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REVIEW ARTICLE

The clinical value of secretin-enhanced MRCP in the functional and morphological assessment of pancreatic diseases

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ABSTRACT

Secretin-enhanced magnetic resonance cholangiopancreatography (S-MRCP) provides a non-invasive way, with which, to evaluate pancreatic duct (PD) anatomy and exocrine pancreatic function. S-MRCP can be added to the routine pancreas MR examination in equivocal cases. Moreover, it can detect subtle PD involvement, allowing diagnosis of early, rather than end-stage, pancreatic diseases. Although S-MRCP is a valuable non-invasive diagnostic method, it is only performed in a few centres due to relative high cost. Furthermore, less familiarity with its indications, the examination technique, and image interpretation also contribute to its limited use. Thus, the purpose of this article is to explain secretin's mechanism of action, the examination technique, the clinically relevant indications, the advantages, and limitations. Finally, we will focus on image analysis and its role in achieving an early and accurate diagnosis of specific pancreatic and PD diseases.

INTRODUCTION

Visualization of the pancreatic duct (PD) is crucial for the detection and characterization of many pancreatic disorders because the vast majority of pancreatic diseases originate from or in proximity to the PD. As 70–90% of pancreatic carcinomas are histologically characterized by a ductal morphology, they are classified as ductal adenocarcinomas, although their ductal origin is still a matter of debate.¹ Chronic pancreatitis (CP), a very common pancreatic disorder, begins in the PD as well.² Therefore, visualization of the entire PD is necessary. In the past, endoscopic retrograde cholangio-pancreatography (ERCP) was the mainstay in the diagnosis of PD pathology,^{3,4} however, this invasive procedure was not only expensive and time-consuming, but also carried a high risk of morbidity and even mortality.^{5–7}

Conventional MRCP was the first non-invasive alternative, a widely utilized technique for the assessment of the pancreaticobiliary ductal system. In addition to its non-invasive nature, MRCP is also quick, requiring less than a minute.^{8,9} Its main disadvantage, however, is that the PD is not always depicted in its entirety.^{10–12} In particular, defining tiny stenoses, and/or small lesions or irregular contours that occur without

PD dilatation, remains a challenge for conventional MRCP. As these are the earliest features of a mass or inflammatory disease, their detection is pivotal for early diagnosis and treatment. These shortcomings were addressed with the introduction of dynamic secretin-enhanced MRCP (S-MRCP) in 1995.¹³ S-MRCP enables visualization of the entire PD, in over 90% of cases.¹⁴ As a consequence, S-MRCP has a much higher sensitivity and specificity, *i.e.* 66 and 85%, respectively, than conventional MRCP.¹⁵ More importantly, its negative-predictive value is 98%,¹⁶ which obviates the need for further invasive evaluation of the PD. Furthermore, S-MRCP can be a useful road-map before therapeutic intervention. Images obtained over the pancreatic bed, sequentially, allow an evaluation of the morphology of the entire PD.¹⁴ Moreover, these serial PD images allow an inference about the ability of the exocrine pancreas to respond to secretin, by visualizing the change in PD calibre over time.^{17–20} Finally, S-MRCP provides both a qualitative and quantitative evaluation of duodenal filling.^{21–23}

S-MRCP is not performed as a routine examination in all MR facilities due to its relatively high cost, increased examination time, and the expertise necessary for interpretation.

S-MRCP reports should include a description of the subtle morphological features of the PD, as well as the functional implications. In this overview, we describe the physiological and potential adverse effects of secretin, the examination technique, the main indications, and, finally, the morphological and functional interpretation of S-MRCP.

Secretin

Secretin is a gastrointestinal hormone (27-amino acid polypeptide) secreted by the duodenal mucosa in response to increased intraluminal acidity.²⁴ Its main physiological effects include stimulation of PD epithelial cells to secrete a bicarbonate-rich fluid, and a transient increase in the tone of the sphincter of Oddi.^{20,25} Whereas, the former increases the volume of fluid in the PD, the latter delays PD fluid drainage into the duodenum, both of which improve visualization of the PD. During S-MRCP, a synthetic secretin-like peptide is administered to the patient intravenously (i.v.).^{16,17,19,26} This induces the two aforementioned effects, and, in addition, inhibits gastric acid secretion and decreases intestinal motility. Currently, three forms of secretin are available on the market: biologic porcine, synthetic porcine, and synthetic human.^{27,28} They can be used interchangeably. The recommended dose of secretin is $0.2 \mu\text{g kg}^{-1}$ (average adult dose of $16 \mu\text{g}$) or $1 \text{ ml } 10 \text{ kg}^{-1}$ of body weight.^{17,25} The peak effect on the PD is usually observed 3–5 min after administration.^{17,20,26,29} As the duodenum begins to fill, the PD returns to its baseline diameter. Typically, the maximum output of pancreatic fluid occurs between 6 and 8 min.²²

