PROCEEDINGS OF THE LATVIAN ACADEMY OF SCIENCES. Section B, Vol. 69 (2015), No. 5 (698), pp. 210–214.
DOI: 10.1515/prolas-2015-0031

IMPACT OF DIFFERENT THYMIC PATHOLOGIES ON THE CLINICAL COURSE OF MYASTHENIA GRAVIS: A POPULATION WIDE STUDY IN LATVIA

Anete Zieda[1#], Kristīne Rāviņa[1], Lelde Pelčere[2], Maruta S. Naudiņa[2], Inese Kamša[2], Nataļja Kurjāne[3], and Viktorija Ķēniņa[2]

[1] Faculty of Medicine, Rīga Stradiņš University, Dzirciema iela 16, Rīga, LV-1007, LATVIA

[2] Department of Neurology, Pauls Stradiņš Clinical University Hospital, Pilsoņu iela 13, Rīga, LV-1002, LATVIA

[3] Clinical Immunology Centre, Pauls Stradiņš Clinical University Hospital, Pilsoņu iela 13, Rīga, LV-1002, LATVIA

[#] Corresponding author; anete.zieda@gmail.com

Communicated by Igors Aksiks

Myasthenia gravis (MG) is an autoimmune disease characterized by autoantibody mediated postsynaptic failure of neuromuscular transmission. The thymus gland has a role in the pathogenesis of MG. The aim of this study was to determine (1) the prevalence of different thymic pathologies in the MG patient population of Latvia; (2) the potential impact of different thymus pathologies on the clinical course of MG; and (3) the effectiveness of surgical treatment of thymic pathologies in Latvia. The results showed that the most common thymus pathology among the patients with MG in Latvia is thymoma. Compared to the published data, the proportion of MG patients diagnosed with thymus hyperplasia in Latvia is very small. Thymus hyperplasia is uncommon among patients 60 years of age and older. MG onset for patients with thymoma is significantly later than that of patients with thymus hyperplasia. Almost all patients with thymoma or thymus hyperplasia develop a generalised form of MG. The presence of a thymus pathology does not significantly affect the electrophysiological test results, clinical symptom severity, frequency of disability or hospitalisation of the patients with MG. Thymectomy in patients with thymoma or thymus hyperplasia has no significant effect on relieving MG symptoms.

Key words: *myasthenia gravis, thymus, thymoma, thymic hyperplasia, thymectomy.*

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disease characterised by autoantibody mediated postsynaptic failure of neuromuscular transmission, resulting in fluctuating muscle weakness and fatigability (Berrih-Aknin *et al.,* 2014). Although MG is considered a rare disease, just like many other autoimmune diseases, it has a comparatively early onset, chronic course, and in most cases it requires continuous pharmacologic treatment. Together these factors impose a considerable effect on public health. Furthermore, during the past twenty years, the prevalence of MG in Western countries has doubled and is still increasing (Avidan *et al.,* 2014).

MG pathogenesis is associated with the production of auto-antibodies to neuromuscular synapse components — acetylcholine receptors (anti-AChR), muscle receptor specific tyrosine kinase (anti-MusK) or low-density lipoprotein receptor-related protein 4 (anti-LRP4), resulting in impaired signal transmission in the neuromuscular junction (Merigioli and Sanders, 2009; Berrih-Aknin *et al*., 2014). Etiology of autoimmune reactions in cases of MG is not precisely known, but it is proven that both genetic factors and thymic pathology play roles in MG pathogenesis and clinical course (Cavalcante *et al.,* 2011).

The thymus gland plays an important role in the maintenance of the immune system homeostasis. T-lymphocyte maturation and selection takes place in this mediastinal organ, resulting in the ability of the immune system to differentiate between self and non-self antigens and adequately respond to them (Lynch *et al*., 2009). Different thymus pathologies are present in up to 80% of anti-AChR seropositive myasthenia patients (Cavalcante *et al*., 2011). The most common thymic pathologies in MG patients are lymphofollicular hyperplasia, thymoma and atrophy with hyperplastic changes (Cavalcante *et al*., 2011).

