# Postoperative ventilatory dependency following thymectomy for myasthenia gravis[1]

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**Thymectomy for the treatment of selected patients with myasthenia gravis results in postoperative prolongation of ventilatory support. A retrospective review of 24 patients undergoing the procedure via midline sternotomy revealed that 17 (71%) were weaned from mechanical ventilation within 48 hours. In the remaining patients, chest wall pain and respiratory muscle weakness prolonged ventilatory support to four days while complications of pneumonia in 2 patients and hydropneumothorax in another patient prolonged support beyond four days. Additional observations suggested that choline-esterase inhibitor therapy is necessary to assist in weaning from mechanical ventilation even if this therapy is reduced from preoperative dosages.**

**Index terms:** Myasthenia gravis, therapy • Respiratory therapy • Thymectomy, adverse effects

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Although the relationship between the thymus gland and myasthenia gravis was first suggested by Laquer and Weigert,[1] in 1910, symptomatic improvement following thymectomy was first reported by Blalock[2] in 1939. Interest in the surgical management of myasthenia gravis has continued, and thymectomy has become a standard mode of therapy in selected patients with myasthenia gravis.[3,4]

Of the various surgical procedures for thymectomy, the midline sternotomy approach is preferred because of more complete removal. Regardless of the surgical approach, however, the peculiarity of myasthenia gravis and its therapy coupled with anesthetic requirements result in postoperative problems that may necessitate prolonged venti-

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**Table 1.** Patient statistics

| Patient No. | Age (yrs) | Sex | Stage | Duration of symptoms | Histology | Days of ventilation |
|---|---|---|---|---|---|---|
| 1 | 22 | F | IIB | 2 yrs | Thymic hyperplasia | 1 |
| 2 | 29 | F | IIB | 2 yrs | Thymic hyperplasia | 1 |
| 3 | 56 | M | IIB | 6 mo | Normal thymus | 2 |
| 4 | 32 | F | IIA | 1 mo | Normal thymus | 9 |
| 5 | 28 | F | IIA | 3 yrs | Thymic hyperplasia | 2 |
| 6 | 59 | F | III | 7 yrs | Adipose tissue | 2 |
| 7 | 24 | F | III | 7 mo | Normal thymus | 1 |
| 8 | 53 | M | IIB | 1 yr | Adipose tissue | 1 |
| 9 | 28 | F | IIA | 7 mo | Follicular hyperplasia | 0 |
| 10 | 19 | M | IIIB | 4 yrs | Thymic hyperplasia | 7 |
| 11 | 71 | M | IIB | 7 mo | Adipose tissue | 2 |
| 12 | 31 | M | IIA | 2½ yrs | Normal thymus | 2 |
| 13 | 58 | M | IIB | 7 yrs | Normal thymus | 2 |
| 14 | 51 | M | III | 5 yrs | Capsulated thymus | 4 |
| 15 | 41 | F | III | 7 mo | Thymic hyperplasia | 0 |
| 16 | 17 | F | IIA | 9 mo | Normal thymus | 10 |
| 17 | 30 | F | III | 4 yrs | Normal thymus | 0 |
| 18 | 67 | M | IIB | 1 yr | Normal thymus | 4 |
| 19 | 22 | F | IV | 3 yrs | Thymic hyperplasia | 4 |
| 20 | 11 | F | IIA | 6 mo | Normal thymus | 2 |
| 21 | 55 | M | IIB | 10 mo | Thymic hyperplasia | 0 |
| 22 | 47 | M | IIB | 1½ yrs | Thymoma | 6 |
| 23 | 18 | F | III | 2 yrs | Thymic hyperplasia | 0 |
| 24 | 43 | F | II | 1 yr | Thymoma | 1 |

latory support.[5,6] We retrospectively reviewed the postoperative courses of patients undergoing thymectomy at our institution. Our goal was to identify factors that might prolong ventilatory support in the postoperative period.

## Material and methods

Twenty-four consecutive patients underwent thymectomy via midline sternotomy between January 1978 and December 1982. Clinical staging of the disease was based on Osserman's criteria.[6] Patients were divided into two groups: group 1 patients required ventilatory support for less than 48 hours, and group 2 patients required ventilatory support for more than 48 hours. This separation was based on observations that most patients undergoing median sternotomies at our institution (i.e., for coronary artery bypass surgery) are weaned from mechanical ventilation on the first postoperative day (Cosgrove DM, personal observation). After 48 hours, factors secondary to the procedure itself, such as pain and alteration in chest wall mechanics or lung parenchyma, are not factors that prolong the weaning process. Group 2 patients were considered to have prolonged postoperative ventilatory dependence.

