LUSTGARTEN FOUNDATION FOR PANCREATIC CANCER RESEARCH

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interview with

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update

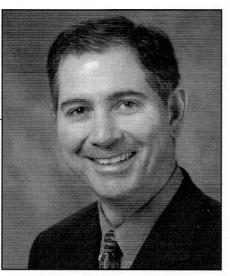
Dr. Reina Marino (RM): What role can surgery play for a patient with pancreatic cancer?

Dr. Doug Evans (DE): Surgery is performed for two reasons. The first is to remove the tumor in the hopes of curing the patient. Generally these surgeries take place when the tumor has not spread beyond the pancreas. The operation performed depends upon where the tumor is located in the pancreas. The most common surgical procedure is pancreaticoduodenectomy, commonly referred to as the Whipple procedure, which involves removing the pancreatic head and associated structures. Most pancreatic cancers that are diagnosed at an operable stage are in the pancreatic head close to the bile duct. The obstruction of the bile duct results in jaundice, causing the diagnosis to be made when the tumor is still relatively small. A distal pancreatectomy is performed when the tumor is located in the body or tail of the pancreas. A total pancreatectomy removes the entire pancreas, but is rarely performed for pancreatic adenocarcinoma. The second reason to perform surgery is for palliation (relief of symptoms despite an incurable situation) to correct problems caused by the tumor that cannot be adequately corrected by other means. This could include surgical bypass of blocked bile ducts in cases where endobilliary stents proved unsuccessful. It could also include gastric bypass, which would be used when the tumor has caused a blockage, or obstruction, of the duodenum

sometimes called the gastric outlet). After this surgery, problems with eating and drinking would hopefully be resolved. There is also an endoscopic stent made for the duodenum, however, the improvement in gastric emptying is quite variable after stenting, and therefore the indications for a stent versus a surgical bypass are based on the unique situation of the individual patient. In general, if we have a patient with locally advanced pancreatic cancer or minimally metastatic pancreatic cancer with gastric outlet obstruction, we would tend to treat them with an operation that would give them the best possible chance of having improved gastric emptying. Unless patients can eat and adequately support themselves nutritionally, chemotherapy or radiation therapy are unlikely to provide any clinical benefit. Some of these operations can be performed laparoscopically, but the majority are performed through a relatively small abdominal incision.

RM: If curative surgery cannot be performed, why wouldn't all patients receive chemotherapy or treatment right away?

DE: Pancreatic cancer patients are often more medically complicated than patients with other solid tumors because of problems such as anorexia (lack of appetite), obstruction of the bile duct or stomach, a predisposition to accelerated clotting of the blood, which may result in deep venous thromboses and occasional pulmonary emboli, and a generalized weakness and loss of energy. Such problems



Douglas Evans, M.D.

may inhibit patients' ability to receive chemotherapy or radiation because patients need to be able to hydrate themselves and take in adequate nutrition before they can receive treatment. If a patient is not feeling reasonably well, anticancer treatment in the form of chemotherapy will not increase their length and quality of life. Because of these complications, sometimes a pancreatic cancer patient may feel as if they need to be their own 'general contractor.' I'll give you an example: Mr. X goes to his medical oncologist and finds out that he has slower than normal flow through the bile ducts, and that he cannot receive chemotherapy until the problem is addressed. Mr. X must now return to the gastroenterologist, or might have to visit a surgeon to deal with the inadequate bile flow. Mr. X is losing valuable treatment time because of these complications, and as a result, he may begin to feel frustrated and helpless.

Unfortunately, the anatomic region where the pancreas is located has created these and other problems, which in turn significantly impairs our ability to treat the patient. Pancreatic cancer, more than any other solid tumor, lends itself to a multi-modality approach requiring the medical oncologist, radiation oncologist, gastroenterologist and surgeon to work together. Such a team approach can provide the support needed to put the patient in the best possible condition to receive treatment. At an NCI-designated Comprehensive Cancer Center (such

(continued)

*Words in bold are defined in the glossary.

as University of Texas M.D. Anderson), the physician and the patient are housed in one series of buildings, which can make potential obstacles to treatment easier to overcome. However, despite our best efforts, some patients cannot recover to a suitable condition to receive any form of anticancer treatment.

