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Kendal Williams (Host): Welcome, everyone, to the Penn Primary Care Podcast. I'm your host, Dr. Kendal Williams. Pancreatic cancer is a disease that affects us all, both in our personal and professional lives. We all know someone who's been affected. My neighbor died of pancreatic cancer two years ago. I've diagnosed two patients in the last six months in my practice with pancreatic cancer, and it's an experience that many primary care physicians will have, if they have not already.

So I wanted to bring some folks on to talk about this disease. One of them you know, Dr. Nuzat Ahmad, is the Associate Director of Endoscopy at HUP, the Vice Chief of the GI division. She's a Gastroenterologist and a Professor of Gastroenterology at Penn. Welcome back, Nuzat.

Nuzhat Ahmad, MD: Thank you, Kendal.

Host: You may remember Dr. Ahmad from our previous discussion of pancreatic cystic lesions and how to work them up. Dr. Ursina Teitelbaum is a Medical Oncologist and the Clinical Director of the Penn Pancreatic Research Center. This is her first time here. Ursina, thanks for coming.

Ursina Teitelbaum, MD: I really appreciate being invited.

Host: Dr. Bryson Katona has an interesting area of research. Dr. Katona is a Gastroenterologist, and he is the Director of the GI Cancer Genetics Program at Penn, and also the GI Cancer Risk Evaluation Program, and has made it his life's work to figure out how to detect cancer early and prevent it. Thank you, Bryson, for coming on.

Bryson Katona, MD: Thank you so much for the invitation. Definitely looking forward to the conversation today.

Host: So, I feel like we're on the defensive with this cancer, and I'm a little bit sick of it. We wait for it to develop. We don't really have any screening that we're actively using. Bryson's going to tell us about more things maybe that we should be using. But it's very common.

Just some statistics, the pancreatic cancer is now the third leading cause of cancer death in the world. It's moving up the charts though. There are nearly 50,000 deaths a year. The lifetime incidence is 1.7%. So it's, you know, one out

of 100 or one out of 200 chance that any single individual will have pancreatic cancer.

And it's a very bad cancer. It's a frustrating cancer to treat because the five year survivals are not great. Five year survival for patients with localized pancreatic cancer is about 37%. That may change. Ursina will update us with that, but that's what it's been historically. It's 12 percent for those with regional disease and only 3.1 percent for patients with advanced metastatic disease. It's one, I think, that many doctors don't want to have themselves in their personal lives and are pretty unhappy to diagnose in their patients. So we want to talk about it. Ursina, let me start with you. Any thoughts? I mean, I just gave just a general intro, but you do this all the time. Anything striking you want to mention up front?

Ursina Teitelbaum, MD: Well, pancreatic cancer has a terrible reputation. We have a lot of new therapeutic combinations just in the past 13 years. And so I think those numbers are probably better. The data hasn't caught up with the new therapies. Pancreas cancer is a relatively chemotherapy resistant tumor and that's been part of the issue. So figuring out how to target it successfully in patients that are very symptomatic is the key. I actually also boarded in Geriatrics and about 10 years ago in Palliative Care and about 70 percent of my practice is pancreatic cancer because it is a cancer of aging and it's a cancer with a high symptom burden.

But I would say I'm actually much more hopeful than I have ever been, about the future of treating pancreas cancer. But to your point, the problem is patients have it. And oftentimes, more often than not, about 85 percent of the time it is, has spread. It is not, or is not operable. And that's the problem. It's almost always found at advanced stages.

Host: So let me just say that for this podcast, we're going to talk about pancreatic adenocarcinoma, which is the primary cancer of the pancreas and the one that you know, we worry about. There are other cancers of the pancreas that are less common and are treated differently, but for today, we'll be talking about pancreatic adenocarcinoma.

I want to talk a little bit about the epidemiology and risk factors. Ursina, you mentioned that it's an older population and from my reading, the median age of diagnosis is 70 years. And, on a broad level, it appears the risk factors, the known risk factors are smoking, potentially obesity, potentially diabetes, potentially alcohol use.

I say potentially because I'm not sure if these have all been sort of tied down as clear risk factors. And then there's a genetic component we're going to highlight in here. So, Bryson, let me go to you. How do you think about this cancer in terms of the risk factors? Of the list of things I said, what do you actually think reverberates as true?

Bryson Katona, MD: I do think that the risk factors play a major role, but when we think about pancreatic cancer in general, we think probably about 90 percent of these are sporadic pancreatic cancers that are, potentially related to some of these personal or environmental risk factors, but this 90 90 percent doesn't have a familial or a hereditary component, whereas about 10 percent of these cancers are found within families either that have a very strong family history of pancreatic cancer or have some sort of germline genetic susceptibility, to pancreatic cancer. But, that group at high risk because of familial or genetic causes is just a very small slice of the pie of all pancreatic cancers.

