

The Increasing Prevalence of Pancreatic Cysts

By Arpan H. Patel, MD

Pancreatic cysts are a rapidly increasing phenomenon in gastroenterology. According to the National Cancer Institute, age-adjusted rates for new pancreatic cancer cases have been rising, on average, 0.4% each year from 2009 to 2018. Keep in mind that this statistic does not include new discoveries of benign pancreatic cysts.

Increased patient imaging and the production of highly detailed images created by improved imaging technology have increased incidental findings of pancreatic cysts. About 50% of my referrals for endoscopic ultrasounds at this time are for patients who had a CT scan for something else and ended up discovering a cyst by chance.

However, the increasing prevalence does not mean all cysts pose significant danger to an individual's health. At Middlesex Digestive, we are seeing an increase in cysts, but very few of them are a cause for concern. The frequency of large or high-risk cysts is minimal. In fact, more than 90% of cysts will be small and possess no high-risk features.

Only about 10% will require further action through biopsies or surgery, and the standard rate of someone developing pancreatic cancer is only 0.5%.

There are several features we look for to determine whether a cyst is high risk. One of the most telling characteristics is size. Cysts that are greater than two centimeters in size are considered to have a greater likelihood of malignancy. The risk of an average cyst (less than two centimeters in size), converting into cancer is 0.01%. For cysts greater than 2 centimeters, the chance of malignancy can increase to 0.2%, which is still relatively low.

Those larger than 3 centimeters are considered particularly risky and will always be sampled to test for the presence of cancer. Other high-risk features include solid components on the cyst and nodules or thickened walls within the cyst. The involvement of the pancreatic duct to the point where it dilates or stretches is also a potential sign of malignant degeneration.

The most common type of cyst is the intraductal papillary mucinous neoplasm (IPMN) cyst, which accounts for 40% of pancreatic cysts. The IPMNs that tend to be precancerous are frequently asymptomatic in patients, which is partly why incidental findings have become more commonplace. If the cysts become large or obstructive, some patients may present with back pain, anorexia or

weight loss, and fatter stools because they cannot process fat.

They may also develop diabetes. Jaundice can also result if the cyst blocks the individual's bile duct. Solid pseudopapillary neoplasms (SPNs), in contrast to IPMNs, are almost always symptomatic. The individual may feel a weight in the abdomen, and may experience nausea, vomiting, or weight loss. The plan of action depends on what type of cyst the patient has.

Pancreatic cancer has a poor prognosis. The only curative intervention is surgery; chemotherapy only delays the inevitable. Large cysts or those with high-risk features are almost always biopsied to detect the possible cancer in its early stages. It's very rare for a cyst to go straight to surgery without sampling, even with the presence of high-risk features. Sometimes large cysts are benign with no precancerous potential. For example, cysts that form as a result of excessive alcohol consumption can reach up to 10 centimeters in size (bigger than a baseball), but tend to have no precancerous potential.

The patient's medical history and sampling of the cyst dictate how aggressive treatment needs to be. The presence of a solid component is the only instance in which a cyst may warrant immediate surgery, as solid cysts are three times more likely to turn into cancer than cysts without solid components.

Surgical cyst removal almost always involves the removal of part of the pancreas, which can be a large and complex operation. To remove the head of the pancreas, the surgeon must also remove the bile duct, small intestine, and stomach in a surgical intervention known as a Whipple procedure. Pancreatic surgery has the potential for complications given the sheer complexity of the surgery. Specialists need to have a complete handle on the nature of the cyst before sending patients to surgery.

Surgery is an option only if the cancer is discovered in its early stages, as more advanced disease will often involve the surrounding vasculature or nearby organs. The goal of pancreatic surgery is curative and, on occasion, if more advanced disease is discovered during

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a surgery, the case is often aborted. To prevent such discoveries, further imaging is usually done in advance of surgery to ensure the cancer has not metastasized.

