NATIONAL HEMOPHILIA FOUNDATION
for all bleeding disorders

MASAC Document #239

MASAC RECOMMENDATIONS ON SCREENING FOR DEVELOPMENT OF HEPATOCELLULAR CANCER IN PATIENTS WITH HEPATITIS C

The following recommendation was approved by the Medical and Scientific Advisory Council (MASAC) on February 27, 2016, and adopted by the NHF Board of Directors on February 28, 2016.

Statement of Problem

Patients with hepatitis C virus (HCV) infection have been shown to have a significantly increased risk of end-stage liver disease, hepatocellular cancer (HCC), and death due to these two complications of HCV infection. The incidence of hepatocellular cancer (HCC) is rising in many countries, including the United States. Cirrhosis due to hepatitis C (HCV) infection is a major driving force behind the increased incidence in the US.

Surveillance for HCC involves determining who is at risk for the development of HCC and deciding how to screen, how frequently to screen, and what the process should be to follow up on abnormal results.

Definition of the At Risk Population

The incidence of HCC in a particular population of patients is used to determine if screening is appropriate for that population. Current guidelines published by the America Association for the Study of Liver Disease (AASLD) are based on a decades-old tenet of cost effectiveness being achieved if an intervention can be done at a cost of about $50,000 per year of life gained. There are published decision analysis/cost effectiveness models for HCC surveillance in chronic HCV infection. The risk of HCC in patients with chronic hepatitis C is highest in patients who have cirrhosis, with an incidence of between 2-8% per year. Patients who are infected with HCV but do not have cirrhosis have such a low risk of developing HCC that screening is not indicated.

Patients who have Been Successfully Treated for their Chronic Hepatitis C Infection

Patients with cirrhosis from HCV infection who are successfully treated and clear the HCV virus are likely to have a reduced risk of developing HCC; however, data quantifying this reduced risk are not clear. It is likely that continued surveillance will become cost-ineffective with time as the liver fibrosis improves and the risk of HCC diminishes. The current guidelines of the AASLD suggest that treated patients with cirrhosis should continue to undergo surveillance for HCC no more often than annually until there is evidence that their cirrhosis has resolved. The timeline for this improvement in fibrosis is unknown.

Patients who are Co-infected with HCV and HIV

Patients with HCV and HIV (HCV-HIV) co-infection are likely to have advanced liver disease. When these patients develop cirrhosis, they are at increased risk of HCC and at higher risk for more aggressive HCC. Therefore, these co-infected patients should undergo HCC surveillance. The criteria for screening are the same as for mono-infected patients.

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How to Screen for HCC

The most widely used radiological test for surveillance for HCC is an ultrasound. Ultrasound has been reported to have a sensitivity of greater than 90% when used as a screening test. The use of a CT scan as a screening tool has been studied; however, its performance characteristics are not known. The theoretical disadvantage of contrast use and high levels of radiation involved in a 4-phase CT scan have limited its use as a screening test for HCC. Strategies for alternating testing modalities (e.g. ultrasound alternating with CT scan or MRI) have no basis.

How to Follow-up Abnormal Screening Results

Patients with a high risk for HCC who enter a surveillance system need to be notified of an abnormal result. An abnormal result is a nodule not seen on a prior study but now noted to be present, regardless of the size of the nodule. An enlarging mass or nodule is always considered abnormal and should lead to further characterization. Most liver centers use an MRI or 4-phase CT to follow-up on an abnormal ultrasound. Individual centers may prefer one modality over the other.

Recommendations

1. Patients with hemophilia and hepatitis C who have documented cirrhosis should be screened for the development of hepatocellular cancer (HCC).
2. Screening for HCC should be done using a high quality ultrasound.
3. Screening for HCC should be done at 6-month intervals. There is no need to change the frequency of the screening examinations for patients with a higher risk of HCC.
4. Patients with cirrhosis who have been treated and have cleared the hepatitis C virus should also continue to be screened to determine the amount of fibrosis with Fibroscan or specialized blood tests annually until their liver fibrosis has improved to the point that they are no longer cirrhotic. This improvement in fibrosis is anticipated but does not always happen. Improvement in fibrosis may take years to reach the point where the risk of HCC is minimal and HCC screening is no longer warranted.

References

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2. Lok AS, Seeff LB, Morgan TR, di Bisceglie AM, Sterling RK, Curto TM, Everson GT, Lindsay KL, Lee WM, Bonkovsky HL, Dienstag JL, Ghany MG, Morishima C, Goodman ZD; HALT-C Trial Group. Incidence of hepatocellular carcinoma and associated risk factors in hepatitis C-related advanced liver disease. Gastroenterology. 2009 Jan; 136(1): 138-48.