Host: If someone were to ask me, how do I avoid having pancreatic cancer? What can I do in my life? My spiel is usually don't smoke, don't drink alcohol, because I think that raises the risk of all cancers. It's a little less clear to me whether it's a risk factor for pancreatic cancer. There's something about, meat eating as well. Is there anything else that we should say or, and are those valuable to even mention?

Ursina Teitelbaum, MD: I would say that age is really number one. You have to live long enough to make enough mutations to make a pancreatic cancer. Correct me if I'm wrong. It's something like close to 70 mutations need to happen. I think smoking is associated, but it's not as strongly as you'd think. You have to smoke a lot to really have it be associated.

And metabolic syndrome, you know, we sort of think of that going along with it obesity and activity, diabetes. But you can have all these things and never develop pancreatic cancer and none of these things and get it. So it's always the number one patient question in my clinic.

How did I get this? And almost never do I have an answer. Although it is a standard of care now, and Bryson can speak to this, that we do genetic testing on every new diagnosis of pancreatic cancer because it may have therapeutic implications for the patient and you never want to, I always tell patients, you're not an island, you're a village. You never want to miss out on a family with a familial cancer syndrome.

Host: The typical scenario for us in primary care is that a patient presents with weight loss, or abdominal discomfort, or jaundice, or all three. The patients I sent to Ursina, one came in with weight loss and fatigue going on for a few months and then came in with jaundice, and I knew something was going on.

The, the second had some non specific abdominal complaints we initially thought were constipation and then came in, it was clear that she had lost some weight and so we investigated and found pancreatic cancer. So we usually get a CAT scan back that has identified a mass in the pancreas, head or tail.

And then what I do, is I call Nuzat or one of her colleagues, Dr. Ahmad in the Endoscopic Center to try and get this worked up. So, Nuzat, can you is that the right thing to do? Number one, when we have a patient we've diagnosed with this, to call you or one of your colleagues? And then what happens to the patient after that?

Nuzhat Ahmad, MD: Yeah, Kendal. So I think in the world of GI and this specific field of advanced endoscopy, we really play a supporting role. We basically support Ursina and her work. So essentially we do endoscopic ultrasound. We use that to look at the mass and biopsy it. We do not use it for staging because, you know, studies have shown that we can overstage masses in the pancreas. So that's usually done by cross sectional imaging. Now over the years, I think the pendulum has swung to getting tissue on almost all cases because, correct me if I'm wrong, Ursina, that we have now moved towards neoadjuvant therapy. So maybe 15 years ago, if you had a mass that looked fairly resectable, the surgeons would say, Hey, look, this is cancer. Looks like a duck, walks like a duck. It's cancer. I'm taking the patient to the OR, but not anymore. Because more and more patients are going, if they're borderline resectable, they're going for neoadjuvant therapy. So we almost always get tissue in all patients. So that's our number one role.

And secondly, if patients have jaundice, then we typically go ahead and do an ERCP and put a biliary stent in to relieve the jaundice. If the patient is going for surgery, the role is somewhat controversial. Do you actually really need to relieve their jaundice? Some patients may have such severe jaundice that they have pruritus, etc.

So, you know, we want to relieve those symptoms. But for the most part, we do go in and put a stent in. And obviously if they're getting chemotherapy, then you definitely want to drain their liver so that they can clear the medications.

Host: Nuzhat, are you able through endoscopic ultrasound to get better images of the pancreas than what you can see on cross sectional imaging? Like is there independent value? Let's say a surgeon, maybe there appears to be a localized resectable lesion, would you do an endoscopic ultrasound to kind of figure out if that is actually the case, or do you think cross sectional is fine?

Nuzhat Ahmad, MD: Ultrasound and cross sectional imaging are complimentary tests. Endoscopic ultrasound definitely has higher resolution than cross-section imaging. We are able to pick up very, very subtle lesions that may be missed on cross-section imaging. And I think that role is very important when we screen for pancreatic cancer, as I'm sure Bryson will talk about. When we have a mass in the, the pancreas, it's less often if it's a solid mass that the EUS will provide additional information, incremental to what cross sectional imaging has provided. And the main role in that is really providing tissue. Staging, I would say, I mean, we almost never use EUS for staging pancreatic cancer.

Host: Can I ask about these biliary stents? So you put in a biliary stent, does it need to be changed? Do they fall out? What are some of the things that we need to think about with biliary stents?

Nuzhat Ahmad, MD: So there are two types of biliary stents. Very broadly speaking, there are plastic, which are temporary and can be removed. And then there are metal stents, which are permanent and typically cannot be removed. There's a third type of stent, but I won't get into that. So when patients come in and we don't have a diagnosis, typically like, you know, we'll do a something we call a double header.

