Secretin-enhanced MR Imaging of the Pancreas

Secretin is a hormone that stimulates the exocrine pancreatic secretion of bicarbonate-rich fluid from the acinar cells of the pancreas that accumulates within the pancreatic duct lumen. The exogenous administration of secretin improves the visualization of pancreatic ducts at magnetic resonance (MR) cholangiopancreatography (MRCP), because of an enlargement of the pancreatic duct system and an increase of the fluid content within the lumen of the pancreatic ducts, responsible of an increase of MR signal. In this review, the technique of secretin-enhanced MRCP, which has the aim to depict the whole pancreatic duct system, the biliary tree, the major and minor papillae, and the duodenum, will be described. Because of the anatomic contiguity between the pancreas and the gastrointestinal tract, the presence of fluid within the stomach may overlap with the pancreatic duct system and therefore the pancreatic duct may be difficult to visualize, representing a potential source of diagnostic pitfalls. The technique to reduce the signal intensity of the static fluid present within the stomach and in the duodenal lumen is also described. The technique of secretin administration will be illustrated, with emphasis on the synchronization of secretin administration and MR image acquisition. Furthermore, the frequency and number of MRCP images necessary to achieve a temporal resolution adequate to visualize the physiologic changes in the pancreatic gland, induced by the administration of secretin, is described. The assessment of pancreatic, morphologic, and functional response to the administration of secretin, as depicted on MRCP images, will be illustrated. Finally, the indications for secretin-enhanced MRCP will be discussed to define which patients will benefit from secretin-enhanced MR imaging for their treatment planning.

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In recent years, magnetic resonance (MR) imaging has increased its role in the detection and characterization of pancreatic diseases. This is most likely due to the capability of MR imaging to simultaneously assess the pancreatic parenchyma and the pancreatic and bile duct systems. This can be achieved by obtaining cross-sectional MR images by using breath-hold T1-weighted gradient-echo sequences performed as two- or three-dimensional gradient-echo, fat-suppression techniques; T2-weighted half-Fourier pulse sequences; diffusion-weighted imaging; and dynamic contrast material–enhanced imaging following the administration of gadolinium chelates that are able to depict and characterize focal pancreatic masses and evaluate diffuse pancreatic diseases. Furthermore, MR cholangiopancreatography (MRCP) is able to diagnose pancreatic and biliary duct disorders in a noninvasive manner, and nowadays MRCP has replaced diagnostic endoscopic retrograde cholangiopancreatography (ERCP) to better help select patients who may benefit from therapeutic procedures, such as endoscopic sphincterotomy, stone removal, or stent insertion (1).

The strengths of MR imaging compared with other diagnostic imaging modalities, such as ultrasonography (US), are the larger field of view and the ability to acquire high-quality images independent of the patient’s body habitus. Compared with computed tomography (CT), the advantages of MR imaging are due to the higher contrast resolution, the ability to directly image the whole pancreatic duct system producing a cholangiography-like image, and the lack of ionizing radiation.

MRCP provides valuable anatomic information of the pancreatic and the biliary ducts; but, in basal conditions, does not give any functional assessment of biliary excretion and pancreatic exocrine function. Dynamic changes of the Vaterian sphincter complex causing biliary outflow obstruction can be diagnosed by serially acquiring MRCP images that enable one to differentiate bile duct stenosis from bile duct contraction (2). In addition, secretin-enhanced MRCP adds functional and anatomic information about the pancreatic ducts and pancreatic exocrine reserve.

In this review, the technique of secretin-enhanced MRCP, including the dose and the method of administration of secretin, will be described. In addition, we will review the analysis of secretin response, and the indications for secretin-enhanced MRCP will be discussed.

## Essentials

- Secretin-enhanced magnetic resonance cholangiopancreatography (MRCP) is indicated in patients with chronic asymptomatic hyperenzymia, recurrent acute pancreatitis, sphincter of Oddi dysfunction, anatomic variants, chronic pancreatitis, and main pancreatic duct stenosis.
- Secretin-enhanced MRCP images are obtained along a coronal or coronal-oblique plane that encompasses the whole pancreatic duct system, the biliary tree, the duodenum, and both papillae; secretin is administered at a dose of 1 clinical unit per kilogram of body weight (0.7–1 mL/10 kg body weight), and MRCP images are acquired with a temporal resolution of 30 seconds for 10 minutes.
- Secretin-enhanced MRCP is able to depict the morphology and enlargement of the main pancreatic duct and of the side branches, improve the visualization of endoluminal filling defects, and evaluate pancreatic output of juice through the duodenal papillae and duodenal filling.

