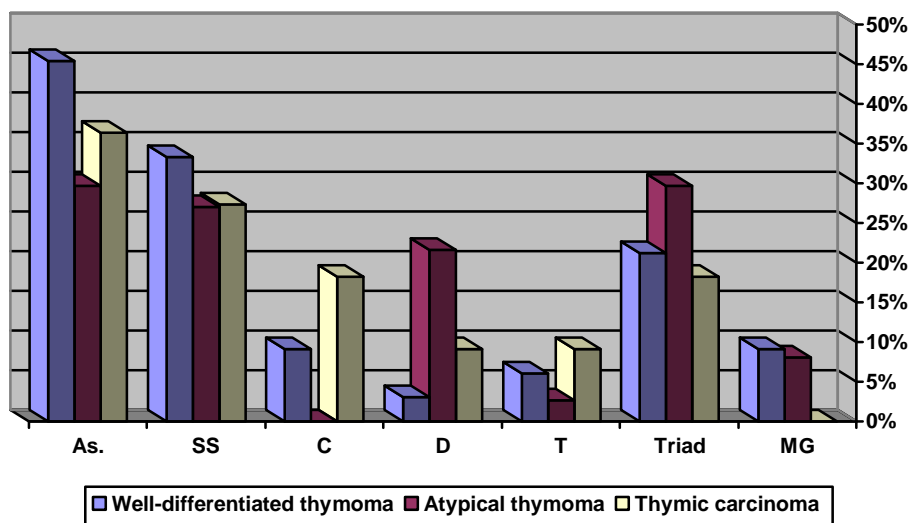


Figure 11 – Clinical presentation in Suster-Moran classification.

(As.) – Asymptomatic; (SS) – Systemic Symptoms; (C) – Cough; (D) – Dyspnoea; (T) – Thoracic pain;

(MG) – Myasthenia Gravis

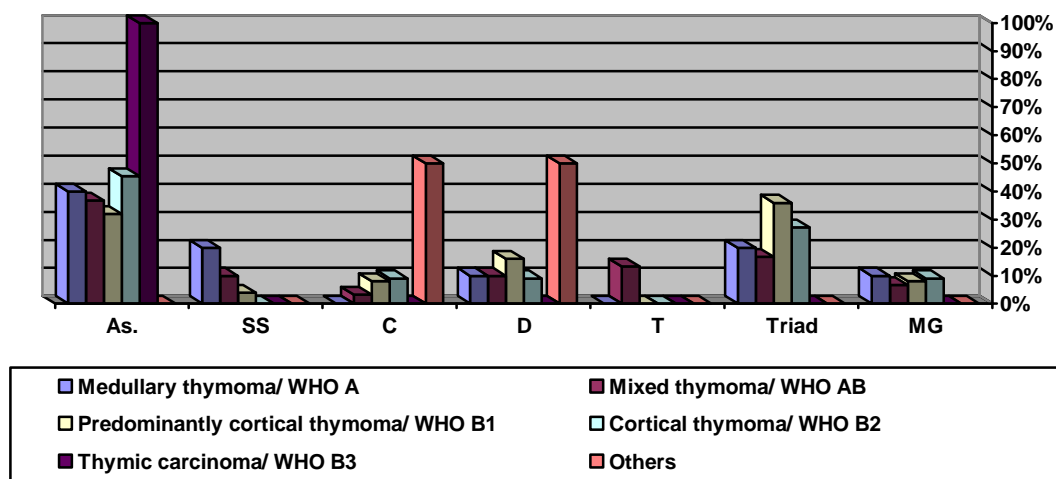


Figure 12 – Clinical presentation in Muller Hermelink/WHO 2004 classifications.

(As.) – Asymptomatic; (SS) – Systemic Symptoms; (C) – Cough; (D) – Dyspnoea; (T) – Thoracic pain;

