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Combatting Pancreatic Cancer: Keys to Early Recognition and Diagnosis

Ana Maria Rosario:
Pancreatic cancer strikes fear into the hearts of every practicing internist, pathologist, oncologist, and general surgeon on behalf of their patients, and unfortunately, for all of us, it's on the rise.

By 2030, it will be expected to climb to the number two spot for causes of cancer death. What new insights can we bring to the recognition and identification of pancreatic cancer to help curb that trend?

You're listening to ReachMD and I'm your host, Ana Maria Rosario and joining me today at Provost GI Insights in New York is Dr. Aimee Lucas, Assistant Professor of Medicine at the Ichan School of Medicine at Mt. Sinai New York.

Dr. Lucas, welcome to the program today.

Dr. Aimee Lucas:
Thank you so much for having me.

Ana Maria Rosario:
Can you give us a basic sense of the shear scope of pancreatic cancer and why it's so difficult to catch and treat?

Dr. Aimee Lucas:
So you're right, pancreatic cancer is a big problem here in the United States. Currently, it's actually the number four killer, cause of cancer deaths in the United States and you're absolutely correct that when we look at mathematical models, looking at what's going to happen over the next 10 to 20 years, we see that pancreatic cancer is actually on the rise and is expected to be the number two cause of cancer deaths within the next 20 year or so.

So we know right now, about 45 thousand or so patients are diagnosed, in the United States, with pancreatic ductal adenocarcinoma every year and the survival rates are actually quite grim. So, five-year survival for pancreatic cancer is really in the single digits and we don't have great ways to detect pancreatic cancer early to treat it adequately and to make sure that patients either don't get pancreatic cancer or can survive from the disease.

Ana Maria Rosario:
So Dr. Lucas, what are some of the select risk factors for pancreatic cancer?

Dr. Aimee Lucas:
So the number one risk factor, probably is tobacco smoke. There are large epidemiology studies that have looked at risk factors for pancreatic cancer and honestly, if you put enough patience into a study, you can probably find some significant results. Cigarette use, pipe use can be associated with pancreatic cancer. Heavy alcohol use and here, we usually think about greater than three alcoholic drinks per day can be associated with an increased risk of pancreas cancer. We are learning more about the association of chronic pancreatitis in the development of pancreatic cancer and so that is also a big risk factor for development of pancreatic cancer, but we're also learning about the role of obesity, particularly with a body mass index or BMI over 40 we're seeing an increased risk of pancreatic cancer.

There are other associations with pancreatic cancer, such as particular blood types, we're learning a little bit more about that. Perhaps, there's a role for infection. The association of some surgeries with pancreatic cancer, we see some increased risk.

Ana Maria Rosario:
Now, how does the family history of pancreatic cancer compares a risk factor to other cancer types?

Dr. Aimee Lucas:
So family history is a really interesting thing and that's one of my particular focuses. So when we look at patients who have breast cancer, or colon cancer, if we see a patient with a young onset breast cancer, or colon cancer, that really raises a lot of red flags for us, or if we see families where we see multiple affected members with breast cancers, ovarian cancers, colon cancers, we start to think about genetic syndromes.

Unfortunately, for pancreatic cancer, what we often say is that we assume that patients either had really bad luck or they sort of brought it upon themselves, you know, they drank too much, they smoked too much and then, they got pancreatic cancer.

What I think is very underappreciated is the role of the family history in the development of pancreatic cancer. So, probably, about 10 percent of pancreatic cancers actually, have a famil component to it. The largest known genetic risk factor for pancreatic cancer, meaning the one that contributes the most that we know about to development of pancreatic cancer, actually, the BRCA mutations that are much better known for breast and ovarian cancer, but those are also associated with prostate cancer and also pancreatic cancer.

There are a number of other genetic mutations that predispose to various different cancers that over time, have been associated with pancreatic cancer. There's the FAMMM syndrome, which is Familial Atypical Multiple Mole Melanoma and that's, associated with an increased risk to get pancreatic cancer. Peutz-Jeghers syndrome, which is a syndrome that involves a lot of hamartomatous polyps throughout the GI tract can be also associated with an increased risk of pancreas cancer.

Lynch syndrome, which is very well known for colon cancer, has actually been found to be associated with pancreatic cancer and then, there's a rare syndrome called Hereditary Pancreatitis, which causes an early onset of pancreatitis in patients and that's associated with pancreatic cancer, as well.

The problem is, we actually don't know what a lot of the genes are that are linked with hereditary type pancreatic cancer. We're learning a little bit more about that with studies of patients who are either at high risk for pancreas cancer because they have multiple affected family members or looking more at patients who have some of these germ line mutations, so we hope to know more in the future.