We'll do an EUSFNA, which is a biopsy, and then we will put in a stent. We will put in a temporary stent because there's no management plan. We don't know exactly which way the patient is going to go. So we'll put in a plastic stent because if the patient goes for surgery, they can just be removed at the same time and it doesn't cause as much scarring as a metal stent does.

So the surgeons tend to like the plastic stents a little bit more than metal stents, if the patient is a surgical candidate. If however, the patient becomes unresectable or is not getting better with neoadjuvant. And we know that this road may not lead to surgery. Then we go in and put permanent stents.

And the difference is that the plastic stents need to be switched out every three months. So, you know, there is, patient has to keep on coming back. Whereas the metal stents can stay for much longer. So the patients don't have to come

back for switches. Up to 30 percent of them, if the patient lives long enough, will develop occlusion, and we have to go in and revise them. But still better than coming in every three months.

Host: That's very helpful. I think one of my patients ended up having an occlusion or I managed a patient recently that had that. Okay. So the tissue, comes from the EUS, tissue comes back from the lab. We all see it. It's adenocarcinoma. And then what should happen in your world? How does the patient go to Ursina from there.

Nuzhat Ahmad, MD: So, I will tell you, sometimes we have patients who have no idea that this is going to be a cancer. Meaning no one's talked to them, they've been told they have a finding on an imaging, and go see you know, the GI for a biopsy. So there's a little bit of this, like who is going to tell the patient because, you know, telling them over the phone with no management plan is just, it's not a position you want to put anyone in. So we activate the wonderful Trish Gambino, who's the nurse navigator,

Ursina Teitelbaum, MD: Who's a dedicated pancreas nurse navigator. We're very lucky in our Penn system to have a pancreas nurse navigator, which is sort of one of our innovations because to Nuzat's point, it gets really tricky at this, at this juncture.

Nuzhat Ahmad, MD: Right? And sometimes when, you know, I talk to them in recovery and I tell them, look, every time we see a mass, this is cancer until proven otherwise, etc. And then I feel more comfortable calling them on the phone and saying, hey, look, the biopsy came back. It's a cancer. But, you know, there are lots of follow up questions that they have, obviously, like what's going to happen next.

So, I try and line up as much as I can. So I talk to Trish Gambino, she will usually get an appointment really quickly for a patient and I'll tell them, hey, you know, you have a surgical appointment, an oncologist appointment lined up, and typically they will end up seeing Ursina mostly, or one of her colleagues, and then we take it from there. We try and communicate back to the primary care physician as well, obviously.

Host: So let's talk about the various stages, if you will. Ursina, you can correct me, but I, I understand sort of practically it breaks down to localized, regional, and metastatic. I'm sure there's a more sophisticated staging.

Ursina Teitelbaum, MD: Even more practically, it breaks down. There's a TNA staging and an M staging, but you're either surgical or you're not surgical. And that's actually the most functional way to look at it. You can have a tiny tumor that's node negative, but if it's up against the wrong vessel and it isn't coming off, it isn't surgical. You can have a large tumor with several nodes around it and if it's up and away from the vessel, that is curable. That is resectable. So, it is actually a very tricky staging. And I confess, first of all, we look at them in, in pancreas tumor board, but also, I have quit being able to accurately predict what the surgeons will call surgical or not surgical, because that line is actually moving.

We have a new category called borderline resectable, which has only been possible because we have more effective chemotherapy. Before we had effective chemotherapy, it was really all or nothing. And now we are able to render some patients resectable with chemo and chemo radiation. But initially, when you have that tissue diagnosis, we need to see on the CT scan, do they have lesions in the liver or in the peritoneum, less often in the lung.

And then that is clearly not surgical and the really confusing part to patients is you can have what looks like a localized tumor, but if there is one spot in the liver, they aren't going to the OR. And patients are savvy enough to know that if it isn't surgical, it isn't curable. Most of the time they understand that, but it is a tricky conversation.

If they are localized and surgical, to Nuzat's point, that's when it becomes an interesting discussion of sequencing. Are they going to get surgery first? And then they get six months of triplet chemotherapy after. Radiation has actually fallen, in the order now, if at all. It's actually controversial whether or not these patients in the post op setting will get radiation at all.

Sometimes, we hold on to the belief that some chemotherapy up front may be advantageous. It's the same amount of chemo. It's sequencing. You're just splitting and giving some up front. Because most of the time when patients recur after surgery, they don't recur in that pancreas bed where the scalpel was. They recur distantly. And the other thing is when someone has a big surgery like a Whipple, you hope to get chemotherapy in after 12 weeks, but we know some patients will never get chemotherapy. So giving chemotherapy up front also ensures that they get some systemic therapy. It may help eradicate micromets.

