

# Actual incidence and long-term consequences of posthepatectomy liver failure after hepatectomy for colorectal liver metastases

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**Introduction.** Posthepatectomy liver failure (PHLF) is a severe complication after hepatectomy for colorectal liver metastases. This study evaluated its actual incidence and its effects on short- and long-term overall survival (OS) in a specialized center.

**Materials and methods.** Between 2006 and 2008, 193 patients who underwent 232 hepatectomies (147 minor and 85 major) for colorectal liver metastasis were studied prospectively. Hepatectomy was performed if the remnant liver volume was >0.5% of body weight. Uni- and multivariate analyses on OS after all hepatectomies (n = 232) or major resection only (n = 85) were then performed on pre-, intra-, and postoperative (including pathological) data to determine the consequences of PHLF by comparison with those of other intra- and postoperative events.

**Results.** The 3-month postoperative mortality rate was 0.8%. PHLF was observed in six patients (7%) after major hepatectomy and in one (0.6%) after minor hepatectomy. With a 25-month follow-up, the 2-year OS rate was 84%. Preoperatively, pulmonary metastasis was the only determinant of OS. Intra- and postoperatively, four factors were determinant of OS: PHLF (risk ratio [RR] = 3.84, P = .04), mental confusion (RR = 3.11, P = .006), fluid collection (RR = 2.9, P = .01) and transfusion (RR = 2.27, P = .009). After major hepatectomy, only PHLF (RR = 4.14, P = .01) and confusion (RR = 3.6, P = .02) were identified.

**Conclusion.** With improvements in postoperative management, PHLF was found to be less responsible for 3-month mortality but remains an event that exerts a major impact on 2-year survival. (Surgery 2014;155:94-105.)

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LIVER RESECTION is the only treatment that offers a chance of long-term survival in patients with colorectal liver metastasis (CRLM) whose 5-year survival is greater than 50% and 10-year survival is between 17% and 25%.<sup>1</sup> A consequence of this has been the development of “onco-surgical strategies,”<sup>2</sup> which include portal vein embolization,<sup>3</sup> two-stage hepatectomy,<sup>4</sup> and measures to protect the liver parenchyma, in combination with chemotherapy, to extend the limits of the resectability of

CRLM.<sup>5</sup> These limits are defined by the minimal amount of functional remnant liver that is theoretically necessary to prevent posthepatectomy liver failure (PHLF). To date, these limits have been defined empirically as a remnant liver inferior to 0.5%<sup>6</sup> and/or inferior to 20% of the standardized total liver volume.<sup>7</sup> During the present study, we assessed (1) the actual incidence of PHLF in a tertiary department that strictly complies with these rules, and (2) the short and long-term effects of PHLF on overall survival by comparison with other intra- and postoperative events and pathological status after hepatectomy for CLRM. To achieve this, we evaluated retrospectively the course of 232 hepatectomies for CRLM operated on within a 2-year period in 193 patients who were prospectively evaluated and followed for at least 3 years if they survived.

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## MATERIAL AND METHODS

We retrospectively analyzed 193 patients who underwent 232 liver resections for CRLM between January 2006 and December 2008 in our department (Centre Hepato-Biliaire, Paul Brousse Hospital, AP-HP, Villejuif, France).

**Therapeutic strategies.** Our therapeutic policy for CRLM has been widely reported elsewhere.<sup>2</sup> In brief, all the patients covered by this study initially were evaluated by a computed tomography (CT) scan with intravenous contrast and/or magnetic resonance imaging and colonoscopy. More recently, selected patients were also staged using positron emission tomography-CT. Preoperative chemotherapy was administered in a neoadjuvant setting to patients with synchronous metastases (diagnosed before, during, or within 6 months of colorectal resection) or patients with multiple metachronous resectable CRLM and/or larger than 5 cm.<sup>8</sup> The response to chemotherapy was determined on a CT scan after every four cycles of treatment according to the RECIST (ie, Response Evaluation Criteria In Solid Tumors) criteria.<sup>9</sup> If the estimated future remnant liver volume was judged to be too small (<0.5% of body weight ratio), portal vein embolization was performed to induce compensatory hypertrophy of the remaining liver.<sup>10</sup> In patients with an estimated future small remnant and multiple bilateral CRLM, a two-stage hepatectomy was planned if the remnant liver contained more than three CRLM.

At the first operation, several limited hepatectomies were performed in the future remnant liver followed by portal ligation of the future resected liver. In the case of synchronous CRLM with colonic cancer in situ, a simultaneous colonic resection was performed during this step. The second step was usually performed 3–6 months after the initial hepatectomy (in the absence of tumor progression under chemotherapy) if the remnant liver had increased in volume.<sup>11</sup> After hepatectomy, adjuvant chemotherapy was systematically administered to patients under appropriate conditions. All treatment decisions were taken during multidisciplinary meetings which included surgeons, medical oncologists, and radiologists.

During an open operative procedure, an intraoperative ultrasound of the liver (Aloka, Japan) was performed in all patients to confirm the number and size of metastases and to define their relationships with intrahepatic vascular structures. Liver sections were performed with CUSA (Compact Ultrasonic Surgical Aspirator) EXcel+ (Integra, New Jersey) and bipolar devices under intermittent

pedicle clamping if necessary. This pedicle clamping was not systematic, but the rule of “clamping rather than bleeding” was always followed. When tumor-free margins could not be obtained because of vascular proximity or the presence of multiple metastases, resection was still performed provided that it was macroscopically complete. Radiofrequency ablation was only used in combination with resection for three or fewer otherwise-unresectable metastases up to 3 cm in diameter in the future remnant liver. Vascular reconstruction was considered in cases with tumor encasement of the major vascular structures. For these resections, total vascular exclusion of the liver was generally applied. A veno-venous bypass with cooling of the liver was performed if it was expected that total vascular exclusion would last for longer than 60 minutes.<sup>5</sup> A silicon 30-F abdominal drainage system was positioned systematically behind the residual liver at the end of the procedure.

After table extubation, the patients were admitted to the intensive care unit for at least one night. They were then transferred on postoperative day (POD) 1 to the hospitalization unit if there was no hemodynamic instability requiring vasopressor support or a need for postoperative mechanical ventilation. Biological data were collected routinely on at least POD 1, POD 2, POD 3, POD 5, and POD 7. Abdominal drainage was removed before POD 5 if the output of ascitic fluid was less than 200 mL/day. An early Doppler ultrasound examination was performed if necessary, and a systematic echography to detect any perihepatic collection and/or asymptomatic vascular or biliary abnormalities was performed between POD 5 and POD 7. A perihepatic collection of more than 5 cm was systematically evaluated by a puncture and drained percutaneously if necessary (presence of bile and/or infection).

**Study methods.** The objective of this study was to describe postoperative mortality and morbidity in a recent series of hepatectomies for CRLM in a tertiary center to evaluate the actual incidence and consequences of PHLF. To achieve this, all pre-, intra-, and postoperative data were collected by our department. Intraoperative data, collected at the end of each procedure, included the type of hepatic resection, minor (or limited;  $\leq 2$  segments) or major ( $\geq 3$  segments), the type, and duration of vascular clamping and the type of hepatectomy-associated procedures performed. Postoperative morbidity and mortality were determined at 90 days after surgery or during the same period of hospitalization, whenever it

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