Right Portal Vein Ligation: A New Planned Two-Step All-Surgical Approach for Complete Resection of Primary Gastrointestinal Tumors with Multiple Bilateral Liver Metastases

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Although complete resection of liver metastases remains the only curative treatment for metastatic liver disease from colorectal and endocrine gastrointestinal (GI) tumors, only a small proportion of patients with liver metastases are candidates for potentially curative surgery.1-20 Among these, 4% to 21% are found to have unresectable disease because of multiplicity of the liver metastases, so a very small proportion of such patients can be eligible for complete resection.6,19,21-26 When the number and distribution of liver metastases create the need for extensive hepatic resection, the risk for postoperative liver failure and morbidity related to the small size of the remnant liver is increased.27-29 Additionally, substantial operative risk results from the combination of extensive hepatic resection with other major abdominal procedures at a single operation, such as extended hepatectomy with colorectal or pancreatic resections.1,30 On the other hand, minor hepatic surgery, such as left liver wedge resection, has been shown to be safe in combination with such extrahepatic procedures as those necessary to treat many GI primary tumors.1,5,19,31,32

So, multistep, multimodality therapies including surgery in several steps have been proposed and usually require resection of the primary tumor in one step, followed by extensive liver resection, with or without the use of percutaneous ablative therapy or systemic chemotherapy.1,10,23,33-35 Improved understanding of the benefits of liver regeneration has led to other approaches using intermediate steps between surgical procedures.24,29,36-39 In patients expected to have a small future liver remnant volume (FLR), most hepatic surgeons perform preoperative portal vein embolization (PVE), mainly to avoid postoperative liver failure and to decrease morbidity either after major hepatectomy in patients with injured liver parenchyma (such as that found in patients after extensive chemotherapy or in patients with chronic liver disease) or when major hepatectomy is associated to major abdominal procedures.24,29,36-39 But some investigators suggest that in patients with bilobar liver metastases from colorectal cancer, hypertrophy of the left liver induced by right PVE might accelerate the progression of left-sided disease and therefore caution against the reckless use of PVE in these cases.40,41

In order to use the benefits of diversion of portal flow to the FLR, to avoid the risk of progression of liver disease, and to minimize the risk and number of procedures necessary to treat patients with GI tumors with bilobar liver metastases, we developed a new planned two-step, totally surgical approach to clear all primary and metastatic disease. In the first step, the primary tumor and all left-sided liver metastases (Couinaud S1 to S4) are resected using straightforward resection techniques. Simultaneously, right portal vein ligation (RPVL) is performed to induce hypertrophy in the left lobe, which has been cleared of all detectable disease. Four to 8 weeks later, after hypertrophy of the disease-free FLR, a second step consisting of a right or extended right hepatectomy is planned to completely clear the remaining right-sided liver metastases (Fig. 1).
TECHNIQUE

Patients were carefully staged using endoscopy, spiral CT with oral and intravenous contrast, and other specialized assessments (octreoscan, CT-portography) when appropriate. Patients were eligible for the two-step procedure when the metastatic disease was limited to the liver (diffuse peritoneal disease excluded) and the primary tumor was intact.

In the first step, usually through a midline incision, complete exploration of the abdomen was performed. The liver was evaluated with bimanual palpation and intraoperative ultrasonography. In the absence of peritoneal carcinomatosis, the primary GI tumor was resected using standard techniques. Then, all left-sided liver metastases (S1 to S4) were removed by wedge resection(s), generally without right liver mobilization. Next, a cholecystectomy was usually performed to facilitate dissection of the right branch of the portal vein. Right portal vein ligation (RPVL) was performed using nonabsorbable suture under ultrasound-Doppler control to ensure that the entire right portal vein, and only the right portal vein, was ligated. Postoperative complications were rigorously detailed prospectively.

Four to 8 weeks later, patients were restaged using thoracoabdominal CT with liver volumetry. The FLR was defined as the liver that would remain after complete anatomic resection of right-sided disease (usually S4 to S8 ± S1). The percent hypertrophy of the FLR was calculated by CT volumetry using the following formula:

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\text{% Hypertrophy} = \left( \frac{\text{FLR volume post-RPVL} - \text{FLR volume pre-RPVL}}{\text{FLR volume pre-RPVL}} \right) \times 100
\]

In the absence of tumor progression on restaging, the second-step operation was performed through a separate incision (J shaped), which provided optimum exposure of

Figure 1. Description of the two-step all-surgical technique using right portal vein ligation for complete resection of primary gastrointestinal tumors with multiple bilobar liver metastases.

**Abbreviations and Acronyms**

- FLR = future liver remnant volume
- GI = gastrointestinal
- PVE = portal vein embolization
- RPVL = right portal vein ligation
the liver and avoided the need for extensive lysis of adhe-
sions from the earlier procedure. The liver was again eval-
uated completely with bimanual palpation and intraoper-
ative ultrasonography with Doppler. Because the right liver
was not unnecessarily mobilized during the first procedure,
and because only necessary hilar dissection was performed
at the first procedure, adhesions were not extensive at the
second step. In the absence of peritoneal carcinomatosis, a
right hepatectomy (resection of S4 to S8) or right lobec-
tomy (S5 to S8 ± S1) was performed using standard tech-
niques39,43 to accomplish complete resection of remaining
hepatic metastases (Fig. 2).