And you also get the biologic behavior of the tumor because you have the tumor in vivo. So we literally give you some treatment and then we look and see, did it

grow? Did it shrink? Whereas if you do it after surgery, I'm committing you to six months of FOLFIRINOX and I don't even know if it works on your tumor because it's not there to follow.

We are often encouraging our surgeons to let us meet the patients at the same time or early and often and be part of the conversation. And it is anxiety provoking for patients because patients want that tumor out yesterday, but there can be an advantage to getting chemotherapy in sooner.

Host: Even for patients that you know are resectable, the point you just made is that after resection, it's three months before they could get chemo, it'd be better for them to get some chemo. So even for those you know are resectable, you consider chemo up front.

Ursina Teitelbaum, MD: The truth is we don't have the data to prove that, and so if you have a patient that is completely resectable and that patient and the surgeon want to go to the OR, we say fine, come back to us soon, like four weeks after, so we can start to prepare you for postoperative therapy. And there is, you know, different surgeons have different practices, to be truthful, so there can be some variety in how they handle it.

Host: And so you mentioned neoadjuvant chemotherapy. So this is, you know, I think by definition, chemotherapy prior to surgery. And so, I guess it's the patients maybe that are in the gray zone, in terms of vascular invasion, where you might do neoadjuvant to try and get it off the vessel so it can be resected?

Ursina Teitelbaum, MD: Sometimes the surgeon will say, you know, Ursina, I could do the surgery today, but if you could shrink it up a little, it would be easier, it would be a better chance of being an R0 resection. They are actually really coming on board because they're seeing that they don't have worse outcomes.

We work really hard. We actually have cancer nutritionists that follow the patients with me. I have a high burden when I'm giving chemo to a potentially resectable patient. I have to keep them nutritionally replete enough to recover from that surgery. So I work really closely with our nutritionists.

We also have palliative care embedded in our clinics. So we have a lot of supports to keep the patients well because I have to deliver them back to the surgeon. So, I'll give two months of chemo, get a scan. Surgeon will look, say, sometimes they'll say, how are they doing? I'm like, great. They're like, give them two more months. And I do. And then sometimes then I give two months

after, like, it's a little bit fluid on how to do it. But it is a high burden for me because I have to keep them well.

Host: Let's talk about the chemotherapy itself. You mentioned the regimen. Can you just take us through, is it the same regimen for all? Is chemo just chemo, or is there, does it depend upon the stage at which they're presenting and so forth?

Ursina Teitelbaum, MD: So in the post operative setting, the optimal regimen is FOLFIRINOX, which is a three drug regimen. It's infusional 5-FU that you wear in a pump for two days at home every two weeks. Oxaliplatin, which is a two hour drip every two weeks. And the major side effects here are neuropathy. Which can be very significant for patients that are frail, that are fall risks, that are diabetic, that have neuropathy for other reasons.

We always say nausea, vomiting, fatigue, decreased blood counts. The third drug in that combination is irinotecan. Some people call it, I run to the can, major side effect, number one, diarrhea, number two, diarrhea, number three diarrhea. And that has hair loss. And with this regimen, you need a port and you need growth factor.

So it is a, an intense regimen. And again, the standard now is that you give six months after, but we're trying to give some before. If you give chemo beforehand in the neoadjuvant or preoperative setting, anothereoption is gem Abraxane. Gem Abraxane isn't validated in the post op setting, but you can give gem nab-paclitaxel as a, a doublet combination. Even though it's just two drugs, doesn't require a port or growth factor, it's actually pretty toxic too. Also has hair loss, decreased blood counts, nausea, vomiting, and neuropathy. So we actually have two combinations in the front line and then one robust combination after surgery.

Host: But it's real chemotherapy in the old style, you know, now we have chemotherapy people take by mouth and go to work and, but this is really, this is a life event.

Ursina Teitelbaum, MD: This is real chemotherapy. What I tell them is the real innovation in the past 25 years has been in our supportive drugs. So we can manage and hopefully prevent nausea in most patients. And by doing that and then limiting neutropenia, infection risk, visits to the ER; we can usually keep patients reasonably well, but with this regimen, you don't feel great the first week. You feel back closer to your baseline the second week, just in time for your next dose.

Host: So you know, I was reading that most people die of pancreatic cancer, who do die of pancreatic cancer, die actually sort of of wasting, right, and malnutrition, both because of the metabolic effect of the tumor itself, but also because it's in a location that affects digestion and affects the desire to eat. So your, your job is kind of tough, and you alluded to that earlier, where you have to sort of balance these factors because you're trying to keep these folks as nutritionally replete as possible through that process so they don't fall behind in that, that overall war that they're fighting.

Ursina Teitelbaum, MD: It is, it is really difficult. We have to keep them nourished. We have to keep them well. A lot of them have malabsorption and then there can be insurance issues, cost issues with getting CREON, with getting pancreatic enzymes. It is a tricky space. But when you get someone to the OR successfully, and then you follow them in surveillance for years, it can be very rewarding.

