

# Greater number of esophageal cancer patients surviving

**B**ecause the nature of the disease has changed, nearly 50% of patients with esophageal cancer who undergo an advanced surgical procedure now survive five years. Previously only 20% survived, according to an article in the April edition of the *Journal of the American College of Surgeons*. Researchers at the University of Rochester Medical Center contend earlier diagnoses, more widespread screening, and individualized care have made surgery the best way to combat esophageal cancer as it is most often diagnosed today.

Whether surgery, chemotherapy, radiation, or some combination of the three should be the standard care has been debated for years. Until recently, surgery was considered the gold standard, but some medical oncologists, based on their assumption surgery comes with a high risk of complications and small chance of survival, have questioned its role. In many cases today, oncologists try chemotherapy and radiation first. Authors of this study argue that the information used to make those decisions is dated, and surgery is the most effective approach in many patients.

“Those who argue against surgery for esophageal cancer cite surgical mortality rates of up to 15% and low 5-year postoperative survival rates of 20% to justify their approach,” said Jeffrey H. Peters, MD, chair of the Department of Surgery at the University of Rochester Medical Center and surgeon in chief of Strong Memorial Hospital. Our study found that the five-year survival of patients after surgical resection for esophageal adenocarcinoma is better than that reported for any other form of therapy,” said Peters, co-author of the article.

## The changing face of esophageal cancer

In the past, the typical esophageal cancer patient had the kind of cancer (squamous cell carcinoma) caused by smoking and was frequently terminal. Patients needed surgery to make swallowing easier. Today, the average patient is younger, diagnosed earlier with a different kind of cancer (adenocarcinoma), and more likely to live longer after surgery.

The relationship of adenocarcinoma to gastroesophageal reflux disease explains the shift toward earlier diagnosis of esophageal cancer. At the point where the esophagus empties into the stomach, a ring of muscle keeps stomach acid from flowing back into the esophagus. For some, the ring malfunctions and allows acid to irritate the cells lining the esophagus, which causes heartburn and GERD. Acid can also cause long-term changes in esophageal cells that make them precancerous.

Approximately 20 million Americans experience severe heartburn. Of those people with frequent heartburn for five years or more, about one in five develop Barrett’s esophagus. Those patients have a 40-fold higher risk of developing GERD-associated adenocarcinoma. Esophageal cancer has increased dramatically in recent years to become the fastest-growing cancer in the United States. The trend is likely to worsen as Americans gain more weight, according to researchers.

The increasing prevalence of GERD resulted in the establishment of Barrett’s surveillance programs and the increasing likelihood that a given patient with severe heartburn will undergo an endoscopy. The rise in GERD, the drop in smoking, and better diagnostics means esophageal cancer is often found earlier, while still confined to the esophagus.

These patients are the best candidates for surgery to completely remove the tumor and cure it.

## A better surgery

Better surgery is also contributing to longer survival, according to the study. Statistical analysis of patient survival found en bloc esophagectomy, which completely removes the cancer and nearby lymph nodes, results in 30% fewer cancer deaths than does transhiatal resection, which leaves the lymph nodes in place. Researchers believe en bloc resection is more effective because it has a better chance of completely removing the cancer.

Although controversial, the authors argue their results add to a growing body of evidence that en bloc resection improves survival rates in esophageal, gastric, and rectal cancer. Refinements in operative techniques and postoperative care have made it much safer as well, the researchers said.

En bloc resection is used less often because it is complex and requires detailed training. Based on the current study, medical center researchers are calling for more widespread use of the technique, particularly in those whose tumor is detected early.

The study also found the number of patients receiving chemotherapy and radiation for esophageal cancer more than doubled during the 10 years in which data was examined—despite a lack of evidence supporting improved survival. One study found radiation and chemotherapy are not beneficial in early-stage cancer, and the side effects might make them more harmful than helpful. Researchers say future work will need to compare survival in patients receiving nonsurgical treatment to survival in patients who have had surgery.