RM: How are most surgical candidates diagnosed?

DE: Most patients with operable pancreatic cancer have tumors located in the pancreatic head that developed in close proximity to the **bile duct**, causing jaundice and eventually leading them to a doctor. If the tumor is not close to the bile duct, it grows unknown to the patient for a significant period of time and is usually inoperable or has spread to other parts of the body (**metastatic**) by the time the diagnosis is made.

RM: What should a patient with pancreatic cancer be looking for in a surgeon or in a medical institution?

DE: Please understand that surgeons are just one part of the health care team needed to maximize a patient's length and quality of life. Patients need to find a knowledgeable doctor whom they trust, and with whom they have a good relationship. They should empower the doctor to serve as their 'general contractor' by seeking the opinions of a trusted medical oncologist, surgeon, and/or a radiation oncologist. This field is so complicated and the pace of new advances so rapid, that it is often impossible for patients to process all of the information at-hand. If I had to offer patients a single piece of advice it would be to find yourself a doctor you trust, and consider this person your 'general contractor.'

RM: Taking all of this into consideration, should patients consider having surgery and other invasive procedures at a hospital that performs a high volume of pancreatic surgeries?

DE: There has been a lot of research on **volume outcome relationships**. This work initially began in cardiac surgery, with the hypothesis, 'If the patient was operated on at a hospital where the surgeon, anesthesiologist, recovery room nurses, and floor nurses all had more experience by repeating the same procedure, the likelihood of a mistake would be lower.'

This has indeed been found true. I also think that of equal, if not greater importance than the technical aspect of the operation, is the institutional focus on the disease, including not only knowledge of the operation, but also when to perform it. This begs the question, 'When should surgery be a part of the overall treatment program?' Operating only on those patients most likely to benefit from surgery is very important, because even if major pancreatic surgery is performed perfectly, there are still a small percentage of patients who will experience a difficult recovery. For these patients the quality of life is negatively impacted by a surgical procedure. This potential for an incomplete or suboptimal recovery is most significant when one is performing a large operation for an aggressive disease that may have a relatively modest life expectancy. With surgery as a component of an overall treatment program, the average length of survival is approximately two to three years, with only 20%-30% of patients being long-term survivors (defined as being without evidence of cancer four or five years after surgery). We do not want a patient to spend precious time trying to recover from an operation that proves to be of no therapeutic benefit. Therefore, sometimes the answer should be not to do the operation. Knowing when to intercede with surgery is probably much more important than spending a lot of time trying to select a doctor for just the technical aspects of the operation. Patients can be relatively reassured that if they find an institution or a group of physicians who have dedicated a major portion of their professional lives to pancreatic cancer, the odds are overwhelming that they will be associated with a group of surgeons who know how to do the operation.

RM: What should a patient expect after the Whipple surgery?

Maria Petzel (MP): Generally, the Whipple operation will take anywhere from five to eight hours, depending on complexity. Patients will then often be in the recovery room or intensive care for the first night. Patients generally do not need to be in a monitored setting for more than one night. Their hospital stay is in the range of 7-12 days, depending on how the patient is doing. The date of discharge (and the length of hospital stay) is usually based on the patient's ability to drink and



QUESTIONS TO ASK YOUR DOCTOR ABOUT SURGERY

The amount of expertise your surgeon has may add months or years to your life. In fact, an experienced surgeon may operate on pancreatic tumors that less experienced surgeons might declare inoperable. Here are some questions for you to ask your surgeon. You have the right to have all questions answered to your satisfaction.