And I, really do feel like we have more patients that are coming through the surgery and coming through recovery and surveillance much more successfully, but it is a labor intensive.

Host: Is there a role for enteral nutrition?

Ursina Teitelbaum, MD: Not really.

Host: Okay. I, I was just curious. It sometimes comes up because you know, we face on our end of these folks that come into the hospital and they, we have these questions about whether or not we should add enteral nutrition. They're losing a lot of weight and families are concerned and so forth. But I gather the evidence has really not shown that adding enteral nutrition has been beneficial.

Ursina Teitelbaum, MD: Not that I'm aware of.

Host: And not part of your practice. Now you mentioned that you feel better about where we're headed with the therapies and that our rates are starting to improve. Can you get into that a little bit?

Ursina Teitelbaum, MD: In 2018 at ASCO, which is our big cancer conference, they showed, the first time with the regimen for FOLFIRINOX after surgery that median overall survival was 56 months. And you have to imagine it used to be 20 months with surgery and chemotherapy and radiation. So we're really moving that needle, and our survival rates are much better. That's why I've said I'm waiting for it to translate into those survival numbers

that you were quoting. And then our chemotherapies are better too. I used to, when I would meet a patient, for example, with metastatic, we used to have gemcitabine and that was it. And was never shown to actually prolong survival.

But it was approved because it made sick people feel better. And it was approved in 1996 and we had nothing since then. A very wise mentor once said, you know, we used to run out of drug before we ran out of patient. And now we have multiple regimens and sometimes we run out of patient before we run out of drug options because we have more treatment options. And we had regimens approved in 2010, 2012, 2015, 2018. So the pace of discovery is much better. And the way I really characterize that with patients is that I used to, I may not be able to cure you, but this is a treatable cancer. And I used to quote survival in months, and now I actually can comfortably often say year or years.

And we can do it with a tolerable quality of life. It has to be life worth living. And so it's become a much more treatable cancer. And we also have a lot of clinical trials, as you can imagine, in this space. Our goal is to figure out how to make immunotherapy work for pancreatic cancer. And that is the focus of a lot of our trials and CAR T.

We're actually working on all of these things. COVID set us back a little bit in terms of trials. This is nationally, globally, really, but we're really perking up and have a lot more in our armamentarium.

Host: I saw a an abstract or something that came across my brain in the last six months or so. I think it was CAR T therapy, and just showing some good numbers.

Ursina Teitelbaum, MD: I think we need time. I'm hopeful we'll crack it, but it takes time, and if we could just detect it earlier, that would be better, and I know that there are a lot of people working on that.

Host: So let's get to that in a second, but I actually want to highlight what you said because it may have gotten lost. You know, I had quoted data from what was published in a it was in a textbook, so, you know, those are a little bit older, too. But, 37 percent five year survival for localized disease, but you're saying median survival now is 56 months, which is almost five years, right?

Ursina Teitelbaum, MD: If they're resectable. I used to quote to fellows, you know, the, the re, the issue with the pancreas is it's like in a superhighway of blood vessels and lymph nodes. So it can be very early and still has the potential to spread. We really think of it as a systemic disease now. So, I used to quote

the fellows, one in five chance of the tumor being surgical, it's about 15-20%, but even with surgery, one in five patients alive at five years, certainly better than that now, and again, I, think 37 percent may be starting to be low.

Host: That's wonderful news. So when we go on the offensive with these tumors, you know, in various scenarios with whether it be had been breast cancer or colon cancer, obviously we've worked on more effective therapies and I'm thrilled to hear we're getting some progress, but a lot of the success has been in both prevention but also early detection, right?

So, Bryson and I'm going to now turn the discussion over to the area that I think is your focus. we talked a little bit about the fact that the risk factors, there, there's no single risk factor. This isn't mesothelioma, right? Where it's just, you know, it's all tied to asbestos. If you avoid asbestos, you can avoid mesothelioma.

This is, has a lot more going on. And you mentioned that the genetics are only a small portion, but let's get into that a little bit. What are you doing in your area now?

Bryson Katona, MD: Yes, I think, for early detection of pancreatic cancer, I see a number of patients who come in and really nobody had any idea that there were any programs for early detection of pancreatic cancer, that pancreatic cancer screening, you know, was even, a thing that people could consider pursuing.

And I think this field of early detection in high risk individuals is one that's kind of progressed so much over the last couple of years. Now I think before I get too much into the weeds here, I think it is important to say that for the average risk, meaning no genetic mutation, no, no strong family history of pancreatic cancer, for the average risk individual who's asymptomatic, there's really, at this point, still no role for pancreatic cancer screening.

