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# MRI assessment of chronic pancreatitis

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ABSTRACT
Magnetic resonance imaging (MRI) plays an important role in the assessment of chronic pancreatitis. By standard MRI techniques, decreased parenchymal signal on T1-weighted fat-suppressed images and delayed gradual enhancement on serial contrast enhanced images represent fibrotic changes caused by chronic inflammation. Magnetic resonance cholangiopancreaticography (MRCP) can reveal ductal changes, including side branch ectasias, that are related to tissue fibrosis and destruction. The exocrine function of the gland and an increased number of side branch ectasias can be evaluated with secretin-stimulated MRCP. Diffusion weighted imaging is an emerging technology that can complement standard MRI to assess the parenchymal changes associated with chronic pancreatitis. The same technique can also quantify the parenchymal response to secretin stimulation. This article reviews standard imaging techniques and new advancements in MRI technology as they relate to the assessment of chronic pancreatitis.

*Key words:* • *magnetic resonance imaging* • *pancreatitis* • *diffusion magnetic resonance imaging* • *secretin*

Chronic pancreatitis is characterized by continued inflammation and destruction that lead to irreversible morphological changes in the pancreatic parenchyma and its ductal anatomy. These changes eventually result in abdominal pain, malabsorption, malnutrition and diabetes mellitus. The diagnosis of chronic pancreatitis relies on clinical symptoms, pancreatic exocrine function testing and imaging (1). Early diagnosis of chronic pancreatitis may help prevent further destruction of the gland. Endoscopic exocrine function testing is considered the most reliable diagnostic tool for chronic pancreatitis and, in some cases, can indicate pancreatitis even before the onset of ductal changes visible by endoscopic retrograde cholangiopancreaticography (ERCP) or magnetic resonance cholangiopancreaticography (MRCP) (1, 2). Imaging results and pancreatic exocrine function status may correlate well, or they may be inconsistent (3). Endoscopic ultrasonography (EUS) is considered a reliable imaging tool for revealing parenchymal and ductal changes. However, EUS is invasive and not available at all treatment centers (4). Conventional computed tomography (CT) and ultrasonography (US) are less sensitive than MRI for the assessment of chronic pancreatitis. MRI can be used for the assessment of chronic pancreatitis in two ways: (a) to evaluate both parenchymal and ductal changes; and (b) to evaluate the exocrine response of the parenchyma and ducts after hormonal stimulation (5).

## Etiology of chronic pancreatitis and morphologic changes caused by the disease

Alcohol ingestion accounts for 70% to 90% of chronic pancreatic cases in Western countries. Tropical pancreatitis is the most common form of chronic pancreatitis in Asia, Africa, and South America. Hereditary pancreatitis, an autosomal dominant disorder associated with trypsinogen gene mutation, is another rare cause of chronic pancreatitis. Obstructive chronic pancreatitis is caused by tumors, scars, cysts or stenosis of the papilla and tends to improve after removal of the obstruction. Chronic pancreatitis can also be idiopathic, without a known underlying cause, and can have an early (in childhood or adolescence) or late (after 60 years of age) onset. Morphologic changes in the parenchyma affect the acinar cells and the main pancreatic duct and/or its side branches. In chronic pancreatitis, the main histopathological changes include sclerosis and fibrosis leading to stricture and dilatation of the pancreatic ductal system as well as diffuse atrophy of the acinar parenchyma and fibrotic parenchymal changes. As a result, focal, segmental or diffuse destruction and/or loss of the exocrine parenchyma occurs. The pancreatic duct can show varying degrees of dilatation and side branch ectasia as a result of underlying sclerosis of the parenchyma. The ducts may contain eosinophilic protein plugs and/or intraductal calcifications (5–7).

