

## Randomized trial of thymectomy in myasthenia gravis

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*Response to:* Tzankov A. Commentary on “Randomized trial of thymectomy in myasthenia gravis”. *J Thorac Dis* 2016;8:E1420-E1422.

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### *To the Editor:*

We appreciate the wide interest in the results from the international extended transsternal thymectomy trial in non-thymomatous myasthenia gravis (MG) (1). Correspondence has been received from several medical communities including neurologists, thoracic surgeons, and pathologists. And we thank Tzankov and Bourque and Warman Chardon for their gracious comments.

Tzankov (2) frames the role of thymectomy in both thymomatous and non-thymomatous MG while Bourque and Warman Chardon (3) summarize the historical record of randomized, controlled treatment trials in the disease. Both single out the evidence gap related to thymectomy we worked to bridge with our trial. The practice parameter by Gronseth and Barohn (4) in 2000 explicitly called for such an effort. There are several points raised by the authors we wish to clarify. The first is the decision to use minimal manifestation status (MMS) as opposed to remission as the clinical endpoint that dictated prednisone dosing changes. Remission in MG, especially when formally defined (5), is relatively uncommon (15–25%), no matter the intervention (6,7). MMS is more commonly encountered and is accepted as a favorable outcome. A clinical status of MMS or better was defined as the treatment goal in the recently published international consensus guidance for MG management (8). As for the thymic tissue, further analysis of the resected

specimens and correlation of histopathological findings with clinical outcomes are in the works.

There is no question that conducting randomized surgical trials presents challenges, and the thymectomy study was no different. Disease duration and upper age limits were modified to boost recruitment; these were the only changes made over the 9-year duration of the trial. We did consider loosening the entry criteria that forbade any immunosuppressive therapy outside of corticosteroids, but concluded such agents would cloud interpretation of study results. Similarly, we weighed the advantages and disadvantages of permitting less invasive thymectomy approaches, but decided against this allowance as well, mandating that the extended transsternal technique be utilized. We were conducting the first randomized trial of thymectomy and felt it imperative to first demonstrate whether there was benefit to an as-complete resection as possible. Nevertheless, our inference is that a similar constellation of benefits can be expected with less invasive approaches as long as the surgeon’s intent is to perform as complete a thymectomy as possible.

The role of thymectomy in double-seronegative and muscle-specific kinase (MuSK) antibody-positive MG deserves final comment. Thymectomy does appear to have a positive impact in double-seronegative patients (7), an observation that may reflect the likelihood that many of

these patients actually harbor anti-acetylcholine receptor antibodies when tested with cell-based assays that cluster the receptor, mimicking the architecture of the post-synaptic membrane (9,10). In most reports, thymectomy in MuSK-antibody positive patients seems to have little if any favorable impact (7,8), providing further emphasis to the need to individualize management approaches for patients with MG.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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