The discovery of a thymoma in a patient with MG is widely accepted as an indication to perform thymectomy. In this case, the need for surgical treatment is justified not only by

the potential decrease of MG symptoms after the surgery, but also by preventing invasive tumour growth and reducing the risk of developing a B-cell non-Hodgkin's lymphoma or a soft tissue sarcoma characteristic to thymomas (Engels, 2010). Widely studied, but still controversial, is the role of thymectomy in patients with non-thymomatous MG. Surgical management of certain thymic pathologies increases the probability of resolving the symptoms of MG, improves the pharmacological control of MG and its symptoms, and decreases the necessity of immunosuppressant therapy subsequently decreasing the significant side effects of long-term corticosteroid use and immunosuppression in patients with MG (Gronseth and Barohn 2000; Luo *et al*., 2014). Results of thymectomy are better if it is performed soon after the onset of MG symptoms, possibly due to autoreactive T and B-cell migration from the thymus to the peripheral lymphoid tissue during the course of the disease, making thymectomy ineffective in MG symptom relief (Marx *et al*., 2010; Berrih-Aknin *et al*., 2014). The period during which thymectomy is most effective is not precisely known, but some studies refer to up to 24 months from the onset of MG symptoms (Huang *et al*., 2005). Patient age less than 50 years at the time of the onset of MG symptoms has also been mentioned as a factor that positively affects the outcome of thymectomy (Budde *et al*., 2001; Huang *et al*., 2005). Data showing the improvement of MG symptoms in post-thymectomy patients with late onset MG have also been published (Kawagauchi *et al*., 2007). This highlights the importance of timely diagnosis and treatment of thymic pathologies in the MG population. The aim of this study was (1) to determine the prevalence of different thymic pathologies in the MG patient population of Latvia; (2) to ascertain the potential impact of different thymic pathologies on the clinical course of MG; and (3) to evaluate the effectiveness of surgical treatment of these pathologies in Latvia.

MATERIALS AND METHODS

The clinical data used in this study were collected from patient records in the archives of Pauls Stradiņš Clinical University Hospital, and also during patient follow-up visits, which were organised as a part of this study. 255 patients who were hospitalised or consulted by the neurologist in an ambulatory setting from 1 January 2010 to 31 December 2014 were included in the study. All of the included patients had a proven diagnosis of myasthenia gravis (ICD-10 code G70.0). Exclusion criteria used in patient selection were (1) MG diagnosis not confirmed by serological and/or electrophysiological testing; (2) diagnosis of myasthenic syndrome, Lambert-Eaton myasthenic syndrome and secondary (symptomatic) myasthenia. Patient data were analysed as a whole as well as divided into subgroups according to gender — male and female; according to the age at the onset of the disease — early onset MG (onset at age < 50 y/o), late onset MG (50–59 y/o), very late onset MG (≥60 y/o); according to the presence or absence of thymus pathology; and according to the specific thymus pathologies — thymic hyperplasia, thymoma, residual thymus tissue and thymus carcinoma. The associations of different thymic pathologies with the following characteristics of the MG patient population were evaluated: the number of patients with MG, the gender and age of patients at the time of the study and at the onset of MG, the presence or absence of a thymic pathology and its type, the subjective results of thymectomy at least three months after the surgery if one was performed, MG form — ocular or generalised, Myasthenia Gravis Foundation of America (MGFA) clinical class, results of electrophysiological testing, seropositivity to AChR, the number of myasthenic exacerbation episodes requiring admission to the neurology ward, the number of myasthenic crisis episodes requiring admission to the intensive care unit, and the number of patients unfit for duty or disabled.

The SPSS 22.0 software was used for data analysis. To determine the normal distribution of quantitative data, the Shapiro-Wilk test, histogram and Q-Q curves were used. To describe parametric quantitative data, the mean value, standard deviation (SD), the value range and the median value were used. To determine the average value of the variability of parametric quantitative data depending on the categorical factors, the ANOVA test was used; to compare variables between subgroups, the independent sample t-test and histograms were used to present the data in graphs. Column charts and graphs were used to present the categorical qualitative data. To determine relationships between categorical data, the Chi-square test and Fisher's exact test were used, if one of the expected values was less than 5. A p value < 0.05 was adopted as statistically significant. To determine the relationship between the data groups with different number of cases (n), the pair exclusion method was used.

