

# Guidelines for the management of hepatocellular carcinoma: still in need of standardization

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Guidelines are meant to assist physicians, patients, health-care providers and health-policy makers in the decision-making process according to evidence based data (1), with the understanding that the recommendations are intended to guide clinical practice in circumstances where all possible resources and therapies are available. This implies that recommendations should adapt to local regulations and capacities, not to forget the impact of cost-benefit analysis. Finally, guidelines are essential instrument to update and advance the research and the knowledge, ultimately contributing to improve patient care.

Despite the blossoming of guidelines for HCC, in the West and East, at a global level, the clinical practice of HCC treatment is still far from being standardized even within each country. There are in fact wide discrepancies in the management of the disease among Academic and non Academic Hospitals (2,3) whereas therapeutic approaches of consolidated efficacy like surveillance of at risk population is not widespread even in resources rich countries like US (4). Indeed, population-based studies in the United States indicate that only a minority of patients with an HCC have undergone regular surveillance and consequently received curative treatments, despite most doctors are aware of potentially lethal consequences of a delayed diagnosis and treatment of HCC.

The Chinese guidelines on primary liver cancer reported in this issue (5) of the Journal represent a potentially breakthrough, since they address the most populous country in the world which is also an hyperendemic area for HCC, due to the prevalence of HBV and exposure to aflatoxin contaminated food. While increasing population's awareness of HCC as a relevant health problem represents

the first step for improving management of the disease, further steps are the definition of surveillance, recall policy and treatment standardization. Despite the driving role of the level of evidence and the strength of the data, several aspects of HCC guidelines still remain to define, mainly as a consequence of discordant results by RCTs which hamper common strategies between the various geographic areas. Not surprisingly, therefore, most recommendations are based on expert opinion and local capacity rather than on RCTs. This makes cost-efficacy of surveillance itself to be questioned by many, because of the lack of solid data on the evidence that HCC mortality is decreased by surveillance everywhere, whereas surveillance is a consolidated standard of care in most countries. This notwithstanding, modalities and timing of surveillance are questioned, as the use of serum tumor markers in surveillance programs are endorsed by Japanese and Chinese guidelines (5,6) whereas they are excluded by European and North American guidelines (1-7). The weak sensitivity and specificity of serum markers and the lack of standardized recall policies being the major reasons for their withdrawal. Thus, in our opinion, the endorsement of AFP in screening and recall policies provided by the Chinese guidelines, needs a prospective validation. Once ultrasound detects a de novo liver nodule in at risk population, the investigation are aimed to the detection of the typical vascular pattern of HCC, defined by an increased enhancement of contrast in the arterial phase, followed by a wash-out in the portal/venous phase, by CT or MRI, which allow the radiological diagnosis of HCC worldwide. The Chinese guidelines highlight the use of hepatic artery digital subtraction angiography (DSA) too, for the radiological diagnosis

of HCC in cirrhosis. From a Western perspective, the use of DSA to diagnose HCC in cirrhosis needs prospective validation. One major advance in the Chinese guidelines, is the concept of palliative resection of the tumor in patients with a multinodular HCC and vascular invasion. Again, we think this innovative policy should be validated by a prospective study, being data on increased survival and/or decreased morbidity far from being supported by evidence-based studies.

In conclusion, it seems that to bridge the gap in screening and management of HCC, educational programs should be implemented to target both patients and stakeholders in the field, while waiting for a breakthrough not only in the strategy of the screening but also for tailoring treatment for each patient, with the aim to improve population's access to the surveillance and to standardized treatments.

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