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Arguments for a selective approach of preoperative portal vein embolization before major hepatic resection

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Abstract
Preoperative PVE can induce hypertrophy of the future liver remnant volume resulting in a decrease of surgical risk after major hepatic resection. However, the number of patients with normal liver at risk is small and there is no arguments for inducing hypertrophy before standard right hepatectomy. Therefore, in patients with normal liver PVE is indicated in patients in whom very extended liver resection or associated major gastro-intestinal surgery is planned. In patients with chronic liver disease and in those with injuried liver (chemotherapy, major steatosis, cholestasis), PVE is indicated before major liver resection.

Key words Portal vein embolization · Hepatic resection

Introduction

In spite of a dramatic improvement in the safety of liver surgery, there is theoretical evidence that an insufficient hepatic functional reserve estimated by a small future liver remnant volume (FLR) after major liver resection can be considered a risky situation.[1–3] Therefore, it could be assumed that portal vein embolization (PVE), which induces hypertrophy of the FLR, can improve the safety and tolerance of major liver resections.[4,5] However, the indications of PVE are still arbitrary, whatever the status of the nontumorous liver parenchyma, including patients with either normal and chronic liver, and whatever the exact quantification of sufficient minimal functional hepatic volume ranging from 25% to 50% of the total liver volume.[6–11] The aim of this article is firstly, to determine the incidence and impact of a small remnant liver volume following major liver resections in patients with normal liver and secondly, to define the subgroup of patients who might obtain benefit from PVE.

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How frequently a major hepatectomy results in a small remnant liver volume

In a large study evaluating the risk of liver resection, we have confirmed that the mortality rate was significantly higher in patients with underlying liver abnormality, including chronic liver disease, cholestasis, and steatosis.[2] As shown in Table 1, the analysis of 662 liver resections in patients with a normal liver showed that the overall mortality rate is 0.9%. The mortality rate of patients who underwent major resection was only 1.5%. Factors significantly associated with an increase of the mortality rate included ASA score >1 and the association of extrahepatic procedure. To investigate whether the volume of the remnant liver had an impact on the postoperative course, we studied a subgroup of 138 patients who underwent an elective solitary major liver resection (removal of three or more Couinaud's segments) with ASA score 1. None of these patients underwent a procedure aimed at hypertrophy of the future remnant liver volume. The number of resected segments was, respectively, three in 18 (13%), four in 88 (64%), five in 22 (16%), and six in 10 (7%) patients. The remnant liver volume (RLV) was expressed a ratio with the preoperative functional liver volume (FLV) calculated by complete preoperative computed tomography-scan volumetric assessments. Patients were divided into five groups based upon their RLV/FLV ratio, ranging from ≤30% to ≥60%.

As shown in Table 2, a small remnant liver, as restrictively defined by an RLV/FLV ratio ≤30%, was observed only in 13 (9.4%) patients, whereas 74 (53%) experienced an RLV/FLV ratio >50%. Interestingly, there was no linear correlation between the

number of resected segments and the volume of the remaining liver. A possible explanation for these observations is that in patients with a large malignant tumor mass, the controlateral liver segments have undergone a progressive compensatory hypertrophy, either because this tumor mass is not functional or because it impairs the adjacent portal blood flow. Therefore our results indicated that a major liver resection, in clinical practice, is rarely associated with a small remnant liver.

Table 1. Univariate analysis of mortality rate after liver resection in 662 patients with normal liver

Variables	*n*	Mortality	*P*
Age			
<70 years	6/603	1%	NS
>70 years	0/59	0%	
ASA			
1	1/444	0.2%	0.01
2–3	5/218	2%	
Resection			
Minor	0/340	0%	NS
Major	6/322	1.5%	
Indication			
Benign	0/291	0%	NS
Malign	6/371	1.6%	
Associated procedure			
Present	4/115	3.4%	0.001
Absent	2/547	0.4%	

NS, not significant

Impact of the remnant liver volume in the postoperative outcome

The analysis of postoperative liver function tests showed that all patients experienced a decrease of prothrombin time on postoperative day 1, without correlation with the RLV/FLV ratio, which progressively normalized thereafter irrespective of the remaining liver volume (data not shown). In contrast, postoperative serum bilirubin was significantly correlated with the RLV/FLV ratio during the first week (data not shown). Therefore, the most accurate postoperative marker of small RLV is serum bilirubin level.[12]

