Original article

Portal vein embolization before major hepatectomy and its effects on regeneration, resectability and outcome

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Background: **This study evaluated the safety of portal vein embolization (PVE), its impact on future liver remnant (FLR) volume and regeneration, and subsequent effects on outcome after liver resection.**
Methods: **Records of 112 patients were reviewed. Standardized FLR (sFLR) and degree of hypertrophy (DH; difference between the sFLR before and after PVE), complications and outcomes were analysed to determine cut-offs that predict postoperative hepatic dysfunction.**
Results: **Ten (8·9 per cent) of 112 patients had PVE-related complications. Postoperative complications occurred in 34 (44 per cent) of 78 patients who underwent hepatic resection and the 90-day mortality rate was 3 per cent. A sFLR of 20 per cent or less after PVE or DH of not more than 5 per cent (*versus* sFLR greater than 20 per cent and DH above 5 per cent) had a sensitivity of 80 per cent and a specificity of 94 per cent in predicting hepatic dysfunction. Overall, major and liver-related complications, hepatic dysfunction or insufficiency, hospital stay and 90-day mortality rate were significantly greater in patients with a sFLR of 20 per cent or less or DH of not more than 5 per cent compared with patients with higher values.**
Conclusion: **DH contributes prognostic information additional to that gained by volumetric evaluation in patients undergoing PVE.**

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Introduction

Major and extended hepatectomies are increasingly performed in patients with hepatobiliary malignancies to achieve a complete resection and provide a chance of cure[1–4]. Extensive resection of liver parenchyma, however, increases the risk of postoperative hepatic dysfunction or hepatic insufficiency. Although the risk of hepatic insufficiency is influenced by multiple factors, recent studies have emphasized an association between volume and function of the residual liver[2,5–9].

Portal vein embolization (PVE) has been used to reduce the risk of postoperative hepatic insufficiency in patients undergoing hepatic resection[10,11]. PVE stimulates hypertrophy of the non-embolized liver, increasing the volume and function of the future liver remnant (FLR)[12–14] and improving the results of postoperative liver function tests[15]. Several studies have demonstrated the clinical value of PVE before liver resection for metastatic tumours[8,16,17], hepatocellular carcinoma[18,19] and biliary tract cancer[2,10].

Despite growing worldwide experience with PVE, postoperative risk in patients who undergo PVE has yet to be clearly quantified. In a preliminary study, a small FLR (20 per cent or less of the estimated total liver volume (TLV)) was associated with worse outcome[20].

The aims of this study were to define the technical and oncological safety of PVE, and to examine the relationship between FLR volume after PVE, degree of liver hypertrophy and outcomes of hepatic resection.

Methods

The records of 112 consecutive patients with hepatobiliary malignancy who underwent PVE in preparation for major or extended hepatectomy between September 1995 and January 2006 were reviewed.

PVE was performed based on volumetry of the anticipated FLR after evaluation by the operating surgeon (E.K.A. or J.-N.V.). PVE was indicated when the FLR