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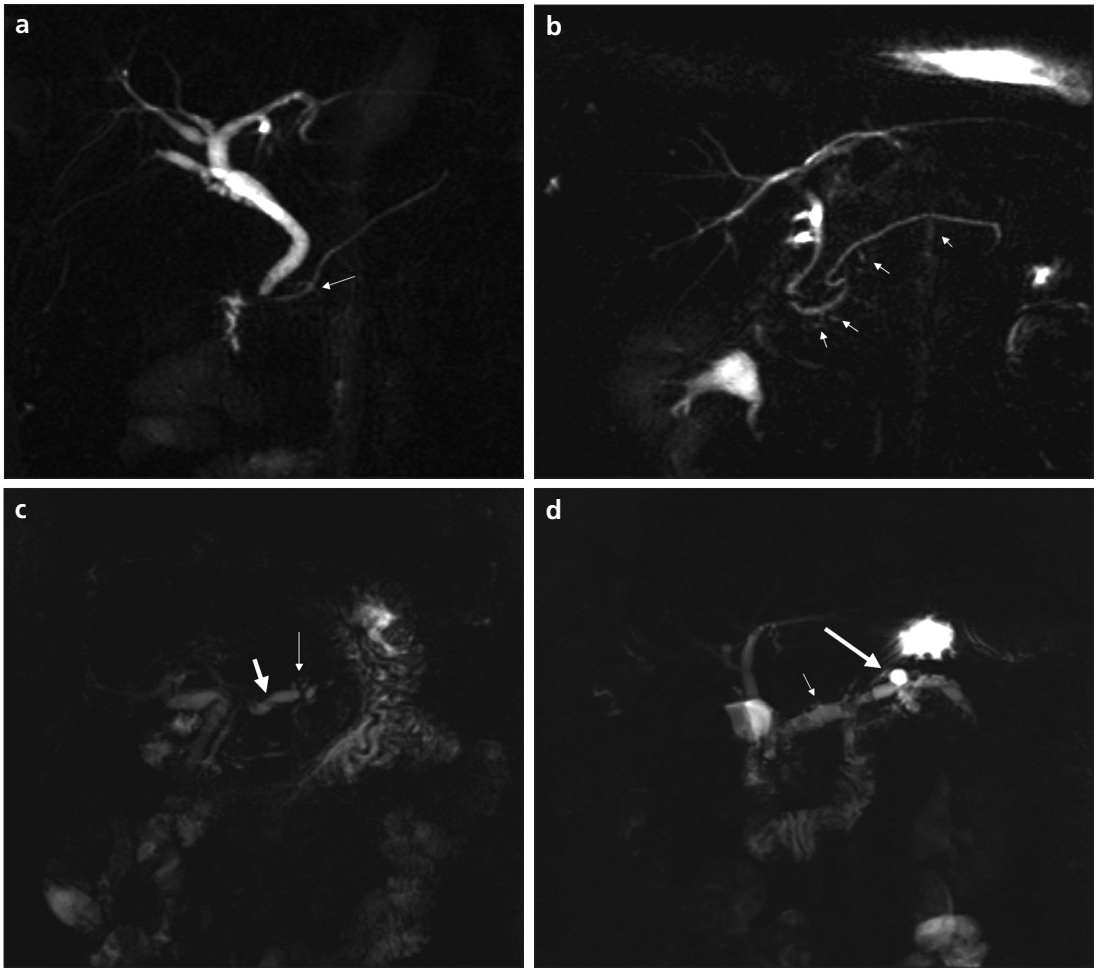


**Figure 1. a–d.** MRCP of a pancreatic duct according to the Cambridge classification: stage 2 ductal changes include fewer than three side branches (*arrow,* **a)**, and stage 3 changes include more than three side branches with preserved main pancreatic duct diameter (*arrows,* **b)**. The findings of stage 4 include side branch ectasias (*thin arrow,* **c)** and a dilated main pancreatic duct (*thick arrow,* **c)**. Stage 5 Cambridge changes manifest as a dilated main pancreatic duct (*short arrow,* **d)** with a cyst in the parenchyma (*long arrow,* **d)**.

### Standard MRI and MRCP to assess chronic pancreatitis

Patients with clinically suspected chronic pancreatitis typically undergo either MRCP alone, to evaluate ductal changes and obstructive causes of chronic pancreatitis such as cholelithiasis, or combined MRI of the pancreas and MRCP to evaluate parenchymal signal changes and gland perfusion on contrast-enhanced images. The presence of periductal fibrosis results in traction of the main pancreatic duct and its side branches, causing dilatation of the main pancreatic duct and its side branches (5–8). Pancreatic ductal findings regarding chronic pancreatitis are evaluated by MRCP according to the Cambridge classification, as shown in Table. Normal pancreatic ductal anatomy, without side branch ectasias, is considered Cambridge stage 1. Cambridge stage 2 consists of two or fewer side branch ectasias. More than three side-branch ectasias of the pancreatic duct is classified as Cambridge stage 3. Cambridge stage 4 is associated with additional stenosis and dilatation of the main pancreatic duct in addition to the ductal changes typical of Cambridge stage 3. When additional calculi and obstructions, cysts, and/or stenosis of the main pancreatic duct are present, these changes are lead to classification as Cambridge stage 5 (Fig. 1) (8).

