The question of how much invasiveness is required for diagnosing liver disease and recognizing cirrhosis is highly relevant for patients, clinicians, and health economists. When a few years ago I suggested to Thierry Poynard that we compare laparoscopically guided liver biopsy with non-invasive testing, he was enthusiastic because, in his words, laparoscopy is the Rolls Royce (or Mercedes Benz) of liver diagnosis. We have not yet managed to organize the study discussed then, and are thus stuck with the present controversy – but I agree, laparoscopy is as good as a Rolls Royce; however, it is cheaper and more versatile, and with the advent of minimally invasive laparoscopy (mini-laparoscopy) the technique has the cost of a Volkswagen, the comfort of a Citroen, the safety of a Volvo, and the reliability of a Mercedes, all with the gain of information of a modern GPS navigation system included.

While I was writing this article, a patient was on my ward with decompensated alcoholic liver disease. She had a bilirubin of 5 mg/dl, an INR of three and ascites. Her fibroscan showed a score of 23 kPa [1]. Was this an obvious case of advanced cirrhosis? In mini-laparoscopy, we saw a swollen fatty liver but no nodules. A biopsy revealed an extremely fatty liver with a moderately severe alcoholic hepatitis, only moderate fibrosis, and no cirrhosis. Does this make a difference? Yes, as she is now being treated with acetylcysteine and steroids, and she is already improving. In addition, as hope represents such an important “drug” in all aspects of medicine, we made sure to deliver it in large amounts.

I was less fortunate with another very recent patient of mine. He was a genotype 1 hepatitis C patient at the age of 58 with no additional risk factors. Diligent as I am in making a reliable and aggressive diagnosis, he underwent liver biopsy prior to the initiation of standard PEG-interferon and ribavirin therapy, but for various reasons biopsy was performed percutaneously using a Menghini-needle; the histology showed moderately active hepatitis C and stage 3 fibrosis. Unfortunately, he failed to respond to treatment, which was, therefore, stopped after three months. As he lived a good distance away, we then lost touch with him until we contacted him because we wanted to include him in a trial for non-responders. He came to the clinic reporting good health. He had just retired as a school teacher, had a new girlfriend, and was looking forward to a happy retirement period. However, his screening laboratory showed an AFP value of 1435 ng/ml, which was quickly explained by advanced HCC with lung metastases. Disease progressed despite local chemoembolization and systemic sorafenib therapy and the patient died a few months later. Had I performed a mini-laparoscopy at the initial diagnosis, I would most probably have seen the cirrhosis, we would then have undertaken a systematic screening programme and we probably would have recognized this AFP-positive HCC early enough for curative treatment.

Are these just isolated cases? All cases are unique, and the list of examples I could present would be very long. When confronted with liver disease, we would need to know the cause, the activity and the degree of fibrosis. All three aspects are best answered by a liver biopsy under macroscopic control. With the exception of viral hepatitis, there are few liver diseases that can be diagnosed by laboratory tests alone, and there is no patient, in whom laboratory tests alone can answer the question of whether the increase of liver enzymes is really due to the suspected causative agent. Alcohol is the most important factor determining the prognosis in hepatitis C [2], and this can best be assessed by histology. Co-morbidity due to co-existing conditions such as NASH, alpha-1 antitrypsin deficiency, iron overload, or rare co-incidences such as schistosomiasis or sarcoidosis may be detected by biopsy and have very relevant therapeutic consequences [3–6]. Thus, even in an apparently obvious liver disease, biopsy often reveals important surprises. This is all the more the case if clinical and laboratory examinations do not make a definite diagnosis.

Biopsy is the most important cornerstone in the detection and differentiation of the causes of liver disease. Biopsy is good, but not excellent, for the staging of liver disease. Sampling error, small biopsies, fractured biopsies, or irregular cirrhosis may all account for an under-diagnosis of cirrhosis by percutaneous or transjugular liver biopsy. Several studies have demonstrated very reliably that the macroscopic assessment of the liver surface by laparoscopy will detect 30% more cases of cirrhosis cases than will liver biopsy alone [7]. This finding was recently confirmed by us in a randomized trial comparing mini-laparoscopy with percutaneous liver biopsy in 857 patients [8]. In addition, mini-laparoscopy proved to be at least as safe as a percutaneous biopsy – and probably much safer than a case of unrecognized cirrhosis, or being treated for the wrong disease. The cost of the procedure...
is low and easily offset by the health benefit resulting from the added information.

If I had chronic liver disease, I would like to know if I have cirrhosis. Of course, knowing does not mean guessing, and all non-invasive tests have significant false positive and false negative rates; inevitably, these will result in worrisome wrong diagnoses, inadequate counselling, and the misallocation of health care resources, which are all much more costly than the test – and more risky as well. Even the best study of Fibroscan found a kPa of 15 or higher only in 85 out of 120 (thus missing 35/120 cirrhotics), but at the same time diagnosed a non-existent cirrhosis in 45 (out of 655) patients [9]. Would you prefer to be amongst the false positives or amongst the false negatives?

With a French counterpart in this debate, I do not want to stick to cars as a comparison: if you want to know the Louvre, what information would you consider adequate: a thoughtful article in a newspaper (laboratory tests including a fibrotest)? The Wikipedia article (laboratory tests including a fibrotest plus fibroscan)? Or would you prefer a good catalogue of the museum with its explanatory notes (a liver biopsy assessed by an expert pathologist)? Personally, I would visit the museum and buy a catalogue to help me interpret my personal impressions (laparoscopy and biopsy). I much prefer the personal visit to the museum: the Louvre is worth it – and your patients with liver disease are also worth it.

References