## MRCP Technique

The basic principle underlying MRCP is to produce high contrast resolution between the fluid-filled pancreatic ducts and the adjacent tissues through the use of T2-weighted imaging with very long echo times (> 600 msec). At these values, the stationary tissues and flowing fluids (which have a short T2 relaxation time) will produce little or no signal because the protons are completely relaxed; whereas stationary fluids, which have a long T2 relaxation time (longer than the echo time), will produce high signal intensity because the protons are still relaxing. The result is an image that resembles those obtained by means of direct cholangiography in a totally noninvasive manner (Fig 1).

Heavily T2-weighted images were originally obtained by using a gradient-echo balanced steady-state free precession technique (3,4). The RARE pulse sequence with a long echo time was then introduced shortly after (5). It had the advantages of a higher signal-to-noise and contrast-to-noise ratios and was less sensitive to motion and susceptibility artifacts than the gradient-echo techniques. Nowadays, half-Fourier pulse sequences are the most frequently used pulse sequences to obtain MRCP images because of their rapid acquisition time, which enables MR image acquisition during breath hold, virtually eliminating motion artifacts (6). To achieve rapid acquisition times, which are useful to obtain MRCP images, half-Fourier pulse sequences exploit the symmetry of the data in k-space, called Hermitian symmetry, which is a basic property of Fourier transformation. With half-Fourier pulse sequences, only slightly more than half of the k-space data of each image (~60) are acquired, the rest are mathematically reconstructed: The data of one-half of the k-space are used to generate the data of the other half. In this manner, the data acquisition time is significantly reduced (2–6 seconds) and MRCP images can be obtained during breath hold and can

Abbreviations:
ERCP = endoscopic retrograde cholangiopancreatography
MRCP = MR cholangiopancreatography
RARE = rapid acquisition with relaxation enhancement

Conflicts of interest are listed at the end of this article.
be repeated frequently in order to obtain dynamic images that are able to depict physiologic movements and/or responses with adequate temporal resolution (6).

Both breath-hold (using half-Fourier pulse sequences) and non–breath-hold techniques (with respiratory triggering or navigator techniques) have been used, with images obtained either as two-dimensional or three-dimensional acquisitions (7). A three-dimensional technique provides a higher signal-to-noise ratio, which can be exploited for thinner contiguous sections. Acquiring images with near isotropic voxels allows improved postprocessing of the images for multiplanar reconstruction, maximum intensity projection, and volume rendering. The introduction of faster gradients and a parallel acquisition technique has resulted in even greater spatial resolution and faster acquisition times (6,7).

MRCP images illustrating the pancreatico-biliary tree are acquired in the coronal or coronal oblique plane, giving a similar appearance as that obtained by direct cholangiography (ie, ERCP or percutaneous transhepatic cholangiography). The MR imaging/MRCP protocol, performed at our institution, is reported in Table 1.

Although MRCP has been widely applied in investigating the biliary ducts, the assessment of pancreatic duct by means of MRCP is less common because pancreatic disease is epidemiologically less frequent than biliary disease and the size of the main pancreatic duct is smaller than that of the common bile duct, resulting in lower signal-to-noise ratios and lower image quality because of the lower signal-to-noise ratio. The normal main pancreatic duct measures between 95 and 250 mm in length. Its diameter is greatest in the pancreatic head, with progressive narrowing toward the tail. An average normal diameter is 3–4 mm in the head, 2–3 mm in the body, and 1–2 mm in the tail (8). Progressive increase in overall diameter is seen with aging (9). As a result, the visualization of the pancreatic ducts on MRCP images is more challenging than visualizing the biliary ducts. As a matter of fact, non–secretin-enhanced MRCP can only clearly show the main pancreatic duct in the head, body, and tail of the gland in 79%, 64%, and 53%, respectively, of the patients (10).