Patient preparation

To visualize the entire PD and eliminate signal intensity (SI) from overlying bowel and stomach, patients should fast at least 4 h prior to the examination.^{23,26,30,31} This also reduces bowel peristalsis and promotes gallbladder distension. In the past, approximately 600 ml of superparamagnetic iron oxide-containing oral contrast agent was consumed before imaging: 300 ml, 30 min before the examination, and another 300 ml immediately before the examination.²⁷ However, this T_2 weighted oral contrast agent (Lumirem®) is no longer commercially available. Thus, we now use LumiVision®, a newly introduced, high-manganese suspension. Alternatively, pineapple or blueberry juice can be used, but these substances are contraindicated in patients with diabetes due to sugar content. Some institutions utilize 1 to 5 ml of gadolinium-DTPA or gadolinium-DOTA mixed in 50 to 200 ml of distilled water. However, this approach is controversial due to lack of safety information about this agent's oral use.³² These paramagnetic alternatives appear dark on T_2 weighted imaging, thus eliminating high SI from residual gastric and duodenal contents. Their drawback, however, is their bright SI on T_1 weighted images, which may obscure portions of the biliary tree, particularly if the liver is being imaged with hepatobiliary contrast agents in the same examination. In general, the use of oral contrast agent is only needed if it is shown that the stomach is not empty and overlies the PD or papilla. In addition, because the patient consumes contrast agent in the supine position, the duodenum remains filled with residual fluid, which acts as a landmark for the papilla area. To reduce peristalsis and motion artefacts, some centres give 20 or 40 mg of i.v. hyoscine

butylbromide (Buscopan®).²³ In cases where Buscopan is contraindicated, Glucagon can be used.³³

Examination protocol

Imaging the pancreaticobiliary ducts relies on heavily T_2 weighted sequences that selectively displays static or slow-moving fluid-filled structures.^{18,34} Sequence parameters differ from institution to institution, depending upon the magnet manufacturer, its field strength, as well as the available applications.^{18,20,31} But, the basic principle of S-MRCP remains the same, i.e. to acquire a thick-slab, single-shot turbo spin-echo or fast spin-echo T_2 weighted images.^{9,35,36} This includes the acquisition of six radial thick-slab images between 30 and 60 mm, depending on the size of the patient.⁹ These images are obtained during breath-hold, each acquired over 2 to 3 s. Then, the radiologist or technologist chooses the best of these images, i.e. that in which the entire PD, CBD, and the papilla of Vater are visualized. For proper evaluation of the PD, images should be acquired dynamically with good temporal and spatial resolution. As a general rule, a single-shot 30–50 mm thick-slab MRCP image is acquired in the coronal plane before secretin injection.^{26,32} The field of view of this image should include the expected location of the PD, CBD, and their junction at the duodenal papilla. A scan of this identical area is then repeated every 30 s, for 10 min, after slow i.v. administration of secretin.^{3,17–19,22,26} The 20 consecutive images generated should be compared with the other serial images to detect subtle changes in the PD diameter. More recent developments include a multisection, thin-slab, single-shot turbo spin-echo T_2 weighted sequence with the possibility of three-dimensional reconstructions that provide better resolution of the PD, both in pathological and normal conditions.³² Acquiring images with near-isotropic voxels facilitates post-processing manipulation of the images with multiplanar reconstruction, maximum intensity projection, and volume rendering. Today, it is common to perform the examination with respiratory triggering, which reduces artefacts when imaging disabled or uncooperative patients.³⁷

Limitations

One of the drawbacks of S-MRCP is the inability to visualize confidently non-obstructing intraluminal stones, especially if they are <4 mm. In addition, stones cannot always be distinguished from blood clots or mucous plugs.^{17,26} Conversely, crossing vessels or air may be mistaken for filling defects.³⁸ To overcome these limitations, the combined use of multiple, thin-slice turbo spin-echo T_2 weighted images with a shorter echo time, and T_1 weighted images with fat suppression, is recommended. But, since an unenhanced CT of the pancreas is far easier to interpret, it is recommended before performing S-MRCP (Figure 1). Next, S-MRCP has all of the contraindications of MRI, i.e. magnet-incompatible patient metalware, claustrophobia, as well as those of secretin, i.e. hypersensitivity etc. Up to 5% of patients may experience adverse effects, mainly nausea, vomiting, flushing and/or abdominal pain, after secretin injection.²⁷ Therefore, some centres inject a test dose of secretin before the examination, to make certain that the patient can tolerate it.²⁰ In our institution, we inject secretin slowly, which has proven effective in keeping adverse reactions negligible. Although the literature mentions acute pancreatitis (AP) as a relative contraindication to secretin administration, some centres, including ours, do not adhere to

Figure 1. The value of CT in depicting intraductal stones in a 70-year-old male with chronic pancreatitis. Three selected images: MRCP, unenhanced CT, and ERCP. (a) Coronal T_2 MRCP image, 5 min after secretin administration. A significant stenosis of the PD within the body, with upstream dilatation (arrows) is observed. Differentiation between a mass- or stone-based upon MRCP is not possible. (b) Axial unenhanced CT image shows at least two concrements. The largest, measuring 6 mm, is intraductal, causing the abrupt cut-off of the main PD (arrow head). (c) ERCP image shows the cannulation of the major papilla with visualization of the proximal part of the Wirsung duct and the abrupt cut-off (arrow head) of the contrast material due to the obstruction caused by the concrement, and thus, the excretion of the contrast material occurs via the Santorini duct. During this procedure, the concrement was extracted (not shown). ERCP, endoscopic retrograde cholangio-pancreatography; MRCP, magnetic resonance cholangiopancreatography; PD, pancreatic duct.

this.²⁰ We believe that the potential harm from delayed diagnosis is greater than that of side effects. Furthermore, in this specific cohort, we have not witnessed any adverse reactions. However, as a safety precaution, we do such examinations only on inpatients,

