What role does surgery play in the treatment of pancreatic cancer, and why is surgery so important?

Surgery is the only potential option for a cure, and even if a patient isn’t cured, surgery usually extends a patient’s life. The big problem, however, is that most patients presenting today already have metastatic disease, which means their pancreatic cancer has spread to distant organs. Surgery is unlikely to benefit these patients, which is why we need a way to detect this cancer earlier, when surgery is still possible.

But the message patients and their loved ones need to hear is that today more patients are becoming candidates for surgery than in the past, and there is hope. The entire paradigm is shifting. Statistics show that only about 20 percent of people upon diagnosis of pancreatic cancer are clear-cut surgical candidates. They have localized disease, meaning the cancer has not spread to distant sites and we can remove it from the pancreas. Another 25 to 30 percent of patients have borderline resectable or locally advanced disease, and most of these patients are now candidates for operations that they would not have been candidates for in the past. This means that many more patients are now living longer and have the potential for a cure.

What’s caused the shift for borderline resectable patients and for those with locally advanced disease?

In patients with borderline resectable disease, the cancer hasn’t spread to other organs, but the cancer involves blood vessels, which makes surgery more challenging. Our ultimate goal is for the cancer to be removed surgically with clean margins, so that no portion of the tumor is left behind. In patients with locally advanced disease, their tumors have more extensive involvement of blood vessels around the pancreas and their cancer may have grown into surrounding organs. Up until now, surgery was not always a viable option because there was a high likelihood of leaving a portion of the tumor behind or having the disease return quickly.

Note: The terms in bold, and their definitions, can be found in the glossary on page 6.
Pancreatic cancer surgery resectability used to have a very strict definition. The tumor couldn’t involve any blood vessels or arteries, and it had to be contained and easy to remove. However, the bar for what we can do now has really been set much higher. Much of that has to do with **vascular resections and reconstructions**, which have become very routine at centers such as ours. If there is vascular involvement, we now routinely remove and/or replace an involved artery or vein with a new vessel, called a graft. If there is vascular involvement, meaning that a tumor is getting too near or actually growing into structures like the superior mesenteric or portal vein, for example, we can often resect the tumor with the vein and reconstruct that vein. That’s a huge advancement for patients that has been made possible by developments in chemotherapy and radiation therapy. Importantly, we now know that performing vascular resections can have similar outcomes to no vascular involvement.

Improvements in systemic therapies have been the major driver in performing these more aggressive surgical procedures. In the past, surgeons avoided more radical operations because there was a high risk of cancer recurrence from the lack of available systemic therapies. Now we finally have effective systemic therapies, making aggressive surgery more appropriate and likely to result in a good oncologic outcome. We now use more upfront, or **neoadjuvant, chemotherapy** that is administered to patients before surgery to treat any potentially microscopic disease that is not seen on imaging, and to shrink patients’ tumors, so they become surgical candidates. Almost all surgical candidates, even those who in the past would have gone straight to surgery and then get **adjuvant chemotherapy** after surgery, will receive some type of upfront chemotherapy before surgery. This is a little controversial, but it’s what’s happening in many large centers. My own opinion, based on our experience and the existing literature, is that all patients who have tumors involving major blood vessels should receive neoadjuvant therapy to optimize their outcome.

We know that pancreatic cancer is both locally invasive and a **systemic disease**, which can affect multiple parts of the body, for most patients at the time of presentation. The truth is that pancreatic cancer is a systemic disease from very early on in its development. I tell patients that currently beating pancreatic cancer requires winning both a local battle (surgery) and systemic battle (chemotherapy). That’s tough for patients to hear but it’s supported by statistics showing that despite surgery and adjuvant treatment, pancreatic cancer can recur. **With neoadjuvant therapy, we have the opportunity to kill off any microscopic cancer cells that are not seen on imaging.** Giving chemotherapy before surgery is helpful in several ways: 1) It ensures that chemotherapy is received by the patient, 2) it treats potentially unseen microscopic disease early, 3) it allows us to test if the chosen chemotherapy regimen works on the individual patient’s tumor, and 4) it improves our chances of achieving negative surgical margins.