RESULTS

Prevalence of different thymic pathologies in the MG patient population in Latvia. Thymus imaging (computer tomography of the mediastinal organs) was performed for 164 patients (64.3%). Of these, in almost one half (49.39%), thymus gland pathology was not detected. Thymoma was found in 19.51% of patients, residual thymus tissue in 21.34%, thymus hyperplasia in 9.15%, and thymic carcinoma in 0.61% of patients (Table 1).

Associations between different thymic pathologies and the MG clinical course and demographic parameters. Statistically significant differences between the prevalence

Table 1

INCIDENCE OF DIFFERENT THYMIC PATHOLOGIES ACCORDING TO AGE AT MG ONSET

	EOMG*		LOMG		VLOMG		MG population	
	N	%	N	%	N	%	N	%
No path.	33	37.93	17	68.00	23	67.65	81	49.39
Hyperplasia	13	14.94	1	4.00	0	0.00	15	9.15
Resid. tissue	26	29.98	3	12.00	4	11.76	35	21.34
Thymoma	15	17.24	4	16.00	6	17.65	32	19.51
Carcinoma	0	0.00	0	0.00	1	2.94	1	0.61

Table 2

DISTRIBUTION OF VARIOUS THYMIC PATHOLOGIES AMONG THE EOMG, LOMG AND VLOMG SUBGROUPS

	EOMG*		LOMG		VLOMG		Sum of cases	
	N	%	N	%	N	%	N	%
No path.	33	45.2%	17	23.3	23	31.5	73	100
Hyperplasia	13	92.2	1	7.1	0	0.0	14	100
Resid. tissue	26	78.8	3	9.1	4	12.1	33	100
Thymoma	15	60.0	4	16.0	6	24.0	25	100
Carcinoma	0	0.0	0	0.0	1	100	1	100
All cases	87	59.6	25	17.1	34	23.3	146	100

* EOMG, early onset MG (2); LOMG, late onset MG (50–59); VLOMG, very late onset MG (≥60).

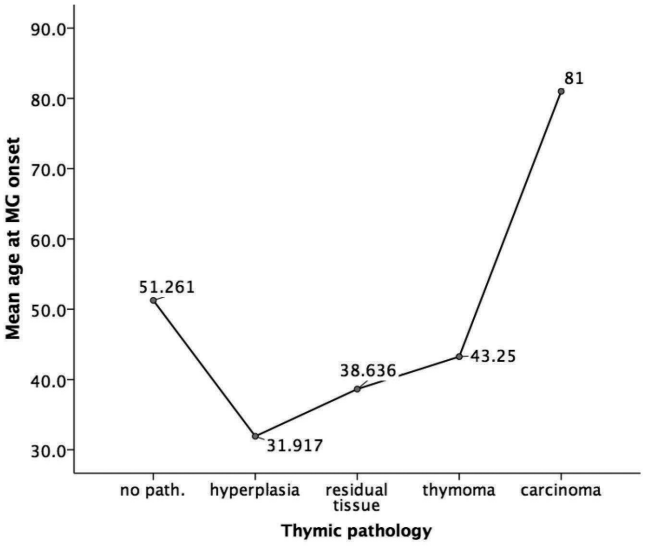

Fig. 1. The association between age at MG onset and different thymic pathologies.

