Managing Pancreatic Cancer, Part 4: Pancreatic Cancer Surgery, Complications, & the Importance of Surgical Volume
Dr. Matthew Katz, Surgeon, MD Anderson Cancer Center, Houston, TX

I’m going to talk a little bit about the most common operation performed for pancreas cancer, which is the pancreaticoduodenectomy, or Whipple operation. Before I do that, I’d like to discuss the normal anatomy so I can describe what the operation entails.

On this slide is the normal anatomy of the upper abdomen. In the central aspect of the cartoon you can see the stomach, which is supplied by arteries in red. Towards the top of the diagram you see a little bit of the liver, which was actually cut for purposes of illustrations here. And then behind the stomach, just above the stomach you can see the pancreas peeking out.

By this picture it’s very easy to see that the pancreas again is in very close approximation to some very important arteries, which are in red, and veins, which are in blue. Again, it’s this anatomy that poses one of the many difficulties that we have with treating pancreas cancer.

This slide depicts the normal anatomy as we would see it surgically. In reddish-brown at the top is the liver, the gallbladder can be seen in green, the bile duct is connected to the gallbladder and is the tube that drains bile from the liver above into the small intestine below. The stomach is usually easily visible and behind the stomach you can see the pancreas itself.

In the pancreas the pancreatic duct drains pancreatic digestive juices from the pancreas into the small intestine and in fact, typically drains those juices into the same common channel with bile coming from the liver through the bile duct.

Food that is eaten comes down the esophagus, which you can’t see, goes into the stomach. That food is then processed, the food is excreted into the duodenum or the first portion of the small intestine, it’s mixed with bile from the liver and pancreatic digestive juices from the pancreas, and then that processed food mixed with enzymes and bile is excreted into the remainder of the small intestine. You also see in this picture the large intestine which is further down in the anatomy.

What you see on this slide is the anatomy that is involved in the pancreatic cancer resection. What I’m talking about relates to tumors in the head of the pancreas; tumors in the head of the pancreas account for approximately two-thirds of new cases of primary pancreas cancer but actually the number of patients with head tumors far outnumber the number of patients with tumors elsewhere in the pancreas who were brought to surgery for a number of different reasons. But again, this operation that I’m describing is for patients with tumors in the head of the pancreas.

What this slide depicts is the anatomy that is removed at the time of the pancreaticoduodenectomy or Whipple procedure. You can see here the organs that are divided as part of this procedure because it’s important to recognize that unfortunately we can’t remove only the pancreatic tumor itself, we have to remove a significant amount of anatomy that surrounds the primary tumor.
In the case of this particular operation, which is the most common operation performed for pancreas cancer, we must remove the gallbladder, the lower aspect of the common bile duct or the tube that drains bile from the liver to the small intestine, the head of the pancreas, the first part of the small intestine called the duodenum, and in many cases part of the stomach.

What you see here is that the stomach has been cut, the small intestine has been cut and the pancreas has been cut. This single surgical specimen in the middle of the diagram is what is what is removed as part of a standard pancreaticoduodenectomy procedure.

Once we remove that portion of anatomy we have to reestablish gastrointestinal continuity, meaning we have to connect all these things that we've divided. So we bring up the small intestine and attach it to the pancreas and then we attach it to the common bile duct and then the we finally attach it to the stomach. And that allows food which is eaten to come through the stomach and then flow directly into the small intestine and go distally. Pancreatic juice takes a more circuitous route, it goes through the pancreatic duct, into the small intestine, mixes with bile, and then goes down that loop of intestine out to the large intestine.

You see here on the left aspect of the diagram two drains which are often placed after the operation. I typically use one drain, some people use no drains, as well as two tubes that can possibly be placed during the operation as well. Some surgeons place a tube in the stomach as you here, to help the stomach be compressed and prevent dilation of the stomach; and some surgeons put a tube in the small intestine such as the one that you see here to assist with the provision of nutrition, following the operation. The use of these tubes is optional, I personally put in a small intestinal tube to feed patients temporarily but I rarely if ever put in a tube into the stomach.

As you can see from these slides, this is a fairly complex operation, the operation can take anywhere upwards of three to four hours to complete, typically takes on the order of five to six hours but certainly can take more depending on the complexity of the tumor, the relationship of the tumor to other organs and other blood vessels, and on the basis of the patients themselves.

Typically after this operation patients stay in the hospital on the order of ten days, anywhere between one and two weeks, and recovery can take some time. I tell my patients personally that they will not recover 100% for about six months, so they won't feel as good as they do prior to the operation for six months. Now, they feel pretty good in about three months and even earlier but it takes a full six months to recover 100% from this operation in my view.