Parenchymal changes may precede ductal changes, as shown in a recent study comparing MRI findings in patients with suspected chronic pancreatitis to the estimated pancreatic exocrine function, as derived from secre-

**Table.** Cambridge criteria of chronic pancreatitis

| Stage | Typical changes on MRCP |
|---|---|
| Cambridge 1 (normal) | Normal appearance of side branches and main pancreatic duct |
| Cambridge 2 (equivocal) | Dilatation/obstruction of less than 3 side branches; normal main pancreatic duct |
| Cambridge 3 (mild) | Dilatation/obstruction of side branches (more than 3); normal main pancreatic duct |
| Cambridge 4 (moderate) | Additional stenosis and dilatation of main pancreatic duct |
| Cambridge 5 (severe) | Additional obstructions, cysts, and stenosis of main pancreatic duct; calculi |

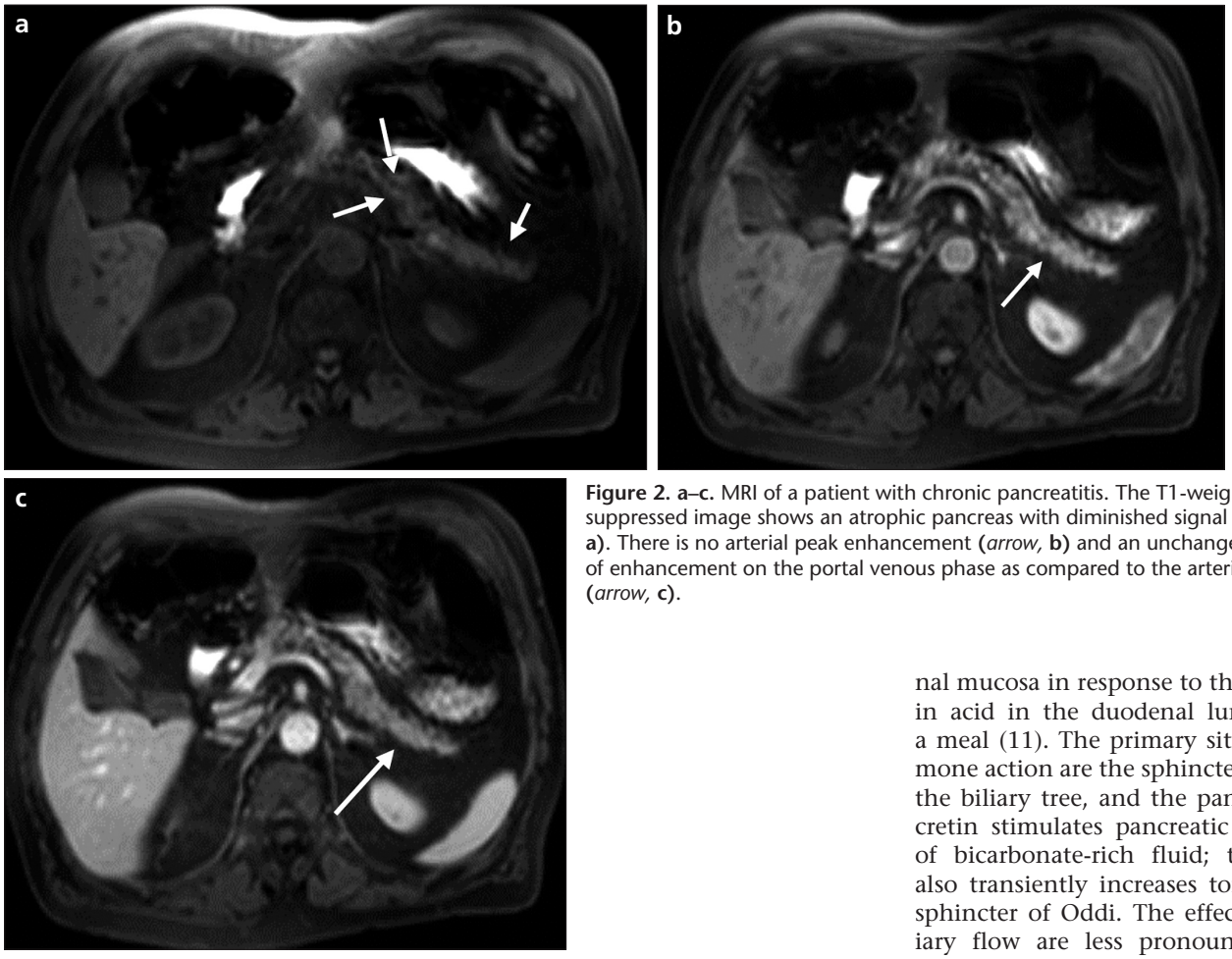


**Figure 2. a–c.** MRI of a patient with chronic pancreatitis. The T1-weighted fat-suppressed image shows an atrophic pancreas with diminished signal **(***arrows,* **a)**. There is no arterial peak enhancement **(***arrow,* **b)** and an unchanged level of enhancement on the portal venous phase as compared to the arterial phase **(***arrow,* **c)**.

tin-stimulated MRCP (9). The following early morphologic changes may occur and may be visualized by MRI (Fig. 2):

1. The anterior/posterior dimensions of the gland are diminished either segmentally or throughout the entire gland due to acinar cell atrophy. Pancreatic size may also decrease with aging, independently of chronic pancreatitis.
2. The pancreatic signal decreases. Low signal intensity on T1-weighted fat-suppressed images reflects the loss of aqueous proteins in the acini of the pancreas. The signal intensity ratio of the pancreas compared to the signal intensity of the spleen or paraspinal muscles is considered to be a reliable measurement method. In a normal gland, this value tends to be greater than 1.
