

## ORIGINAL ARTICLE

# Right hepatectomy with extra-hepatic vascular division prior to transection: intention-to-treat analysis of a standardized policy

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## Abstract

**Background:** Right hepatectomy (RH) is the most common type of major hepatectomy and can be achieved without portal triad clamping (PTC) in non-cirrhotic liver. The present study reviews our standardized policy of performing RH without systematic PTC.

**Methods:** One hundred and eighty-one consecutive RH were performed in non-cirrhotic patients, with division of the right afferent and efferent blood vessels prior to transection, without systematically using PTC. Prospectively collected data were analysed, focusing on the following endpoints: need for salvage PTC, ischaemic time, blood loss and post-operative outcome.

**Results:** Extra-hepatic division of the right hepatic vessels was feasible in all patients, but was ineffective in 48 patients (26.5%) who required salvage PTC during transection. In those patients, the median ischaemic time was 20 min. The median blood loss was 500 ml (50–3000). Six patients (3.3%) experienced post-operative liver failure. Overall morbidity, severe morbidity and mortality were 42%, 12.1% and 1.6%, respectively, with peri-operative transfusion rate (16.6%) being the only factor associated with morbidity.

**Discussion:** By performing RH with extra-hepatic vascular division prior to transection, PTC can be safely avoided in the majority of patients.

Received 15 February 2012; accepted 21 May 2012

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## Introduction

During a hepatectomy, the need for bleeding control has generalized the use of continuous or intermittent total portal triad clamping (PTC).<sup>1</sup> However, PTC induces significant ischaemia/reperfusion injuries on the remnant liver. These injuries constitute a determinant factor in liver dysfunction,<sup>2</sup> which is known to be a main cause of post-operative mortality,<sup>3</sup> particularly in major hepatectomy. Moreover, it has been demonstrated that liver metabolism and tissue oxygenation were markedly affected by occlusion of the liver hilus.<sup>4,5</sup> Finally, ischaemia/reperfusion injuries have been associated with tumour growth in experimental models.<sup>6,7</sup> Whereas not demonstrated in human colorectal metastases,<sup>8</sup> a longer PTC time has been recently identified as a predictor of shorter survival in patients undergoing liver resection for hepatocellular carcinoma (HCC).<sup>9</sup> Therefore, techniques of

selective vascular exclusion<sup>10</sup> have been developed in order to protect the remnant liver without significant increased blood loss.

Since the description of the first right hepatectomy under hemi-occlusion of the afferent blood flow extra-hepatically by Lortat-Jacob in 1952,<sup>11</sup> the safety of liver resection under selective vascular clamping has been demonstrated.<sup>12–15</sup> Improvement of this technique with concomitant control of the ipsilateral outflow and preservation of the caval flow has further been reported.<sup>10,16</sup> The technique has reached a high feasibility rate, as demonstrated in the recent intention-to-treat study by *Viganò et al.*,<sup>17</sup> in which the requirement for salvage clamping was only 9.8%. Most of these series, however, have included both cirrhotic and non-cirrhotic patients or have involved various types of hepatectomy (minor or major, anatomic or not), thus precluding any reliable interpretation of the results with regard to the advantages of this technique in each individual patient.

A right hepatectomy is the most common major hepatectomy performed by specialized and even non-specialized surgeons, in patients without liver cirrhosis. As a result of the anatomy of the right primary branch of the glissonian pedicle tree, which is always located under the Glisson's sheath<sup>18</sup> and can be easily encircled in most cases, a right hepatectomy may be especially appropriate for extra-hepatic ligation and division of the ipsilateral portal vein, hepatic artery and hepatic vein. Therefore, the aim of the present study was to investigate, in a large cohort of patients without chronic liver disease, the feasibility and the results of a right hepatectomy initially performed without PTC, using extra-hepatic vascular division prior to transection.

## Methods

### Patients

From January 2000 to December 2010, 281 consecutive right hepatectomies were performed without systematic PTC for benign or malignant diseases in the same institution. A right hepatectomy was defined as resection of Couinaud's segments 5 to 8 according to the Brisbane classification.<sup>19</sup> After the exclusion of patients with tumours involving the hepatocaval confluence (36 patients), resection of the middle hepatic vein (13 patients), concomitant resection of the caudate lobe (13 patients), concomitant resection in the left liver (26 patients) or underlying chronic liver disease, i.e. F3 or F4 fibrosis, according to the METAVIR classification<sup>20</sup> (31 patients), a total of 181 hepatectomies were analysed. A hundred and fifteen patients had liver metastases of whom 62 (53.9%) have received a median of six cycles (range: 2–15) of pre-operative chemotherapy. Baseline characteristics are summarized in Table 1. Informed consent for the prospective collection of clinical data was obtained from each patient. The conduct of surgery and research was in accordance with the ethical guidelines issued by the 2000 revision (Edinburgh) of the 1975 Declaration of Helsinki.