Ana Maria Rosario:
Well, if you're just tuning in, you're listening to ReachMD and I'm your host Ana Maria Rosario and I'm joined by Dr. Aimee Lucas from the Ichan School of Medicine at Mt. Sinai in New York.

So Dr. Lucas, turning our attention to the precancerous lesions, can you first give us a rundown of the important types and then, we can discuss here how to go about identifying them before they develop into pancreatic cancer?

Dr. Aimee Lucas:
Sure. So one of the things we're seeing a lot of now with a lot of cross-sectional imaging and by cross-sectional I mean, CAT scans or MRIs. We're seeing a lot of cysts in the pancreas and this raises, rightfully, a lot of concern in caregiver's eyes.

So there's a few important things to think about when we're thinking about cystic lesions of the pancreas and one is, do they have any cancer potential or not and one of the ways that we determine whether or not there's cancer potential is trying to figure out whether or not the cysts are what we call mucinous and there's certain characteristics of cysts that can tell us whether or not a cyst is mucinous and therefore has cancer potential, or if it's just a simple cyst, like a pseudocyst that might be a result of an episode of pancreatitis or something like that and really is a benign condition.

So we're seeing more and more of these cystic lesions and it's important to work closely with your gastroenterologist to differentiate them.

So the ones we see a lot are Intraductal Papillary Mucinous Neoplasms and these seem to be almost everywhere now a day, IPMNs are what we call them and they are cystic lesions of the pancreas. They can be found throughout the pancreas, either in the main of some of the cytology sampling of the fluid duct of the pancreas, or in the branch ducts of the pancreas and those are called Branch Duct IPMNS.

We can use the various different tools and imaging techniques to try to figure out what kind of cysts we're dealing with, whether or not it's mucinous by sampling, perhaps, some of the fluid inside and then, we can start to understand also, some of the features of the cyst, such as are there concerns for cancer development within the cyst lining on some of the cytology sampling of the fluid or other concerning features like that.

There's another cyst that does have cancer potential and that's called a Mucinous Cystic Neoplasm. These are more often found in women, actually, and when we look at the cyst lining, they stain positive for estrogen receptor and progesterone receptor. They do have

cancer potential, often located in the body, or the tail of the pancreas. We can also differentiate those cysts from, let's say the pseudocyst by characteristic imaging findings, and also sampling some of the tissue.

There's another precancerous lesion that's important to understand. Those are the pancreatic intraepithelial neoplasia lesions or PanIN lesions for short. These are small intraductal lesions that are formed by abnormal proliferation's of ducts and they actually vary in degree of dysplasia from PanIN-1, which is, let's say the most benign to PanIN3, which verges on basically, carcinoma in situ.

Some pancreatic cancers arise from PanIN, but not all PanINs actually become cancers and the tricky part about them is that we don't really think at this point we have a great way to image them on a CAT scan or an MRI. We might think that there are some changes that we could see on a very specialized technique called endoscopic ultrasound when we're looking at the pancreatic parenchyma that might suggest the presence of PanIN, but oftentimes, we're not able to tell that those lesions are actually present.

When we look at autopsy studies, however, you know, patients that have passed away for various different reasons, they walk across the street, get hit by a bus and pass away that way, we actually see that PanINs are very prevalent in your average American, but we do also know that we see more PanIN lesions and more advanced PanIN lesions in patients who have pancreas cancer.

So when we look at, let's say, the resections, the pancreatic resections, for patients who have pancreatic cancer, we see a lot of PanIN-3 lesions and PanIN-2 lesions in the area surrounding the pancreas, so we do think there's a clear association and a fairly well defined genetic sequence of events that lead to the development of cancer.

Ana Maria Rosario:
Let's focus on the best imaging options to capture the pancreas, what are your recommendations?

Dr. Aimee Lucas:
What often happens is that patients will have a CAT scan first and so this is either happening directly to look at the pancreas or because of something else, perhaps, we're looking for appendicitis or gallbladder disease or something else and we happen to capture the pancreas. So I think that CAT scans are a very valuable technique in looking at the pancreas, particularly if they're pancreatic protocol CAT scans.

Other techniques to image the pancreas include MRI exams and those can really, in conjunction with a cholangiogram that we do through the MRI, can really give you a nice look at the pancreatic ducts, the side branches, and investigate for any cysts.

