Twenty years after: from Milan criteria to a "blended" approach

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When Milan criteria (MC) were first proposed in 1996, they rapidly became the cornerstone for the selection of patients with hepatocellular cancer (HCC) waiting for liver transplantation (LT) (1). The use of the MC consented to very well select patients at low risk for post-LT recurrence, thus obtaining excellent survival rates (2). However, twenty years later, it is now clear that the MC are a too restrictive selection criterion, unfortunately excluding too many patients from the potentially curative strategy of LT. Several innovations have been recently introduced in the specific field of tumor oncology and transplant, putting the bases for the creation of new and more refined allocation and selection processes (3).

For example, several enlarged criteria have been proposed in the last years, all aimed at improving the ability to select patients. Apart criteria based on morphology only (4), new scores combining radiological and biological aspects are now presenting a growing interest for the scientific community: alpha-fetoprotein (5), inflammatory markers (6), and des-gamma carboxy-prothrombin (7) all represent recent and promising areas of research.

The improved ability of loco-regional therapies has been contemporaneously reported in the last decade, with the introduction of innovative strategies like the trans-arterial radio-embolization (TARE). TARE looks to be able not only to more efficaciously treat advanced HCCs (8), but also to consent to downstage and then transplant initially excluded HCC cases with macrovascular invasion (9).

The combination of sorafenib with other strategies has been also largely investigated in recent years, with the intent to better clarify if its use in a neo-adjuvant or adjuvant fashion should be of some utility: until now, discordant data have been shown (10), and new and more solid results are awaited.

Immunosuppression (IS) represents another field in which no definitive data have been produced: new studies are required aimed at identifying both the connection of IS with the risk of recurrence or specific protocols able to protect against tumor progression (11,12).

Finally, several technological evolutions in the field of surgery have been done in this latter period, all aimed at improving our ability to manage HCC patients. For example, the implementation of the laparoscopic hepatic resection (13), the more liberal use of living-donor LT, even in Western countries (14), or finally the growing use of perfusion machines with the intent to improve the use of marginal grafts (15) all represent new opportunities for the physicians involved in the management of HCC patients waiting for LT.

Twenty years after the MC introduction, the time is arrived for a new revolution based on a "blended" management and selection approach (16).

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Footnote

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Translational Gastroenterology and Hepatology, 2017

Page 2 of 2

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