

Removing Stomach to Prevent Cancer Has Lasting Consequences

For people with an inherited risk of a lethal stomach cancer, a total gastrectomy may be lifesaving—but at what cost?

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By Shana Spindler

For one young woman, the diagnosis came with regular feelings of “grief, anxiety, and fear.” Another wrote, “I would be lying if I said I didn’t think about [it] ... every day.”

Both were recounting what it was like to find out that they had inherited a genetic mutation that put them at very high risk of developing a lethal form of [stomach cancer](#). And both made the difficult decision to essentially eliminate that risk by having their stomach surgically removed.

They and others like them who have had this preventive surgery—known as a total [gastrectomy](#)—acknowledge that the procedure likely saved their life. And they have learned to live full lives without a stomach.

Now, based on the findings of the largest study of its kind, there’s a clearer picture of the impact this surgery may have on those who choose to get it. The take-home finding: The surgery often has harmful long-term consequences that may require additional support to manage beyond a few postoperative check-ups.

The study included 126 people who received a total gastrectomy at the NIH Clinical Center to prevent [hereditary diffuse gastric cancer](#), the highly lethal form of stomach cancer caused by certain inherited mutations in a gene called CDH1. The researchers followed about half of the participants, all of whom carried a harmful variant of the gene, for at least 2 years after their surgery.

More than 90% of participants who were followed for more than 2 years after surgery [experienced at least one chronic complication during this period](#), and about a quarter of them said the complications were life altering, according to findings recently published in the Journal of Clinical Oncology.

“We do this [operation] to prevent cancer and help people,” said the study’s lead investigator, Jeremy Davis, MD, of NCI’s Center for Cancer Research. “Patients return to the clinic and say they

feel okay, but all you have to do is sit with them for a little while and stuff comes out; problems with family dynamics or not being able to get through the workday because of symptoms.”

The more he has talked with his patients after they’ve had their stomachs removed, the more he has learned about the procedure’s impact on their lives, Dr. Davis explained. And that information, he continued, may be surprising to surgeons who often stop meeting with a patient after the initial healing is complete.

A long-term [observational study](#) like this one is intended to provide a different type and quality of information than a clinical trial, Dr. Davis said. Using its findings, clinicians can better counsel somebody considering a total gastrectomy about not only what the procedure and the short-term recovery will be like, but also about how it may impact their life over the long term.

Having this sort of information available, he continued, will allow doctors to assemble a team of health professionals who can help patients navigate the long-term consequences from gastrectomy. And as new [surveillance](#) options and preventive treatments emerge, people at risk of [hereditary diffuse gastric cancer](#) considering gastrectomy can better weigh the potential harms and benefits of all options.

“It’s not that [surgery] might change your life, it will change your life,” Dr. Davis emphasized. Now, he said, surgeons can be “more deliberate in our conversations with patients about the real impact of this operation.”

Daniel Coit, MD, of Memorial Sloan Kettering Cancer Center, who helped write the current treatment guidelines for people who carry high-risk CDH1 variants but was not involved in the study, said the information provided in the study will be meaningful to people with these genetic variants and the surgeons who treat them.

The study and the findings, Dr. Coit said, “are enormously important.”

A Minority Report diagnosis of stomach cancer

The 2002 movie *Minority Report* depicts a futuristic time when the police have crime-predicting technology and can arrest somebody for “pre-crimes.” Today, in the real world, genetic testing provides a similar power to identify those with a greatly increased cancer risk, allowing the option for preventive treatments before cancer develops.

One of the best-known examples of such a preventive measure is [prophylactic mastectomy](#), the removal of the breasts, in people who have inherited harmful variants of BRCA1, BRCA2, or certain other genes that dramatically increase the risk of developing breast cancer.

Similarly, people who have specific inherited changes in CDH1 have a high likelihood of developing stomach cancer and can opt for prophylactic stomach removal. Gastrectomy is currently recommended for this population because, unlike the more common form of stomach cancer that

tends to originate as a single tumor in the stomach, this inherited form of the disease usually snakes throughout the tissue that encases the stomach. One consequence of this sprawling pattern of growth is that the cancer typically isn't detected until it has spread to other parts of the body.

People who carry one of the dangerous CDH1 variants have around a 40% chance of developing stomach cancer over their lifetime, according to Dr. Davis—although some studies have pegged that number to be as high as 80%. Of those diagnosed with gastric cancer, only about a third are alive 5 years later.

“That sets the stage for why you would think about taking out your stomach,” he said.

As most people might imagine, removing a stomach is complex and involves rejoining the esophagus to the small intestine. Without a stomach, patients must modify how much and how often they eat, and they almost always require the lifelong use of certain nutritional supplements.

