Diagnosis of mild chronic pancreatitis (Cambridge classification): Comparative study using secretin injection-magnetic resonance cholangiopancreatography and endoscopic retrograde pancreatography

Jin Kan Sai, Masafumi Suyama, Yoshihiro Kubokawa, Sumio Watanabe

AIM: To investigate the usefulness of secretin injection-MRCP for the diagnosis of mild chronic pancreatitis.

METHODS: Sixteen patients having mild chronic pancreatitis according to the Cambridge classification and 12 control subjects with no abnormal findings on the pancreatogram were examined for the diagnostic accuracy of secretin injection-MRCP regarding abnormal branch pancreatic ducts associated with mild chronic pancreatitis (Cambridge Classification), using endoscopic retrograde cholangiopancreatography (ERCP) for comparison.

RESULTS: The sensitivity and specificity for abnormal branch pancreatic ducts determined by two reviewers were respectively 55%-63% and 75%-83% in the head, 57%-64% and 82%-83% in the body, and 44%-44% and 72%-76% in the tail of the pancreas. The sensitivity and specificity for mild chronic pancreatitis were 56%-63% and 92%-92%, respectively. Interobserver agreement (κ statistics) concerning the diagnosis of an abnormal branch pancreatic duct and of mild chronic pancreatitis was good to excellent.

CONCLUSION: Secretin injection-MRCP might be useful for the diagnosis of mild chronic pancreatitis.

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Key words: Magnetic resonance cholangiopancreatography; Endoscopic retrograde cholangiopancreatography; Mild; Chronic pancreatitis; Diagnosis

INTRODUCTION
Chronic pancreatitis is morphologically characterized by irregular sclerosis associated with destruction and permanent loss of the exocrine parenchyma which may be either, focal, segmental or diffuse. These changes may present together with varying degrees of dilatation of the duct system at different segments\(^1\). Chronic pancreatitis is classified according to morphologic changes of the pancreatic ducts, as defined in the 1983 Cambridge Symposium\(^2\).

MR cholangiopancreatography (MRCP) is a useful non-invasive technique to depict the projection images of the pancreatico-biliary tree, and is expected to become a valuable alternative to endoscopic retrograde cholangiopancreatography (ERCP)\(^3\). However, visualization of the branch pancreatic ducts by MRCP is not good\(^9\), and there are few reports about the diagnostic value of MRCP in mild chronic pancreatitis (Cambridge classification). On the other hand, secretin injection-MRCP might allow better visualization of the pancreatic ductal system\(^12\).

The purpose of this study was to evaluate the usefulness of secretin injection-MRCP for the diagnosis of abnormal branch pancreatic duct in patients with mild chronic pancreatitis.

MATERIALS AND METHODS

Patients
The MRCP image obtained after secretin injection was examined in 16 patients (32-39 y.o.; mean 36 y.o.) having
mild chronic pancreatitis according to the Cambridge classification, and in 12 control subjects (31-37 y.o.; mean 35 y.o.) showing no abnormal findings on the pancreatogram, who had already undergone ERCP. In the Cambridge classification mild chronic pancreatitis is defined as “more than 3 abnormal side branches with a normal main pancreatic duct”. In the present study, we selected patients in their 30’s, because we wanted to exclude those with ductal changes associated with aging. In all the patients the maximum diameter of the main pancreatic duct was within 2 mm and the ultrasonogram and CT revealed no findings suggestive of chronic pancreatitis, such as atrophy, calcification, dilatation or stenosis of the pancreatic duct. The control subjects had no pancreatic diseases and were selected from a population that had undergone ERCP for a suspected biliary disease. Patients with mild chronic pancreatitis were selected from a population that had been subjected to ERCP for recurrent attacks of abdominal pain associated with increased serum levels of amylase and lipase in the absence of conclusive US or CT findings of chronic pancreatitis. The symptomatic period was between 15 and 54 mo. Secretin injection-MRCP was performed within 4 wk after ERCP. Informed consent was obtained from all patients after explanation of the examination process. The study protocol was approved by the ethical committee of our institution.