Secretin-enhanced MRCP

To improve the sensitivity of MRCP to visualize the pancreatic duct system, the administration of secretin has been suggested during MRCP image acquisition (11–15). Secretin is a 27-amino acid polypeptide hormone secreted by S cells of duodenal mucosa in response to luminal acid that occurs after a meal. It stimulates the exocrine pancreatic secretion of bicarbonate-rich fluid and increases the amount of fluid within the ducts that subsequently reaches the duodenal lumen through the duodenal papillae (16).

In endoscopic manometric studies conducted in healthy volunteers, it has been shown that the secretin effect is transient and associated with an increase in pancreatic duct pressure after 1 minute, with an almost complete return to basal values within 5 minutes (17). The increase in pressure within the lumen of the pancreatic duct system is the result of an augmented endoductal fluid content and simultaneous increased tone of the sphincter of Oddi, which inhibits the release of fluid through the papilla of Vater during the first 5 minutes (18).

Table 1

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<th>MRCP Protocol: Pulse Sequences and Parameters</th>
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<td>Pulse Sequence</td>
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Note.—HASTE = half Fourier single-shot turbo spin-echo, 2D = two-dimensional.
The exogenous administration of secretin during MRCP image acquisition improves pancreatic duct visualization because it is responsible for two simultaneous and concomitant effects on the pancreatic gland and on the pancreatic ducts detectable on MR images: (a) increase in caliber of the pancreatic duct system due to the increased production of pancreatic juice produced by the acinar cells, primarily 3–5 minutes after administration; and (b) stronger MR signal because of higher number of protons within the lumen of the pancreatic duct due to increased amount of water and bicarbonates present in the pancreatic juice fluid (Fig 2) (12,14,19).

Therefore, secretin can be used as a contrast agent because it improves the visualization of the pancreatic ducts (Fig 2), but at the same time can provide functional information on the physiologic pancreatic response to secretin.

**Figure 2:** Dynamic secretin-enhanced MRCP in physiologic conditions. (a) Coronal fat-suppressed T2-weighted half-Fourier single-shot RARE (∞/1000) image in basal conditions shows normal-caliber intra-and extrahepatic bile ducts and the Wirsung duct (arrows). (b) Three minutes after intravenous administration of secretin in a dose of 1 clinical unit per kilogram of body weight, an enlargement and an increase in signal intensity of the Wirsung duct in all its segments (arrow) are visible. The accessory duct of Santorini is visible (arrowhead), as well as fluid within the duodenal bulb up to the genu inferior (∗). (c) Five minutes after secretin administration, duodenal filling due to pancreatic juice output through the major and minor papilla (∗) is visible. The Wirsung duct remains enlarged but shows an initial reduction in signal intensity (arrows). (d) Ten minutes after secretin administration, the Wirsung duct is reduced in size and signal intensity, returning to its basal conditions (arrows), and there is duodenal filling up to the duodeno-jejunal junction (Treitz angle) (∗).
As a matter of fact, when secretin is administered in combination with high-temporal-resolution MR imaging, pancreatic exocrine secretion can be visualized on MR images. Therefore, secretin-enhanced MRCP enables morphologic and functional evaluation of the pancreas.

To detect changes in the pancreatic ducts induced by secretin, MRCP images should be acquired dynamically with a temporal resolution of one or more images per 30 seconds for the first 5 minutes following the intravenous administration; whereas, between 5 and 10 minutes after the administration, the temporal resolution can increase up to one image per 60 seconds. It is also important to prescribe the appropriate coronal or coronal-oblique plane, with a section thickness that encompasses the entire pancreatic ducts: Wirsung and Santorini ducts, their emergence in the duodenum and the common bile ducts (Fig 2). For this purpose, two-dimensional half-Fourier pulse sequences are those that better meet this need because of their rapid acquisition time (2 seconds per slab); whereas three-dimensional MRCP have acquisition time of 2–4 minutes (depending on the respiratory triggering) and therefore insufficient temporal resolution.

Fasting by the patient for 4–6 hours prior to the examination will reduce peristalsis, a potential source of motion and/or blurring artifacts. A negative contrast agent consisting of 50–150 mL of superparamagnetic iron oxide particles should be routinely administered to the patient 5–10 minutes before initiating the MRCP acquisition to eliminate the possibility of obscuring visualization of the pancreatic ducts due to overlapping fluid-containing structures in the stomach. Pineapple or blueberry juice can also be used for this purpose, with less efficient signal suppression of static fluid within the stomach.