- 1. Why will I have this surgery?
- 2. What are the risks and benefits of this surgery?
- 3. How many pancreatic surgical procedures have you done, and how often do you do them?
- 4. How many pancreatic surgical procedures are done at this hospital, and how often?
- 5. How long will the surgery take?
- 6. How long will I be in the hospital?
- 7. What are all of the complications that can occur?
- 8. Do I have to make a decision right now, or can I take time to get a second opinion?
- 9. How much time do I have to think about other options, or to get a second opinion?

Excerpted from Understanding Pancreatic Cancer: A Guide for Patients and Caregivers. ©2007 The Lustgarten Foundation for Pancreatic Cancer Research

eat enough to support themselves and the patient's general level of strength to take care of themselves. They need to be able to shower, get dressed and go for walks before they can go home. Occasionally, there are complications from pancreatic surgery and I would group them into three main categories: First, there could be an infection due to the unique aspect of the surgery. After the tumor has been taken out, the pancreas, the bile duct and the stomach all have to be reconnected to the intestinal tract. Whenever you reconnect human anatomy, there is the possibility for a leak at the point of connection. The most common place for a problem is where the pancreas is reconnected - if there is a small leak in that area between the pancreas and the intestine, it could result in an infection, which would then usually require the placement of an additional drainage catheter to help the area heal.

The second generalized category of complication is related to surgery done on older patients or those with pre-existing heart or lung disease. When such patients undergo this large an operation with the inherent stress of surgery, they could have a small heart attack or experience post-operative pneumonia or problems with breathing.

These are relatively uncommon problems, but ones that could nevertheless delay a patient's recovery. The last generalized category of complication would be those issues related to the physiology of putting the patient's gastrointestinal tract back together again. Despite the fact that people are put back together completely, correctly and with a great deal of skill, a couple of things can happen, including: the stomach may not empty normally and not as well as it did prior to the operation. This delayed emptying occurs in about 1 out of 5 patients and can necessitate a longer period of specialized support to achieve adequate nutrition and fluid intake. That is why many surgeons place feeding tubes in the small bowel to assist with fluid and nutritional intake when the stomach isn't emptying normally. Second, the opposite may happen; a few weeks after surgery, food and liquid will travel through the gastrointestinal tract too quickly. This doesn't happen right away, but could begin anytime from three weeks to a couple of months after the operation. This phenomenon of rapid transit of fluid and nutrients can result in dehydration and nutritional depletion. This, too, is uncommon, occurring in less than 5% of patients. However, it can be a source of significant frustration and affected patients may occasionally require intravenous nutrition.

Though patients will be ready to be released from the hospital in 7-12 days they will require additional time for recuperation and recovery upon returning home. It is often 2-3 months after surgery before patients can expect to feel "normal." In the 2-3 months after surgery patients are gradually adapting to changes in diet and digestion, finding the right pancreatic enzyme dosage, and gradually increasing physical activity.

RM: Are there any medications that patients may need to take for the rest of their lives following pancreatic surgery?

DE and MP: There are. These medications include agents to prevent an ulcer from forming, and those should be taken indefinitely. Following pancreatic surgery patients should take either a histamine blocker, such as Zantac or Pepcid or a proton pump inhibitor such as Prilosec or Nexium. In addition, the majority of patients will require pancreatic enzymes. They will know that they need enzyme supplements if their bowel movements are more frequent, greasy, and/or have an odor. An excessive amount of rumbling in their abdomen after they eat or excessive amounts of burping or flatulence are also indications of a need for enzyme supplements. Patients need to titrate the enzyme that they take with their meal based upon their digestive function and the amount of fat in the meal. If their bowel movements become constipated, they may be able to decrease the amount of enzyme they use. If their bowel movements have an odor, are greasy, or are frequent, then they need to increase the amount of enzyme. Some patients will need medications for blood glucose control. A few non-obese patients will be insulin dependent diabetics after the removal of the pancreatic head. Obesity greatly increases the likelihood that insulin will be necessary. In a patient who is not obese and has normal blood sugar prior to surgery, the likelihood that they will require insulin after surgery is relatively low (25% or so). A patient who is hyperglycemic prior to surgery is likely to require insulin after surgery. The removal of one-third to one-half of the pancreas in those patients is usually enough to move them from using oral agents to control their hyperglycemia to the need for insulin. The whole area of blood sugar control is now a very hot topic. Today, most hospitals have physicians who specialize in blood sugar control. At M.D. Anderson, we have a blood sugar management team, under the direction of the endocrinology department, who work with pancreatic surgery patients on a routine basis. The treatment team, which is run by an endocrinologist and a nurse practitioner. will see patients on the first or second day following pancreatic surgery.