Figure 2. A 54-year-old male with normal pancreatic function. Four selected images before and after secretin injection of 20 serial, heavily T_2 weighted, long TE HASTE MRCP images, obtained over 10 min, show normal filling of the duodenum with opacification beyond the genu. (a) Scout coronal MRCP image shows both the dorsal (long arrow) and ventral pancreatic duct (short arrow) draining into the major papilla. Note a 1 cm cystic lesion (thick arrow), consistent with a side-branch IPMN in the pancreatic tail, with connection to the main PD. High signal intensity material within the stomach lumen and duodenum is due to residual fluid (arrow heads). (b, c) Coronal MRCP images, 3 and 5 min after secretin administration, show clear delineation of the entire main pancreatic duct, with enlargement of the calibre and increase in signal intensity of the Wirsung (long arrow) and Santorini pancreatic ducts (short arrow) due to secretin stimulation. There is moderate duodenal filling, limited to the duodenal bulb (*). (d) 10 min after secretin administration, the Wirsung (long arrow) and Santorini (short arrow) ducts are again reduced in diameter and signal intensity, returning to their baseline conditions due to their normal elasticity. There is duodenal filling up to the duodenojejunal junction (Treitz angle*), indicating normal exocrine function. IPMN, intraductal papillary mucinous neoplasm; MRCP, magnetic resonance cholangiopancreatography; PD, pancreatic duct.

so that medical treatment can be promptly given, even in the event of a delayed adverse reaction.

Image interpretation

Normal pancreatic duct

In healthy patients, the main PD is smooth, tapers at the tail, and measures less than 3 mm in the body of gland.^{27,30} A non-diseased main PD should distend 1–2 mm in response to secretin and return to baseline within 10 min, as its contents drain into the duodenum (Figure 2).³⁹ However, in judging the main PD diameter, the patient's age should be taken into account since the size of the PD increases with age.⁴⁰ Even so, in patients <60 years, the PD should not exceed 3 mm in the head and body of the pancreas.³⁰ A dynamic S-MRCP examination should be evaluated for: (a) elasticity, *i.e.* amplitude of distention of the PD; (b) time to peak PD diameter; (c) presence or absence of prolonged dilatation (during the 10 min post-secretin administration); (d)

Figure 3. Impaired pancreatic exocrine function in a 53-year-old female with CP and recurrent upper abdominal pain. Note, the multiple saccular structures on the left of the image, consistent with renal cysts as incidental finding. (a) Scout coronal MRCP image shows slightly narrowing (secondary to CP) of Wirsung's duct (arrows) with a small pseudocyst in the pancreatic tail (arrow head). (b) 10 min after secretin administration, Wirsung's duct (arrows) remains unchanged in calibre due to loss of its elasticity and there is no duodenal filling (*) consistent with exocrine dysfunction. CP, chronic pancreatitis; MRCP, magnetic resonance cholangiopancreatography.

presence of side-branches (their number, location, morphology, and the presence or absence of communication with cystic lesions); and (e) sphincter Oddi dysfunction.⁴¹ One caveat is that the PD calibre should not increase in response to secretin administration in patients who have undergone prior pancreatic sphincterotomy unless post-op scar tissue has formed causing some degree of obstruction.²⁰

Duodenal filling evaluation

It is proven that the volume of fluid secreted from the pancreas, in response to secretin, provides a functional analysis of its exocrine reserve. In CP, both endocrine (e.g. insulin production), and exocrine function (e.g. bicarbonate secretion) decrease. Studies have found that quantification of the fluid accumulation in the duodenum and proximal small bowel correlates very well with the degree of CP.²⁷ In patients with normal exocrine function, after secretin administration, fluid promptly appears in the peri-ampullary duodenum, then fills and distends the duodenal bulb and progresses past the genu (Figure 2).^{20,27,30}

There are various approaches with which to evaluate the volume of secretion and rate of secretion.

First, Matos et al¹⁷ suggested a simple, qualitative grading system in which duodenal filling is defined as:

- Grade 0—no fluid is observed (Figure 3).
- Grade 1—fluid is limited to the duodenal bulb.
- Grade 2—fluid partially fills the duodenum up to the genu.
- Grade 3—fluid fills beyond the genu (Figure 2).

The lower the grade, the lower the bicarbonate concentration.^{39,42} Pancreatic exocrine function is considered impaired in any patient with <Grade 3. The main drawback of the Matos grading system is that it cannot differentiate between patients with early or established CP,³⁹ unlike two quantitative methods, which estimate both the rate and volume of secretions.^{22,23,27} For these functional, quantitative assessments of the pancreas, the mean secretory volume (MSV) can be calculated by drawing a region of interest (ROI) around the fluid-filled duodenum and proximal

jejunum on each image of the post-secretin coronal sequence. The area (cm²) of the ROIs are then added and the total multiplied by the slice thickness to obtain the total fluid volume (ml) secreted in response to secretin. In patients without exocrine function impairment, the MSV should be approximately 57 ml, and an MSV of 50 ml is equivocal. In patients with suspected pancreatitis, an MSV of 40 and 22 ml suggests early and established disease, respectively.²⁷

Bali et al quantified the pancreatic exocrine function using S-MRCP by calculation of pancreatic flow output and total excreted volume. Pancreatic flow output and total excreted volume were derived from a linear regression between MR-calculated volumes and time.⁴³ However, despite validation of these techniques, we do not use it in our routine work because such calculations are quite time-consuming and require special applications.

