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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. So often people have different kinds of 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 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? 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 hepatitis 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 overweight 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, 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, 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
Cancer associated with obesity and diabetes and one important thing to understand in terms of liver cancer is that whereas we try to focus on one risk factor as a matter of fact, patients with liver cancer, have several risk factors. It is not unusual to find a patient that is overweight, maybe is diabetic, which goes with being overweight and he didn’t know he had hepatitis C so lived a normal life with drinking more than his liver could stand, and so here we are and maybe even he was smoking. So just a regular guy that had accrued four risk factors for liver cancer. So this is very important to understand when they add to each other the increasing the risk factor is exponential. I want to pick up on the viral hepatitities which increase the risk of developing hepatocellular cancer. So hepatitis B and hepatitis C, interestingly, as we’re living through Covid right now, another viral disease for which we have a vaccine, it’s important to understand that there are vaccines for hepatitis B&C.
0:07:20.57 –> 0:07:23.432 Have those vaccines had any
0:07:23.432 –> 0:07:26.109 impact on reducing the rates
0:07:26.109 –> 0:07:28.67 of hepatocellular cancer?
0:07:28.67 –> 0:07:30.718 We have vaccination available
0:07:30.718 –> 0:07:34.363 for hepatitis A&B. Hepatitis A is not
0:07:34.363 –> 0:07:37.279 associated with liver cancer, it is the
0:07:37.279 –> 0:07:40.72 hepatitis that is actually acquired
0:07:40.72 –> 0:07:43.248 through eating shellfish,
0:07:43.25 –> 0:07:48.403 or seafood. Hepatitis B,
0:07:48.403 –> 0:07:51.709 we have a vaccine which is extremely
0:07:51.709 –> 0:07:55.208 efficient and we have data showing that,
0:07:55.21 –> 0:07:58.521 for example, in some country in Africa
0:07:58.521 –> 0:08:01.999 where they had a very high incidence
0:08:01.999 –> 0:08:05.694 of a hepatocellular cancer because of the
0:08:05.694 –> 0:08:09.699 maternal fetal transmission of hepatitis B,
0:08:08.97 –> 0:08:12.138 they implemented a mass
0:08:12.138 –> 0:08:13.722 vaccination program there.
0:08:13.73 –> 0:08:17.018 And the incidence of liver cancer dropped
0:08:17.02 –> 0:08:18.62 dramatically, so yes,
0:08:18.62 –> 0:08:22.163 it is there and we can decrease the
0:08:22.163 –> 0:08:25.319 incidence with vaccination and in fact
0:08:25.319 –> 0:08:29.209 most people in the younger generation
0:08:29.21 –> 0:08:31.09 are vaccinated for it.
0:08:33.44 –> 0:08:36.038 Unfortunately we never made it with
0:08:36.038 –> 0:08:39.35 trying to find a vaccine for hepatitis C because of
0:08:39.35 –> 0:08:42.344 this high variability of the virus.
0:08:42.35 –> 0:08:45.032 But we were lucky because
0:08:45.032 –> 0:08:47.6 we were able to devise
0:08:47.6 –> 0:08:50.295 pharmacological treatment and so now
0:08:50.295 –> 0:08:54.232 we have very effective ways to eradicate
0:08:54.232 –> 0:08:57.694 the virus using small molecule compounds.
And that is important information. And 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 also liver cancer are preventable. 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 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.
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 with liver cancer have more than one risk factor. So if I only eliminate the virus and eradicate it, I decrease a very important risk factor. 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
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 and therefore all patients are
0:14:43.406 –> 0:14:45.722 treated with FDA approved first line
0:14:45.722 –> 0:14:47.854 medications for smoking cessation as
0:14:47.854 –> 0:14:50.119 well as smoking cessation counseling
0:14:50.119 –> 0:14:52.596 that stresses appropriate coping skills.
0:14:52.596 –> 0:14:55.386 More information is available at
0:14:55.386 –> 0:14:57.06 yalecancercenter.org you’re listening
0:14:58.97 –> 0:14:59.41 Welcome back to Yale Cancer Answers.
0:15:01.6 –> 0:15:05.096 This is doctor Anees Chagpar and
0:15:05.1 –> 0:15:07.728 I’m joined tonight by my guest
0:15:07.728 –> 0:15:09.48 doctor Mario Strazzabosco.
0:15:09.48 –> 0:15:12.108 We’re discussing the care of patients
0:15:12.108 –> 0:15:14.734 with liver cancer and right before
0:15:14.734 –> 0:15:17.534 the break Mario you were telling us
0:15:17.534 –> 0:15:20.317 about this plethora of factors that
0:15:20.317 –> 0:15:23.025 increase people’s risk of
0:15:23.025 –> 0:15:25.86 liver cancer and the fact that
0:15:25.86 –> 0:15:29.077 while we do have interventions for
0:15:29.077 –> 0:15:31.696 hepatitis there frequently are other
0:15:31.696 –> 0:15:34.75 factors that are involved.
0:15:34.75 –> 0:15:37.162 You mentioned a few that I’m
0:15:37.162 –> 0:15:40.205 going to lump together,
0:15:40.205 –> 0:15:42.885 which are metabolic syndrome.
0:15:42.89 –> 0:15:44.93 So obesity and diabetes,
0:15:44.93 –> 0:15:47.48 as well as alcohol which
0:15:47.48 –> 0:15:50.017 can lead to fatty liver.
