Role of Gd-EOB-DTPA enhanced MR Imaging in the evaluation of the transplanted liver: Advantages and Limitations

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GOALS AND OBJECTIVES

✓ To review the properties of Gd-EOB-DTPA in liver MR imaging.
✓ To discuss advantages of using Gd-EOB-DTPA in post-transplant liver MR imaging.
✓ To discuss limitations of using Gd-EOB-DTPA as the contrast agent in post-transplant liver MR imaging.

TARGET AUDIENCE

✓ Fellow and attending radiologists specializing in abdominal imaging
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Gd-EOB-DTPA = Gadolinium ethoxybenzyl di-ethylenetriamine penta-acetic acid (Gadoxetic disodium, Eovist™, Primovist™, Bayer HealthCare, Germany)
• **Introduction**
  ✓ Chemical properties and Pharmacodynamics of Gd-EOB-DTPA

• **Common post-transplant pathologies and role of Gd-EOB-DTPA enhanced MRI:**
  1. **Biliary pathologies**
     • *Biliary leak/biloma*
     • *Biliary obstruction and anastomotic stricture*
     • *Limitations*
  2. **Recurrent fibrosis/cirrhosis**
  3. **Recurrent hepatocellular carcinoma**
     • *Detection*
     • *Limitation in patients with advanced liver dysfunction*
  4. **Vascular complications**
     • *Arterial complications*
     • *Venous complications*
     • *Limitations*

• **Conclusion**
  ✓ *Summary of advantages and limitations of use of Gd-EOB-DTPA in post-transplant liver*
Chemical Properties of Gd-EOB-DTPA

- Paramagnetic contrast with features of both extracellular contrast agent and hepatocyte-specific agent (uptake by hepatocytes with subsequent biliary excretion).
- Paramagnetic component, gadopentetate dimeglumine, is covalently linked to lipophilic ethoxybenzyl (EOB) moiety.
- Relatively high T1 relaxivity allows lower dosage compared to other gadolinium chelates.
- Its blood pool properties are less intense, and shorter, than extracellular agents.
Pharmacokinetics of Gd-EOB-DTPA

- Lipophilic ethoxybenzyl (EOB) side chain has high affinity to ATP-dependent organic anion transporter polypeptide 1 (OATP1). OATP1 transports Gd-EOB-DTPA from extracellular space into hepatocytes.
- Subsequent excretion into the biliary canaliculi via the canalicular multispecific organic anion transporter (cMOAT).
- With normal liver and renal function, approximately 50% is excreted via the hepatobiliary pathway, with the rest through renal excretion. Plasma half-life is approximately 56 minutes (shorter compared to conventional extracellular contrast agents).
- Hepatobiliary phase reached by approximately 20 minutes after administration and lasts for 120 minutes.

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Introduction

Potential con’s and pro’s for use of Gd-EOB-DTPA

- Hepatobiliary phase images, which are routinely acquired by 3-D volumetric T1-weighted technique, high signal-to-noise ratio (SNR) offering high-contrast cholangiographic images and increased sensitivity for detection of focal hepatic lesions.

- Hepatobiliary phase images can help with characterization of focal lesions.

- Gd-EOB-DTPA has less intense blood-pool characteristics compared to extracellular agents; hence, early post-contrast images may have inferior contrast-to-noise ratio (CNR). Additionally, “transient severe motion” can be seen during arterial phase with higher frequency than other agents.

- Biliary excretion of Gd-EOB-DTPA is dependent on normal hepatocyte and normal excretory function. In patients with hepatocellular dysfunction or high-grade biliary obstruction, hepatobiliary phase imaging will be markedly compromised by lack of biliary excretion of contrast.
Biliary Applications

- Biliary complications occur in 5-15% of hepatic transplantations. Usually seen in the early postoperative period (less than 3 months after surgery).

- Gd-EOB-DTPA-enhanced hepatobiliary-phase MRI has higher SNR than T2-weighted MRCP and may offer better delineation of the biliary tree. In particular, Gd-EOB-DTPA is superior for evaluation of small non-dilated bile ducts.

- Because of functional cholangiography properties, Gd-EOB-DTPA-enhanced MRI is an excellent diagnostic modality for evaluation of bile duct injuries and leaks. It may also help differentiate between biliary and non-biliary pathologies (e.g., biloma vs. other fluid collection).
Biliary Anastomosis. 65 year-old male with a history of orthotopic liver transplantation for HCV cirrhosis. Coronal (A) and sagittal (B) reformats of hepatobiliary phase MR images (obtained 20 minutes following injection of Gd-EOB-DTPA) nicely delineate the choledocho-choledochal anastomosis (arrow).

**Biliary Applications: Delineation of Biliary Anatomy**
Biliary Anastomosis. 34 year-old male with a history of orthotopic liver transplantation for PSC. Coronal (A) and sagittal (B) reformats of hepatobiliary phase MR images (obtained 20 minutes following injection of Gd-EOB-DTPA) nicely delineate the choledocho-jejunal anastomosis (arrow).