### Surgical procedure

There was no laparoscopic right hepatectomy. Open liver resections were performed using a right or bilateral subcostal incision, except in seven patients in which a midline incision was selected because of concomitant extrahepatic surgery or a previous midline incision. The hepatic pedicle was always encircled in order to perform salvage PTC whenever needed. An anterograde cholecystectomy was performed and a C-tube was inserted into the cystic stump. Secondly, the right branch of the hepatic artery and the right branch of the portal vein were encircled and clamped. At this time, an ischemic demarcation line could identify both right and left livers and indicate the future parenchymal section line. This might also eliminate any anatomical variation of the right vascular pedicle distribution. Therefore, the right branch of the portal vein could be safely stapled and divided using a linear stapler (ATW35; Ethicon Endo-Surgery, Paris, France) and the right branch of the hepatic artery was also ligated and divided. In case of trifurcation of the portal trunk, the anterior and posterior

**Table 1** Baseline characteristics in 181 patients undergoing a right hepatectomy with systematic extra-hepatic vascular division prior to transection

Patient characteristics	n = 181
Age (years)	59 (17–82)
Male gender	107 (59.1%)
BMI (kg/m <sup>2</sup> )	24 (15–37)
ASA score	
I	55 (30.4%)
II	87 (48.1%)
III	29 (16.0%)
Not specified	10 (5.5%)
Diabetes mellitus	29 (16.0%)
Indication for right hepatectomy	
Liver metastases	115 (63.5%)
Hepatocellular carcinoma	32 (17.7%)
Cholangiocarcinoma	8 (4.4%)
Benign disease	26 (14.4%)
Previous cholecystectomy	8 (4.4%)
Re-hepatectomy	24 (13.3%)
Preoperative chemotherapy <sup>a</sup>	62 (53.9%)
Pre-operative PVE	10 (5.5%)
Tumour size ≥8 cm	50 (27.6%)
Concomitant extra-hepatic surgery:	25 (13.8%)
Colectomy	5
Ileostomy closure	1
Nephrectomy	3
Adrenalectomy	8
Resection of the common bile duct + 'Roux-en-Y'	5
Left pancreatectomy	1
Parietal surgery	2
Liver fibrosis <sup>b</sup>	
F0	150 (82.9%)
F1	15 (8.3%)
F2	16 (8.8%)
Liver steatosis	
<30%	161 (89.0%)
≥30%	20 (11.0%)

<sup>a</sup>The proportion of patients with pre-operative chemotherapy was calculated in the subgroup of patients with liver metastases. Only pre-operative chemotherapy performed less than 12 weeks before surgery was considered as having a potential impact on intra- and post-operative outcome.<sup>63</sup>

<sup>b</sup>According to the METAVIR classification.<sup>20</sup>

Age and BMI are expressed as median (range).

BMI, body mass index; ASA, American Society of Anesthesiologists; PVE, portal vein embolization.

sectorial branches of the right portal vein were separately ligated and divided. Some secondary portal branches for the right part of segment I were eventually ligated. After mobilization of the right ischaemic liver by section of the right triangular ligament, the posterior aspect of segments VI and VII was separated from the vena cava by ligating the caudate veins. After section of the hepatocaval ligament, the right hepatic vein was stapled and divided using a linear stapler (ATW35; Ethicon Endo-Surgery). Parenchymal transection was systematically begun without PTC and performed along the ischaemic demarcation line with an ultrasonic dissector (Dissectron®; Satelec Medical, Integra™, Mérignac, France). The right hepatic duct was found while separating segment V from segment IV and ligated at the right border of the hilar plate. To limit backflow from the suprahepatic veins, infused fluids were restricted, as tolerated by the haemodynamic status, until parenchyma transection was complete.<sup>21</sup> The thresholds for red blood cell (RBC) transfusion were a haemoglobin concentration of 7 g/dl for healthy patients 64 years of age or younger and 8 g/dl for patients 65 years of age or older or with pre-existing cardiopulmonary disease. These criteria were consistent throughout the study period.

During the parenchymal dissection, a salvage PTC was performed in the following situations: (i) major bleeding from portal or hepatocaval origin; (ii) cumulative blood loss exceeding 500 cc from the beginning of the parenchymal transection; and (iii) difficulties in achieving correct control of the rough surface, because of excessive oozing. This salvage PTC was continuous except when the predictable ischaemic time was superior to 20 min. In this case, an intermittent PTC was applied, with 15 min of ischaemic time separated by reperfusion periods of 5 min.

### Data collection and statistical analyses

Demographic and operative data, post-operative outcome and pathological findings were prospectively collected. The three main endpoints were intra-operative blood loss, requirement for a salvage PTC and post-operative outcome. Intra-operative blood loss was quantified by measuring suction bag volume and by weighing the swabs. Major intra-operative blood loss was defined as blood loss >1000 ml (90<sup>th</sup> percentile). The post-operative RBC transfusion rate was calculated within the 7 post-operative days. The mortality rate was defined using either the 30-day mortality or the in-hospital mortality. Morbidity was classified according to the Dindo and Clavien classification.<sup>22</sup> Severe morbidity was defined as grade III and more. Post-hepatectomy liver failure was defined using the '50–50' criteria.<sup>3</sup> A biliary fistula was defined as fluid in the abdominal drain with either the presence of biliary salts or a bilirubin concentration at least three times greater than in the serum on or after postoperative day 3, or as the need for radiological intervention because of biliary collections or relaparotomy resulting from bile peritonitis (this definition was slightly modified from Koch *et al.*<sup>23</sup>).

Continuous variables were expressed as median (range). Differences between groups were explored using the Mann–Whitney

U-test. Categorical variables were reported as the number of patients (prevalence in percentage) and differences between subgroups were compared using the two-sided Pearson's  $\chi^2$  test or Fisher's exact test when appropriate. Pre- and intra-operative variables that reached a univariate *P*-value < 0.1 were entered into a logistic regression model, using a forward stepwise method, to define which parameters were independently associated with major intra-operative blood loss and morbidity. A *P*-value < 0.05 was considered statistically significant. The statistical analysis was done using SPSS version 15.0 software (SPSS Inc., Chicago, IL, USA).

