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ORIGINAL ARTICLE

Measurement of liver function using hepatobiliary scintigraphy improves risk assessment in patients undergoing major liver resection

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Abstract

Background: ^{99m}Tc-mebrofenin-hepatobiliary-scintigraphy (HBS) enables measurement of future remnant liver (FRL)-function and was implemented in our preoperative routine after calculation of the cut-off value for prediction of postoperative liver failure (LF). This study evaluates our results since the implementation of HBS. Additionally, CT-volumetric methods of FRL-assessment, standardized liver volumetry and FRL/body-weight ratio (FRL-BWR), were evaluated.

Methods: 163 patients who underwent major liver resection were included. Insufficient FRL-volume and/or FRL-function <2.7%/min/m^2 were indications for portal vein embolization (PVE). Non-PVE patients were compared with a historical cohort (n = 55). Primary endpoints were postoperative LF and LF related mortality. Secondary endpoint was preoperative identification of patients at risk for LF using the CT-volumetric methods.

Results: 29/163 patients underwent PVE; 8/29 patients because of insufficient FRL-function despite sufficient FRL-volume. According to FRL-BWR and standardized liver volumetry, 16/29 and 11/29 patients, respectively, would not have undergone PVE. LF and LF related mortality were significantly reduced compared to the historical cohort. HBS appeared superior in the identification of patients with increased surgical risk compared to the CT-volumetric methods.

Discussion: Implementation of HBS in the preoperative work-up led to a function oriented use of PVE and was associated with a significant decrease in postoperative LF and LF related mortality.

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Introduction

As the management of postoperative liver failure after major liver resection is difficult and remains mainly supportive,[1] more emphasis should be placed on the preoperative assessment of the future remnant liver (FRL) in order to prevent this potentially lethal complication. Traditionally, FRL assessment is performed using Computed Tomography (CT) volumetry. However, volumetric measurement of the FRL does not provide any information on the FRL-function. This may lead to an under-detection of patients at risk for postoperative liver failure, especially patients with compromised liver parenchyma as the quality of the parenchyma is usually unknown pre-operatively.[2] Other mathematical methods of preoperative FRL assessment such as FRL/body-weight ratio

(FRL-BWR) and standardized liver volumetry, claim to overcome this limitation through individualizing CT volumetry of FRL by calculating the minimally required FRL-volume relative to patients' weight and body surface area (BSA), respectively.[3,4]

^{99m}Tc-mebrofenin hepatobiliary scintigraphy (HBS) with SPECT-CT is a quantitative method of liver functional assessment,[5] which allows measurement of the FRL-function depending on quality of the liver parenchyma rather than volume alone.[6] HBS can therefore be applied in both patients with compromised and non-compromised liver, using the previously calculated cut-off value of 2.7%/min/m^2.[7] Patients with FRL uptake function below the cut-off value have a risk of postoperative liver failure of 2.4% with negative predictive value of 97.6% and a likelihood ratio for negative test result of 0.12. The positive predictive value of HBS is 57.1% with a likelihood ratio for positive test result of 6.8. Since the identification of the cut-off value, HBS is being used at our center as standard preoperative assessment of FRL together with CT volumetry, in patients scheduled for major liver resection.

The impact of HBS on preoperative management and the postoperative outcomes has not been assessed since its implementation. The aim of this study was to evaluate the value of preoperative HBS in a subsequent series of patients eligible for major liver resection. Data were compared with FRL-BWR and standardized liver volumetry as alternative, mathematical methods of FRL assessment for identification of patients at risk for developing postoperative liver failure.

Methods

Patients

All patients who had undergone preoperative HBS and CT-volumetry followed by major liver resection (≥3 Couinaud liver segments) at the Academic Medical Center in Amsterdam, The Netherlands, from November 2006 to June 2014, were included. HBS was performed in patients with increased surgical risk, i.e. patients suspected of perihilar cholangiocarcinoma (PHC) and patients scheduled for extended hemihepatectomy or right hemihepatectomy, except when an evident surplus of FRL-volume was determined on CT imaging. A historical cohort (May 2000–November 2006) was used for the comparison of the postoperative outcomes before and after the implementation of HBS in our preoperative routine. This historical cohort consisted of 55 patients from a previous series in whom HBS wasn't part of the standard preoperative work-up but was performed for the calculation of the HBS cut-off value only.[7] The study has been approved by the institutional review board, and the need for written informed consent was waived.

Volumetric measurements

Volumetric measurements were performed using CT images in portal-venous phase. Three-dimensional reconstructions of the liver were made using 5 mm thick axial slices. Portal and hepatic veins were used as landmarks for segmental division. The total liver, tumor and FRL were outlined manually. Integrated software (Mx-View 3.52, Philips Medical Systems) was used to calculate total liver volume, tumor volume and FRL volume. FRL volume is expressed as a percentage of total liver volume. The volumetric cut-off value for safe resection was set at FRL-volume of at least 25% for patients in whom healthy liver parenchyma was expected. In patients diagnosed with PHC typically associated with (post)cholestatic livers, 35% of the total liver volume was considered as minimum for resection.

For the purpose of this study, the required FRL was additionally calculated using the FRL-BWR method[3] and standardized liver volumetry as proposed by Vauthey.[4] According to the FRL-BWR, the minimal FRL-volume should be at least 0.5% of patient's weight.[3] The standardized liver volumetry uses a validated mathematical formula in order to estimate the total liver volume (estimated total liver volume). The ratio of the FRL-volume, measured with CT-volumetry, and the estimated total liver volume represents the percentage of liver tissue that will remain after the resection and is called standardized FRL-volume.[4]

Liver function assessment

HBS was performed after a 4 h fast, as food consumption stimulates hepatic function and bile flow, which might influence test results. When patients presented with jaundice, HBS was performed after biliary drainage. Patients were positioned supine on the imaging table of a large-field-of-view (FOV) SPECT/CT camera (Symbia T16; Siemens) positioned over the liver and heart region. The SPECT/CT camera was equipped with low-energy high-resolution collimators. After intravenous administration of 200 MBq freshly prepared ^{99m}Tc-mebrofenin (Bridatec; GE-Amersham Health), dynamic acquisition was obtained (36 frames of 10 s/frame, 128 matrix), which was used for calculation of the hepatic mebrofenin uptake rate (MUR). Subsequently, a fast SPECT acquisition was performed (60 projections of 8 s/projection, 128 matrix), centered on the peak of the hepatic time–activity curve, which was used for the 3-dimensional assessment of liver function and calculation of functional liver volume. Immediately after SPECT, a low-dose, non-contrast-enhanced CT scan was obtained for attenuation correction and anatomical mapping. In order to evaluate biliary excretion a second dynamic acquisition (15 frames of 60 s/frame, 128 matrix) was obtained. Data were processed on a Hermes workstation (Hermes Medical Solutions, Sweden).

The HBS parameters related to MUR in the total liver and FRL were calculated as described before.[5,8,9] A cut-off value of 2.7%/min/m^2 was used to discriminate normal from decreased FRL uptake rate as was described in a previous study.[7]

Preoperative portal vein embolization

Patients with insufficient FRL-volume, i.e. <25% in patients with presumed healthy liver parenchyma and <35% in patients