In adults, to assess pancreatic exocrine secretions, secretin is administered in a dose of 1 clinical unit per kilogram of body weight (0.7–1 mL/10 kg body weight). This dose, considered as the standard dose, is responsible for a maximal stimulation of the exocrine pancreas (20). However, neither visual nor significant difference in the mean pancreatic flow output and total excreted volume was found by using a dose of 0.3 clinical unit per kilogram of body weight (19), meaning that pancreatic duct visualization and pancreatic response are not impaired by the reduction of the secretin dose administered.

Image Evaluation

Morphology

Secretin improves the visualization of the full length of the main pancreatic duct, improving the diagnostic accuracy in depicting congenital anomalies/malformations and in confirming or excluding diseases (Fig 2). In most patients, the main pancreatic duct is not visualized throughout its length and therefore the assessment of its morphology and the presence abnormalities cannot be confidently performed. Visualization is commonly difficult in patients with normal or minimally dilated pancreatic ducts, in the body-tail of the gland, and in younger patients (21,22). Secretin administration is also very helpful in the visualization of dilated side branches on MRCP images, which might not be seen in basal condition because of their small size.

Secretin administration also improves visualization of the endoluminal filling defects. This improvement is however not substantial in patients with severe chronic pancreatitis, since the main pancreatic duct is already enlarged at baseline, containing a larger amount of fluid that surrounds the low intensity protein plugs that may be present along most or all their circumference. This improvement afforded by secretin administration is therefore particularly important in patients with mild or moderate chronic pancreatitis who have minimal dilation of the main pancreatic duct, where there might be insufficient pancreatic duct fluid to delineate the whole circumference of the protein plugs. At early stages of chronic pancreatitis, the removal of stones or plugs can lead to symptom remission, so the detection of endoluminal filling defects, namely their dimension and position, is important in planning adequate treatment such as interventional ERCP and/or lithotripsy.

Function

The dynamic assessment, obtainable with rapid imaging after secretin administration, provides information about the main pancreatic duct flow dynamics and about the hydrodynamic changes induced by the increased endoluminal pressure within the pancreatic duct system, increased fluid secretion within the duct, and subsequent pancreatic juice secretion into the duodenum.

Sphincter of Oddi dysfunction can be noninvasively diagnosed by means of secretin-enhanced MRCP by analyzing the time of onset and the amount of duodenal filling over time (Fig 3) (23). Another treatable cause of impeded pancreatic secretion outflow is the santorinicle, when it occurs in patients with pancreas divisum (Fig 4).

The assessment of the pancreatic exocrine reserve represents a medical need in patients with pancreatic diseases, especially in patients with chronic pancreatitis, to monitor disease progression and treatment response. There are direct and indirect tests to assess pancreatic exocrine reserve. The direct tests are represented by collection of pancreatic juice, after secretion stimulation, by means of cannulation of the papilla of Vater during ERCP or of duodenal juice by means of ECRP (24–26). These are invasive techniques that directly measure bicarbonate output and enzyme concentration within the pancreatic juice (26). The indirect test is represented by the fecal elastase-1, which is noninvasive and easy to perform but has low sensitivity in the mild to moderate forms of pancreatic insufficiency.

Secretin-enhanced MRCP also allows noninvasive assessment of pancreatic exocrine reserve by measuring the duodenal filling after secretin stimulation. The measurement of the duodenal filling, index of the pancreatic exocrine reserve, may be performed both in a semiquantitative or quantitative manner (13,14,27,28). The limitation of secretin-enhanced MRCP in assessing
Most appropriate imaging technique for investigating subjects with chronic asymptomatic pancreatic hyperenzymemia (31). In these patients, MRCP imaging depicted a pancreatic disease in 27.5% cases; whereas secretin-enhanced MRCP depicted abnormal findings in 50% of the patients. The most frequent abnormalities diagnosed on secretin-enhanced MRCP images were diffusely dilated side branches (25.6%), diffuse main pancreatic duct dilation, pancreatic exocrine reserve is the inability to assess the enzyme content within the pancreatic juice.