## Results

### Intra-operative course

The median duration of surgery was 300 (175–630) min. The right hepatic pedicle and the right hepatic vein were ligated before the hepatectomy in all patients. In the 10 patients with previous portal vein embolization, only one had pronounced inflammation with difficulties in dissecting the right glissonian pedicle, which was surrounded by an hypervascularized shift. In the eight patients with a previous cholecystectomy, no technical difficulty was noted during hilar dissection. There was no arterial or portal injury in these 18 patients. Forty-eight patients (26.5%) required a salvage PTC during transection. In these patients, the median blood loss were significantly higher compared with patients without PTC (600 vs. 400 ml; *P* < 0.0001) and the median clamping time was 20 min (range 5–96 min), including 18 patients (37.5%) up to 15 min, 17 patients (35.4%) from 16 to 30 min, 8 patients (16.7%) from 31 to 60 min and 5 patients (10.4%) more than 60 min. Intermittent PTC (*n* = 20; 41.7%), was performed when total ischemic time exceeded 20 min, with a maximum of 96 min. As shown in Table 2, steatosis  $\geq 30\%$  was the only significant determinant factor for the requirement of a salvage PTC (*P* = 0.047). However, 5 of the 10 patients with pre-operative portal vein embolization (PVE) also required a salvage PTC (*P* = 0.083).

The median intra-operative blood loss was 500 ml (50–3000). Fourteen patients (7.7%) had an intra-operative RBC transfusion, with 2 (range 1–4) RBC units per transfused patient. Significantly increased intra-operative blood loss was observed in male patients (500 vs. 375 ml; *P* < 0.001) or in patients with a body mass index (BMI) of 30 kg/m<sup>2</sup> or higher (650 vs. 450 ml; *P* = 0.026), hepatocellular carcinoma (600 vs. 442 ml; *P* = 0.014), tumour size over 8 cm (550 vs. 500 ml; *P* = 0.037) and steatosis  $\geq 30\%$  (625 vs. 450 ml; *P* = 0.013). (Table 3). Nineteen patients (10.5%) had major intra-operative blood loss (>1000 ml). In univariate analysis (Table 4), only male gender (84.2% vs. 56.2%; *P* = 0.019) was significantly associated with major intra-operative blood loss. There was a trend to significance for BMI (25 vs. 24 kg/m<sup>2</sup>; *P* = 0.052) and diabetes mellitus (42.1% vs. 21.6%; *P* = 0.082) to also be associated with major intra-operative blood loss. On multivariate analysis, only male gender (OR = 5.624; 95% CI: 1.239–25.520; *P* = 0.025) was independently associated with major intra-

**Table 2** Univariate analysis of determinant factors of salvage PTC during transection

Factors	No PTC (n = 133)	Salvage PTC (n = 48)	P-value
Age	61 (17–82)	63 (26–80)	0.887
Male gender	74 (55.6%)	33 (68.8%)	0.113
BMI (kg/m <sup>2</sup> )	24 (15–37)	24 (18–34)	0.992
ASA score III	22 (17.7%)	7 (14.9%)	0.658
Diabetes mellitus	35 (26.3%)	8 (16.7%)	0.178
Malignant disease	113 (85.0%)	42 (87.5%)	0.662
Liver metastases	84 (63.2%)	31 (64.6%)	0.865
Previous cholecystectomy	4 (3.0%)	4 (8.3%)	0.211
Re-hepatectomy	16 (12.0%)	8 (16.7%)	0.417
Pre-operative chemotherapy <sup>a</sup>	47/84 (56.0%)	15/31 (48.4%)	0.470
Pre-operative PVE	5 (3.8%)	5 (10.4%)	0.083
Tumour size ≥8 cm	35 (26.3%)	15 (31.3%)	0.514
Concomitant surgery	21 (15.8%)	4 (8.3%)	0.207
F1-F2 liver fibrosis <sup>b</sup>	24 (18.0%)	7 (14.6%)	0.585
Steatosis ≥30%	11 (8.3%)	9 (18.8%)	0.047

<sup>a</sup>The proportion of patients with pre-operative chemotherapy was calculated in the subgroup of patients with liver metastases. Only pre-operative chemotherapy performed less than 12 weeks before surgery was considered as having a potential impact on the intra- and post-operative outcome.<sup>63</sup>

<sup>b</sup>According to the METAVIR classification.<sup>20</sup>

Age and BMI are expressed as median (range).

PTC, portal triad clamping; BMI, body mass index, ASA, American Society of Anesthesiologists; PVE, portal vein embolization.

operative blood loss. No patient experienced a clinical air embolism or accidental devascularization of the left hemiliver.

### Post-operative course

Three patients (1.6%) died post-operatively. One patient developed an acute thrombosis of a previous aorto-bifemoral bypass at post-operative day one and required reoperation. He then developed fatal multiple organ failure syndrome at postoperative day 5. The second patient had a massive cerebrovascular stroke and died at postoperative day 5. The third patient developed a fatal myocardial infarction 10 days after hepatectomy.