Going beyond short-term follow-up after total gastrectomy

Patients' reports on the short-term effects of total gastrectomy in the current study matched those seen in previous reports. They included manageable surgical complications, such as leaks where the esophagus was surgically connected to the intestines, bleeding, and infections—which were all treatable—and expected short-term side effects, such as weight loss and challenges adjusting to life without a stomach. Nearly all patients lost weight within the first year—an expected consequence given the restrictive diet required following the procedure.

However, until now, Dr. Coit said, no studies have followed patients in a “meticulous and systematic way” to understand how total gastrectomy affects a person over their lifespan.

About half (68 of the 126) participants in the study were more than 2 years out from their surgery. With the help of a comprehensive clinical questionnaire and one-on-one discussions with these participants, Dr. Davis and his team found that long-term issues following gastrectomy were pervasive in that group.

“Yes, you can do the operation safely,” Dr. Davis said, “but you look a year or 2 down the line, and people are all dealing with consequences that disrupt their daily lives.”

The long-term, or chronic, consequences of total gastrectomy

Overall, 94% of the patients who had had surgery at least 2 years earlier reported at least one chronic complication, such as bile entering the esophagus, difficulty swallowing, and problems absorbing certain nutrients.

Bile reflux—which can cause abdominal pain, heartburn, and nausea—was the most common

chronic complication. Almost three-quarters of patients reported the condition, and for about a quarter of patients it interfered with daily activities.

In addition to the physical ailments caused by gastrectomy, Dr. Davis and his team documented the lifestyle changes and psychological costs of the procedure.

They found that the social and emotional well-being of their patients decreased in the first month after surgery but improved to their presurgery baseline 6 months later, according to quality-of-life surveys. However, Dr. Davis said, it was apparent that these quality-of-life surveys did not capture the full picture of how their lives had changed.

Only during the one-on-one interviews did participants begin to reveal the true impact gastrectomy had on their lives. For example, about a quarter of the patients changed their employment for reasons directly related to total gastrectomy—such as nausea, fatigue, and an inability to eat frequent meals while working. Some said the impacts of the surgery led to alcohol dependence and divorce.

“Patients have come to me over the years and said that we didn’t talk enough about the mental or psychological aspects of this operation before surgery,” Dr. Davis said. “Everybody experiences some consequence of this operation, and in some cases those consequences are disruptive to their daily lives,” he added. “Just talking about it and describing it is important.”

Now, when Dr. Davis meets with a new patient, he talks not only about the operation and chance of infection or other short-term risks, but also about the ways the procedure could impact the patient’s life overall. The “global picture,” he said.

Avoiding preventive gastrectomy altogether

A surgical procedure of this magnitude is a huge decision that few people face, Dr. Coit said.

For some people with harmful mutations in CDH1, the decision to go ahead with total gastrectomy is driven by significant cancer-related anxiety, he continued. For them, removing the stomach brings peace of mind.

By contrast, other individuals, after weighing the pros and cons of stomach removal, choose to forgo the preventive procedure in favor of frequent monitoring for signs of stomach cancer—known as surveillance.

Like the predicted crimes in the movie, whether a lethal cancer will occur in a patient with one of the CDH1 variants is ultimately unknown. This uncertainty makes preventive treatment decisions tricky, especially if those treatments can worsen the person’s quality of life.

The experiences reported in this study can now help guide these discussions and decisions, Dr. Davis said. And other recent work he’s done may help as well.

In early 2023, Dr. Davis and some NCI colleagues reported that surveillance every 6 to 12 months by endoscopy—the use of a long, flexible tube that reaches down the esophagus and allows the doctor to see inside the stomach and obtain a sample of stomach tissue—provides [a possible alternative to gastrectomy in patients who have harmful CDH1 gene variants](#).

Stopping the cancer cell invasion before it starts

Now Dr. Davis and his team are trying to identify other information—such as markers in a patient’s biopsy samples or blood—that can help guide decisions about prophylactic surgery or surveillance.

For some, gastrectomy may be the clear-cut best choice, he said. But for others, “maybe surveillance is a reasonable alternative.”

Another possibility they are investigating: an entirely new prevention strategy. But in this case, instead of interviewing patients, he and his colleagues are interrogating cancer-like cells in the laboratory.

Each gastrectomy that Dr. Davis performs offers a rare glimpse at the earliest stages of stomach cancer, including cells in the stomach lining that resemble signet rings.

Nearly all stomachs of people with the inherited CDH1 variants contain at least a few of these oddly shaped cells. And although their presence does not mean that cancer has set in, these cells are the seeds that can grow and become an invasive cancer.

By studying these cells, Dr. Davis wants to learn how CDH1 mutations lead to stomach cancer so they can identify potential targets for drugs that could stop cancer from developing.

His hope, he said, “is that we won’t have to take out as many stomachs because we’ve found, through our basic science research, some [other] way of preventing stomach cancer.”

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