Clinical Radiology 68 (2013) 1121–1127

Contents lists available at SciVerse ScienceDirect

Clinical Radiology

journal homepage: www.clinicalradiologyonline.net

Gadoxetate uptake as a possible marker of hepatocyte damage after liver resection-preliminary data

S. Bickelhaupt [a], P. Studer [b], C. Kim-Fuchs [b], D. Candinas [b], J.M. Froehlich [a], M.A. Patak [a,c,*]

[a] Department of Radiology, University Hospital Zürich, Zürich, Switzerland
[b] Department of Visceral Surgery, Bern University Hospital, 3010 Bern, Switzerland
[c] Institute of Radiology, Bern University Hospital, 3010 Bern, Switzerland

ARTICLE INFORMATION

Article history:
Received 7 April 2013
Received in revised form
27 May 2013
Accepted 4 June 2013

AIM: To determine the feasibility of evaluating surgically induced hepatocyte damage using gadoxetate disodium (Gd-EOB-DTPA) as a marker for viable hepatocytes at magnetic resonance imaging (MRI) after liver resection.

MATERIAL AND METHODS: Fifteen patients were prospectively enrolled in this institutional review board-approved study prior to elective liver resection after informed consent. Three Tesla MRI was performed 3–7 days after surgery. Three-dimensional (3D) T1-weighted (W) volumetric interpolated breath-hold gradient echo (VIBE) sequences covering the liver were acquired before and 20 min after Gd-EOB-DTPA administration. The signal-to-noise ratio (SNR) was used to compare the uptake of Gd-EOB-DTPA in healthy liver tissue and in liver tissue adjacent to the resection border applying paired Student's *t*-test. Correlations with potential influencing factors (blood loss, duration of intervention, age, pre-existing liver diseases, postoperative change of resection surface) were calculated using Pearson's correlation coefficient.

RESULTS: Before Gd-EOB-DTPA administration the SNR did not differ significantly ($p = 0.052$) between healthy liver tissue adjacent to untouched liver borders [59.55 ± 25.46 (SD)] and the liver tissue compartment close to the resection surface (63.31 ± 27.24). During the hepatocyte-specific phase, the surgical site showed a significantly ($p = 0.04$) lower SNR (69.44 ± 24.23) compared to the healthy site (78.45 ± 27.71). Dynamic analyses revealed a significantly lower increase ($p = 0.008$) in signal intensity in the healthy tissue compared to the resection border compartment.

CONCLUSION: EOB-DTPA-enhanced MRI may have the potential to be an effective non-invasive tool for detecting hepatocyte damage after liver resection.

Introduction

Recent advances in preoperative liver imaging have improved planning for liver resection and estimation of its perioperative risks, while improvements in the relevant surgical techniques have lowered the incidence of intra- and postoperative complications. Despite these advances, this complex surgical procedure is still associated with some risk of intra- and postoperative complications.[1,2] The major complications are haemorrhage of the resection surface, biliary leakage, and post-hepatectomy liver failure (pHLF).[3–5] Intraoperative handling techniques during liver resection aim to reduce blood loss from the highly perfused

* Guarantor and correspondent: M.A Patak, University Hospital Zürich, Department of Radiology, Rämistrasse 100, 8091 Zürich, Switzerland. Tel.: +41 44 255 30 50; fax: +41 44 255 44 43.
E-mail address: Michael.Patak@hirslanden.ch (M.A. Patak).

0009-9260/$ – see front matter © 2013 The Royal College of Radiologists. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.crad.2013.06.007

liver, while at the same time minimizing tissue damage in the remaining part of the liver. Despite these measures, intraoperative procedures may still damage liver tissue adjacent to the resection surface. This might adversely affect patients with borderline liver volumes, as this secondarily induced tissue damage could further reduce the volume of postoperative functional liver tissue. MRI in combination with liver-specific contrast agents, one of the standard imaging methods for detection and characterization of focal liver disease, has been shown to be superior to computed tomography (CT).[6,7] Gadoxetate disodium (Gd-EOB-DTPA; Primovist, Gd-EOB, Bayer-Schering Pharma, Berlin, Germany) is a hepatocyte-specific paramagnetic contrast agent that is selectively taken up by an active transporter present in hepatocyte cell membranes, organic anion transport protein (OATP 1B1/3), due to its ethoxybenzene side-chain (EOB) and partially excreted into the bile (MRP2 secretion) without biotransformation.[8] Although still limited in number, the first studies in humans indicate that Gd-EOB-DTPA-enhanced MRI might serve as a reliable, non-invasive tool for estimating overall and regional liver function and viability.[9–12] The present prospective feasibility study investigates the potential of Gd-EOB-DTPA-enhanced MRI for evaluation of liver tissue viability after liver resection in the compartments adjacent to the resection border.