**Indications for Secretin-enhanced MRCP**

**Chronic Asymptomatic Hyperenzymemia**

Chronic asymptomatic pancreatic hyperenzymemia is a persistent abnormal increase in the serum concentrations of the pancreatic enzymes (amylase and lipase), without pancreatic symptoms or evidence of pancreatic diseases at imaging (29). The medical need in these patients is to differentiate undiagnosed pancreatic disease and other extrapancreatic conditions that may induce an increase in serum concentrations of amylase and lipase, including chronic viral hepatitis, renal failure, celiac disease, hyperparathyroidism, and neoplasms (30). Secretin-enhanced MRCP is the most appropriate imaging technique for investigating subjects with chronic asymptomatic pancreatic hyperenzymemia (31). In these patients, MRCP imaging depicted a pancreatic disease in 27.5% cases; whereas secretin-enhanced MRCP depicted abnormal findings in 50% of the patients. The most frequent abnormalities diagnosed on secretin-enhanced MRCP images were diffusely dilated side branches (25.6%), diffuse main pancreatic duct dilation.

**Figure 3:** Sphincter of Oddi dysfunction diagnosed at dynamic secretin-enhanced MRCP in a 41-year-old man with recurrent episodes of pancreatic-like abdominal pain. (a) Coronal fat-suppressed T2-weighted half-Fourier single-shot RARE (600/1000) image at baseline shows a normal size of the Wirsung duct (arrows). (b) Three minutes after administration of secretin, enlargement and increase in signal intensity of the Wirsung duct (arrows) are visible. Dilated side branches can be observed mainly in the head of the pancreas (arrowheads). Three minutes after administration of secretin there is only minimal duodenal filling, limited to the duodenal bulb. (c) Five minutes after secretin administration, there is enlargement of the Wirsung duct, dilated side branches (arrowheads), and minimal duodenal filling (arrows). (d) Ten minutes after secretin administration, the Wirsung duct remains dilated and does not return to its basal condition and the duodenal filling is limited to the duodenal bulb, suggesting pancreatic juice outlet obstruction at the major papilla (+).
Recurrent Episodes of Acute Pancreatitis

Acute pancreatitis is an inflammatory process of the pancreatic parenchyma that can affect peripancreatic tissues and distant sites (32). When patients have more than one clinical episode of acute pancreatitis they are given the diagnosis of acute recurrent pancreatitis (ARP) (33). In 70%–90% of the patients with ARP a cause can be diagnosed, whereas in 10%–30% of the patients a cause cannot be identified and therefore the diagnosis of idiopathic ARP is made (33,34). The diagnosis of a cause of ARP and its treatment represent a medical need, this is because more than 50% of untreated patients with ARP experience further recurrent episodes that may eventually lead to chronic pancreatitis (33).

Some etiologies of acute pancreatitis are identified by analyzing clinical history and findings, including laboratory data, to identify alcohol abuse, drug-induced pancreatitis, presence of infection, or family history of pancreatitis. Other causes of acute pancreatitis such as gallstones, microlithiasis, neoplasia of the ampulla or pancreas, or congenital anomalies of the pancreatic duct system (annular pancreas, pancreas divisum) may be identified with diagnostic imaging techniques including, US, CT, and MR imaging.

There are however some causes of recurrent acute pancreatitis that require a functional assessment of the pancreas in addition to a morphologic assessment. These include sphincter of Oddi dysfunction, presence of santorinicele in patients with pancreas divisum, biliary cystic disease (choledochal cyst or choledochocoele/duplication cyst), with anomalous pancreatico-biliary junction that may be responsible of reflux of bile within the lumen of the Wirsung duct and pancreatic juice within the biliary tree (35).

**Sphincter of Oddi dysfunction.**—Sphincter of Oddi dysfunction is the term used to describe the spectrum of motility disorders of the Sphincter of Oddi encompassing both stenosis and dyskinesia (23). The Sphincter of Oddi dysfunction is estimated to affect 13% of patients with right upper quadrant pain after cholecystectomy, and it is in these patients that most data have been published. It is also thought to affect 0.9% of patients with an in situ gallbladder (36). Currently, the reference standard to diagnose sphincter of Oddi dysfunction is manometry, which is able to directly measure sphincter pressure elevation in these patients. Furthermore, manometry is able to classify the sphincter of Oddi dysfunctions to three different types, according to the Milwaukee classification, which is based on the presence of biliary pain, elevated liver function tests, delayed drainage of contrast medium at ERCP, and dilated common bile duct (Table 2). Manometry is also useful in identifying which patients will benefit from endoscopic sphincterotomy (37,38). Favorable outcomes are most common in type I sphincter of Oddi dysfunction and less common in types II and III. However, manometry is invasive and carries a significant risk of pancreatitis, more common in type III Oddi dysfunction (23). Secretin-enhanced MRCP represents an alternative to manometry in diagnosing sphincter of Oddi dysfunction.

