Myasthenia gravis and thymectomy: many doubts and few certainties

Giuseppe Marulli* and Federico Rea

Department of Cardiologic, Thoracic and Vascular Sciences, Thoracic Surgery Unit, University of Padova, Padova, Italy

* Corresponding author. Department of Cardiologic, Thoracic and Vascular Sciences, Thoracic Surgery Unit, University of Padova, Via Giustiniani 2, 35100 Padova, Italy. Tel: +39-49-8218740; fax: +39-49-8212249; e-mail: giuseppe.marulli@unipd.it (G. Marulli).

Keywords: Myasthenia gravis • Thymectomy • Robotic surgery • Thymoma

Myasthenia gravis (MG) is a rare autoimmune disease affecting neuromuscular transmission. The thymus plays a central role in the complex pathogenesis and perpetuation of this disease, being implicated in mechanisms of self-tolerance and autoimmunity.

Since the study of Blalock [1] in 1944, who published the results of transternal thymectomy in a series of 20 patients affected by MG, thymectomy has become an essential part of the integrated treatment of this disease, yielding positive results in terms of improvement and remission of symptoms.

The report by Keijzers et al. [2] in this issue of EJCTS provides the neurological and surgical results of robotic thymectomy in a large cohort of patients affected by MG. This study summarizes the main concerns regarding the role of thymectomy in MG patients.

Despite a general agreement on the beneficial role of thymectomy for MG patients, to date no prospective randomized trials have addressed the question whether thymectomy is superior to medical treatment. This question is the subject of an ongoing international multicentre randomized clinical trial comparing thymectomy and prednisone therapy with prednisone alone [3]. The best available data come from a meta-analysis of 28 controlled but non-randomized studies that showed MG patients undergoing thymectomy were twice more likely to attain medication-free remission than unoperated patients, 1.6 times more likely to become asymptomatic and 1.7 times more likely to improve [4].

In addition to this low level of evidence supporting thymectomy, several controversies still exist regarding the selection of candidates for surgery, the extent of thymic resection and the best surgical approach to be used [5]. Thus, a consensus on the best clinical practice has never been reached. For these reasons, when considering thymectomy for MG patients, clinicians have to think imperatively over the ratio between expected benefits and risks guaranteeing the best balance between the extent of resection, morbidity, patient acceptance and results.

In our view, three key points are of paramount importance:

(i) Surgical risk-benefit balance: A variety of surgical approaches have been described for thymectomy ranging from open (basic transternal or the more aggressive extended transcervical and transternal maximal thymectomy), to minimally invasive approaches (transcervical or video-assisted thoracoscopic thymectomy). When compared, each approach has its benefits and drawbacks. At this time, only non-randomized retrospective case series are available for comparison of various operative approaches. The heterogeneity of patient selection, the different timing and type of surgery, the several clinical classifications used, the different methods applied for the evaluation of results and many other confounding factors have made the analysis complicated, if not impossible (Class III evidence) [6]. Ideally, the less invasive surgical technique is desirable, assuming the results are equivalent. Minimally invasive techniques have become increasingly popular due to their low procedural morbidity and mortality, short hospital stay, optimal cosmesis, minor surgical access trauma and postoperative pain, better preservation of pulmonary function and better acceptability, particularly by young patients. Thoracoscopic thymectomy has been proposed as a valid alternative to open approaches for patients with MG in an attempt to find the best compromise between achieving a complete resection of the thymus and minimizing the effect of the surgery on the patient. The introduction, in the last decade, of robotic instrumentation was oriented to increase the potential of standard thoracoscopy in terms of technical skill and safety, and eventually to improve clinical results [7, 8].

(ii) Probability of clinical benefits (remission and improvement of symptoms): To date, only a few studies adopted the recommendations for clinical research standards classification proposed in 2000 by the Myasthenia Gravis Foundation of America (MGFA) [9]. The available results, coming from recent papers, reported a complete stable remission (CSR) rate ranging between 28 and 42.8% for conventional thoracoscopic thymectomy series and between 27 and 42% for robotic series [10]. A similar wide range of CSR is reported for open transternal and transcervical approaches. This variability may result from several factors: different length of follow-up, heterogeneity of patients’ characteristics (e.g. thymomatous and non-thymomatous, ocular and generalized MG with different classes of severity, variable length of preoperative symptoms), clinical evaluation sometimes not performed by a neurologist, different practice among neurologists with regard to medication prescription and management strategy for weaning off the drugs after thymectomy etc. These factors are still confounding and represent a serious limitation for a comprehensive and definitive evaluation of clinical results after thymectomy, making the judgment about what is the better surgical approach to adopt also difficult.

(iii) Reduction of medications: Thymectomy allows an important reduction or suspension of drugs [4]. This benefit is often...
underestimated, poorly considered and few times reported in the studies. In our opinion, this is an advantage of paramount importance for two reasons: firstly, a significant reduction of potential adverse effects of the medications may be obtained, together with a reduction of the risks related to the prolonged immunosuppressive therapy (oncological and infective risks). Secondly, the thymectomy could have a significant economic impact: the costs related to a virtual lifetime of medical treatment are enormous, thus a reduction or suspension of medication translates into a reduction of costs for the Health Care System.

In conclusion, well-designed controlled prospective studies should be required to answer some of the numerous open questions concerning thymectomy in the treatment of MG. However, the rarity and the intrinsic characteristics of MG make it difficult to design and perform prospective studies aimed at comparison of thymectomy techniques. As suggested by Jaretzki [5], alternative valid non-randomized studies should be employed based on the systematic use of the ‘MGFA Recommendations for Clinical Research Standards’. The analysis of CSR and improvement following thymectomy must be performed by the Kaplan–Meier method in order to uniformly compare the results of different techniques.

REFERENCES


