Thymus/Thymoma Tracheal Resection

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Disclosures

• None
Thymectomy

Myasthenia Gravis
Thymoma
Thymectomy

**Myastenia Gravis**
- 40,000 – 60,000 pts annually
- Autoimmune etiology
- ~ 20% have a thymoma

**Thymoma**
- #1 primary mediastinal malignancy
- 400 patients annually in US
- 33% have some autoimmune disorder
  - Myasthenia gravis most common
Randomized Trial of Thymectomy in Myasthenia Gravis


ABSTRACT

BACKGROUND

Thymectomy has been a mainstay in the treatment of myasthenia gravis, but there is no conclusive evidence of its benefit. We conducted a multicenter, randomized trial comparing thymectomy plus prednisone with prednisone alone.

METHODS

We compared extended transsternal thymectomy plus alternate-day prednisone with alternate-day prednisone alone. Patients 18 to 65 years of age who had generalized neurethromonous myasthenia gravis with a disease duration of less than 5 years were included if they had Myasthenia Gravis Foundation of America clinical class II to IV disease (on a scale from I to V, with higher classes indicating more severe disease) and elevated circulating concentrations of acetylcholine-receptor antibody. The primary outcomes were the time-weighted average Quantitative Myasthenia Gravis score (on a scale from 0 to 39, with higher scores indicating more severe disease) over a 3-year period, as assessed by means of blinded rating, and the time-weighted average required dose of prednisone over a 3-year period.

RESULTS

A total of 126 patients underwent randomization between 2006 and 2012 at 36 sites. Patients who underwent thymectomy had a lower time-weighted average Quantitative Myasthenia Gravis score over a 3-year period than those who received prednisone alone (0.15 vs. 8.05; P<0.001). Patients in the thymectomy group also had a lower average required for alternate-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 (6% vs. 37%; P=0.001). The number of patients with treatment-associated complications did not differ significantly between groups (P=0.78), but patients in the thymectomy group had fewer treatment-associated symptoms related to immunosuppressive medications (P=0.001) and lower distress levels related to symptoms (P=0.003).

CONCLUSIONS

Thymectomy improved clinical outcomes over a 3-year period in patients with neurethromonous myasthenia gravis. (Funded by the National Institute of Neurological Disorders and Stroke and others; MGTX ClinicalTrials.gov number, NCT00294696.)
Benefit of Thymectomy

MGTX Trial, NEJM 2016
Thymectomy for Myasthenia: Unanswered Questions

- What ages to offer resection
- What stage of disease
- Optimal preop preparation
- Sternotomy vs MIS
  - Transcervical
  - VATS (right vs left)
  - Robotic (right vs left)

Perioperative risk
- Myasthenic crisis
- Phrenic nerve injury
Thymoma
Surgical-Pathologic Staging: Masaoka

Remains within the capsule of the thymus

Stage I
Stage II

Extends through the thymic capsule into the fat or pleura.

IIa microscopic
IIb macroscopic*
Stage III

Macroscopic invasion of neighboring organs.

In this case Ascending aorta, SVC and perhaps LUL
Stage IVa

Pleural and/or pericardial dissemination
## Histologic Grade: WHO

<table>
<thead>
<tr>
<th>WHO Type</th>
<th>Histologic Description</th>
<th>Incidence&lt;sup&gt;a&lt;/sup&gt; (%)</th>
<th>10-Year Survival&lt;sup&gt;b&lt;/sup&gt; (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Medullary thymoma</td>
<td>9</td>
<td>97</td>
</tr>
<tr>
<td>AB</td>
<td>Mixed thymoma</td>
<td>24</td>
<td>95</td>
</tr>
<tr>
<td>B1</td>
<td>Predominantly cortical thymoma</td>
<td>13</td>
<td>92</td>
</tr>
<tr>
<td>B2</td>
<td>Cortical thymoma</td>
<td>24</td>
<td>81</td>
</tr>
<tr>
<td>B3</td>
<td>Well-differentiated thymic carcinoma*</td>
<td>15</td>
<td>62</td>
</tr>
<tr>
<td>C</td>
<td>Thymic carcinoma*</td>
<td>15</td>
<td>29</td>
</tr>
</tbody>
</table>

<sup>a</sup> The incidence of histologic classes of thymoma were reported in 11 retrospective...
Thymectomy for Thymoma: Unanswered Questions

- Surgical planning
  - Approach Open vs MIS (conversions)
- What can “go”
  - Pericardium, Lung, Phrenic nerve
  - SVC and/or innominate vein
  - Venous reconstruction?
- Pathology
  - Completeness of resection
  - Masaoka Stage
  - WHO Grade
- Adjuvant radiation therapy
- Complications (phrenic nerve)
Tracheal Resection
Case Report: 37 yo woman presents with stridor. Prior history of 2 week intubation after an opiate overdose 3 months ago.
Cautery Incision of the Stricture
Balloon Bronchoplasty
Tracheal Resections STS Thoracic Database

