Editorial

Surgery for hepatocellular carcinoma can provide the same life-expectancy as transplant of that of general population

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When deciding for the optimal treatment to adopt in patients suffering from hepatocellular carcinoma (HCC), the surgical approach is commonly considered as the most curative option (1,2). The scarcity of donors for liver transplantation (LT) led surgeons to bridge patients until an eventual future transplant (salvage LT), opting in first instance and when feasible for hepatic resection (HR) also for those patients otherwise transplantable (2). In the study published by Pinna and colleagues in Annals of Surgery 2018, it was verified in what measure LT and HR can provide for HCC the same mortality expected in the general population, defining the so called "statistical cure" (3).

Data from 1,218 HCC patients treated with LT and from 2,068 HCC patients treated with HR were used to estimate the "statistical cure" after surgery, however, as first it should be clearly explained its definition. "Statistical cure" occurs when the mortality of patients treated for a specific disease returns to the value expected in the general population (3,4). In other easier words, it is a single percentage able to answer to the specific patient's question: "*what are my chances to return to having a normal life expectancy, as if I had never been sick with cirrhosis and HCC?*". A specific event and temporal endpoint should be defined and in the present work, the time from surgery until death or recurrence was correctly used as the primary survival measure [disease-free survival (DFS)], since it is questionable to define "as cured" by the tumor a patient who, even if alive, has HCC recurrence (2). However, Authors argued that in presence of increased efficacy of therapies for HCC recurrence after resection, these patients can experience long-term survivals even after tumor relapse (3,5). Therefore, statistical cure was also calculated considering the time elapsed from surgery until solely patient's death [overall survival (OS)]. By this way, Authors considered HCC as a "*chronic illness requiring continuing therapeutic options*" (3). In the recent years, several neoplastic and non-neoplastic diseases have been treating as chronic illness.

Finally, cure probabilities after LT were adjusted for potential drop-out rates during waiting-time.

Results showed that LT outperforms HR in providing the highest chances of being alive and without HCC recurrence, even in presence of a drop-out from the LT waiting-list up to 20%. That is, considering DFS, the cure fraction after LT was 74.1% and after HR was 24.1%. Such a difference is consequent to the fact that LT not only removes the tumor but also the underlying cirrhosis which is the main cause of HCC occurrence, providing the most powerful radical therapy. However, not all that glisters are gold. It is well known that LT is not an accessible option for all HCC patients, being HR daily adopted and still able to provide some chances of long-term life expectancy; even the recent AASLSD (American Association for the study liver disease) guidelines for the treatment of HCC stated that for single tumor larger than 25 mm, liver resection is the treatment of choice (6). Pinna and colleagues showed that when considering LT drop-out rates and using OS as the survival measure for cure definition, the benefit of LT over HR became small or even negligible for single tumors

<5 cm. This finding can be summarized as follows: in some clinical scenario, HR can provide the same life-expectancy of LT from an intention-to-treat point of view, avoiding the transplant procedure but at the cost of continuum of cares for both cirrhosis and eventual HCC recurrence (3).

Overall, the study gives to transplant surgeons the relief from the regret of not having transplanted all single HCC patients, providing that most of candidates to HR (single tumor <5 cm; >70% of patients) received a therapy which returned the same life-expectancy expected after enlistment for LT. This is a very important issue especially in Western countries in whom the last decades were afflicted by hepatitis C virus (HCV) untreatable recurrence after LT (7). The 67.1% of resected patients in the present study were HCV positive, in a period (2000 to 2016) where only the latter years offered direct-acting anti-viral (DAA) availability for HCV cure (7,8). Thus, Authors showed how they avoided transplant and possible deadly HCV recurrence in most of HCC patients, eventually determining a reasonable life-expectancy after resection, so as to allow to these patients to have access to DAA therapy and further life-expectancy prolongation. Unfortunately, despite this latter aspect, it must be emphasized that early HCC recurrence is the main unfavorable event to expect after HCC surgery (9). DAA therapy stops the progression of cirrhosis, reduces the de-novo HCC risk but early HCC recurrence depends from metastases from the primary removed tumor. In this sense, it should be noted that HCC recurrence after LT inevitably determines the patient's death as a result of the effect of the immunosuppression; on the contrary, and fulfilling the Author initial reasoning, increased efficacy of therapies for HCC recurrence after resection, can determine long-term survival even after tumor relapse (3,5), confirming the present end-results.

Taking all these aspects together it can be finally stated that present results provided evidence that the decision-making to resect rather than transplant patients in an era affected by HCV was justified in a long-term perspective. The introduction of DAA will dramatically change this scenario in the future, both reducing HCC patients in need for LT as well as reducing HCC overall. However, it should emphasize that for well compensated patients with single lesion less than 5 cm, LR remains one of the best treatment options with a chance of cure (3,6).

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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