3. The perfusion of the pancreatic gland is evaluated on serial contrast-enhanced images. A normal pancreatic gland demonstrates arterial capillary peak enhancement with venous washout of the contrast. In chronic pancreatitis, enhancement peaks in a gradual fashion on venous phase contrast-enhanced images. This pattern is attributed to the presence of fibrous tissue present in cases of chronic pancreatitis that impairs blood capillary flow and leads to late enhancement. A time-related perfusion model with improved temporal resolution has been investigated. The arterial enhancement slope can be quantitatively determined with this technique, with a higher upslope in normal subjects compared to the plateau-like enhancement in patients with chronic pancreatitis (10).

### Use of secretin-stimulated MRCP (s-MRCP) for the assessment of chronic pancreatitis

Secretin is a 27-amino-acid polypeptide hormone secreted by the duodenal mucosa in response to the increase in acid in the duodenal lumen after a meal (11). The primary sites of hormone action are the sphincter of Oddi, the biliary tree, and the pancreas. Secretin stimulates 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 the effects on the pancreas. Four to ten minutes after secretin administration, distension of the pancreatic duct occurs. After secretin administration, the usual pancreatic duct distension is most visible between four and ten minutes after administration. This distension helps to visualize the pancreatic duct. Secretin is a safe pharmaceutical agent with a very small incidence of serious adverse effects and is easy to administer (11–13).

Patients should fast for four to six hours before examination. Administration of an oral contrast agent is required 30 minutes before the start of the examination to control for any preexisting fluid signal in the duodenum. The oral contrast agent should shorten the T2 time by acting as a negative T2 agent. An oral ferumoxsil suspension (300 mL) or 5 mL of gadolinium DTPA mixed in 75 mL of distilled water can shorten the T2 time. Gadolinium has been used as an alternative for ferumoxsil suspensions. Secretin is administered via a slow intravenous injection for one minute to avoid the potential adverse effect of abdominal pain that

