Support for Yale Cancer Answers comes from AstraZeneca, dedicated to advancing options and providing hope for people living with cancer. More information at astrazeneca-us.com. Welcome to Yale Cancer Answers with your host doctor Anees Chagpar. 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’s a conversation about liver cancer with Doctor Mario Strazzabosco, professor of medicine and clinical program leader of the liver Cancer program at the Yale School of Medicine, where Doctor Chagpar is a professor of surgical oncology. Mario, maybe we can start off by you telling us a little bit about liver cancers. Sometimes cancers have started somewhere else and go to the liver and sometimes cancers start in the liver. Can you give us a framework of how to think about liver cancers?
We distinguish cancers that start in the liver and we call them primary liver cancer, from cancer that goes into the liver with the primary cancer somewhere else. Those are called secondary liver cancer and in essence they are metastasis from a primary tumor. Today the topic will be cancer that happens in the liver as a primary site. And those are less common than the cancers that spread to the liver from other sites, is that right? That is right they are definitely less common, but it is true that primary liver cancer is actually one of the few cancers that are still increasing in terms of incidence and also in terms of mortality. So tell us a little bit more about primary liver cancers. Are there different types? Yes, there are several types. The two main types are hepatocellular carcinoma, which is the cancer that starts from the liver cells. It is the most common of them and the other is called cholangiocarcinoma.
and that starts from the bile ducts inside or outside of the liver. And this is less common. You mentioned that the incidences was increasing. What are the risk factors for getting liver cancer? This is a very important question. So liver cancer is increasing as a result of several worldwide epidemiological trends. The main risk factor is one, having liver disease. Two having hepatis c, three having hepatitis B, four, having an excessive consumption of alcohol, five, having what we call metabolic syndrome, which is the result of being obese or having diabetes, or having other cardiovascular risk factors. In addition to that, there is a 6th epidemiological trend which is very important, which is the poor access to care in certain countries. These are the main factors that contribute to increasing the incidence of primary liver cancer, and particularly of hepatocellular carcinoma. Of course, the combination of these factors changes according to the geographical area. It used to be that in the US, the incidence of HCC was lower than Asia, Africa, for example, than Asia, Africa, or other places.
But now with migration and other factors, it tends to become more equal in terms of distribution of risk factors and also the risk factors are changing, so we used to have a very big impact of hepatitis C. Now with the new treatments we see a rise in the hepatocellular cancer which is a consequence of the metabolic risk factor such as diabetes, so the incidence in the US vs Asia has increased. You mentioned that was due to in part to migration i.e. people from Asia moving to the US which might imply some genetic factors. So is there a genetic underpinning to some of these cancers as well? I think this is more exposure to viral hepatitis. For example, one of the main factors in hepatitis B which is a direct oncogenic virus and it used to be lower here and higher for example, in the Mediterranean countries and in Asia. And changes in the worldwide population may change that. But one peculiar thing in the US is actually the increase
0:05:56.828 → 0:05:59.208 of metabolic risk factors.
0:05:59.21 → 0:06:01.54 Cancer associated with obesity
0:06:02.6 → 0:06:05.78 and diabetes and one important thing
0:06:05.78 → 0:06:08.82 to understand in terms of liver cancer
0:06:08.82 → 0:06:11.802 is that whereas we try to focus on
0:06:11.802 → 0:06:14.566 one risk factor as a matter of fact,
0:06:14.566 → 0:06:16.15 patients with liver cancer,
0:06:16.15 → 0:06:18.526 have several risk factors. It is not unusual
0:06:18.53 → 0:06:20.912 to find a patient that is
0:06:20.912 → 0:06:22.5 overweight, maybe is diabetic,
0:06:22.5 → 0:06:25.14 which goes with being overweight and
0:06:25.14 → 0:06:28.573 he didn’t know he had hepatitis C
0:06:28.573 → 0:06:31.63 so lived a normal life with
0:06:32.456 → 0:06:35.347 drinking more than his liver could stand,
0:06:35.35 → 0:06:37.8 and so here we are and maybe
0:06:37.8 → 0:06:39.64 even he was smoking.
0:06:39.64 → 0:06:42.52 So just a regular guy that had
0:06:42.52 → 0:06:45.49 accrued four risk factors for liver cancer.
0:06:45.49 → 0:06:48.22 So this is very important to understand
0:06:48.22 → 0:06:50.99 when they add to each
0:06:50.99 → 0:06:53.282 other the increasing the risk factor
0:06:53.29 → 0:06:53.942 is exponential.
0:06:53.942 → 0:06:56.55 I want to pick up on the viral
0:06:56.623 → 0:06:59.047 hepatitities which increase the risk
0:06:59.047 → 0:07:01.869 of developing hepatocellular cancer.
0:07:01.87 → 0:07:04.678 So hepatitis B and hepatitis C,
0:07:04.68 → 0:07:06.764 interestingly, as we’re living
0:07:06.764 → 0:07:09.372 through Covid right now, another
0:07:09.372 → 0:07:13.548 viral disease for which we have a vaccine,
0:07:13.55 → 0:07:16.81 it’s important to understand that
0:07:16.81 → 0:07:20.57 there are vaccines for hepatitis B&C.
Have those vaccines had any impact on reducing the rates of hepatocellular cancer? We have vaccination available for hepatitis A&B. Hepatitis A is not associated with liver cancer; it is the hepatitis that is actually acquired through eating shellfish, or seafood. Hepatitis B, we have a vaccine which is extremely efficient and we have data showing that, for example, in some country in Africa where they had a very high incidence of a hepatocellular cancer because of the maternal fetal transmission of hepatitis B, they implemented a mass vaccination program there. And the incidence of liver cancer dropped dramatically, so yes, it is there and we can decrease the incidence with vaccination and in fact most people in the younger generation are vaccinated for it. Unfortunately we never made it with trying to find a vaccine for hepatitis C because of this high variability of the virus. But we were lucky because we were able to devise pharmacological treatment and so now we have very effective ways to eradicate the virus using small molecule compounds.
And that is important information. Overall I think one message that it would be very important to get through to the public, is that most formal liver disease and therefore liver cancer are preventable. And also treatable in terms of liver disease. So you can prevent risky behavior for viral hepatitis, you can use vaccination. You can treat the virus if you realize you are infected before having a cirrhosis. Avoid, of course, excessive use of alcohol. You can act on the lifestyle if you have diabetes. If you are obese, you can lose weight. You can increase your exercise. You can control those factors and so all of them are actually preventable, acting both at a personal level and public health action. Let’s pick up on on that. You mentioned a number of preventative measures, so if somebody gets vaccinated against hepatitis B, for example, and never contracts hepatitis B, it’s understandable then that
they’ve eliminated that risk factor, but if they get hepatitis C and are treated for it, does that eradicate the risk of developing hepatocellular carcinoma? Or is the fact that they already had hepatitis C even though it was treated, does that still increase their risk?

