Clinical and serological features of thymoma-associated Myasthenia Gravis: a retrospective analysis on 346 patients

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Background and aim

TAMG (Thymoma-associated MG) represents one of the subtypes of MG associated with autoantibodies against the acetylcholine receptor (AChR-Ab). We analyzed the clinical and serological features of patients with thymoma and relapsed thymoma, at different time points, in order to identify a possible relationship among relapses, clinical features and changes in AChR-Ab titres overtime.

Methods

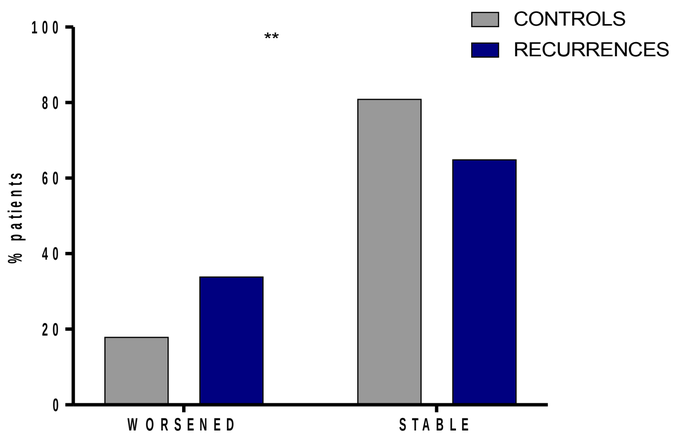
We enrolled 346 MG patients with AChR-Ab and thymoma: 318 with TAMG and 28 (8,8%) who experienced one or more recurrences of thymoma. We then retrospectively assessed: age of MG onset, MG clinical status according to MGFA (Myasthenia Gravis Foundation of America), time of thymectomy, surgical approach, post-thymectomy status and oncological features (according to histological classifications: WHO and Masaoka-Koga). AChR-Ab serum titres have been closely monitored overtime. GraphPad Prism 7.03 was used to perform Statistical analysis and p-values < 0.05 were considered statistically significant.

Results

Clinical features	no recurrences	recurrences	p value
N° of patients	318	28	
Age at onset	51.7±14.2	38.35±10.2	*p<0,0001*
EOMG (< 40)	248	16	
LOMG (≥ 40)	70	12	
Age at diagnosis	52.5±13.6	39.4±10	*p<0,0001*
Gender			
Female	158	18	
Male	160	10	
Age at thymectomy	52.2±14	39.1±10.7	*p<0,0001*

***Table 1**: Clinical features of Pisa's cohort of thymomas (t-test). EOMG: early onset MG; LOMG: late onset MG*

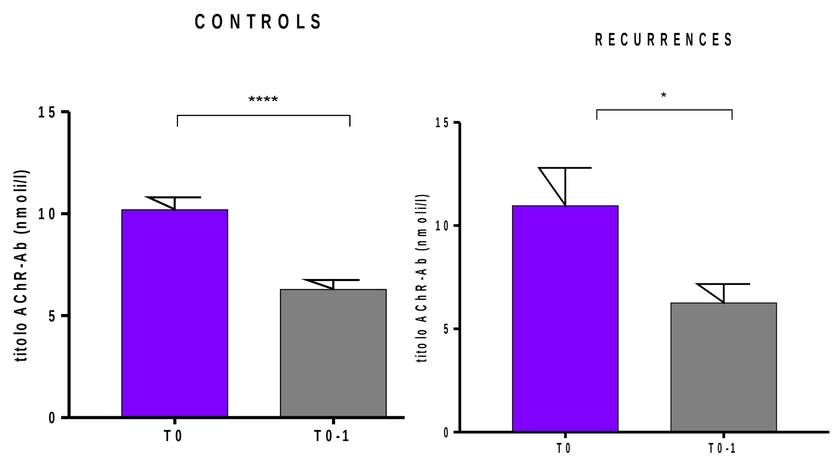
➢Patients with relapsed thymoma were younger then those without recurrences (unpaired t test, p<0,0001) (Table 1), with an average neoplastic disease-free time of about 3.7 years.



