Thymectomy for the management of Myasthenia Gravis. Does the open approach confer the best results for long-term remission?

"The Athens Crossroad" Congress
Athens  Greece  November 8-10, 2018
Disclosure:

None

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Background

Torino, Italy
There continues to be a debate about the effectiveness of Thymectomy in the management of non-thymomatous MG and which thymectomy technique is the procedure of choice.
This debate persists primarily because the lack of controlled randomized prospective studies
Anatomy & implications

Torino, Italy
The Thymus

The thymus is not “two well-defined lobes that appear almost as distinct as do the two lobes of the thyroid” as Blalock described in 1931.
A highly variable anatomy has been described, having profound surgical implications discussing radical thymectomy and the correct surgical approach to the Thymus.

Ectopic thymic tissue has been detected in 32%-98% of patients receiving extended thymectomy.

Alfred Jaretzki III et al.: Semin Neurol 2004;24:49
It’s crucial to emphasize that the thymus is a functional entity, not limited to the glans itself as well as that thymic cells may be also found outside the main capsule.

The recommendation is that as much mediastinal thymic tissue as possible should be removed in MG non-thymomatous patients.
MG treatment

- Thymectomy is generally indicated in patients with early onset MG and positive Ach receptor antibodies, or in case of associated Thymoma.

- Patients with AchR antibodies and generalized disease are more likely to improve their symptoms.

- Thymectomy is NOT recommended for patients with MUSK antibodies.
Indications for surgery

- Young patients have better response rate to thymectomy than the elderly
- The benefits of thymectomy may decrease with the age of patient
- Patients with short duration of illness prior to surgery, are reported to be more likely to benefit

Therefore, there is a clear indication to perform thymectomy as early after disease onset, and at as early as feasible.
Randomized Trial of Thymectomy in Myasthenia Gravis


CONCLUSIONS—Thymectomy improved clinical outcomes over a 3-year period in patients with nonthymomatous myasthenia gravis. (Funded by the National Institute of Neurological Disorders and Stroke and others; MGTX ClinicalTrials.gov number, NCT00294658.)

day prednisone (44 mg vs. 60 mg, P<0.001). Fewer patients in the thymectomy group than in the prednisone-only group required immunosuppression with azathioprine (17% vs. 48%, P<0.001) or were hospitalized for exacerbations (9% vs. 37%, P<0.001). The number of patients with treatment-associated complications did not differ significantly between groups (P=0.73), but patients in the thymectomy group had fewer treatment-associated symptoms related to
<table>
<thead>
<tr>
<th>Open approach</th>
<th>Minimally invasive techniques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transsternal (full median sternotomy)</td>
<td>VATS</td>
</tr>
<tr>
<td>Transcervical</td>
<td>RATS</td>
</tr>
<tr>
<td>Partial sternotomy</td>
<td>Subxifoid approach</td>
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<tr>
<td>Lateral thoracotomy</td>
<td>Cervicotomy + VATS/RATS</td>
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<tr>
<td>Hemi-clam shell incision</td>
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<tr>
<td>Clam shell incision</td>
<td></td>
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<tr>
<td>Procedure</td>
<td>Description</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Transcervical T1</strong></td>
<td>T1a basic TCT</td>
</tr>
<tr>
<td></td>
<td>T1b extended TCT</td>
</tr>
<tr>
<td></td>
<td>T1c extended with partial sternal split</td>
</tr>
<tr>
<td></td>
<td>T1d extended TCT with videoscopic technology</td>
</tr>
<tr>
<td><strong>Videoscopic T2</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Transternal T3</strong></td>
<td>Historically proposed surg approach</td>
</tr>
<tr>
<td><strong>Combined Transcervical-transternal T4</strong></td>
<td></td>
</tr>
</tbody>
</table>
Total thymectomy has always been considered the goal of surgery for MG.

Although total thymectomy appears indicated in the treatment of MG, the optimal approach that balances extent of resection, morbidity, patient acceptance, and results remains controversial.
Extended transsternal thymectomy

- En bloc resection of ALL fat & thymic tissue in the neck and mediastinum, from the inferior part of the thyroid lobes to the diaphragm and, laterally, from one phrenic nerve to the contralateral one
Transcervical approach

**Approccio Transcervicale (TCT)**

<table>
<thead>
<tr>
<th>T-1a</th>
<th>Basic</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-1b</td>
<td>Extended</td>
</tr>
<tr>
<td>T-1c</td>
<td>Extended + Split sternale</td>
</tr>
<tr>
<td>T-1d</td>
<td>Extended + VATS</td>
</tr>
</tbody>
</table>

There continues to be debate concerning which thymectomy technique is the procedure of choice in the treatment of myasthenia gravis (MG). This debate persists primarily because of the lack of consistently prospective studies. It also because of the varying presentations and clinical courses of MG patients. Analysis has been complicated by the absence, until very recently, of large, well-designed, prospective, randomized trials that prospectively compare different procedures. Without a clear advantage in one technique by properly designed prospective studies, there can be no scientifically valid comparison of the various thymectomy techniques. In this review, attempts have been made to clarify some of the controversial issues concerning the selection of a thymectomy technique in the treatment of myasthenia gravis and to make limited recommendations based on the best available evidence.