Number one, there’s a lot of people that have hepatitis C and don’t know it, particularly in the so called baby Boomer. #2 this drug that I was mentioning, DAA, direct active antivirus, are extremely good and can eradicate the virus in most cases. Then the question becomes at what stage did you apply that treatment?

Did you have just a minor chronic hepatitis or were you already progressed to have more fibrosis and cirrhosis. And the risk decreases in a different way whether you treated hepatitis before becoming cirrhotic or when you were already cirrhotic?

In this second instance, the decrease in the risk is less important. The thing that we learned after treating
many patients and erradicating the virus is that the risk of having liver cancer was decreasing, but was not zero. So there is still a substantial risk, even if it is, let’s say halved. And there is a big controversy in the literature, but I won’t go into that, but I think that one of the problems is, the timing in the Natural History of disease in which you apply the treatment and just to go back to the beginning of this conversation, we said most patients have more than one risk factor. So if I only eliminate the virus and eradicate it, I decrease a very important risk factor. But I don’t zero the risk factor because the patient may be diabetic, the patient may be overweight, but the patient may be drinking or go back to drink because now he doesn’t have the virus. So again, one of the important messages is that liver cancer is a very comprehensive approach. Eliminating the virus is just step one. We’re going to pick...
0:13:34.93 up on how we deal with all of the other lifestyle factors right after we take a quick break it for a medical minute. Please stay tuned to learn more about advances in liver cancer with my guest doctor, Mario Strazzabosco. Support for Yale Cancer Answers comes from AstraZeneca, working to eliminate cancer as a cause of death. Learn more at astrazeneca-us.com. 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’s 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 patients 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. 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’re listening to Connecticut Public Radio. 