Material and methods

Patients

From May 2010 to September 2011, 15 consecutive patients [six male, nine female, mean age 61.4 ± 9.56 (SD) years, range 44–77 years] scheduled for clinically indicated elective liver resection were prospectively enrolled in this pilot clinical study. Each of the 15 patients gave written informed consent prior to enrolment. The study protocol was approved by the institutional and governmental ethics committees.

Inclusion criteria were elective hemihepatectomy. General exclusion criteria were patient unable to speak the local language and, thus, unable to understand study documents; age less than 18 years; atypical liver resection; profound liver cirrhosis; or kidney insufficiency (creatinine clearance <60 ml/min/1.73 m^2).

Patient exclusion criteria related to MRI were pacemaker; implanted cardioverter defibrillator, or other electronic implant or device; vascular clips in place for less than 2 weeks; metallic prosthesis not compatible with MRI; severe claustrophobia; pregnant or breastfeeding; auricular fibrillation.

Exclusion criteria related to Gd-EOB-DTPA were hypersensitivity to Primovist: severe cardiovascular disease; moderate or severe renal impairment [glomerular filtration rate (GFR) <60 ml/min/1.73 m^2]; concomitant treatment with rifampicin. Three of the 15 patients were excluded from the study after giving their approval because MRI could not be performed due to their poor postoperative clinical status. The remaining cohort consisted of six males (mean age 62.16 ± 11.53 years, range 38–77 years) and six females (mean age 61.8 ± 10.34 years, range 44–72 years) with an overall mean age of 62 years (±10.43 years, range 44–77 years). The causes for the elective liver resection in the study population were equally distributed between cholangiocarcinoma in 3/12 patients (25%), hepatocellular carcinoma (HCC) in 3/12 patients (25%), alveolar echinococcosis in 3/12 patients (25%), and metastatic surgery [gastrointestinal stromal tumour,[1] colorectal cancer[2]] in 3/12 patients (25%).

Surgical/clinical methods

Intraoperative manual measurement of the resection surface area was performed using the surface of the resected liver as a surrogate marker of the resection surface area of the remaining liver. The resected liver was placed on a transparent foil with the resection surface facing the table surface. Carbon paper was placed underneath the foil and a pen was used to trace the resection borders through the carbon paper onto white bond paper. The borders marking the resection surface area were digitalized and the surface area in square centimetres (cm^2) was calculated using ImageJ software (version 4.2, National Institutes of Health, Bethesda, MD, USA).

Surgical protocols were analysed with regard to the following parameters: intraoperative blood loss, pre-existing chronic liver diseases, and duration of liver resection.

Imaging protocol

MRI was performed 3–7 days after liver resection using a 3 T MRI system (Verio, Siemens, Siemens Medical Solution, Erlangen Germany) using body-array surface coils (Siemens Medical Solutions, Erlangen, Germany) covering the upper abdomen with the patient lying in supine position. After acquisition of a standard localizer, the following sequences were measured: T1-weighted (W) FLASH sequence [fast low-angle shot two-dimensional sequence with fat saturation, 74 ms repetition time (TR), 6.15 ms echo time (TE), 6 mm section thickness, 7.2 mm intersection gap, 178 mm × 320 mm field of view, 240 × 320 matrix] without and 10 min after intravenous administration of Gd-EOB-DTPA (0.025 mmol/kg of body weight, flow rate 2 ml/s followed by 20 ml saline flush using a cubital intravenous line); T1W VIBE (3D volumetric interpolated breath-hold gradient echo) sequence with fat selective prepulse (4.27 ms TR, 1.51 ms TE, 2.5 mm section thickness, 240 mm × 350 mm field of view, 220 × 320 matrix, 9° flip angle) were acquired before and 30 s, 90 s, 3 min, 10 min, and 20 min after Gd-EOB-DTPA administration; T2W HASTE (half-Fourier axial single-shot fast spin-echo) sequences (93 ms TE, 1800 ms TR, 6 mm section thickness, 190° flip angle, 337 × 399 mm field of view) were acquired 15 min after administration of the contrast agent.