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Early phase detection of bile leak after hepatobiliary surgery: value of Gd-EOB-DTPA-enhanced MR cholangiography

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Abstract

Objectives: To assess the value of gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)-enhanced MR cholangiography for early phase detection of bile leaks after hepatobiliary surgery.
Methods: Twenty-three patients with symptoms suggestive of bile leak underwent conventional fat-suppressed T1- and T2-weighted MR cholangiography followed by Gd-EOB-DTPA-enhanced MR cholangiography using gradient-echo (GRE) T2-weighted sequences and fat-suppressed T1-weighted 3D gradient-echo sequences 20 min after an intravenous bolus of Gd-EOB-DTPA. The results of Gd-EOB-DTPA-enhanced MR cholangiography correlated with clinical findings, surgical repair, and the results of endoscopic retrograde cholangiopancreatography and percutaneous transhepatic cholangiography.
Results: The results of Gd-EOB-DTPA-enhanced MR cholangiography were negative in 13 patients (cholecystectomy 5, liver transplantation 2, liver resection for focal lesions 2, cholangiocarcinoma 1, and partial hepatectomy after liver injury 1). In 10 patients in whom bile leaks were detected, this complication occurred after liver resection for focal lesions in 3, cholecystectomy in 4, liver transplantation in 2, and liver resection for intrahepatic cholangiocarcinoma in 1. The diagnostic accuracy of Gd-EOB-DTPA-enhanced MR for the detection or exclusion of bile leaks was 100%.
Conclusions: Gd-EOB-DTPA-enhanced MR cholangiography is a highly reliable technique for the detection of bile leaks after hepatobiliary surgery and may avoid the use of other, potentially risky invasive diagnostic techniques.

Key words: Gd-EOB-DTPA—Cholangiography—Bile ducts—Postsurgical complications—Bile leak

The increase in the number of hepatobiliary surgical interventions (e.g., laparoscopic cholecystectomy and adult living donor liver transplantation) during the past decade has been accompanied by an increase in the incidence of postoperative complications such as bile leaks, which must be diagnosed and treated early to limit associated morbidity and mortality [1, 2]. Diagnostic imaging plays a key role in the treatment of patients with suspected postoperative bile leaks. Magnetic resonance (MR) cholangiography with hepatocyte-specific contrast agents that are excreted through the biliary system has recently been introduced in clinical practice. Gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA) is a paramagnetic contrast solution that combines the features of an extracellular contrast agent with those of a hepatocyte-specific agent. Gd-EOB-DTPA makes it possible to assess hepatic parenchymal enhancement on dynamic MR images, to obtain specific images of the cellular uptake of Gd-EOB-DTPA, and to visualize the functioning of the biliary tree. Therefore, Gd-EOB-DTPA may also be suitable for biliary imaging and could reveal postoperative biliary complications. However, only a few isolated case reports have evaluated postoperative biliary leakage using MR cholangiography with Gd-EOB-DTPA [3, 4].

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The purpose of the present study was to assess the value of Gd-EOB-DTPA-enhanced MR cholangiography for early phase detection of bile leaks after hepatobiliary surgery.

Materials and methods

The study population comprised all consecutive patients who had undergone hepatobiliary surgery between March 2009 and April 2010 and presented with clinical symptoms and/or abnormal liver function test results suggestive of bile leak in the immediate postoperative period. Clinical data and diagnostic results were collected retrospectively and analyzed. Clinical symptoms included persistent fever for more than 48 h after surgery, abdominal pain, vomiting and/or paralytic ileus, and bilious or biliopurulent fluid from the surgical drain. A noninvasive radiologic study (abdominal ultrasound and/or computed tomography [CT]) was performed before Gd-EOB-DTPA-enhanced MR cholangiography. All MR-cholangiography results were read and interpreted independently by two abdominal radiologists from our department. The exclusion criteria were as follows: hypersensitivity or intolerance to paramagnetic contrast agents; presence of pacemakers, defibrillators, or neurostimulators; presence of implants or prosthetic devices in the inner ear; presence of ferromagnetic vascular clips incompatible with MR; presence of Starr-Edwards heart valves; and presence of metallic particles in vital areas. Also excluded were patients with poor biliary excretion of contrast 20–30 min after injection, probably due to severe liver dysfunction. Two patients previously diagnosed with severe chronic liver disease (Child-Pugh B/C) were excluded. Patients provided their written informed consent and the Ethics Committee of Reina Sofia University Hospital, Córdoba (Spain) approved the study.

