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ORIGINAL ARTICLE

# Measuring future liver remnant function prior to hepatectomy may guide the indication for portal vein occlusion and avoid posthepatectomy liver failure: a prospective interventional study

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## Abstract

**Background:** Estimation of the future liver remnant function (eFLRF) can avoid post-hepatectomy liver failure (PHLF). In a previous study, a cutoff value of 2.3%/min/m$^2$ for eFLRF was a better predictor of PHLF than future liver remnant volume (FLRV%). In this prospective interventional study, investigating a management strategy aimed at avoiding PHLF, this cutoff value was the sole criterion assessing eligibility for hepatectomy, with or without portal vein occlusion (PVO).

**Methods:** In 100 consecutive patients, eFLRF was determined using the formula: eFLRF = FLRV % × total liver function (TLF). Group 1 (eFLRF >2.3%/min/m$^2$) underwent hepatectomy without preoperative intervention. Group 2 (eFLRF <2.3%/min/m$^2$) underwent PVO and re-evaluation of eFLRF at 4–6 weeks. Hepatectomy was performed if eFLRF had increased to >2.3%/min/m$^2$, but was considered contraindicated if the value remained lower.

**Results:** In group 1 (n = 93), 1 patient developed grade B PHLF. In group 2 (n = 7) no PHLF was recorded. Postoperative recovery of TLF in patients with preoperative eFLRF <2.3%/min/m$^2$ occurred more rapidly when PVO had been performed.

**Conclusion:** A predefined cutoff for preoperatively calculated eFLRF can be used as a tool for selecting patients prior to hepatectomy, with or without PVO, thus avoiding PHLF and PHLF-related mortality.

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## Introduction

Post-hepatectomy liver failure (PHLF) is a major and potentially life-threatening complication following major hepatectomy in normal livers. It more readily occurs after minor resections in livers compromised by steatosis, steatohepatitis, chemotherapy associated liver injury (CALI)[1] or cirrhosis. Although liver function correlates well with liver volume in uncompromised livers, this relationship is less clear in patients with coexisting parenchymal liver disease.[2,3] Estimation of remnant liver function instead of remnant liver volume is a better predictor of clinical outcome after liver resection in patients with decreased liver function.[4] In planning a liver resection, not only should the future liver remnant volume ratio (FLRV%) and total liver function (TLF) be measured, the estimated future liver remnant function (eFLRF) should be calculated. This is particularly important for compromised livers. In a previous pilot study,[5] a tool for assessing eFLRF was developed by combining FLRV% (measured by Magnetic Resonance Imaging – MRI) with TLF (measured using $^{99m}$Tc-mebrofenin hepatobiliary scintigraphy – HBS). A cut-off value for eFLRF at 2.3%/min/m$^2$ was defined by receiver-operating-characteristic (ROC) analysis. This cut-off for eFLRF seemed to be a better predictor for PHLF than FLRV%. In

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this pilot study, mortality related to PHLF may have been avoided if the eFLRF criterion had been used instead of FLRV%.

### Objective of this study

The objectives of this study were to validate the eFLRF cutoff value of 2.3%/min/$m^2$ as (i) a criterion of eligibility for hepatic resection and (ii) as an indication for portal vein occlusion (PVO), as part of a predefined, stepwise hepatic resection strategy, aiming to avoid PHLF and PHLF-related mortality.

## Methods

### Inclusion criteria

The study was approved by the Medical Ethics Committee of the Antwerp University Hospital. Written informed consent was obtained from each participating patient. Consecutive patients undergoing hepatectomy between April 2012 and January 2014 were included. Indications for liver resection were: benign liver tumor, colorectal and non-colorectal liver metastasis, intrahepatic/perihilar cholangiocarcinoma and hepatocellular carcinoma, all diagnoses being confirmed *post hoc* by pathological examination of the resection specimen. The outlying liver parenchyma was reported as follows: normal, cirrhotic (diagnosed on clinical/biochemical evaluation and/or imaging and/or liver biopsy, if available) and at-risk for chemotherapy-associated liver injury (CALI), based on preoperative administration of chemotherapeutic agents. Cirrhosis Child-Pugh A and suspected CALI were never considered as a contraindication for resection. Exclusion criteria were: cirrhosis Child-Pugh B/C, age under 18 years and pregnancy.

