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## Pancreatic Cancer: Associated Signs, Symptoms, Risk Factors and Treatment Approaches

Narrator:

Welcome to Medical Breakthroughs from Penn Medicine, *Advancing Medicine Through Precision Diagnostics and Novel Therapies*.

Dr. Caudle:

You're listening to ReachMD, and I'm your host, Dr. Jennifer Caudle, and with me today is Dr. Major Kenneth Lee, Assistant Professor of Surgery at Penn Medicine. And today, we will be discussing Pancreatic Cancer: Associated Signs, Symptoms, and Risk Factors and Treatment Approaches. Dr. Lee, welcome to the program.

Dr. Lee:

Thanks very much. I'm happy to be here.

Dr. Caudle:

So, let's start with how common is pancreatic cancer and what are some of the signs and symptoms associated with this diagnosis?

Dr. Lee:

As much as we often hear about pancreatic cancer, it's actually a relatively rare disease. It's estimated

that there will be about 50,000 new cases of pancreatic cancer this year, so 2017, by estimate. And, actually, that's only a slight increase from where things have been for quite a while. For the sake of comparison, there are about 250,000 breast cancers to be expected this year, and 220,000 lung cancers, and probably 125 to 150,000 colorectal cancer cases. And so, relative to the other diseases that we hear a lot about, it's uncommon. For one individual person, without significant risk factors or family history, your lifetime risk of pancreatic cancer is about 0.5%. So that's low. The reason that people hear so much about it, I think, in part, is because it's an aggressive disease and we haven't made as much progress as we would like in treating it. So, even though it's the 9<sup>th</sup> or 10<sup>th</sup> most common cancer, overall, it's the number 4 cause of cancer deaths, and it probably will be 2<sup>nd</sup> by the year 2020. So, most cancers in the U.S. are in decline, in terms of numbers, and we are kind of getting better and better at treating most cancers, but pancreatic cancer is pretty steady in terms of the number. We still have a ways to go in how we treat it. As far as the signs and symptoms, one of the issues with pancreatic cancer is that it can be hard to catch when it's early in stage. And so, the actual signs and symptoms tend to depend on where it's located in the pancreas. The cancers that arise in the body and tail of the pancreas often are asymptomatic until they get fairly sizable, and then they typically can present with abdominal pain, weight loss, more typical things, back pain occasionally, especially if the cancer is invasive. The tumors in the head of the pancreas tend to get picked up earlier because they cause problems. They can block up the duodenum, which is the first part of the intestine, or they can block the bile duct and cause people to become jaundiced. So, those typically present with pain, jaundice, and weight loss, and tend to get picked up a bit earlier.

Dr. Caudle:

You mentioned something at the beginning of your statement about how by 2020, I believe you said, you felt that pancreatic cancer would either become more common or more deadly. Can you please clarify what you meant by that and maybe explain a little bit why that's the case?

Dr. Lee:

It's actually not that the pancreatic cancer itself will be more common or more deadly. It probably will be about the same. The issue is that we've made a lot more headway with other types of cancers, and, therefore, pancreatic cancer tends to stand out because we haven't made as much progress. So, lung cancer is a common cancer and it's also quite deadly. Now, by contrast, colorectal cancer; so colorectal cancer is much more common than pancreatic cancer, but we are much better at treating it than pancreatic cancer, between surgery and the other therapies, especially chemotherapy and radiation, and so forth. And so, when somebody's diagnosed with colon cancer, the odds that they will be alive in 5 years are much higher than a patient who's diagnosed with pancreatic cancer. So, it's not that pancreatic cancer will change in terms of how common it is, or how deadly it is. What it more so is

is that we haven't gotten much better at treating pancreatic cancer, while we have gotten much, much better at treating things like colon cancer, breast cancer, prostate cancer, and so forth. So, pancreatic cancer tends to be coming more and more to the forefront in America, because it sort of stands out, because we have not found great ways to treat it yet, relative to other cancers that we seem to be getting better and better at treating.