Gd-EOB-DTPA-enhanced MR cholangiography was performed at 1.5 T (Signa LX Release 9.1, General Electric, Milwaukee, USA) using a four-coil phased array, with a section thickness of 4 mm or less and covering only the upper abdomen. The MR protocol was as follows: (a) non-enhanced breath-hold axial image acquisition with fast gradient-echo (GRE) sequences for fat-suppressed T1- and T2-weighted images; (b) intravenous administration of Gd-EOB-DTPA (Primovist®, Bayer Schering Pharma AG, Berlin, Germany) using a prefilled syringe (7.5 mL [0.25 mmol/mL]) followed by a 20-mL saline infusion using an automated injector (MR Spectris®, Medrad, PA, USA) at a rate of 2 mL/s through a peripherally inserted 20G vascular catheter; (c) axial T2-weighted fast GRE images obtained immediately after the administration of Gd-EOB-DTPA; and (d) fat-suppressed T1-weighted 3D GRE sequences acquired 20 min after the intravenous bolus of Gd-EOB-DTPA (hepatobiliary phase).

Abdominal fluid collections appeared markedly hyperintense on T2-weighted sequences and hypointense on T1-weighted sequences, although the nature of the fluid could not be determined. The images obtained in the hepatobiliary phase revealed significant and homogeneous enhancement of both the biliary tree and those areas where the contrast was visible outside the bile ducts, a finding that was interpreted as positive for the diagnosis of bile leak. In those cases where there was no evidence of contrast material outside the biliary system, the procedure was considered negative. In all cases, the findings of Gd-EOB-DTPA-enhanced MR-cholangiography correlated with those obtained later by endoscopic retrograde cholangiopancreatography (ERCP), percutaneous transhepatic cholangiography (PTCA), clinical follow-up, or surgical repair of the biliary tree.

Results

The study sample comprised 23 patients (10 men and 13 women) with a mean age of 59 years (range, 30–87 years). The mean interval between the initial surgical procedure and the presence of signs and symptoms suggestive of bile leak was 12 days (range, 2–20 days). Gd-EOB-DTPA-enhanced MR cholangiography was well tolerated by all patients, and no adverse reactions or complications were observed. Bile leak was detected in 10 patients: after liver resection for focal lesions in 3, cholecystectomy in 4, liver transplantation in 2, and liver resection for intrahepatic cholangiocarcinoma in 1. In the remaining 13 patients, Gd-EOB-DTPA-enhanced MR cholangiography was negative. Individual details of the study population are shown in Table 1. All patients were followed for at least 4 weeks after ERCP, PTCA, or surgical repair.

In the 10 patients with bile leaks, contrast material was found in the bile collections or bilomas in 4, in bilomas and the free intraperitoneal fluid in 5, and in free intraperitoneal fluid in 1. In the 13 patients with negative results, Gd-EOB-DTPA-enhanced MR cholangiography pointed to alternative diagnoses for the bile leak, such as abscess collection (7 patients), intrahepatic abscess (1 patient), seropurulent free fluid (2 patients), dehiscence of the biliodigestive anastomosis (1 patient), dysfunction of liver graft (1 patient), and stenosis of the biliobiliary anastomosis in a liver recipient (1 patient). Imaging with Gd-EOB-DTPA was able to detect all bile leaks (100%) that appeared early at 20 min after administration of the contrast. These were those leaks that because of the high debit required surgical repair or other interventions, such as ERCP or PTCA.

Discussion

Detecting and locating postsurgical bile leaks is difficult. Clinical and laboratory findings are frequently nonspecific, and diagnosis requires a high degree of clinical

Table 1. Characteristics of 23 patients with suspicion of bile leak undergoing MR cholangiography with Gd-EOB-DTPA

