Surveillance of the patients at high risk for developing hepatocellular carcinoma in Europe - between guidelines and reality

Hepatocellular carcinoma is the sixth most common cancer, and the third cause of cancer related death worldwide [1]. The pattern of HCC occurrence has a clear geographical distribution, with the highest incidence rates in several regions from East Asia and sub-Saharan Africa.

In Europe, the incidence and mortality rates reported are heterogeneous. The GLOBOCAN 2008 database [2] reports similar HCC incidence and mortality rates for Central and Eastern European countries (for males – incidence 9.9%, mortality 10%; for women – incidence 4.9%, mortality 5.5%). There are slightly higher rates reported for Western Europe countries: crude incidence rate is 13.6% for males and 5.1% for women. Mortality rates are similarly high when compared to Central and Eastern European countries, with a 12.9% crude rate for men and a 5.5% crude rate for women. The highest crude incidence rate is reported for Southern Europe countries: 19.8% for male and 8.9% for women. These countries have also the highest crude mortality rate: 17.1% for men and 8.6% for women.

Hepatocellular carcinoma is a suitable target for a cancer surveillance program because:
- It has a high incidence, mortality and morbidity
- There is a target population easily identifiable
- The screening test can be repeated at a default interval
- The patients diagnosed and treated in an early stage have a higher survival rate than those with advanced disease
- Ultrasound as a screening test is an accurate, simple, repeatable, cost-efficient technique which can be easily accepted by the patient

Over 90% of HCC patients have a known underlying risk factor. This is a good reason why a target population is easy to be identified in order to facilitate the screening and surveillance program. The majority of HCC patients have liver cirrhosis (over 80%). Thus, a screening test should be offered to all patients with liver cirrhosis irrespective of the etiology. Moreover, the fact that one-third of cirrhotic patients will develop HCC during their lifetime represents one more reason for the surveillance of these patients. Worldwide, more than half of cases appear in patients with HBV infection (about 400 million people), while only one third of patients with HCV infection will develop hepatocellular carcinoma (about 170 million people). On the contrary, in the developed Western world, chronic hepatitis C is the major risk factor, while hepatitis B virus infection is responsible for only 20% of cases. Patients with chronic HBV or HCV infection are at risk of HCC development even in the absence of cirrhosis. Therefore, non-cirrhotic HBV carriers with active hepatitis or family history of HCC and non-cirrhotic patients with chronic hepatitis C and advanced liver fibrosis F3 must be considered for a screening program according to the most recent guidelines [1].

Another reason for the surveillance of patients at risk is that their survival depends on the stage of the disease at diagnosis. Thus, for people with early-stage liver cancer who are able to have a liver resection or transplant, the 5-year survival rate is in the range of 50-75%, while for those who have symptomatic liver cancer is less than 10% [3].

Taking into consideration the rate of tumor growth up to the limit of its detectability, the interval of surveillance for HCC is six months, according to the European Association for the Study of the Liver guideline [1]. Ultrasonography performed by highly skilled operators is the most recommended surveillance method, being accepted due to its advantages: the absence of risks, non-invasiveness, good acceptance by patients and relatively moderate cost.

When applied as a method of detection of a focal liver lesion in a patient at risk, echography has high specificity, over 90%, but a lower sensitivity, about 58-89% [4, 5]. Nevertheless, when surveillance is realised by highly skilled operators, this method is able to detect even small lesions, under 2 cm, in over 95% of cases [6].

All these data related to the surveillance of the patients at high risk for developing HCC are generally accepted and stated in clinical practice guidelines.

What happens in reality?
- Is surveillance correctly applied according to current recommendations?
- Are there national programs subsidized by health insurance funds?
- Is there enough patient compliance?
- Is the surveillance program performed by experienced physicians?
- Is there a good performance of the ultrasound equipment used in the surveillance program?
- Do the patients have access to the diagnostic methods recommended by

EFSUMB
Lynne Rudd
28 Portland Place, London W1B 1LY, United Kingdom
Tel: +44 (0) 20 7099 7140
Email: efsumb@efsumb.org
current guidelines (4-phase multide
ctor CT scan or dynamic contrast-enhanced MRI)?

