Myasthenia Gravis

Which Type of Surgery Is Best?

Steven Karceski, MD

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Related Article

Impact of the Surgical Approach to Thymectomy Upon Complete Stable Remission Rates in Myasthenia Gravis: A Meta-analysis

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In their study “Impact of the Surgical Approach to Thymectomy Upon Complete Stable Remission Rates in Myasthenia Gravis: A Meta-analysis,”¹ Dr. Solis-Pazmino and colleagues tried to answer what sounds like a simple question: what type of surgery is best for myasthenia gravis (MG)? Most would agree that the “best” surgery is the one that has the most effect with the fewest complications. Another way of saying this is that the best surgery has the lowest risk with the highest benefit. Nowadays, there are many different types of surgery for MG. As technology has advanced, so have surgical approaches. Modern approaches often use minimally invasive techniques, sometimes with the aid of robots. These delicate surgeries can achieve goals that previously could only be accomplished with more invasive methods. The question asked by Dr. Solis-Pazmino et al. seems simple at first, but the path to finding the answer turns out to be complicated.

How Was the Study Done?

The most straightforward way to answer a question like this would be to perform a randomized clinical trial (RCT). In this trial, the investigators would divide people into 1 of 2 groups. One group would receive one type of surgery, and the other would have a second type. Then, in following the groups over several years, the researchers could measure which group did better. They could also monitor both groups for complications of the surgery. But what if there are many surgical approaches, as there are for MG? To compare all of the different types, the researchers would have to divide the group of patients into many different groups. Suddenly, the trial is much more complex, and much more difficult to complete.

Instead of an RCT, Dr. Solis-Pazmino and colleagues performed a meta-analysis. The investigators looked through the medical literature to identify studies that had already been completed about the types of surgeries they were researching. Using statistical analysis techniques, they compared the different surgical techniques in these studies to see which ones had the greatest benefit with the lowest risk.

Before the investigators started their analysis, they decided on certain rules they would use to choose the studies they would include in their assessment. First, they determined they

would only look for studies that included large numbers of people. Next, they looked for studies that followed patients for at least 3 years after surgery. The reason for this is that in MG, surgery does not work immediately. People with MG continue to achieve remission years after surgery has been completed (see “What is Myasthenia Gravis?”). In addition, the researchers carefully evaluated each of the trials for biases. Biases occur due to the way a trial is set up. When carefully constructed, a trial eliminates most of the possible causes for error (or bias).

Using these rules, the investigators analyzed 13 studies that had low bias. There were 12 cohort studies (a type of study that looks at a group of people who share certain characteristics over a set period of time) and 1 RCT. The RCT the authors analyzed in their study has generally been viewed as the standard study on this topic.² In the trials the authors analyzed, there were a total of 1,598 patients. The patients were on average 20–43 years old, 65% were women, 22% were taking an anticholinesterase drug (see “What is Myasthenia Gravis?”), and 21% were taking steroids (like prednisone). Some of the patients had a thymoma (a mass in the thymus), and others did not.

The studies the researchers analyzed described surgeries that involved removing the thymus gland to treat MG. In the studies, there were several ways the surgeons removed the gland. Some removed just the gland itself; this is called a basic thymectomy. One problem with this approach is that there can sometimes be smaller areas of the thymus, located outside of the main gland, called ectopic thymus. Because of this, other surgeons removed both the thymus and the area surrounding it. This approach is called an extended thymectomy. Some surgeons used robots to assist them. Some approached the thymus from above the sternum (called a transcervical approach), while others went from below the sternum (called a subxiphoid

approach). Some came in from the left, others from the right, and others approached the thymus from both sides.

With so many approaches to removing the thymus, Dr. Solis-Pazmino and colleagues needed to categorize the different types of surgery. They broke them down into 4 groups. The first 2 were traditional surgery (trans-sternal [through the sternum]) vs minimally invasive surgery. The other 2 were basic surgery (removal of just the main part of the thymus) vs extended surgery (removal of the thymus and surrounding areas to be sure to eliminate ectopic thymus tissue).

What Did the Study Show?