Sex/age	Diagnosis	Surgical procedure	Clinical symptoms	Laboratory abnormalities	Interval days	Prior radiologic studies: findings	Confirmation of diagnosis
Positive MR cholangiography with Gd-EOB-DTPA (n = 10)							
F/73	Hepatic hydatid cyst	Cystectomy	Bilious drain	No	9	CT scan: collection	ERCP
F/65	Cholecystitis	Cholecystectomy	Fever, abdominal pain, bilious drain	No	3	Ultrasound: collection	Surgical repair
M/57	Hemangioma	Right hepatectomy	Paralytic ileus, bilious drain	No	2	CT scan: collection	Surgical repair
M/31	Liver injury	Hemostasis/suture	Fever, abdominal pain, bilious drain	No	2	CT scan: collection	ERCP
M/58	Cholecystitis	Cholecystectomy	Bilious drain	No	3	CT scan: collection	ERCP
F/51	Metastases, colon cancer	Resection metastases	Bilious drain	No	13	Ultrasound: collection	ERCP, PTCA, surgical repair
F/31	Familial intrahepatic cirrhosis	Liver transplantation	None	↑ Bilirubin, cholestasis enzymes	7	Ultrasound: collection	ERCP
M/50	Alcoholic cirrhosis	Liver transplantation	Bilious drain	No	4	Ultrasound: collection	PTCA
F/63	Cholecystitis	Cholecystectomy	Bilious drain	No	6	Ultrasound: collection	ERCP
F/70	Cholangiocarcinoma	Left hepatectomy	Bilious drain	No	10	CT and ultrasound: collection	ERCP
Negative MR cholangiography with Gd-EOB-DTPA (n = 13)							
F/63	Cholangiocarcinoma	Duodenopancreatectomy	Fever, abdominal pain	No	3	CT scan: collection	PTCA, wound dehiscence repair
M/62	Cholecystitis	Cholecystectomy	Fever, abdominal pain	No	2	Ultrasound: collection	Clinical follow-up
M/76	Cholecystitis/choledocholithiasis	Cholecystectomy	Fever, abdominal pain	↑ Bilirubin, leukocytosis	7	CT and ultrasound: collection	ERCP, surgical repair
F/87	Cholecystolithiasis	Cholecystectomy	Biliopurulent drain	Leukocytosis, ↑ transaminases	3	Ultrasound: free fluid	ERCP
F/56	Liver cirrhosis	Liver transplantation	Ascites, vomiting, abdomen distention	Altered liver function tests	5	CT and ultrasound: collection	Clinical follow-up
F/70	Metastases, colon cancer	Resection metastases	Bilious drain	No	14	CT scan: collection	Clinical follow-up
F/79	Cholecystitis	Cholecystectomy	Fever	Leukocytosis	3	CT and ultrasound: collection	Clinical follow-up
M/45	Alcoholic cirrhosis	Liver transplantation	Altered consciousness	↑ Bilirubin, ↑ transaminases	6	CT and ultrasound: bile duct dilatation	ERCP (stenosis biliary anastomosis)
M/44	Alcoholic cirrhosis	Liver transplantation	Ascites, vomiting, distention abdomen	Altered liver function tests	2	CT scan: free fluid	Clinical follow-up
F/74	Cholelithiasis	Cholecystectomy	Bilious drain	No	2	CT scan unrevealing	ERCP
M/77	Cholecystitis	Cholecystectomy	Fever, abdominal pain	Leukocytosis	2	CT scan: collection	PTCA (purulent abscess drain)
M/30	Liver injury	Right hepatectomy	Purulent drain	Leukocytosis	20	CT scan: collection	PTCA
F/55	Metastases, colon cancer	Resection metastases	Purulent drain	Leukocytosis	7	CT scan: collection	Surgical repair

ERCP, endoscopic retrograde cholangiopancreatography; *PTCA*, percutaneous transhepatic cholangiography