These are all very important because, for some patients, there can be delays in adjuvant therapy post-surgery and treating patients with chemotherapy after surgery may result in picking the wrong drug regimen for that patient’s specific tumor. We now have data showing that a significant percentage of patients who go directly to surgery may never receive adjuvant treat- ment because their health worsens, or they experience surgical complications. This is crucial because as I said, the systemic treatment is equally if not more important in this disease.

**How effective is neoadjuvant treatment in getting patients with locally advanced disease or borderline resectable disease into the operating room?**

My goal is to get as many patients as possible into the operating room and have a great outcome for them. Studies are ongoing, but what is clear is that many more patients who never would have been surgical candidates before are surgical candidates today. We have learned that the vast majority of patients on neoadjuvant therapy will have either a response or no progression on that therapy based on imaging. However, we have also learned that radiography can be an unreliable predictor of whether they actually responded or not. It is very important to understand that patients with locally advanced disease who are treated with neoadjuvant therapy need to be evaluated by an experienced pancreas surgeon who is familiar with operating on these tumors. Patients who have stable disease are often actually having a response that can’t be seen on imaging. If patients are told their tumors are inoperable, they should seek out second and third surgical opinions early in the treatment process. Many patients we have cured had first been told they had inoperable and incurable tumors.

For the minority of patients who progress on neoadjuvant therapy, there is hopefully still an opportunity to change regimens. It is sometimes hard for patients and providers to hear but knowing this before surgery may prevent them from undergoing a large operation that was not going to extend their life. In addition, it may offer the opportunity to change regimens early and ensure a higher chance of successful surgery.

**Patients need to know that there have been vast improvements in not only the diagnosis and staging of pancreatic cancer, but also in the surgical intervention itself, and in anesthesia and post-operative care.**

**What exactly can neoadjuvant treatment offer potential surgical candidates?**

As a surgeon, I am a huge proponent of neoadjuvant treatment. The studies are evolving, but generally what we are seeing is that neoadjuvant treatment increases resectability of borderline and locally advanced disease, meaning that more patients are eligible for surgery. That’s because the treatment can potentially decrease tumor bulk and vessel involvement and increase the clean surgical margins that all surgeons want for their patients. Upfront chemotherapy also seems to reduce the likelihood of lymph node involvement at the time of surgery.
Does radiation have a role in neoadjuvant treatment?
Through ongoing research, we’re learning more about radiation’s role in pancreatic cancer treatment. Generally, radiation can be used after neoadjuvant chemotherapy in select patients. Patients with resectable disease might consider conventionally fractionated radiation therapy or stereotactic body radiation therapy after surgery. For some borderline resectable and locally advanced patients, chemoradiation, chemotherapy plus radiation, may actually be used prior to surgery. I am a very big proponent of neoadjuvant stereotactic radiation therapy for treating borderline and locally advanced tumors because the data convincingly show that it improves the likelihood of achieving negative surgical margins and decreases lymph node metastases at the time of surgery. However, the timing of surgery after radiation is absolutely crucial in my experience, and I normally try to operate four to six weeks after radiation is completed.

Once a person makes it to the operating room, what is the most common surgical procedure used to treat pancreatic cancer?
By far, the most common surgical procedure to treat pancreatic cancer is the Whipple procedure, or what’s called a pancreaticoduodenectomy. It’s a major procedure where we remove the head of the pancreas, the duodenum, which is the first part of the small intestine that connects to the stomach, and the end of the bile duct. The gallbladder is also removed. We then reconnect the intestines, bile duct and pancreas to restore normal digestive function after surgery. The procedure can take approximately four to six hours.

Patients need to know that there have been vast improvements in not only the diagnosis and staging of pancreatic cancer, but also in the surgical intervention itself, and in anesthesia and post-operative care. There was a time when the death rate from the Whipple was about 25 percent. Now, it’s about 4 percent nationally, and for tertiary centers such as ours, it should be less than 2 percent. That’s why it is so important to make sure patients are treated surgically at a center that has experienced surgeons and skilled, extensive medical teams who perform a high volume of these procedures. The quality of life after a Whipple operation is important and returning to normal can be optimized by choosing an experienced surgical team. We developed and utilize a comprehensive peri-operative enhanced recovery pathway for Whipple procedures, which optimizes a speedy recovery and improves surgical outcomes.