Sixty-four (47%) patients experienced one or more complications, including pulmonary complications in 25 patients, abdominal infection, biliary leakage, or bilioma in 17 patients, ascites in 17 patients, liver failure in 7 patients, and postoperative hemorrhage in 6 patients. As shown in Fig. 1, the overall rate of complications was not statistically different between patients with a small or larger RLV. However, patients with RLV/FLV ≥60% had a tendency to present more biliary complications (18%), probably due to the tumor

Table 2. Relation between the RLV/FLV ratios and the number of segments resected

RLV/FLV ratio	<30%	30%–40%	40%–50%	50%–60%	>60%
No. of patients (%)	13 (9%)	23 (17%)	29 (21%)	29 (21%)	44 (32%)
No. of segments resected					
6 (n = 10)	2	0	2	3	3
5 (n = 22)	3	3	7	5	4
4 (n = 88)	8	19	18	18	25
3 (n = 18)	0	1	2	3	12

RLV/FLV ratio, ratio of remnant liver volume / functional liver volume

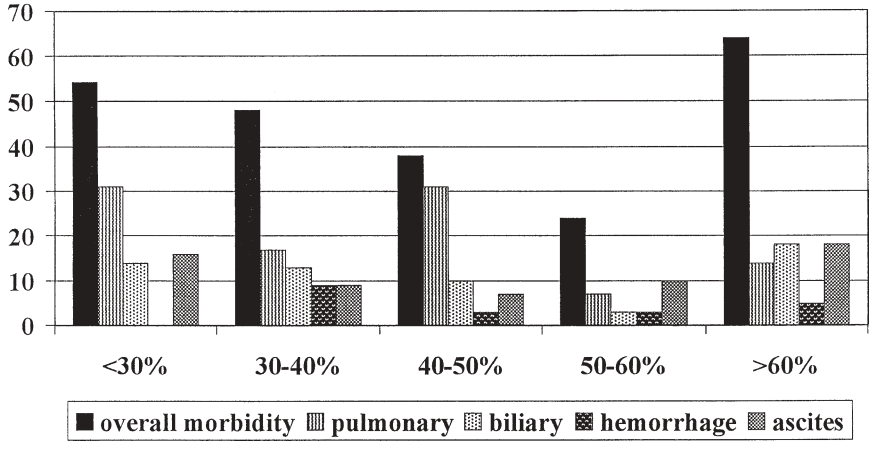

Fig. 1. Relationship between the rate of postoperative complications and the remnant liver volume in a subgroup of patients with normal underlying liver who underwent major liver resection

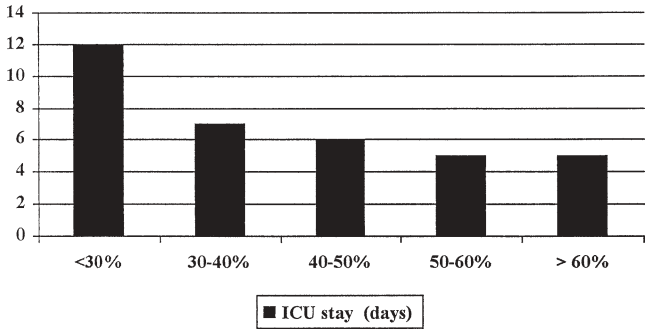

Fig. 2. Duration in the intensive care unit (*ICU*) according to the remnant liver volume in a subgroup of patients with normal underlying liver who underwent major liver resection

