Dynamic Secretin-enhanced MR Cholangiopancreatography

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Secretin causes temporary dilatation of pancreatic ducts, principally by increasing pancreatic exocrine secretions, and thus allows better visualization of the ducts at magnetic resonance (MR) cholangiopancreatography. Secretin-enhanced MR cholangiopancreatography is useful for detection and diagnosis of a variety of congenital, inflammatory, and neoplastic conditions of the pancreas. Although MR cholangiopancreatography without secretin is a reliable method for evaluating the pancreatic ductal system, the authors believe that secretin-enhanced MR cholangiopancreatography gives additional valuable functional and anatomic information about the pancreatic duct and pancreatic excretory capacity.

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Abbreviations: ERCP = endoscopic retrograde cholangiopancreatography, IPMT = intraductal papillary mucinous tumor

RadioGraphics 2006; 26:665–677 • Published online 10.1148/rg.263055077 • Content Codes: GI MR

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Introduction

Magnetic resonance (MR) cholangiopancreatography is a noninvasive technique for evaluation of the pancreatic ducts and biliary tree. The method has been available for more than a decade and is based on the use of heavily T2-weighted MR sequences to suppress the signal from most soft tissues and allow the stationary fluid in the ducts to be visualized. Use of a contrast agent is not necessary at MR cholangiopancreatography, and the imaging examination is often performed without it. However, we have found that the use of secretin, a hormone that stimulates pancreatic secretion, improves our ability to assess the pancreatic duct system. In this article, we discuss and illustrate the utility of secretin-enhanced MR cholangiopancreatography in the detection of various pancreatic diseases.

Secretin is a 27–amino acid polypeptide hormone secreted by the duodenal mucosa in response to luminal acid, typically after a meal (1). It has numerous physiologic effects, including actions on the sphincter of Oddi, the biliary tree, and the pancreas. An important action is its stimulation of the pancreatic secretion of bicarbonate-rich fluid; the agent also transiently increases tone in the sphincter of Oddi. The effects on biliary flow are less pronounced than those on the pancreas. As a result, secretin usually produces distention of the pancreatic duct that is most visible 4–10 minutes after administration.

Prior to 1999, secretin was available commercially in the United States in a form purified from porcine duodenum. The porcine form of the hormone differs from the human form in two amino acid residues; however, the biologic properties are believed to be identical. In 1999, the biologic porcine form became unavailable in the United States, and a synthetic form was developed. Synthetic porcine secretin is now approved by the Food and Drug Administration and is commercially available in the United States (SecreFlo; Repligen, Waltham, Mass), as is a synthetic form of human secretin (Chirhostim; ChiRhoClin, Burtonsville, Md).

Most MR cholangiopancreatographic studies are probably still performed without secretin because of the cost and inconvenience of using the hormone. However, secretin is safe to use, with a very small incidence of serious side effects, and is easy to administer. Most important, it can significantly enhance the depiction of pancreatic ducts on MR cholangiopancreatographic images. While the agent produces little change in the appearance of the biliary tree, visualization of pancreatic ductal anatomy is often substantially improved, and use of the hormone is recommended in cases in which a detailed evaluation of the pancreatic duct is desired or when it is important to obtain a qualitative indication of the exocrine function of the pancreas.

In our routine practice, secretin-enhanced MR cholangiopancreatography is performed in all patients whose symptoms might be related to the pancreas and in whom visualization of pancreatic ducts is important, especially in those with unexplained abdominal pain that continues after noncontributory conventional examinations. In this article, we review our experience with 295 dynamic secretin-enhanced MR cholangiopancreatographic examinations. The MR cholangiopancreatography–based diagnoses included acute pancreatitis (n = 19), chronic pancreatitis (n = 49), pancreas divisum (n = 33), intraductal papillary mucinous tumor (IPMT) (n = 12), other pancreatic cancers (n = 14), and various conditions after Whipple surgery (n = 14).

