Editorial

Radiological simultaneous portohepatic vein embolization (RASPE) and major hepatectomy with hepatocellular carcinoma (HCC)

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Radiological simultaneous portohepatic vein embolization (RASPE) is a relatively new technique, which aims to rapidly increase the future liver remnant (FLR) in patients with very small FLR in order to undergo major hepatectomy.

It was initially described by Hwang *et al.* as a two stages procedure, which, included portal vein embolization (PVE) first, followed by embolization of right hepatic vein (HVE) after several days (1). They concluded that sequential application of PVE and HVE is safe and leads to a stronger compensatory regeneration of the FLR than does PVE alone. Recently, the process of simultaneous portohepatic vein embolization has been reported by Guiu *et al.* (2). Briefly the procedure was done under general anesthesia. The right HV (and accessory right HV when present) were accessed first. Then the distal part of the right HV was punctured under US and the right PV branch was assessed with US-guided technique. Embolization was conducted using a mixture of iodized oil and n-butyl-cyanoacrylate. It was concluded that simultaneous PVE and HVE induces safe and rapid hypertrophy of the FLR before right hepatectomy (2).

Furthermore, two very recent studies by Laurent *et al.* (3) and Guiu *et al.* (4), mainly with patients with liver metastases and inadequate FLR, showed that RASPE or liver venous deprivation (LVD) which is a similar term, is safe and induces faster and greater FLR, with better functional capacity in comparison to PVE, with less risk of post-operative liver failure. For this reason RASPE could be considered a safer "radiological associating liver partition and portal vein ligation" (ALPPS) for staged hepatectomy.

It would certainly be interesting to explore the potential applications of RASPE in patients with hepatocellular carcinoma (HCC).

HCC is the 5th most common cancer worldwide and the 3rd most common cause of death. Despite the vaccination for hepatitis B and the effective anti-viral treatment for hepatitis B and C the world incidence is increasing. This is mainly due to the increase in non-alcoholic fatty liver disease (NAFLD) and steatohepatitis which are the hepatic components of metabolic syndrome (5).

HCC is mainly developed in chronic liver disease, where there is hepatic steatosis, fibrosis or cirrhosis. Liver resection and liver transplantation are the main treatment options in order to achieve long term survival or cure. Liver transplantation offers very good results, but has many limitations, as it is usually applied in selected patients which mainly fulfil the Milano criteria (single tumor <5 cm, 3 tumors <3 cm each). Liver resection is the treatment of choice for large HCCs with preserved liver function. Recent evidence suggests that liver resection can expand its indications as it can be applied even in advanced stages of the disease (multinodular HCCs, HCCs with limited macrovascular invasion) with satisfactory long-term results (6,7). Furthermore, anatomic resections with broad surgical margins (>1 cm) provide better results, as HCC has a tendency to invade the small branches of portal vein, and to cause intrahepatic dissemination. However, major liver surgery is prohibited by the presence of chronic liver disease, which can have a significant impact on portal

venous pressure and significantly decreases the capacity for liver regeneration.

The gold standard for patients with HCC and inadequate FLR is PVE. The main indications for PVE, in patients with HCC and presence of liver fibrosis or cirrhosis, are FLR <40% when liver function is good (ICGR15 <10%) and FLR <50% when liver function is affected (ICGR15: 10–20%) (8). However, PVE has limitations: it can not be applied effectively when FLR is very small (<25%) and a long waiting period (>4 weeks) is required before liver resection, in order that adequate hypertrophy of FLR can be achieved. Furthermore, segement IV embolization is technically very demanding, when an extended right hepatectomy is required.

In order to increase the regeneration of the FLR, the ideal method should be safe, induce rapid liver regeneration with good FLR functionality and be associated with low postoperative mortality.

ALPPS, which is the alternative of PVE in patients with small FLR, provides rapid liver regeneration but not with good functionality. A recent systematic review assessed the role of ALPPS in 176 patients with HCC and inadequate FLR. They concluded that ALPPS is safe and feasible to treat selected patients with initially unresectable HCC but with high 90-day mortality (17.6%) and, as yet unclear oncological outcomes (9).

RASPE has the potential to overcome the disadvantages of PVE and ALPPS: it increases the FLR rapidly and effectively, with preservation of liver function (FLR-F) as expressed by the use of Technetium (99mTc) mebrofenin scintigraphy (4), is safe and with low post-operative mortality. Furthermore, embolization of middle HVE facilitates the performance of extended right hepatectomy.

The increase in regeneration rate *vs.* PVE could be due to several factors: embolization of the HVE could prevent persistent portal inflow and could reduce porto-portal collaterals. Furthermore, RASPE can increase liver injury since occlusion of HVE out-flow and simultaneous PVE could reduce the flow in the hepatic artery through the hepatic arterial buffer response.

There are, of course, several questions which have to be answered: what will be the effect of RASPE in patients with liver fibrosis or cirrhosis, where liver regeneration capacity is reduced? The majority of patients, where RASPE has been done, are patients with colorectal metastases, where liver is not fibrotic. Also, as the combination of TACE and PVE seems to be more effective in patients with large HCCs or satellite lesions (8), what will be the risks for the liver after sequential application of TACE and RASPE?

RASPE is also a technically demanding procedure and it still has to be shown if it is easily reproducible.

The randomized trial which is running for the effect of RASPE *vs.* PVE in patients with colo-rectal liver metastases should provide several answers, on the FLR changes at 3 weeks after the procedure (10). However, a similar trial should be conducted with patients with HCC, as the regeneration process is different in diseased liver.

Overall, RASPE has the potential to become the procedure of choice in patients with HCC and small FLR (<25%).

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