Biliary Applications: Delineation of Biliary Anatomy

Choledocho-jejunal anastomoses are usually reserved for patients with history of PSC, biliary atresia, or prior biliary complications.
**Biliary Applications: Biloma**

**Biloma.** 24 year-old male with history of PSC. Axial T2-weighted image (A) shows a large fluid collection within the native liver. Hepatobiliary-phase MRI (B; obtained 20 minutes following injection of Gd-EOB-DTPA) shows contrast (arrow) within the collection – a finding confirming a biloma. ERCP (C), which was performed for therapeutic purpose, again confirms the leak.

*Gd-EOB-DTPA-enhanced MRI is the non-invasive modality of choice for evaluation of bile leak and biloma.*
Biliary Applications: Bile Leak

• Bile leak has reported prevalence of 4.3% after transplantation.

• Bile leak occurs with similar frequency after choledocho-choledochal and choledocho-jejunal anastomosis.

• Possible site of leak:
  ✓ Biliary anastomosis (choledocho-choledochal or choledocho-jejunal anastomosis)
  ✓ Cystic ducts remnant
  ✓ T-tube site
  ✓ Cut edge of liver (in case of living liver transplantation)

• Treatment options include biliary diversion, stenting, and surgical reconstruction.
Biliary Applications: Biliary Obstruction

- Causes of biliary obstruction include:
  - stricture, choledocholithiasis, and biliary cast.
- Stricture are divided into anastomotic and non-anastomotic types.
- Most biliary strictures are extrahepatic and occur at the anastomosis due to scar formation.
- Etiology of nonanastomotic biliary strictures include:
  - Ischemia (resulting from hepatic artery thrombosis or stenosis)
  - Infectious cholangitis
  - Pretransplantation sclerosing cholangitis.
**Biliary Applications: Anastomotic & Non-anastomotic Stricture**

**Biliary Stricture.** (A) Coronal MIP MRCP in 53-year-old male with history of OLTX, 3 years earlier, shows marked narrowing at the biliary anastomosis (arrow). (B) Coronal MIP MRCP in 64-year-old male with history of OLTX, 4 years earlier, shows long-segment stricture of common hepatic duct and biliary confluence (encircled). Patient had a history of hepatic arterial thrombosis.
Biliary Applications: Limitations in Advanced Liver Disease

- Biliary excretion of Gd-EOB-DTPA is dependent on normal hepatocyte and normal excretory function. In patients with hepatocellular dysfunction or high-grade biliary obstruction, hepatobiliary phase imaging will be markedly compromised by the lack of biliary excretion of contrast.

- Gd-EOB-DTPA uptake is mediated by same transporter for bilirubin. As such, biliary obstruction or hepatobiliary dysfunction can lead to reduced or no visualization of the biliary tree.

- More delayed imaging (up to 40 minutes) may be necessary to improve hepatobiliary phase enhancement.

- Absent biliary opacification by 30 minutes strongly correlated with significant hepatocyte dysfunction or high-grade biliary obstruction.
**Suboptimal Hepatobiliary Phase.** 62 year-old male with history of recurrent PSC in liver allograft. Delayed Gd-EOB-DTPA-enhanced axial T1-weighted image, obtained after a 30 minutes delay, fails to show biliary excretion of contrast. Note the dysmorphic liver morphology and intrahepatic biliary ductal dilatation - features compatible with recurrent PSC.
Recurrent Fibrosis. 62 year-old male with history of orthotopic liver transplantation for primary sclerosing cholangitis. Axial hepatobiliary phase MR image (A), obtained 20 minutes following injection of Gd-EOB-DTPA, shows non-focal and lace-like areas of signal alteration suggestive of recurrent fibrosis. The diagnosis was confirmed on subsequent MR elastography (B). The average hepatic parenchymal stiffness was calculated at 11 kPa, compatible with cirrhosis.
Recurrent Fibrosis. 28 year-old male with history of ulcerative colitis and primary sclerosing cholangitis who underwent orthotopic liver transplantation 6 years earlier. Axial hepatobiliary phase MR image (A), obtained 20 minutes following injection of Gd-EOB-DTPA, shows non-focal and segmental areas of signal alteration in posterior segment – an appearance suggestive of recurrent fibrosis. The gross photograph of explanted liver (B) shows diffuse nodularity of liver and innumerable regenerative nodules.
Recurrent Hepatocellular Carcinoma

- 5-year risk of recurrent HCC, in patients undergoing liver transplantation based on Milan criteria, is 10-15%.

- Due to its high CNR, hepatobiliary phase images increase sensitivity for detection of focal lesions.

**Limitations:**

- The quality of images acquired during the hepatic arterial phase may be compromised by ring and motion artifacts.