Clinical indications for MRCP

S-MRCP is an established tool for: (1) the detection of anatomic variations and/or anomalies in patients with recurrent pancreatitis but without risk factors (such as alcohol abuse or biliary causes); (2) the evaluation of a morphological cause of pancreatitis or disconnected PD syndrome in patients with severe AP; (3) the differentiation between adenocarcinoma and its mimickers, i.e. autoimmune or groove pancreatitis (GP) ("duct-penetrating" sign); (4) the determination of whether a cystic lesion arises from or lies in proximity to the PD; (5) in cases where ERCP has failed to show the entire PD or to define the length of a tight stricture, i.e. as a road map before therapeutic ERCP (Figure 4); (6) the evaluation of the patency of the pancreaticoenteric anastomosis in post-pancreatectomy patients; and (7) an estimation of reserve exocrine function in post-sphincterotomy patients.^{18–20,44}

Pancreas divisum

Pancreas divisum is due to failure of the dorsal and ventral buds of the PD to fuse during embryologic development. In more than 90% of individuals, the proximal one-third of the dorsal PD regresses as it fuses with the ventral duct, forming the main PD.^{19,45} Pancreas divisum is found in 15–20% of patients with unexplained pancreatitis.³² There are two main types of pancreas divisum, complete and incomplete.⁴⁶ In complete pancreas divisum, the small ventral duct, or duct of Wirsung, drains via the major papilla, and the large dorsal duct, or duct of Santorini, drains via the minor papilla. With incomplete pancreas divisum, small rudimentary branches connect the ventral and dorsal PDs. Sometimes, the major papilla is non-patent, so the entire PD drains via the minor papilla.^{19,45,47} All of these conditions cause prolonged stasis of pancreatic juices within the PD, and thus, may have similar manifestations.^{47–50} S-MRCP has a very high diagnostic accuracy for pancreas divisum (Figure 5); sensitivity is between 73 and 100%, while specificity approaches 100%.^{20,51,52}

Santorinicele and wirsungocele

S-MRCP allows clear delineation of Santorinicele and Wirsungocele; there is a focal saccular distention of the terminal parts of the dorsal (Santorini) (Figure 6) or ventral (Wirsung) ducts where they enter into the duodenal wall.²⁰ Some authors think that Santorinicele or Wirsungocele may be formed as a result of

Figure 4. The value of S-MRCP as a road-map, pre-ERCP or after unsuccessful ERCP, in 56-year-old female who had undergone partial pancreatectomy and pancreaticojejunal anastomosis as a child due to a car accident. The patient had forgotten this history and did not tell the gastroenterologist. The patient recently presented with recurrent upper abdominal pain and signs of chronic pancreatitis. ERCP was unsuccessful, and she was referred for S-MRCP for further evaluation. (a) On the scout coronal MRCP image, the tail and adjacent part of the body of the main pancreatic duct and side branches (arrows) appear dilated. The remainder of the main duct is not visualized, after an abrupt transition point (arrow head). (b) Coronal MRCP image, 8 min after secretin administration, clearly shows a high-grade, short stenosis at a pancreaticojejunal anastomosis (arrow head). However, a large amount of pancreatic juice has filled the jejunum and adjacent small bowel (**). Due to the anastomotic stenosis, the remnant pancreatic duct is persistently enlarged (arrows). Due to its loss of elasticity, it does not return to its baseline calibre, explaining the symptoms of chronic pancreatitis. ERCP, endoscopic retrograde cholangio-pancreatography; MRCP, magnetic resonance cholangiopancreatography; S-MRCP, secretin-enhanced MRCP.

impaired flow across the minor papilla, with increased intraluminal pressure in combination with weakness of the distal duct wall.^{19,52,53} Patients with the combined pathology, *i.e.* pancreas divisum/Santorinicele/Wirsungocoele have an increased risk of recurrent acute pancreatitis (RAP).^{53,54}

Anomalous pancreaticobiliary junction

S-MRCP may help in the detection of this congenital anomaly, a malunion of the main PD and CBD before they enter the duodenal wall.⁵⁵ Because there is an absence of a true sphincteric muscle, these patients are prone to reflux into the PD and

Figure 5. Pancreas divisum in a 55-year-old female referred to MR examination because of nonspecific upper abdominal pain. (a) Scout coronal MRCP image shows that the main pancreatic duct is barely visible in its entire length (arrows). The common bile duct (thick arrow) and the main pancreatic duct (arrows) appear to intersect one another. (b) Coronal MRCP image acquired 5 min after secretin administration shows that the diameter of the main pancreatic duct is markedly increased, with improved delineation of the ductal anatomy (arrows). The main pancreatic duct drains into the minor papilla (arrow head), which then empties into the duodenum. Findings are definitive for pancreas divisum. MRCP, magnetic resonance cholangiopancreatography.

CBD, predisposing them to bouts of pancreatitis and cholangitis, as well as stone formation.⁵⁶ They are also at increased risk of biliary tract or gallbladder cancer.^{45,57,58} On the post-secretin images, one may see gallbladder distention, an indirect sign of reflux. This malunion, however, may not be seen if it is too short. However, indirect reflux should be sufficient to make a confident diagnosis. Another confident sign is the direct reflux of hepatobiliary contrast agent into the PD using combined secretin and gadoteric acid-enhanced MRI (Figure 7) in this very short APBJ.

Annular pancreas

This is a congenital anomaly due to failed or incomplete rotation of a portion of the ventral pancreas during embryological development.⁵⁵ Although S-MRCP depicts an annular duct encircling the descending duodenum,⁴⁵ this diagnosis can be made on routine pancreas MRI.