of different thymic pathologies in different age groups (p = 0.005) were found (Table 2). 92.2% of all thymus hyperplasia cases were observed in the early onset MG group (EOMG, onset at age 2); there were no thymus hyperplasia cases observed in the very late onset MG group (VLOMG, onset at age ≥60). Thymoma was found in 17% (16.0% to 17.65%) of patients in all age groups. The presence of different thymic pathologies had significant associations with the age at the onset of MG ($p < 0.001$; F = 6.692, η^2 = 0.167) (Fig. 1). For younger patients (mean age 31.9 years at the beginning of the disease), the most characteristic thymus pathology was shown to be thymus hyperplasia. Presence of a thymoma was associated with older age (mean age 43.25 years) at the onset of the disease. Various thymus pathologies were observed with similar frequency in both women and men. No differences in the proportion of seropositive AChR patients were found between patient groups with various thymic pathologies. There were also no significant differences in the proportion of seropositive individuals in the thymic pathology group and the group without the identified thymus pathology ($p > 0.05$) (Table 3). Significant differences in qualitative or quantitative results of myasthenic reaction were not found between various thymic pathologies, nor between patients with and without thymus pathologies ($p > 0.05$). No significant differences were found in the frequency of MG forms (generalised or ocular) ($p > 0.05$) (Table 4), MGFA class ($p > 0.05$), need for hospitalisation or admission to the intensive care unit ($p > 0.05$), fitness for duty ($p > 0.05$), or disability ($p > 0.05$) frequency in patients with and without thymus pathologies and between thymic pathology groups.

Table 3

INCIDENCE OF ANTI-ACHR ANTIBODIES IN CASES OF VARIOUS THYMUS PATHOLOGIES

	Positive anti-AChR antibodies	Negative anti-AChR antibodies
No pathology	74.5	25.5
Hyperplasia	66.75	33.25
Residual tissue	70.6	29.4
Thymoma	88.8	11.2
All cases	75.4	24.6

Table 4

INCIDENCE OF OCULAR OR GENERALISED MG FORMS IN CASES OF VARIOUS THYMUS PATHOLOGIES

	Ocular form	Generalised form
No pathology	19.2	80.8
Hyperplasia	0.0	100
Residual tissue	25.0	75.0
Thymoma	6.9	93.1
Carcinoma	0	100
All cases	8.0	92.0

Effectiveness of thymectomy in patients with different thymic pathologies. Thymectomy was carried out in 84.4% of MG patients with thymoma, 33.3% of patients with thymus hyperplasia, 11.4% of patients with residual thymic tissue, in no patients with thymic carcinoma, and in no patients without thymic pathology. When evaluating the subjective condition of patients at least three months after the surgery (Fig. 2), none of the thymus gland pathology groups showed significant thymectomy efficiency — overall subjective improvement ($p > 0.05$).

DISCUSSION

Thymic examination at least once after diagnosing a patient with MG was carried out in 65% of patients. Thymus gland pathology was not detected in half of the patients (49.4%), which does not comply with the literature data on coincidence of these pathologies. According to the literature data, up to 80% of MG patients have one of the thymus gland pathologies (Muller-Hermelnik *et al*., 1999; Berrih-Aknin *et al*., 2009; Marx *et al*., 2010). Also, "residual thymic tissue" was the most commonly found pathology in patients of all age groups (12% LOMG and VLOMG and 30% EOMG); these patients most likely should also belong to the group

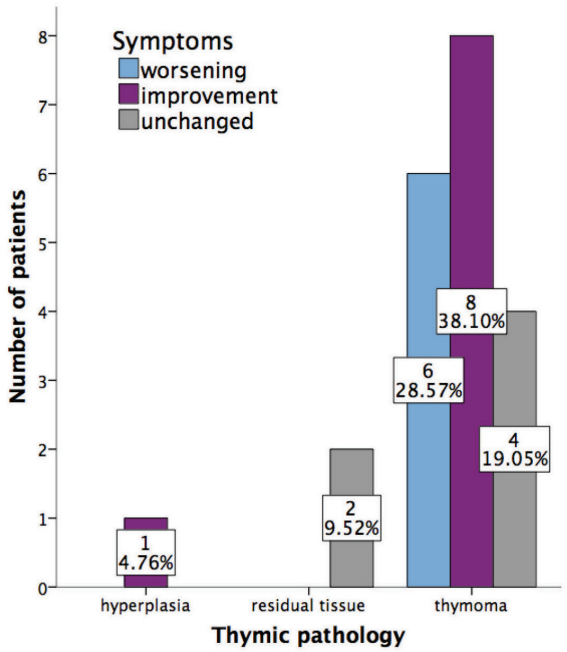

Fig. 2. Subjective results of performed thymectomies in cases of various thymic pathologies.