The median hospital stay was 9 days (range 5–55). The overall morbidity rate was 42%, including 107 post-operative complications, detailed in Table 5. Severe morbidity occurred in 22 patients (12.1%). Nineteen patients (10.5%) required post-operative RBC transfusions, with 2 (range 2–7) RBC units per transfused patient. These patients had a significant higher intra-operative blood loss compared with patients without a post-operative transfusion (700 vs. 475 ml;  $P = 0.004$ ). The overall peri-operative (intra- and post-operative) RBC transfusion rate was 16.6%. The median transaminases peaks on postoperative day 1 were 369 UI/l (range 78–3312) and 423 UI/l (34–3920) for aspartate amino-transferase and alanine amino-transferase, respectively. Six patients (3.3%) developed post-hepatectomy liver failure and this complication was associated with one post-operative death. The prothrombin time ratio and serum bilirubin level on postoperative day-5 were 75% (range 38–100) and 37  $\mu\text{mol/l}$  (range 4–89), respectively. Ten

patients (5.5%) had transient renal insufficiency, of whom one patient required dialysis. There was no digestive fistula in the 11 patients with concomitant gastrointestinal resection or 'Roux-en-Y' procedure.

On univariate analysis, operative time (315 vs. 285 min;  $P = 0.022$ ), intra-operative blood loss (500 vs. 400 ml;  $P = 0.041$ ) and the peri-operative transfusion rate (23.7% vs. 11.4%;  $P = 0.028$ ) were associated with post-operative morbidity (Table 6). In multivariate analysis, only peri-operative transfusion rate was an independent determinant of morbidity (OR = 2.33; 95% CI: 1.043–5.207;  $P = 0.039$ ).

### Discussion

For an anatomic major hepatectomy, an attractive strategy is to use a partial hepatic devascularization technique to avoid ischaemia of the remnant liver, splanchnic congestion (especially in the case of concomitant gastrointestinal surgery) and haemodynamic variations induced by continuous or intermittent PTC.<sup>24</sup> Moreover, extra-hepatic division of the ipsilateral vessels before transection induces selective ischaemia to the removed liver, enables the surgeon to easily delineate the future cutting plan on the liver surface and gives time for meticulous parenchymal dissection and haemostasis, avoiding the haemorrhagic uncomfortable revascularization periods frequently associated with intermittent PTC. Finally, it might decrease the risk of air embolism<sup>25</sup> owing to the ligation of the ipsilateral hepatic vein. For all

**Table 3** Values of intra-operative blood loss according to pre-operative factors

		Intra-operative blood loss (mL)	P-value
Age	≤60 years	500 (50–2400)	0.873
	>60 years	500 (50–3000)	
Gender	Male	500 (50–3000)	<0.001
	Female	375 (50–1350)	
BMI (kg/m <sup>2</sup> )	<30	450 (50–3000)	0.026
	≥30	650 (50–2000)	
ASA score	I-II	500 (50–3000)	0.582
	III	400 (200–2900)	
Diabetes mellitus	No	500 (50–3000)	0.572
	Yes	450 (50–2900)	
Malignant disease	No	400 (50–1400)	0.386
	Yes	500 (50–3000)	
Hepatocellular carcinoma	No	442 (50–3000)	0.014
	Yes	600 (50–2000)	
Liver metastases	No	500 (50–2400)	0.205
	Yes	500 (50–3000)	
Previous cholecystectomy	No	500 (50–3000)	0.860
	Yes	400 (200–900)	
Re hepatectomy	No	500 (50–3000)	0.790
	Yes	500 (100–2900)	
Pre-operative chemotherapy <sup>a</sup>	No	500 (50–3000)	0.177
	Yes	400 (50–2900)	
Pre-operative PVE	No	500 (50–3000)	0.586
	Yes	525 (50–1700)	
Tumour size	≤8 cm	500 (50–3000)	0.037
	>8 cm	550 (50–2900)	
Concomitant surgery	No	500 (50–2900)	0.435
	Yes	400 (150–3000)	
Liver fibrosis <sup>b</sup>	F0	450 (50–3000)	0.111
	F1-F2	500 (100–1700)	
Steatosis ≥30%	No	450 (50–2900)	0.013
	Yes	625 (200–3000)	

<sup>a</sup>The proportion of patients with pre-operative chemotherapy was calculated in the subgroup of patients with liver metastases. Only preoperative chemotherapy performed less than 12 weeks before surgery was considered as having a potential impact on the intra- and post-operative outcome.<sup>63</sup>

<sup>b</sup>According to the METAVIR classification.<sup>20</sup> BMI, body mass index, ASA, American Society of Anaesthesiologists; PVE, portal vein embolization.

these reasons, we have adopted this technique since 2000 as a systematic procedure for a right hepatectomy in non-cirrhotic liver.

Several previous studies and three systematic reviews have compared various clamping and non-clamping techniques in liver resection.<sup>1,24–46</sup> Apart from the superiority of intermittent PTC

**Table 4** Univariate analysis of determinant factors of major intra-operative blood loss (>1000 ml)

Factors	≤1000 ml (N = 162)	>1000 ml (N = 19)	P-value
Age	61 (21–82)	63 (17–77)	0.704
Male gender	91 (56.2%)	16 (84.2%)	0.019
BMI (kg/m <sup>2</sup> )	24 (15–37)	25 (19–35)	0.052
ASA score III	24 (14.8%)	5 (26.3%)	0.195
Diabetes mellitus	35 (21.6%)	8 (42.1%)	0.082
Malignant disease	139 (85.8%)	17 (89.5%)	0.493
Hepatocellular carcinoma	26 (16.0%)	5 (26.3%)	0.332
Liver metastases	104 (64.2%)	11 (57.9%)	0.541
Previous cholecystectomy	8 (4.9%)	0 (0%)	0.404
Re hepatectomy	21 (13.0%)	3 (15.8%)	0.722
Pre-operative chemotherapy <sup>a</sup>	55/104 (52.9%)	7/11 (63.6%)	0.496
Pre-operative PVE	9 (5.6%)	1 (5.3%)	0.717
Tumour size ≥8 cm	30 (18.5%)	6 (31.6%)	0.217
Concomitant surgery	25 (15.4%)	2 (10.5%)	0.743
F1-F2 liver fibrosis <sup>b</sup>	27 (16.7%)	4 (21.1%)	0.747
Steatosis ≥30%	16 (9.9%)	4 (21.1%)	0.235