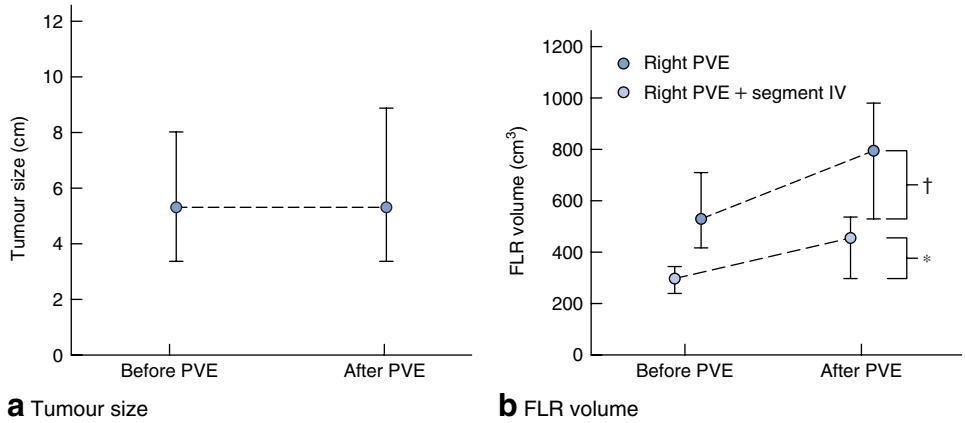

Fig. 1 **a** Change in tumour size after portal vein embolization (PVE) and **b** changes in future liver remnant (FLR) volume after right PVE (21 patients) and right PVE extended to segment IV portal branches (right PVE + segment IV) (85 patients) in patients without severe fibrosis or cirrhosis. Values are median with interquartile ranges. *$P = 0{\cdot}007$, †$P < 0{\cdot}001$, (Wilcoxon test)

volume was 20 per cent or less of the estimated TLV in patients with normal liver, 30 per cent or less in patients with fibrosis or severe liver injury[7,21] and 40 per cent or less in patients with cirrhosis[22,23].

The FLR volume was measured directly using computed tomography (CT) combined with three-dimensional CT volumetry as described previously[11,15]. TLV was calculated from the patient's body surface area (BSA) using a mathematical formula (TLV [cm^3] = $-794{\cdot}41 + 1267{\cdot}28 \times$ BSA [m^2])[24,25]. The ratio between FLR volume and TLV was defined as the standardized FLR (sFLR). The difference between the sFLR before and after PVE was defined as the degree of hypertrophy (DH). Patients with cirrhosis were excluded from the analysis of sFLR and DH after PVE in relation to postoperative outcome after hepatic resection.

PVE was performed as described previously[26,27]. Embolization of segment IV was performed when an extended right hepatectomy was planned on the basis of tumour location.

All patients underwent abdominal CT with three-dimensional CT volumetry 2–8 weeks after PVE to assess the extent of compensatory hypertrophy. Tumour response to PVE was reviewed retrospectively by a single radiologist and evaluated according to Response Evaluation Criteria in Solid Tumors[28] in patients for whom both pre- and post-PVE scans were available.

All patients underwent extended right or right hepatectomy with or without caudate lobectomy. The surgical technique, intraoperative management and postoperative care were as described previously[1,29]. All patients with hilar cholangiocarcinoma underwent percutaneous or endoscopic biliary drainage of the FLR before PVE to achieve a bilirubin level of less than 34·2 μmol/l.

Perioperative morbidity was reported according to the classification proposed by Dindo *et al.*[30]. Grade I and II complications were defined as minor, and grade III and IV complications as major. Postoperative mortality was defined as any death within 90 days after surgery or within the hospital stay during which the surgery was performed. Hepatic dysfunction was defined as a peak postoperative bilirubin level greater than 51·3 μmol/l[1] or a prothrombin time longer than 18 s[5]. Hepatic insufficiency was defined as a peak postoperative bilirubin level greater than 171 μmol/l unrelated to biliary obstruction and/or clinically significant ascites or hepatic encephalopathy[1].

Statistical analysis

Continuous data were expressed as median (95 per cent confidence interval), unless indicated otherwise, and compared using the Mann–Whitney *U* test or Wilcoxon test. Dichotomous variables were compared by means of the χ^2 test or Fisher's exact test, as appropriate. The relationship between liver regeneration and clinical outcome was investigated using the sFLR after PVE and the DH. Receiver–operator characteristic (ROC) curve analysis was used to identify cut-off values of sFLR and DH that predicted hepatic dysfunction. Cut-off values were determined by seeking the largest sum of the sensitivity and specificity values while maintaining the lowest likelihood ratio of a negative test and the highest likelihood ratio of a positive test. $P < 0{\cdot}050$ was considered statistically significant.

