Laparoscopic-Assisted Colectomy Is Safe and Effective

Points to Remember

- Minimally invasive laparoscopic colon surgery is a safe and effective alternative to open surgery for the treatment of colon cancer in selected patients.
- Mayo Clinic recently led 47 other institutions in a 7-year-long, National Institutes of Health-funded international study that enrolled 872 patients to determine the safety and efficacy of this procedure.
- Advantages of the laparoscopic approach include shorter hospital stay and less postoperative pain.

Scope of Problem

This year, an estimated 100,000 people in the United States will be diagnosed as having colon cancer. More than 90% of them will require surgery to remove all or part of the colon to eliminate the cancer.

As a result of a 7-year, Mayo Clinic-led, NIH-funded, multicenter international study examining the safety and efficacy of laparoscopic treatment of colon cancer, patients now have a choice of surgical procedures. The study’s central finding: In the hands of an experienced laparoscopic colon surgeon, the minimally invasive approach produces nearly identical rates of recovery and complications to that of traditional open surgery and offers reduced length of hospitalization, use of less pain medication, and swifter recovery time.

Traditional Approach to Treatment

Traditionally, a 15- to 20-cm-long abdominal incision is used for open surgery on the small bowel, colon, or rectum. Patients usually require 6 days of hospitalization postoperatively to allow the return of normal bowel function and ability to eat a regular diet. Patients are usually advised to avoid strenuous activity for 6 weeks to reduce the risk of hernia formation.

A New Approach: Minimally Invasive Laparoscopic Surgery

In contrast to traditional open surgery, laparoscopic surgery is minimally invasive. It typically involves the creation of three 1-cm incisions through which the laparoscope and surgical instruments are inserted. One of the smaller incisions is lengthened to about 4 to 6 cm to bring the colon out of the abdomen, cut away the cancerous portion, reconnect the 2 healthy parts, and reinsert the colon inside the abdomen. Patients are hospitalized for 5 days and must avoid strenuous activity for 6 weeks, but usually can return to ambulation immediately and light activities within a few weeks.

About the Study

When first introduced, laparoscopic techniques posed concerns that their use to resect a diseased colon would lead to higher rates of cancer recurrence as a result of “seeding.” To address this question, the NIH sponsored a Mayo Clinic-led study to compare the safety, efficacy, and rate of cancer recurrence between laparoscopic and...
This current study is the largest—with 872 patients and 66 surgeons at 48 medical centers in the United States and Canada—and the longest of its kind. To participate in the study, a surgeon had to become credentialed and show that he or she had performed at least 20 laparoscopic colon surgeries. During the study, an audit committee evaluated randomly selected, unedited videotapes submitted by each surgeon to assure proper technique was followed.

Advantages of Laparoscopic Surgery
- Smaller incisions: 2 inches vs 6 to 8 inches in standard surgery. As one man stated after returning to work 5 days after surgery: “The incision looked like a couple of cat scratches.”
- Average hospital stay: 5 days vs 6 days for standard surgery.
- Need for IV pain medication: 3 days vs 4 days for standard surgery.
- Though not quantified in the study, many participants reported a return of energy faster than patients who had undergone traditional surgery.

Disadvantages
- Surgical team needs advanced training and experience.
- Not suitable for all patients (see below).
- As with any laparoscopic procedure, if the surgical field can’t be well visualized or other problems occur, the surgery may need to be converted to an open procedure. In this study, in about 20% of the patients randomly assigned to undergo laparoscopic surgery, the procedure was converted to an open procedure because of the identification of advanced disease, the inability to visualize critical structures, or the presence of severe adhesions.

Inclusion Criteria
- Cancer of the colon that has not spread to other organs.

Exclusion Criteria
Success of laparoscopic-assisted colectomy depends on careful selection of patients. Those not suited to this approach include patients who have:
- Locally advanced bulky tumor.
- Acute obstruction from the cancer or colonic perforation from the cancer.
- Other conditions that preclude laparoscopic surgery, such as multiple previous abdominal procedures with adhesions.

For more information or to refer patients for evaluation for laparoscopic surgery for colon cancer, contact 507-538-0882. On the Internet, go to www.mayoclinic.org/coloncancer.

Graves’ Orbitopathy: Medical and Surgical Management Options

Scope of Problem
Systemic Graves’ disease (GD) is the most common autoimmune disorder in the United States and the world. The overall age-adjusted incidence rate for women is 16.0 cases per 100,000 population per year. The rate for men is 2.9 cases per 100,000 population per year.

Graves’ disease also can affect the eyes in a condition known as Graves’ orbitopathy (GO). GO is clinically apparent in 25% to 50% of patients with GD. It is caused by a positive feedback cycle of mechanical, immunologic, and cellular processes that induce proptosis (forward protrusion of the globe) and other changes within the orbital tissues which can seriously disturb or damage vision.