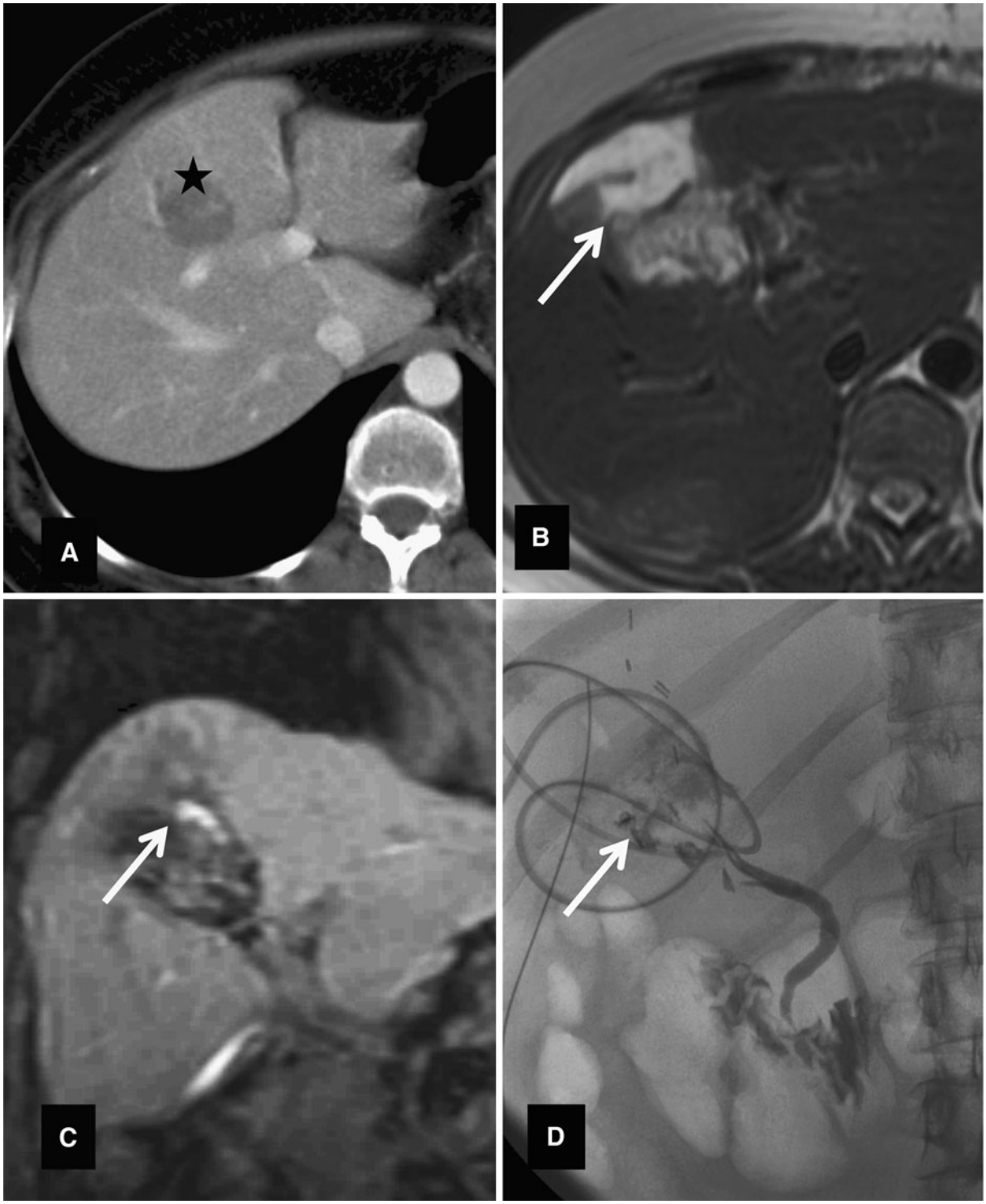

Fig. 1. A 51-year-old woman was diagnosed with hepatic metastasis by CT imaging (**A**) and underwent resection of the lesion; T2-weighted MR showed a collection of liquid (hyperintense) in the surgical bed with subhepatic spread (**B**); T1-weighted MR with Gd-EOB-DTPA and fat suppression revealed a biliary fistulous tract in continuity with the collection (**C**); bile leak was confirmed by ERCP.

suspicion. However, an early and reliable diagnosis is mandatory to insure adequate treatment and to avoid high associated morbidity and mortality rates [1, 2]. Noninvasive techniques, such as CT scanning and sonography, may disclose the presence of intraparenchymal hepatic lesions and abdominal collections,