Secretin-enhanced MR Imaging Technique

Fasting by the patient for 4–6 hours prior to the examination, along with the administration of 300 mL of ferumoxsil oral suspension as a negative oral contrast agent (Gastromark; Mallinckrodt Medical, Raleigh, NC), helps to avoid obscuration of the pancreatic ducts by high signal
intensity in the overlying stomach and duodenum (Fig 1). We give the oral contrast medium approximately 30 minutes before initiating the MR cholangiopancreatographic acquisitions. Secretin is given intravenously over 1 minute to avoid abdominal pain that may occur with a bolus injection. An adult dose of 2 μg per kilogram of body weight is used. At the commencement of the injection, a baseline image is obtained, followed by acquisition of a coronal single-shot turbo spin-echo image (acquisition time, 2 seconds) every 30 seconds for 15 minutes.

After the acquisition of axial locator images, the pancreatic duct is imaged by applying a single-shot fast spin-echo pulse sequence within a single 40-mm-thick coronal slab positioned over the pancreas. The matrix size for most patients is 256 × 256; the field of view varies from patient to patient but is generally 22 × 22 cm. Echo time is typically more than 750 msec. Fat saturation is used in all patients. Acquisition times are approximately 1–2 seconds per section, and images are acquired during breath holding. The examination parameters are listed in Table 1.

### Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tr>
<td>Echo time (msec)</td>
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<tr>
<td>Echo train (no. of echoes)</td>
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<tr>
<td>Variable field of view (cm)</td>
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<tr>
<td>Matrix</td>
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<tr>
<td>Flip angle (degrees)</td>
<td>180</td>
</tr>
<tr>
<td>Slab thickness (mm)</td>
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</table>

(a) Image obtained without secretin and ferumoxsil shows high signal intensity in the fluid-distended stomach (arrow) and small bowel (arrowhead) that obscures the pancreatic ducts. (b) Image obtained with the use of oral ferumoxsil (Gastromark; Mallinckrodt) as a negative contrast material shows a near absence of signal from the stomach and duodenum, a condition that allows better visualization of the pancreatic (arrow) and biliary ducts.

Figure 1. A comparison of MR cholangiopancreatographic images shows the value of oral ferumoxsil. (a) Image obtained without secretin and ferumoxsil shows high signal intensity in the fluid-distended stomach (arrow) and small bowel (arrowhead) that obscures the pancreatic ducts. (b) Image obtained with the use of oral ferumoxsil (Gastromark; Mallinckrodt) as a negative contrast material shows a near absence of signal from the stomach and duodenum, a condition that allows better visualization of the pancreatic (arrow) and biliary ducts.
maximal effect of intravenous secretin is observed at 5–7 minutes after the start of the injection (Fig 2). The caliber of the main pancreatic duct increases by at least 1 mm, and high signal intensity is seen in the descending and transverse duodenum in normal individuals after secretin injection.

The most common adverse effects of secretin are abdominal cramps, abdominal discomfort, nausea, vomiting, bloating, bradycardia, decreased blood pressure, diaphoresis, and diarrhea. However, in our experience, adverse effects occur infrequently. Only one (0.3%) of our patients developed severe abdominal pain requiring 4 hours of observation.
Pancreas Divisum

The pancreas derives from dorsal and ventral buds that develop from the embryonic foregut. The ventral system also gives rise to the hepatobiliary system. At approximately 6–8 weeks of gestation, the ventral pancreas rotates posterior to the duodenum and comes to rest inferior and slightly posterior to the head portion of the dorsal pancreas. Fusion of the ductal system occurs in more than 90% of individuals, but variations occur that may affect the patency of the accessory duct (Santorini duct). Figure 3 shows variations of the ductal anatomy (2).

