ALPPS procedure for hepatocellular carcinoma with macrovascular thrombosis: a new opportunity?

Giovanni Battista Levi Sandri, Quirino Lai, Michel Rayar, Laurent Sulpice

treatment. We are pleased to learn that this hypothesis was confirmed by Halfon *et al.* in their clinical practice.

In summary, the combination therapy of PegIFN alfa-2a and NA can be beneficial, but the optimal strategies for combination remains to be determined. With newly developed therapeutic regimens appearing in the near future, including cytokines, HBV entry blockers, Toll-like receptor agonists, and therapeutic vaccines, it is conceivable that use of these additional immunomodulators rather than IFN, might be of synergic benefit in the restoration of innate and adaptive immune responses in CHB patients (Fig. 1). Currently two randomized, multicentre, comparative and prospective clinical trials (Endeavor and Anchor study), involving combination therapies of IFN, NA and immunomodulators (cocktail therapy) for NA-treated CHB patients, are under way in China to explore this hypothesis.

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Conflict of interest

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Di Wu
Meifang Han
Qin Ning*
Department and Institute of Infectious Disease, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China
*Corresponding author. Address: Department and Institute of Infectious Disease, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1095 Jiefang Avenue, 430030 Wuhan, China. Tel./fax: +86 27 83662391.
E-mail address: qning@vip.sina.com

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To the Editor:

We read with interest the recent article entitled, "Surgical treatment of hepatocellular carcinoma associated with hepatic vein tumour thrombosis" published by Kokudo *et al.* [1]. We congratulate the authors for their study, based on an experience of over 1500 liver resections. The authors conclude that surgical treatment of patients with tumour thrombosis, involving major hepatic veins (mHVTT), does not differ in terms of mortality, length of hospital stay and frequency of complications compared with patients with microscopic invasion (pHVTT). We agree with the authors' conclusion. Major hepatectomy was performed in 67% of the cases in the mHVTT group, including four where right extended or left hepatectomy was required. We would like to draw attention to those selected patients. Since the first two-staged hepatectomy reports [2], liver resection indications have been implemented with new surgical treatments, such as the Associating Liver Partition and Portal vein ligation for Staged hepatectomy (ALPPS) procedure. Vennarecci *et al.* [3] described the ALPPS procedure for hepatocellular carcinoma (HCC) with major vascular invasion and concluded that this technique may increase

the rate of curative liver resections for tumours previously considered unresectable. Kokudo *et al.* [1] considered surgical resection of cases where preoperative characteristics jeopardize oncological radicality, only with the intent to prevent embolic complications or tumour rupture. The authors suggested that this aggressive surgical approach should be considered only in Child-Pugh class A patients, in which liver function is still acceptable. We agree with this statement. A multicentre analysis recently confirmed that the ALPSS procedure offers a better chance for complete resection in patients with primarily unresectable liver tumours [4]. In another study, ALPPS has been described for cirrhotic patients with HCC [5], in which all resected cases had preserved liver function (Child-Pugh class A). An increase in the future liver remnant (FLR) from 33% to 43% was observed within one week; this increase reached 54% after hepatectomy. These important results suggest that it is possible to achieve R0 resection in patients with mHVTT as long as patients present preserved liver function. Notwithstanding, ALPPS represents a suitable indication only in a small number of patients with portal vein thrombosis (PVT). In fact, patients treatable with ALPPS should be carefully selected and evaluated in order to draw a benefit in terms of survival. Model for end-stage liver disease (MELD) and portal hypertension (PHT) are two crucial factors in decision making for surgical resection, especially when major liver resection or the ALPPS procedure are contemplated. As previously described, liver resection in cirrhotic patients with MELD score >14 is not recommended [6], and when the score is >9 other treatment modalities should be considered [7]. PHT was for a long time considered an absolute contraindication for liver resection. However, recent experiences suggest that liver surgery can be safety achieved also in the presence of PHT, mainly in the case of limited hepatic resections in patients with Child-Pugh A [8–10]. Nevertheless, we believe that PHT must remain a contraindication for ALPPS procedure as well as for major hepatic resections. According to the classification of PVT by Shi *et al.* [10] we suggest type III-IV as contraindications for the ALPPS procedure, whilst type I-II can be safely approached with this surgical technique. The suboptimal effect on the regeneration of truncal with respect to segmental/subsegmental PVT must also be taken into account. Various grades of liver atrophy consequent to truncal/main PVT can be preoperatively evaluated with volumetric computed tomography (volCT), calculating in this way the liver remnant to body weight ratio (BWR). The volCT scan can be repeated after the first surgical step, starting from postoperative day 7. Patients can be scheduled for the second step when a liver remnant to BWR of 0.8 was achieved. Consistent with these arguments, ALPPS seems to be an intriguing strategy, which should be explored in the next future. ALLPS can represent a valid approach also in patients with mHVTT, with the intent to increase the surgical indications.

In conclusion, we hope that further studies will focus their attention on patients with HCC that are presently considered unresectable. Multicentre studies are aimed to better define indications for HCC in cirrhotic patients with hepatic vein tumour thrombosis.

Conflict of interest

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Giovanni Battista Levi Sandri[1,2,*]
Quirino Lai[2]
Michel Rayar[1]
Laurent Sulpice[1]
[1]*Department of General Surgery and Organ Transplantation, Umberto I Policlinic of Rome, Sapienza University of Rome, Rome, Italy*
[2]*Service de Chirurgie Hépatobiliaire et Digestive, Centre Hospitalier Universitaire de Rennes, Université de Rennes 1, France*
*Corresponding author. Address: CHU Rennes, Service de Chirurgie Hépatobiliaire et Digestive, Université de Rennes 1, F-35033 Rennes, France. Fax: +33 299 28 41 29.
E-mail address: gblevisandri@gmail.com