Dr. Solis-Pazmino and colleagues found that when comparing the minimally invasive extended thymectomy surgery to the trans-sternal surgery, the benefits were the same. At 3 years after extended thymectomy, the rates of remission were identical between the groups. However, there were significant differences between the groups with regard to the rates of healing and problems related to surgery. People who had minimally invasive surgery recovered faster and spent less time in the hospital. These patients also had fewer complications. Of the complications that were studied, there were fewer people who had heart rate irregularities (cardiac arrhythmias) following the minimally invasive procedures. In short, Dr. Solis-Pazmino and colleagues found that the minimally invasive extended thymectomy procedure was just as effective as traditional trans-sternal surgery and had fewer risks. Their findings suggest that the minimally invasive approach should be used unless there is a reason the person is unable to have one of those procedures.

About Myasthenia Gravis

What Is Myasthenia Gravis?

MG is a rare condition that can affect anyone, at any age, although it mostly affects young women (under 40) or older men (over 60). MG is not genetic, and it is not contagious. People with MG develop muscle weakness. The weakness worsens when the person uses the muscles, as in exercising, and gets better when resting. The muscle weakness can also affect the muscles in the eyelids or the muscles that control eye movement, causing “droopy” eyelids or double vision. In some people, the muscles of the face and neck can be affected, causing slurred speech or trouble swallowing. If the chest muscles are affected, a person could experience trouble breathing or shortness of breath.

What Causes MG?

MG affects the way the nerves send signals to the muscles. There is constant communication between the nerves and muscles across a very small space in the muscle called the neuromuscular junction. The nerves send a neurotransmitter called acetylcholine into the neuromuscular junction. The acetylcholine molecule crosses this space and connects with a receptor on the surface of the muscle cell called the acetylcholine receptor. When the molecule activates the receptor, a chain of events is set in motion, causing the muscle to contract.

When a person has MG, the person’s immune system starts making an antibody to itself (this is called an autoimmune disease). The antibody attaches itself to the acetylcholine receptor. When the antibodies attach to the receptors, they tag or mark them as something that the body needs to get rid of. The body then removes the receptors, which means the muscle can no longer respond correctly to the signals the nerve is sending. In a way, it is like a telephone with a faulty receiver—only some of the conversation gets through. When communication between nerves and muscles is broken, weakness is the result.

The thymus gland is an important part of the immune system. It is a gland under the sternum, or breastbone. In the thymus is a certain kind of white blood cell that is important in helping our bodies fight off viruses and other infections. These cells fight infection by making antibodies. In people with MG, these cells begin making antibodies against an important part of the muscle system, the acetylcholine receptor. One-fifth (21%) of people with MG have an enlarged thymus, called a thymoma. One question that remains unanswered is why the immune system of people with MG mistakenly makes antibodies to their own acetylcholine receptors.

Treatments for MG

There are many treatments for MG. Most people with MG take medication. The medication helps the muscles remain strong for a longer period of time. Some people take medication that suppresses the immune system, and this then suppresses the production of the antibodies attacking their acetylcholine receptors. The antibodies can also be removed from the blood by a process called plasmapheresis. Recently, the US Food and Drug Administration approved the use of an antibody treatment called eculizumab, which affects the workings of the immune system.

In many people, removing the thymus gland (called a thymectomy) is a powerful way to improve or stop the autoimmune process that occurs in MG. The National Institute for Neurologic Disorders sponsored a randomized clinical trial to evaluate the effectiveness of thymectomy in MG. The trial, referred to as the MGTX Trial, took place in 36 medical centers from 2006 to 2012.³ It was published in the *New England Journal of Medicine* in August 2016. In this trial, 126 people with MG underwent a thymectomy. Following these people for 3 years, the investigators found that thymectomy was far better than medication for treating MG. The people who had a thymectomy were taking less medication, had fewer side effects, and required hospitalization much less for their MG.

In this trial, the thymectomy was performed using the transsternal approach. In other words, the thymus was removed using a more invasive approach. In the trial, this was the only type of thymectomy that could be performed. None of the less invasive surgeries was allowed. In a clinical trial, this makes sense. To avoid errors and faulty data, the treatments all had to be the same. But with advances in surgical techniques that came about after that study was completed, including minimally invasive approaches, an excellent question arose: which technique is the best? This was the basis for the study that Dr. Solis-Pazmino and colleagues proposed.

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