And that's actually been stated pretty point blank by the U. S. Preventative Services Task Force, where they have explicitly come out and said those, those individuals at average risk should not be screened. But that being said, you know, we do have many high risk groups where screening is now formally recommended.

Those come in two flavors. One is based on a family history alone. And so we consider individuals who have familial pancreatic cancer, and that's where you have two relatives with pancreatic cancer who are directly related to one another

and then your patient is directly related to one of those two individuals. Those patients, are eligible for pancreatic cancer screening, typically starting around age 50. And then you also have the gene mutation carrier. So we know many genes are associated with increased pancreatic cancer risk. So some of the most common ones we see are, are individuals with the BRCA1 or BRCA2 mutation.

Some of the other breast cancer risk genes, such as ATM or PALB2, the Lynch syndrome genes, and then some of the rarer syndromes, such as Peutz-Jeghers syndrome. Most of those high risk individuals, they don't need two family members with pancreatic cancer. Oftentimes they're eligible for screening with just one family member.

And to be honest, actually some, the pendulum has been swinging such that just carrying the gene mutation itself, regardless of the family history, is oftentimes enough to get screened because, you know, especially when you're talking about cancer risk syndromes, people may have died earlier of other cancers.

You may have small family histories or sometimes patients don't know their family history. And so when you use family history to determine who's eligible or who's an eligible screening candidate, you know, it certainly can bias who that decision is made for.

Host: So who should we be referring for genetic testing? I mean, I can envision this. It's, it's fairly obvious if a patient comes in and says, you know, my dad had pancreatic cancer, my brother just died of pancreatic cancer, I'm really worried, right? So, that seems obvious, but these genetic syndromes work that one family member has, there may be breast cancer heavily in the family, right?

And, or you might have colon cancer heavily in the family. And so what are some signals we should be looking for as primary care just to then go ahead and refer them for genetic counseling and testing?

Bryson Katona, MD: Yeah, so you know, our bar for doing genetic testing has gotten infinitely lower over the last five years. Just to a little bit to our CNS clinic, so when patients are diagnosed with pancreatic cancer, there's actually now a genetic counselor who's embedded in the pancreatic cancer clinic who, does point of care germline genetic testing on any patient who's diagnosed.

On patients who you see in the office, nowadays, anybody that's had a first degree relative with a pancreatic cancer, where that relative didn't have genetic testing, technically is eligible. So, you know, somebody comes in, their father died of pancreatic cancer 30 years ago, you know, clearly before the time of any

genetic testing, that individual would be eligible for testing based on that single family history point alone. And you know, I think the nice thing, regardless of whether or not, maybe it's a strong family history of colon cancer. Maybe it's a strong family history of breast cancer. The way that genetic testing is being done now is that, we don't necessarily have to you know, pigeonhole ourselves into just a small range of syndromes that we test for, but when someone comes in for testing, if they want, we can test them for it all.

Whether we test for one gene or 80 genes, the process for the patient, the price for the patient and the cost for the patient, is all exactly the same.

Host: So, the bar is pretty low if, uh, there's a strong family history of cancers. And, I guess, pancreatic cancer, though, is, like, you're not going to necessarily worry about somebody who's has a family history of sarcoma, for instance, right? So, it's really, just want to go through this. This is for my own benefit.

Breast cancers, there's an alignment, right? Colon cancer, there's an alignment. Pancreatic cancer, for sure. Any other cancers that would raise a flag in your mind that says, okay, you know, I should send somebody?

Bryson Katona, MD: For the BRCA kind of genes, you know, if you see families that are high risk in breast, ovarian or prostate cancer; those are individuals that may be harboring genetic risk for pancreatic cancer as well as those other ones. And then kind of the other big group is the Lynch syndrome, patients.

And so if you're seeing colon cancer, uterine cancer, potentially stomach cancer or urinary tract cancers, you know, those kind of cluster together, as well. You know, I think a lot of people don't realize how cheap and easy genetic testing is now, but we basically can do it with a saliva sample.

And even if patients decide to totally forego their insurance and just pay out of pocket for the genetic testing, max cost is only $249 now regardless of the number of genes that are tested.

Ursina Teitelbaum, MD: And we're really lucky with our genetics program, Kendal, and all of our Penn hospitals. You can have a patient come in with a fulminant diagnosis or presumed diagnosis of pancreas cancer. I have called them and said, I think this patient is dying in the next few days. Can you come and test this person so we can capture this family's risk? And they will come to the bedside in the hospital.

Host: That's tremendous. I think I may have even heard that like Ancestry. com and some of these other places that you can send your saliva to get tested are actually now testing for some genetic cancer syndromes. Is that right? Bryson?

Bryson Katona, MD: The, the, issue with some of these commercial genetic testing companies and 23 and Me is the one that, that is advertising that, so they actually do report that they test for, some BRCA1 and 2 variants.