Welcome back to Yale Cancer Answers. This is doctor Anees Chagpar and I’m joined tonight by my guest doctor Mario Strazzabosco. We’re discussing the care of patients with liver cancer and right before the break Mario you were telling us about this plethora of factors that increase people’s risk of liver cancer and the fact that while we do have interventions for hepatitis there frequently are other factors that are involved. You mentioned a few that I’m going to lump together, which are metabolic syndrome. So obesity and diabetes, as well as alcohol which can lead to fatty liver. So can you tell us a little bit more about fatty liver, and whether that impacts the development of liver cancer and whether there’s any quote safe amount
What we call fatty liver is a very common condition which is identified by an increased deposition of fat in the liver cells. Fatty liver can be the result of several problems, but most likely it’s due to the effect of obesity, the affect of diabetes, hyperlipidemia, and what we call metabolic syndrome, which is a complex of changes that are increasing the risk of cardiac disease. This is how we recognize this at the beginning and we used to think that fatty liver was a relatively benign condition, but now we understand that some patients with fatty liver will develop an inflammatory condition of the liver that is not any more benign but can lead to chronic liver disease like cirrhosis and can be associated with the development of liver cancer. Clearly the amount of people that are affected by this condition is very high, so the question is how do we follow those patients? What do we do? It would be important to try to prevent it,
and so how do you prevent it? There is data that shows if you lose 10% of your body weight the risk decreases. This 10% of your body weight should be lost in your abdominal fat because this is a fact that is more associated with this complication. An increase in physical activity is going to play a role. We see that with patients that have this predisposition, a low carbohydrate diet is preferred. They should avoid sodas and so on. I do understand this is a change in lifestyles which are very very difficult to achieve. But addressing this metabolic factor is really part of the constellation of medical action that we need to take. It seems like this really, that constellation to exercise more, lose weight, eat right, that’s really a constellation for good health in general, and it has so many really important health benefits. But one question that people may be wondering about is, if I’ve been overweight all my life and we know that there is an uptick now even in childhood obesity.
So if somebody has been overweight, obese, they then lose a bunch of weight, is the damage to their liver already done such that you're having a relatively small impact on reducing hepatocellular carcinoma? Or is this really reversible? If you eliminate the damaging condition to the liver, you can to a certain extent reverse the chronic damage. We learned this when we started to treat patients with hepatitis B and antivirals. They were very effective in suppressing the virus and that patient went from a complete cirrhosis to an incomplete cirrhosis. So yes, there is a remodeling of your liver and this is not complete in how much it happens. It depends how far you went, but there is to a certain extent a remodeling or the liver and we saw that happening in patients we stopped drinking alcohol. All of them have an improvement. And we saw that with patients treated for hepatitis. Now to what extent this is going to impact the natural history of metabolic liver.
disease is less certain,
but it’s very likely that we can,
for example, if you
decrease your body weight,
your risk decreases.
Now the trick is that when
you decrease your body weight,
you don’t need to get it back,
So it’s very easy to decrease 10%
of your body weight,
but what it counts is 2 years after.
Did you maintain that 10%
decrease because that is what
counts in terms of
risk reduction.
So you want to
make sustainable lifestyle changes now.
One of the things that you
mentioned was that you’ve seen the
fact that you can reduce risk in
people who have stopped drinking,
so abstained from alcohol,
but some people may be wondering,
is there any quote safe limit for alcohol?
So if you used to drink 4 drinks a night,
is it OK to drink one drink a night?
Is there any safe level of
alcohol to which the damage to your
liver is minimal and the risk of
hepatocellular carcinoma is minuscule?
Or is all alcohol going to be
somewhat toxic to your liver?

We used to think that there was a threshold, and this is being kind of revised,

but it’s very well known that a little amount of alcohol can actually improve your metabolic risk.

However, how little is enough, it doesn’t really depend on a fixed dose.

It depends what your genes are and what your history is.

So if you’re drinking alcohol but you have hepatitis C, it’s zero, there’s no even smelling it.

So it’s a difficult question to reply.

In general your advice is abstinences is the gold standard.

It depends on what your overall risk profile is.