Dr. Caudle:

That makes a lot of sense and I appreciate you clarifying that. It's very interesting. Can you talk about risk factors? Are there certain risk factors that patients should be aware of, and is screening available?

Dr. Lee:

With respect to risk factors, there are definitely genetic components to it. There are some people who have known genetic syndromes that predispose them to pancreatic and other cancers, like for instance, the BRCA mutations predispose you to pancreatic cancer and others. But there are also people with affected first-degree relatives or multiple affected first-degree relatives who are at increased risk. So, our antenna, in terms of pancreatic cancer is definitely up in any of the patients who have an extensive family history, or in patients who are known to have one of the relevant gene mutations. Outside of hereditary factors, we do know that smoking is a definite risk factor, as it is for most cancers, so that is yet another reason to stop smoking. Diabetes is possibly a risk factor. It probably is a bit of a risk factor, but the interplay of diabetes and pancreatic cancer is kind of complicated. And so, how much a person's risk escalates if they have diabetes, is a little bit unclear. There is a disorder known as chronic pancreatitis where patients develop chronic inflammatory changes of the pancreas and that's associated with about a 3-fold increased in pancreatic cancer. And so, those are probably the main things, if we're looking at things that apply to a fair number of people, both the hereditary components and then smoking, diabetes, and chronic pancreatitis. Screening is interesting. My wife is a primary care doctor, and that's a question that comes up a fair amount for her. The shorter answer is that there is no way to effectively screen most people for pancreatic cancer. The easiest and cheapest way to screen people is by blood test. There is a blood test called CA-19-9 that goes along with pancreatic cancer, but it's not always elevated in people who have pancreatic cancer, and it can be elevated in people who don't have pancreatic cancer. So, it's a bit imperfect, and so the yield is pretty questionable in people who don't have a symptom. As an alternate, it's kind of impractical to screen people for pancreatic cancer by CAT scan or by endoscopy, because, as I said earlier, it's still a relatively rare disease, but it's also aggressive. So, you'd have to screen far too many people to find one, and then you'd have to find that person at the exact right time to intervene. And it's hard to accomplish that. So, those things don't go very well. Since we know that it doesn't work that great to screen everybody with pancreatic cancer, we have tried to restrict the screening to these high-risk

individuals who have a genetic predisposition or have a significant family history. And so, for instance at Penn, we do have a pancreatic cancer screening program headed by one of the interventional GI people that focuses on these high-risk groups, but it's not yet clear whether screening works, even in these high-risk people, but it's certainly a better approach than trying to screen everybody, because we know that doesn't work very well.

Dr. Caudle:

Let's talk a little bit about pancreatic cysts. And it was helpful for you to talk a little bit about screening, in general, but let's say a patient presents with a pancreatic cyst. What should the next steps be for that patient and their care and their treatment?

Dr. Lee:

That's a question that is becoming more and more relevant every year and probably will keep coming more and more relevant. The issue is that pancreatic cysts are actually quite prevalent because our imaging is pretty good at finding them. So, if you take people who are over 70, about 10% of people have pancreatic cysts. And in people younger than 70, probably somewhere in the 2.5 to 5% of people have pancreatic cysts. And so, the classic story we get is that somebody goes and they get a CAT scan for something completely unrelated and a pancreatic cyst is identified and so they come to see us, because people don't want to miss anything pancreatic. And when I see the patients, I tell them that there are several types of cysts that can develop in the pancreas. Some of them are benign and will never become a cancer. And then some of them do, at least, carry the potential to become a cancer, and we're pretty good at identifying which is which when they have some size, but it can be harder to tell which is which when they're smaller. The easiest answer to cysts is that they should be followed for at least a short while, and they probably should preferably be followed by somebody with some expertise like a surgeon or a gastroenterologist. They're typically followed by either an MRI or CAT scan or a third modality which is a type of endoscopy, and how we utilize those kind of depends on the patient. How long we follow them, and if and when we should remove them is actually kind of complicated and we struggle with that ourselves, to some extent. There are some broad guidelines, but you have to tailor everything to an individual patient, in terms of what's their age, what's their level of fitness, what's their personal history, family history, and what's been the natural history of the cyst? And then, if there's a specialist following them, then they can put all of these things together and decide kind of where to take it. We have a Multidisciplinary Cyst Conference here at Penn which we think is helpful, because it can get complicated, and it's nice with all these things to have people putting their heads together so that the patient can get a consensus opinion from multiple people with some expertise on the matter.