The issue is, is that they actually only perform dedicated testing for three Ashkenazi Jewish founder BRCA1 and 2 variants, and they don't do complete BRCA1 and 2 testing. So we've actually had individuals from very high risk families that have had 23 and Me, they get a negative BRCA1 and 2 report back from them, and they think they're in the clear, but in fact they're carrying a BRCA2 mutation that just doesn't fall within those three founder mutations.

And basically tell patients that direct to consumer genetic testing is for fun, but I don't, don't really trust it for true clinical decision making.

Host: Well, I hope that question wasn't painful, but I actually found it really valuable the answer because I, this comes up. I mean, I, know that because somebody mentioned it to me, family member or patient. So that's actually really valuable. I do not order genetic testing, outside of the context of your counseling program. Because I really don't know how to counsel people and I don't like getting lab tests back that I don't know how to interpret. I suppose that's probably best practice?

Bryson Katona, MD: Yes, definitely. There are a few things, you know, we always definitely discourage providers from ordering the genetic testing directly for several reasons. One important part of the counseling actually is that while there are protections in place to protect against health insurance discrimination or workplace discrimination that could result from a positive genetic testing result; there are currently no protections in place for disability insurance, for life insurance, for long term care insurance. And so if a patient has genetic testing sent without any appropriate counseling, and they're found to have say, a BRCA1 gene mutation, their chance of getting a reasonably priced policy has sailed. The other issue is, is that a lot of times these genetic testing reports come back with uncertain findings. So these uncertain findings are always subject to change, down the road. And, the issue is, is that once you're the ordering provider for someone's genetic test, you're basically on the hook for their uncertain findings for life.

We have, through the cancer genetics program, we have a, a good mechanism where we have fantastic genetic counselors that follow up on all these altered or changing test reports. But this could be very difficult and cumbersome for, you know, a practice that isn't as fortunate to have so many genetic counselors.

Host: Once you do define somebody as having a genetic syndrome, I think you guys do all the screening, right? It, it's through you that they get, let's say, an MRI of their pancreas on a however often you do it and so forth, right?

Bryson Katona, MD: Correct. Yeah, we have, uh, several different, depending on what type of gene mutation they're found to have. I typically will follow a lot of the individuals with Lynch syndrome. And, we have the Basser Center where they try to, do the comprehensive care for like BRCA1 and 2 carriers. But, yeah, the goal of seeing one of the cancer genetics physicians is really to outline a cancer risk management strategy and plan.

And try to serve as the conductor to make sure that, you know, all of these different pieces are really getting accomplished.

Host: So let's go back to the average risk, folks, which you said clearly there's no, you know, the USPSTF has said there's no value for screening and that's obviously because we don't have any study that shows value, right. We don't have any evidence that there's anything that we can do. I'm sure we're trying though, right? So about a year or so ago, Richard Wender was on the podcast and talked about screening for cancer generally and did mention a little bit about these newer sort of commonly known as liquid biopsy, you know, detection of genetic material that can be done and where that is at. That's sort of out there. But what's going on in terms of the average risk and trying to build an evidence base that may ultimately satisfy guideline groups like the USPSTF?

Bryson Katona, MD: Great question. And maybe I'll just comment quickly on these multi cancer early detection tests, that I think really are, you know, a lot of people are talking about them, a lot of patients. Of course there's the Galleri test, and then there's a few others that are kind of coming onto the market.

There was also recently a pancreas specific blood test, a test called the IMMray PanCan-d test which actually was just with, withdrawn back off the market a couple months ago due to, uh, the company wanting to retool it. But as far as these multi cancer early detection tests, you know, I think the performance characteristics for early stage resectable pancreatic cancer are just not there.

Galleri, for example, for stage one and stage two, specificity is only, you know, in the 50 to 60 percent range, which is just, really not good enough. You know, they're very good at detecting stage four pancreatic cancers, but by that point, it's fairly limited utility.

As far as for the average risk individuals, I don't know that any pancreatic cancer screening will, any pancreatic cancer screening technique will ever be good enough for the average risk individuals. And that's just because pancreatic cancer is a rare cancer. And, if you think about the number you would need to screen to find an early lesion, it's just too high.

It's a tenth of the risk of getting breast cancer. Pancreatic cancer, it's a tenth of the risk of getting prostate cancer, so it's just a very rare, rare, cancer. I think where the research is really aiming is trying to find other high risk groups amongst what we would consider the average risk population that could then be targeted for screening.

One area, for example, is new onset diabetics, which I know that there has been some work in this area that maybe this is a subgroup that at least for a few years after their diabetes diagnosis, should potentially be targeted for pancreatic cancer screening.