## Study details

Researchers reviewed the medical records of 263 patients who underwent esophagectomy for adenocarcinoma between January 1992 and December 2002. Ninety-seven (37%) had cancer in stage 1; 63 (24%) were stage 2; 93 (35%) were stage 3; and 10 (4%) were stage 4. The cancer spread into nearby lymph nodes in 52% of the patients, and Barrett's esophagus was identified in 62%.

Forty-five percent of study patients had en bloc resection and 18% received neoadjuvant therapy. Seventeen percent of the patients were identified in a Barrett's surveillance program. The overall five-year survival was 46.5%; for the last five years of the study, it was 50.4%. The overall five-year survival for stage 1 was 81%; for stage 2, 51%; for stage 3, 14%; and for stage 4, 0%. The data reinforce the importance of early detection. Complications occurred in 61% of patients, and there were 12 deaths related to surgery.

## First implantable radiation sensor receives clearance

Sicel Technologies Inc. received 510(k) clearance from the FDA for its wireless, implantable radiation sensor and reader. Clearance was based on a multicenter clinical study of breast cancer patients, most of whom were implanted with two-dose verification system sensors prior to radiation therapy. Using a handheld reader, physicians determined the actual dose of radiation delivered to the tumor after each course of therapy. Implantation of the DVS sensor did not lead to any adverse events in the clinical trial.

DVS is the first permanently implantable, wireless, telemetric, radiation sensor for human use to be commercially available in the United States. Using proprietary telemetric technology, Sicel's miniature (20 mm x 2 mm) DVS sensor pinpoints the target during a patient's treat-

ment cycle and measures the amount of radiation received by the tumor.

According to Sicel, almost every cancer center already has the equipment required to visualize the DVS sensor. Although there are several methods available to facilitate tumor localization, none provide actual dose information.

# FDA FYI

For more information on these drugs, visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

## Approved

### *Dry mouth*

The FDA approved IMPAX Laboratories' abbreviated new drug application for **pilocarpine hydrochlorine**, a generic version of MGI Pharma's Salagen. IMPAX said they plan to market the product, to treat dry mouth from salivary gland hypofunction caused by radiotherapy treatment for head and neck cancer, in the near future.  
[www.impaxlabs.com](http://www.impaxlabs.com); 510.476.2000

## Phase 2

### *Bladder cancer*

Spectrum Pharmaceuticals reported positive data from a multi-center study of 46 patients with superficial bladder cancer. Patients underwent surgical removal of all but one marker lesion and then received six weekly instillations of **EOquin** into the bladder. Complete disappearance of the tumor was documented in 30 patients. Spectrum reports the drug was well tolerated.  
[www.spectrumpharm.com](http://www.spectrumpharm.com); 949.788.6700

### *Colorectal cancer*

Vertex Pharmaceuticals began a phase 2-development program for **VX-680** to target Aurora kinase. The open-label nonrandomized study will enroll patients who received up to three prior treatments. Codeveloper Merck said they expect to initiate a phase 2 clinical study for VX-680 in patients with advanced lung cancer this year.  
[www.vrtx.com](http://www.vrtx.com); 617.444.6100

### *Colorectal cancer*

Pro-Pharmaceuticals announced preliminary data that showed a partial response in a patient in stage 1 of a two-stage phase 2 trial of **Davanat** with **5-flourouracil**. The trial gives patients, whose cancer spread despite treatment, monthly cycles of the combination for at least two cycles or until their disease progresses.  
[www.pro-pharmaceuticals.com](http://www.pro-pharmaceuticals.com); 617.559.0033

## Phase 1

### *Chemotherapy-induced immune suppression*

ProMetic Biosciences began enrollment for its phase 1b/2 trial of **PBI-1402**. In animal studies, the drug promoted growth of red blood cells and protected the spleen and bone marrow from the toxic effects of chemotherapy.  
[www.prometic.com](http://www.prometic.com); 973.812.9880

### *Lymphoma*

Reata Pharmaceuticals received FDA clearance to begin clinical testing on **RTA 402** for patients with solid tumors, lymphoma, and myeloma. The drug exploits physiological differences between cancerous and noncancerous cells by modulating oxidative stress response pathways.  
[www.reatapharma.com](http://www.reatapharma.com); 972.865.2200