Do the patients have access to a potentially curative treatment (transplant, resection, ablation)?

Although Europe is one of the regions with considerable human and financial resources (unlike Africa for instance), the few published studies so far have demonstrated poor HCC surveillance practices in real-world settings. In Western Europe we found a percentage of 47% [7] and 61.6% respectively [8] of HCC patients diagnosed by screening. Nevertheless, despite the recommendations of national societies of gastroenterology and hepatology [9], the screening program from most Eastern European countries is insufficiently subsidized by health insurance funds. Thus, in Romania, The National Health Service provides a 6.62 Euro discount for an abdominal ultrasound examination. Taking into account this situation, highly skilled operators with high-performance ultrasound systems will never sign a contract with The National Health Service and they will never perform free ultrasound examinations in ambulatory care sites. Therefore, guidelines recommendations to perform an ultrasound exam every 6 months using high-performance ultrasound equipment are applicable only for patients who are able to pay for this investigation. In Western Europe there is not an ideal situation either. A study published last year for example [10] analysed the socioeconomic characteristics of Swiss hepatitis C patients who develop HCC, taking into consideration three socioeconomic factors: professional occupation, education level and annual income. The authors found a lower risk for HCC for the patients with higher education and no significant difference between employed and unemployed patients. Although, the largest differences of HCC risk was seen when comparing the patients’ annual income. The authors find two explanations for which the patients with low socioeconomic status have a higher risk for HCC: 1. they have additional co-factors and 2. these patients do not seek medical attention and thereby are less likely to be treated.

In spite of unfavorable socioeconomic status, according to a recent study, a simple and low-cost intervention, as the patients education, could considerably improve the clinical effectiveness of HCC screening programmes [11].

A good reason to survey the patients at risk is that their survival rate in case of early detection of liver cancer and early treatment is highly different from those with symptoms.

But do the patients diagnosed through a screening program have access to the diagnostic procedures and treatment as recommended by guidelines? A multicenter French study published in summary in 2010 [12], as well as a multicenter Italian study published this year [13] show low adherence to the both diagnostic and therapeutic guidelines in clinical practice, particularly in patients with early-stage HCC. Thus, despite recommendations, in most patients with HCC under 2 cm the diagnosis was based on a single imaging procedure and, in some cases, only on CEUS. This situation happens because contrast enhanced MRI is less accessible and there is a long waiting time for a patient suspected of hepatocellular carcinoma. Also, more than a half of patients detected with HCC with BCLC stage A did not receive curative therapies (transplant, resection or ablation) [13]. Although there are no published studies on this topic, the situation seems to be even more difficult in Eastern and Southern Europe.

All these barriers depending on the physician, on the patient or on the financial resources available in every country lead to a disappointingly low adherence to guidelines in clinical practice even in Europe.

Larisa Sândulescu, Adrian Săftoiu
Research Center of Gastroenterology and Hepatology, University of Medicine and Pharmacy Craiova, Romania

References
EUROSON 2014

Congratulations to Dr Andreas Schuler, DEGUM President of EUROSON 2013 and Dr Fabio Piscaglia EFSUMB President of EUROSON 2013 on the successful Congress in Stuttgart, Germany.

The next Congress will take place in Tel Aviv, Israel. EUROSON 2014 will bring together leading key specialists and the medical ultrasound community to share their vision on the current state of ultrasound in medicine and biology, and the direction our field will take in the upcoming years.

EUROSON 2014 will be a great opportunity to learn about the latest in ultrasound technology, clinical applications and practice through a comprehensive program of educational sessions, scientific papers, practical training programs and technical exhibition.

EUROSON 2014

Telefax: +972-3-5767711
E-Mail: secretariat@euroson2014.com
Website: www.euroson2014.com

Forthcoming Euroson Schools

See www.efsumb.org for more information and other future schools