Is the Whipple always done as an “open” procedure, versus a minimally-invasive approach?
Minimally-invasive Whipple procedures are becoming more common at large centers. This operation requires a unique skillset and experience level. Therefore, the vast majority of Whipple operations performed across the United States are still done using the conventional open approach. Most capable surgeons will choose between a minimally-invasive and open procedure, depending on the patient’s situation. Even though we use smaller incisions, it takes us somewhat longer to do a minimally-invasive surgery compared to a traditional open procedure. However, it’s easier on the patient since there’s less blood loss and potentially less recovery time. We perform open and minimally-invasive operations based upon both patient and tumor characteristics.

What about complications?
There can be complications with any surgery, whether it’s open or minimally-invasive. However, if you are in the right hands with an experienced surgeon and medical team, the chances of serious complications with a Whipple are minimized. A somewhat common complication after a pancreatectomy is the formation of pancreatic fistulas. These fistulas are like channels that can cause leakage from the site of the pancreas connection to the bowel. There can also be issues with diarrhea, diabetes, and sometimes slow emptying of the stomach. Infections can happen, but a skilled team and excellent post-operative care will minimize the chance of infections. Most patients experience weight loss, but that weight can be regained in most cases.

SOME COMPLICATIONS OF SURGERY
- Problems digesting different foods
- Insufficient pancreatic enzymes or hormones
- Leaking from the various connections made by the surgeon
- Infection
- Bleeding
- Diabetes


Is recovery difficult?
Generally, most patients are released from the hospital in five to seven days. The first night or two after surgery will be spent in the Intensive Care Unit, and then patients are transferred to a general medical-surgical floor. Once patients are tolerating a diet, feeling well and are stable, they can go home. In surgical terms, stable means that patients have no infection and no fever. They have to be able to function fairly well without help, which means tasks of daily living like brushing their teeth or toileting should be able to be done unassisted. Sometimes older patients may require more help so they may go to a rehabilitation facility for a few weeks. It is important for patients to know that they should recover to their normal quality of life within two to three months.

Is there anything special that patients and their caregivers need to know about recovery at home?
I think one of the hardest things for patients is that they can’t eat the way they used to right away. Patients really worry about that, but we discuss these concerns with a team that includes a dietitian. First, patients are probably not going to be that hungry. And second, and most important, the body needs time to adjust after any gastrointestinal surgery, especially one as complicated as the Whipple. It’s normal for patients to have some difficulties with eating.

Nausea and some heartburn are common, and some patients may experience vomiting. All of these symptoms happen because the stomach can be temporarily paralyzed, a condition called delayed gastric emptying. Fortunately, it resolves in as little as a few weeks post-surgery for most patients. In some patients, however, it can take up to a few months to resolve.
Every patient is an individual. I’ve had patients who are back to normal after a month, but for most, full recovery takes about eight weeks. Most surgeries, especially complex ones like this, can cause fatigue. That’s expected, and rest can be the best medicine. However, patients should do light exercise like walking to help beat fatigue and speed up the recovery process.

Are there any tips to help with nutrition?

Patients should seek guidance from valuable resources like clinical dietitians and gastroenterologists who can help patients get back to a more normalized eating pattern. During surgical follow-up visits, I’ve often heard patients say they do well with eating small, frequent meals every few hours because that’s less taxing on their digestive system. Proteins are always recommended to help patients regain muscle mass they may have lost. Patients generally figure out through trial-and-error what works for them in terms of foods that don’t cause diarrhea or gas. Some patients may need to take pancreatic enzymes to help with nutrition after a Whipple procedure as these enzymes help break down fats, proteins and carbohydrates. We offer a comprehensive dietary assessment and program, which patients find very valuable, as part of our multidisciplinary management.

What about post-operative pain at home?

It is important for patients to stay ahead of the pain and recognize they don’t have to suffer. They should take any pain medications the doctor prescribes, as prescribed. Pain does nothing to help with recovery; in fact, it can absolutely make the recovery process longer and more difficult than it needs to be. However, most patients are feeling quite well and are free of significant pain by discharge. Few will require narcotics more than a week or two after surgery.

Do some patients experience emotional changes/challenges after surgery?