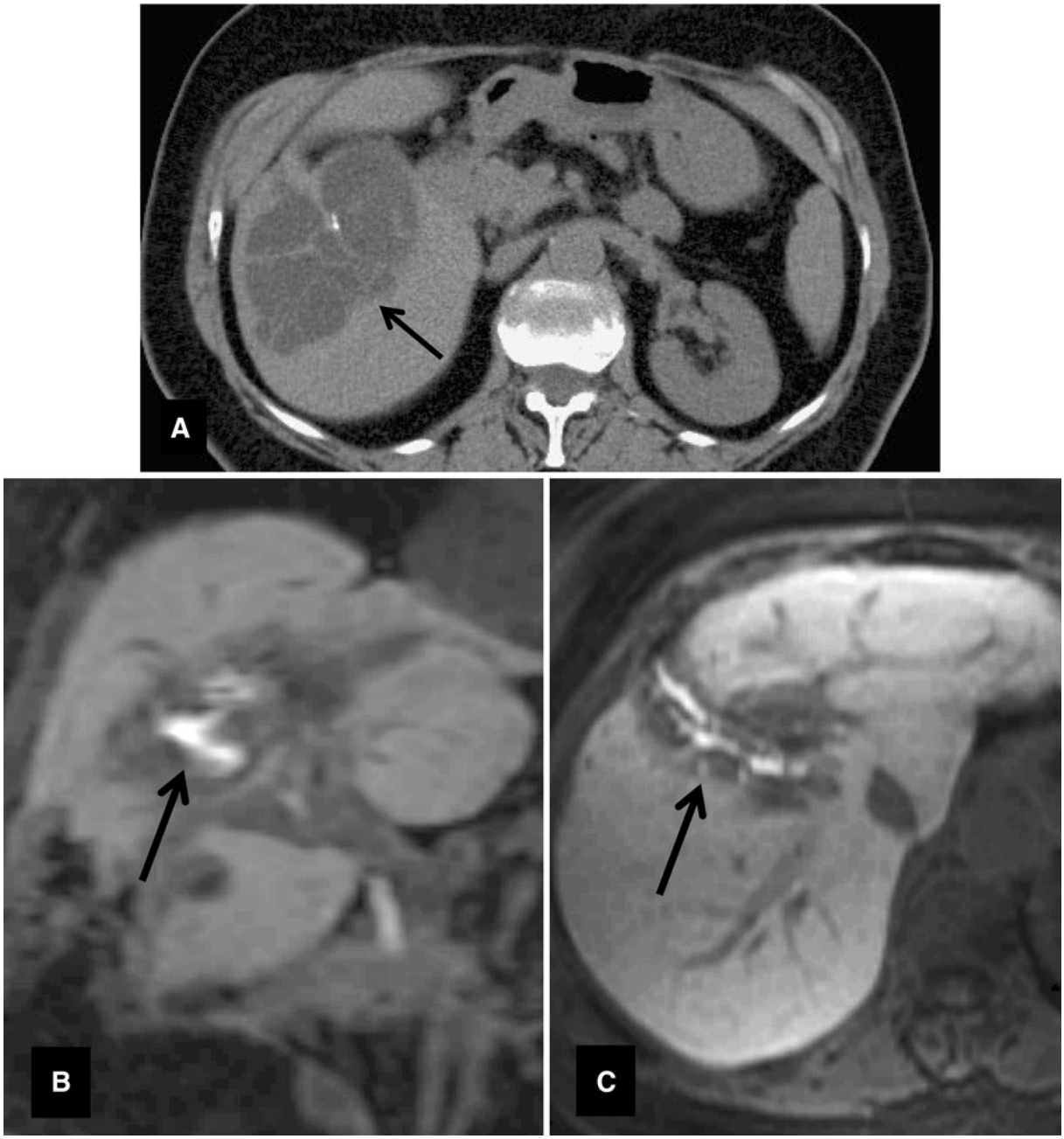

Fig. 2. A 76-year-old woman underwent resection of a hydatid cyst, as shown by axial CT imaging (**A**). Sagittal (**B**) and axial (**C**) fat-suppressed T1-weighted MR with Gd-EOB-DTPA shows leak of the contrast agent outside the biliary tree compatible with a bile leak.

although they do not reveal the characteristics of the content or provide adequate opacification of the biliary system. Functional hepatobiliary Tc-99 m HIDA scintigraphy has a high sensitivity in detecting the presence and site of bile leaks; however, this expensive technique cannot provide information on the anatomy of the bile ducts [5]. Invasive techniques such as ERCP and PTCA are very useful for assessing the site and severity of leaks, as well as for stent insertion and percutaneous drainage, although they are costly, invasive, and potentially risky [6]. Moreover, extrabiliary abnormalities cannot be observed. Therefore, it would be reasonable to postpone the use of these techniques until the anatomic and functional data of the biliary system provided by Gd-EOB-DTPA-enhanced MR cholangiography are available.