RM: Is there compelling research on pre- and/or post-surgery treatments?

DE: At M.D. Anderson, we are in the business of trying to find better treatments for patients in the future. As such, we always have ongoing clinical trials to examine the benefits of both pre-operative therapy (neoadjuvant therapy) and post-operative therapy (adjuvant therapy). It is important for patients to understand, when considering a clinical trial, that physicians would never develop a trial if they did not believe it would offer a patient the best possible chance of being cured. Right now at our institution, for those patients who have potentially resectable (removable) pancreatic cancer with no evidence of cancer anywhere else, we have a trial of pre-operative chemotherapy with or without radiation followed by surgery. And for those patients who have had surgery first (either at M.D. Anderson or elsewhere), we have a clinical trial of chemotherapy and radiation after surgery. We know that 80 to 90% of those patients who do have a potentially removable primary pancreatic cancer (with no cancer anywhere else) will still have microscopic cancer cells outside the pancreas. There is some evidence to suggest that if you can attack the cancer cells when they are relatively smaller in number, then the treatments may be more effective. Giving those patients chemotherapy with or without radiation may prove more effective than waiting for the cancer cells to grow and treating the patient when the metastases are visible on CT images or X rays.

RM: In the near future, do you think there will be any surgical techniques that will enable doctors to remove tumors now considered inoperable?

DE: Inoperable tumors are usually larger, and most patients who have large tumors also have metastatic disease. We have suggested specific criteria for which tumors are (or are not) removable. This is intended to result in fewer people who will go to the operating room for surgery that proves unsuccessful. That is very important, because patients experience tremendous confusion after an unsuccessful surgery. They often do not understand why the tumor could not be removed. The development of a clear and precise understanding of which tumors are removable, which are not, and why, would be a tremendous advance.

RM: We know people who have survived in excess of 10 years. How long have you had patients survive this disease?

DE: We, and a number of other surgeons across the country, have operated on patients who we think are cured of pancreas cancer. Visit our Web site (www.mdanderson.org/diseases/pancreas) for feature stories on some of our survivors and a list of other valuable resources. Our most recently published analysis of patients who survived 5 years from diagnosis demonstrated that almost 30% of patients reached this milestone; a wonderful advance due to the innovations made in cross-sectional imaging, surgery, and the delivery of chemotherapy and radiation.



contributors

Glossary

DOUGLAS EVANS, M.D.

Dr. Evans joined the faculty of the University of Texas M.D. Anderson Cancer Center in 1990 and has devoted his professional career to the research and treatment of pancreatic and endocrine tumors. In January, 2009 he assumed the chair of the department of surgery at The Medical College of Wisconsin in Milwaukee. Dr. Evans is a graduate of Bates College and Boston University School of Medicine. He received his surgical training at Dartmouth Medical School before joining the faculty of M.D. Anderson Cancer Center.

REINA A. MARINO, M.D.

Dr. Marino is a board certified diagnostic radiologist based in the Philadelphia area. Dr. Marino is the author of Courage To Conquer: Breast Cancer Survivors Share Their Personal Stories. In addition, Dr. Marino has been a health columnist for the Philadelphia Daily News and consultant and speaker for the American Cancer Society. Her professional interests include cancer awareness and prevention, nutrition and stress management. Dr. Marino became involved with The Lustgarten Foundation after losing her father to pancreatic cancer.

