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Welcome to Yale Cancer Answers with doctors Anees Chagpar, Susan Higgins and Steven Gore. I am Bruce Barber. Yale Cancer Center Answers is our way of providing you with the most up-to-date information on cancer care by welcoming oncologists and cancer specialists who are on the forefront of the battle to fight cancer. This week Dr. Steven Gore welcomes Dr. Mario Strazzabosco for a conversation about liver cancer. Dr. Strazzabosco is Director of Liver Cancer Program at Smilow Cancer Hospital and Dr. Gore is Director of Hematological Malignancies.

Gore Tell us about liver cancer. Many of our listeners may think of any cancer that has gone to the liver as being liver cancer. That is not exactly right, am I correct there?

Strazzabosco Correct, the most frequent forms of this are called secondary liver cancer, otherwise called liver metastasis where the liver is a target organ of other malignant tumors elsewhere in the body and they metastasize to the liver.

Gore Something like breast cancer or colon cancer.

Strazzabosco Breast cancer, colon cancer and so on. These are metastatic cancers that develop in the normal liver. The big difference from the one that we are talking about today, which is a primary liver cancer is that the liver is almost never normal. The liver cancer is actually one of the dreadful complications of having chronic liver disease. Sometimes, liver cancer can develop in a patient with an otherwise normal or semi-normal liver. Most of the time, I would say 90% of the time, in our geographic area, it is actually a complication of long-standing liver disease. For example, among the patients with liver cirrhosis, liver cancer arises with an incidence of 5% per year.

Gore So 5% per year in people with cirrhosis.

Strazzabosco And this is one of the reason why these people are usually screened for liver cancer with ultrasound every 6 months. It is a very important issue because if you can diagnose liver cancer in an early stage, this also can be done, whereas if you do not do the screening and the cancer at the moment of the diagnosis is already advanced, there is little that can be done actually. This opens several other questions like how do I know that I have liver cirrhosis, for example.

Gore That was one of my next questions, but maybe before we get there, does it matter what the cause of cirrhosis is, I know there are many forms of cirrhosis, right?

Strazzabosco It does matter a lot, and there are many forms of cirrhosis. The most frequent one is due to hepatitis C, hepatitis B, alcoholic liver disease and more recently, this new entity of nonalcoholic steatohepatitis.

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Gore Fatty liver.

Strazzabosco Yeah, the bad kind of fatty liver basically, which is associated with metabolic liver disease, diabetes and obesity.

Gore Well there is none of that in our country.

Strazzabosco It is pretty common here. You see less of it for example in Italy where people are leaner and eat in a different way.

Gore Mediterranean diet.

Strazzabosco Yes, a Mediterranean diet.

Gore They fit into those skinny jeans and everything there.

Strazzabosco When I was practicing in Italy, I was a little skeptical about the existence of this form but now that I am practicing here, I do see it. I would say that nowadays these are the 4 most common causes of liver disease epidemiologically speaking and the important thing is that they are all preventable and treatable.

Gore And do they all have a predilection to having liver cancer develop?

Strazzabosco Yes, independent of the form of cirrhosis. They do it with different mechanisms, of course, but hepatitis B virus is an oncogenic virus.

Gore Maybe even it causes cancer.

Strazzabosco It causes cancer, it can integrate in the genome, it is a direct cause of cancer. It is one of the few cases where you can have liver cancer in the absence of cirrhosis, just with moderate liver disease. For example, when these are acquired very early, the inflammatory component does not start to develop severe liver disease but the cancer is there and can integrate in the genome and activate some oncogenes. Hepatitis C is different because there is not a direct oncogenic action but it is the overall inflammation and repair chronically. Alcohol is more or less the same action.

Gore Inflammatory?

Strazzabosco Inflammatory and anti-inflammatory is also there. The pathogenesis of the hepatitis connected with fatty liver.

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Gore I see, so you were saying with hepatitis B if I understand correctly is that DNA from the virus actually becomes part of our DNA?

Strazzabosco Yeah, there is integration.

Gore I see.

Strazzabosco And this can activate some oncogenes.

Gore Some genes which can lead to cancer.

Strazzabosco Yeah but you still have to have some sort of even moderate damage to promote proliferation.

Gore For the cells to start growing.

Strazzabosco Right, so I think this is a direct action. We should spend some time talking about prevention and also treatment once you identify the liver disease, now you can treat it. Hepatitis C has great drugs. You can eradicate the virus now. Hepatitis B, you do not eradicate the virus but you suppress the virus replication so the inflammation goes down.

