Is the American Association for the Study of Liver Diseases recommendation for hepatocellular carcinoma screening a cul-de-sac?

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Abstract

The American Association for the Study of Liver Diseases just confirmed a grade I recommendation for hepatocellular carcinoma (HCC) screening despite growing controversy. Why should HCC be an exception in the long list of other cancers where the feasibility and the efficacy of screening were investigated by randomized trials? Only 12.0% of United States patients are screened, a fact that precludes efficacy, and there are no relevant figures on the benefit-risk ratio. The ethics of belief is a treacherous reef. Screening is not just performing a test, but is a public health issue: a national program is needed to ensure minimal participation, quality controls and evaluation of the results to improve the process.

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Core tip: Why should hepatocellular carcinoma be an exception in the list of long other cancers where the feasibility and the efficacy of screening were investigated by randomized trials? The ethics of belief is a treacherous reef. Screening is not just performing a
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Italian survey which showed that 90% of patients would refuse participation in a RCT, preferring to undergo screening (see 29 in 1). This did not provide evidence that a trial is not possible, it only showed that the patients did not receive balanced and unbiased information about screening. Randomized controlled trials are always difficult, however, why should HCC be an exception in the long list of other cancers where the feasibility and efficacy of screening were investigated by randomized trials? For example, French and United States urologists, whose associations have strongly promoted prostate cancer screening for a long time, did not hesitate to recruit patients for large multi-national trials. Everyone must support the trial recently submitted to the VA Cooperative Studies Program.

The maintenance of the grade 1 level cannot mask the fact that the recommendation has not been implemented. Only 12.0% of United States patients are screened, a fact that precludes efficacy.[3] Indeed, there are no relevant figures on screening to inform patients about the benefit-risk ratio, a pre-request for compliance. The benefit may be very limited, e.g., the 5-year HCC risk is 1.9% in patients with alcoholic cirrhosis.[6] With regard to harm, overdiagnosis is the inevitable trade-off involved in early cancer detection. Cancer overdiagnosis means that some cancers never progress or progress slowly and the patient dies of other causes before symptoms are apparent. Such patients, as patients with false-positive results, do not benefit from diagnostic procedures and unnecessary treatments, and can only be harmed by them.[1]. The magnitude of overdiagnosis is estimated to be about 25% in mammographically-detected breast cancers and 60% in prostate-specific antigen-detected prostate cancers.[7] No data are available for HCC screening, and stating that “the risk of this is felt to be small” is not the best way to reassure patients.[3] Moreover, both the European Association for the Study of the Liver and AASLD noninvasive recall strategies for nodules of 10-30 mm in the cirrhotic liver, based on the vascular pattern, have a false-negative rate of approximately 20%.[8] Ultrasound screening is far from being a simple and non-invasive procedure, because the next step findings are frequently discordant on both computed tomography and magnetic resonance imaging, supporting the use of biopsy for the diagnosis of small HCCs.[3][8]

The ethics of belief is a treacherous reef when practiced at the bedside, and is without hope for improvement and progress. Screening is not just performing a blood test or a radiological exam, it is a complex issue which is beyond the scope of any clinical disciplines. It is a public health issue: a national program is needed to ensure minimal participation, quality controls (even more mandatory here as the algorithms are complex for recall strategies), and evaluation of the results to improve the process. Moreover, although on the rise, HCC is only the ninth leading cause of cancer deaths in the United States and has to compete with other priorities in a cost-constrained economy.[1].

Finally, the conflict of interest section is puzzling.[3] It contrasts with a previous statement where both authors of the recommendation stated they served on the Speaker’s Bureau of Bayer[3]. Bayer markets sorafenib, the $5000/mo drug for advanced HCC, which is now being investigated for the prevention of early HCC recurrence after local ablation (NCT01126645). Early HCC could be a huge market for Bayer. Moreover, AASLD which edits Hepatology receives grants from Bayer for its practice guidelines program and Bayer also held three different booth spaces during the last AASLD meeting (see http://www.aasld.org/practiceguidelines/Pages/Ar chivePracticeGuidelines.aspx and http://www.aasld.org/lm2012/2012/exhibits/Pages/currentexhibitors.aspx).

REFERENCES


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