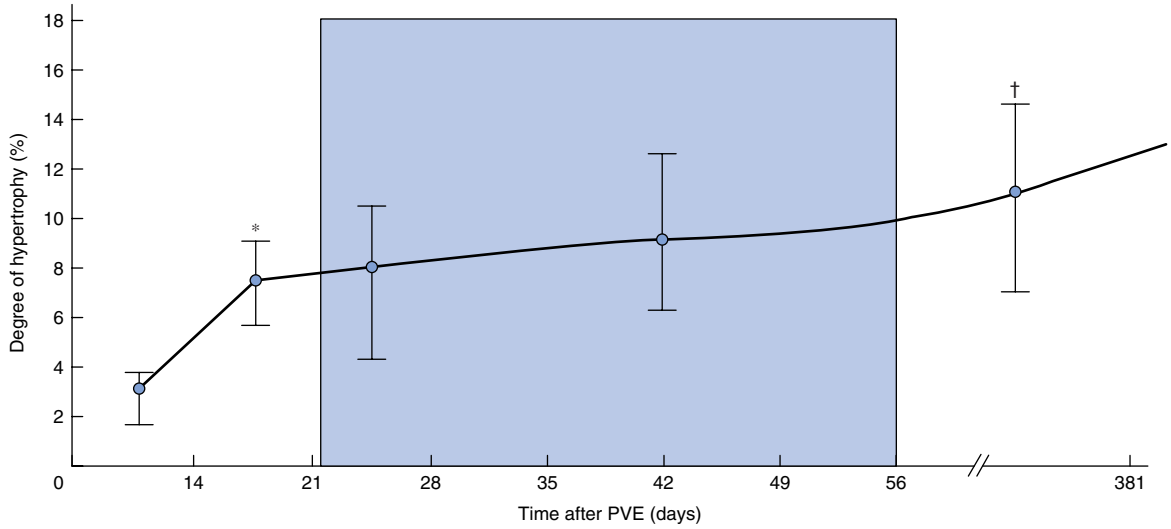

Fig. 2 Kinetics of future liver remnant (FLR) growth, plotted as median (with interquartile ranges) degree of hypertrophy (DH) after portal vein embolization (PVE). The shaded zone (days 22–56 after PVE) identifies the 'plateau' period during which the DH did not change significantly between measurement points. The number of measurements indicates the number of three-dimensional computed tomography (CT) volumetric scans evaluated at each interval after PVE. The number of patients whose last CT evaluation occurred during each interval is also shown. *$P = 0{\cdot}004$ *versus* days 0–14; †$P = 0{\cdot}008$ *versus* days 22–28 (Mann–Whitney U test)

Results

Clinicopathological features of the 112 patients studied are shown in *Table 1*. The indications for PVE were hepatic metastases in 65 patients (58·0 per cent) and primary hepatobiliary malignancy in 47 (42·0 per cent). Only four patients (3·6 per cent) presented with severe fibrosis or cirrhosis (Ishak score[32] 5–6). The remaining 108 patients had unremarkable pathological findings (77 patients), hepatic injury (five) or fibrosis (26). Twenty-eight patients with colorectal liver metastases received chemotherapy before PVE (median 4 (range 2–12) cycles), which was discontinued a median of 6·5 weeks before PVE. Five of these patients received more chemotherapy treatment less than 2 weeks after PVE.

Technical and oncological safety of portal vein embolization

Primary technical success of PVE was accomplished in 111 (99·1 per cent) of the 112 patients. One patient required a second intervention to occlude an incompletely embolized portal branch of the right anterior sector. PVE procedures are summarized in *Table 1*. One patient underwent PVE limited to segment IV because of pre-existing right portal vein thrombosis.

