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0:00:15.5 → 0:00:46.1 Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it is a conversation about pancreatic cancer with Dr. Jill Lacy. Dr. Lacy is Professor of Medicine in the Section of Medical Oncology at the Yale School of Medicine. Dr. Gore is a Professor of Internal Medicine and Hematology and Director of Hematologic Malignancies at the Yale Cancer Center.

0:00:46.1 → 0:00:48.4 Jill, thanks so much for joining me.

0:00:48.4 → 0:00:52.3 And thank you for having me.

0:01:07.9 → 0:01:17 So Alex Trebek is the latest in a slew of famous people who have been diagnosed with pancreas cancer. What's up with that?

0:01:17 → 0:02:18.5 It is true that a number of celebrities have been diagnosed with pancreatic cancer. I think we all remember Patrick Swazye, Michael Landon, Pavarotti, Sally Ride and unfortunately like most patients who are diagnosed with pancreatic cancer, they succumb to their disease in a relatively short period of time. So, there is something different about pancreatic cancer relative to other cancers that are commonly diagnosed. And that difference is that the likelihood of surviving pancreatic cancer after diagnosis is lower than for almost every other cancer and certainly much lower than for the common cancers. So, we often talk about 5-year survival rates in the cancer world because that sort of gives us some metric as to how we are doing in terms of curing patients or if not curing them, prolonging their life. And the statistic for pancreas cancer is that the 5-year survival rate is 8.7%.

0:02:18.5 → 0:02:21.9 Still too low?

0:02:21.9 → 0:03:29.4 It is improving, but if you contrast that with other common cancers, breast cancer over 90%, prostate cancer over 98%, colorectal cancer 65%, and all cancers, it is about two-thirds of patients are 5-year survivors. So, it is a dismal statistic and I think that is why this diagnosis has a different impact than many other cancer diagnoses. I would point out that it seems like it is a common cancer because so many famous people have been diagnosed with pancreas cancer and they do get a lot of publicity, but it is actually an uncommon cancer, only about 3% of all cancer diagnoses are pancreatic cancer. The incidence is not increasing, so we do not have an epidemic of pancreatic cancer fortunately, but it is going to move into second place as the second leading cause of cancer-related deaths after lung cancer, probably in about 1 or 2 years - the reason being is that we are making progress in other cancers through early diagnosis or screening and treatments are improving at a more rapid pace

in other cancers compared to pancreas cancer.

0:03:29.4 -> 0:03:45 To what extent is the problem with pancreas cancer the biology of the cancer and to what extent is it just because of the location of the pancreas such that symptoms do not appear until the patients have fairly advanced disease, or is it a combination?

0:03:29.4 -> 0:06:03.4 A combination. So, it is true that about 80% of patients who are diagnosed with pancreas cancer are inoperable at diagnosis and therefore incurable or treatable, and we can prolong life but the cure is illusive for those patients. Only about 20% of patients present with operable pancreatic cancer and that really is the only path to cure at present. And so, this is really in sharp contrast to many other cancers where the majority of patients who are diagnosed with cancer are diagnosed at an early stage where it is curable. And I think there are really 3 major reasons for that. One is as you indicated the inherent biology of pancreatic cancer. This is a cancer that has a predisposition to spread early on in its natural history to distant sites in the body. So, a very small pancreatic cancer may already have spread into the liver or the belly cavity at diagnosis and it is also a somewhat aggressive cancer. It grows relatively quickly, so there is a narrower window for early diagnosis. The second reason is that there is often a modest delay in seeking medical attention. The pancreas is an organ that lies deep in the belly cavity and tumors can get quite large in the pancreas before patients have any symptoms at all and when they do develop symptoms, they are often quite nonspecific and vague and discounted by the patient and often by their physician. So, many patients will have, for example, vague abdominal complaints, some pain particularly after eating, some gassiness, bloating, their stool habits may have changed, but nothing that really raises a red flag. About 40% of patients will present with jaundice, which is yellowing of the skin, the eyes and darkening of the urine. And that can be an early symptom and sign of pancreas cancer. Those are the patients who are most likely to be operable and so that is the one symptom that may present early.

0:06:03.4 -> 0:06:12.8 And that is because the tumors that do that are in the part of the pancreas that is closest to the bowel right and it happens right away or earlier on?