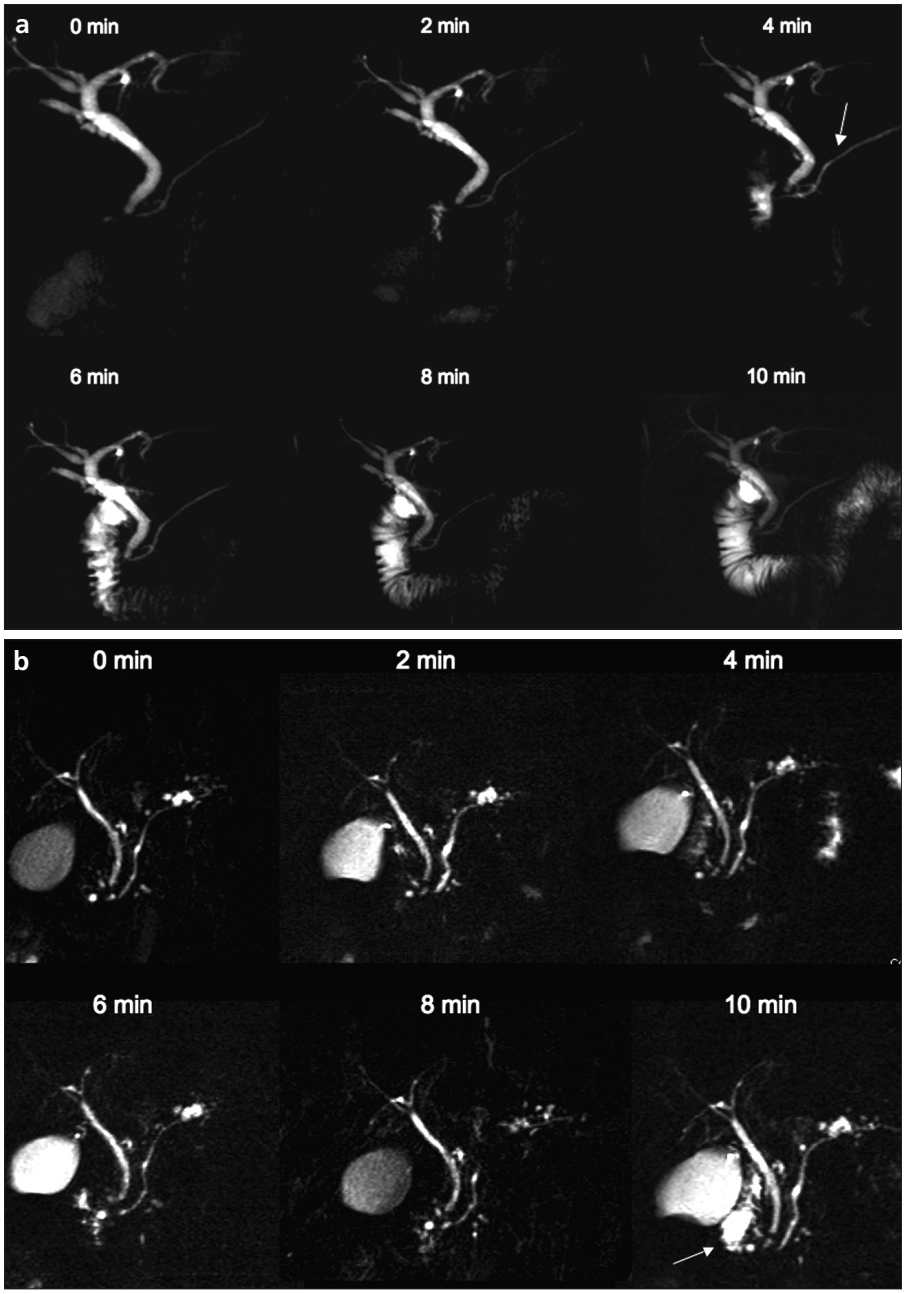


**Figure 3. a, b.** Secretin-stimulated MRCP of a patient with normal estimated pancreatic exocrine function **(a)**. The pancreatic duct diameter increased four minutes after secretin stimulation **(***arrow,* **a)**, and grade 3 duodenal filling was detected. A patient with diminished pancreatic exocrine function showed grade 1 duodenal filling **(***arrow,* **b)**.

can occur with a bolus injection. The injection dosage is 0.2 μg/kg body weight. At the commencement of the injection, a baseline scan is obtained, followed by a coronal single-shot fast spin echo image (2-second scan time) every 30 seconds for 15 minutes (9,13).