Table 1 Patient characteristics

Sex ratio (M : F)	83 : 29
Mean (range) age (years)	60 (36–78)
Diabetes mellitus	
Yes	35 (31·2)
No	77 (68·8)
Body mass index (kg/m^2)	
Mean (range)	27·7 (19·4–48·4)
<25 kg/m^2	34 (30·4)
≥ 25 kg/m^2	73 (65·2)
Not available	5 (4·5)
Diagnosis	
Colorectal metastases	50 (44·6)
Hepatocellular carcinoma	24 (21·4)
Hilar cholangiocarcinoma	14 (12·5)
Gallbladder cancer	6 (5·4)
Other malignant tumours	18 (16·1)
Non-tumorous liver	
No pathological changes	77 (68·7)
Steatosis $>30\%$ or steatohepatitis*	5 (4·5)
Fibrosis (F1–4†)	26 (23·2)
Severe fibrosis/cirrhosis (F5–6†)	4 (3·6)
Portal vein embolization	
Right PVE + segment IV	86 (76·8)
Right PVE	24 (21·4)
Left PVE	1 (0·9)
Segment IV only	1 (0·9)

Values in parentheses are percentages unless indicated otherwise. *Kleiner score 4 or more[31]. †Fibrosis score according to Ishak *et al.*[32]. Right PVE + segment IV, right portal vein embolization (PVE) extended to segment IV portal branches.

Eight patients experienced complications after right PVE extended to segment IV portal branches (right PVE + segment IV). Four patients had partial portal vein thromboses, which were treated with preoperative anticoagulant therapy (one), surgical removal of the clot (two), or left untreated because of systemic progression of disease (one). One patient had a complete portal vein thrombosis, which was treated with a 30-h local infusion of recombinant tissue plasminogen activator and mechanical thrombolysis. One patient developed a subcapsular haematoma, and one had an oesophageal haemorrhage. In one patient, a single coil migrated into the segment III portal branch but this did not preclude regeneration of the involved segment or subsequent liver resection. One patient experienced a complication after right PVE; migration of a coil and embolizing material to the portal bifurcation was noted at the time of surgery, and removed uneventfully. There was no difference in the incidence of complications after right PVE + segment IV and right PVE alone ($P = 0{\cdot}417$). The patient who underwent PVE limited to segment IV developed a left portal vein thrombosis, and surgical resection was not possible because of this and tumour progression. The patient who underwent left PVE did not experience complications.

Pre- and post-PVE scans were available for comparison in 103 patients. Tumours were not measurable in 23 patients, 13 patients with hilar cholangiocarcinoma, six with gallbladder cancer and four with colorectal metastases. In the remaining 80 patients the median tumour size was 5·3 (2·2 to 12·8) cm at baseline and 5·4 (1·9 to 15·2) after PVE (*Fig. 1a*).

Regeneration after portal vein embolization

In 85 patients without cirrhosis who underwent right PVE + segment IV, the absolute FLR volume increased from 290 (180 to 505) cm^3 before to 440 (294 to 716) cm^3 after PVE ($P = 0{\cdot}007$) (*Fig. 1b*). The sFLR increased from 16·6 (10·9 to 28·0) to 25·8 (16·8 to 40·0) per cent ($P = 0{\cdot}007$), giving a median DH of 8·8 (2·8 to 17·7) per cent. In the 21 patients without cirrhosis who underwent right PVE, the absolute FLR volume increased from 518 (274 to 945) cm^3 before to 798 (269 to1352) cm^3 after PVE ($P < 0{\cdot}001$) (*Fig. 1b*), and the sFLR increased from 28·1 (20·4 to 53·7) to 43·7 (21·1 to 67·8) per cent ($P < 0{\cdot}001$); the median DH was 10·9(1·4 to 24·6) per cent.

Among patients without cirrhosis, the absolute FLR volumes and sFLRs measured before and after PVE, and DH for segments I, II and III, were similar in patients who underwent right PVE + segment IV and those who had right PVE alone. The higher DH in patients who had right PVE was due to significant growth of segment IV. The absolute segment IV volume increased from 227 (120 to 476) to 284 (145 to 544) cm^3 ($P < 0{\cdot}001$), and the standardized segment IV volume (calculated as [segment IV volume/estimated TLV] × 100) increased from 13·1 (6·6 to 25·1) to 17·1 (10·6 to 26·8) per cent ($P < 0{\cdot}001$). Segment IV DH was 3·4 (0·0 to 10·2) per cent.