Each patient was ventilated via an endotracheal tube with a volume-cycled ventilator. Criteria for extubation were based on adequate oxygenation (the ability to maintain arterial $PO_2$ at 80 mm Hg with inspired oxygen concentration being less than 40% while breathing spontaneously for two hours) and adequate respiratory muscle strength (the ability to maintain a vital capacity of 15 mL/kg for two or more hours after spontaneous ventilation commenced).[7] As patients recovered from anesthesia, these parameters of spontaneous ventilation and oxygenation were measured. If patients met the criteria for extubation, they were extubated and transferred to the medical intensive care unit for 24-hour observation. Otherwise, mechanical ventilation was continued until the following day when weaning was again attempted. Intermittent mandatory ventilation was used to wean patients if they could not be extubated in the recovery room.[8] The weaning process was started when the oxygen requirement was less than 40% and initial vital capacity was at least 5 mL/kg. Ventilator breaths (tidal volume, 15 mL/kg) were decreased by one to two breaths per minute every four to six hours depending on the patient's ability to maintain spontaneous respiratory rates below 20 per min-

**Table 2.** Medication dosages and rationale (group 1)

| Patient No. | Medication | | Day restarted | Rationale for treatment |
|---|---|---|---|---|
| | Preoperative | Postoperative | | |
| 1 | Pyridostigmine (250 mg) | Pyridostigmine (120 mg) | 1 | $PCO_2$, 50 mm Hg; vital capacity adequate |
| 2 | Pyridostigmine (360 mg) | Pyridostigmine (120 mg) | 1 | Facial weakness, diplopia |
| 3 | Prednisone (50 mg) | Pyridostigmine (120 mg)<br>Prednisone (50 mg) | 1 | Diplopia, vital capacity adequate, shoulder weakness |
| 5 | None | None | | |
| 6 | Pyridostigmine (270 mg) | Pyridostigmine (135 mg) | 1 | Not recorded |
| 7 | Pyridostigmine (240 mg) | Pyridostigmine (90 mg) | 4 | Ptosis, ileopsoas weakness |
| 8 | Pyridostigmine (360 mg) | Pyridostigmine (180 mg) | 1 | Diplopia, edrophonium test—44% vital-capacity increase |
| 9 | Pyridostigmine (240 mg) | Pyridostigmine (300 mg) | 1 | Dysphagia |
| 11 | Pyridostigmine (360 mg)<br>Prednisone (80 mg)* | Pyridostigmine (504 mg)<br>Prednisone (80 mg)* | 1 | Vital capacity increased 25% with pyridostigmine administered intramuscularly |
| 12 | Pyridostigmine (120 mg) | Physostigmine (45 mg) | 3 | Ptosis |
| 13 | Prednisone (50 mg)* | Prednisone (50 mg)* | 2 | Ptosis |
| 15 | Pyridostigmine (480 mg) | Pyridostigmine (1,440 mg) | 1 | Edrophonium test—67% vital capacity increase |
| 17 | Pyridostigmine (180 mg) | Pyridostigmine (400 mg) | 1 | Vital capacity, 20%; predicted normal |
| 20 | Pyridostigmine (180 mg)<br>Prednisone (20 mg) | Pyridostigmine (300 mg)<br>Prednisone (20 mg) | 1 | Ptosis, neck weakness |
| 21 | Pyridostigmine (240 mg) | Pyridostigmine (240 mg) | 1 | Dysphagia |
| 23 | Pyridostigmine (90 mg)<br>Prednisone (20 mg) | Pyridostigmine (90 mg)<br>Prednisone (20 mg) | 1 | Not recorded |
| 24 | Pyridostigmine (240 mg) | Pyridostigmine (240 mg) | 1 | Ptosis |

* Every-other-day dosage

ute and an arterial $PCO_2$ between 35 mm Hg and 45 mm Hg. The decision to reinstitute choline-esterase inhibitor therapy was made by the attending neurologist.

## Results

Patient statistics are listed (*Table 1*). All had normal vital capacities before surgery except patients 16, 19, 20, and 23 who had vital capacities of 76% 74%, 59%, and 75% of predicted vital capacity, respectively. No correlation was found between the severity of myasthenia gravis, preoperative vital capacity, or smoking history and postoperative ventilatory dependence. There was likewise no correlation between the histological findings of the thymic tissue and the postoperative course.

Preoperative and postoperative dosages of choline-esterase inhibitors and the rationale for reinstitution of these medications for group 1 patients are listed (*Table 2*). Patients 8, 11, 15, and 17 clearly required choline-esterase inhibitor medi-

**Table 3.** Medication dosages and rationale (group 2)

| Patient No. | Medication | | Day restarted | Rationale for treatment |
|---|---|---|---|---|
| | Preoperative | Postoperative | | |
| 4 | Pyridostigmine (720 mg) | Pyridostigmine (12 mg, intramuscular) | 1 | Vital capacity reduced to 20%, predicted normal |
| 10 | Pyridostigmine (840 mg) | Pyridostigmine (32 mg, intramuscular) | 2 | Edrophonium test—30% vital-capacity increase |
| 14 | Prednisone (60 mg)<br>Prednisone (15 mg) | Pyridostigmine (12 mg)<br>Prednisone (15 mg) | 2 | Vital capacity, 20%; predicted normal |
| 16 | Pyridostigmine (240 mg)<br>Prednisone (40 mg) | Pyridostigmine (360 mg)<br>Prednisone (40 mg) | 3 | Edrophonium test—50% vital-capacity increase |
| 18 | Pyridostigmine (240 mg) | Pyridostigmine (400 mg) | 3 | Edrophonium test—25% vital-capacity increase |
| 19 | Pyridostigmine (1,920 mg)<br>Prednisone (90 mg) | Pyridostigmine (930 mg)<br>Prednisone (90 mg) | 1 | Vital capacity, < 20%, predicted normal; stage IV disease |
| 22 | Pyridostigmine (180 mg) | Pyridostigmine (240 mg) | 3 | Hypercarbia, diplopia |

cations to increase vital capacity to meet extubation criteria. There was no correlation between requirements for analgesia and reduced vital capacity in these patients.

