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Hepatic venous pressure gradient after portal vein embolization: An accurate predictor of future liver remnant hypertrophy

Kayvan Mohkam[a,b,*], Agnès Rode[c], Benjamin Darnis[a], Anne-Frédérique Manichon[c], Loïc Boussel[c], Christian Ducerf[a], Philippe Merle[d], Mickaël Lesurtel[a], Jean-Yves Mabrut[a,b,*]

[a] Department of General Surgery and Liver Transplantation, Hospices Civils de Lyon, Croix-Rousse University Hospital, Lyon, France
[b] Ecole Doctorale EDISS 205, EMR 3738, Claude Bernard Lyon 1 University, Lyon, France
[c] Department of Interventional Radiology, Hospices Civils de Lyon, Croix-Rousse University Hospital, Lyon, France
[d] Department of Hepatology, Hospices Civils de Lyon, Croix-Rousse University Hospital, Lyon, France

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ABSTRACT

Background: The impact of portal hemodynamic variations after portal vein embolization on liver regeneration remains unknown. We studied the correlation between the parameters of hepatic venous pressure measured before and after portal vein embolization and future hypertrophy of the liver remnant after portal vein embolization.

Methods: Between 2014 and 2017, we reviewed patients who were eligible for major hepatectomy and who had portal vein embolization. Patients had undergone simultaneous measurement of portal venous pressure and hepatic venous pressure gradient before and after portal vein embolization by direct puncture of portal vein and inferior vena cava. We assessed these parameters to predict future liver remnant hypertrophy.

Results: Twenty-six patients were included. After portal vein embolization, median portal venous pressure (range) increased from 15 (9–24) to 19 (10–27) mm Hg and hepatic venous pressure gradient increased from 5 (0–12) to 8 (0–14) mm Hg. Median future liver remnant volume (range) was 513 (299–933) mL before portal vein embolization versus 724 (499–1279) mL 3 weeks after portal vein embolization, representing a 35% (7.4–83.6) median hypertrophy. Post–portal vein embolization hepatic venous pressure gradient was the most accurate parameter to predict failure of future liver remnant to reach a 30% hypertrophy (c-statistic: 0.882 [95% CI: 0.727–1.000], $P < 0.001$). A cut-off value of post–portal vein embolization hepatic venous pressure gradient of 8 mm Hg showed a sensitivity of 91% (95% CI: 57%–99%), specificity of 80% (95% CI: 52%–96%), positive predictive value of 77% (95% CI: 46%–95%) and negative predictive value of 92.3% (95% CI: 64.0%–99.8%). On multivariate analysis, post–portal vein embolization hepatic venous pressure gradient and previous chemotherapy were identified as predictors of impaired future liver remnant hypertrophy.

Conclusion: Post–portal vein embolization hepatic venous pressure gradient is a simple and reproducible tool which accurately predicts future liver remnant hypertrophy after portal vein embolization and allows early detection of patients who may benefit from more aggressive procedures inducing future liver remnant hypertrophy. (Surgery 2018;143:1-2.)

Major hepatectomy often represents the best chance for long-term survival in patients with primary or metastatic liver malignancies.[1–3] After hepatectomy, a minimal volume of the future liver remnant (FLR) ranging from 20% to 40% of total liver volume is required to avoid the risk of postoperative liver failure.[4–6] When such a threshold cannot be achieved in first intent, portal vein embolization (PVE) may be undertaken in an attempt to increase FLR volume.[7–9]

Unfortunately, up to 20% of patients undergoing PVE will not achieve sufficient FLR hypertrophy, which precludes operative resection.[10,11] Thus, PVE is also considered as a functional test allowing a selection of potential candidates for major resection.[12,13] Such a test, however, requires a waiting period of up to 3 weeks before assessing the actual FLR hypertrophy.[6,14] In this context, it would be of great interest to find a predictor for failure of FLR hypertrophy at the time of PVE. This would allow consideration of an

* Corresponding author: Hospices Civils de Lyon, Croix-Rousse University Hospital General Surgery and Liver Transplantation 103, Grande Rue de la Croix-Rousse 69317 CEDEX 04 Lyon France
E-mail addresses: kayvan.mohkam@chu-lyon.fr (K. Mohkam), jean-yves.mabrut@chu-lyon.fr (J.-Y. Mabrut).

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alternative strategy for obtaining FLR hypertrophy, such as associated liver partition and portal vein ligation for staged hepatectomy (ALPPS)[15] or combined hepatic and portal vein embolization.[16]

The impact of portal hemodynamics in the pathophysiology of liver regeneration has been suggested in several works in the past.[17,18] It is well-established that portal venous pressure (PVP) increases to varying degrees after PVE.[12] In contrast, however, the exact role of PVP change on liver regeneration is not known. While an increased postoperative PVP has been identified as a predictor of postoperative liver failure in both cirrhotic[19] and non-cirrhotic patients,[20] it has also been suggested that portal pressure represents a trigger for hepatic regeneration after hepatectomy.[17,18] We hypothesized that changes in parameters of PVP could be correlated with FLR hypertrophy after PVE, and thus we aimed to assess the impact of various parameters of PVP before and after PVE on FLR hypertrophy after PVE.