(MG) – Myasthenia Gravis

## Prognosis

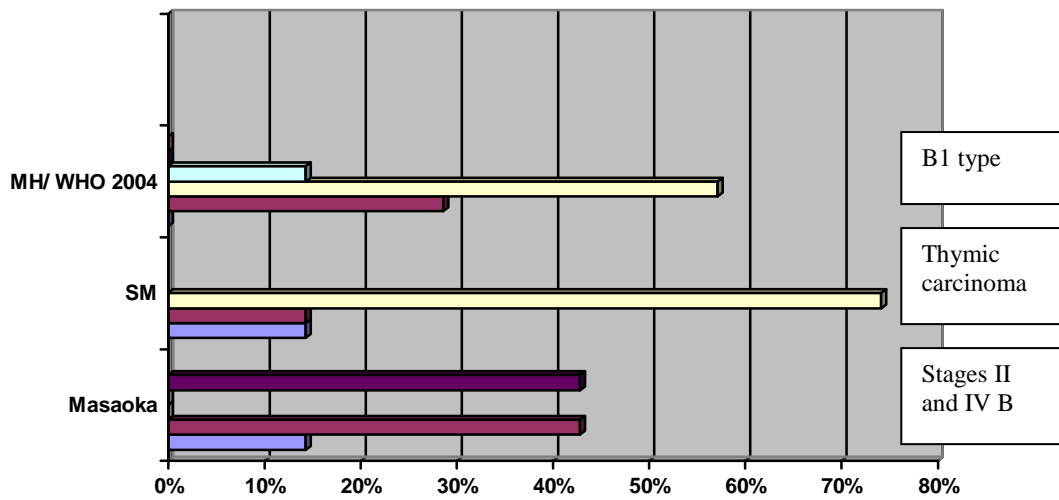
According to Tables IX and X and Figure 13, the prognosis was associated with surgical staging of Masaoka and the applied histological classifications of Suster-Moran and Muller Hermelink/WHO 2004 revealed equivalence in both incidence and death discrepancy.

Table IX – Mortality by classification system.

Masaoka		Suster-Moran		MH/WHO	
<b>I</b>	(1) 14,3%	<b>Thymoma</b>	(1) 14,3%	<b>AB</b>	(2) 28,6%
<b>II</b>	(3) 42,8%	<b>Atypical thymoma</b>	(1) 14,3%	<b>B1</b>	(4) 57,1%
<b>IV B</b>	(3) 42,8%	<b>Thymic carcinoma</b>	(5) 71,4%	<b>B2</b>	(1) 14,3%

*Table X – Equivalence of histological classifications by WHO 2004 (Muller Hermelink) and Suster-Moran classifications to the surgical Masaoka classification.*

<b>Masaoka</b>	<b>WHO 2004 (MH)</b>	<b>n/ %</b>	<b>SM</b>	<b>n/ %</b>
<b>I</b>  <i>WHO – 52%</i> <i>SM – 52%</i>	A	9/ 11%	Thymoma	32/ 39,5%
	AB	16/ 19,8%	Atypical thymoma	8/ 9,9%
	B1	12/ 14,8%	Thymic carcinoma	2/ 2,5%
	B2	2/ 2,5%		
	B3	2/ 2,5%		
	Thymic carcinoma	1/ 1,23%		
<b>II</b>  <i>WHO – 37%</i> <i>SM – 37%</i>	A	1/ 1,23%	Thymoma	2/ 2,5%
	AB	11/ 13,6%	Atypical thymoma	23/ 28,4%
	B1	9/ 11,1%	Thymic carcinoma	5/ 6,2%
	B2	8/ 9,9%		
	B3	1/ 1,23%		
	Thymic carcinoma	0		
<b>III</b>	—	—	—	—
<b>IV A</b>	A	0	Thymoma	0
	AB	0	Atypical thymoma	1/ 1,23%
	B1	1/ 1,23%	Thymic carcinoma	0
	B2	0		
	B3	0		
	Thymic carcinoma	0		
<b>IV B</b>  <i>WHO – 9,9%</i> <i>SM – 9,9%</i>	A	0	Thymoma	0
	AB	2/ 2,5%	Atypical thymoma	4/ 4,9%
	B1	3/ 3,7%	Thymic carcinoma	4/ 4,9%
	B2	2/ 2,5%		
	B3	0		
	Thymic carcinoma	1/ 1,23%		



**Legend:**

	<i>Masaoka</i>	<i>Suster-Moran</i>	<i>Muller-Hermelink</i>	<i>WHO</i>
	<i>I</i>	<i>Well-differentiated thymoma</i>	<i>Medullary thymoma</i>	<i>A</i>
	<i>II</i>	<i>Atypical thymoma – Moderately differentiated</i>	<i>Mixed thymoma</i>	<i>AB</i>
	<i>III</i>	<i>Thymic carcinoma – Undifferentiated</i>	<i>Predominantly cortical thymoma</i>	<i>B1</i>
	<i>IV A</i>	—	<i>Cortical thymoma</i>	<i>B2</i>
	<i>IV B</i>	—	<i>Well-differentiated thymic carcinoma</i>	<i>B3</i>
	—	—	—	<i>Thymic carcinoma</i>

**Figure 13 – Deaths among the several stages of the different classifications.**

## Discussion

The mean age of thymomas presentation was 57 years, and the difference in genders is insignificant (48% feminine versus 52% masculine), however, there is a higher prevalence in women with MG (63% feminine versus 37% masculine), which is in concordance with the reference data<sup>1</sup>. The calculated prevalence of MG is higher in this study (23,4%) when compared with the pointed prevalence of 15%<sup>2,3,4</sup>.