Pancreas divisum occurs if there is a lack of fusion of the dorsal and ventral anlagen. Between 5% and 10% of the general population have this anatomic variant (3). Endoscopic retrograde
Figures 4, 5. (4) Incomplete pancreas divisum. Secretin-enhanced MR image shows the continuity of the main duct (curved white arrow) with the dorsal duct (black arrowhead) and of the ventral duct (black arrow) with the distal common bile duct (straight white arrow), features suggestive of pancreas divisum. However, a tenuous connection (white arrowhead) between the ventral and dorsal duct systems indicates incomplete division. (5) Complete pancreas divisum. (a) Presecretin MR image does not clearly depict the main pancreatic duct. (b) MR image obtained 5 minutes after secretin injection clearly shows the main duct in the body of the pancreas (white arrow) and the dorsal duct (arrowhead) in continuity with the main duct. Note that the main duct does not join with the distal common bile duct (black arrow), a finding that indicates complete pancreas divisum. (c) Corresponding ERCP image obtained after injection via the minor papilla helps confirm pancreas divisum and shows a santorinicele (arrow) at the minor papilla.
cholangiopancreatographic (ERCP) studies have shown that in 10%–15% of patients, pancreas divisum is incomplete; that is, there is a minor communication between the dorsal and ventral ducts (Fig 3, C) (2,4). This percentage may be an underestimate, as a vigorous injection of contrast material into the ventral duct would be required to show the connection. The significance of a bifid pancreas has been debated. The small diameter of the minor papilla orifice results in increased dorsal and main duct pressures that may cause pain or pancreatitis. About 15%–20% of patients with unexplained pancreatitis have pancreas divisum. Minor papilla sphincterotomy is the usual treatment for recurrent pancreatitis or disabling abdominal pain in patients with a divided pancreas. Traditionally, incomplete pancreas divisum was thought less likely than complete divisum to be associated with pancreatitis, since high pressure in the dorsal pancreatic duct system could be decreased via a connection to the ventral duct (Fig 4); however, this notion has been challenged by some investigators (5). The sensitivity of MR cholangiopancreatography for detection of pancreas divisum is considerably increased with the use of secretin (3,6,7) (Fig 5). Dynamic MR cholangiopancreatography also can depict a cystic distention of the distal accessory duct or Santorini duct (a so-called santorinicele) (Fig 6), probably as a result of impaired flow through the minor papilla. It has been suggested that patients with a pancreas divisum and a santorinicele have a higher risk of pancreatitis (8).

Figure 6. Santorinicele. (a) Presecretin MR image shows possible mild enlargement of the distal tip of the dorsal duct (arrowhead) and the presence of pancreas divisum. (b) Postsecretin MR image shows increased signal intensity in the duodenum from the exocrine response to secretin. The fusiform enlargement (santorinicele) of the tip of the dorsal duct also is more prominent (arrows).

Acute Pancreatitis

Computed tomography (CT) is the principal method for evaluating the severity of pancreatitis and determining whether complications are present. MR cholangiopancreatography with or
without secretin for contrast enhancement is an excellent alternative method of evaluating the pancreatobiliary system in patients with an elevated creatinine level or a severe allergy to iodinated contrast material. It is also superior to CT for the detection of choledocholithiasis. The use of secretin in patients with acute pancreatitis has caused concern in the past; however, we encountered only one instance of abdominal pain and no exacerbations of pancreatitis after secretin injection in 295 examinations. Secretin enhancement is occasionally useful for determining whether the main pancreatic duct is completely disconnected or only stenosed in patients with necrotizing pancreatitis, an important distinction when surgical intervention is being considered (9) (Figs 7, 8).

### Chronic Pancreatitis

Pancreatologists use the Cambridge criteria for grading chronic pancreatitis at ERCP (Table 2). The use of secretin improves visualization of the main pancreatic duct and its side branches to such a degree at MR cholangiopancreatography that it is possible to use the same criteria for disease severity (Figs 9, 10). While parenchymal calculi are not seen as clearly at MR cholangiopancreatography as they are at CT, intraductal calculi are well demonstrated as filling defects at secretin-enhanced MR cholangiopancreatography. In

<table>
<thead>
<tr>
<th>Grade Description</th>
<th>ERCP Findings</th>
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<td>Main Duct</td>
<td>Side Branches</td>
</tr>
<tr>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Equivocal</td>
<td>Three or fewer abnormal</td>
</tr>
<tr>
<td>Mild chronic pancreatitis</td>
<td>More than three abnormal</td>
</tr>
<tr>
<td>Moderate chronic pancreatitis</td>
<td>Abnormal</td>
</tr>
<tr>
<td>Marked chronic pancreatitis</td>
<td>Abnormal, with calculi, obstruction, or cavity</td>
</tr>
</tbody>
</table>

Note.—Adapted, with permission, from reference 10.