Complications of GO
When intraorbital inflammation develops, fat and muscle tissues expand within the orbit. This may result in proptosis, or forward protrusion of the globe. In addition, involvement of muscle structures within the eyelid may lead to eyelid retraction and widening of the palpebral fissure. Proptosis and
eyelid retraction may, in turn, result in drying of the cornea with ocular irritation and with potential ulceration and loss of vision.

The most common symptom of GO is ocular irritation. Involvement of the extraocular muscles may cause double vision.

The most worrisome complication of GO is compression or stretching of the optic nerve due to extraocular muscle or fatty tissue swelling behind the eye. This puts the patient at risk of permanent loss of vision. Also important from the patient’s perspective are the psychosocial and quality-of-life concerns associated with the significant appearance changes which may be associated with this disorder.

Traditional Treatments
Medical approaches are the standard first-line treatment for mild cases. They include artificial tears and ointments to address ocular surface drying. Patients may also be fitted with glasses that provide lateral shielding of the eyes to protect the vulnerable cornea. More advanced approaches have traditionally included the use of immunosuppressive therapies, including oral or intravenous corticosteroids and cyclosporine, or orbital irradiation.

More severe cases of GO require surgical intervention to relieve elevated intraorbital pressure (orbital decompression surgery), address diplopia (eye muscle surgery), and improve ocular surface exposure (eyelid retraction repair).

Limits of Traditional Treatments
In terms of medical approaches to GO, only approximately 65% of patients respond to immunosuppressive or radiation regimens. Recent research at Mayo Clinic and elsewhere has raised questions regarding the effectiveness and potential complications of orbital radiotherapy. The side effects of systemic immunosuppressive therapy may be significant and may limit therapy on a long-term basis.

In terms of traditional surgical approaches, decompression surgery can reduce pressure on the optic nerve and allow the eye to settle into a more normal position. Because a number of surgical approaches are possible—each with advantages and disadvantages—it is generally most helpful for surgeons to customize their approach to each patient. Mayo Clinic offers all available approaches (including transantral, endoscopic, and neurosurgical approaches), with surgery performed by a multidisciplinary team of ophthalmology, otolaryngology, and neurosurgery specialists.

New Approach to Medical Treatment
In our experience, the optimal care of GO patients is based on an integrated team approach that crosses specialty lines. Mayo Clinic researchers serve as vital collaborators in patient care, and they believe GO develops from a positive feedback cycle involving the mechanical elements of trauma and fluid pressure, an accumulation of immune cells and subsequent stimulation of metabolic processes, and activation of orbital fat production and fibrosis in response to this stimulation. Mayo Clinic researchers work closely with clinicians to develop new medical treatments based on staging the disease and assessing its activity at a given stage. Investigators at Mayo Clinic are currently recruiting patients to participate in a study of the effectiveness of a novel immunosuppressive agent in the treatment of severe GO.

Indications for Treatment
Medical treatment is the first line of treatment unless vision is acutely threatened. Decompression
surgery is indicated when there is optic neuropathy, severe ocular surface exposure, globe subluxation, or in some cases for cosmetic considerations.

Double vision may be corrected by repositioning the extraocular muscles so the patient can regain single vision. Strabismus surgery is indicated when the patient experiences functionally significant double vision, usually in primary (straight-ahead) or down gaze.

Upper and lower eyelid surgery may be performed to correct eyelid retraction associated with ocular surface exposure and/or cosmetic change. In general, orbital decompression surgery is performed initially, when required, followed by strabismus surgery and eyelid surgery.

Complications vary by type of surgical procedure. They include a worsening of double vision, sinus inflammation, asymmetrical eyelid position, and, rarely, loss of vision.

For More Information
To inquire about enrolling patients in the Mayo Clinic research study of a new immunosuppressive agent, or to refer a patient to Mayo Clinic for evaluation of GO by a multidisciplinary team,
Atypical Advanced Atherosclerosis and a New Approach to Treatment

The Mayo Clinic Chest Pain and Coronary Physiology Clinic offers specialized therapeutic options for patients with advanced atherosclerosis. Enhanced external counterpulsation is a noninvasive technique that applies intermittent balloon pressure to the lower extremities to augment diastolic pressure. This is delivered by having the patient wear specially designed pants with inflatable balloon pressure cuffs in them. In studies conducted at Mayo Clinic over a 3-year period, investigators noted symptomatic improvement in the majority of patients treated with this technique.

Transmyocardial laser revascularization is a procedure in which the surgeon uses a laser to create a number of small holes in the myocardium in an attempt to improve blood flow into the heart.

Atypical Early Atherosclerosis and a New Approach to Treatment

Many patients with early atherosclerotic disease have classic symptoms but have either normal arteries or minimally diseased arteries on coronary angiography. These patients are uniquely challenging to manage because of the recurrent nature of their pain syndrome. They have frequently undergone extensive, costly, and sometimes uncomfortable evaluations to identify noncardiac sources of chest pain, including gastrointestinal and psychological examinations.