0:06:12.8 -> 0:07:14.3 Correct. These are tumors that arise in what is called the head of the pancreas, and in the head of the pancreas, you have the bile duct which traverses through it and the tumor in the head of the pancreas does not need to be very large before it is blocking the bile duct and the bile backs up and that causes the jaundice. Other presenting symptoms - diabetes, a significant percentage of patients who are diagnosed with pancreatic cancer had a new diagnosis of diabetes within the past year. We see this very commonly. And the reason for that is, pancreatic cancer actually causes diabetes. It is sort of a symptom of the disease through inflammation of adipose tissue and causing insulin resistance. There actually has been some discussion of whether every adult who is diagnosed with new-onset diabetes should undergo screening for

pancreas cancer but that certainly is not a recommendation at this time.

0:07:14.3 -> 0:07:19.3 How would one screen if one wanted to, is that a CAT scan?

0:07:19.3 -> 0:08:23.7 Right. The other challenge with pancreas cancer, the third challenge in early diagnosis, is exactly that - screening. We do not have an effective validated screening tool for pancreatic and that is the reason why many patients present with advanced disease. And again, contrast this with all the other common cancers - mammograms for breast cancer, PSA for prostate cancer, CAT scanning for lung cancer, colonoscopy for colon cancer, Pap smears and HPV testing for cervical cancer. There is not an easy way to screen for pancreas cancer, you would think imaging modalities like CAT scans would be effective, but pancreas tumors often are quite subtle and difficult to see on imaging such as CAT scanning which has had a major impact in screening for lung cancer, for example. We do not yet have a blood test, but there is intensive research in this area. It is a very, very important area for research in pancreatic cancer.

0:08:23.7 -> 0:08:33.2 And are there any family predispositions in pancreas cancer? Can there be?

0:08:33.2 -> 0:10:33 There are some risk factors for this disease that potentially can increase one's risk of developing pancreatic cancer and we will talk about family history, that is important. First and foremost is age. Many cancers are disease of aging, as is pancreatic cancer. So, the typical age at diagnosis is right around age 70, give or take a few years, but about 15% of patients are in their 50s, so we do see this in younger patients and even patients in their 40s and rarely in their 30s. Other risk factors, there is a slightly increased risk for African-Americans versus non-African-Americans, for males versus females, smoking is a risk factor about threefold increased risk if you are smoker and probably about 20-30% of pancreatic cancers are smoking related. Longstanding diabetes is a slight risk factor, about twofold. Obesity is a modest risk factor, about twofold and then family history. So, there is tremendous awareness of the importance of our family history in determining our risk for developing cancer and this is due to the wide availability of genetic testing through companies like 23 and Me and through the public disclosure of a cancer carrying gene by people like Angelina Jolie who carries the BRCA gene, which predisposes to pancreas and ovarian cancer. And so, for pancreas cancer, about 20% of patients will have a family history that suggest that this cancer is hereditary or familial in some way. And if you do genetic testing for genes such as BRCA, you will find a faulty gene that you inherited either from your mother or your father.

0:10:33 -> 0:10:35.3 5% of pancreas cancer patients?

0:10:35.3 -> 0:11:13.8 Right. It is not a big number, but it is not an insignificant number and because of that, it is now recommended and this is a recent recommendation from our professional societies, that all patients and any patient who is diagnosed with pancreatic cancer should undergo genetic testing to

see if they carry a gene that has predisposed them to pancreatic cancer. That probably has implications for them in terms of their treatment and certainly has implications for their family members. So, that is a new recommendation.

0:11:13.8 → 0:11:30.6 Wow and that is big, right because you turn things up, it is not just as you pointed out, it is not just how it is going to effect your treatment but it is now what you do with that information in terms of understanding the risk to your relatives and disclosing that risk potentially.

0:11:30.6 → 0:12:35 It is huge. And we are picking up the familial form of pancreatic cancer in patients with pancreatic cancer and no family history whatsoever. So, we talk about the family history a lot and it is very important, but in this disease now we have shifted to genetic testing. And there are implications for family members. So, I said there is no screening. There is no screening for the general population, but if you are at particularly high risk because for example you inherited BRCA, BRCA does predispose to pancreas as well as ovarian and breast, you can enter into a screening program. Now, the screening is somewhat investigational, but I think it is very important for family members to know this and to potentially participate in screening. Screening involves doing imaging, either an ultrasound through the endoscope called the endoscopic ultrasound or MRI imaging or blood testing.

0:12:35 → 0:12:39 And how often would a patient have that for a nonpatient.

0:12:39 → 0:12:45.3 Well, that has not been worked out fully, so that is a moving target.