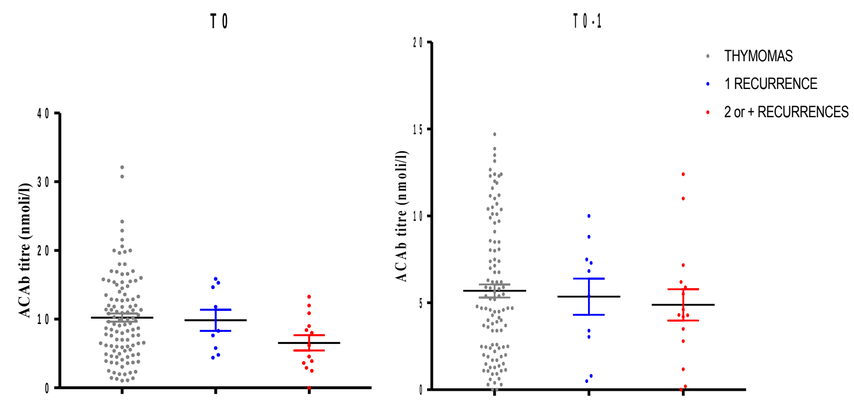
➢In relapsed thymomas symptoms worsened immediately after the first thymectomy (Chi-square test, p<0,0001). However, MG symptoms did not get worse by the time of recurrence of thymoma.

➢Relapsed thymomas had a higher Masaoka stage than non-relapsed thymomas (Chi-square test, p<0,0001).

ACHR-AB TITRES BEFORE AND IMMEDIATLY AFTER THYMECTOMY

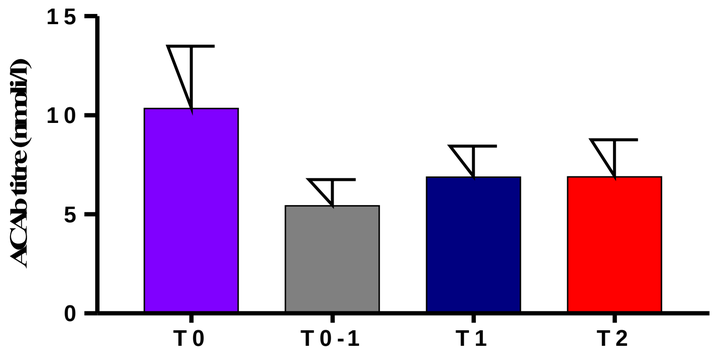


➢Overall, AChR-Ab titres in patients with thymoma declined immediatly after thymectomy (Wilcoxon test; thymomas: p<0,0001; relapsed thymomas: p<0,02)



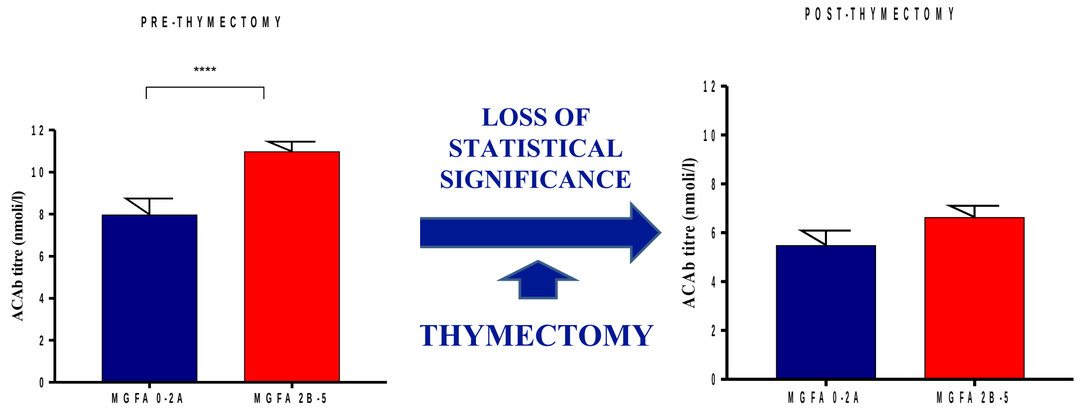
➢There was no statistical difference in AChRAb titres before (T0) and immediatly after (T0-1) thymectomy between patients with relapsed thymoma and patients without relapses (Kruskal-Walis test;T0: p>0,4; T0-1: p>0.8).