Patients and methods

Study population and design

Between April 2014 and August 2017, all patients who were eligible for major hepatectomy and had an indication for PVE were enrolled in this study. During the PVE procedure, all patients underwent simultaneous measurement of parameters of hepatic venous pressure. All data were collected prospectively and analyzed retrospectively. The study protocol conformed to the precepts of the 1975 Helsinki declaration.

Portal vein embolization

Percutaneous, transhepatic PVE was performed under general anesthesia using a contralateral approach through the FLR. The latter approach was used, because an ipsilateral approach does not allow final portography and measurement of PVP, and prior studies have shown no differences in terms of adverse events between the 2 approaches.[11,21] A distal portal branch was accessed under ultrasonographic guidance, punctured with a 15 cm-long, 16-gauge introducer needle. After a vascular sheath was secured with an 11 cm-long, 5-French introducer set, flush portography was performed to assess the portal anatomy. Embolization was conducted using a mixture of 1 to 5 mL of ethiodized oil (Lipiodol; Guerbet, Aulnay-sous-Bois, France) and 1 mL of n-butyl-cyanoacrylate (Glubran 2; GEM Srl, Viareggio, Italy). When needed, segment IV was embolized using microcoïls (2 mm 3 cm) (Nester; Cook Medical, Bloomington, IN) in each subsegmental (IVa and IVb) branch. A final portography was performed to check the completeness of the embolization.

Pressure measurements

Portal venous pressure was measured at the beginning and at the end of embolization, at the same level in the portal vein. After puncture of the right femoral vein, monitoring of the central venous pressure was performed through a 5-French catheter located in the inferior vena cava at the level of the hepatic vein. Measurement of hepatic venous pressure parameters were recorded with a PowerLab 4/35 DAQ System (LabChart Software; ADInstruments, Dunedin, New Zealand) and Pressure Gauge Kit (ADInstruments). The pressure transducer was placed in a fixed position at the midaxillary line of the recumbent patient. A zero measurement with the transducer open to air started the study. Measurements were repeated until stability was achieved, and two consecutive values were consistent. The hepatic venous pressure gradient (HVPG) was calculated as the difference between the PVP and the central venous pressure.

Endpoints and definitions

The primary endpoint was FLR hypertrophy, defined as growth of FLR volume expressed in percentage. Computed tomography or magnetic resonance imaging-based hepatic volumetry was performed before and 21 days after PVE to determine the volumes of the total liver, the part planned to be resected, the total tumor mass, and the FLR. The FLR hypertrophy was expressed in percentage and calculated according to the following formula: %FLR hypertrophy = [FLR volume after PVE – FLR volume before PVE] / FLR volume before PVE x 100%. The FLR was also normalized to the body weight and to the standardized total liver volume based on the calculation of body surface area.[22] We also compared patients with an FLR hypertrophy of at least 30% with those who failed to reach 30% hypertrophy after PVE. Postoperative morbidity was graded according to the Clavien–Dindo classification.[23]

Statistical analysis

Categorical variables were expressed in counts and percentages and compared with Pearson's χ^2 statistic or Fisher's exact tests as appropriate. Continuous variables were expressed in median values and interquartile range or range between minimum and maximum values, and compared using the Mann–Whitney *U* test. Continuous variables before and after PVE were compared using the Wilcoxon signed-rank test. The distribution of each of the pressure parameters according to the degree of hypertrophy was assessed graphically by means of dot charts, and their discrimination capacity to predict failure of FLR hypertrophy was determined by building receiver operating characteristic (ROC) curves and calculating the area under the receiver operating characteristic curve (AUROC) (c-statistic). The impact of baseline patient and tumor-related variables as well as the impact of pressure parameters on FLR hypertrophy was assessed by univariate and multivariate linear regression analyses. All calculations were performed with SPSS software version 20.0 (IBM Corp., Armonk, NY). All tests were two-tailed.

Results

Patient characteristics

Over the study period, 26 patients underwent successful PVE with simultaneous measurements of parameters of hepatic venous pressure and were enrolled in this study. One additional patient suffered from hepatic necrosis after PVE and was not included in the study because he did not have the appropriate measurements of hepatic volumetry. For that patient, the cause of hepatic necrosis was related to an undiagnosed, pre-existing hepatic artery stricture due to tumor compression. None of the 26 patients included in the analysis suffered from any procedure-related complication.

There were 21 males and 5 females with a median age of 63⁻64 years (IQR: 54–73). The majority of patients (65.%) presented with an underlying liver disease, including 7 (27%) patients with non-alcoholic steatohepatitis, 5 (19%) with hepatitis C virus, 3 (12%) with hepatitis B virus and 2 with alcohol-related liver diseases. Eight (31%) patients had no peri-portal fibrosis, whereas an F1, F2, F3, and F4 fibrosis was present in 5 (19%), 1, 5 (19%), and 7 (27%) patients, respectively. Six (23%) patients with no evidence of peri-portal fibrosis had undergone previous chemotherapy with a median of 6 cycles (range: 3–9). The main indication for hepatectomy was hepatocellular carcinoma (54%, $n = 14$), followed by hilar cholangiocarcinoma (27%, $n = 7$) and colorectal liver metastasis (19%, $n = 5$).

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