I think most patients understandably have a very difficult time with a diagnosis of pancreatic cancer. Coping with depression following a pancreatic cancer diagnosis is the subject of some ongoing research. One of the issues I see is there is so much misinformation and outdated information about pancreatic cancer available. For example, people hear about the Whipple from a TV show or from the Internet and they become afraid that it’s the worst procedure imaginable and they shouldn’t bother undergoing it because their prognosis is grim.

There is no doubt that it is a major procedure, and there is no doubt that pancreatic cancer is very tough to treat. What I want patients to realize, though, is real progress is being made. More patients are having surgery and getting treatment based on molecular profiling of the disease to determine if there are any mutations in a patient’s inherited DNA or in a patient’s tumor that would indicate a particular treatment is likely to be effective. There is more hope than ever before. We may not be able to cure every patient we operate on, but we can potentially provide patients with a longer life with a good quality of life and more time with friends and family. I wouldn’t be a pancreatic cancer surgeon if this wasn’t the case.

Any major surgery can cause emotional challenges, and the Whipple is a major surgery. People can be afraid of anesthesia, believing they will never wake up from it. They may be concerned that they will never have their old life again. It is so important to bring these concerns up with the entire medical team. The team can help guide patients and caregivers by answering questions, addressing concerns and helping patients get extra help as needed. That assistance can be anything from counseling to a nutritionist to a home health aide to help out around the house while the patient is recovering from surgery.

As part of our multidisciplinary pancreatic cancer team, we actually now screen patients for depression. Strong emotional feelings related to a diagnosis of pancreatic cancer are very common, and there are now resources to help with what I consider appropriate feelings. I am committed to treating every aspect of pancreatic cancer patients, and emotional challenges are part of that.

There was a time you could count on one hand the number of trials that were exploring pancreatic cancer. Now, there’s just a sea-change in the amount of quality research being conducted. Organizations like the Lustgarten Foundation that are dedicated solely to funding pancreatic cancer research can filter through these trials, recognize work that has serious potential to help more pancreatic cancer patients and then fund it.

How do you find the right team to treat your pancreatic cancer? How do you find the right surgeon?

There are no hard-and-fast rules, and access can be an issue for many. But there are some important things people should know since pancreatic cancer surgery is complicated and difficult for a patient to undergo. I recommend that patients have their surgery performed by an experienced surgeon who has significant expertise treating pancreatic cancer patients and who performs many Whipple procedures each year. Studies show that high-volume centers with experienced surgeons have much better outcomes, and that’s what is most important for patients and their loved ones. Although the number of such operations being considered as high volume is somewhat arbitrary, I know from experience that the more operations I do, the better I perform and the outcomes improve. At the very least, surgeons should know and share how many operations they perform yearly and what the outcomes are of those operations.

Quality pancreatic cancer care is a multi-disciplinary effort, and patients need a team that will work together to get the best possible outcome. Aside from a surgical oncologist, patients need experts in pancreatic cancer from medical oncology, gastroenterology and radiology (including radiation oncology and interventional radiology). Patients also need an experienced
Intensive Care Unit team, skilled nursing care, dietitians and social workers. Studies clearly demonstrate that patients treated by a team of providers have better outcomes. I always tell my patients and their caregivers they are stuck with me for life. I follow my surgical patients indefinitely because they have become my friends and I care for them a great deal on a personal level. These patients continue to have several questions about their prognosis and disease even many years after surgery. At some point, though, the visits become more social, and that is the best part of my profession.

Clearly, the Whipple is the most common of pancreatic cancer surgeries. Are there other types of surgeries?

Yes, but they aren’t used quite as often due to the nature of the disease. If imaging shows cancer in the tail and body of the pancreas, we can perform a distal pancreatectomy. We’ll take out the tail of the pancreas, some of the body of the pancreas and generally the spleen. A total pancreatectomy is very seldomly used because there is rarely an advantage to removing the entire pancreas for cancer. In this procedure the spleen, gallbladder and part of the stomach and small intestine are also removed. People will become diabetic once their pancreas is completely removed, and that adds another serious problem on top of the cancer.