Recently there have been some technical advances in pancreatic cancer surgery. Many surgeons now have gained experience with minimally invasive approaches and many patients are requesting to at least learn about these different approaches to pancreatic cancer surgery. Minimally invasive surgery is typically performed through multiple small incisions as you see in the upper left hand portion of this slide.

Trocars or these tubes as seen in the lower left hand portion of the slide are placed through these small incisions into the abdomen and then the abdomen is inflated with gas and this provides working room within which instruments, such as the ones in the lower right hand of this slide, can be inserted into the abdomen and the operation can be performed.

The entire operation is visualized on video screens. Theoretically these operations are associated with lower length of stay and less pain but the advantages associated with these operations have not yet definitively proven and at this point, particularly for cancer, I think their use should be
restricted to certain centers and certain patients, preferably in some sort of experimental trial format.

Robotics has also become an option for pancreatic cancer surgery. Robotics, such as the robot depicted here, offers enhanced magnified 3D optics and imaging, improved dexterity over earlier generation laparoscopic technologies, and are ergonomic for the surgeon, which makes these long operations somewhat more comfortable for the surgeon.

What you're looking at here is a surgeon on the left operating at the robotic console. Across the room the surgical robot with its multiple surgical arms positioned over the patient lying in the center of the screen.

These robots are actually quite incredible. They offer 3D views with high definition optics, they give a wide angle of the surgical field, you can zoom in and out, and in fact you can see small aspects of anatomy more brightly, more sharply, and more clearly than this anatomy is even viewable in a standard operation.

But it's important to remember that these robotic and laparoscopic operations are not right for everybody, certainly patients with advanced tumors are often not a consideration for these techniques and only certain individuals with an extensive experience with these techniques should be performing them.

Whatever the route taken, whether it by minimally invasive or standard approach, the Whipple operation is associated with certain post operative changes that again are due to body changes that occur secondary to removal of the pancreas and changes in the pathways that food must use to go from the stomach out to the body.

First of all, removing some of the pancreas can lead to diabetes. I typically tell my patients that if you’re not diabetic prior to the operation, the chance of becoming diabetic after the operation is about 10%. When I say that, that typically does not mean insulin requiring but it does mean that about 10% of patients who were not diabetic require some sort of oral medication to control diabetes after the operation. Diabetics who undergo the Whipple procedure, about 10-20% of them can anticipate worsening in their diabetes following the operation.

The second issue is exocrine insufficiency. Patients who lose a piece of their pancreas may have some difficulty digesting food the same way that they did before, due to the relative absence of digestive enzymes and the different anatomy of the small intestine. We typically recommend that oral pills are used to replace digestive enzymes after the operation. These pills are typically taken with each and every meal.

Finally, there are dietary changes that come about both because of the altered pancreatic anatomy and altered small intestinal anatomy. I typically advise my patients to eat frequent small meals as opposed to three meals a day and to limit their dietary choices to choices relatively low in fats.

A common question I get asked in my clinic by patients who are considering this operation is ‘What will my life be like after?’ and there have been several studies which have documented quality of patients’ lives following surgery. This is some of our own data from my group here at MD Anderson in which we evaluated various questions assessing patients’ quality of life. All of these patients were asked these questions after surgery as they embarked on their postoperative
chemotherapy. We followed their quality of life by having them answer this series of questions at various time points from surgery, all the way to the five-year mark after surgery.

What you’re looking at in this slide is a summary of the group’s response to the question ‘To what extent have you been troubled by side-effects of treatment?’ On the Y-axis you can see the responses varying from not at all to very much and along the X-axis you can see the time that the questions were asked.

The curve that is generated from these data points shows that early after treatment, between the baseline measurement and three months, the side-effects were somewhat troublesome, but those troubles resolved by three months and that the three months mark stayed fairly minimally bothersome until the five-year mark or 60-month mark.

This slide shows the responses from patients asked two questions – on the top, ‘How would you rate your overall health?’ and on the bottom, ‘How would you rate your overall quality of life?’ On the Y-axis, responses from very poor to excellent, and on the X-axis the time point at which those responses were obtained. Baseline meaning immediately following surgery, through the chemotherapy, and then measured at 3, 6, 9, 12, 15, 21, 24, 28, 32, 36, 42, 48, 54, and 60 months following surgery.

What you can see in both of these curves is that patients in general rate their overall health not very well immediately after the operation but by three to six months feel like their overall health is good and that their overall quality of life is close to excellent.

Last I want to touch on the volume outcome relationship, i.e. the relationship between the number of procedures performed by a surgeon at a hospital and the short- and long-term results of their patients with surgical therapy.