"without pathology" since about 10% of thymic tissue remains physiologically functional until about 70 years of age (Steinmann *et al*., 1985). There were no patients with thymus atrophy with hyperplastic changes found in our study group (about 20% prevalence in MG patients according to the literature data (Cavalcante *et al*., 2011)). The diagnosis of this thymic condition requires histological analysis, which is almost never carried out due to the lack of indications for surgical treatment or specific modifications in pharmacological therapy for this condition. Thymus hyperplasia has been mentioned as the most common thymic pathology in MG patients, especially in early onset MG — 50–70% of MG patients (Muller-Hermelnik *et al*., 1999; Berrih-Aknin *et al*., 2009). We found thymoma to be the most common thymic pathology in Latvian MG patients in all age groups with almost equal frequency of 16.0–17.45%, similar to the average frequency in the world — 10–30% of MG patients (Marx *et al*., 2010). While the frequency of thymoma in the Latvian MG patients corresponds to the average in the world, the frequency of the other pathologies is dramatically lower, which most likely indicates that the diagnostics of non-thymomatous pathologies in Latvia is inefficient. This might arise because the only widely accepted indication to carry out thymectomy is the detection of thymoma (Engels, 2010). While results of many studies show the effectiveness of thymectomy in the case of thymus hyperplasia, thymectomy for patients with thymic hyperplasia is performed relatively rarely in Latvia (about 30% of patients). This observation cannot be explained by the age of the patients at the time of diagnosis. Age can be a barrier to safe surgical treatment because of the various comorbidities or due to a relatively lower effectiveness of thymectomy in patients over 50 years of age at the time of diagnosis (Huang *et al*., 2005; Budde *et al*., 2001). Similarly as elsewhere in the world (Muller-Hermelnik *et al*., 1999; Berrih-Aknin *et al*., 2009), thymus hyperplasia in Latvia is mainly found in early onset MG patients (patients younger than age 50) and, according to the data of this study, it was not found in MG patients older than 60 years of age. On the other hand, this might be explained by delayed diagnosis of thymus hyperplasia. Studies have shown that surgical treatment is most effective within the first 24 months after the onset of symptoms (Huang *et al*., 2005), as later MG may become self-sustaining even after the thymectomy (Marx *et al*., 2010; Berrih-Aknin *et al*., 2014). The results of the first randomised class I study on the effectiveness of thymectomy in the case of non-thymomatous MG will be available in 2016. Possibly, the results of this study will serve as the basis for new, evidence-based recommendations for thymectomy that could motivate to improve the efficiency of the radiological diagnosis of thymus hyperplasia.

In this study, a significant ($p < 0.001$) correlation was found between patient age at the beginning of the disease and the existence of certain thymic pathologies — younger MG patients (average age at the beginning of the disease — 31.9 years) most often were diagnosed with thymus hyperplasia; older MG patients (mean age at the beginning of the disease — 43.3 years) with thymoma. These findings are consistent with literature data (Muller-Hermelnik *et al*., 1999; Berrih-Aknin *et al*., 2009; Marx *et al*., 2010). Significant differences in the prevalence of antibodies to AChR were not found between groups of patients with various thymic pathologies, nor between patients with and without identified thymus gland pathologies. Taking into consideration the role of thymus in the production of anti-AChR antibodies (Cavalcante *et al*., 2011; Marx *et al*., 2003), the absence of seropositivity differences between patients with and without thymus pathology seems unlikely. These results might be explained by the relatively small proportion of patients tested for the antibodies or the frequency of undiagnosed thymic pathologies. Up to 100% of patients with identified thymoma or thymus hyperplasia had generalised symptoms (mean in Latvia MG population — 82%). However, this difference was not statistically significant ($p > 0.05$), likely due to the relatively small number of cases. No significant differences in electrophysiological examination, MGFA clinical classes, need for hospitalisation or admission to ICU, as well as the inability to work and disability parameters were found between groups of patients with various thymic pathologies. It should be noted that in the evaluation of these parameters, patients who had had a thymectomy were included in the "thymoma" group.