Sometimes surgeries are performed to help relieve symptoms such as jaundice, nausea, vomiting and pain in order to improve quality of life. Surgeons can bypass blockages of the pancreatic or bile ducts or gastrointestinal tract to relieve these symptoms. Surgeons can also perform nerve blocks to reduce pain. Sometimes, unfortunately, we’ll start an operation and find out the cancer has spread, and surgery isn’t an option. Fortunately, with advances in pre-operative imaging, finding inoperable disease at the time of surgery is rare these days.

After surgery, patients still need more treatment, correct?

Yes, after surgery, patients still typically need more treatment, and if they didn’t receive neoadjuvant therapy, it is essential that they receive adjuvant chemotherapy. For patients who received neoadjuvant therapy, the decision on additional therapy is a complex and individualized one. However, it’s absolutely vital for patients to receive chemotherapy at some point to increase survival. Recent studies show that combination regimens – modified FOLFIRINOX or gemcitabine and paclitaxel – lead to longer survival in patients who undergo adjuvant chemotherapy after surgery. There are several regimens in the pipeline that could offer similar improvements in survival but those are the two main regimens frequently utilized.

If you look at the whole patient population of those eligible for surgery, one unfortunate statistic is that about 20 percent of patients are too sick after surgery to get adjuvant treatment in a timely manner. Everyone is working hard to improve that.

One thing we didn’t touch on yet is the presence of pancreatic cysts. Surgeons are seeing more of these types of cysts, correct?

Absolutely. I see patients every week, and many of these visits are due to cysts showing up incidentally on CT and MRI scans done for a different reason. The numbers have exploded. Most people have no symptoms and cysts never cause them any problems. Determining which cysts might develop into pancreatic cancer and those that are benign is still difficult, and sometimes people may undergo surgeries they don’t need. Researchers are working on ways to better identify cysts that may cause problems and those that won’t. For example, I was involved with Lustgarten-funded researchers at Johns Hopkins who are developing a Comprehensive Cyst (CompCyst) test, which combines clinical, radiological, genetic and protein marker information to distinguish if pancreatic cysts can develop into pancreatic cancer or remain as benign cysts. We are currently developing a pancreatic cyst screening program at Northwell Health Cancer Institute because these are such common findings.

Are there different types of cysts, some which most likely may lead to cancer?

Cysts are fluid-filled growths, and there are many types. The three main types that we often see are intraductal papillary mucinous neoplasms (IPMNs), mucinous cystic neoplasms (MCNs), and serous cystadenomas (SCAs). Improvements in imaging tests over the past decade have led to a significant increase in the number of patients found to have a pancreatic cyst. Most of these cysts are harmless and can safely be followed and monitored.

Almost all SCAs are benign. However, some people unfortunately might get jaundiced or be uncomfortable as these cysts grow, or if the cyst is positioned in such a way that it’s causing problems. In that case, surgery is an option but rarely required. Otherwise, in the absence of other symptoms or concerns, surveillance, most commonly using MRI scans, is the best option.

The mucin-producing cysts are the most troublesome. Mucin is just mucus, formed by many proteins. IPMNs are the most common type of pre-cancerous cyst. It’s hard to predict if and when they will turn malignant. IPMNs are essentially polyps of the pancreas. Depending on several factors, and if there’s a low chance of malignancy, surveillance again is the most likely treatment path. However, some IPMNs need to be removed due to a high chance of cancer development. MCNs are also pre-cancerous growths that usually require removal.

What we try to do is balance the risk of pancreatic cancer versus the risk of surgery for a cyst that may never become malignant. Our job is to identify the name of the cyst so that we can try to best predict the potential malignancy risk and then determine whether surgery is indicated. Pancreatic resection carries risks, but obviously so does missing a pancreatic tumor. Removal of a pre-malignant cyst is the best chance of a cure.

How are organizations like the Lustgarten Foundation contributing to the research on pancreatic cancer surgery?