**MRCP**

After a 6-h fast, MR studies were performed on a 1.5 T scanner using a phased-array multi-coil. With the patients in the supine position, 100 U of secretin (Eisai Corporation, Tokyo, Japan) was injected intravenously. Half-Fourier fast echo sequences with the single slice method were obtained in the coronal plane and left and right oblique planes to emphasize the pancreatic body, head and tail, respectively. MRCP images of axial planes were also added on demand. The sequence parameters were: effective echo time, 250 ms; echo train length, 212; matrix, 384 × 384; FOV, 25 to 35 cm. A thin slice, thickness of 10-30 mm, was adopted to delineate the fine structure of the minimally dilated branches. The acquisition time for an image was 3 s with complete breath-holding. Acquisition was repeated every 30 s during 10 min.

**Image analysis**

Only clear MRCP images of the pancreatic ducts were regarded as acceptable. MRCP images were reviewed using ERCP as the gold standard. Two sets of MRCP films and one set of ERCP films were prepared so that each reviewer could work separately on the films. MRCP images were interpreted independently by two reviewers (Sai J and Takayashi Y) and ERCP images by another reviewer (Kubokawa Y); all of them were experienced in pancreaticobiliary imaging. Each MRCP and ERCP film was randomly numbered, and reviewers were blinded to the clinical information associated with each film. Abnormal branches of the pancreatic ducts were documented with markings on the duplicate films of ERCP and MRCP by each reviewer, who did not participate in the examination; visible branch pancreatic ducts were regarded as abnormal branch pancreatic ducts on MRCP images because they are not detectable on MRCP except in pathologic cases. Then MRCP images were compared with the ERCP images for the number and location of the abnormal branch pancreatic ducts, lesion by lesion under consensus.

**Statistical analysis**

The sensitivity and specificity for the diagnosis of abnormal branch pancreatic ducts and mild chronic pancreatitis (Cambridge classification) determined by each reviewer was examined. Regarding the diagnosis of ectatic branch pancreatic duct and mild chronic pancreatitis on MRCP images, the interobserver agreement was analyzed with k statistics: values were classified as excellent (above 0.75), fair to good (0.40 to 0.75), or poor (below 0.40).

**RESULTS**

Successful MRCP images were obtained after secretin injection in patients with mild chronic pancreatitis and control subjects. The rates for visualization of the main pancreatic duct on MRCP were 100%.

Abnormal branch ducts delineated on MRCP images correlated with ERCP images, lesion by lesion. The sensitivity and specificity for the diagnosis of abnormal branch pancreatic ducts determined by the two reviewers were 55%-63% and 75%-83% in the head, 57%-64% and 82%-83% in the body, and 44%-44% and 72%-76% in the tail of the pancreas, respectively (Table 1a, b). The sensitivity and specificity for the diagnosis of mild chronic pancreatitis (Cambridge classification) was 56%-63% and 92%-99%, respectively (Table 2). Interobserver agreement (k statistics) for identifying abnormal branch pancreatic ducts and for diagnosing mild chronic pancreatitis was good to excellent (Table 3).

**DISCUSSION**

Early-stage chronic pancreatitis is difficult to diagnose because less obvious changes occur over time, before the development of overt exocrine or endocrine insufficiency and visible structural abnormalities. Therefore, a major diagnostic challenge occurs when patients have clinical signs suggestive of chronic pancreatitis, in the absence of demonstrable pancreatic abnormalities on ultrasonography and CT. Reversely, in patients with advanced disease, findings such as atrophy, calcification, dilatation and stenosis of the pancreatic duct are obvious. One of the earliest findings of chronic pancreatitis is an abnormal branch of the pancreatic duct detected by ERCP. ERCP is the sensitive method for the diagnosis of early-stage chronic pancreatitis; however, it is invasive and associated with complications, because sufficient contrast medium must be injected to the peripheral branches of the pancreatic ducts when mild changes of chronic pancreatitis are sought.

Today, diagnostic ERP is challenged by MRCP, which is a noninvasive alternative to diagnostic ERP for the evaluation of normal and diseased pancreatic ducts. However, it is difficult to delineate minimally dilated...
Sensitivity and specificity of MRCP for abnormal branch pancreatic ducts as compared with ERCP by Reviewer 1.