Thymectomy was carried out in 84.4% of MG patients with thymoma, 33.3% of patients with thymus hyperplasia, 11.4% of patients with residual thymic tissue, in none of the patients with thymic carcinoma (refused treatment) and in none of the patients without thymus gland pathology. The efficacy of thymectomy was assessed at least three months after surgery. The majority (38.10%) of patients after thymectomy due to thymoma noted improvement, but 28.57% of the patients noted deterioration of the condition. As a result, this study fails to show significant thymectomy effi-

cacy (relief of symptoms) ($p > 0.05$). It is difficult to compare these data to those of other studies, mainly because this study did not use any objective evaluation criteria for the pre- and post-operative disease severity, such as Quantitative MG Score for Disease Severity, which is usually used for measurement of therapeutic effectiveness in patients with MG (Jaretzki *et al*., 2000) during the early years of the study period. This scale was introduced in the Neuromuscular Disease Clinic of the Pauls Stradiņš Clinical University Hospital only in 2014, when it was included in the patient exam questionnaire of this study, but it has never been used to assess the pre-surgical condition of patients.

Using the data collected and analysed in this study, as well as additional data about MG patient clinical condition, treatment, its efficiency and other parameters (obtained with patient permission), the PSKUS Neurology Department has started to develop a computerised database of MG patients. This database will help to optimise MG treatment, and allow attending physicians to obtain clear data on performed tests and their results, which may help to optimise timely diagnosis and treatment of thymic pathologies, as well as serve as a basis for other studies of myasthenia gravis in Latvia.

ACKNOWLEDGEMENTS

The authors are grateful to the collective of the Neurology Clinic of Pauls Stradiņš Clinical University Hospital for their support. There is no financial support or conflict of interests to disclose.

REFERENCES

Avidan, N., Panse, R., Berrih-Aknin, S., Miller, A. (2014). Genetic basis of myasthenia gravis: A comprehensive review. *J. Autoimmun.*, **52**, 146–153.

Berrih-Aknin, S., Ruhlmann, N., Bismuth, J., Cizeron-Clairac, G., Zelman, E., Shachar, I., Dartevelle, P., de Rosbo, N. K., Le Panse, R. (2009). CCL21 overexpressed on lymphatic vessels drives thymus hyperplasia in myasthenia. *Ann. Neurol.,* **66** (4), 521–531.

Berrih-Aknin, S., Panse, R. (2014). Myasthenia gravis: A comprehensive review of immune dysregulation and etiological mechanisms. *J. Autoimmun.,* **52**, 90–100.

Budde, J., Morris, C. D., Gal, A. A., Mansour, K. A., Miller, J. I. (2001). Predictors of outcome in thymectomy for myasthenia gravis. *Ann. Thor. Surg.,* **72** (1), 197–202.

Cavalcante, P., Le Panse, R., Berrih-Aknin, S., Maggi, L., Antozzi, C., Baggi, F., Bernasconi, P., Mantegazza, R. (2011). The thymus in myasthenia gravis: Site of 'innate autoimmunity'? *Muscle & Nerve,* **44** (4), 467–484.

Engels, E. A. (2010). Epidemiology of thymoma and associated malignancies. *J. Thor. Oncol.*, **5** (10), suppl. 4, s260–265.

Gronseth, G. S., Barohn, R. J. (2000). Practice parameter: Thymectomy for autoimmune myasthenia gravis (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology,* **55** (1), 7–15.

Huang, C. H., Hsu, H. S., Huang, B. S., Lee, H. C., Kao, K. P., Hsu, W. H., Huang, M. H. (2005). Factors influencing the outcome of transsternal thymectomy for myasthenia gravis. *Acta Neurol. Scand.*, **112** (2), 108–114.

Jaretzki, A., Barohn, R. J., Ernstoff, R. M., Kaminski, H. J., Keesey, J. C., Penn, A. S., Sanders, D. B. (2000). Myasthenia gravis: Recommendations for clinical research standards. Task Force of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America. *Ann. Thor. Surg.*, **70** (1), 327–334.