<sup>a</sup>The proportion of patients with pre-operative chemotherapy was calculated in the subgroup of patients with liver metastases. Only pre-operative chemotherapy performed less than 12 weeks before surgery was considered as having a potential impact on the intra- and post-operative outcome.<sup>63</sup>

<sup>b</sup>According to the METAVIR classification.<sup>20</sup> Age and BMI are expressed as median (range). BMI, body mass index, ASA, American Society of Anaesthesiologists; PVE, portal vein embolization.

over continuous PTC in patients with chronic liver disease,<sup>34</sup> there is no evidence to support one technique of vascular control over another. In particular, one recent meta-analysis<sup>47</sup> failed to demonstrate any advantage of the hepatic vascular exclusion approaches. However, most of the studies investigating the role of one-sided selective clamping techniques (Table 7) have included both cirrhotic and non-cirrhotic patients or have involved various types of hepatectomy (minor or major, anatomic or not). In addition, occlusion of the ipsilateral outflow was not routinely performed in many of these studies. This may bring about various confounding variables and preclude any reliable conclusion about the role of a hemi-clamping approach in each individual patient. The present study is the first report of a large cohort of patients without underlying chronic liver disease undergoing a unique type of major hepatectomy with the same procedure of vascular control and parenchymal dissection (Table 7). A right hepatectomy was selected because this largely used standard operative procedure is reproducible with few anatomical variations. In addition, the access to the right portal pedicle and to the right hepatic vein is safe and makes extra-hepatic division of the right liver vessels an easy procedure to perform.

**Table 5** List of 107 post-operative complications in 76 patients<sup>a</sup>, according to the Dindo and Clavien classification of morbidity<sup>22</sup>

Complication	I	II	IIIa	IIIb	Iva	IVb	V	Total
Liver-related complications								
Liver failure <sup>b</sup>	5	–	–	–	–	–	1	6
Biliary fistula	4	–	7	3	–	–	–	14
Ascites	11	3	–	–	–	–	–	14
<b>Total liver-related complications</b>	<b>20</b>	<b>3</b>	<b>7</b>	<b>3</b>	<b>–</b>	<b>–</b>	<b>1</b>	<b>34</b>
Haemorrhage								
Blood effusion or collection	–	4	3	–	–	–	–	7
Gastrointestinal bleeding	–	–	1	–	–	–	–	1
Pulmonary complications								
Pleural effusion	15	–	1	–	–	–	–	16
Pneumonia	–	4	–	–	–	–	–	4
Pulmonary embolism	–	1	–	–	–	–	–	1
Acute respiratory distress syndrome	–	–	–	–	1	1	–	2
Non-pulmonary infections								
Catheter infection	1	–	–	–	–	–	–	1
Urinary infection	–	1	–	–	–	–	–	1
Undetermined fever	–	2	–	–	–	–	–	2
Subphrenical abscess	–	–	4	–	–	–	–	4
Wound complications								
Wound haematoma	9	–	–	–	–	–	–	9
Evisceration	–	–	–	1	–	–	–	1
Other								
Acute renal failure	–	9	–	–	1	–	–	10
Transient neurological confusion	6	–	–	–	–	–	–	6
Peripheral venous thrombosis	–	3	–	–	–	–	–	3
Thrombosis of a previous aortobifemoral bypass	–	–	–	1	–	–	–	1
Transient cardiac failure	–	1	–	–	–	–	–	1
Myocardial infarction	–	–	–	–	–	–	1	1
Cerebrovascular stroke	–	–	–	–	–	–	1	1
Multi-organ failure syndrome	–	–	–	–	–	–	1	1
<b>Total</b>	<b>51</b>	<b>28</b>	<b>16</b>	<b>5</b>	<b>2</b>	<b>1</b>	<b>4</b>	<b>107</b>

<sup>a</sup>23 patients had more than one complication.

<sup>b</sup>Liver failure was defined using the '50–50' criteria.<sup>3</sup>

Indeed, in the present series, vascular dissection and ligatures could always be performed before parenchymal dissection and this strategy was successful in nearly three-quarters of the patients without the need for a salvage PTC. The rate of salvage PTC requirement was slightly higher to the 21% rate, as previously reported by Malassagne *et al.* in 43 patients with right and left hepatectomies.<sup>10</sup> This could be explained by a high proportion of patients with pre-operative chemotherapy or steatosis. Indeed, steatosis was the only determinant factor for salvage PTC requirement in the present series. The fragility of the steatotic parenchyma, with a high risk of damaging some tributaries to the middle hepatic vein, may explain unexpected bleeding from the left liver raw surface in spite of ischaemia of the right liver. Pre-

operative right PVE may be thought to be another cause of failure of the extra-hepatic portal pedicle division, because of the difficulty in dissecting the right portal vein. In the present series, the division of the right portal vein was feasible in all 10 patients receiving pre-operative PVE. Pronounced inflammation with difficulties in dissecting the right glissonean pedicle was described in only one of these patients, but five required a salvage PTC, although the PTC rate was not significantly higher compared with patients without PVE ( $P = 0.083$ ). In spite of the high rate of salvage PTC, the total ischaemic time was brief, below 30 min in the vast majority of patients, suggesting that, on an intent-to-treat basis, this policy was effective for ischaemia sparing of the remnant liver and may contribute to the low peak of