0:12:45.3 → 0:12:49.1 Right, I mean endoscopy is not a big deal, but if it is a big deal if you needed to have it every 6 months for example.

0:12:49.1 → 0:12:52 Yes it is a procedure and requires some light anesthesia, correct.

0:12:52 → 0:13:10.2 Wow, that is fascinating. We are going to have a lot more to talk about in pancreas cancer Jill, this is, as always, a very sobering subject but right now, we would like to take a short break for a medical minute. Please stay tuned to learn more about treatment options for pancreas cancer with Dr. Jill Lacy.

0:13:10.2 → 0:13:27.5 Medical Minute Support for Yale Cancer Answers comes from AstraZeneca, working side by side with leading scientists to better understand how complex data can be converted into innovative treatments. Learn more at astrazeneca-us.com.

0:13:27.5 → 0:14:26.3 This is a medical minute about smoking cessation. There are many obstacles to face when quitting smoking as smoking involves the potent drug nicotine, but it is a very important lifestyle change especially for patients undergoing cancer treatment. Quitting smoking has been shown to positively impact response to treatments, decrease the likelihood that patient will develop second malignancies and increase rates of survival. Tobacco treatment programs

are currently being offered at federally designated comprehensive cancer centers and operate on the principles of the US Public Health Service Clinical Practice guidelines. All treatment components are evidence based and therefore all patients are treated with FDA approved first-line medications for smoking cessation as well as smoking cessation counseling that stresses appropriate coping skills. More information is available at YaleCancerCenter.org. You are listening to Connecticut Public Radio.

0:14:26.3 → 0:15:28.9 Welcome back to Yale Cancer Answers. This is Dr. Steven Gore. I have been joined tonight by my guest Dr. Jill Lacy, and we have been discussing treatment options and identification, natural history of pancreatic cancer. Jill, you really impressed upon me the difficulty of early diagnosis and the often somewhat grim prognosis for many patients in terms of long-term survival, but it seems to me that compared to what I learn when I was training in oncology, things seem to have gotten somewhat better. I mean, when I started there were basically no effective chemotherapy drugs for pancreatic cancer and sometime I guess in the 90s, gemcitabine was approved as the first drug approved for pancreas cancer granted, it was approved on a clinical trial that showed a rather small benefit but it was real benefit it seemed for some patients.

0:15:28.9 → 0:16:31 Yes, I think that is absolutely true. I would like to emphasize that although those statistics are disappointing and we have a long ways to go, we are clearly making progress. If you just look at those 5-year survival rates, over the past decade, the 5-year survival rate has doubled. So, it has gone from about 3.5 to 4% 20 years ago, now to 8-9%. So, the absolute number is small but the trajectory is favorable. And the biggest advances have come really in the last 5-8 years. And you are right, prior to that, there was a sense of nihilism about this disease. As an oncologist, we often felt that there was not a lot that we could do to really change the natural history of pancreatic cancer and improve and prolong patients' lives. But that has changed and there really have been some advances in the field that are noteworthy.

0:16:31 → 0:16:30.6 Can you let us know what some of those are?

0:16:30.6 → 0:18:15.2 Yeah. So, about 8 years ago now, so it has been a while, there was a big breakthrough in treating metastatic pancreatic cancer. Up to that point, as you mentioned, we were using a drug called gemcitabine that modestly improved survival for patients, about 6 months survival compared to 3 months with best supportive care. And so about 8 years ago, we heard about the results from a French study where patients with metastatic pancreatic cancer were treated with a standard treatment gemcitabine or with this new 3-drug cocktail of chemotherapy agents called FOLFIRINOX. And the results of that study were really quite stunning, in that the FOLFIRINOX doubled the average survival to about a year, but notably a subset of patients were surviving many years and in addition, it appeared that FOLFIRINOX substantially improved not only length of life but also quality of life. So, that was a big game changer in a field that had really stalled out for several decades in terms of advances in the field. So, that has been the big advance for treating metastatic disease

and since then, we now have another 2-drug regimen that is also better than gemcitabine alone. It is a little gentler, a little easier. So, we often will use that in patients who may be a little bit older or have a lot of medical comorbidities and would not tolerate some more intensive 3-drug regimen of FOLFIRINOX.

0:18:15.2 -> 0:18:27.2 Gotcha. So, that is making it a little bit better for patients who have had spread of the pancreatic cancer right, but what about for the patients who are dealing with localized disease?