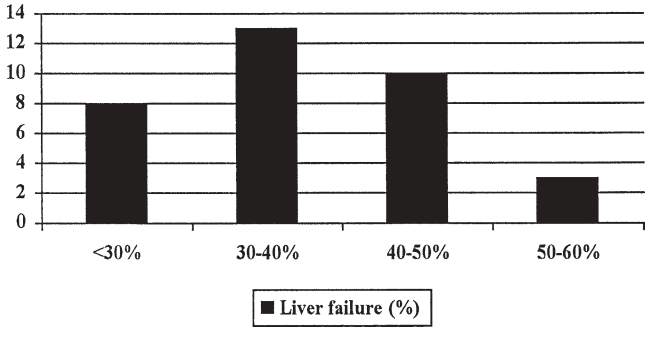

Fig. 3. Rate of postoperative liver failure according to the remnant liver volume in a subgroup of patients with normal underlying liver who underwent major liver resection

volume and technical difficulties. When excluding patients with RLV/FLV ratio >60% the rate of complications such as pulmonary, biliary, ascites, and both intensive care unit (ICU) and hospital stays appeared to increase linearly with RLV. The ICU stay duration was higher in patients with the smallest RLV (Fig. 2). Surprisingly, the incidence of liver failure was not strictly correlated with the size of the RLV in this study (Fig. 3). Accordingly, the true minimum liver volume that must be preserved after liver resection in patients with normal liver remains undefined. Therefore, even in patients with an RLV below <30% it is difficult to justify routine performance of PVE.

Results of PVE before right hemihepatectomy in patients with normal liver

To assess the impact of liver hypertrophy of the future liver remnant volume induced by PVE on the immediate postoperative complications after a standardized major liver resection, we prospectively compared two groups of patients with normal liver who underwent an elective right hemihepatectomy.[13] Despite an increase of the left liver volume of 45% in the PVE group, a similar postoperative course was observed between patients with an RLV/FLV ratio of 31% when compared to patients having an RLV/FLV ratio of 47% after PVE. As shown in Table 3, intraoperative blood loss, incidence and type of postoperative complications, postoperative kinetics of liver function tests, and the duration of in-hospital stay were remarkably similar in patients undergoing right hepatectomy with or without preoperative PVE. Therefore, it appears that the significant hypertrophy of the left liver induced by PVE before a standardized right hemihepatectomy brought no measurable impact in terms of postoperative complications.[13]

Table 3. Postoperative course after right hemihepatectomy with or without preoperative portal vein embolization in patients with normal liver

Resection	Without PVE (n = 14)	With PVE (n = 13)
Liver volume (cc)	442 ± 138	626 ± 172
RLV/FLV ratio (%)	31%	47%
Morality	0	0
Transfusion (n)	3	4
Morbidity	3 (21%)	3 (23%)
Hospital stay (days)	12 ± 4	12 ± 4

PVE, portal vein embolization

Risks and complications of PVE

Patients who are considered for PVE are most often those with malignant tumors. PVE can increase both the resectability of patients with multiple tumors and the safety of the surgery. However, the compensatory increase of the arterial flow in the embolized lobe and the growth of the parenchyma in the nonembolized lobe may stimulate tumor cell developments.[11,14] It has been shown that the growth of liver metastases present in the future remnant liver can be stimulated by PVE.[14] Kokudo et al. confirmed that PVE increases tumor growth with a decrease of disease-free survival after liver resection for colorectal metastasis.[15] Recently it has been shown that PVE before major hepatic resection for hepatocellular carcinoma can be associated with a higher rate of extrahepatic metastasis.[16] Although these studies need to be confirmed, we believe that the achievement of PVE should be seriously discussed case by case because of a possible described risk of tumor growth induced by PVE in the controlateral liver. The rate of technical complications of percutaneous transhepatic PVE is approximately 10%, including

hematoma, hemobilia, and migration of the embolized substance in the controlateral lobe.[9]

Conclusions

Although Vauthey et al. suggested that PVE be carried out in patients with normal liver when the percentage of future functional remnant volume is ≤25%, the inferior limits of functional liver volume in patients with normal parenchyma in order to avoid postoperative liver failure remain to be known.[17] We did not find arguments for inducing hypertrophy of the future liver remnant before standard right hemihepatectomy in patients with a normal liver. In patients with a normal liver, preoperative PVE should be restricted to those in whom a very extended liver resection or associated major gastrointestinal surgery is planned.[1,6] In contrast, we strongly advocate including PVE in the management of patients with chronic liver disease or with injured livers (i.e., chemotherapied livers, major steatosis, or cholestasis) before any major liver resection.[6,8,17,18] In these patients, the absence of hypertrophy of the nonembolized liver following successful PVE should be considered as an indicator of the absence of liver capacity to regenerate, and therefore a contraindication for major liver resection.[13]

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