The pancreas is a highly vascular organ containing critical blood vessels. If there is any involvement of the cancer with these blood vessels, the patient is not a good candidate for surgery. Borderline resectable candidates, where the cancer's involvement with local lymph nodes or larger vessels is greater than is preferred, neoadjuvant chemotherapy can shrink the tumor to make the patient a better surgical candidate.

Unfortunately, due to the asymptomatic nature of cancerous IPMN cysts, many patients present late in the process, an unfortunate situation compounded by the fast-growing nature of the tumor. The transformation of the cyst from when it becomes malignant to when it becomes irremovable is rapid.

The most common way pancreatic cysts are diagnosed is with a routine CT scan: a frequent imaging modality that is used to help diagnose a variety of abdominal ailments. The pancreas is very well visualized on CT scans, so the presence of a cyst is clear; however, the characterization of the cyst (especially when it is smaller), including whether it has any high-risk features, is often not clear through a CT scan. In such cases patients are sent to a gastroenterologist to determine the next course of action.

Two important types of exams are performed on patients with large cysts:

endoscopic ultrasound (EUS) and MRI. Both tests are more than 90% accurate in detecting and characterizing cysts, though EUS is thought to be more sensitive by a few percentage points. EUS has several benefits over MRI: not only does EUS provide a characterization of a cyst's appearance, but it can also provide sampling in the same procedure.

To determine whether the cyst is a cancerous or precancerous IPMN, a fluid-based analysis is required to test for key tumor markers and genetic mutations to determine the individual risk for each patient. This is typically achieved by inserting a needle into the cyst, which can only be done through EUS or surgery. Surgery, however, is rarely used in biopsies today, as EUS offers a less complex and safer alternative. MRI helps characterize what a cyst looks like, but there is no choice but to sample with EUS anyway if it does have high-risk features.

While MRIs offer a noninvasive study of potentially dangerous cysts, EUS has become the gold standard of care for pancreatic biopsies. EUS is usually less expensive than MRI, and while there is a risk because of the sedation EUS requires, most risk is minimal. There is less than a 1% chance of tear or perforation, and antibiotics are given to combat any risk of infection as a result of the biopsy. EUS is also preferred for patients with pacemakers or metal in the body, who are ineligible for MRIs.

Smaller cysts or cysts with classically benign appearances are rarely biopsied

and almost never surgically removed. In general, annual surveillance of pancreatic cysts for at least five years is recommended to ensure stability in smaller cysts. The consensus guidelines alternate EUS with MRI throughout the five years. At Middlesex Digestive, we often start with EUS if the cyst is greater than 2 centimeters to ensure it has no precancerous qualities.

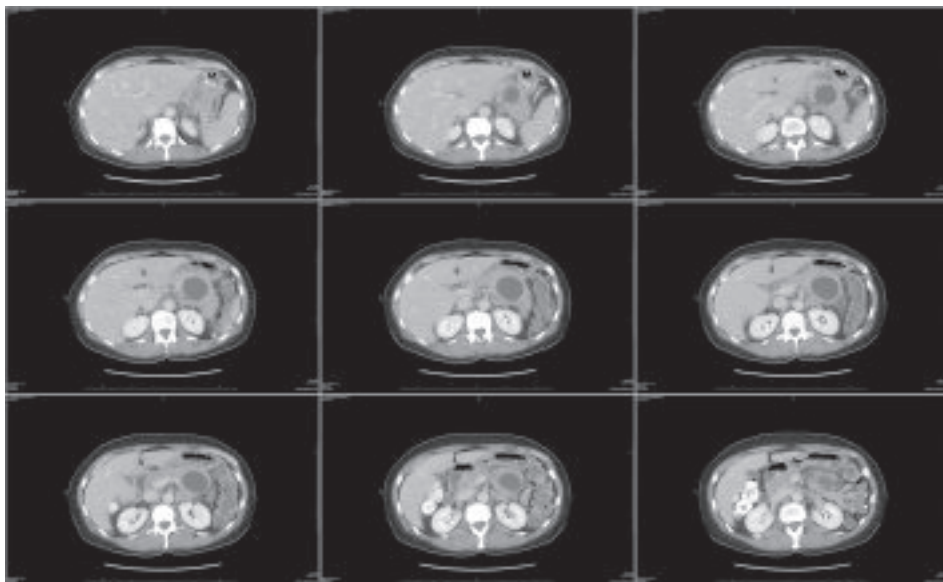
One prevalent issue faced by gastroenterologists is the limited availability of EUS technology. Most US hospitals and clinics do not have EUS, so they must rely on imaging technologies like MRI to diagnose patients. Higher-volume communities may have EUS equipment and expertise, but many places—especially rural communities—do not have access to more advanced technology or, more importantly, experts trained in that technology.