MARIA PETZEL, R.D., C.S.O., L.D., C.N.S.D

Maria is a graduate of the University of Oklahoma and joined the University of Texas M.D. Anderson Cancer Center in 2001. She received a joint appointment in Department of Surgical Oncology in 2006 and specializes in the nutritional management of patients following major hepatobiliary and pancreatic surgery.

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About The Lustgarten Foundation

The Lustgarten Foundation For Pancreatic Cancer Research is a not-for-profit organization dedicated to advancing the diagnosis, treatment, cure and prevention of pancreatic cancer. The Foundation was named for Marc Lustgarten, Vice-Chairman of Cablevision Systems Corporation, who was diagnosed with pancreatic cancer.

The Lustgarten Foundation concentrates on stimulating the scientific community to conduct the research necessary to find a cure for pancreatic cancer. The Foundation has sponsored international research conferences, launched a national public awareness campaign, and committed \$20 million in support of promising pancreatic cancer research. Today, The Lustgarten Foundation is the nation's largest private supporter of pancreatic cancer research.

To help support these activities, the Foundation has established a Scientific Advisory Board of renowned researchers and clinicians to help direct its research funding activities, and a Corporate Advisory Board of leading cable and media executives to support a national pancreatic cancer public awareness campaign. Former President Jimmy Carter, Honorary Chairman of the Foundation's Corporate Advisory Board, leads the public awareness campaign. The campaign includes public service announcements (PSAs) featuring President Carter, actor Matthew Modine, and "Last Lecturer" Dr. Randy Pausch. The PSAs appear on major television and cable networks nationwide, and print versions of the PSAs appear in major print vehicles.

The Lustgarten Foundation also distributes a comprehensive handbook for pancreatic cancer patients and their families. "Understanding Pancreatic Cancer" offers up-to-date information on the disease. Copies are available free-of-charge by request to The Lustgarten Foundation.

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(osi) oncology

Bile Duct – tube that connects the liver and gallbladder to the small intestine.

Catheter - thin, flexible tube.

Comprehensive Cancer Center – an institution recognized by the National Cancer Institute as one that performs research in 3 major areas: basic research, clinical research and cancer prevention, control and population based research. It must also conduct outreach activities and provide education and information that is directed toward and accessible to health care providers and the lay community.

Deep Venous Thrombosis (DVT) – blood clots in deep veins of the arms or legs.

Endobilliary Stent – small metal mesh tube used to prop open a bile duct.

Endocrinologist – a physician specializing in the diagnosis and management of hormonal abnormalities. A hormone is a chemical substance produced in the body that controls the activity of cells or organs. For example, insulin and estrogen are hormones.

Gastric Outlet Obstruction – blockage of normal flow of food or fluid out of the stomach.

Hyperglycemic - high blood sugar.

Intravenous (IV) – refers to a thin tube inserted into a vein to deliver fluid or medication.

Jaundice – yellowish pigmentation of skin, body tissues and fluids caused by deposition of bile pigments. Bile is a yellow-green fluid secreted by the liver, stored in the gallbladder and passed into the small bowel to help digest fats. Jaundice can occur when there is an abnormality in the production or breakdown of bile or if there is excessive breakdown of red blood cells.

Metastatic - spread of disease to other body tissues.

Multi-modality - many disciplines or methods.

Pancreatic Adenocarcinoma – the most common type of pancreatic cancer.

Pulmonary Emboli - blood clots in lung arteries.

Surgical Bypass – surgical procedure where a new pathway is created for the flow of blood, fluid or other bodily substances.

Titrate - adjust.

Volume Outcome Relationship – the connection between the number of procedures performed and how patients do following that procedure.

Whipple Procedure – a type of surgery where the head of the pancreas, duodenum, portion of the stomach and other nearby tissues are removed.