Among patients without cirrhosis, the response to PVE was similar in 28 patients who received preoperative chemotherapy and 80 who did not. The two groups did not differ with respect to absolute FLR volumes and sFLR before and after PVE ($P = 0{\cdot}654$, $P = 0{\cdot}723$ and $P = 0{\cdot}658$, $P = 0{\cdot}617$, respectively). Likewise, the DH values were similar (9·0 (2·6 to 18·3) per cent in those who had chemotherapy and 8·5 (2·7 to 24·6) per cent in those who did not; $P = 0{\cdot}212$).

In 31 patients with fibrosis or liver injury, both the absolute FLR volume and the sFLR significantly increased after PVE, from 435 (203 to 945) to 707(330 to 1197) cm^3 ($P < 0{\cdot}001$) and from 25·2 (12·5 to 53·8) to 34·9 (21·5 to 66·6) per cent ($P < 0{\cdot}001$) respectively. The DH was 9·6 (1·7 to 22·5) per cent. There was no difference in DH between patients with and without underlying liver disease ($P = 0{\cdot}126$).

Of the 112 patients, 94 were re-evaluated with one and 18 with multiple CT scans between 9 and 381 days after

Table 2 Surgical procedures and postoperative complications in 78 patients who had hepatic resection

	No. of patients
Procedures	
Right PVE + segment IV	61 (78)
Extended right hepatectomy	34
Extended right hepatectomy + extrahepatic procedure*	27
Right PVE	17 (22)
Right hepatectomy	13
Right hepatectomy + extrahepatic procedure†	4
Two-stage resection	10 (13)
Postoperative complications	34 (44)
Minor (grade I–II)	18 (23)
Major (grade III–IV)	16 (21)
Hepatic dysfunction	12 (15)
Hepatic insufficiency	6 (8)
Death within 90 days (grade V)	2 (3)

Values in parentheses are percentages. Complications were graded according to the classification of Dindo *et al.*[30]. Extrahepatic procedures: *resection of bile duct ($n = 10$), bile duct and portal vein ($n = 2$), portal vein or inferior vena cava ($n = 4$), pancreas ($n = 2$), diaphragm ($n = 5$), bowel ($n = 2$), lung ($n = 1$) and adrenal gland ($n = 1$); †resection of diaphragm ($n = 2$), pancreas ($n = 1$) and lung ($n = 1$). Right PVE + segment IV, right portal vein embolization (PVE) extended to segment IV portal branches.

PVE. Serial CT was carried out in some patients because of insufficient FLR growth or other factors leading to a delay in the planned surgery.

Volumetric data obtained from all scans were used to analyse the kinetics of FLR growth after PVE in patients without cirrhosis (*Fig. 2*). The FLR volume significantly increased in the first 3 weeks after the procedure (DH 3·2 (1·5 to 5·7) per cent for days 1–14 *versus* 7·4 (0·3 to 11·3) per cent for days 15–21; $P = 0·004$). After this initial increase, the DH reached a plateau phase of minimal regeneration (DH 7·4 (0·3 to 11·3) per cent for days 15–21 *versus* 8·0 (0·4 to 14·9) per cent for days 22–28, $P = 0·530$; DH 8·0 (0·4 to 14·9) per cent for days 22–28 *versus* 8·9 (2·8 to 20·3) per cent for days 29–56, $P = 0·154$) (*Fig. 2*). A slower rate of liver regeneration continued in the following months: in the 14 patients followed for more than 2 months (median 98 (57 to 339) days) the DH was 10·9 (4·2 to 24·7) per cent. However, given the wide time distribution between these measurements and the significant difference in DH values recorded ($P = 0·008$ for days 22–28 *versus* days 57–381), only measurements recorded during the plateau period – between days 22 and 56 – were considered to be homogeneous and therefore comparable regardless of the time of acquisition.