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**Figures 7, 8.** (7) Disconnected pancreatic duct syndrome. (a) Presecretin MR image shows a lack of continuity of the main pancreatic duct (arrow) in the region of the pancreatic neck and proximal body. (b) Postsecretin MR image demonstrates the absence of duct connection (arrowhead) and lack of stenosis. Note the curved drain catheter at the site of a peripancreatic fluid collection (arrow). (c) ERCP image helps confirm disruption of the main duct in the pancreatic head (arrowhead). The patient subsequently underwent pancreateojunostomy and percutaneous drain placement. (8) Pancreatic duct stenosis following acute pancreatitis. (a) Presecretin MR image shows discontinuity of the main duct at the level of the pancreatic neck (white arrowhead), an adjacent high-signal-intensity fluid collection (black arrowhead), and diffuse ascites (arrow). (b) MR image obtained 7 minutes after secretin injection shows stenosis of the main pancreatic duct in the pancreatic neck (white arrowhead) and diffuse ascites (arrow). The fluid collection adjacent to the pancreatic neck (black arrowhead) appears brighter than on the presecretin image, a feature suggestive of a connection to the duct. (c) ERCP image helps confirm the presence of stenosis (white arrowhead) and absence of disconnection of the duct. The fluid collection (black arrowhead) is filled with injected contrast material, which indicates disruption of the duct. The patient underwent percutaneous placement of a pancreatic stent (not shown) and did not need open surgery.
addition to depicting the ductal anatomy, secretin-enhanced MR cholangiopancreatography is useful also for qualitatively evaluating the exocrine secretory function in patients with intraductal calculi (11,12).

Pancreatic Adenocarcinoma
Pancreatic adenocarcinoma is the fourth most common cause of death due to cancer in the United States. MR imaging with gadolinium can be used for problem solving and for staging of the tumor in patients for whom contrast-enhanced CT is contraindicated. MR cholangiopancreatography with secretin is not usually required for diagnosis of a tumor or detection of tumor growth. In our experience, MR cholangiopancreatography with secretin is not accurate for differentiating between benign and malignant strictures of the main pancreatic duct. Occasionally, the etiology of ductal stricture in the pancreatic head is not determined preoperatively, and a Whipple procedure, which involves radical resection of the pancreatic head, duodenum, common bile duct, right half of the omentum, and local nodes, is performed.

Intraductal Papillary Mucinous Tumor
IPMTs originate from the main pancreatic duct or side branches and can mimic chronic pancreatitis–related changes such as dilated ducts or filling defects. The tumor produces thick mucin, which is usually visible at ductal cannulation during ERCP. About 90% of these tumors are benign or are carcinomas in situ. The prognosis, however, is considerably worse if the tumor becomes invasive. MR imaging is as sensitive as CT, if not more sensitive, for the diagnosis and staging of IPMT (13). Unfortunately, neither CT nor MR imaging enable differentiation of thin mucin from pancreatic juices. Such differentiation is possible with ERCP and endoscopic ultrasonographically guided fine-needle aspiration. However, in our experience, thick mucin balls may have decreased signal intensity on T2-weighted images and may appear as 1–3-mm filling defects.

Figure 9. Mild chronic pancreatitis. (a) Presecretin MR image shows no abnormality of the main pancreatic duct (arrow). (b) MR image obtained 5 minutes after secretin injection shows a normal main pancreatic duct (arrow) and dilatation of several side branches (arrowhead), findings consistent with mild (grade 3) chronic pancreatitis. (c) ERCP image shows dilatation of more than three side branches (arrowheads) without irregularity in the main duct (arrow), findings that confirm mild chronic pancreatitis.
in affected ducts (Fig 11). By definition, IPMTs communicate with the main pancreatic duct. Theoretically, small tumors should increase in size after secretin injection, as they fill with exocrine secretions. However, in 21 cases of side branch IPMT that we reviewed, no significant change in tumor size followed secretin injection. In these cases, a mucous plug may have impeded the filling of the cystic tumor by secreted juices.

Chronic pancreatitis is a frequent complication of IPMT because of long-term obstruction of

**Figure 10.** Severe chronic pancreatitis. (a) MR image obtained 7 minutes after secretin injection shows severe cystic dilatation of side branches in the pancreatic head and irregular dilatation of the main pancreatic duct, with low-signal-intensity filling defects (arrows). The exocrine response to secretin was poor, as demonstrated by the lack of high signal intensity in the duodenum. (b) Corresponding ERCP image helps confirm the presence of main duct filling defects consistent with calculi (arrows), findings indicative of grade 5 chronic pancreatitis. MR cholangiopancreatography has lower sensitivity than does ECRP for depicting pancreatic ductal calculi.

