

**RAY KIM:** My name's Ray Kim. I'm a hepatologist and associate professor of medicine at Mayo Clinic College of Medicine in Rochester, Minnesota. I am so thrilled to talk to you about our paper that's upcoming in the January issue of the Mayo Clinic proceedings. And title of the paper is Hepatocellular Carcinoma in Olmsted County between 1976 and 2008.

As a way of background, I'd like to tell you a little bit about hepatocellular carcinoma, or liver cancer. Liver cancer is a leading cancer cause of death in the world, particularly in developing countries. In the US, it has been well demonstrated that the incidence of liver cancer has been increasing over the past two decades. This is in contrast to many other cancers whose instance is decreasing because of many other public health efforts.

As to why the incidence might be increasing, there has been some speculations that the reason is not clear at this point and it is one of the reasons why we perform this study to find out what's going on in the community. The other thing about liver cancer, is that it has extremely poor survival probability. In patients with liver cancer, especially in the developing countries, if one is diagnosed with liver cancer, that is almost a death sentence and then there is a very poor survival. So it's an important disease to study.

The third thing about liver cancer, is that it doesn't occur in people at random. It tends to occur in people with chronic liver disease. So that has some public health implications, in that you can identify people who are at risk of developing this awful disease.

So what we found in this study, is that Olmsted County, liver cancer has been increasing for the study period that we looked at. I need to give you a little bit of background because Olmsted county is unique because the health care that is provided to the older community members, is limited to the county itself. In other words, the community residents don't go outside the community to get health care. And based on some research infrastructure that has been developed in the past decades, we can capture all of the health care that goes on in the community.

So we were able to utilize this community based health records to identify all people who have been diagnosed with liver cancer between 1976 and 2008. And applying strict diagnostic criteria, we were able to identify 104 individuals, or community residents, with the diagnosis. And these patients were usually in their 60s and about 2/3 of them were male. As I discussed earlier, the incidence of liver cancer we demonstrated that it increased in Olmsted county, as well as in the United States. And numerically it was 3.5 per 100,000 people per year, at the beginning of this study in the late 70s. To a double of that number, to 6.9 per 100,000 people per year, at the end of the study. So for the past three decades, in subset county the occurrence of liver cancer doubled, basically.

And what we saw was that the driving factor for the rise in the incidence of liver cancer was hepatitis C virus infection. Hepatitis C virus is a blood borne infection. It's actually the most common chronic blood borne infection in the United States. And it's mostly transmitted, in the past, by transfusion but currently most of the patients that we see pick up the virus from injection drug use. And it is most commonly seen in patients who were born between 1945 and 1964, namely the baby boomer generation.

So as these people grow older, Hepatitis C virus lingers and causes liver disease and then eventually liver cancer. And that's the scenario and that's the epidemiologic phenomenon that we're observing that the epidemic of hepatitis C virus is now translating into a big occurrence of liver cancer in our community. The other well known predisposing factors for liver cancer, are hepatitis B and obesity related to fatty liver disease. These factors didn't come out as strong in our data. So mostly in our data, hepatitis C was the driving factor.

It is not very well known that the number one cancer that's associated with obesity is liver cancer, particularly in male. And along with this public attention to obesity epidemic, liver cancer should be one of the items that people need to think about.

The other finding that we thought was encouraging, was that liver cancers are being diagnosed earlier in the latter period than in the earlier period. And that was associated improved survival in patients with the disease. However, this is a case of glass half full because the 5 year survival went from 3%, at the beginning of the study, to 15% at the end of the study. So there was a significant increase in survival rate. But as you can tell, 15% we have a long way to go to make the treatment result acceptable.

So what does our data mean to our practicing physicians? We have to go back to the fact that liver cancer occurs in patients with chronic disease, particularly liver cirrhosis. In our data, 70% of patients with liver cancer had underlying liver cirrhosis. So as a practicing physician, it is important for you to recognize that liver cancer is a constant threat in patients who are dealing with liver cirrhosis. So if you have a patient with chronic liver disease, advanced liver disease, and cirrhosis, liver cancer is something that you need to think about.

And there is the guidelines that tell you who are those patients that need to be under surveillance to pick up early case of liver cancer. So you need to apply that guidelines and in those patients. The reason for surveillance is because early diagnosis does lead to improved outcome, as we demonstrated in this study, unlike in the old days when liver cancers are diagnosed late and the patients come in with a large tumor that cannot be treated with any curative modalities. Right now there are multiple things, not only the surgery but also local ablation therapies, and other things that we can apply to improve outcome and potentially cure patients.

Like to finish with what's next for our project. Again, we are not happy with the survival results that we're seeing. And the realistic way to improve survival in our population is early diagnosis and then applying effective treatment modalities for those patients. Our emphasis is preventive research. So what can be done to diagnose patients early, and who are the candidates, and what's the best modality to pick up those early cases.

And in a smaller scale, we would like to repeat this study maybe in another 10 years. And we might be able to see changing epidemiologic trends. Perhaps by then hepatitis C may not be as important but the obesity related fatty liver disease may come in as an interesting or important risk factor. So we look forward to that possibility.

It is also important for patients to recognize what this data mean. And that is that again, liver disease causes liver cancer, and oftentimes liver disease dubbed as a silent killer. And and that's because you don't get symptoms until you have very advanced liver disease or liver cancer. So it is important for individuals to realize if someone has a liver disease risk factor, and as we demonstrated in this study, hepatitis C is a major risk factor for liver disease, particularly if you belong in the baby boom generation. And the CDC is preparing to come out with a public announcement that if you belong in the baby boom generation, everyone needs to be tested for hepatitis C, because it is that common in that generation. So think about that.

And the second factor may be that obesity related liver disease is also increasing, as you can imagine, as Americans get bigger each year it seems like. The prevalence of chronic liver disease associated with the fatty liver disease that occur in the setting of obesity, that is also increasing. So again, to the degree that most liver disease has no symptoms, you need to be cognizant of the possibility that if you have those risk factors, you may indeed have liver disease that may be important. Thank you.

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