Resectability and outcome

Seventeen patients (15·2 per cent) did not undergo surgery after PVE because of extrahepatic (nine patients) or intrahepatic (one) progression of disease, inadequate hepatic regeneration (five) or significant medical co-morbidities (two). Of the 95 patients who underwent surgical exploration, 17 patients were excluded from hepatic resection because of unexpected extrahepatic (ten patients) or intrahepatic (two) disease precluding resection, severe cirrhosis (two), severe intraoperative hypothermia leading to coagulopathy (one), diffuse haemorrhage (in a patient who had previously received prolonged chemotherapy by hepatic arterial infusion) and hepatitis (one). A total of 78 patients underwent hepatectomy (resection rate 69·6 per cent). The surgical procedures performed are summarized in *Table 2*. Of note, 27 (44 per cent) of 61 patients who underwent extended right hepatectomy and four of 17 who had right hepatectomy also had a synchronous extrahepatic procedure.

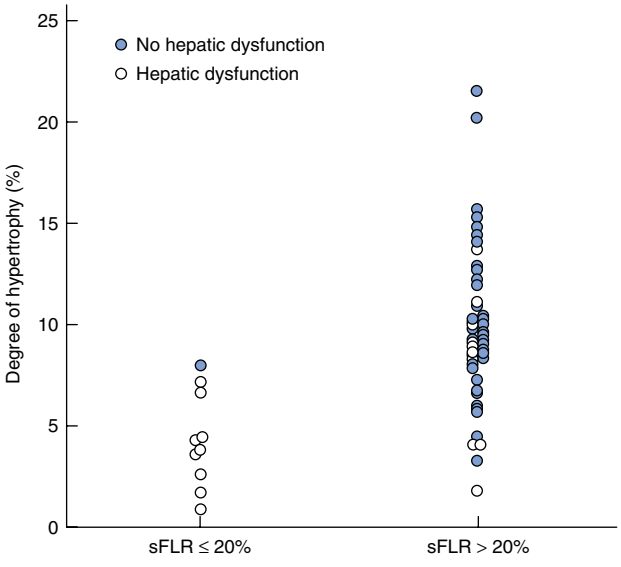

Fig. 3 Scatter plot of the incidence of hepatic dysfunction according to degree of hypertrophy, stratified by standardized future liver remnant (sFLR)

Table 3 Diagnostic capability of standardized future liver remnant, hypertrophy rate and combined criteria in predicting hepatic dysfunction

	sFLR ≤ 20%	DH ≤ 5%	sFLR ≤ 20% or DH ≤ 5%
Sensitivity (%)	60	67	80
Specificity (%)	98	96	94
Positive predictive value (%)	90	83	80
Negative predictive value (%)	89	91	94
LR+	30·6 (4·2, 222·5)	17·0 (4·2, 69·3)	13·6 (4·4, 42·0)
LR−	0·41 (0·22, 0·76)	0·35 (0·17, 0·71)	0·21 (0·08, 0·59)

Values in parentheses are 95 per cent confidence intervals. Only 66 patients with degree of hypertrophy (DH) calculated in the 'plateau' period were considered. sFLR, standardized future liver remnant; LR+, likelihood ratio of positive test; LR−, likelihood ratio of negative test.

Thirty-four patients (44 per cent) experienced postoperative complications. Grade II complications in 18 patients (23 per cent) included self-limiting biliary fistula (four), hepatic dysfunction (seven), pneumonia (two), atrial fibrillation (one), fluid overload (one), urinary tract infection (one) and wound infection (two). Eleven patients (14 per cent) experienced grade IIIa complications, including bile leak/biloma (six), intra-abdominal fluid collection (three), pleural effusion (one) and pancreatic fistula (one). Two patients (3 per cent) underwent reoperation for small bowel perforation (grade IIIb complication). Three patients (4 per cent) had grade IVa (life-threatening) complications: liver insufficiency (one), pulmonary embolism (one) and respiratory insufficiency (one).