### Preoperative evaluation

Age and Body Mass Index (BMI, kg/$m^2$) were recorded for all patients. The physical status was estimated using the American Society of Anaesthesiologists (ASA) score. MRI of the liver, a few weeks prior to surgery, is the standard diagnostic tool in our department. Consecutive slices of this diagnostic MRI examination were used by an expert radiologist to perform liver volumetry. The volume to be resected was delimited in close collaboration with the surgeon.

$^{99m}$Tc-mebrofenin HBS was performed to measure global liver function and expressed in %/min, regardless of the tumor volume. To compensate for variations in individual metabolic needs, the clearance was normalized by dividing the obtained value by the Body Surface Area (BSA), calculated by the Mosteller formula ($BSA^2$ = body weight (kg) × body length (cm)/3600). The liver function measured by HBS, was divided by the body surface area (BSA) and expressed as total liver function (TLF).[5] In this article, TLF refers to this BSA-normalized value.

FLRV% was calculated by dividing the future liver remnant volume (in mL) by the total functional liver volume (in mL). It was expressed as % (FLRV% = FLRV × 100/TLV). Potential effects of large tumor volume were anticipated by subtracting the tumor volume from TLV.

eFLRF was calculated by multiplying the future liver remnant volume ratio by the total liver function (eFLRF = FLRV % × TLF/100).

Methodology of MRI volumetry, $^{99m}$Tc-mebrofenin HBS, FLRV% and eFLRF calculations were performed as previously described.[5]

### Portal vein occlusion

When eFLRF was >2.3%/min/$m^2$, hepatectomy was performed without further preoperative intervention (Group 1). When eFLRF was <2.3%/min/$m^2$, PVO was performed (Group 2). PVO could consist of a portal vein embolization (PVE) or a portal vein ligation (PVL). PVE was the treatment of first choice, except when a two-stage hepatectomy was planned: here, PVL was performed during the first procedure.

PVE was performed under general anesthesia by the interventional radiologist. The portal vein was punctured percutaneously with an 18 gauge trocar/needle under ultrasound guidance. The punctured portal vein branch was normally one of the branches intended to be embolized. A short 4 French introducer sheath (Terumo®) was introduced into the punctured portal vein to secure the access. A 0.035 inch guidewire was then used to advance a 4 French Simmons/Sidewinder 1 Glidecath Terumo® catheter through the sheath into the common portal vein, and a diagnostic venogram performed to illustrate the portal vein anatomy. A Prograt 2.7 Terumo® microcatheter was subsequently positioned in the selected branches of the portal vein. Embolization in these selected portal branches was carried out by careful injection of diluted glue, consisting of 1 part Glubran 2 (Gem Italy®) and 5 parts Lipiodol (480 mg/L iodide, Guerbet®). The microcatheter was meticulously flushed with a glucose solution in order to prevent occlusion of the microcatheter lumen by the glue. After successful embolization, the catheters and sheath were carefully removed, simultaneously gluing or gelfoaming the intrahepatic puncture track.

PVL was performed at laparotomy as part of the first step of a two-stage hepatectomy. For example, after resection of tumors in the left liver, the right portal vein was dissected and isolated. Interruption of the portal flow in all right hepatic segments was verified using intraoperative Doppler-ultrasonography by selectively clamping the right portal vein. When portal flow occlusion was confirmed, the right portal vein was sutured and transected. Sclerosis of the right portal vein system was subsequently achieved by injecting 10 mL of ethanol 96% into the right portal vein stump.

Complications related to PVE or PVL were registered according to the Dindo–Clavien classification.[6]

Four to 6 weeks after PVO, MRI and $^{99m}$Tc-mebrofenin HBS were repeated. FLRV% and TLF were measured and eFLRF was re-calculated. If eFLRF after PVO was >2.3%/min/$m^2$, hepatectomy was performed. If post-PVO eFLRF remained <2.3%/min/$m^2$, hepatectomy was considered to be contraindicated and alternative treatments were proposed.

 

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