Dr. Caudle:

Well, you know, that makes a lot of sense and I think that's very helpful, not only for me as a family practitioner, but I think for our listeners as well. Because it can be complicated and I do understand your recommendation of sort of a multidisciplinary approach and how it can be helpful, certainly in the case of cysts and others.

If you're just tuning in, you're listening to Medical Breakthroughs from Penn Medicine on ReachMD. I'm your host, Dr. Jennifer Caudle, and with me is Dr. Major Kenneth Lee, and today we are discussing pancreatic cancer.

So, let's move forward a little bit. Can you tell us a little bit about your approach to treatment and which patients, what types of patients, rather, do you recommend receive surgery right away versus those who should receive chemotherapy and then surgery, and maybe which patients would not be candidates for surgery?

Dr. Lee:

So, I think just from my first meetings with a lot of people who have pancreatic cancer, I think one thing that is important, to start, by saying is that every patient who gets a diagnosis of pancreatic cancer gets chemotherapy, unless they are not fit enough to receive chemotherapy, for one reason or another. And the reason why I think it's important to mention that is because some patients, especially when you first meet them, think of surgery as a way to avoid chemotherapy, and that's not really the case. Chemotherapy would be recommended even in the case of a small tumor that's easily removed, because we think that the best way to improve peoples' survival in this disease would be a combination of surgery and chemotherapy, if that's applicable. So, the real question is sort of how to sequence surgery with these other therapies, like chemotherapy and radiation. And so, every one patient is different, but to try to simplify things, I would say that when a patient gets diagnosed with pancreatic cancer, they basically get put into 1 of 4 groups. And so, one group we call resectable, and so that means that there's no evidence that the tumor has spread anywhere, and the tumor looks well-contained, and away from the larger blood vessels there associated with the pancreas. And those patients are at least candidates for upfront surgery. The other end of the spectrum would be patients with metastatic disease, meaning the tumor has spread somewhere, like the liver, the lungs, or elsewhere, at the time of diagnosis. And those patients are essentially non-candidates for surgery and would be treated with chemotherapy generally. And then there are two middle grounds we call "borderline resectable" and "locally advanced." And that's just terminology, but, essentially, for both of those, what it means is that the tumor hasn't spread anywhere, but it's less favorable, because it's either involving or at least potentially involving some of the larger arteries and veins in the area of the pancreas that would make the tumor unresectable, or would at least require a bigger operation with a vessel resection. And so, I would say that most surgeons would start those groups of people on

chemotherapy first to try to shrink the tumor, and make the operation more likely to be successful. So, that's not kind of the entire story, because every patient's different, and they're always exceptions to paradigms, but that's probably a reasonable broad description. What I didn't talk about are trials, and I do think that clinical trials have a very important role. And, at least here, we try to think of most people in the context of some sort of trial, and we enroll a lot of people in trials. And we have trials at Penn for all of these people: resectable, metastatic, borderline, and I do think that's the main way that we'll continue to make some progress with this disease is to keep thinking about it in a multidisciplinary way and to keep trying to translate our scientific knowledge to the clinical venue.