Eighteen patients developed hepatic dysfunction, six of whom experienced hepatic insufficiency and one died from liver failure. Another patient died after surgery as a result of a methicillin-resistant *Staphylococcus aureus* perihepatic

Table 4 Short-term clinical outcome by standardized future liver remnant, degree of hypertrophy and combined criteria

	sFLR			DH			sFLR or DH		
	≤ 20% ($n = 10$)	> 20% ($n = 56$)	P†	≤ 5% ($n = 12$)	> 5% ($n = 54$)	P†	≤ 20% or ≤ 5% ($n = 15$)	> 20% and > 5% ($n = 51$)	P†
Any complication	9 (90)	22 (39)	0·003	10 (83)	21 (39)	0·006	12 (80)	19 (37)	0·003
Major complication	5 (50)	9 (16)	0·028	5 (42)	9 (17)	NS	7 (47)	7 (14)	0·011
Liver-related complication	9 (90)	13 (23)	< 0·001	10 (83)	12 (22)	< 0·001	12 (80)	10 (20)	< 0·001
Hepatic dysfunction	9 (90)	6 (11)	< 0·001	10 (83)	5 (9)	< 0·001	12 (80)	3 (6)	< 0·001
Hepatic insufficiency	3 (30)	1 (2)	0·009	2 (17)	2 (4)	0·148	3 (20)	1 (2)	0·034
Death within 90 days	1 (10)	1 (2)	0·282	1 (8)	1 (2)	0·332	2 (13)	0 (0)	0·049
Duration of hospital stay (days)*	8 (6–53)	8 (5–28)	0·312‡	8.5 (6–53)	7 (5–28)	0·213‡	8 (6–53)	7 (5–28)	0·119‡

Values in parentheses are percentages unless indicated otherwise; *values are median (range). Only 66 patients with degree of hypertrophy (DH) calculated in the 'plateau' period were considered. sFLR, standardized future liver remnant. †χ^2 test or Fisher's exact test unless indicated otherwise; ‡Mann–Whitney U test.

collection complicated by haemoperitoneum. The 90-day mortality rate was 3 per cent.

The median hospital stay after hepatic resection was 8 (range 5–53) days and there was no significant difference between patients with a normal liver and those with fibrosis or liver injury (7·0 *versus* 8·0 days; $P = 0·891$).

ROC curve analysis was performed to determine the value of sFLR after PVE in predicting hepatic dysfunction. The area under the curve was 0·81 (0·68 to 0·95) and the cut-off value was 20 per cent. *Fig. 3* shows the relationship between postoperative hepatic function and DH in patients stratified using the 20 per cent cut-off value for sFLR after PVE. Hepatic dysfunction was more common in patients with a small sFLR, and appeared to be related to a small DH.

ROC curve analysis of DH in predicting hepatic dysfunction yielded an area under the curve of 0·84 (0·70 to 1·00) with a cut-off value of 5 per cent. To avoid bias from inclusion of patients with liver in a significant regeneration phase, only the 66 patients with the DH calculated in the plateau period were considered.

These analyses indicated that patients with a sFLR of more than 20 per cent or a DH of more than 5 per cent had good outcomes. In contrast, patients with a sFLR of 20 per cent or less, regardless of DH, and patients with a DH of 5 per cent or less, regardless of sFLR, had poor outcomes. *Table 3* shows the diagnostic characteristics of sFLR and DH cut-off values in the plateau period population. Considered separately, both sFLR and DH displayed high specificity but low sensitivity. The combination of sFLR and DH had a specificity of 94 per cent and a sensitivity of 80 per cent (*Table 3*). The combination of sFLR and DH was also useful in predicting clinical outcomes (*Table 4*).