In comparison with T2-weighted images obtained with the single-shot fast spin-echo technique of conventional MR cholangiopancreatography [7], Gd-EOB-DTPA-enhanced

Fig. 3. In a 57-year-old man with a history of partial resection of a giant hepatic hemangioma, fat-suppressed T1-weighted Gd-EOB-DTPA-enhanced MR reveals the presence of a bile leak (hyperintense tract) in three spatial planes.

MR cholangiography allows a better assessment of bile duct lesions and provides information on the dynamics of liver parenchyma enhancement and biliary excretion, as well as on possible associated abnormalities such as cholecystitis, functional stenosis of the biliary tract (e.g., sphincter of Oddi dysfunction), and bile leak secondary to ductal lesions [8].

Other hepatocyte-specific MR imaging contrast agents have been developed, including mangafodipir trisodium (Mn-DPDP; Teslascan®, Nycomed Amerham, Oslo, Norway) and gadobenate dimeglumine (Gd-BOPTA; MultiHance®, Bracco Imaging, Milan, Italy). Mn-DPDP-enhanced MR cholangiography has high sensitivity and specificity [9, 10]. However, Gd-EOB-DTPA has some advantages over Mn-DPDP and Gd-BOPTA [8, 11–14]. Mn-DPDP is a pure hepatocyte-specific agent. In addition, a slow intravenous infusion (at least 20 min) is necessary to prevent adverse reactions, thus enabling bile ducts to be evaluated for around 3 h after injection. Gd-BOPTA and Gd-EOB-DTPA combine the features of