Acute pancreatitis (AP)

AP, usually due to alcohol abuse or biliary stones, is a clinical diagnosis. According to the Atlanta Criteria, imaging is only required if the clinical course is severe, or if the patient has no risk factors for pancreatitis.⁵⁹ CT is usually the study of choice. However, MRI may be performed if there is uncertainty about the aetiology of AP or in the setting of recurrent pancreatitis.^{14,29} S-MRCP should be added if: (1) there is suspicion that a congenital anomaly caused the AP (Figure 6); or (2) there is concern about the integrity of the PD, *i.e.* fistula, rupture, or discontinuity of the main PD. S-MRCP may show the extent and location of the leak and whether or not it communicates with a pseudocyst to optimize patient management. In the case of a disconnected PD syndrome, S-MRCP shows intrapancreatic fluid collection along the expected course of the main PD (Figure 8), with PD obstruction at the level of this fluid collection.^{19,20,30} Also, S-MRCP helps to characterize a stricture that could be revealed by AP.

Figure 6. Pancreas divisum with Santorinicele in a 28-year-old female with recurrent episodes of pancreatic-like abdominal pain. (a) Scout coronal MRCP image shows the main drainage of the pancreas through the dominant dorsal pancreatic duct of Santorini. The main pancreatic duct is depicted in its entirety (thin arrows). (b) Coronal secretin-enhanced MRCP image 3 min after injection, shows pancreas divisum. Small saccular dilatation of the terminal part of the dorsal pancreatic duct (arrow head) represents a Santorinicele. (c) On secretin-enhanced MRCP image, obtained 10 min after secretin injection, there is intense diffuse parenchymal hyperintensity (short arrows) indicating mild diffuse acinarization (blush). (d) MRCP cropped and magnified obtained 10 min after secretin injection, shows the swelling at tip of main pancreatic duct (arrow head), which is consistent with "Santorinicele." Secreted fluid has moved into distal duodenum (arrows). MRCP, magnetic resonance cholangiopancreatography.

Recurrent acute pancreatitis (RAP)

Strictures, either post-surgical or post-traumatic, as well as inadequate drainage of pancreatic fluid, are the main cause of RAP.^{44,60} Hereditary pancreatitis is a diagnosis of exclusion in which S-MRCP is very helpful.² S-MRCP is ideal, in such settings, because it can visualize the PD beyond a tight stricture (Figure 9), or show the drainage of the main PD into the minor papilla, *i.e.* pancreas divisum and accessory ducts, as mentioned above (Figure 5). Although the connection between RAP and pancreas divisum is a current topic of discussion, some studies have shown a higher frequency of pancreas divisum in patients with RAP.⁴⁴ In addition, it was reported that sphincterotomy at the minor ampulla, in cases of divisum, reduces the frequency of RAP.^{44,61} S-MRCP may show the focal cystic dilation of the accessory or the main PD, *i.e.* Santorinicele or Wirsungocoele (Figure 6).²⁷ Furthermore, a blush (acinarization) of the pancreatic parenchyma may be seen on post-secretin, T_2 weighted S-MRCP images due to elevated pressure in the side-branches, which leads to distention of pancreatic

Figure 7. Sphincter of Oddi dysfunction in a 46-year-old female referred for MRI because of recurrent upper abdominal pain. (a) Scout coronal MRCP image shows that the common bile duct (arrow) and the main pancreatic duct (arrow head) appear to drain into the major papilla, as is normal. (b) Coronal MRCP image, 5 min after secretin administration. There is severe distension and increased signal intensity of the main pancreatic (arrows) and common bile ducts (arrow heads), with sufficient filling of the whole duodenal C-loop, indicating normal exocrine function (**). (c) Coronal MRC T_1 weighted image, 20 min after gadoteric acid administration, shows excretion of the hepatobiliary contrast agent into the CBD (arrow heads), with contrast reflux into the main pancreatic duct (arrows), indicating an APBJ associated with a sphincter of Oddi dysfunction (*). APBJ, anomalous pancreaticobiliary junction; MRCP, magnetic resonance cholangiopancreatography.

acini with fluid (Figure 6). That may be a sign of impaired outflow, related to AP.⁵² Moreover, S-MRCP may show a reduction in exocrine function in patients with RAP.⁴⁴

Chronic pancreatitis (CP)

If not treated early, recurrent pancreatitis can progress to CP in which fibrous tissue gradually replaces the glandular elements

Figure 8. Pancreatic duct rupture in a 20-year-old male referred for MRI because of necrotic pancreatitis and suspicion of main pancreatic duct discontinuity. (a) Scout coronal MRCP image. The pancreatic duct is barely visible. Residual fluid within the stomach and duodenal loop appear high in signal intensity (**). (b) Post-secretin coronal MRCP image, after oral administration of Lumirem®. The high signal intensity from gastric and duodenal liquid disappears (white **). The main pancreatic duct is not visible and there is no normal filling of the duodenal C loop (**). Instead, the intrapancreatic fluid collection, *i.e.* the drainage of the pancreatic juice, is seen along the expected course of the main pancreatic duct in the pancreatic tail adjacent to the stomach (arrow heads). This implies a main pancreatic duct rupture as a result of necrotic pancreatitis. MRCP, magnetic resonance cholangiopancreatography.