RESULTS
Between 1996 and 2001, this two-step strategy was ap-
plied in 20 patients (11 women, 9 men, mean age
57 ± 13 years). All patients had diffuse, bilobar liver
metastases and intact primary GI tumors. Tumor types
were colorectal adenocarcinoma in 12 patients and neuro-
endocrine tumors in 8 patients. Colorectal cancers in-
cluded four rectal and eight colon primaries. Neuroen-
docrine primaries were located in the ileum (one
patient), gastric antrum (one patient), and in the left
pancreas (six patients). The number of metastatic nod-
ules determined by preoperative CT (or CT postogra-
phy) and intraoperative ultrasound was confirmed by
pathologic analysis (mean 5.3 ± 5 lesions in the right
liver [range 1 to 15 metastases] and 2.5 ± 2 in the left
liver [range, 1 to 5 metastases]).

At the first-step procedure, 75% of the patients (15 of
20) underwent exploration through a midline incision.
All patients underwent complete macroscopic resection
of the primary and resection of one to five left-sided liver
metastases (S1 to S4). The RPVL was performed in all

![Figure 2. (A and B) Preoperative CT scan of a patient with primary gastrointestinal tumor and multiple bilobar neuroendocrine liver metastases. (C) Left liver segment hypertrophy seen in a CT scan 4 weeks after the first step including the resection of both the primary tumor and left-sided liver metastases including those in segment 4, associated with right portal vein ligation. (D) Postoperative CT scan 8 weeks after the second step including right liver hepatectomy.](image)
patients without intraoperative incident. In 17 patients (94%), cholecystectomy with minimal hilar dissection was performed to facilitate RPVL. After the first step, there were no major complications related to RPVL. A single major complication occurred (bronchopulmonary infection requiring antibiotic therapy [5%]). Nine minor postoperative complications occurred (45%), including urinary infection, asymptomatic pleural effusion, wound infection, and superficial phlebitis. The mean hospital stay after the first step was 12 days (range 6 to 20 days). First-step metastasectomies were margin-negative except in one patient who had five left-sided liver metastasectomies of colorectal origin (microscopic margin was positive despite a grossly negative margin).

After a median interval of 6 weeks (range 4 to 8 weeks), the mean volume of the left liver (S2 + S3 + S4) increased from 478 ± 132 mL pre-RPVL (range 276 to 625 mL) to 632 ± 184 mL post-RPVL (range 253 to 924 mL). The percent hypertrophy of the left liver (see Technique section) was 32% ± 9%. The mean volume of left lateral segments (S2 + S3) increased from 273 ± 85 mL (range 162 to 475 mL) preoperatively to 390 ± 114 mL (215 to 634 mL) post-RPVL, an increase of 43% ± 13%. There were no tumor recurrences on the left liver after RPVL and before the second step.

Fifteen patients (75%) underwent the second-step operation. One patient died 1 month after the first step after acute myocardial infarction and one refused the second operation for personal reasons. Three patients with colorectal primaries did not undergo the second-step operation because restaging CT scan showed subcentimeter pulmonary metastases; one of these patients had concomitant progression in size and number of his multiple right-sided liver metastases. At the second-step laparotomy, one patient was found to have diffuse peritoneal carcinomatosis that was not visible on restaging CT scan before surgery. Finally, at the second step, 14 of 15 patients operated on (70% of the total population) underwent the planned right liver resection, including right hepatectomy (n = 8), and right extended hepatectomy to part or all of segment 4 (n = 6). An elective J-shaped incision was used in 10 patients (71%) and bisubcostal incision in 4 patients (29%). There were no major complications after the second-step operations including no liver failure. The kinetics of liver function changes after the first and the second steps did not deviate from the normal changes expected after hepatectomy, and returned to baseline in the expected period postresection.44,45 The rate of minor complications was 36% (asymptomatic pleural effusion detected by chest radiography or CT, urinary infection, and minor wound infection). The median duration of in-hospital stay after the second step was 13 days (range 9 to 20 days). Among patients who underwent the second-stage procedure, no patient was left with gross residual disease and a complete (R0) resection was accomplished in all except one (R1).

**DISCUSSION**

Planned two-step surgery, including RPVL, is safe, effective, and enables complete removal of gross primary GI tumors and synchronous diffuse liver metastases in about 70% of patients with diffuse bilateral liver metastases. Patients with colorectal cancer with synchronous liver metastasis, particularly when liver metastases are unresectable, have a poor prognosis with a 5-year survival from 0% to 8% and a median survival of just less than a year.46,47 When primary tumor-related complications such as intestinal obstruction or bleeding are not present, patients with primary GI tumors and apparently unresectable liver metastases are often treated with palliative intent without referral for specialized surgical opinion. Indeed, in the setting of widely metastatic disease, resection of the primary tumor may be unnecessary. Resection of an asymptomatic primary tumor when hepatic metastatic disease is unresectable is generally not recommended except for intestinal endocrine tumors, which are at higher risk for local complications.48 Even when resection of all of liver metastases is technically possible, the patient’s overall performance status, complexity of the surgical procedures, and the volume of the planned future liver remnant size may impact surgical decision making, especially when major hepatic resection is considered simultaneously with extrahepatic surgery.1,36-49,50