The answer to that is simple: organizations like the Lustgarten Foundation are increasing awareness that surgery may be an option for more patients than previously thought and that research into this disease is moving at an incredible pace. I’m a surgeon and also a scientist. I’ve been involved in many clinical trials. There was a time you could count on one hand the number of trials that were exploring pancreatic cancer. Now, there’s just a sea-change in the amount of quality research being conducted. Organizations like the Lustgarten Foundation that are dedicated solely to funding pancreatic cancer research can filter through these trials, recognize work that has serious potential to help more pancreatic cancer patients and then fund it.
Lustgarten is also very involved in funding translational research, bringing the most promising research from the lab bench to the patient’s bedside to make significant changes in actual practice. The work that is taking place at the dedicated Lustgarten Foundation Laboratory at Cold Spring Harbor Laboratory is incredible. Northwell Health Cancer Institute, where I am the deputy physician-in-chief and director of surgical oncology, is also a partner in that work.

How do you see pancreatic cancer surgery evolving over the next decade?

I think it will be more than just surgery evolving. Clearly, there will most likely be improvements in the technologies used in minimally-invasive approaches. But the real change is going to come in the form of treatment prior to surgery and after surgery. There is so much going on in molecular profiling and personalized medicine that change is inevitable. Any real change is going to be multi-modality, with various disciplines working together to refine treatment.

My kids come with me sometimes on the weekends when I do hospital rounds to see patients. I tell them that in their lifetime I think surgeons like me are going to become obsolete. If that happens in my lifetime, that’s great, because that would mean a major surgery for pancreatic cancer is no longer necessary. There would be earlier detection, better up-front treatment, less complicated surgeries, better everything. That change is coming for patients. I truly believe that.

For more information about pancreatic cancer surgery and Dr. Weiss, please contact Northwell’s patient navigator at 1-833-762-7327.

ABOUT THE LUSTGARTEN FOUNDATION

The Lustgarten Foundation is the largest private funder of pancreatic cancer research in the world. Based in Woodbury, N.Y., the Foundation’s mission is to cure pancreatic cancer by funding scientific and clinical research related to the diagnosis, treatment, and prevention of pancreatic cancer; providing research information and clinical support services to patients, caregivers and individuals at high risk; and increasing public awareness and hope for those dealing with this disease. Thanks to separate funding to support administrative expenses, 100 percent of your donation goes directly to pancreatic cancer research. For more information, visit www.lustgarten.org.

GLOSSARY

Adjuvant treatment: In cancer, adjuvant treatment refers to treatment after surgery, generally with chemotherapy and/or radiation.

Borderline resectable pancreatic cancer: The cancer has not spread to other organs, but does approach nearby structures, such as a major artery or vein. There is concern the cancer might not be able to be surgically removed with clean margins.

Clean margin: When a tumor is removed through surgery, the tissue surrounding the tumor is free of malignant tissue.

Conventional fractionated radiotherapy: A full dose of radiation is divided into smaller doses called fractions to allow healthy cells to recover between treatments.

Distal pancreatectomy: A surgical procedure in which the tail and body of the pancreas are removed, usually along with the entire spleen.

FOLFIRINOX: A drug combination of FOL (folinic acid), F (fluouracil), IRIN (irinotecan), and OX (oxiplatin); modified FOLFIRINOX is a slightly less toxic version.

Gemcitabine: A chemotherapy drug, commonly called GEMZAR.

Locally advanced pancreatic cancer: The cancer is confined to the area around the pancreas but can’t be surgically removed because the tumor may be intertwined with major blood vessels and may have invaded surrounding organs.

Metastatic cancer: Cancer that has spread to distant parts of the body from the original tumor site.

Neoadjuvant treatment: In cancer, neoadjuvant treatment refers to treatment prior to surgery, generally with chemotherapy and/or radiation.

Stereotactic body radiation therapy: A type of external beam radiation in which extremely precise, intense doses of radiation are targeted at cancer cells while minimizing damage to healthy tissue.

Systemic disease: A disease that affects certain parts of the body and sometimes the whole body.

Total pancreatectomy: Procedure now rarely used to remove the entire pancreas and spleen in patients with pancreatic cancer.

Vascular reconstruction: A procedure in which a vascular surgeon replaces a blocked or damaged artery or vein with a new vessel, called a graft.

Whipple procedure (pancreaticoduodenectomy): Surgical procedure, usually for cancer, that removes part of the stomach, the duodenum (first part of the small intestine), the head of the pancreas, part of the bile duct, the gallbladder and lymph nodes in the area of the pancreas.