0:15:50.02 –> 0:15:53.282 So can you tell us a little
0:15:53.282 –> 0:15:56.129 bit more about fatty liver,
0:15:56.13 –> 0:15:59.688 and whether that impacts the development
0:15:59.69 –> 0:16:02.355 of liver cancer and whether
0:16:02.355 –> 0:16:05.02 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? It would be important to try to prevent it,
0:17:55.26 –> 0:17:58.368 and so how do you prevent it?
0:17:58.37 –> 0:18:02.375 There is data that shows if you lose
0:18:02.375 –> 0:18:05.49 10% of your body weight the risk decreases.
0:18:05.49 –> 0:18:08.118 This 10% of your body weight
0:18:08.118 –> 0:18:10.849 should be lost in your
0:18:10.849 –> 0:18:13.079 abdominal fat because this
0:18:13.079 –> 0:18:17.187 is a fact that is more
0:18:17.187 –> 0:18:19.327 associated with this complication.
0:18:24.66 –> 0:18:28.628 An increase in physical activity is going to play a role.
0:18:28.63 –> 0:18:31.6 We see that with patients that
0:18:31.6 –> 0:18:33.085 have this predisposition,
0:18:33.09 –> 0:18:36.066 a low carbohydrate diet is preferred.
0:18:36.07 –> 0:18:40.525 They should avoid sodas and so on.
0:18:40.53 –> 0:18:44.832 I do understand this is
0:18:44.832 –> 0:18:49.097 a change in lifestyles which
0:18:49.097 –> 0:18:52.88 are very very difficult to achieve.
0:18:52.88 –> 0:18:56.45 But addressing this metabolic factor is
0:18:56.45 –> 0:19:01.51 really part of the constellation of medical
0:19:01.51 –> 0:19:04.52 action that we need to take.
0:19:10.73 –> 0:19:15.032 I mean it seems like this really,
0:19:15.04 –> 0:19:17.902 that constellation to
0:19:17.902 –> 0:19:20.768 exercise more, lose weight, eat right,
0:19:20.768 –> 0:19:23.63 that’s really a constellation for good
0:19:23.707 –> 0:19:27.46 health in general, and it has so many
0:19:27.46 –> 0:19:29.372 really important health benefits.
0:19:29.38 –> 0:19:31.985 But one question that people
0:19:31.985 –> 0:19:34.59 may be wondering about is,
0:19:34.59 –> 0:19:37.845 if I’ve been overweight
0:19:37.845 –> 0:19:41.479 all my life and we know that there is
0:19:41.48 –> 0:19:44.686 an uptick now
0:19:44.69 –> 0:19:46.502 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 treating 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
0:21:11.46 -> 0:21:13.1 disease is less certain,
0:21:13.1 -> 0:21:16.493 but it’s very likely that we can,
0:21:16.5 -> 0:21:18.008 for example, if you
0:21:18.008 -> 0:21:20.27 decrease your body weight,
0:21:21.305 -> 0:21:23.375 Now the trick is that when
0:21:23.375 -> 0:21:25.55 you decrease your body weight,
0:21:25.55 -> 0:21:28.175 you don’t need to get it back,
0:21:28.557 -> 0:21:31.196 So it’s very easy to decrease 10%
0:21:31.2 -> 0:21:32.948 of your body weight,
0:21:32.948 -> 0:21:36.87 but what it counts is 2 years after.
0:21:36.87 -> 0:21:38.71 Did you maintain that 10%
0:21:38.71 -> 0:21:41.095 decrease because that is what
0:21:41.095 -> 0:21:44.38 counts in terms of
0:21:44.38 -> 0:21:46.04 risk reduction.
0:21:46.04 -> 0:21:47.7 So you want to
0:21:47.7 -> 0:21:49.78 make sustainable lifestyle changes now.
0:21:49.78 -> 0:21:52.204 One of the things that you
0:21:52.204 -> 0:21:54.65 mentioned was that you’ve seen the
0:21:54.65 -> 0:21:57.261 fact that you can reduce risk in
0:21:57.261 -> 0:21:59.737 people who have stopped drinking,
0:21:59.74 -> 0:22:01.4 so abstained from alcohol,
0:22:01.4 -> 0:22:04.72 but some people may be wondering,
0:22:04.72 -> 0:22:08.04 is there any quote safe limit for alcohol?
0:22:08.04 -> 0:22:12.19 So if you used to drink 4 drinks a night,
0:22:12.19 -> 0:22:16.447 is it OK to drink one drink a night?
0:22:16.45 -> 0:22:19.802 Is there any safe level of
0:22:19.802 -> 0:22:22.963 alcohol to which the damage to your
0:22:22.963 -> 0:22:27.503 liver is minimal and the risk of
0:22:27.503 -> 0:22:30.278 hepatocellular carcinoma is minuscule?
0:22:30.28 -> 0:22:33.472 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, or 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 you 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 hepatits 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 ultrasounds 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 have 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
with advanced liver disease is too high because we do have again ways to prevent the cancer, ways to screen to get an early diagnosis and it is important because we now have several ways to approach liver cancer and therapeutic approaches are increasing every year. So it’s very important to get diagnosed and to go to a center where you have a multispecialty program so that all aspects of the care can be addressed at the highest professional level. And it brings back one of the other risk factors that you mentioned which was access to care people who don’t have good access to care, and I wonder whether you mentioned that as a risk factor. Because if you don’t have access to care, you can’t get appropriate screening. is that right? You cannot and appropriate care is something that we will be investigating next because it’s really a pity that you have ways to prevent it, but people don’t even get close to that opportunity. It’s really saddening. Doctor Mario Strazzabosco is a 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.