Figure 9. Recurrent pancreatitis progressed to chronic pancreatitis with impaired pancreatic exocrine function in a 42-year-old female with recurrent upper abdominal pain. She was referred for MRI because the gastroenterologist could not pass the orifice of the main pancreatic duct during ERCP. (a) Initial examination in 2014 with a coronal MRCP image, 5 min after secretin administration. The main pancreatic duct is mildly increased in calibre (arrows). Contour irregularities and slight stenoses of the duct are seen in the region of the pancreatic head (arrow heads). There is little duodenal filling, limited to the duodenal bulb (**), comparable with early-stage recurrent pancreatitis. (b) Follow-up examination in 2016. Coronal secretin-enhanced MRCP image, at 10 min. There has been an interim increase in the main pancreatic duct diameter and the contour irregularities are worse. Multiple dilated side-branches are seen in the head and body of the pancreas (arrows). The pancreatic duct remains dilated rather than returning to its baseline calibre and the stenoses within the head and uncinate process of the pancreas (arrow heads) have progressed. Duodenal filling is nearly absent (*), suggesting pancreatic exocrine dysfunction as seen in late-stage recurrent pancreatitis. ERCP, endoscopic retrograde cholangio-pancreatography; MRCP, magnetic resonance cholangio-pancreatography.

of the pancreas.²⁷ In the past, CP was diagnosed and graded by ERCP, according to the Cambridge classification.⁶² However, S-MRCP has now replaced its invasive counterpart. The diagnosis of CP is made on S-MRCP if any of the following findings are seen:^{20,27,30}

- $\geq$ three side-branch ducts, carried over from the Cambridge criteria (Figure 4);
- strictures and/or sacculations of the main PD (Figure 9);
- loss of the main PD tapering within the pancreatic tail (Figure 3);
- the main PD is rigid in response to secretin (Figure 3);
- duodenal filling is reduced and/or delayed (Figure 9).

However, some authors²⁶ find that the use of secretin will not help in diagnosing CP. Since the PD system is already dilated, the elasticity of the main PD walls is lost and the pancreatic juice production is reduced or lost. In these patients, however, secretin might be useful in assessing significant stenoses of the main PD and in non-invasively assessing the pancreatic exocrine reserve by analysing the amount of pancreatic juice collected within the duodenal lumen.

Figure 10. A 53-year-old-woman with established autoimmune pancreatitis, before (a–b) and after (c–d) treatment. (a) Axial T_2 weighted DWI FS ($b = 50$) shows diffuse enlargement and oedema of the whole pancreatic gland, with loss of the normal pancreatic lobulations (***). (b) Scout coronal MRCP examination shows multiple stenoses of Wirsung's duct due to autoimmune pancreatitis (arrows), with a dominant stenosis in the body of the pancreas (arrow head). (c) Axial DWI T_2 FS ($b = 50$) shows significant decrease of the swelling and resolution of oedema of the pancreatic gland (***). (d) Post-treatment coronal MRCP images, 5 min after secretin administration. Both dominant and trivial stenosis (arrows and arrow head), seen in (b) have resolved (duct-penetrating sign) and there is greater filling of the duodenum at this time. DWI, diffusion-weighted imaging; FS, fatsat; MRCP, magnetic resonance cholangiopancreatography.

The morphological changes of CP do not necessarily correlate with the degree of exocrine dysfunction. Therefore, to establish the diagnosis of CP, one should rely on both morphological and functional features.^{27,63} Moreover, the presence of normal duodenal filling after secretin administration does not exclude mild exocrine impairment.³⁰

Specific types of pancreatitis

Autoimmune pancreatitis (AIP)

AIP is an autoimmune reaction in/around the PD, which results in inflammation and fibrosis.⁶⁴ At least two forms of AIP exist: Type 1, which is part of an IgG4 systemic disease; and Type 2, which has granulocytic epithelial lesions on histology and represents a primary pancreatic disorder.⁶⁵ Diagnosis is usually based upon laboratory tests, imaging findings, histology, and response to corticosteroid therapy.^{64,66,67} Whereas, CT or MR show diffuse pancreatic enlargement in Type 1 AIP, focal swelling, usually of the head, may occur in Type 2 AIP.⁶⁸ S-MRCP may be useful in AIP Type 1 or 2, in particular, if there is any concern that the focal pancreatic mass is really an adenocarcinoma.²⁶ S-MRCP, by showing the patency and elasticity of the PD in response to secretin, *i.e.* the “duct-penetrating” sign, can largely exclude adenocarcinoma^{30,69,70} (Figure 10). Conversely, most patients with pancreatic cancer have an abrupt cut-off of the main PD.⁷⁰ Furthermore, follow-up S-MRCP can confirm the diagnosis of AIP, in equivocal cases, showing that the PD calibre increases or returns to normal,

Figure 11. A 46-year-old male with established chronic groove pancreatitis, who presented with several episodes of acute abdominal pain. (a) Axial T_1 W GRE FLASH 2D shows a large, inhomogeneous 3 cm mass in the pancreatic head and uncinate process (arrow heads). (b) Scout coronal MRCP image. The pancreatic duct is barely visible (arrows). Huge fluid collections in the stomach and less pronounced in the duodenal loop appear of high signal intensity (*). (c) Coronal MRCP images, 5 min after secretin administration, show enlargement and an increase in signal intensity of the main pancreatic duct, with irregularity along its entire length, as well as some dilated side-branches (arrows). Note that the duct traverses the mass, *i.e.* the “duct-penetrating” sign. There is mild duodenal filling along the entire duodenal bulb (**). (d) Coronal MRCP, 10 min after secretin administration. Wirsung’s duct is reduced in calibre and signal intensity, returning to its baseline diameter (arrows), and there is duodenal filling up to the distal part (**). 2D, two-dimensional; MRCP, magnetic resonance cholangiopancreatography.