0:18:27.2 -> 0:19:11 Right. So, at diagnosis, we categorize patients based on their staging, studies of a CAT scan as metastatic or operable, able to go to surgery and that is about 20% of patients and then about 30-40% of patients do not have metastatic disease, the tumor has not spread, but it has encroached upon and is growing around major blood vessels such that a surgeon cannot operate on that patient and get the disease out. So, when we talk about patients with operable disease, that is about 20% of patients, and those are the patients where we know we have a path to cure. Surgery alone cures only about 10% of those patients.

0:19:11 -> 0:19:13.1 10% of the 20%?

0:19:13.1 -> 0:19:31.5 Right. And about 15 years ago, we learned that if you add a drug such as gemcitabine to the surgery, it is usually given for 6 months after surgery, about 20% of patients are cured, 80% of patients will still recur.

0:19:31.5 -> 0:19:33.8 The 20% as opposed to 10%.

0:19:33.8 -> 0:19:42.1 As opposed to 10%, so that is a doubling. So, that was a breakthrough, but still just 20% of patients with potentially curable cancer.

0:19:42.1 -> 0:19:43.6 And it is a big surgery for a lot of people.

0:19:43.6 -> 0:19:50.8 It is a big surgery, although the surgical outcomes have really improved.

0:19:50.8 -> 0:19:53.7 That is a separate story we can talk about maybe after some time.

0:19:53.7 -> 0:21:12.4 So, again, another big breakthrough in 2018 and again, this is a study that was done in France by our French colleagues and they were the ones that discovered FOLFIRINOX, and so they conducted a study for patients who had surgery, the Whipple procedure or distal pancreatectomy for operable pancreas cancer, and half of the patients were given the standard of care, which is 6 months of gemcitabine after surgery and half of the patients were given this cocktail of 3 drugs FOLFIRINOX and again really simply stunning results. The FOLFIRINOX essentially appears to have doubled the cure rate. So, with FOLFIRINOX, it looks like we are now curing about 40% of patients. So, if you think about surgery alone, 10%; gemcitabine after surgery for 6 months - 20-25%; and now FOLFIRINOX, 40%. That is a huge advance in the field. So, we are really very excited about that and it brings us back to this question of early diagnosis. So, now that we can cure a substantial percentage

of patients who are operable, it is becoming critically important to diagnose patients when they are operable.

0:21:12.4 -> 0:21:28.7 Gotcha. So, you said that the surgical outcomes had also improved all by themselves for these pancreatic cancer so-called Whipple procedures. What has changed there?

0:21:28.7 -> 0:21:28.6 I am not a surgeon, so I am a little bit out of my wheelhouse here.

0:21:28.6 -> 0:21:33.5 But you see the results a lot.

0:21:33.5 -> 0:21:39.8 Yeah. I mean you probably remember for medical school after Whipple procedure, patients were really quite sick and in the hospital for weeks and weeks.

0:21:39.8 -> 0:21:41.5 Surgery was almost 12 hours a lot of the times.

0:21:41.5 -> 0:23:06.7 Right, and now, the surgical techniques have improved. Often, patients are discharged by day 4. Part of that is that, we are doing a better job in selecting patients for surgery in part because of better imaging. So, now every patient with pancreatic cancer who does not have evidence of distant spread on a CAT scan will undergo a special CAT scan procedure called a pancreatic protocol, and a pancreatic protocol CAT scan allows us to see the relationship of the tumor to the blood vessels, and we know from decades of experience that if this tumor is encroaching on blood vessels, touching or certainly wrapping around blood vessels, surgery can either be impossible or can be very difficult with a much higher risk of bad outcomes. So, now the practice has changed to administering chemotherapy before surgery and most commonly we are using FOLFIRINOX given its effectiveness in patients who have blood vessel involvement. Really any blood vessel involvement. If it is possible to shrink the tumor, pull the cancer off the blood vessels, the surgical outcomes will be better. So, that is another reason why the surgical outcomes are improving.

0:23:06.7 -> 0:23:15.7 It sounds like you need to be involved with your medical oncologist and your surgical oncologist and everybody else really before anything has happened?

0:23:15.7 -> 0:23:46.6 Multidisciplinary assessment is absolutely critical in this disease. Certainly, any patient who does not have overt metastasis, involvement of the liver or the lungs on that first staging CAT scan should have a multidisciplinary evaluation. They should have that CAT scan with the pancreatic protocol and their case should be discussed in a multidisciplinary setting, either formally at a tumor board or in a multidisciplinary clinic.