Total Volume Per Year

Indication

N by Indication

- Malignant
- Benign

75%
Approach

N by Approach

- Thoracic
- Cervical

81%
### Mortality, LOS, Readmission

<table>
<thead>
<tr>
<th>Surgical Approach</th>
<th>Surgical Indication</th>
<th>Mortality</th>
<th>Length of Stay (Days)</th>
<th>30-day Readmission Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td></td>
<td>P-value</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Variable</td>
<td></td>
<td>P-value</td>
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</tr>
<tr>
<td>Variable</td>
<td></td>
<td>P-value</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Mortality**: 15 (1.1%), 5 (1.6%), 0.77, 14 (1.1%), 6 (1.5%), 0.10
- **Length of Stay (Days)**: 10.3 +/- 14.1, 10.6 +/- 12.8, 0.80, 10.9 +/- 15.1, 8.9 +/- 8.7, 0.014
- **30-day Readmission Rate**: 65 (5%), 40 (13%), 0.001, 84 (7%), 21 (5%), 0.20

## Morbidity by Approach

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cervical N=1295</th>
<th>Thoracic N= 309</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Complication</td>
<td>249 (19.2%)</td>
<td>93 (30.1%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>31 (2.4%)</td>
<td>22 (7.1%)</td>
<td>0.001</td>
</tr>
<tr>
<td>ARDS</td>
<td>4 (0.3%)</td>
<td>5 (1.6%)</td>
<td>0.016</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>30 (2.3%)</td>
<td>22 (7.1%)</td>
<td>0.001</td>
</tr>
<tr>
<td>DVT</td>
<td>5 (0.4%)</td>
<td>8 (2.6%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Empyema</td>
<td>0 (0%)</td>
<td>2 (0.6%)</td>
<td>0.037</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>4 (0.3%)</td>
<td>4 (1.3%)</td>
<td>0.049</td>
</tr>
<tr>
<td>Return to OR</td>
<td>67 (5.2%)</td>
<td>25 (8.1%)</td>
<td>0.056</td>
</tr>
<tr>
<td>Ventilator &gt; 48 hrs</td>
<td>32 (2.5%)</td>
<td>12 (3.9%)</td>
<td>0.18</td>
</tr>
<tr>
<td>PE</td>
<td>1 (0%)</td>
<td>2 (0.6%)</td>
<td>0.097</td>
</tr>
<tr>
<td>Reintubation</td>
<td>47 (3.6%)</td>
<td>16 (5.2%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>41 (3.2%)</td>
<td>5 (1.6%)</td>
<td>0.18</td>
</tr>
<tr>
<td>UTI</td>
<td>22 (1.7%)</td>
<td>9 (2.9%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Recurrent Nerve Injury</td>
<td>12 (0.9%)</td>
<td>5 (1.6%)</td>
<td>0.35</td>
</tr>
<tr>
<td>Anastomotic Complication</td>
<td>3 (0.2%)</td>
<td>3 (1%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Wound Infection</td>
<td>60 (4.6%)</td>
<td>15 (4.9%)</td>
<td>0.88</td>
</tr>
</tbody>
</table>
# Predictors of Morbidity and Mortality

Table 3. Summary of Multivariable Logistic Regression Model for Morbidity or Mortality Composite Endpoint

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (OR)</th>
<th>OR 95% Confidence Interval (CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zubrod Score: 2, 3, 4 or 5 vs 0 or 1</td>
<td>2.44</td>
<td>1.61 3.69</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Approach: Thoracic vs. Cervical</td>
<td>1.65</td>
<td>1.12 2.43</td>
<td>0.011</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.54</td>
<td>1.04 2.26</td>
<td>0.030</td>
</tr>
<tr>
<td>ASA Class: III, IV or V vs I or II</td>
<td>1.50</td>
<td>0.95 2.38</td>
<td>0.083</td>
</tr>
<tr>
<td>CAD</td>
<td>1.52</td>
<td>0.95 2.41</td>
<td>0.081</td>
</tr>
<tr>
<td>Obesity: BMI &gt; 30 kg/m² vs BMI ≤ 30 kg/m²</td>
<td>1.33</td>
<td>0.94 1.87</td>
<td>0.11</td>
</tr>
<tr>
<td>Most Recent Creatinine Level</td>
<td>0.81</td>
<td>0.63 1.04</td>
<td>0.11</td>
</tr>
<tr>
<td>Pulmonary Hypertension</td>
<td>2.87</td>
<td>0.75 10.99</td>
<td>0.12</td>
</tr>
<tr>
<td>Gender: Male vs. Female</td>
<td>1.29</td>
<td>0.92 1.82</td>
<td>0.14</td>
</tr>
<tr>
<td>Indication: Malignant vs. Benign</td>
<td>1.19</td>
<td>0.78 1.80</td>
<td>0.42</td>
</tr>
</tbody>
</table>
## Volume-Outcome Relationship