**Table 6** Univariate analysis of overall morbidity<sup>a</sup>

	Patients without morbidity (N = 105)	Patients with morbidity (N = 76)	P-value
Age	60 (17–82)	64 (21–82)	0.147
Male gender	59 (56.2%)	48 (63.2%)	0.347
BMI (kg/m <sup>2</sup> )	24 (15–36)	24 (16–37)	0.632
ASA score III	14 (13.3%)	15 (19.7%)	0.250
Diabetes mellitus	25 (23.8%)	18 (23.7%)	0.984
Malignant disease	91 (86.7%)	65 (85.5%)	0.826
Liver metastases	70 (66.7%)	45 (59.2%)	0.421
Previous cholecystectomy	4 (3.8%)	4 (5.3%)	0.722
Re-hepatectomy	12 (11.4%)	12 (15.8%)	0.393
Preoperative chemotherapy <sup>b</sup>	40/70 (57.1%)	22/45 (48.9%)	0.386
Preoperative PVE	5 (4.8%)	5 (6.6%)	0.744
Tumour size ≥8 cm	17 (16.2%)	13 (17.1%)	0.893
F1-F2 liver fibrosis <sup>c</sup>	16 (15.2%)	15 (19.7%)	0.428
Steatosis ≥30%	11 (10.5%)	9 (11.8%)	0.772
Operative time (min)	285 (175–530)	315 (180–630)	0.013
Concomitant surgery	16 (15.2%)	11 (14.5%)	0.887
PTC requirement	24 (22.9%)	24 (31.6%)	0.190
Ischaemia time (min)	0 (0–91)	0 (0–96)	0.198
Blood loss (mL)	450 (50–2900)	500 (50–3000)	0.047
Peri-operative transfusion	12 (11.4%)	18 (23.7%)	0.029
Intra-operative transfusion	5 (4.8%)	10 (13.2%)	0.052
Post-operative transfusion	9 (8.6%)	10 (13.2%)	0.320

<sup>a</sup>Overall morbidity was defined as Dindo and Clavien<sup>22</sup> grade I or more.

<sup>b</sup>The proportion of patients with pre-operative chemotherapy was calculated in the subgroup of patients with liver metastases. Only pre-operative chemotherapy performed less than 12 weeks before surgery was considered as having a potential impact on the intra- and post-operative outcome.<sup>63</sup>

<sup>c</sup>According to the METAVIR classification.<sup>20</sup>

Age, BMI operative time and blood loss are expressed as median (range).

BMI, body mass index; ASA, American Society of Anesthesiologists; PVE, portal vein embolization; PTC, portal triad clamping.

transaminases and the high rate of post-operative liver recovery (97% after post-operative day 5).

The median operative time was 5 h, which is similar to operative times reported in the literature for a major hepatectomy without PTC (221–318 min),<sup>10,36,45</sup> but higher compared with some series of major hepatectomy under PTC (180–220).<sup>30,45,48</sup> Thus, it is likely that the unclamping technique is associated with an increase in operative time, as suggested by a recent retrospective study.<sup>45</sup> In terms of intra-operative blood loss and transfusion rate, the present series compares favourably with previous reported series of a major hepatectomy in non-cirrhotic patients,<sup>28,30,40,48–51</sup> in which the median blood loss varied from 250 to 989 ml. A recent Japanese study reported a 14% rate of blood loss exceeding 1500 ml in patients without underlying liver disease.<sup>52</sup> This rate was only 5.5% in the present series. The peri-operative RBC transfusion rate (17%) was also similar to previous series of major hepatectomy in non-cirrhotic patients, in which it varies largely from 6% to 63%, as it may depend on centres transfusion policies.<sup>10,26,27,30,48,49,51,53,54</sup> In addition, as expected from the

partial outflow control enabled by the technique,<sup>25</sup> the incidence of clinical air embolism was nil in the present series, although damage to the middle hepatic vein is still possible.

Two classic hazards have been raised against the use of extra-hepatic division of the vessels: there is a risk of hepatic vein or vena cava injury during the extrahepatic dissection of the hepatic veins and a risk of devitalizing the remnant liver by an erroneous ligation of a glissonian pedicle in the hilum, which is increased by the frequency of anatomical abnormalities. Thus, Bismuth advocated in 1982 not to divide the inflow vessels prior to transection and reported a technique combining the advantages of the Lortat-Jacob and the Ton That Thung approaches:<sup>12</sup> the ipsilateral pedicle was dissected and clamped but not divided until the portal elements were identified by a superior approach inside the parenchyma. Also, the right flank of the retrohepatic inferior vena cava was freed without systematically attempting to dissect the right hepatic vein. However, thanks to the improvement of the knowledge of the retrohepatic and hepatocaval confluence anatomy, which is especially associated with the progresses in liver trans-