Clinicians in the Mayo Clinic Chest Pain and Coronary Physiology Clinic and Cardiac Laboratory perform a comprehensive assessment of these patients’ coronary physiology, categorizing problems as stemming from endothelial or nonendothelial causes.

Patients with endothelial dysfunction are treated with agents that have been shown to improve vascular health such as angiotensin-converting enzyme inhibitors, arginine, lipid-lowering agents, and exercise. Patients may be eligible also to participate in studies of novel therapies. Genetic tests are performed to establish abnormalities associated with endothelial dysfunction and premature atherosclerosis.

Through this multidisciplinary approach to both patient groups—those with advanced disease and those with early atherosclerotic disease—the Mayo Clinic Chest Pain and Coronary Physiology Clinic can provide an individualized approach to cardiac chest pain patients who challenge traditional treatment modalities.

For more information or to refer patients to the Mayo Clinic Chest Pain and Coronary Physiology Clinic, call 507-255-4244.
**Mayo Clinic Briefings**

**MayoClinic.com Adds Dietary Supplements Search Tool**

Many patients increasingly look to their physicians for advice on the effectiveness of herbal treatments. Questions such as “Does ginseng really improve memory?” or “How much soy is recommended to reduce high cholesterol?” are becoming commonplace—yet many physicians are not trained in this area, and the data on these topics change rapidly. As a result, many physicians have difficulty giving quick, accurate responses to these kinds of questions. To help provide answers, MayoClinic.com has launched a new search tool on its Web site.

The tool is called the Natural Standard Supplement Database. It’s intended to provide Web visitors with extensive and timely evidence-based information about many common nutritional supplements. During office visits, this database can easily be brought up on the computer screen so physicians can go over the information with patients.

The site currently contains information on 86 herbs, vitamins, and other supplements—all easily accessible by following these simple steps:

2. Click on the “Drugs and Supplements” tab, at the top of the Web page.
3. Search for a supplement by name, or browse through the alphabetical index.

Each entry offers helpful information about the supplement’s background, alternative names, uses, proven effectiveness, dosage, and safety. Readers can:

- View summarized results of scientific studies testing the effectiveness of supplements.
- Consult the convenient A to F grading scale rating the strength of scientific evidence for or against each supplement’s uses.
- Find out how particular supplements affect allergies, pregnancy, and breast-feeding.

New entries will be added periodically to provide information on 105 supplements by the end of the year.

---

**Mayo Clinic to Examine Neurostimulator in Patients With Epilepsy**

Researchers at Mayo Clinic are enrolling participants in a clinical trial to determine if a Responsive Neurostimulator surgically implanted in the brain can suppress seizures in patients who have epilepsy.

Cardiac pacemakers were once thought of as novelties and medical miracles, but today they are commonplace and are regulating the heartbeats of thousands of patients around the world. This neurostimulator, a pacemaker for the brain, can be implanted in epilepsy patients who have not responded to treatment.

Epilepsy is a chronic disorder of the brain that causes recurrent seizures and affects nearly 3 million people in the United States. Antiepileptic medication can leave most patients free of seizures or lessen their frequency and intensity. Those who do not respond to medications may be candidates for surgical removal of the brain tissue responsible for triggering the seizure. In most cases, however, these patients still require medication to control seizures. The neurostimulator would eliminate the need to remove brain tissue from these patients.

The self-contained device, not much bigger than a watch, is implanted by neurosurgeons under the scalp and is connected to wires placed in the brain. The neurostimulator constantly monitors the brain’s electrical activity for onset of seizure activity. When seizure activity is detected, the neurostimulator delivers mild electrical stimulation through the wires in an attempt to stop the seizure before the patient experiences symptoms.

Participants are being enrolled in a preliminary observation study for a minimum of 3 months. Participants keep a seizure diary and see a study physician each month. If the participant meets the seizure frequency criterion of 4 seizures per month for 3 consecutive months, he or she is eligible to receive the implanted neurostimulator. After the device is implanted, participants will be followed for 2 years. Seizure type and frequency are assessed monthly, and physical and emotional health are assessed regularly.

Mayo Clinic is 1 of 13 US medical centers conducting this clinical trial. If you have questions about the study or wish to refer a patient, please contact the research study coordinator at 507-284-1588.
Aromatase Inhibitors: New Adjuvant Hormonal Therapy Options for Postmenopausal Breast Cancer Patients

Scope of Problem
An estimated 276,000 cases of breast cancer (217,000 invasive, 59,000 in situ) are diagnosed annually in the United States. Approximately 90% of the patients with invasive cancer present with localized (stage I or II) disease. Most of these malignancies occur in postmenopausal women.