<table>
<thead>
<tr>
<th></th>
<th>Volume Per Year ≥ 4 N=9</th>
<th>Volume per Year &lt; 4 N= 98</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Volume</strong></td>
<td>540</td>
<td>529</td>
<td></td>
</tr>
<tr>
<td><strong>30-day Mortality</strong></td>
<td>7</td>
<td>8</td>
<td>0.80</td>
</tr>
<tr>
<td><strong>Total Morbidity</strong></td>
<td>93</td>
<td>141</td>
<td></td>
</tr>
<tr>
<td><strong>Total Composite endpoint</strong></td>
<td>94</td>
<td>145</td>
<td></td>
</tr>
<tr>
<td><strong>Composite Endpoint Incidence</strong></td>
<td>17.4%</td>
<td>27.4%</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
Summary

In STS reporting centers:

- Tracheal resection is performed with low mortality
- Morbidity higher than expected
- Volume is highly concentrated in few centers
- There is likely a volume-outcome relationship
- Expand the database to capture relevant variables
  - Preoperative interventions
  - Resection length
  - Release maneuvers
  - Airway complications
Post-intubation stenosis

Grillo et al, *JTCVS* 1995

- N = 503
- Era 1965-1992
- Length 1-7.5 cm (mean 3.3 cm)
- Follow-up > 3 years
Approach

- Cervical: 69%
- Partial Sternotomy: 29%
- Thoracotomy: 2%
Anastomotic Level

- Trachea: 64%
- Cricoid: 23%
- Thyroid: 12%
Results by Level

<table>
<thead>
<tr>
<th>Failure Risk</th>
<th>a</th>
<th>b</th>
<th>c</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>324</td>
<td>117</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>2.2%</td>
<td>6%</td>
<td>8.1%</td>
</tr>
</tbody>
</table>
Predictors of Failure

• **Preoperative**
  • Previous tracheostomy
  • Previous repair
  • TEF
  • Extensive malacia

• **Intraoperative**
  • Higher anastomosis
  • Need for release maneuver

• **Postoperative**
  • Reintubation
Tracheal Resection: Unanswered Questions

1. Tracheal Resection

Pre-Operative
- Current Airways: □ Native □ Oral ETT □ Trach □ T-Tube
- Prior tracheotomy: □ Yes □ No
- Prior intubation: □ Yes □ No
- Prior Tracheal Resection: □ Yes □ No

Recent Bronchoscopic Intervention (within 6 weeks): □ Yes □ No (includes: core out, dilation, ablation, stent)

Recurrent nerves intact: □ Yes □ No □ Unknown

If not intact: Which nerve? □ Right □ Left □ Both

Airway management during resection (check all that apply):
- Cricoid - table ventilation: □ Yes □ No
- VA ECMO: □ Yes □ No
- Cardiopulmonary bypass: □ Yes □ No

Incision (check all that apply, must have at least one indicated):
- Cervical □ Yes □ No
- Partial sternotomy □ Yes □ No
- Full sternotomy □ Yes □ No
- Right thoracotomy □ Yes □ No
- Camshell □ Yes □ No

Length of tracheal resection:_mm (Surgical or pathologic measurement acceptable)

Cricoid resection required: □ Yes □ No

Carinal resection required: □ Yes □ No

Release Maneuvers: □ Yes □ No

If yes: □ Suprahyoid □ Suprahyoid □ Hilar

Additional Post-Operative Events
- Anastomotic dehiscence requiring drainage, revision, stent, tracheostomy, T-tube □ Yes □ No
- Anastomotic stricture requiring intervention □ Yes □ No
- Airway obstruction requiring intervention (e.g., unscheduled bronchoscopy) □ Yes □ No
- Recurrent nerve palsy: □ Yes □ No

Additional Post-Operative Events
- Did the patient leave the hospital with tracheal appliance? (tracheostomy, T-tube or stent) □ Yes □ No □ Patient Died in Hospital

At 30 Days Post-Operative Patient is:
- Short/Tube free □ Yes □ No □ Patient Died Within 30 Days of Procedure

At 90 Days Post-Operative Patient is:
- Short/Tube free □ Yes □ No □ Patient Died Within 90 Days of Procedure

- Preoperative evaluation and preparation
- Key intraoperative variables
- Specific airway complications
Thank you

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