Gore Using medication.

Strazzabosco Using medication, antivirus, and it is clear that if you are able to identify and treat this disease before it gets cirrhotic, you do prevent significantly the development of liver cancer. It is different when you apply this treatment in a patient who already has cirrhosis, then the risk of liver cancer decreases but does not go to zero and alcoholic liver disease of course is preventable with sacrifice.

Gore That is not easy for people who really suffer from alcoholism. It is a terrible problem.

Strazzabosco Yes, though sometimes it is not really being an alcoholic. One of the things that is good to understand is that often liver cancer is the result of not one single cause but the combination of different causes. It is very easy, you do not know that you have hepatitis C, so you live a normal life, you eat and drink socially, you do not get drunk and you grow fat, so now you are acquiring 3 different risk factors for liver cancer and they do not just add together. They multiple, so the risk is tremendously increasing if you have 3 risk factors and these 3 risk factors are so common; hepatitis C is so prevalent among baby boomers for example. Gore The curse of our generation.

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Strazzabosco It is the curse of our generation, and it is very easy to have 3 major risk factors and not know it, so that is one of the difficulties we are facing. They can be prevented and progression to advanced chronic disease can be prevented by etiologic treatment of behavior, change in lifestyle and whatever and then you have the screening phase, which is an oncologic surveillance in the population at risk. Physicians should be able to identify patients with risk factors and these patients should do an ultrasound and see what the liver morphology is. Now there are also ways to understand how fibrotic the liver is. For example, there is an easy test called FibroScan, and you measure the elasticity of the liver.

Gore How spongy it is, how bouncy it is, right?

Strazzabosco Exactly, you hit the abdominal wall and record how it progresses. Is it progressive through some sort of wood or sponge, it is not rocket science.

Gore Are they hitting it physically or are they hitting it with something?

Strazzabosco There is a little probe that you apply on the abdominal wall.

Gore It gives you a little thump.

Strazzabosco Yes, and then we record the wavelength of how this elastic wavelength came back and there you have a number.

Gore But it does not hurt?

Strazzabosco No not at all and above a certain number, you have significant fibrosis and should probably see a hepatologist and start doing several things that would prevent you to go on to cirrhosis and to liver cancer.

Gore We probably have several baby boomers, quite a few in our audience, how common is liver cancer, should all these boomers in our listening audience be running to their doctor and saying, I need a FibroScan?

Strazzabosco I do not want to frighten my fellow baby boomers, okay.

Gore We have enough to worry about.

Strazzabosco The advice is to take good care of your health as you would do for any other disease. Strangely enough, most of the risk factors are the same for cardiac disease and for liver disease and many other cancers, diabetes is a risk factor as already found.

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Gore And obesity.

Strazzabosco And obesity as well, it is basically a set of genes that predisposes you to have this sort of problem, so do not panic, but the bad part is that actually liver cancer incidence is rising in the Western Countries. It used to be very high in Africa, Asia.

Gore Asian countries.

Strazzabosco Following the epidemiology of hepatitis B or nephrotoxin, but now it is more widespread also in the western society and particularly in the US, this is due to some generational aging or migrations, by people coming from high risk countries, but that the latest statistics are about 6.1 per 100,000 people.

Gore Six cases of liver cancer per 100,000 people.

Strazzabosco Yes, and Connecticut in particular is one of the States with higher incidence, I do not know why.

Gore We are glad you are here.

Strazzabosco It is about 7.5. We ran some estimates, very limited, but there are more than 200 new cases per year just in Connecticut and these are patients that are very complex because the characteristics of liver cancer as I said before is that you have this liver cancer in a patient with chronic liver disease and so you have 2 components, one is the oncologic component.

Gore The cancer per se.

Strazzabosco Right, and the other is a failing organ, so it is the cancer in an organ which is failing and that is the complexity.

Gore Right sure.

Strazzabosco You do not have a failing colon, you just take it out and do all the other things that you need to do but here you have a patient with very complex internal medicine syndrome which is end-stage liver disease, so you have all sorts of complications, and you want to cure the cancer in a patient with liver disease.

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Gore Well we are going to pick this up after the break, but at this point, we are going to take a short break for a medical minute. Please stay tuned to learn more information about liver cancer with Dr. Strazzabosco.