Secretin-enhanced MRCP signs indicative of sphincter of Oddi dysfunction, due to the obstructed pancreatic juice outflow at the major papilla, are represented by a delayed duodenal filling and persistent dilation of the main pancreatic duct 10 minutes after the administration of secretin, compared with baseline (Fig 3) (39). Ten minutes after secretin administration, the mean...
maximum diameter of the main pancreatic duct in patients with papillary stenosis was significantly larger than that in control subjects without papillary stenosis; furthermore, there was no overlap between the observed individual values in patients with papillary stenosis and those in control subjects (Fig 3) (39).

These findings are frequently associated with side-branch dilation, an expression of early chronic pancreatitis, most likely secondary to pancreatic outlet obstruction, and subsequent upstream increase of endudodal pressure. The strength of secretin-enhanced MRCP in this setting is the lack of invasiveness; however, the weakness is the reduced accuracy compared with that of manometry. Studies reported a global sensitivity of secretin-enhanced MRCP of 37%–57.1% and a specificity of 85%–100% (27,40–42); better accuracies were reported in types I and II sphincter of Oddi dysfunction (73%) compared with type III (46%) (41).

**Pancreas divisum.**—Pancreas divisum is a congenital anomaly of the pancreas caused by the lack of fusion between ventral and dorsal pancreatic ducts during the 6th-8th week of gestation. The frequency of pancreas divisum in Western countries ranges from 4% to 14% in autopsy series and from 2% to 8% in ERCP series (43–46). Because the major part of the pancreatic secretion must flow through the minor papilla, patients with pancreas divisum are at a higher risk for obstructive pancreatopathy, causing both pancreatitis and pancreatic type pain, up to the development of severe chronic pancreatitis. These issues are still controversial and ERCP studies provide conflicting results (47–52), being limited by the fact that endoscopic access to the minor papilla is substantially more difficult to achieve than for the major papilla, a possible selection bias in referral centers (51). MRCP is able to diagnose pancreas divisum by depicting the anatomy of the pancreatic duct system in relationship to the minor and major papilla (Fig 4). Diagnostic criteria useful in the diagnosis of pancreas divisum are dorsal duct in direct continuity with the main pancreatic duct and of the same caliber, main pancreatic duct crossing the common bile duct, lack of communication between dorsal and ventral duct (53). Secretin administration improves the visualization of pancreas divisum on MRCP images in 5%–23% of patients, because it allows better visualization of the relationship between the dorsal and ventral pancreatic duct (54,55).

Besides pancreas divisum, there are other anatomic variants that share the feature of excretion of the major fraction of pancreatic secretions via the dorsal duct orifice (Fig 4). These variants, characterized by an incomplete pancreas divisum with dominant dorsal duct, are found in nearly 10% of the population, double the prevalence of pancreas divisum. Often the thin duct connecting Wirsung and Santorini duct in patients with incomplete pancreas divisum is not visible in basal conditions. Dynamic MRCP after secretin stimulation improved detection of pancreas divisum in 23% of the patients (Fig 4) (11). The dominant dorsal duct anatomic variants may be responsible for recurrent episodes of acute pancreatitis because of the obstruction of pancreatic outlet at the minor papilla due to its smaller size.

**Santorinicele.**—Santorinicele is a cystic dilation of the distal dorsal duct, just proximal to the minor papilla, in analogy with ureteroceles and choledochoceles, and is believed to result from a combination of relative obstruction and weakness of the distal duct wall, either acquired or congenital (56). Santorinicele has been suggested as a possible cause of relative stenosis of the accessory papilla that may become clinically relevant when it occurs in association with pancreas divisum or dominant dorsal duct (37). In these conditions, the temporary obstruction of the minor papilla during passage of protein aggregates, which most likely occurs, is responsible for upstream increase in pressure within the lumen of the Santorini duct, resulting in recurrent episodes of acute pancreatitis (54,58). With time, the above-mentioned mechanism is responsible for dilation of the Santorini duct and of the side branches (57,59,60) (Fig 4).