To overcome these problems, many multistep treatments have been proposed including preoperative chemotherapy.22-24,33,34,51-53 For example, after primary tumor resection, systemic or hepatic-directed chemotherapy may be instituted for a period of time, followed by reevaluation for potential second-stage resection of down-staged liver disease.23 A more aggressive approach includes resection of the primary tumor followed by percutaneous ablative treatment or resection of unilateral liver disease. Next, when indicated, intercurrent portal vein embolization is performed in preparation for
major resection of remaining disease a few weeks after embolization.33,36,39 On the other end of the spectrum, some patients will undergo no surgical treatment, with chemotherapy only.

The concept of the reported technique was to maximize the proportion of patients who can safely undergo potentially curative therapy of GI primary tumors with diffuse, bilobar liver metastases. This new alternative was developed to accomplish the following principal goals: 1) to achieve complete (R0) resection of all tumors with acceptable morbidity, 2) to resolve the problems and potential problems related to the primary GI tumor (primarily obstruction, bleeding, and perforation), and 3) to prepare patients for safe resection of their diffuse liver metastatic disease (surgical cure) by initiating hypertrophy of the disease-free left liver. Secondary goals are important as well: 1) the primary procedure should not interfere with standard intercurrent treatments, including preoperative systemic chemotherapy or even segmental PVE when indicated, and 2) the primary procedure should not create extensive adhesions (peritoneal or hepatic hilar) that would greatly increase the difficulty or complexity of the major hepatic resection planned for the second step.

All these stated goals were accomplished using the described technique. The potential additive morbidity of major abdominal surgery and simultaneous major liver surgery was avoided because primary tumor resection was combined with straightforward liver resection, and the major hepatic resection was performed as a separate procedure. The liver hypertrophy induced by RPVL was effective, indeed similar to that seen after PVE despite the theoretic risk for recanalization.54 RPVL was not associated with morbidity, and the risk for disease progression in the left liver was avoided. Because there is no contraindication to systemic chemotherapy after the first step, even those who were found to have progressive disease before or at the time of the second laparotomy remained candidates for traditional adjuvant therapy. Those with progression were likely spared the risk of major hepatic resection as a result of the discovery of previously unidentifiable disease found during the window of observation between steps.

Importantly, because major hepatic resection is not combined with primary tumor resection, the attendant risks of combined major resection with extrahepatic abdominal surgery are avoided and the goal of minimum morbidity is better achieved. Indeed, an essential part of the first-stage procedure is to prepare for the second step. At each part of the procedure, attention is directed toward safe, complete resection of the primary or left liver disease without unnecessary dissection or mobilization that could impact the difficulty of the second step. In a majority of the cases, different incisions are possible to further minimize adhesion-related difficulties at the second step. Excessive dissection of the porta hepatis is always avoided to facilitate redissemination at the second procedure. We believe that the avoidance of cholecystectomy when possible could facilitate dissection at the second procedure. But in patients with neuroendocrine diffuse liver metastases, if the planned second step is considered unachievable, we suggest performing a cholecystectomy without RPVL because further intraarterial chemoembolization might be indicated.55,56 Uniform form of intraoperative ultrasonography ensures accurate staging and complete resection of the left-sided metastases during the period of hypertrophy of the left liver.57 Finally, although the dissociation of primary GI tumor and major liver resection may by itself reduce the postoperative morbidity, we believe that apart from volumetric considerations, a large proportion of patients with liver metastases may have injured liver parenchyma as a result of a long period of systemic or intraarterial chemotherapy, so are likely to benefit from hypertrophy induced by portal vein ligation before major liver resection.56

In conclusion, an oncologic, all-surgical approach to patients with gastrointestinal primary tumors and bilobar liver metastases is feasible. Resection of the primary GI tumor and all left-sided liver metastases with RPVL at the first step provides left liver hypertrophy without the risk for progression of disease in the FLR in preparation for the second, curative major liver resection to remove the remaining right-sided liver disease. In distinction to other techniques, liver hypertrophy induced after portal vein ligation is initiated in a liver cleared of metastatic disease, which limits the risk of tumor progression during the observation period. Other therapies, including portal vein embolization and systemic chemotherapy, could be administered if desired in selected cases after the first step. An observation period is necessary for recovery from the first-stage procedure, which enables better selection of patients for major hepatic resection at the second step. This planned, two-step surgical approach using portal vein ligation may be considered in patients who might previously have been consid-
ered only for palliative or supportive treatment because of the presence of primary GI tumors with apparently "unresectable" diffuse, bilobar liver metastases. Further study is necessary to assess the potential impact of this strategy on longterm survival in patients with intact primary GI tumors and synchronous diffuse bilobar liver metastases.

Author Contributions
Study conception and design: Belghiti
Acquisition of data: All authors
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REFERENCES