**Figure 11.** IPMT with diffuse duct disease. (a) Postsecretin MR image shows severe dilatation of the main duct in the pancreatic body and tail. The appearance of the duct resembles that in chronic pancreatitis, but dilatation is diffuse, and there is no stricture. Cystic dilatation of the main duct is visible in the head of the pancreas (white arrow). Small low-signal-intensity filling defects in the duct (arrowheads) are likely to be mucous concretions. The ventral duct (black arrow) appears normal. (b) ERCP image shows an extrusion of mucus from a bulging major papilla. There is marked dilatation of the proximal main pancreatic duct (arrowhead). The ventral duct (black arrow) appears normal. The cystic dilatation of the main duct in the pancreatic head is not as well depicted as at MR cholangiopancreatography, but a mucin-related filling defect (white arrow) that was not visible on the MR images is shown. Thin mucin is indistinguishable from pancreatic juices at MR imaging.
Figure 12. Recurrence of IPMT. (a) Postsecretin MR image, obtained 3 years after surgery with the Whipple procedure for IPMT, shows cystic dilatation of the duct in the remnant pancreatic tail (arrow). Low-signal-intensity foci with diameters of 2–3 mm (arrowheads), features likely due to viscid mucus, are seen within the duct. (b) Axial T2-weighted MR image shows a distended duct in the pancreatic tail (arrowheads) and the postsurgical site of pancreatojejunostomy (arrow). IPMT recurrence was found at pathologic analysis of a resected specimen. Right-sided hydrenephrosis due to a ureteropelvic junction obstruction (not shown) was an incidental finding.

Figure 13. Whipple procedure. (a) Presecretin MR image obtained after Whipple surgery does not show any residual pancreatic duct. (b) MR image obtained 7 minutes after secretin injection clearly depicts the pancreatic duct in the body and tail (white arrow), mild stenosis at the junction with the roux limb of the jejunum (black arrow), and dilatation of a side branch (arrowhead). (c) ERCP image obtained with cannulation of the pancreatojejunostomy helps confirm mild distention of the main pancreatic duct and side branch.
pancreatic ducts by viscid secretions. MR features that support a finding of IPMT more than that of chronic pancreatitis include diffuse dilatation without stricture; septation; and a mural nodule within a dilated ductal side branch. Features associated with a higher risk of malignancy in IPMT include the presence of diabetes, age of more than 70 years, a tumor larger than 3 cm, a mural nodule larger than 1 cm, a bulging papilla, or main pancreatic duct dilatation of more than 1 cm (14–16). MR imaging is useful for postoperative follow-up of IPMT. Features suggestive of tumor recurrence include a recurrent cystic pancreatic mass, increased dilatation of ducts in the pancreas, and a solid extrapancreatic lesion (17) (Fig 12).

**Postoperative Anatomy**

After a pancreatic surgical resection (eg, the Whipple procedure, or pancreatostomy with the Puestow or Frey procedures for chronic pancreatitis), ERCP is more difficult to perform. MR cholangiopancreatography is the predominant method of investigating disease in the residual pancreas. Mild distention of the main pancreatic duct, a finding that becomes more obvious after the administration of secretin, is commonly seen following Whipple surgery and is attributed to the near-universal presence of anastomotic stenosis (Fig 13). The volume of fluid seen in the efferent jejunal limb may be an indirect measure of remnant pancreatic exocrine function after the Whipple procedure (18). The current practice among surgeons at our institution is to insert a stent at the anastomotic site. Following the Puestow operation, the main pancreatic duct may be invisible unless there is a recurrence of chronic pancreatitis.

**Conclusions**

Secretin is a safe, albeit costly, agent that improves visualization of the main and side pancreatic ducts in normal and pathologic states during MR cholangiopancreatography. Dynamic MR cholangiopancreatography after secretin administration also provides valuable information about the secretory reserve capacity of the pancreas. Yet, a lack of awareness of the value of secretin-enhanced MR cholangiopancreatography among radiologists and referring clinicians has limited the use of this technique.

**References**

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RadioGraphics 2006; 26:665–677 • Published online 10.1148/rg.263055077 • Content Codes: [DT] [MR]

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