in response to steroid therapy (Figure 10), thus excluding cancer.⁷¹

Groove pancreatitis (GP)

GP is a rare segmental CP confined to the pancreatoduodenal groove, *i.e.* a potential space bordered by the head of the pancreas, duodenum, and CBD.⁷² Because GP occurs in the same patients at risk for pancreatic adenocarcinoma, the diagnosis of GP is extremely challenging⁷³ (Figure 11). Once again, the “duct-penetrating” sign on S-MRCP can help confirm GP by showing the patent PD coursing through the inflamed pancreatic head⁶⁹ (Figure 11d). The ancillary finding of small pseudocysts in the duodenal wall further confirms the diagnosis of GP, also known as cystic dystrophy of the duodenal wall.²

Solid pancreatic tumours

S-MRCP may help to differentiate an inflammatory pancreatic mass from pancreatic carcinoma. Whereas, patency of the PD (“duct-penetrating” sign) implies the presence of a soft mass, an abrupt obstruction of the PD (“double duct” sign, if the CBD is simultaneously seen) suggests a rigid mass^{18,30} (Figure 12). However, a patent PD on S-MRCP does not exclude pancreatic adenocarcinoma located remote from the PD. S-MRCP may also be useful in showing the proximity of a tumour to the main PD lesions, including neuroendocrine tumours (NETs), side-branch intraductal papillary mucinous neoplasms (IPMNs),

Figure 12. Ductal adenocarcinoma. A 62-year-old female with an obstructed main pancreatic duct at the level of the body of the pancreas. Following surgical resection, histopathology confirmed the presence of a small T_1 adenocarcinoma. (a) Axial post-contrast T_1 weighted image shows a small lesion at the level of the pancreatic body with an abrupt cut-off of the main pancreatic duct (arrow head). (b) On the scout coronal T_2 MRCP image, the main pancreatic duct is dilated and its contour irregular within the body of the pancreas (arrows). (c) Coronal T_2 MRCP image, 3 min after secretin administration, shows better visualization of the entire main pancreatic duct (arrows) and of its abrupt cut-off (arrow head). (d) Coronal T_2 MRCP, 10 min after secretin administration, shows a persistent stenosis (arrow head), without the “duct-penetrating” sign. The remaining Wirsung’s duct is reduced in calibre and signal intensity, returning to its baseline condition (arrows). The duodenum (***) is opacified up to the duodenojejunal junction (Treitz angle) (*). The upstream pancreatic duct is markedly dilated (thick arrows). MRCP, magnetic resonance cholangiopancreatography.

and even mucinous cystic neoplasms more than 10 mm away from the main PD, which can be removed by enucleation rather than surgical resection.⁷⁴ S-MRCP can be used to measure the distance and even to guide a stent placement in the PD to prevent post-enucleation fistula.⁷⁵ Furthermore, S-MRCP may be able to distinguish between different solid pancreatic tumours, such as NETs, lymphoma, and angiomyolipoma from adenocarcinoma. This ability is of high clinical relevance. Although all these tumours may appear similar on all imaging modalities, it is, based on our experience, in the vast majority of cases, only adenocarcinoma that can completely obliterate the PD. All other tumours may demonstrate the “duct-penetrating” sign (Figure 13). The additional MR features, including fat content on in- and opposed-phase images, diffusion restriction, and arterial-phase hypervascularity, can help us to favour the diagnoses of angiomyolipoma, lymphoma, and NET (Figure 13), respectively. Finally, S-MRCP may help exclude a solid pseudopapillary epithelial neoplasm (SPEN), which has a predilection for young females and does not affect the PD. This tumour represents the transition between solid and cystic tumours of the pancreas and does not cause obliteration of the pancreatic duct⁷⁶

Figure 13. A 29-year-old female with a 3 cm solid mass within the head of the pancreas (arrows) without duct obstruction. (a) Axial T_1 2D GRE FLASH image shows a 3 cm solid mass within the pancreatic head with compression of the pancreatic parenchyma, but without duct dilatation (arrows). (b) Coronal T_2 MRCP image, 5 min after secretin administration confirms the uniform calibre of the main pancreatic duct along its whole length *i.e.* the “duct-penetrating” sign (arrows), and duodenal filling up to the genu inferius, indicating sufficient exocrine function (**). (c) Axial PET-CT image after administration of ^{18}F -fluorodopa shows a 3 cm tracer-avid solid mass within the pancreatic head (arrows), indicating a NET. 2D, two-dimensional; MRCP, magnetic resonance cholangiopancreatography; NET, neuroendocrine tumour.