The main clinical presentation was composed by the triad of cough, dyspnoea and thoracic pain (16%), with each of the symptoms occurring alone in 8,6%, 6,2% and 4,9% of the cases, respectively. Paraneoplastic symptoms in this serie were not even notified. Asymptomatic findings and systemic symptoms were frequent, (38% and 18,75%, respectively) and should not be considered patognomonic due to their unespecificity and high prevalence in other diseases. However, thymoma should be suspected in a previous diagnosed MG patient who suddenly develops those systemic manifestations. Thoracic X-ray and thoracic-CT together are able to identify thymomas in 89% of the patients. These procedures should be encouraged in patients with the mentioned symptomatic triad. Other more invasive exams are unnecessary and only increase the hospital costs. Once more, the uncertainty about how to manage these patients is reflected in the percentage of bronchofibroscopies (19,8%) made. A high percentage of patients had already once in life had a neoplasm (18,5%) and 17,3% of them were smokers. More work should be done in this area to conclude if these findings are only epidemiologic associations or if there really is a molecular or genetic pattern.

In advanced stages of the disease and/or when there were extra-thymic manifestations, radiotherapy schemes were implemented (12,3%). The radiation dosage used was nearly similar among all the patients, with satisfactory responses and with only one case of radiation pneumonitis documented, 7,4% were submitted to a combination of radio and chemotherapy. Chemotherapy schemes alone

were only applied on those patients whose clinical condition and/or co-morbidities were prohibitive to radiotherapy. The drugs used were always the same (cisplatin, epirubicin and etoposide), always in the same dosages, with no significant toxicity notified. The success of the chemotherapy schemes on thymomas can be explained by the action of all these anti-cancerous on the DNA (cisplatin; epirubicin links to DNA and interferes with calcium and sodium transports; etoposide stimulates the topoisomerase-II)<sup>25</sup>. In fact, the scheme was extrapolated from the bronchogenic carcinoma, area in which much more data is available<sup>26</sup>.

Masaoka I (encapsulated type) was the more frequent stage among this surgical classification, with a prevalence rate of 51,8%. The less common was Masaoka stage III, with none reported case.

Suster-Moran “atypical thymoma” was the most frequent histological type (45,7%), being the “thymic carcinoma” the less common one (only 13,5% of all the cases).

WHO 2004 AB thymoma (corresponding to Muller Hermelink “mixed thymoma”) was the most prevalent within these classifications, with a prevalence rate of 35,8% (versus 43% in other clinical trials<sup>2</sup>).

The most frequent patterns of classification associated with clinical presentation were: Masaoka I (prevalence of 51,8%), where 48% patients were asymptomatic; Muller Hermelink/ WHO 2004 “mixed thymoma/ AB type” (prevalence of 35,8%), where 36,7% patients were asymptomatic; Suster-Moran “atypical thymoma” (prevalence of 45,7%) where 29,7% patients were asymptomatic and other 29,7% presented with the symptomatic triad. It can be concluded that absence of symptoms was the commonest way of presentation, without correlation either with Masaoka surgical staging nor with the used histological classifications.

Masaoka related mortality was as follows: Masaoka II ( prevalence of 37%) and IV B (9,9%), with 3 deaths each (42,8% mortality); in Suster-Moran “thymic carcinoma type” (prevalence of 13,5%) there were 5 deaths (71,4% mortality) and in Muller Hermelink/ WHO 2004 “predominantly cortical thymoma/ B1 type” (prevalence of 30,9%) there were 4 deaths (57,1%).



The histological classifications revealed correlation with prognosis in Suster-Moran thymic carcinoma (5) and WHO 2004 B1 type (4).

While WHO 2004 and Muller Hermelink classifications consider histogenesis and morphogenesis, allowing the knowledge of evolution of the thymus, Suster-Moran classification is based in pure morphological criteria, seeming to be easier to be applied in daily routine. The common types of thymomas with epithelial cells expressing high affinity to lymphocytes, and the other way around, may be difficult to be interpreted under Suster-Moran criteria<sup>3, 10</sup>.

Following modern medicine tendency to search support in molecular pathology, WHO 2004 classification continues to be the up to date one as in thymomas clinical behaviour and follow up, reinforced a clear role for Masaoka's surgical strategy in this study.

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