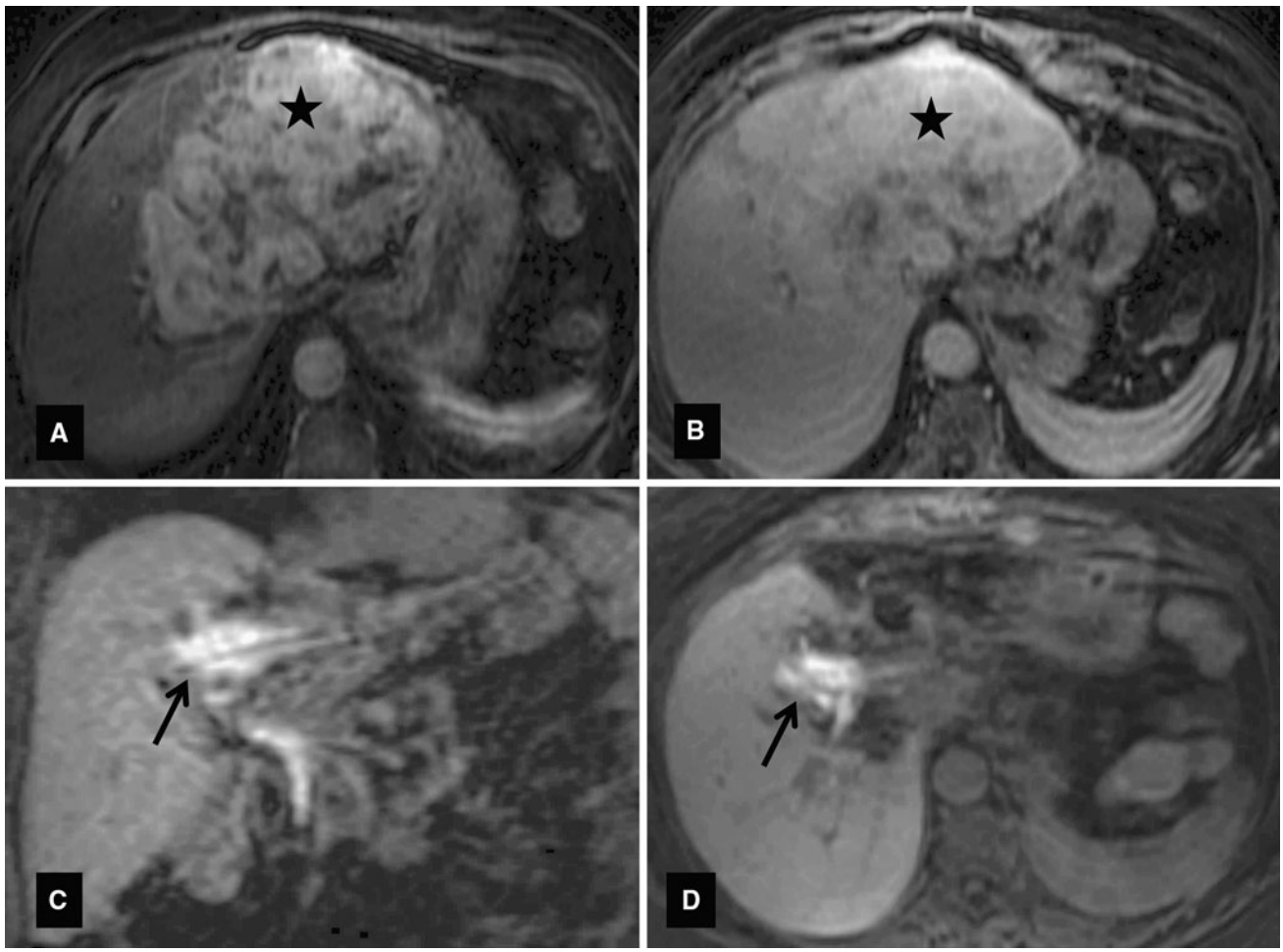

Fig. 4. MR images of a 70-year-old woman with cholangiocarcinoma reveal a heterogeneous lesion in the left hepatic lobe with early uptake of the contrast agent in the arterial phase (**A**) and maintenance of enhancement in the late venous phase (**B**). Gd-EOB-DTPA-enhanced MR reveals a bile leak with formation of bilomas in the surgical bed (**C** and **D**).

an extracellular contrast agent and a hepatocyte-specific agent; however, with Gd-EOB-DTPA 50% of the administered dose is excreted in bile, whereas approximately 3–5% of the dose of Gd-BOPTA is excreted in bile. The high percentage of bile excretion with Gd-EOB-DTPA allows adequate biliary imaging about 20 min after injection compared to approximately 45 min with Gd-BOPTA.

Despite its potential advantages over other radiodiagnostic techniques, Gd-EOB-DTPA-enhanced MR cholangiography is expensive and requires breath-hold during examination [8]. Furthermore, the presence of chronic liver disease significantly affects the signal intensity of the bile duct in Gd-EOB-DTPA-enhanced MR cholangiography [15, 16]. Another disadvantage to be considered is the possibility of false negative results when only a contrast post-injection phase with an early delay of 20 min is used, particularly in low grade bile leaks and in those in which a pressure gradient is established between the biloma and biliary tree (i.e., subcapsular localization). In these cases, new serial post-contrast phases with delays greater than 20 min (e.g., at 40–60–90 min) may be used as well as hepatobiliary scintigraphy, which is a very sensitive technique for the detection of these type of leaks, although the diagnostic window is delayed up to 2–4 h [8, 17].

The value of Gd-EOB-DTPA-enhanced MR cholangiography in detecting hepatocyte-selective enhancement of focal lesions and differentiating primary hepatocellular carcinoma from metastasis is well established [18, 19]. Moreover, Gd-EOB-DTPA-enhanced MR cholangiography can reduce costs by improving preoperative planning and decreasing intraoperative treatment changes and unnecessary surgery [20].

To our knowledge, Gd-EOB-DTPA-enhanced MR cholangiography for the diagnosis of bile leak has not been evaluated in a series as large as that presented here. Previous experience is limited to isolated case reports in

postcholecystectomy bile leak (3, 4). Our results show not only the usefulness of Gd-EOB-DTPA-enhanced MR cholangiography in visualizing bile leaks, but also its ability to detect postoperative bile leaks in several surgical procedures, including cholecystectomy, liver resection, duodenopancreatectomy with biliodigestive anastomosis, and liver transplantation. This preliminary experience in 23 patients with clinical suspicion of post-surgical bile leaks is encouraging, because all bile leaks (100%) that could be observed early after 20 min of the administration of Gd-EOB-DTPA were detected. These bile leaks were those with a high debit requiring surgical repair or other intervention procedures, such as ERCP or PTCA.

In conclusion, Gd-EOB-DTPA-enhanced MR cholangiography is a highly reliable diagnostic technique for early phase detection of bile leaks after a variety of hepatobiliary operations and may obviate the need for other, potentially risky invasive diagnostic techniques (Figs. 1, 2, 3, 4).

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