Even in Massachusetts, a state renowned for its medical community, specialists proficient in EUS are relatively rare. Most physicians are now required to perform additional training after their gastroenterology fellowship to get enough exposure to be proficient in endoscopic ultrasound. As applications to these programs increase, hopefully the growing number of trained professionals will spur more communities to invest in EUS technology.

Individual risk for pancreatic cysts varies greatly from person to person. Patients with familial or genetic risk have a higher likelihood of cancer. Genetic predisposition to cysts may result in a larger number of cysts and a faster timeline toward pancreatic cancer. BRCA mutations can increase the risk of developing pancreatic cancer, as can disorders such as Lynch syndrome and hereditary pancreatitis. Smokers and alcoholics are populations that warrant increased attention.

One notable improvement in the scientific community is the ability to test cyst fluid for genetic mutations that increase risk. This makes it easier to prognosticate the cyst's risk for converting into a malignancy.

Debate exists as to whether more people are getting pancreatic cysts or whether their increased prevalence is due to



more advanced imaging technology and medical practices; however, the past four decades have yielded a decrease in risky behaviors that have been proven to lead to pancreatic cysts.

One of the biggest risk factors for pancreatic cysts is tobacco use, with smokers twice as likely to get pancreatic cancer as nonsmokers. Despite a significant decrease in tobacco use in the United States since the 1970s, pancreatic cysts are more common than ever. The decrease in significant risk factors such as smoking suggests that advanced technology is at least partially responsible for the uptick in cyst discovery.

Some modifiable risks, however, have not decreased with time. In the United States, pancreatic cancer is the fourth leading cause of cancer-related death in the country. Excessive alcohol consumption is widely regarded as a significant risk factor, as are obesity and low levels of physical activity. Individuals with a BMI of at least 30 have a 1.7 times greater risk of getting pancreatic cancer than those with BMIs lower than 30.

The increase in pancreatic cysts often forces medical professionals to be objective about what the data states regarding cysts. Attempting to biopsy every cyst would overwhelm the healthcare system; it also increases the risk of complications for patients.

Personally, the increase in incidental findings has reminded me to take a step back and closely examine individual patient data and corresponding risk factors before sending a cyst to biopsy.

For many patients, cysts are not concerning at all. Nevertheless, because of the potential for cancer, there is concern for all patients who present with a cyst, regardless of its size. It's important to discuss treatment strategies and reassurances regarding individual risk with each patient, those with both low- and high-risk features. Specialized, individual patient care is necessary to yield the best health outcomes for all.


Dr. Patel, a gastroenterologist at Massachusetts-based Middlesex Digestive Health & Endoscopy Center, has expertise in numerous areas of gastroenterology, including advanced

interventional endoscopy procedures and therapies such as ERCP and ablative therapies for Barrett's esophagus, endoscopic ultrasound and managing complex bariatric (weight-loss) procedures.

Dr. Patel was accepted out of high school into Northwestern University's Honors Program in Medical Education—a joint acceptance to both the undergraduate pro-


gram and the University's Feinberg School of Medicine—and received his medical doctorate in 2012. While an undergraduate, he received the J.G. Nolan Scholarship, given to students who have excelled in their studies, and in later years was honored as a Liver Emerging Scholar by the American Association for the Study of Liver Diseases and as a Chief Gastroenterology Fellow by the University of Michigan Division of Gastroenterology and Hepatology. Dr. Patel is licensed to practice in Massachusetts and six other states.

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