Dr. Caudle:

You've talked a lot about individualizing the treatment for the patient, which certainly makes a lot of sense. Let's talk about surgical techniques. With regards to surgery, are either laparoscopic or robotic pancreatic surgeries an option, and which is more favorable, or which is done more commonly, and what are your thoughts about those?

Dr. Lee:

They're both options, and, in fact, they're both fairly well-entrenched, but I don't think we yet know how it will all shake out, how far it's worth pushing the envelope. You could put both laparoscopic and robotic under the heading of minimally invasive pancreatic surgery. And, for instance, here, we definitely do minimally invasive pancreatic surgery as do many people at high-volume centers. I think minimally invasive, whether laparoscopic or robotic, is sort of starting to become the standard of care for many of these lesions that we see in the body and tail of the pancreas, because the operation that it takes to remove tumors in the body and tail of the pancreas, is a smaller operation, and it can be relatively low impact, if it's done in a minimally invasive way. But, by contrast, there is more debate about the role for minimally invasive resections of the pancreatic head, which is what we call a Whipple procedure. I think that most people would admit that a Whipple procedure is a high-impact operation, no matter how we do it, and it's debatable, whether making the incision smaller, will make the operation any better. And there are studies that argue both ways on that, but I think the bottom line is probably that minimally invasive pancreatic surgery is here to stay. At places like this, they do a lot of pancreatic surgery and we're just figuring out how far to safely carry it. I don't think that there is a great consensus and probably not a great differentiation to be made between laparoscopic and robotic pancreatic surgery. They're both minimally invasive. They both allow you to do the operation through smaller incisions, and so, they're probably essentially equivalent. And whether you would prefer straight standard laparoscopy or robotics, is probably a little bit dependent on who the surgeon is and what their experience and comfort is with one technique versus the other. So, really, the discussion is minimally invasive versus open surgery, and we do know that minimally invasive pancreatic surgery is



here to stay, but we haven't yet figured out how far we're going to take it all.

Dr. Caudle:

In conclusion, are there any final thoughts about pancreatic cancer diagnosis and the prognosis or treatment options that you can share with us?

Dr. Lee:

I really think that the key is multidisciplinary care. There are some diagnoses for which surgery is the answer, and is kind of the cut-and-dry answer, and the only answer. And then there are other diagnoses where you really do need multi-modality therapy. And pancreatic cancer is certainly, in its current form, a diagnosis that requires multi-modality therapy. So, I think that any patient who gets a diagnosis of pancreatic cancer is best off coming to a place like this and seeing a surgeon, if surgery is an option; seeing a medical oncologist, potentially seeing a radiation oncologist, and being informed about clinical trials, so that we start to put together a plan of care that has multiple angles to it. I think it would be a mistake -- although, it can be, when you first meet patients, a lot of times they would like to jump to surgery: How do I get this out of me? And I think that upfront surgery can be the thing to do, but I think that what you want to do is have a bigger view to it and explain to the patients that their treatment is going to be multi-modal, they will need surgery, but they will need other components to therapy. And then, figuring out what the approach is for each individual, because what we're trying to do is improve people's survival with a plan of care, and surgery can be a part of that and other things are often a part of that also. And so, we try to focus on survival and putting together a plan of care that's best for each patient.

Dr. Caudle:

I definitely really appreciate those comments and, again, as a family practitioner myself, and I know so many people are listening, pancreatic cancer can be so difficult. We all know this. And it's sometimes very difficult with our patients and it's hard. I really appreciate you talking about the importance of individualized care. As I mentioned before, the importance of thinking about multi-modal care and involving multiple specialties, and really coming up with a treatment plan that works best for each patient because it can be different for each patient. And so, Dr. Lee, I really want to thank you so much for being with us today and just sharing your insights.

Dr. Lee:

Thanks a lot. I was happy to be here and hopefully people are able to learn something from my comments, but thanks for having me.

Dr. Caudle:

Oh absolutely. I know they will. I'm your host, Dr. Jennifer Caudle, and thank you so much for

listening.

Narrator:

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