**Table 7** Main series including major hepatectomies performed without portal triad clamping in the past 15 years

Authors	Year	Type of study	Number of patients (MH / RH)	Chronic liver disease (%)	Vascular control <sup>a</sup>	Intra-operative blood loss (ml)	Transfusion rate or blood unit per patient	Overall morbidity	Severe morbidity	Mortality
Malassagne <i>et al.</i> <sup>10</sup>	1998	Cohort	43 / 36	14%	r-SHVE or l-SHVE	Ns	35%	18.6%	11.6%	2%
Descottes <i>et al.</i> <sup>49</sup>	2003	Cohort	87 / 73	0%	r-Inflow	980	52%	26%	NS	4.6%
Scatton <i>et al.</i> <sup>51</sup>	2004	Cohort	50 / 26	12%	None or r-Inflow or l-Inflow	250	26%	16% (surgical) 20% (medical)	6%	0%
Moug <i>et al.</i> <sup>16</sup>	2007	Cohort	59 / 30	3%	r-SHVE or l-SHVE	450	0%	20%	1%	0%
Ercolani <i>et al.</i> <sup>31</sup>	2008	Cohort	393 / ns	27%	PTC or r-Inflow or l-Inflow or THVE	Ns	0.59 unit	23.4%	NS	2.1%
Fu <i>et al.</i> <sup>42</sup>	2011	Ran-domized control trial	108 / 52	60%	r-Inflow or l-Inflow vs. MPV vs. PTC	354	6.7%	20%	NS	0%
Li <i>et al.</i> <sup>50</sup>	2011	Cohort	60 / 60	0%	r-Inflow	595	0.42 unit	35%	8.4%	0%
Wong <i>et al.</i> <sup>45</sup>	2011	Cohort	124 / 124	31%	r-Inflow (or none) vs. PTC	450	10.3%	22.4%	NS	1.7%
Viganò <i>et al.</i> <sup>17</sup>	2011	Cohort	171 / 92	8%	r-SHVE or l-SHVE	450	14.3%	38.3%	NS	1.2%
Present series		Cohort	181 / 181	0%	r-SHVE	500	16.6% 0.45 unit	42%	12%	1.6%

Studies that focused exclusively on a hepatectomy in patients with cirrhosis have been excluded.

When data were available for distinct groups, only those from the group with major or a right hepatectomy without portal triad clamping have been presented.

<sup>a</sup>Techniques of vascular control: PTC, total portal triad clamping (continuous or intermittent). r-Inflow/l-Inflow, clamping/division of the right/left portal vein and hepatic artery. r-SHVE/l-SHVE, clamping/division of the right/left portal vein and hepatic artery + clamping/division of the ipsi-lateral hepatic vein (selective hepatic vascular exclusion/devascularization). THVE, Total hepatic vascular exclusion without preservation of the caval flow. MPV, Clamping of the main portal vein.

MH, major hepatectomy; RH, right hepatectomy; NS, not specified.

plant surgery, and the use of low central venous pressure during liver surgery, accidental injuries of hepatic veins or vena cava during the retrohepatic dissection step have become rare and mostly as a result of huge liver masses or a previous hepatectomy. Moreover, in contrast to a more challenging liver resection such as a mesohepatectomy<sup>55</sup> or a hepatectomy in cirrhotic livers, the encirclement of the right hepatic vein during a right hepatectomy in non-cirrhotic livers is a safe and easy step in the majority of patients. Regarding the risk of right glissonian pedicle division prior to parenchymal dissection, there was no accidental devascularization of the left remnant hemi-liver in the present series. In fact, anatomical variations of the extrahepatic portal vein are infrequent and mostly located to the left side. One of them is the anterior right portal vein originating from the left portal vein, which is observed in 2% of the subjects<sup>56</sup> and may explain the risk of right remnant hemi-liver devascularization after left hepatectomy. In contrast, the symmetrical variation has never been

described and extra-hepatic division of the portal vein before transection in a right hepatectomy may not be as risky as in a left hepatectomy. In addition, checking the ischaemic liver territory by clamping the right portal pedicle prior to division is undoubtedly a key step in performing this technique safely. Infrahepatic vena cava clamping has been another means to reduce bleeding during parenchymal dissection. By lowering the central venous pressure, this manoeuvre decreases the venous backflow that occurs along the liver cut surface in spite of portal triad clamping.<sup>57</sup> Two randomized studies assessing the role of concomitant infrahepatic vena cava clamping are available in the literature with conflicting results. The first one<sup>58</sup> included mostly patients undergoing minor hepatectomies and failed to show any reduction of bleeding in the clamping group. The second trial<sup>59</sup> showed a significant decrease in intra-operative blood loss but without any impact on morbidity or mortality. Half clamping of the infra-hepatic vena cava with a tourniquet, in association with portal triad clamping, has also



been reported to be associated with a lower central venous pressure and a significant decrease in intra-operative blood loss.<sup>60</sup> Although never performed in the present series, this manoeuvre may be associated with hemivascular control of the right liver in a right hepatectomy, as it might decrease supra-hepatic backflow even in the absence of portal triad clamping and, therefore, might decrease the probability to require salvage portal triad clamping during transection. It might also be useful in case of vena cava injury during the hepatocaval dissection prior to transection.

Post-operative mortality and morbidity rates (1.6% and 42% respectively) were comparable to previous series of major hepatectomy in non-cirrhotic patients.<sup>10,26,27,30,40,48,49,51,53,54</sup> The prospective collection of post-operative data and the strict accordance to the five-tier grading of the Dindo and Clavien classification,<sup>22</sup> may explain the high rate of overall morbidity, whereas less than 20% of patients experienced morbidity of grade II and more. Moreover, every single complication and its associated grade of severity was reported in detail (Table 4) in order to present a comprehensive analysis of the outcome after a right hepatectomy with the unclamping policy. The rate of biliary fistula was 7.7%, but only 5.5% of patients required percutaneous or surgical management. By reducing the time constraint with regard to ischaemic insult to the remnant liver, the unclamping technique may give more time for the surgeon to perform meticulous ligations of the biliary stumps. Another advantage of the unclamping technique is the avoidance of haemodynamic changes and splanchnic congestion associated with total interruption of the liver inflow, and the hypothesis that it may reduce the risk of post-operative renal failure. Interestingly, none of the 11 patients with a concomitant gastrointestinal resection or 'Roux-en-Y' procedure experienced a digestive fistula and only one patient required post-operative dialysis. Classic factors of post-operative morbidity were found, i.e. operative time, intra-operative blood loss and peri-operative transfusions, the latter being independently associated with morbidity as already demonstrated.<sup>61</sup>