Ursina Teitelbaum, MD: But you could imagine, you get one of these tests and it says you have a pancreatobiliary cancer, cancer cells. And then you get a scan and you don't see anything. So that's going to raise tremendous anxiety. No surgeon's going to take out a healthy looking organ. So that's sort of the conundrum and who's going to take care of those patients then again, like if you ordered that test, they're yours because without tissue, I'm not going to see them.

Host: I remember sharing this with my brother, who's a very, uh, pragmatic primary care physician, very, very well trained. And, you know, I told him about this after Dr. Wender had mentioned it, and I said, and he said, that sounds like a nightmare.

Ursina Teitelbaum, MD: I think it's, I think it's a nightmare. And, I actually wanted to get back to Nuzhat's discussion about biopsy. She's right. They didn't always require biopsy to take patients to the OR, but just like Bryson's talking about wanting to know the germline, the genetic characteristics of the patient; we're increasingly wanting to know the genetic molecular characteristics of the tumor, which we do through next generation sequencing of the tumor. Now it's a very tricky space because the sneaky secret and patients get very upset

because PanCan, which is one of the patient advocacy groups, you know, they have this logo, know your tumor, and you can know your tumor with pancreas and there really are no targetable mutations, beyond BRCA with PARP inhibitors. So it is really tricky. And the other thing I would say is it's very difficult to biopsy pancreas cancer. Sometimes it takes a couple times, which is very frustrating even with an obvious tumor. And we are starting to use circulating tumor material, in that regard, liquid biopsy, if we're not able to get a biopsy with a needle, maybe we can get one from a blood sample. And so that would be in a more appropriate usage of a liquid biopsy if we're really not able to get an actual biopsy safely, which happens sometimes.

Host: So this has been a great discussion, and I, really appreciate you all coming on. It sounds like we're getting close to going on the offensive with this thing. At least we can start to identify higher risk groups, as Bryson has outlined, and, Ursina, it sounds like you and your colleagues all over the world are making progress, so we can feel a little bit better about this. Is there, anything you'd like to leave our audience with?

Ursina Teitelbaum, MD: I like the, even when it's not curable, it's treatable. I often will tell patients it's getting much better, and I encourage some of them not to tell everyone it's pancreas cancer because everyone's face falls and it's all sad, when in fact I think there's a lot of optimism among us that we're doing better; longer lives, better quality of life. I don't think it is the same diagnosis it was 20 years ago, certainly.

Host: You know, I remember the discussion of HIV and back when it was, uh, you know, incredibly deadly and the Surgeon General at the time saying, we're just trying to turn it into a disease like diabetes, where it becomes a chronic disease that we manage over time and people are not, never cured of it, but we keep it at bay. And we've done that with HIV. And so hopefully we can get there with pancreatic cancer, even if we can't cure it. Right?

Ursina Teitelbaum, MD: I think we're moving the needle. It's slow, but it's steady.

Host: Well, that was a great discussion. I really appreciate it. I really appreciated also the practical discussion of what do we do with our patients? How do we get them to you? Let me just ask another question.

I do it through Epic, I email people I know, but is there a main number you can call that says I have a patient needs, you know, has got a pancreatic mass and

needs a sort of an expedited workup? Is there a way that folks either outside of our system or even within, but, don't know you guys directly?

Nuzhat Ahmad, MD: If you want to send for the first step, which is like a biopsy, obviously you can email us, but you can use the consult to GI order in Epic. And we have actually retooled it, and it's going to have urgency levels in it. So just so that there can be an auto triage of the urgent patients.

Host: So if it says pancreatic mass and they're just diagnosed on CT, those patients will be prioritized.

Nuzhat Ahmad, MD: Yes, exactly.

Ursina Teitelbaum, MD: The other path I've seen, is patients go get referred to a surgeon, and the surgeons are often able to coordinate an expedited GI evaluation also, and then you get that extra input as to whether or not it's resectable. And actually, I have to put a plug in Cristabella and Christine Cianci at Presby pioneered this diagnostics clinic.

We recognize it's very difficult in the internal medicine space and even just patients that come into the ER, trying to get all of the work up. So we are now willing to see, and we actually started it now in PCAM, in the main hospital where we will actually, you have a patient with a mass, we will direct the workup.

So we used to say, I said before, if they don't have tissue, we won't see them. That's actually not true. If they clearly have cancer, with a mass, we are happy to help with that now directly. We recognize it is difficult in the primary care space to facilitate everything. And sometimes it's just easier knowing what we are looking for. For example, we prefer a triple phase CT, a pancreas protocol CT. That's what our surgeons prefer. So there are things we can do to make it little bit more streamlined.

Host: I'm glad I asked that question. That was really valuable information. I want to thank our guests for coming on and talking about this very important topic. As we get more, farther down the road with treatment and prevention, we'll bring you back, with some updates. And I hope that's soon.

So thanks to our guests for joining us and thank the audience for joining the Penn Primary Care Podcast. See you again next time.

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