0:23:46.6 -> 0:23:56.8 And the surgery is still not for the faint of heart right? This is not something where you go to average Joe surgeon down the corner ideally right?

0:23:56.8 -> 0:24:06.5 Ideally, you want any complex surgery to be done by a surgeon who does a lot of that procedure, that is important, absolutely.

0:24:06.5 -> 0:24:32.7 Yeah, that is a lot for patients. I think people hear the word pancreas cancer and I think it is such an emotional thing, I have seen it in my family, because the reputation of the disease is so devastating. As you pointed out, it need not necessarily be.

0:24:32.7 -> 0:25:06.2 It need not necessarily be, that's right. And many patients when they are diagnosed and they often will get the diagnosis first from a gastroenterologist who has done the endoscopic ultrasound and there is a few days before that result and seeing a specialist in pancreas cancer, they start going on the internet, their learning things about pancreas cancer, some of which is accurate and some of which is very frightening, so they will come to you often quite informed, also mixing with some misinformation, but also very anxious and very fearful.

0:25:06.2 -> 0:25:07.4 And without any context right?

0:25:07.4 -> 0:25:34.2 Correct. So, it is very important to go through the information they bring to you with them to make sure they understand that it is not always a death sentence and that we can cure many patients and for those that we cannot, we can prolong their life and improve their quality of life, and a subset of those patients will live many years.

0:25:34.2 -> 0:25:52.1 Well, that is certainly much more positive than it used to be, right. And what about the quality of life issues, I know that for some patients pain control can be a real problem with advanced pancreas cancer due to its location around nerves and stuff, have we done better with that and appetite of course is another one right?

0:25:52.1 -> 0:27:09.5 Yes, I do think we are better at managing symptoms in many cancers including pancreatic cancer. We talk a lot about getting palliative care involved early on in patients with advanced cancers and that is important in pancreas cancer. Pain is a big problem for many patients with advanced pancreatic cancer. So, it is important to optimize pain regimens, sometimes we can do a procedure called a celiac nerve block that can help with pain, so that is important. Oftentimes, patients will have reduced appetite and there are things that we can do for that. Many patients with pancreatic cancer will have a syndrome called pancreatic insufficiency, which means that the pancreas is not making enough digestive enzymes to properly digest their food and for the patient what that means is a lot of gas, a lot of cramping, a lot of bloatedness, a lot of just gastrointestinal distress that can really effect their quality of life. So, it is very important to get those patients on pancreatic enzyme supplements, which you can take by mouth, that can really alleviate those symptoms. So, all of those supportive care interventions are extremely important in maintaining quality of life.

0:27:09.5 -> 0:27:56.1 Yeah, you know I may have not discussed this with you

previously, Jill, but my mom had pancreas cancer from which she expired and celiac plexus nerve block was amazing for her, which we had done reasonably early on into her course, but she was having pain and she was not dealing well with narcotics and she was essentially pain-free for the rest of her course with minimal or no narcotics. It was an incredible blessing for her. So, I am big proponent of making sure that those kinds of modalities at least be found out about, not that narcotics are not also very wonderful drugs and very important and other things we can do, but it was so nice to have her be not clouded for her last few months.

0:27:56.1 -> 0:28:06.3 Absolutely. Celiac access or celiac nerve block can be a gamechanger for many patients, not everyone but for those that benefit as you say, it is huge.

0:28:06.3 -> 0:28:45.3 It was huge, yeah. She was at a place where we kind of had to talk them into it, which also gets the whole thing about patient advocacy because had I not been an oncologist, who knows, so as much as we often say be aware of what you find on the internet, it is wonderful to have access to at least discussion on the internet where hopefully you will have a physician who has got time and patience to at least listen to reasonable things that you have seen and be able to contextualize them and say yeah that is a good idea, I have not thought about that or yeah this is why that is, of course I thought about that and this is why it is not appropriate for you or for your loved one.

0:28:45.3 -> 0:28:52.9 Yes, it is very important to go through the information that patients bring to the visit and take everything seriously.

0:28:52.9 -> 0:28:55.3 Right, so easy to blow people off right or to be blown off?

0:28:55.3 -> 0:29:02 Right, and I have to say I have learned a lot from my patients. You listen, you will learn. It is very important.

0:29:02 -> 0:29:26.2 Dr. Jill Lacy is a Professor of Medicine in the Section of Medical Oncology at Yale School of Medicine. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at YaleCancerCenter.org. We hope you will join us next week to learn more about the fight against cancer here on Connecticut Public Radio.