Santorinicele was detected in three of 107 (3%) patients at MRCP and in seven of 107 (6%) patients at secretin-enhanced MRCP; in all cases santorinicele occurred in patients with pancreas divisum (54). The treatment of choice for santorinicele is endoscopic sphincterotomy of the minor papilla. Following sphincterotomy, the drainage of the Santorini duct, through the minor papilla, is improved and symptoms are relieved, most likely because of the reduction in endoductal pressure (58,61). After sphincterotomy, there is also a reduction in caliber of the Santorini duct and duodenal filling occurs earlier, compared with equivalent pretreatment images; these changes support the hypothesis that the santorinicele is a cause of pancreatic juice outlet obstruction at the level of the minor papilla (54).

**Annular pancreas.**—Annular pancreas is a rare anomaly, with an incidence of one in 20,000 individuals (62). In annular pancreas, a band of pancre-
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Figure 5: Annular pancreas. Secretin-enhanced MRCP in 16-year-old girl with recurrent episodes of pancreatic-like abdominal pain and vomiting. (a) Coronal fat-suppressed T2-weighted half-Fourier single-shot RARE (2.3/1000) image at baseline shows a normal size of the Wirsung duct (arrow) and of the Santorini duct that has, however, an arcuate path (arrowheads). (b) Ten minutes after secretin administration, there is duodenal filling due to intraluminal pancreatic juice collection. The duodenal filling outlines a substenosis of the duodenal lumen (arrows) due to annular pancreas, as confirmed on (c) axial contrast material–enhanced volumetric fat-suppressed T1-weighted gradient-echo image (4.66/1.87) during the pancreatic phase (arrow).

in pediatric population with this condition (Fig 5).

Anomalous pancreatico-biliary junction.—Anomalous pancreatico-biliary junction (PBJ) is a rare congenital anomaly in which the pancreatic and biliary ducts are joined outside the duodenal wall (63–65). In anomalous PBJ, a long common channel (15 mm on ERCP images) comprises the common bile duct and the main pancreatic duct (63–65). Anomalous PBJ is present in 90%–100% of patients with congenital choledochal cyst, but it can also be found in patients without congenital cystic dilation of the bile ducts (63,64,66). Reflux of pancreatic juice within the lumen of the bile ducts of a patient with choledochal cysts has been proven by showing progressive gallbladder and common bile duct...
filling during dynamic MRCP using secretin stimulation (Fig 6) (67,68). Patients with anomalous PBJ have a higher incidence of pancreatic disease (38%), most commonly, acute pancreatitis (31%) (63). The reflux of pancreatic juice within the lumen of the biliary tree has been postulated as a cause of increased incidence of the high incidence of biliary carcinoma in patients with anomalous PBJ, ranging between 15.6% and 36.0% (64,66).

**Chronic Pancreatitis**

Chronic pancreatitis is characterized by progressive fibrotic destruction of the glandular tissue. The exact pathophysiological mechanisms initiating and maintaining the development of fibrosis in the pancreas are poorly understood; however, fibrosis of the pancreatic parenchyma is the end result of different processes, including necrosis, inflammation, and/or duct obstruction (69). They result in the formation of extracellular matrix in the interstitial spaces and in the areas where acinar cells disappear or duct cells are injured. This eventually leads to a loss of the lobular architecture of the pancreas, grotesque distortion of the large ducts, and severe changes in the arrangement and composition of the islets (69).

In its early phase, the above-mentioned process of inflammation and/or duct obstruction can be appreciated in the side branches that assume a club-like appearance, which represents the hallmark sign of chronic pancreatitis detected on ERCP images (70) (Fig 7). Because of their small size, the side branches are not routinely seen on MRCP images. Secretin administration improves the visualization of the side branches (from 4% to 63% of the patients), helping in this manner in diagnosing chronic pancreatitis in its early stage (Fig 7) (12). This improved visualization of the dilated side branches has made secretin-enhanced
MRCP preferable to diagnostic ERCP, because in this manner we can avoid the risk of ERCP-induced severe acute pancreatitis, which occurs in 1%–7% of ERCP procedures, and the asymptomatic increase in pancreatic enzymes, which occurs in up to 70% of patients following ERCP (22,71). The risk of ERCP-induced severe acute pancreatitis increases in patients with preserved pancreatic exocrine function and normal-size main pancreatic duct and biliary ducts (22); therefore, ECRP should be limited to therapeutic indications.