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Gore Welcome back to Yale Cancer Center answers. This is Dr. Steven Gore and I am joined tonight by my guest, Dr. Mario Strazzabosco. We are discussing the diagnosis and treatment of liver cancer. The audience will probably not realize that I am trying to modify my pronunciation of the Os in your name after the dialogue we had off mic but that is too complicated for my pidgin Italian that I get mainly from travelling in Europe. So, before the break you were telling me about how complicated it is to treat liver cancer because it is usually in the context of a failing liver. Are you a surgeon or medical physician?

Strazzabosco I am an hepatologist, which is a branch of internal medicine.

Gore Gotcha, but large part of therapy for liver cancer is surgical, is that correct?

Strazzabosco It is in part, so let us begin by saying most medical oncology, chemotherapy do not really work in this cancer for two main reasons, the reason #1 is this as I said is a failing liver, you have to be very careful with drug toxicity. Gore Sure because we need the liver to metabolize drugs.

Strazzabosco Right, exactly, so you have to be careful and you cannot use the full strength and the second thing is that the liver is actually the organ that usually metabolizes the drug and so it is actually specifically designed, not to be offended.

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Gore Right, oh! I see, it takes care of itself.

Strazzabosco Right, metabolizing enzymes and pumps that push the drug outside in the body and this cancer, if they have not completely lost their differentiation, they do remember the job that they were doing before and somehow they become resistant to most of the use of chemotherapeutic agents. There are in the pipeline some targeted small molecules that would interfere with some important transaction mechanism, some of them already, one of the aspects it is already being used; other we cannot, but they still limit the number of patients that can be treated in this way, they have to have an almost perfect liver function and usually we use these drugs in patients who have failure of treatment; so what are the other treatments. First of all, they apply mostly on patients with early to intermediate stage.

Gore Okay.

Strazzabosco This is one more reason to have an early diagnosis.

Gore Get screened, right.

Strazzabosco So depending on the stage and several other local factors, local meaning where is it in the liver, the patient can undergo resection.

Gore Meaning surgical removal.

Strazzabosco Surgical removal of the cancer, taking away a piece of the liver or of different size, okay. As you know, the liver can grow back and that does not happen that often if your cirrhosis is advanced, so you have to take this into account. For example, one thing is taken away in metastasis, one thing is taken away as primary liver tumor because the regeneration in potential of the liver is different.

Gore So what you are saying is that if it is a colon cancer that has spread with one or two metastases to a normal liver, you can sometimes cut out those metastases and help.

Strazzabosco Right.

Gore But in this case, the liver cancer because it is growing in a sick organ, the liver may not grow back.

Strazzabosco You can still cut out the tumor but you have to make sure that there are certain parameters that are satisfied.

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Gore Okay.

Strazzabosco For example, there cannot be varices, the bilirubin has to be below 1. There are certain criteria that limits the applicability, still it is one of the best treatment you can do.

Gore I see.

Strazzabosco Then, if the patient cannot undergo surgery, you can use several different interventional radiology treatment, just to give you an example, one is called radiofrequency ablation, you insert a probe in the tumor and you use microwave to cook the tumor basically, this is what you do.

Gore Lovely.

Strazzabosco It is very efficacious.

Gore Is the probe inserted through the skin?

Strazzabosco Yes, that can be done, mostly it is done percutaneously.

Gore Through the skin.

Strazzabosco Right, sometimes can be done laparoscopically depending on the location. If the location is difficult to access through the skin or it is too risky, otherwise it is just like a biopsy. It is not painful.

Gore It sounds painful.

Strazzabosco No it is not and because you know the liver only has pain nervous termination on the capsule.

Gore Outside the liver.

Strazzabosco Right, the capsule...

Gore That surrounds the liver.

Strazzabosco Surrounds the liver, that has pain

Gore But not inside the liver.

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Strazzabosco Not inside the liver.

Gore Interesting.

Strazzabosco Right, so the results are outstanding particularly if tumors are small.

Gore Okay.

Strazzabosco If tumors are a little larger or they have a clear arterial evaluation, you can use TACE. TACE is the acronym for transarterial chemoembolization and basically you go through the hepatic artery, cannulate very selectively the feeding artery.

Gore That goes to the tumor.

Strazzabosco The tumor, because the normal liver gets most of its blood from the portal vein. Gore Which comes from the gut.

Strazzabosco Which comes from the gut, yes and the tumor gets its feeding from the artery, so we can clearly isolate that portion of the liver from the surrounding portion, you can embolize, but also you can add some chemotherapeutic agents, a very high concentration locally and they stay there.

