# New study supports surgery as treatment for myasthenia gravis

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In a global study of myasthenia gravis, an autoimmune disease that causes muscle weakness and fatigue, researchers found that surgical removal of an organ called the thymus reduced patients' weakness, and their need for immunosuppressive drugs. The study, published in the *New England Journal of Medicine*, was partially funded by the National Institutes of Health.

"Our results support the idea that thymectomy is a valid treatment option for a major form of myasthenia gravis," said Gil Wolfe, M.D., Professor and Irvin and Rosemary Smith Chair of Neurology, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, New York, and a leader of the study.

The Thymectomy Trial in Non-Thymomatous Myasthenia Gravis Patients Receiving Prednisone (MGTX) was a randomized, controlled study conducted on 126 patients aged 18-65 between 2006 and 2012. The researchers compared the combination of surgery and immunosuppression with the drug prednisone with prednisone treatment alone. They performed extended transternal thymectomies on 57 patients. This major surgical procedure aims to remove most of the thymus, which requires opening of a patient's chest.

On average the researchers found that the combination of surgery and prednisone treatment reduced overall muscle weakness more than prednisone treatment alone. After 36 months of prednisone treatment, both groups of patients had better QMG scores, a measure of muscle

strength. Scores for the patients who had thymectomies and prednisone were 2.84 points better than patients who were on prednisone alone.

The researchers also found that patients who had surgery required lower daily doses of prednisone than the patients receiving prednisone alone, 44 mg versus 60 mg, respectively. They had less need for additional immunosuppressant drugs as well. Finally, surgery reduced the occurrence of adverse events from 93 for patients taking prednisone alone to 48 for ones who had surgery and prednisone, primarily reflected in a reduction in hospitalizations.

"This is a study that the myasthenia gravis community has needed for a long time," said Robin Conwit, M.D., program director, at NIH's National Institute of Neurological Disorders and Stroke (NINDS). "We hope it becomes a model for rigorously testing other treatment options."

Affecting 36,000 to 60,000 patients in the United States, myasthenia gravis describes a group of chronic autoimmune neuromuscular diseases which causes varying degrees of muscle weakness and fatigue. The disorders may affect eye and eyelid movements, facial expressions, chewing, talking, swallowing, breathing, and neck and limb movements. About 80 percent of patients have elevated levels of antibodies against acetylcholine receptors, proteins on the muscle used to detect signals sent from nerve endings in the form the chemical acetylcholine.

Often patients are initially treated with acetylcholinesterase inhibitors, drugs that elevate acetylcholine levels. If that does not resolve the weakness then patients are treated with immunosuppressive drugs, including corticosteroids. Because chronic corticosteroid treatment can cause side effects, doctors carefully monitor patients and prescribe the lowest effective doses.

Over the last 50 years, many studies suggested that the thymus, an organ

in the chest involved with immune cell development during childhood, regulates production of antibodies to the acetylcholine receptor and that removing the thymus reduced symptoms. Acetylcholine receptors found in the thymus may trigger the immune system to generate antibodies that circulate through the blood stream and block the receptors in the patients' muscles. Moreover about 30 percent of people who have a thymoma, a thymus tumor, also suffer from myasthenia gravis and removal of the tumor alleviates the myasthenic symptoms.

Patients were selected for the study if they had the disease for fewer than five years, elevated levels of acetylcholine receptor antibodies and no thymomas. Neurologists and thoracic surgeons worked together at 67 centers in 18 countries. Other leaders included the late John Newsom-Davis, M.D., Oxford University, U.K.; Henry J. Kaminski, M.D., George Washington University School of Medicine & Health Sciences; Alfred Jaretzki III, M.D., and Joshua R. Sonett, M.D., Columbia University Medical Center, New York City.

"We greatly appreciate the gamble patients took when they agreed to be subjects and are grateful for the help they provided in answering this 50 year old question," said Gary R. Cutter, M.S., Ph.D., Professor of Biostatistics at the University of Alabama at Birmingham School of Public Health and a leader of the trial.

The researchers noted surgery can be expensive and not without risks. An examination of hospital records provided by the Agency for Healthcare Quality and Research showed that in 2013, hospitals charged an average of $86,000 per extended transternal thymectomies, not including doctors' fees.

"Our results suggest surgery is a legitimate option for patients to consider," said Dr. Wolfe. "We hope that it will help doctors and patients weigh the costs and benefits of how best to reduce the disability

that may impact myasthenia gravis patients on a daily basis as they go about their lives."

**More information:** Wolfe et al. "Thymectomy in Non-thymomatous Myastenia Gravis: Results from MGTX," *New England Journal of Medicine*, August 10, 2016. DOI: 10.1056/NEJMoa1602489

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