LIVER BIOPSY – IS STILL AN OPTION?

Why this question? Maybe, because many papers which have appeared in hepatological literature in recent times have assessed different modalities for the evaluation of liver diseases. Here we refer to diffuse illnesses starting with the "classical" liver biopsy and progressing to non-invasive tests, such as biological tests, where blood results are used together for evaluation, or elastographic methods such as ultrasound based techniques.

These present times can be confusing for many people as we are in a transitional period. There are still many physicians that believe that the liver biopsy is the only method that can give a correct answer concerning the severity of a hepatic disease. However, a cohort of researchers have found that biological tests or elastographic methods can replace the liver biopsy, offering the same accuracy.

Let’s take a look at this controversy. Liver biopsy was the first method for evaluation in the hepatological field and for more than 50 years was the gold standard. The severity of a disease was diagnosed by this method and also the prognosis and decision of the treatment was decided. This was the standard of care in these times and possibly the patient was not always the first consideration! Criticism of this method was the invasivity, the pain for the patient and sometime complications with rare fatalities. However, is it not normal to have some fatalities when you are conducting an initial research, not just trying to cure? Secondly, we must examine the performance of a liver biopsy (or performance in the "intent to diagnose"): how often do we have a very correct morphologic diagnosis in which we can trust? For a long time, this was not a real preoccupation of the physician, but when the competition of non-invasive methods appeared, the performance began to count. And here the statistical results are not very good. From the past we know that a liver biopsy can miss liver cirrhosis in approx. 20% of cases. More recently, in large cohort of patients, we found that an optimal morphological fragment is obtained in percutaneous liver biopsy in only approx. 40% of cases. Other methods of histologic evaluation (tranjugular liver biopsy) offered less hepatic tissue while additional factors such as interobserver variability between pathologists are well known. Some pathologists demonstrated that short liver specimens can underestimate the severity of the lesions, finally resulting in an incorrect histological appreciation. As a result of this and on account of the invasivity of the liver biopsy, researchers started to search for non-invasive modalities for liver evaluation, in patients with diffuse liver diseases.

Advantages: first for patient! No pain, no stress before this evaluation, repetitivity, not very high cost! The development of these methods was made first in Europe and France was the leader in this field. They developed biological tests, well known, like FibroTest-ActiTest (for activity and fibrosis evaluation) and later FibroMax (activity, fibrosis, steatosis, nonalcoholic and alcoholic steatohepatitis evaluation). In the field of ultrasound based elastography, FibroScan (Transient Elastography) was developed in France too. Many publications concerning the non-invasive evaluation of liver in comparison with liver
biopsy came from France (Poynard, Castera and others). From France came the first recommendation in the guidelines for the use of non-invasive modalities for liver evaluation as an alternative to liver biopsy. Later, the EASL (European Association for the Study of the Liver) Guideline proposed non-invasive modalities like an alternative to liver biopsy. During time, non-invasive modalities for liver evaluation were spread in other European countries (but, not only European). Others biological test were developed (like ELF, Hepascore, Lok, others) and other ultrasound based elastographic methods appeared and started to be evaluated (in comparison with liver biopsy and in the last time with Transient Elastography), like ARFI (Acoustic Radiation Force Impulse Elastography) or 2D-SWE (2D-Shear Wave Elastography, SuperSonic Imagine).

These non-invasive modalities for liver evaluation have spread everywhere in the world, from Japan, China and Korea to Canada and Brazil. Increasing number of patients are evaluated with these methods now, decreasing in the real world, the number of liver biopsies. Only in the USA there is still a delay for this introduction, maybe in connection with the severity of FDA regulations for the approval of such methods.

In this moment, many meta-analyses or large cohorts of patients have demonstrated very good results of these non-invasive methods for the evaluation of fibrosis (elastographic methods) or inflammation, steatosis and fibrosis (in biological tests such as FibroMax). These methods are good for the "intention to diagnose" a case, the failure rate being quite low and can be repeated as often as is necessary while being excellent for establishing the diagnosis of moderate or severe fibrosis (accuracy more then 85-90%). On the other hand, in some diseases, such as C chronic hepatitis, we have now very potent drugs, than can cure the vast majority of patients, irrespective of the degree of fibrosis. If we consider prioritising these patients, non-invasive methods are quite good.

Therefore, in the future, everywhere we shall see a decreasing number of liver biopsies (including in more conservative countries such as the USA). Probably, in a percentage of patients, the liver biopsy is still necessary (maybe in autoimmune hepatitis, cholestatic diseases, B chronic hepatitis or others), or maybe for some academic studies.

For focal liver lesions (which is not the topic of our discussion), probably we shall see an increasing need for biopsy (echoguid-ed), regarding the molecular medicine perspective or personalized treatment for every patient.

Finally to answer the question in the title: liver biopsy - is it still an option? Yes, is a good option, but in many cases it can be now replaced by non-invasive modalities of liver evaluation. Biological tests or elastographic methods or a combination of these two modalities (this combination can increase confidence) will replace many liver biopsies. The comfort and the safety for patients, their reasonable price and the excellent accuracy of these methods are the main arguments in the future for this new direction of evolution, from an invasive procedure (liver biopsy) to the non-invasive modalities of evaluation.