- Gd-EOB-DTPA has less intense blood-pool characteristics compared to extracellular agents; hence, early post-contrast images may have an inferior contrast-to-noise ratio (CNR).

- In patients with hepatocellular dysfunction or high-grade biliary obstruction, hepatobiliary phase imaging may be markedly compromised by the lack of biliary excretion of contrast.
**Recurrent HCC.** 75 year-old female with history of primary biliary cirrhosis complicated by HCC who underwent OLTX 4 years earlier. Axial hepatobiliary phase MR image (A), obtained 20 minutes following injection of Gd-EOB-DTPA, shows a 1.5 cm hypointense lesion in segment 4A (arrow). Corresponding arterial-phase (B), venous phase (C), and T2-weighted (D) images show arterial hyperenhancement, washout, and T2 hyperintensity compatible with recurrent HCC.
Vascular Complications: Arterial Complications

- Hepatic artery thrombosis is the most common vascular complication (seen in 2-12% of liver transplant patients).

- Other vascular complications include: hepatic artery stenosis and pseudoaneurysm formation.

- Hepatic artery thrombosis and stenosis can result in biliary ischemia, as the hepatic artery is the sole source of vascular supply to the bile ducts.

- Risk factors of thrombosis includes allograft rejection, end-to-end anastomosis, short warm ischemia time, and pediatric transplantation.
Vascular Complications: Arterial Complications

Hepatic Artery Pseudoaneurysm. Axial arterial-phase MR image (A), following injection of Gd-EOB-DTPA, suggests dilatation of proper hepatic artery (arrow) in this liver transplant patient. Axial image from CTA (B) confirms this finding.

- Pseudoaneurysms: extrahepatic (most commonly at the anastomosis, or results from angioplasty), intrahepatic (due to percutaneous biopsy, biliary procedures, infection).
- Ruptured intrahepatic pseudoaneurysm can result in portal or biliary fistulas.
- Treatment includes coil embolization, stent placement, or surgical resection.
Hepatic Artery Pseudoaneurysm (continued). Due to size of pseudoaneurysm, no intervention was performed. Follow up MRI (C), using Gadobenate dimeglumine, shows decreased size of pseudoaneurysm presumably due to partial luminal thrombosis. Note the higher CNR and less motion in figure C.

Due to its less intense blood pool characteristics, arterial phase Gd-EOB-DTPA-enhanced MRI may have a lower contrast to noise ratio (CNR).
Vascular Complications: Venous Complications

- Includes venous narrowing or venous thrombosis affecting portal veins, hepatic veins, or IVC

- Portal vein complications, which are the most common ones, are seen in up to 13% of OLTX patients.

  ✓ **Portal vein**: stenosis usually occurs at the anastomosis. Portal vein thrombosis often involves the main extrahepatic segment, although intrahepatic branches can be affected as well.

- IVC and hepatic venous complications are less common (seen in 1-2%).

  ✓ **IVC**: stenoses are due to anastomotic narrowing or extrinsic compression (graft swelling, fluid, hematoma). IVC thrombosis are extremely rare and are due to either iatrogenic factors or underlying hypercoagulable state.

  ✓ **Hepatic vein**: stenoses are typically seen in living donor transplantation.
Portal Venous Thrombosis. 39 year-old female with history of biliary atresia who underwent orthotopic liver transplantation, with hepatico-jejunal anastomosis, 17 years earlier. Axial T2-weighted image (A) and venous-phase contrast-enhanced T1-weighted image (B) show T2-hyperintense, nonenhancing tubular structures along the portal triads. At times, it might be very difficult to differentiate intrahepatic venous thrombosis from biliary dilatation or peribiliary cysts with certainty.
Portal Venous Thrombosis (continued). Axial (C) and coronal (D) hepatobiliary phase MRI, obtained 20 minutes following administration of Gd-EOB-DTPA, confirm that the tubular structures do not fill with excreted contrast and represent portal venous thrombosis. Note normal, non-dilated bile ducts (arrow). Opacification and delineation of bile ducts allows one to differentiate between biliary dilatation, peribiliary cyst, and venous thrombosis.
Summary of Advantage and Disadvantages

ADVANTAGES:

• High-resolution delineation of biliary tree and improved diagnostic efficacy for evaluation of biliary complications
• High sensitivity for detection of focal hepatic lesions
• Increases diagnostic accuracy for characterization of focal hepatic lesions

LIMITATIONS:

• Arterial-phase images may have lower CNR and be compromised by motion and ring artifact
• Hepatobiliary-phase images may be compromised in advanced hepatocyte dysfunction and high-grade biliary obstruction
• Cost
Conclusion

There are potential advantages with use of Gd-EOB-DTPA for evaluation of transplanted liver. Use of this agent in selected post-transplant patients can result in improved diagnostic efficacy. Knowing the potential pitfalls helps with patient selection.
Selected References


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