Cystic pancreatic lesions

S-MRCP may have a role in the differentiation of cystic pancreatic lesions by showing their relationship to the PD.²⁰ If the lesion arises from the PD, it is an IPMNs, either side-branch (Figure 14), main duct (Figure 15), or mixed type.⁷⁷ Of course, a pseudocyst may show a direct connection to the PD, but, in this case, the clinical history and post-pancreatitis status should be known. Otherwise, the differential diagnosis includes pseudocyst. However, the study results are conflicting, with some authors finding that there is no added value for S-MRCP in the differentiation of pancreatic cystic lesions.⁷⁸ Interestingly, in the majority of cases, there is no increase in the size of the IPMN

after secretin administration due to mucus plugging between the non-pathologic part of the duct and the tumour.¹⁹ If there is no connection between the cystic lesion and the PD, the lesion is unlikely to be IPMN.²⁷ However, the following caveat is worth mentioning. If, on serial images, the SI of a cyst continues to increase post-secretin stimulation, this is proof of its communication with the PD, implying it is an IPMN, rarely a pseudocyst.²⁷ On the contrary, mucinous and serous cystic neoplasms, and rarely, congenital cystic lymphangioma, may lie in very close proximity to the PD, but have no direct contact with it. Furthermore, factoring in the age and gender of the patient,⁷⁹ as well as the clinical history, morphological appearance, and the presence

Figure 14. Multiple side-branch IPMNs in a 71-year-old female baseline (a), and 8 min (b), MIP reconstruction, after secretin administration. (a) Coronal T_2 MRCP image shows multiple intercommunicating cystic lesions within the uncinate process of the pancreas and along the entire pancreatic duct (arrows), as well as a solitary cystic lesion in the tail of the pancreas (arrow head). (b) Coronal T_2 MRCP image, 8 min after secretin administration. The pancreatic ductal system is better-delineated and it is also possible to appreciate the relationship between the lesions and Wirsung's duct (arrows). IPMN, intraductal papillary mucinous neoplasm; MRCP, magnetic resonance cholangiopancreatography.

Figure 15. An 83-year-old female with IPMN of the main-duct type and symptoms of recurrent chronic pancreatitis, who presented with upper abdominal pain. (a) Axial T_2 weighted image with FS image shows a 3 cm cystic mass at the level of the pancreatic body and tail (arrows). (b) Scout coronal MRCP image suggests that this lesion communicates with the main pancreatic duct in the tail. The relationship between cystic lesions and the main pancreatic duct in the body is unknown. (c) Coronal MRCP image, 3 min after secretin administration, clearly shows a connection of this cystic mass with the Wirsung's duct (arrow head), indicating a segmental IPMN of the main-duct type (arrows). Note the diffuse multiple tiny cystic lesions of the liver ("starry sky"), indicating Von Mayenburg complexes or hamartomas (**). FS, fatsat; IPMN, intraductal papillary mucinous neoplasm; MRCP, magnetic resonance cholangiopancreatography.

or absence of direct communication with the PD, can help to make the correct diagnosis.

Finally, S-MRCP is not indicated for the follow up of an IPMN of the side-branch type. The exception is for the follow up of a main duct-type IPMN (Figure 15) where visualizing the progression or postoperative recurrence of tumour is based on PD evaluation.

Postoperative patients

Pancreatectomy (especially exceeding $\geq 30\%$ reduction of pancreatic tissue) may lead to a decrease of endocrine and exocrine pancreatic function, with consequent metabolic and nutritional disorders.^{80–83} Atrophy of the remaining pancreatic parenchyma is common. These complications could be secondary to the deregulation of pancreatic neurohormonal stimulator mechanisms or to stenosis of the pancreatojejunal or pancreatogastric anastomosis.⁸³ S-MRCP is indicated to check the patency and contour of the pancreatojejunal anastomosis.⁸⁴ The jejunal filling volume is semi-quantitatively evaluated at 10 min and is

graded according to the method of Matos *et al.*¹⁷ In patients who have undergone a sphincterotomy, S-MRCP may be performed to assess exocrine function. Even in the absence of increased sphincter tone, pancreatic secretions may suffice to distend the PD.⁸⁵ (Figure 16)

S-MRCP in children

Secretin can be administered in an off-label use, according to specific indications, in paediatric patients.⁸⁶ This is a fast, non-invasive method to evaluate the PD in children. A normal S-MRCP may obviate the need for ERCP (Figure 9). Abnormalities detected on S-MRCP can then direct further interventions.⁸⁷

CONCLUSIONS

S-MRCP is a safe, noninvasive technique for the evaluation of PD anatomy and pancreatic diseases, and provides morphological and functional information simultaneously. Moreover, it is highly sensitive for early disease detection, since the PD is the

Figure 16. The value of S-MRCP in assessing exocrine function after sphincterectomy. (a) Coronal T_2 MRCP image, of a 50-year-old female patient who underwent sphincterectomy. The baseline MRCP shows the moderate dilated PD (arrows) and CBD (arrow heads), as well as the residual fluids in the stomach (*). (b) Coronal MRCP image, 3 min after secretin administration, shows better delineation of the entire main pancreatic duct, with only slight enlargement of the calibre and moderate increase in signal intensity of the Wirsung duct (arrows) due to secretin stimulation. There is moderate duodenal filling, limited to the duodenal bulb (arrow heads). Note the decrease of fluid signal in the stomach after ingestion of 300 ml LumiVision (*). (c) 10 min after secretin administration, the Wirsung duct (arrows) is again slightly reduced in diameter and signal intensity, returning to baseline conditions due to the decreased elasticity. However, there is duodenal filling up to the duodenojejunal junction (Treitz angle*), indicating normal exocrine function after sphincterectomy. PD, pancreatic duct; S-MRCP, secretin-enhanced MRCP.

origin of most pancreatic disorders. An understanding of the adequate indications, an optimal examination protocol, and an

exact interpretation of the findings enable the correct diagnosis and management of the patient.

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