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Median operative time: 45 min (range: 35-135 min)

No intraoperative/postoperative mortality

Minor complications:
- Postop. Limited pneumothorax
- Skin wound seroma
- Prolonged mediastinal drainage

Mean hospital stay: 3 days
Torino, Italy

Results
Results

MGFA standards of measurements:
- MG classes of clinical severity (Class I-V) preoperative assessment
- MG postintervention MGFA categories:
  - Complete stable remission (CSR)
  - Pharmacological remission (PR)
  - Minimal manifestations
The primary focus of comparative analysis of thymectomy for MG should remain complete stable remission.

The analysis of uncorrected crude data has been the most common method employed in the appraisal of the results of thymectomy.

Crude data does not include important follow-up information and should have no place in the comparative analysis of results of thymectomy.
## Results

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Surgical approach</th>
<th>Pts</th>
<th>Mean FU (months)</th>
<th>Remission (%)</th>
<th>Improvement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shrager</td>
<td>2006</td>
<td>TC</td>
<td>151</td>
<td>83</td>
<td>37.1</td>
<td>79.5</td>
</tr>
<tr>
<td>de Perrot</td>
<td>2003</td>
<td>TC</td>
<td>120</td>
<td>48</td>
<td>41</td>
<td>NA</td>
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<tr>
<td>Calhoun</td>
<td>1999</td>
<td>TC</td>
<td>100</td>
<td>63.6</td>
<td>35</td>
<td>85</td>
</tr>
<tr>
<td>Ruffini</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Meyer</td>
<td>2009</td>
<td>VATS</td>
<td>48</td>
<td>72</td>
<td>34.9</td>
<td>95.4</td>
</tr>
<tr>
<td>Tomulescu</td>
<td>2006</td>
<td>VATS</td>
<td>105</td>
<td>36.4</td>
<td>59.5</td>
<td>97.2</td>
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<tr>
<td>Manlulu</td>
<td>2005</td>
<td>VATS</td>
<td>36</td>
<td>69</td>
<td>22.2</td>
<td>91.6</td>
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<tr>
<td>Mineo</td>
<td>2000</td>
<td>VATS</td>
<td>31</td>
<td>40</td>
<td>36</td>
<td>96</td>
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</tbody>
</table>

The reported TCT remission rates are comparable with those after VATS approach.
Extended transcervical thymectomy results in non-thymic myasthenia gravis: Comparison of cumulative incidence of CRS/PR.

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Figure 3: Cumulative incidence of remission by the duration of MG symptoms before thymectomy (<6 vs >6 months). MG: myasthenia gravis.

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Cumulative incidence of CRS/PR
Results

<table>
<thead>
<tr>
<th>Author</th>
<th>year</th>
<th>Surgical approach</th>
<th>pts</th>
<th>Crude remission rate</th>
<th>Cumulative remission (5-y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jaretzki</td>
<td>1988</td>
<td>Maximal TC</td>
<td>95</td>
<td>46</td>
<td>NR</td>
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<tr>
<td>Prokakis</td>
<td>2009</td>
<td>Transternal</td>
<td>78</td>
<td>37</td>
<td>15</td>
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<tr>
<td>Cheng</td>
<td></td>
<td>TCT</td>
<td>168</td>
<td>46</td>
<td>25 (3-y)</td>
</tr>
<tr>
<td>Calhourn</td>
<td>1999</td>
<td>TCT</td>
<td>100</td>
<td>35</td>
<td>NR</td>
</tr>
<tr>
<td>Shrager</td>
<td>2006</td>
<td>TCT</td>
<td>151</td>
<td>29</td>
<td>33</td>
</tr>
<tr>
<td>Bodde</td>
<td>2001</td>
<td>TCT</td>
<td>113</td>
<td>21</td>
<td>NR</td>
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<tr>
<td>Ruffini</td>
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<td>TCT</td>
<td>224</td>
<td>38</td>
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</table>

The reported TCT remission rates are comparable with those after transsternal approaches.
Conclusions

Torino, Italy
Thymectomy has been demonstrated to be effective in MG non-thymomatous patients

The optimal surgical technique should be the one that balances the extent of the resection, morbidity, patient’s acceptance and general results. Minimizing morbidity & mortality in MG patients becomes paramount

TCT as an open procedure, is less invasive and morbid compared to the classic transternal approach.

TCT CR rates have been demonstrated to be comparable to those following extended transternal & VATS/RATS thymectomy
Thank you very much for your attention

Torino, Italy

Pier Luigi Filosso, MD
University of Torino, Department of Thoracic Surgery
The analysis of uncorrected crude data has been the most common method employed in the appraisal of the results of thymectomy. Uncorrected crude data analysis in either form does not include important follow-up information and should have no place in the comparative analysis of results of thymectomy. Improvement” and changes in “mean grade,” widely used in comparing data and as determinants of success, are also unreliable measurements because objective criteria, such as a quantitative scoring system, have not been applied in most instances.
Surgery for MG

Surgical approaches to the Thymus

The indications should be:

- Discussed within a multidisciplinary setting
- Based on surgeon’s experience & preference

thymic hyperplasia
Non-encapsulated thymic foci were observed:

- Pretracheal & anterior mediastinal fat (from the level of the thyroid till to the diaphragm)
- Bilaterally beyond each phrenic nerve

Alfred Jaretzki III et al.: Semin Neurol 2004;24:49
The success of a thymectomy for MG primarily depends on the amount of thymic tissue resected.

The choice of the optimal surgical approach depends on:

- the neurological outcome
- the extent of the mediastinal tissue resection
- the potential morbidity of the surgical technique adopted