Therefore, the depiction of side-branches abnormalities on secretin-enhanced MRCP images helps make the diagnosis of early chronic pancreatitis, which may be difficult in some patients by means of clinical and laboratory tests, addressing a medical need in gastroenterology. In many forms of chronic pancreatitis, side-branches abnormalities occur before the onset calcified endoductal stones; the calcifications are difficult to diagnose at MR imaging.

In severe chronic pancreatitis, the inflammation/fibrosis process is more advanced, with involvement of the main pancreatic duct that appears dilated with multiple stenoses (Fig 8) (72,73). The use of secretin will not help in making the diagnosis of chronic pancreatitis. Since the pancreatic duct system is already dilated, the elasticity of the main pancreatic duct walls is lost and the pancreatic juice production is reduced or lost. In these patients, secretin might be useful in assessing hydrodynamically significant stenoses of the main pancreatic duct and in non-invasively assessing the pancreatic exocrine reserve by analyzing the amount of pancreatic juice collected within the duodenal lumen (Fig 8) (14,27,28).

**Main Pancreatic Duct Stenosis**

Ductal stenosis is a secondary sign of pancreatic neoplasms, both adenocarcinoma and neuroendocrine neoplasms (74–76); however, a ductal stenosis may occur also in patients with chronic pancreatitis or autoimmune pancreatitis and as a late complication of abdominal trauma. In some patients, the differential diagnosis between a neoplastic and a benign cause of ductal stenosis is complicated by the coexistence in benign disease of a focal pancreatic enlargement due to inflammation, granulation tissue or lymphocytes, and plasma cell in a periductal infiltrate.

Some studies suggest that benign causes of ductal stenosis tend to have a nonobstructed main pancreatic duct, which can be seen to penetrate the mass on US or ERCP images (77,78), and this is called the duct-penetrating sign (79). On MRCP images, the duct-penetrating sign was present in benign stenoses in 85% of the studies and was absent in ductal stenoses due to pancreatic malignancies in 96% of the patients (79). On secretin-enhanced MRCP images, the presence or absence of the duct-penetrating sign is easily assessed because of the increased amount of fluid within the lumen of the pancreatic duct system that better assesses the entity of the ductal stricture, helping in this manner in the differential diagnosis between malignant and benign causes of ductal stenosis (Fig 9).

Autoimmune pancreatitis is also a cause of ductal stenosis due to periductal infiltration of lymphocytes and plasma cells, which represents the histologic hallmarked of the disease. The secretin-enhanced MRCP sings useful in making the diagnosis of autoimmune pancreatitis are the duct-penetrating
Figure 8: Severe chronic pancreatitis. Dynamic secretin-enhanced MRCP in 52-year-old man with recurrent severe abdominal pain and steatorrhea. (a) Coronal fat-suppressed T2-weighted half-Fourier single-shot RARE (\(\tau/1000\)) image before secretin administration shows enlargement of the Wirsung duct and of multiple side branches (arrowheads) with endoductal filling defects, suggesting severe chronic pancreatitis. (b) Five minutes after secretin administration, there is neither enlargement nor increase in signal intensity of the Wirsung duct and of the side branches. Duodenal filling is limited to the duodenal bulb (+). (c) Ten minutes after secretin administration, duodenal filling is limited to the duodenal bulb up to the genu inferius (+), suggesting reduced pancreatic exocrine reserve.

Figure 9: Autoimmune pancreatitis with multiple ductal stenoses and penetrating-duct sign at dynamic secretin-enhanced MRCP in 29-year-old man with recurrent episodes of pancreatic-like abdominal pain. (a) Coronal fat-suppressed T2-weighted half-Fourier single-shot RARE (\(\tau/1000\)) image in basal conditions shows multiple stenoses of the Wirsung duct due to autoimmune pancreatitis (arrowheads), with a dominant stenosis in the body of the pancreas (arrow). (b) One minute after secretin administration, there is resolution of the dominant stenosis and of all other stenoses detected in basal conditions (duct-penetrating sign) (arrow).
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secretin administration will stimulate the pancreatic parenchyma to produce water and bicarbonates; if this is obtained during dynamic acquisition of MRCP images, with high temporal resolution we can image the pancreatic response in physiologic condition, gathering morphologic and functional information useful for diagnosis.

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