Kawaguchi, N., Kuwabara, S., Nemoto, Y., Fukutake, T., Arimura, K., Osame, M., Hattori, T. (2007). Effects of thymectomy on late-onset myasthenia gravis without thymoma. *Clin. Neurol. Neurosurg.*, **109** (10), 858–861.

Luo, Y., Pan, D. J., Chen, F. F., Zhu, M. H., Wang, J., Zhang, M. (2014). Effectiveness of thymectomy in nonthymomatous myasthenia gravis: A systemtic review. *J. Huazhong Univ. Sci. Technol.*, **34** (6), 942–949.

Lynch, H. E., Goldberg, G. L., Chidgey, A., Van den Brink, M., Boyd, R., Sempowski, G. D. (2009). Thymic involution and immune reconstitution. *Trends Immunol.,* **30** (7), 366–373.

Marx, A., Muller-Hermelink, H., Strobel, P. (2003). The role of thymomas in the development of myasthenia gravis. *Ann. NY Acad. Sci.,* **998**, 223–236.

Marx, A., Willcox, N., Leite, M. I., Chuang, W. Y., Schalke, B., Nix, W., Ströbel, P. (2010). Thymoma and paraneoplastic myasthenia gravis. *Autoimmunity*, **44** (5–6), 413–27.

Meriggioli, M. N., Sanders, D. B. (2009). Autoimmune myasthenia gravis: Emerging clinical and biological heterogeneity. *Lancet Neurol.,* **8** (5), 475–490.

Muller-Hermelink, H., Marx, A. (1999). Pathological aspects of malignant and benign thymic disorders. *Ann. NY Acad. Sci.*, **2**, 5–14.

Steinmann, G. G., Klaus, B., Müller-Hermelink, H. K. (1985). The involution of the ageing human thymic epithelium is independent of puberty. *Scand. J. Immunol.,* **22 (**5), 563–575.

Received 12 May 2015

AIZKRŪTS DZIEDZERA PATOLOĢIJU IETEKME UZ *Myasthenia gravis* KLĪNISKO GAITU: POPULĀCIJAS PĒTĪJUMS LATVIJĀ

Myasthenia gravis (MG) ir autoimūna saslimšana, ko raksturo muskuļu vājums un pastiprināta nogurdināmība auto-antivielu izraisītu neiromuskulārās pārvades traucējumu dēļ. Šo auto-antivielu produkcijā ir iesaistīts aizkrūts dziedzeris. Šī pētījuma mērķis bija noskaidrot (1) dažādu aizkrūts dziedzera patoloģiju sastopamību MG pacientiem Latvijā; (2) dažādu aizkrūts dziedzera patoloģiju potenciālo ietekmi uz MG klīnisko gaitu un saistību ar pacientu demogrāfiskajiem rādītājiem; un (3) aizkrūts dziedzera patoloģiju ķirurģiskās ārstēšanas (timektomijas) efektivitāti MG simptomu mazināšanā Latvijā. Pētījuma rezultāti liecina, ka visbiežāk sastopamā aizkrūts dziedzera patoloģija MG pacientiem Latvijā ir timoma. Salīdzinot ar citu starptautisku pētījumu datiem, Latvijā ievērojami retāk kā citās pasaules valstīs tiek diagnosticēta aizkrūts dziedzera hiperplāzija. Tā netika konstatēta nevienam pacientam pēc 60 gadu vecuma. Pacientiem ar konstatētu aizkrūts dziedzera hiperplāziju raksturīgs ievērojami agrāks MG pirmo simptomu parādīšanās vecums nekā pacientiem ar konstatētu timomu. Praktiski visiem pacientiem ar timomu vai hiperplāziju attīstās ģeneralizēta MG forma. Pētījumā neizdevās statistiski ticami pierādīt aizkrūts dziedzera patoloģiju ietekmi uz elektrofizioloģisko testu rezultātiem, klīnisko simptomu smagumu, hospitalizāciju biežumu, tostarp intensīvās terapijas nodaļā, sakarā ar MG paasinājumu vai krīzi, darba nespēju vai invaliditāti. Netika statistiski ticami pierādīta arī timektomijas efektivitāte MG simptomu mazināšanā.