Although an overall grading system for different stages of chronic pancreatitis does not exist using s-MRCP, the following findings are associated with the disease (Fig. 3) (13):

1) **Inadequate pancreatic duct distension or lack thereof.** The minimum expected distension of the pancreatic duct after secretin administration is 1 mm greater than baseline; less than 1 mm of distension is associated with impaired ductal compliance. An exception to this criterion involves a past history of sphincterectomy. In cases of an incompetent sphincter, a ductal response is not visualized, even with the lack of pressure at the orifice (14).
2) **An increased number or new recognition of side branch ectasias.** Secretin stimulation increases the inflow of pancreatic secretions into ductal side branches that flow towards the primary pancreatic duct. In normal glands, dilatation of the side branches is not evident. However, subtle fibrosis of a main pancreatic ductal side branch junction may interrupt the seamless passage of secretions. This interruption will cause either dilatation of new side branches in addition to preexisting dilated side branches or, in the very early stages of chronic pancreatitis, side branch ectasias that were not visible on the baseline MRCP images.
3) **Diminished duodenal filling after secretin stimulation.** Duodenal filling after secretin stimulation serves as an estimate of exocrine function of the pancreatic gland, which is expected to decrease in cases of chronic pancreatitis. Filling of the duodenum is graded according to duodenal anatomy. Grade 1 duodenal filling occurs when pancreatic excretion is confined to the duodenal bulb. Grade 2 duodenal filling represents fluid collection in the first and second portions of the duodenum. In grade 3 duodenal filling, pancreatic fluid passes through the inferior duodenal genu and reaches the third portion of the duodenum. Diminished pancreatic exocrine function is estimated in cases of grade 1 or 2 duodenal filling or in the absence of duodenal fluid accumulation in the duodenal lumen.

### Diffusion-weighted imaging for chronic pancreatitis

Diffusion-weighted imaging (DWI) has been used for the assessment of chronic pancreatitis. Apparent diffusion coefficient (ADC) values for patients with chronic pancreatitis are lower than those found for patients with normal pancreases. This finding is attributed to the replacement of normal pancreatic parenchyma with fibrous tissue and/or reduced exocrine function that may reduce the amount of diffusible tissue water and result in decreased ADCs (Fig. 4) (15). The exo-