Standard Hormonal Treatments
Patients with locally treated breast cancer (ie, by surgery, radiotherapy, or both) have variable risk of recurrence on the basis of their presenting factors. To reduce their risk, many elect to take systemic therapy—hormonal therapy, chemotherapy, or both. Since the early 1980s, tamoxifen has been the hormonal treatment of choice for both premenopausal and postmenopausal patients. Studies have shown that taking tamoxifen for 1 to 2 years is more effective at preventing breast cancer recurrence than placebo, and taking tamoxifen for 5 years is more effective than taking it for 1 to 2 years.

Continuing tamoxifen beyond 5 years may be associated with a higher chance of cancer recurrence. This is why it is generally recommended that tamoxifen be stopped after 5 years.

A New Approach: Aromatase Inhibitors
New studies indicate that aromatase inhibitors may be effective in addition to, or instead of, tamoxifen for postmenopausal women with hormone receptor–positive breast cancer.

Aromatase inhibitors are compounds that interfere with the enzyme aromatase, which is present in fat cells and other cells of all women. In postmenopausal women, aromatase produces low concentrations of estrogen from androgens, such as androstenedione, which is produced in the adrenal gland. Aromatase inhibitors, therefore, block this enzymatic transformation of androgens into estrogens.

Aromatase inhibitors differ from tamoxifen in that they actually reduce the amount of estrogen in the body.

Tamoxifen, on the other hand, blocks estrogen’s effect on tissues by competing with estrogen at the estrogen receptor binding site.

Pivotal Clinical Trials
Three recent studies of aromatase inhibitors are changing the field of adjuvant hormonal therapy for postmenopausal breast cancer patients.

1. The Anastrozole vs Tamoxifen—ATAC—Trial, published in 2002. Approximately 9,000 women were randomly assigned to 1 of 3 treatments: tamoxifen for 5 years, anastrozole (an aromatase inhibitor) for 5 years, or a combination of both for 5 years. Results, so far, have shown a 2% to 3% absolute decrease in breast cancer recurrence for the aromatase inhibitor group compared with the tamoxifen and combination-therapy groups.

2. Letrozole vs Placebo After 5 Years of Tamoxifen Trial, published in fall 2003. Some 5,000 postmenopausal women who had completed 5 years of adjuvant tamoxifen were randomly assigned to receive either letrozole (another aromatase inhibitor) for 5 years or placebo for 5 years. Early results revealed a 6% absolute benefit—93% vs 87% 4-year disease-free survival. This early analysis led to closure of the study, allowing the placebo patients to switch to letrozole and allowing the data to be published earlier than originally planned.

3. Exemestane vs Tamoxifen, Following 2-3 Years of Tamoxifen, published in early 2004. This trial of about 5,000 patients involved postmenopausal women with hormone receptor–positive breast cancer who had received 2 to 3 years of tamoxifen. They were...
then randomly assigned to continue tamoxifen for a total of 5 years or to switch to the aromatase inhibitor exemestane to complete a 5-year period of adjuvant hormonal therapy. Results showed an absolute disease-free survival benefit of 5% favoring the group receiving exemestane.

Advantages of Aromatase Inhibitors
Aromatase inhibitors may be more effective than tamoxifen in preventing cancer recurrence. Also, they are associated with a decreased incidence of blood clots and uterine cancers.

Disadvantages of Aromatase Inhibitors
Aromatase inhibitors are generally well tolerated. However, all 3 studies reported adverse effects, including myalgias and arthralgias, which were bothersome in up to 5% to 10% of the patients. Another adverse effect appears to be an increased tendency for osteoporosis. It is not clear whether treatment of osteoporosis with calcium, vitamin D, and other drugs can prevent this.

Cost is another consideration. Because Medicare generally does not pay for oral agents, patients may need to fund 5 years of treatment out-of-pocket. Aromatase inhibitors cost between $200 and $300 per month compared with $40 to $100 per month for tamoxifen.

Implications for Practice
With this new clinical trial information, 3 new basic treatment scenarios have emerged:
1. To take tamoxifen for 5 years, then consider taking an aromatase inhibitor for an additional length of time.
2. To begin with tamoxifen, and after 2-3 years switch to an aromatase inhibitor such as exemestane for the remainder of a 5-year treatment cycle.
3. To take an aromatase inhibitor exclusively—such as anastrozole—for 5 years.

In addition, Mayo Clinic oncologists are participating in a clinical trial that randomly assigns eligible women to 1 of 2 aromatase inhibitors, anastrozole or exemestane, for 5 years. The trial involves a second randomization to test 3 years’ treatment with the nonsteroidal anti-inflammatory drug celecoxib vs placebo.

For information about this clinical trial and its enrollment criteria or to refer a patient to Mayo Clinic Medical Oncology, contact 507-284-4137.