Abdominal ultrasounds are not used often and that's because it's very challenging to visualize the pancreas, given its position in the body on a trans abdominal ultrasound, but what we can do is we can place an ultrasound probe into the stomach and into the first part of the small intestine by using an endoscope and then, ultrasound at the end of the endoscope. This is a technique called endoscopic ultrasound and that actually, nicely allows us to visualize the pancreas, get a good look at the entire organ and the nice thing about endoscopic ultrasound is that if we see any abnormalities, if we see a mass or if we see a cyst that's of adequate size, we can actually sample some of that fluid and image the pancreas and makes a diagnostic decisions at that same time, so endoscopic ultrasound is also a nice tool to image the pancreas.

Ana Maria Rosario:
So what is your general thought process for monitoring pancreatic cysts? Is it a watch and wait pattern are something more proactive?

Dr. Aimee Lucas:
So pancreatic cysts are a challenging problem as we discussed earlier on and when we look back at our older literature, we used to think that the risk of pancreatic cancer in some of the IPMNs was actually very, very high, particularly in the main duct IPMN.

So we used to think that cancer risk was somewhere between 30 and possibly even 70 percent in some of these patients with IPMNs and that's because when we looked at our studies, we had looked at patients who had undergone surgical resections of the pancreas and looked at how many of those patients actually had cancer or dysplasia in the pancreas, but more recently, we've looked at larger, more epidemiology type approaches to figuring out what actually happens with these pancreatic cysts.

So, some groups have actually pulled the ICD9 or the billing codes for pancreas cysts from large health data sets, such as the Kaiser data set and Bretchin Woo (11:30) did this out of Kaiser and they can look at all patients with pancreatic cancer and sort of follow to see what happens over time.

What his studies have showed is that the risk of cancer is actually quite low and much lower than we thought it was in some of the previous surgical literature and that we see the pancreatic cancers, particularly very early on once patients are diagnosed with a cyst, we often see the pancreas cancers within three to six months of the cyst diagnosis. Then, your risk of pancreas cancer is actually decently low from that point on.

Now, that being said, it doesn't mean that it's low enough that one can ignore the risk of pancreas cancer if we identify a patient with an IPMN or an Intraductal Papillary Mucinous Neoplasm, so we have certain criteria where we can sort of use these criteria to determine next steps for the surveillance and management of pancreatic cysts.

These have been modified over time so that we can figure out what the really high risk criteria are and what can sort of place our minds at ease. So when we look at a cyst, we look for some of the high risk stigmata of cancer and that's really a patient with obstructive jaundice, meaning the ducts are blocked because of a cyst in the head of the pancreas, an enhancing solid component within the cyst, or if we have a main pancreatic duct that's greater than about 10 mm and if a patient has any of those characteristics in the presence of a cyst, then, we do recommend thinking about surgery and consultation with your local pancreatic surgeon.

If the patient doesn't, we look at some worrisome features. From a clinical perspective, that can be pancreatitis in from an imaging perspective, it's whether or not the cyst is large, meaning about 3 cm or larger, it has a thickened or enhanced wall, the pancreatic duct is somewhere between5 mm and 9 mm, there's a non-enhancing mural nodule, or just an abrupt change in the caliber of the pancreatic duct with some distal pancreatic atrophy.

If we see any of those things, then, we moved to an endoscopic ultrasound, the technique I mentioned earlier, and then, from there, we can make some further decisions on whether or not to go to surgery. If we don't see any of those things, then, we can look at the size of the largest cyst we can really determine surveillance intervals from there.

I mean, we have guidelines that were published in Pancreatology a few years back that suggest the interval for monitoring some of these cysts. So if the cyst is large, meaning over 3 cm, we follow them quite closely, perhaps, every three to six months, perhaps with an MRI, alternating with an endoscopic ultrasound.

Whereas, a smaller cyst, perhaps, something that's less than a centimeter, you can really probably get away with a CAT scan or an MRI in about two or three years. Then, cyst sizes that are in between those two, you think about some sort of intermediate surveillance interval.

Ana Maria Rosario:
Are there any closing thoughts on this topic before we wrap up our discussion today?

Dr. Aimee Lucas:
No. I think you've raised a lot of important points today. One of my main concerns is always trying to figure out ways to better prevent patients from getting pancreatic cancer because then, I think we can really make an impact on disease morbidity and mortality and then, also, investing really in a lot of pancreatic cancer research so that we can figure out better ways to treat those patients who are diagnosed with pancreatic cancer so that we can improve their survival.

Ana Maria Rosario:
Well, with that, Dr. Lucas, thank you for being here and I'd like to thank you for your time and insights on identifying pancreatic cancer.

I'm Ana Maria Rosario for ReachMD. To access this and other important interviews, please visit www.reachmd.com and thanks as always for listening.