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The Patient Bomb: Sustained Viral Response after Hepatitis C in Cirrhosis

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Keywords

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Cirrose e resposta virológica mantida

Palavras Chave

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The paper by Pereira Guedes et al. [1], analyzing data from a real-world Portuguese cohort with advanced liver disease, provides us with some interesting ideas, with translation into our clinical and real practice. The study, albeit retrospective, has evaluated data from 237 patients in a tertiary university hospital; 99% completed treatment, and the sustained viral response (SVR) was 98%, similar to the best trial results [2]. Almost two-thirds of the patients were cirrhotics, one-third having intense fibrosis. Patients have been included in the first years of medical therapy with direct antiviral agents (DAA) in Portugal [3].

The overall mortality rate in this study was 19/1,000 person-years, and the liver-related mortality rate was 9.5/1,000 person-years. The hepatic decompensation incidence rate was 25/1,000 person-years, and the hepatocellular carcinoma (HCC) incidence rate was 11.6/1,000.

SVR is associated with a low risk of, but does not prevent, evolution to HCC disease progression, especially in the presence of other causes of liver injury [4]. It is recommended that these patients be kept under close surveillance [5]. There are two main messages: even with cirrhosis, it is possible to eliminate individually the virus, sustained some years after the end of therapy. There is no recurrence of HCV as is the case for HBV. Albeit, cirrhosis is a disease for life. We can talk about real "cure" for patients without cirrhosis but not for patients with intense fibrosis or cirrhosis. It is different to cure the virus only (cirrhosis) and to cure both the virus and the disease (if no cirrhosis).

Some authors call for a need of simplification, saying that it is not necessarily the best evaluation of liver fibrosis. The two best methods for grading fibrosis are liver biopsy and elastography (Fibroscan®). We know the utility and the accuracy of some scores like AST to Platelet Ratio Index (APRI) and others like FIB-4, but they are not as good as elastography. If we live in a setting in which we have access to Fibroscan®, as is the case of the majority of Western Medicine, for example in Portugal. Liver cirrhosis is an oncogenic disorder, one of the most oncogenic situations that we know in medicine, with a 10–40% risk of evolution to HCC at 10 years.

In the paper by Pereira Guedes et al. [1], elastography, liver biopsy and clinical evaluation was used before therapy. After DAA treatment, there is a reduction of the value of elastography. Specially in patients with values close to 12.5 kPa, after therapy, it will be less than 12.5 kPa, with a value of "no cirrhosis" – a false negative…

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Why in the name of simplification, put the safety in question in a pre-oncogenic situation? The risk stills persist after SVR, even though at a lower level.

In this study, the average age was 58 years, 16.6% had esophageal varices and the average level for elastography was 20.73 KpA. 70% have had cirrhosis. In fact, patients with advanced disease need treatment as soon as possible. We can say that to treat liver cirrhosis with hepatitis C is a "liver emergency." Almost 50% of the patients had been treated with interferon, which means that they were "difficult" patients. The adhesion has been fantastic, never seen in other situations. Even in patients with difficult situations, like People Who Injected Drugs (PWID), the adhesion has been globally almost 100% [6].

The follow-up of this cohort is too short, only 2.5 years after EOT, but the liver mortality was 2.2% (19/1,000 person-years). Four patients (1.7%) died of HCC.

De novo HCC appeared in 10 patients, in 4 patients during treatment. Mortality was higher in patients with cirrhosis, in patients with higher values of MELD (Models for End-Stage Liver Disease, >10), and in patients with a previous history of decompensation.

In the first years of DAA, we have been dealing with difficult patients (i.e., advanced cirrhosis), especially in the very beginning. Saying so, we are dealing with one of the highest oncogenic diseases in medicine. The risk of HCC is between 10 and 40% at 10 years.

Another question is related to the quality of the diagnosis of HCC with ultrasound [7]. If HCC appears during treatment or a short time after the end of treatment, we can conclude that it was there at the time of the last ultrasound, perhaps with small dimensions. But it is known the high dependency from the operator, that lack of control of the practice of doctors who perform the liver ultrasounds. Besides a basic education in digestive ultrasound, we should create a specific and official competence recognized by the Portuguese Board of Doctors (Ordem dos Médicos) (and/or a periodic recertification).

In conclusion, it is recommended to keep these patients under surveillance. Cirrhosis is a disease for life, and we must keep in mind an important message when communicating the SVR to patients with cirrhosis/intense fibrosis. The "Diploma/Clinical Report" should say: "We have viral elimination for life, but you need to do an ultrasound with a good radiologist or a doctor very keen on digestive ultrasound every 6 months. For life."

Finally, SVR is associated with a low risk of, but does not prevent, HCC occurrence or disease progression, especially in the presence of other causes of liver injury. Patients should avoid alcohol [8], lose weight [9], stop smoking, control diabetes [10], and drink coffee.

It is a second-hand harm reduction risks and a damage control. The elastography done before therapy can help with the risk estimation [11].

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