Preoperative and postoperative dosages of choline-esterase inhibitors and postoperative treatment rationale for group 2 (prolonged ventilator dependency) are listed (*Table 3*). Chest tube and sternotomy pain prolonged ventilatory dependency in patients 16, 18, and 22. Attempts to wean these patients resulted in tachypnea and shallow respirations from splinting of the chest wall because of pain. Control of pain with narcotics resulted in decreased spontaneous minute ventilation and hypercarbia. In addition to these factors, respiratory muscle weakness was a major factor in ventilator dependency in all patients in this group. Patients 14, 18, and 19 were each extubated within four days after optimal regulation of their choline-esterase inhibitor medication. Patients 4, 10, 16, and 22 had additional factors that were believed to prolong ventilatory dependency. Patient 4 had bilateral lower lobe *Staphylococcus aureus* pneumonia and required 10 days of nafcillin therapy. Patient 10 had a large hydropneumothorax, which required chest tube drainage. Patient 16 had a left lower lobe *Hemophilus influenza* pneumonia, requiring 10 days of ampicillin therapy, and had a large left pleural effusion that required chest tube drainage. Patient 22 met criteria for extubation within two days, but because of sleep deprivation, required marked sedation that led to reduction in vital capacity. This patient also had resection of the left phrenic nerve during surgery because of the extent of the spread of thymoma, but this did not appear to prolong the weaning process as bilateral diaphragmatic paralysis persisted up through discharge from the hospital.

## Discussion

The postoperative course of thymectomy can be complicated by respiratory failure due to multiple factors including respiratory muscle weakness, decreased lung compliance from atelectasis, retained secretions, pneumonia, and other such problems related to mechanical ventilation.[4,5,9] Advanced age, preoperative vital capacity below 2 L, and the presence of thymoma had reportedly prolonged mechanical ventilation beyond 12 days.[5] Although only 2 of our patients had a thymoma, we did not find that age or preoperative vital capacity were predictive of postoperative ventilatory dependency. Overall, the mean postoperative time of ventilatory dependency was only 2.6 days, and in the more complicated patients in group 2, the mean duration was only 5.7 days. These findings are in contrast to previous studies[5,9] and are partly due to advancement in postoperative ventilator care and a better understanding of the respiratory muscles.[10] In addition, our findings are in contrast with more recent

findings by Gracey et al[11] who noted a high incidence of postoperative respiratory failure in patients with Osserman classification group III and IV. Although 3 of 8 patients who required mechanical ventilation beyond 48 hours were classified as either III or IV, 1 (patient 14) had a hemothorax, which may have prolonged ventilator dependency. Furthermore, 3 patients with group III classification required ventilation less than 48 hours. Statistical significance between ventilator dependency and disease classification was not noted.

We did find that most of our patients (group 1) were weaned from mechanical ventilation within two days. Under these circumstances, ventilator dependency was most likely secondary to usual postoperative factors encountered after sternotomy. On the other hand, group 2 patients required a longer period of ventilatory support. All patients in this group required adjustments in dosages of choline-esterase inhibitors with 3 of 7 patients being weaned from mechanical ventilation within four days. The remainder of the patients in group 2 had other complications of prolonged ventilator dependency, which appeared to prolong the weaning process.

Some clinicians believe that choline-esterase inhibitors should be withheld in the first 24 hours after surgery as there are reduced needs during this time, leaving the patient vulnerable to cholinergic toxicity. Our data suggest that while the initial requirement may need to be reduced from the preoperative level, a delay in reinstitution of therapy after the first postoperative day may be associated with prolonged mechanical ventilation. This was evidenced by the majority of patients in group 2 in whom choline-esterase inhibitor therapy was started beyond the first postoperative day.

## Summary

Our observations suggest that prompt institution of choline-esterase inhibitor therapy is necessary to assist in weaning from mechanical ventilation, even if it is reduced from preoperative levels. In addition, ventilatory dependency beyond two days should suggest that either further regulation in choline-esterase inhibitor therapy is necessary or that problems related to mechanical ventilation should be considered in the differential diagnosis. We are unable to determine whether or not additional factors prolong ventilator dependency beyond four days. In a similar manner, we did not consider plasmapheresis in any of the patients so that we cannot comment on the utility of this therapy in patients who required mechanical ventilation beyond 48 hours.

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