<table>
<thead>
<tr>
<th>Location of abnormal branch pancreatic ducts</th>
<th>Number of lesions</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td>25</td>
<td>25/40 (63)</td>
<td>40/53 (75)</td>
</tr>
<tr>
<td>Body</td>
<td>16</td>
<td>16/28 (57)</td>
<td>88/106 (83)</td>
</tr>
<tr>
<td>Tail</td>
<td>4</td>
<td>4/9 (44)</td>
<td>19/25 (76)</td>
</tr>
</tbody>
</table>

TP: True positive; TN: True negative; FP: False positive; FN: False negative; Numbers are numbers of patients (numbers in parentheses are percentages).

Sensitivity and specificity of MRCP for abnormal branch pancreatic ducts as compared with ERCP findings by Reviewer 2.

<table>
<thead>
<tr>
<th>Location of abnormal branch pancreatic ducts</th>
<th>Number of Lesions</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td>22</td>
<td>22/40 (55)</td>
<td>44/53 (83)</td>
</tr>
<tr>
<td>Body</td>
<td>18</td>
<td>18/28 (64)</td>
<td>87/106 (82)</td>
</tr>
<tr>
<td>Tail</td>
<td>4</td>
<td>4/9 (44)</td>
<td>18/25 (72)</td>
</tr>
</tbody>
</table>

TP: True positive; TN: True negative; FP: False positive; FN: False negative; Numbers are numbers of patients (numbers in parentheses are percentages).

branch pancreatic ducts on MRCP despite its improved resolution because while on ERCP images the collapsed branches and main pancreatic duct are distended by the contrast medium, MRCP reflects the physiologic state of the pancreatic duct.

Since Takehara et al. first reported the MRCP images of moderate to severe chronic pancreatitis obtained after the injection of secretin; several authors have reported the usefulness of secretin injection-MRCP in the diagnosis of chronic pancreatitis. Secretin stimulates fluid secretion in the ductal system; and increases the tonus of the sphincter of Oddi during the first 5 min, inhibiting the release of fluid through the papilla of Vater. Therefore, secretin increases the absolute volume of intraductal free water and fills the collapsed branches with fluid, facilitating the detection of mild ductal changes in patients with mild chronic pancreatitis, even when no abnormalities can be demonstrated by MRCP under physiologic conditions. According to Mansfredi et al., visualization of the pancreatic duct branches improved from 71% to 100% in 93 patients with severe chronic pancreatitis and from 4% to 63% in 84 patients suspected of having pancreatic disease. Since the pancreatic juice secretion decreases in patients with advanced chronic pancreatitis, secretin injection-MRCP could be of diagnostic value for those with early-stage chronic pancreatitis, although the occurrence of mild chronic pancreatitis was underestimated by secretin injection-MRCP compared with ERCP in the present study.

In conclusion, secretin injection-MRCP might allow an earlier diagnosis of chronic pancreatitis and reduce the rate of false-negative cases detected with MRCP.

### COMMENTS

#### Background

Early-stage chronic pancreatitis is difficult to diagnose because less obvious changes occur over time. One of the earliest findings of chronic pancreatitis is an abnormal branch of the pancreatic duct detected by endoscopic retrograde cholangiopancreatography (ERCP). On the other hand, MR cholangiopancreatography (MRCP) is expected to become a valuable alternative to ERCP. However, diagnosis of mild ductal changes of chronic pancreatitis using magnetic resonance cholangiopancreatography (MRCP) is quite challenging, because visualization of the branch pancreatic ducts is not good.

#### Research frontiers

We examined the diagnostic accuracy of secretin injection-MRCP regarding abnormal branch pancreatic ducts associated with mild chronic pancreatitis (Cambridge classification) using ERCP for comparison, and there were no other related or similar studies.

#### Innovation and breakthrough

The sensitivity and specificity for the diagnosis of mild chronic pancreatitis (Cambridge classification) were 56%-63% and 92%-92%, respectively. Secretin injection-MRCP might allow an early diagnosis of chronic pancreatitis.

#### Application

The application of this study could be expanded to diagnose early chronic pancreatitis in larger series.

#### Terminology

Secretin injection-MRCP was acquired as follows: with the patients in the supine position, 100 U of secretin was injected intravenously. MRCP was repeated every 30 s during 10 min.

#### Peer review

Secretion injection-MRCP could be a useful method for the diagnosis of mild chronic pancreatitis (Cambridge Classification), although the occurrence was underestimated compared with ERCP.

#### REFERENCES

1. Hayakawa T, Kondo T, Shibata T, Noda A, Suzuki T, Nakano...