What I want to show you in this slide is that while I described a single operation to you, that operation can be performed a number of different ways. The results obtained by that operation are quite variable and one of the most important things that can affect the outcomes associated with a surgeon’s operation that they perform is the number of operations they do perform on a yearly basis.

At the top of the slide you can see a chart which shows the number of surgical cases, the estimated number of patients treated yearly, and the operative mortality or the number of patients or the percentage of patients that die from pancreatic cancer operations in hospitals who treat very low, low, medium, high, and very high number of pancreatic cancer patients.

What you can see first of all is that to be rated a very high volume hospital for pancreas cancer you only have to operate on 15 pancreas cancer patients yearly. Most high volume pancreas cancer centers, such as M. D. Anderson or Johns Hopkins or Mass General or any of these other pancreas centers operate on well over 100 patients yearly, but you can see in this table that at least according to this system very high volume hospitals were those treated greater than 13 patients per year.

So, what you can see in this slide is that patients who are treated at very low volume hospitals have a risk of death from the operation that I described to you before of approximately 16%, whereas patients who were treated at hospitals who treat a large number of these patients have a risk of dying from the operation of only 4%. So it is imperative that patients with pancreas cancer...
seek out treatment facilities that are familiar with pancreas cancer treatment and treat a large number of patients.

On the lower-left aspect of the slide is a chart that is comparing on the Y-axis the life expectancy of patients treated at different hospitals and on the X-axis the type of hospital they were treated at, whether they were very low volume hospitals, low volume hospitals, medium-volume hospitals, high volume hospitals or very high volume hospitals.

What this chart is showing you is that the difference in survival, on average, of patients treated at very high volume hospitals is almost two years longer than the median survival of patients treated at very low volume hospitals.

On the lower-right of this slide is a chart that shows that that difference in survival of patients that are treated in low and high volume hospitals can not only be explained by differences in complications or problems that occur in the perioperative period. So, the fact that patients treated at high volume hospitals live two years longer than patients treated at low volume hospitals is not only because the mortality from surgery is higher in those low volume hospitals, that also has something to do with the way that the operations are performed in those high volume hospitals i.e. while the operation may seem standard from one institution or another, there are subtle differences in the operations that are performed that can lead to long-term differences in cancer-related outcomes.

I’ve mentioned that surgical therapy is the only treatment that has historically been viewed as curative for patients with pancreas cancer but let me show you this survival curve. Again, this is a Kaplan-Meier survival curve, meaning that on the Y-axis is the percentage of patients that are still alive after surgery for pancreas cancer at any given point. And those time points are the number of months following surgery, as shown on the X-axis. The flatter and higher a line is, indicates a group of patients that are doing better over time.

The first thing you can see in this slide is that – again, these are all patients who have undergone pancreas cancer surgery for resectable pancreas cancer, but none of the curves on this chart are flat. That indicates that the rate of actual cure following pancreas cancer surgery itself is actually not 100% and in fact, even in the best curves in this slide the rate of cure is about 20%, or the number of patients who are still alive after potentially curative pancreas cancer operations after five years is only about 20%.

The second thing that is important to recognize in this slide is that despite improvements in perioperative care and operative techniques that we’ve been making over the past 30-40 years, there have not been significant changes in the outcome of patients following pancreas cancer surgery throughout that time. What this slide is actually showing you is groups of patients with resectable pancreas cancer who underwent surgeries in the 1970s, in the 1980s, in the 1990s, and then in this last decade. And unfortunately what this slide is showing is that the survival rates of patients treated in all of those four decades are relatively equal.

Why is that? Well, this is recent famous paper which shows what is going on with pancreas cancer on the cellular level. In fact, when I have patients that are newly diagnosed with pancreas cancer, many of those patients believe that those tumors have been growing over the past several days or maybe several weeks, some may believe those tumors have been there even for several months, but in fact what this slide actually shows is that the initiating events for pancreas cancer development and pancreas cancer growth may occur 10-15 years prior to the diagnosis cancer clinically.
Once those cellular events occur, tumors begin to grow and may disseminate early in the growth process. What this cartoon is showing is that cells in maroon are breaking off from the primary tumor in this representative patient about 6.8 years prior to diagnosis. What that means is that when we diagnose patients with pancreas cancer, certainly many of them have disease outside the pancreas when that cancer is diagnosed but what it also implies is that patients with localized cancers or cancers that appear to be localized on CAT scan also have cells either floating throughout the blood stream or cancerous cells in the liver or lungs that cannot be detected by CAT scan or other imaging methods.