The main limitation of the present study is represented by its retrospective design and the lack of a control group. This precludes drawing any firm conclusion about indications, timing and effectiveness of a salvage PTC during transection. In addition, any comparison of outcome between patients with and without PTC was omitted, as the two groups were obviously not comparable. We also failed to determine any pre-operative factor associated with major intra-operative blood loss, which would give an indication to perform an initial PTC prior to transection, except male gender. Although we did not find any confounding variables, such as hepatocellular carcinoma, this association must be carefully interpreted. It seems difficult to conclude that portal triad clamping should initially have been performed in men and that extrahepatic vascular control should only be indicated in women. BMI and diabetes mellitus were other factors that tend to be associated with major intra-operative blood loss, although not significantly. As a result of the small size of the group of patients with major intra-operative blood loss, it is likely that this study lacked power

to demonstrate a significant association with high BMI and diabetes mellitus. We might then suggest that performing initial portal triad clamping prior to transection would have been better in this subgroup of patients.

Overall, given the size and the homogeneity of the cohort, the present study brings evidence to validate the policy of a selective use of PTC during transection rather than a systematic upfront PTC in right hepatectomy. In addition, it provides comprehensive data on the expected results of a right hepatectomy performed with this procedure of vascular control. Although this technique was performed by a single team, there are some arguments to think that wide applicability of the reported results is likely. All hepatectomies of the present series were performed over a 10-year period by several faculty surgeons or graduating chief residents. We report herein the overall results of the technique, regardless of the presumable heterogeneity in the surgeons' technical skills. The technique of extra-vascular control of hepatic pedicles prior to transection has become a standard that several surgeons performing liver resection have adopted worldwide and whose reproducibility has already been demonstrated.<sup>14,15,17</sup> As a result of favourable anatomical conditions, vascular control of the right glissonean pedicle and right hepatic vein may be performed easily in a high reproducible manner in most cases. In addition, the ischaemic line drawn on the liver surface after division of the right pedicle enables the surgeon to easily delineate the future cutting plan. Therefore, this technique of a right hepatectomy in non-cirrhotic livers is considered in our team as one of the essential surgical procedures for graduating chief residents to achieve competence in hepato-pancreato-biliary surgery.

There are, however, some tricks and pitfalls we may discuss from our technical experience with this technique, and especially from what we learned during the study period:

#### **Safe extrahepatic division of the right portal vein**

As discussed above, the primary branches of the portal vein are always extrahepatic, i.e. located below the reflection line of Glisson's capsula. Two anatomical conditions may however induce technical difficulties in dissecting the right portal vein. First, the length of the common trunk may be very short before the origin of the sectional branches. At most, the surgeon may deal with a portal vein trifurcation. In this case, the posterior branch should first be ligated and divided, then the encirclement of the anterior branch would be easier. Second, the shape of the parenchyma surrounding the right part of the hilum may be very different in each subject. In some cases, the right portal vein, although remaining extracapsular, enters into a deep valley made by the convexity of segments IV,V,VI and I on each side of the hilum. In this case, safe access to the right portal vein may be more difficult and a vascular ligation should be preferred than vascular stapling.

In all cases, in order to lengthen the right portal vein, the right branch of the hepatic artery should first be ligated and divided and all the tributaries to segment 1, arising from the posterior aspect of the right portal vein, should also be ligated and divided.

When the vascular stapler can not be used, the right branch of the portal vein can be ligated by a silk ligature and divided. This ligature should be placed without pulling the vein out to avoid any portal vein stenosis and, as it may slip from the venous stump like a champagne cork, it can be secured to the venous wall, using a polypropylene stitch. Finally, the origin of the left portal vein should be carefully identified by extensively dissecting the anterior aspect of the main portal trunk.

### Division of the right glissonean pedicle should come before hepatocaval dissection

This has many advantages. After division of the right glissonean pedicle, every clamp can be removed from the portal triad. Thus, the liver rotation to the left around the vena cava may be easier. Additionally, as the right liver has been devascularized, its mobilization becomes easier and any haemorrhage on the capsula or on the hepatic stump of the accessory hepatic veins is minimal and can be easily controlled.

### Optimizing parenchymal dissection

The so-called hanging manoeuvre has been reported as part of the anterior approach technique.<sup>62</sup> However, it can easily be used after hepatocaval dissection and right hepatic vein transection to facilitate the exposure of the deeper part of the parenchyma, anterior to the vena cava. During parenchymal dissection, bleeding may sometimes be because of fluid overload. Adequate communication between surgeons and anaesthesiologists is of utmost importance, especially during right liver mobilization.

In conclusion, in spite of an increasing challenging patient population with pre-operative chemotherapy or liver steatosis, systematic extra-hepatic vascular division prior to transection and selective use of PTC during transection can be safely performed in a right hepatectomy. This policy will avoid any ischaemic insult to the remnant liver in the majority of patients while minimizing the cumulative ischaemic time in the remaining patients.

### Conflicts of interest

None declared.

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