Impaired liver regeneration after PVE was not associated with any of the patient factors tested (sex, age, diabetes and body mass index) or liver-related factors (presence of fibrosis, or steatosis/steatohepatitis); there was no significant difference between DH 5 per cent or less *versus* more than 5 per cent for any factor ($P = 0·503$, $P = 0·187$, $P = 0·408$, $P = 0·169$, $P = 0·270$ and $P = 0·567$ respectively).

Discussion

Embolization of the entire tumour-bearing liver before hepatic resection is safe both technically and oncologically. It appears that DH contributes additional prognostic information beyond that provided by volumetric evaluation in patients undergoing PVE before hepatic resection.

Analysis of hepatic regeneration after PVE in patients without cirrhosis revealed an early phase of regeneration during the first 3 weeks followed by a plateau during which the FLR volume increased only slightly. The present study expands on the results of a previous analysis[33]. Although some authors re-evaluate patients after 2 weeks[33–36], the present results show that a steady state of regeneration has not been reached by this time and that 21 days is the minimum interval needed before the hypertrophic response to PVE is assessed. Patients who exhibit slow liver growth and those with small sFLRs after 3 weeks are unlikely to experience rapid regeneration beyond this time point, and this should be taken into account when planning treatment.

Identification of the plateau period permitted definition of a homogeneous group of patients in a steady-state phase of liver growth. This provided the basis for analysis of the significance of the 'static' (sFLR) and 'dynamic' (DH) information obtained by CT volumetry. The FLR

volume and the sFLR provide no information about change in volume over time, whereas the DH, a measure of liver growth, is a dynamic, time-dependent variable. The findings of the present study indicate that approximately 75 per cent of the growth in the FLR in the first 2 months after PVE occurs in the first 3 weeks, so early evaluations may underestimate the real response to the hypertrophic stimulus and result in overestimation of the postoperative risk.

Both sFLR after PVE (20 per cent or less) and DH (5 per cent or less) accurately predicted the likelihood of postoperative hepatic dysfunction. Individually, sFLR and DH had high specificity and relatively low sensitivity, but when combined predicted hepatic dysfunction with high sensitivity and correlated with clinical outcome. Patients with a sFLR of 20 per cent or less or DH of not more than 5 per cent had a significantly higher risk of overall, major and liver-related complications, and hepatic dysfunction and insufficiency. They also had a higher 90-day mortality rate (*Table 4*).

The optimal extent of PVE before planned extended right hepatectomy has been debated[27]. Embolization of segment IV portal branches in patients with segment IV involvement has been criticized because of the risk of inadvertent occlusion of the portal veins supplying the anticipated FLR[37]. Segment IV embolization is advised for both technical[27] (hypertrophy of this segment increases the parenchymal transection area) and oncological[38,39] (segment IV hypertrophy may be associated with tumour growth in the non-embolized segments) reasons. The present study has confirmed the safety and effectiveness of right PVE + segment IV. Only one patient (1 per cent) experienced reflux of embolizing material into the portal veins of the FLR, compared with 6·3 per cent after 188 right PVEs reported by Di Stefano and colleagues[40]. Consistent with previous findings[40,41], adverse events occurred in ten (8·9 per cent) of 112 patients in the present study, but there was no difference in the incidence of complications after right PVE and right PVE + segment IV.

In patients with colorectal liver metastases, PVE is frequently part of a multimodal treatment that includes preoperative chemotherapy. Liver injuries associated with systemic chemotherapy have been recognized[42–44], which raises the concern that chemotherapy might impair the regenerative response to PVE. However, in keeping with previous findings[45,46], preoperative chemotherapy did not impair hepatic regeneration after PVE in the present series.

This study has demonstrated the importance of the hypertrophic response of the liver to PVE, and the role of low sFLR and DH values as predictors of poor clinical outcome. The cut-off values in this series were determined in patients with moderate hepatic injury at worst and further studies are required to define the most appropriate values for patients who have cirrhosis[6] or hepatic injury from extensive chemotherapy[42].

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