But let’s say if you drink once in a while, that is clearly not a problem,

But if it’s your habit, it may become a problem.

This doesn’t say that if you go out for dinner, you can drink a glass of wine.

Of course you can, even eating a candy is OK.

But not OK if you have diabetics.

This brings us to the point of surveillance of the liver, right?
How can we tell how damaged our liver is, whether it’s from diabetes, whether it’s from obesity, whether it’s from alcohol, or whether it’s from hepatitis. As you mentioned before the break, we may not even know that we have. Are there ways of looking at the liver? Yes, so everything starts from understanding whether your liver is damaged or not, so you may for any reason do some laboratories tests that include liver function tests. You may get an ultrasound or you may get tested for hepatitis C for example if you were born a baby boomer, so if you had a risky behavior anything that may increase risk, then a way to understand how chronic is your damage, you can use a fiber scan so it’s like a machine that looks like an ultrasound, but it is not ultrasound because this measures how elastic is your liver and that can give us an estimate whether you have significant fibrosis or not. Or you can do an MRI, there are
several ways to understand if you
liver disease, and
then if you have chronic liver
disease with significant fibrosis,
the current guidelines are that
you should be doing an ultrasound,
every six months.
And there is very good evidence that
this can help diagnose liver cancer
in early stage and therefore in a
stage when the treatment can be successful.
There are other patients that may
need screening, like patients
mainly from Asia that have hepatitis.
and are less than 40 years of age.
Or for example, a patient with hepatitis C that
has been treated,
but they have significant fibrosis.
So the screening is a very important
component of our strategy, but
still we see patients coming to the
clinic with advanced stage cancers.
Or cancer that is beyond curative options.
And that is a failure of screening,
but of course you can have the
situation in which the patient
didn’t know he had liver disease,
because a lot of times liver disease
can be significant but not
symptomatic.
So still the amount of patients that come
0:27:15.508 → 0:27:18.037 with advanced liver disease is too high
0:27:18.04 → 0:27:21.595 because we do have again
0:27:21.595 → 0:27:25.249 ways to prevent the cancer, ways to screen
0:27:25.25 → 0:27:28.505 to get an early diagnosis and it
0:27:28.505 → 0:27:31.452 is important because we now have
0:27:31.452 → 0:27:34.374 several ways to approach liver cancer
0:27:34.38 → 0:27:37.592 and therapeutic approaches
0:27:37.592 → 0:27:41.607 are increasing every year.
0:27:41.61 → 0:27:44.053 So it’s very important to get diagnosed
0:27:44.053 → 0:27:47.823 and to go to a center where you have a
0:27:47.823 → 0:27:50.083 multispecialty program so that all
0:27:50.083 → 0:27:52.526 aspects of the care can be addressed
0:27:52.53 → 0:27:54.35 at the highest professional level.
0:27:55.44 → 0:27:57.82 And it brings back one of the other
0:27:57.82 → 0:27:59.677 risk factors that you mentioned
0:27:59.677 → 0:28:02.351 which was access to care people who
0:28:02.351 → 0:28:04.538 don’t have good access to care,
0:28:04.54 → 0:28:06.26 and I wonder whether you
0:28:06.26 → 0:28:08.55 mentioned that as a risk factor.
0:28:08.55 → 0:28:11.83 Because if you don’t have access to care,
0:28:11.83 → 0:28:13.51 you can’t get appropriate screening,
0:28:13.51 → 0:28:14.518 is that right?
0:28:15.6 → 0:28:17.338 You cannot and appropriate care
0:28:20.71 → 0:28:23.559 is something that we will be
0:28:23.559 → 0:28:25.5 investigating next because it’s really
0:28:25.5 → 0:28:28.38 a pity that you have ways to prevent it,
0:28:28.38 → 0:28:30.683 way ato treat it, but people don’t
0:28:30.683 → 0:28:33.12 even get close to that opportunity.
0:28:33.12 → 0:28:34.218 It’s really saddening.
0:28:35.03 → 0:28:37.148 Doctor Mario Strazzabosco is a
0:28:37.148 → 0:28:38.99 professor of medicine and clinical
program leader of the Liver Cancer
program at the 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’ll join us next week to
learn more about the fight against
cancer here on Connecticut Public Radio.