ACHR-AB TITRES OVERTIME (AT EACH RECURRENCE)



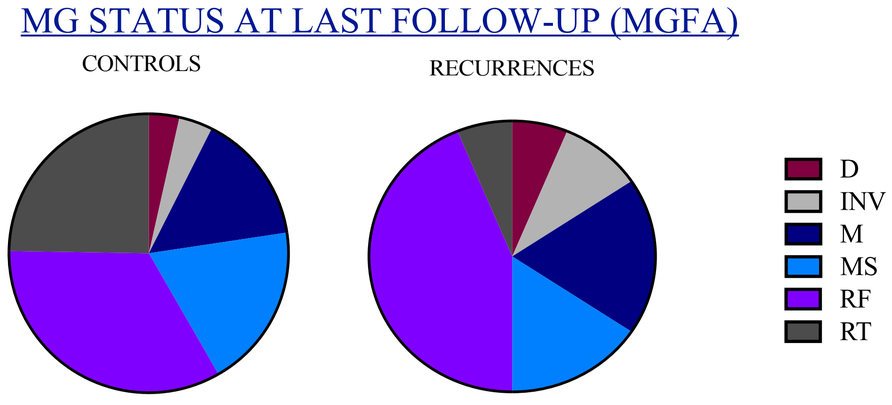
➢AChR-Ab titres remained unchanged overtime (Kruskal-Walis test, p=0.8). There was no statistical significantly difference of AChRAb tires performed at first (T1) and second (T2) recurrences in relapsed thymomas

CORRELATION BETWEEN ACHR-AB TITRE AND SEVERITY OF MG



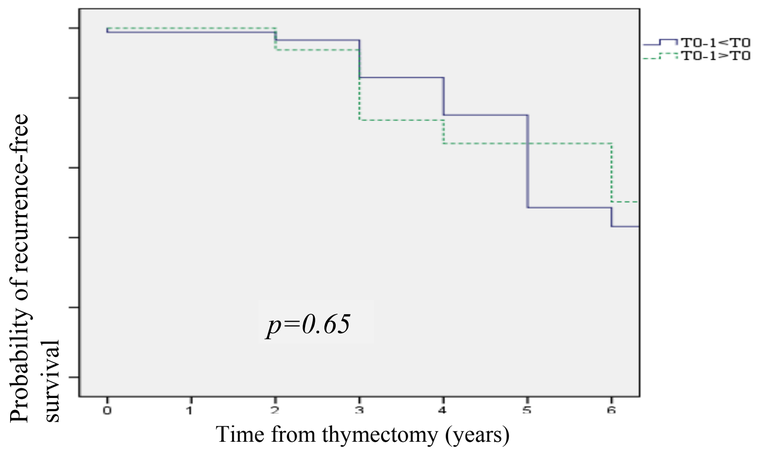
➢Before thymectomy there was a direct correlation between the severity of the disease and the antibody titre; after thymectomy this significance got lost

MG STATUS AT LAST FOLLOW-UP (MGFA)



➢The overall remission rate (RT+RF) was almost the same in the two groups (controls vs. recurrences: 58,2% vs 50%) *CSR: complete stable remission; PR: pharmacological remission; I: improved; MM: minimal manifestations; U: unchanged*

ACHR-AB TITRE AND THE PROBABILITY OF RECURRENCE-FREE SURVIVAL



➢No statistical difference has been found between the group that after thymectomy had an increase of antibody titre and the group that experienced a decrease of antibodies

AChR-Ab titre is not related to the probability of recurrence-free survival

Conclusion and discussion

- Our study shows, for the first time, that thymoma recurrences are associated with the age of the patient and the worsening of symptoms immediately after thymectomy, although at the time of recurrence there is no change in MG status.
- In both relapsed and non relapsed-thymoma patients AChR-Ab titre significantly declines after thymectomy, although it does not rise at the time of recurrence, even though there is an incremental trend.
- The dramatic reduction in the antibody titer together with the loss of statistical correlation between AChR-Ab level and the severity of the disease after surgery could support the role of thymectomy as "disease modifying" in TAMG.
- In the long-term, pharmacological and complete stable remission is achieved in a high percentage of both groups.
- Although rare, relapsed thymoma does occur, and further studies would need to be carried out to identify possible biomarkers of reccurrence.