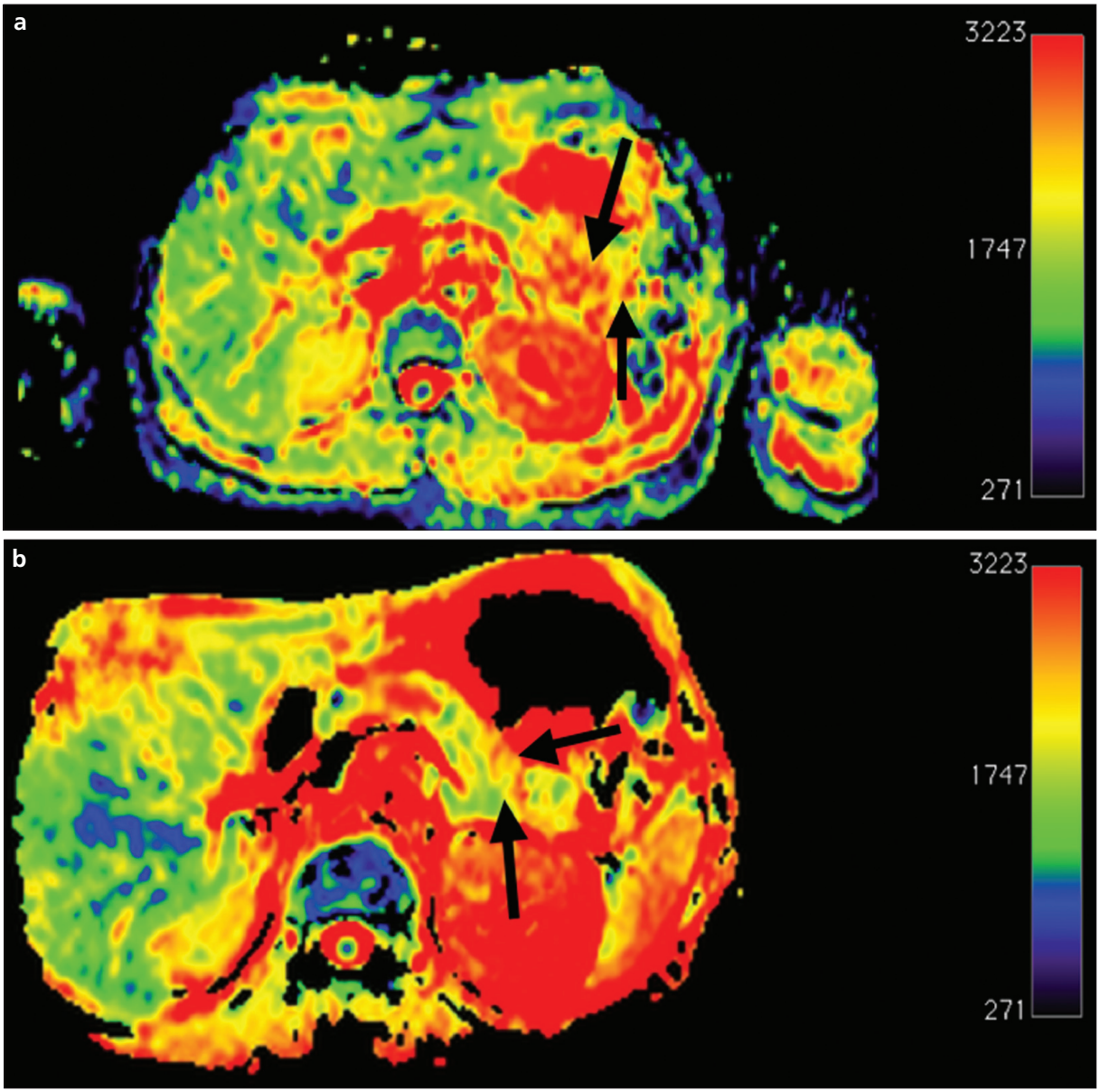


**Figure 4. a, b.** Colored ADC map derived from diffusion-weighted MRI (DWI) of the pancreas. A normal pancreas with associated ADC values and colors is shown (*arrows,* **a**). A patient with clinically established chronic pancreatitis shows decreased ADC values with corresponding colors (*arrows,* **b**).

crine functional reserve capacity of the acinar cells can also be quantitatively estimated by DWI after secretin stimulation. The first study of DWI after secretin stimulation investigated the peak ADC changes after secretin stimulation and the time to peak ADC in three different patient groups. Patients without pancreatic disease showed a 57% to 120% (median, 75%) increase in ADC values compared with the initial ADC value before secretin stimulation. The peak ADC value was obtained 5 minutes and 30 seconds (median, 2 minutes) after secretin stimulation. A group of patients with habitual alcohol consumption was selected as a high-risk group, revealing similar peak ADC values but prolonged time to ADC peaks after secretin stimulation. All patients with chronic pancreatitis and a few patients in the high-risk group had no constant ADC peak but, instead, had subtle fluctuations in ADC values after secretin stimulation (16). A more recent study investigated the correlation between severity of chronic pancreatitis and ADC values, as measured by secretin-enhanced DWI. Statistically, there was no significant difference between the percentage increases of ADC peak values from baseline among groups with different severities of chronic pancreatitis, but the baseline ADC values decreased with increasing pancreatitis severity. In contrast to the earlier study, all patients revealed ADC peaks after secretin stimulation, regardless of the severity of chronic pancreatitis. There was also no significant difference among the times to peak ADC of the groups with different severities of pancreatitis. A cutoff ADC peak of $1.79 \times 10^{-3}$ $mm^2/s$ was found to be the determinant value for differentiating between patients without chronic pancreatitis and those with chronic pancreatitis (17).

In conclusion, MRI assessment of chronic pancreatitis allows for the visualization of parenchymal signal changes on T1-weighted fat-suppressed images, the visualization of arterial contrast enhancement patterns on serial contrast enhanced images and measurement of pancreatic size. Ductal changes visible on static images and changes evident by secretin-stimulated MRCP can indirectly determine the degree of parenchymal fibrosis and severity of the disease. Estimation of pancreatic exocrine function by grading duodenal filling during the same session provides additional information about the functional status of the gland. DWI is an emerging technique that will have a potential role in quantifying the parenchymal response of the pancreatic gland to secretin stimulation.

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