Gore So you are injecting the chemo right into the tumor.

Strazzabosco Right, you can use microsphere, you can use some oil, like Lipiodol that gets engulfed by the cells, so the concentration of the chemotherapeutic agent is even higher and then there are several variations of this.

Gore I see.

Strazzabosco In some cases rather than injecting chemotherapeutic agent, you can inject a radiotherapeutic agent like Yttrium-90. Gore Radioactive material.

Strazzabosco Right, so it stays there because this tumor actually is very sensitive to radiation. It is very difficult and dangerous to irradiate the whole liver because of the hilum and so on but with this system, you can actually hit with a high radiation in a small area in the liver and then

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again, there are several variations of this main sort of treatment, alright. The thing is it is not clear immediately which patient should get what because basically these are all treatments that are reserved to patients with early or intermediate cancer but then to go on the nitty-gritty of which one or the other is not so easy and this is one on the main message that I hope to convey that these are patients that need to be seen by specialized centers, not being treated by whatever is available in a certain community or certain hospital. You need that has very good result with each of these techniques and so that is what is usually done around the Multidisciplinary Tumor Board that include hepatologists, transplant surgeons.

Gore Radiation oncologists.

Strazzabosco All the people that provide care. They are together and discuss the case and this is what we call personalized medicine in this cancer so far, waiting for some more biological and molecular biology clues and leads. Last is the chance of transplantation. This is the only solid organ that can be treated by transplant, so the result of transplantation is outstanding.

Gore You are talking about transplanting the whole liver.

Strazzabosco Transplanting the whole liver.

Gore Oh, my gosh.

Strazzabosco Because you take care of both diseases, you take care of the cancer, you take care of the cirrhosis. Now, there are limitations to your ability to do so. The cancer has to be in a stage where the likelihood of metastasis is absolutely zero, livers are few, and so on, but you know, the transplantation is part of the possibilities that we can offer to our patients and again the matter is these patients should seek care and be referred to places that run this multidisciplinary approach because sometimes, the treatment is sequential, it is multidisciplinary and sequential, you start by resecting a patient and then you do a TACE and then you do an RFA and finally, this patient is still in stage in which he can be transplanted and he will be transplanted or you will list the patient with transplantation but in the meanwhile that you wait you need to take care of the patient so it does not grow out of the stage and so you do everything you need to do in order to keep it at bay while the liver camps, so I would say that with respect to several years ago, the prognosis is improving because of all these treatments, but the complexities remain high and unfortunately, liver cancer is still one of the few or very few tumors in which mortality is not decreasing yet.

Gore Not decreasing.

Strazzabosco No, so all the other cancers as you will teach me are improving, the prognosis is improving, the liver is still not but they are surviving much better.

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Gore Is that because people are still being diagnosed at a higher stage?

Strazzabosco Because of that, because you do have liver disease, because, for example, until a couple of years ago, we did not have the new antivirals for hepatitis C and we are expecting that the prognosis will change, so sometimes you treat the cancer but still the liver does not go as it should, so it is a very complex environment where you will need to have the collaboration of many different providers but the point is that this collaboration must not be random, otherwise the patient's itinerary is several points of entry and several different outcomes.

Gore It is very confusing, right, overwhelming.

Strazzabosco Right and so that is reason why many centers are actually organizing themselves in a multidisciplinary program.

Gore Basically one stop shopping.

Strazzabosco Exactly.

Gore So how does somebody find, you know let us say somebody does not live in our area where obviously we have a center for example, are there online resources for center for excellence for liver cancer or...

Strazzabosco Yeah, of course you can look up at the website and you know there are master major institutions.

Gore Should have such as.

Strazzabosco Should have such as, okay I think the big point is go to centers of excellence and refer your patient to centers of excellence.

Gore As them a question, are you a center of excellence, right or are you, well, I think you know obviously people want to take care of their patients the best way, so hopefully, they will refer patients if they do not really feel like they are adequately...

Strazzabosco It would be nice if all the centers would put their outcomes in volumes and in the public domain.

Dr. Mario Strazzabosco is Director of Liver Cancer Program at Smilow Cancer Hospital. If you have questions for the doctors, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at yalecancercenter.org. I am Bruce Barber reminding you to tune in each week to learn about the progress being made in the fight against cancer here on WNPR, Connecticut's Public Media Source for news and ideas.