Dynamic MR Cholangiography after Fatty Meal Loading: Cystic Contractility and Dynamic Evaluation of Biliary Stasis

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Purpose: Dynamic MR cholangiography was conducted on patients with cholelithiasis or choledocholithiasis who had consumed a fatty test meal (Molyork) and the cystic contractility and dynamics of biliary stasis was evaluated.

Subjects and Method: The subjects were 25 with intracystic cholelithiasis, 10 with choledocholithiasis and 10 normal controls. For an imaging sequence, the rapid acquisition with relaxation enhancement (RARE) method was employed and imaging was conducted for 40 min (every 30 s following Molyork administration) without breath-holding. The gallbladder contraction ratio was computed and the contractile ratio for the common bile duct was calculated. To determine the bile flow to the duodenum, the high-intensity signal, indicating the flow from the lower common bile duct, and perfusion of the duodenum were observed in dynamic mode on the monitor with the naked eye and interpreted as positive bile flow. The frequency of this flow was visually monitored.

Results: The gallbladder contractile ratio was significantly reduced in patients with cholelithiasis or choledocholithiasis compared with the controls. In a comparison with the normal controls, no sequential changes were noted in the mean contractile ratio of the common bile duct of the patients with cholelithiasis or choledocholithiasis. The mean frequency of bile flow observed for each 40 min period was 13 ± 2.4, 6 ± 2.2, and 4 ± 1.3 times for the controls, those with intracystic cholelithiasis, and those with choledocholithiasis, respectively. Compared with the controls, the latter two patient groups showed evident reductions in the frequency of bile flow to the duodenum (p < 0.001).

Conclusion: Dynamic MRC combined with Molyork loading makes it possible to compute cystic contractile ratios and perform a dynamic examination of bile flow under non-invasive, near-physiological conditions.

Keywords: dynamic MR cholangiography, choledocholithiasis, Molyork

Introduction

Magnetic resonance cholangiopancreatography (MRCP)1,2 makes it possible to visualize the cholangiopancreatic system completely and non-invasively. It does not require the use of contrast media and allows one to conduct a morphological evaluation of the cholangiopancreatic system under physiological conditions. When combined with anti-gastrin agents (e.g., secretin), it also enables dynamic observation by utilizing the exocrine function of the pancreas.3,4 Standard MRCP can be conducted even when the patient is in an acute stage of pancreatitis or cholangitis. Its efficacy has been widely recognized.

Among clinical cases, a frequent cause of acute pancreatitis is cholelithiasis. Currently, the therapeutic modality is often selected with consideration given to the time required for the treatment and the expense involved. Thus, laparoscopic cholecystectomy has become the mainstay treatment at many institutions.5 However, it must be remembered that this procedure is sometimes associated with risks such as stenosis of the common bile duct caused by postoperative cholangitis or
re-occlusion of this duct due to a recurrence of cholelithiasis. Evaluation of the physiological functions of the biliary system is important when a patient is to be conservatively treated while preserving the gallbladder.

Ultrasonographic evaluation has been reported as a method by which the contractility of the gallbladder and common bile duct can be studied. The success of this method is often dependent on the skill of the operators and on the physical constitution of the subject. However, as of this writing, no report has used MRC for a functional evaluation of the biliary system. MRCP is independent of the operator and, in the biliary tree evaluation, it is believed to be more valuable for evaluation of the biliary function.

In the present study, dynamic magnetic resonance cholangiography (DMRC) under fatty meal (Molyork®; Toho Kagaku, Tokyo, Japan) loading was conducted on patients who had intracystic calculi or choledocholithiasis with co-existing intracystic calculi. The presence (or absence) of contractility of the gallbladder and common bile duct and the presence (or absence) of bile flow and its extent were evaluated in these patients.

Materials and Methods

Materials

The group comprised 35 patients (ages from 27 to 85 years; mean, 55; 11 males and 24 females). This group included 25 with intra-cystic cholelithiasis (ages: 27 to 84 years, mean: 62.3, 9 males and 16 females, diameter of calculi: 3 to 20 mm, mean: 9.5 [6.4 mm]) and 10 with choledocholithiasis with co-existing intracystic calculi. The presence (or absence) of contractility of the gallbladder and common bile duct and the presence (or absence) of bile flow and its extent were evaluated in these patients.

Study Method

To calculate the cystic and choledochal contractile ratios, nine images (taken immediately after Molyork loading) were recorded on the DMRC. The imaging apparatus employed was a 1.5T superconductive device (Symphony, Siemens, Germany). The subject fasted for the preceding 12 hours and immediately before the test he ingested 6 g of FerriSeltz (Otsuka Seiyaku, Tokyo, Japan) dissolved in 150 ml of water. The subject was then subjected to routine magnetic resonance cholangiography (MRC) during which coronal and axial views were recorded by means of half-Fourier single-shot turbo spin echo (HASTE method). The imaging parameters were as follows: TR1500/TE: 120 ms, flip angle: 90°, matrix: 204 × 256, field of view: 30.5 mm, excitation number: 1, imaging time: 0.22 s, and slice thickness: 2 mm. This study was begun after this routine MRC. The patient was instructed to drink, through a straw while supine, 13 g of fatty meal (Molyork®, Toho Kagaku, Tokyo, Japan) dissolved in 50 ml of water, followed by DMRC every 30 s for 40 min without breath-holding. For the DMRC sequence, rapid acquisition with relaxation enhancement was employed (RARE method). The imaging parameters were as follows: TR8000/TE: 20 ms., flip angle: 90°, matrix: 240 × 512, excitation number: 1, imaging time: 9.5 s, and slice thickness: 60 to 80 mm. These parameters were set so that both the gallbladder and common bile duct would be included in each tomographic image. The procedure was thoroughly explained to the patients and their oral consent was obtained prior to the test.

1) Evaluation of cystic contractility

The long and short diameters of the gallbladder were measured on the DMRC and its volume was calculated with the following formula:

\[
\text{Volume immediately after Molyork loading} = \frac{\text{Long diameter} \times \text{short diameter}}{6}
\]

(a variation of the sum-of-cylinders method by Dodds et al.).

The result was used to calculate the cystic contractile ratio with the following formula:

\[
\text{Cystic contractile ratio} = \frac{\text{Volume immediately after Molyork loading} \times \text{volume immediately after Molyork loading}}{100}
\]

2) Evaluation of the contractility of the common bile duct

The diameter at the mid-point of the common bile duct on the DMRC image was measured and the contractile ratio of the duct was calculated with
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Fig. 1. Graph showing the mean cystic contractile ratios for normal individuals and those with cholelithiasis and choledocholithiasis. Significant differences were noted, beginning 15 min after fatty meal loading (P < 0.005).

the following formula:

\[
\frac{\text{Diameter of common bile duct after Molyork loading}}{\text{Diameter of common bile duct immediately after Molyork loading}}
\]

3) Evaluation of bile flow

To observe the bile flow, images were taken every 30 s for 40 min, beginning immediately after Molyork loading. A total of 80 images were examined in dynamic mode on a monitor. The frequency of bile secretion in the controls and in those with intracystic and common bile duct calculi was counted with the naked eye and the manner in which the papillary sphincters underwent contraction and relaxation was noted. The high-intensity signals that emanated from the lower common bile and shifted to the duodenum were interpreted as positive signs of bile secretion during the 40 min immediately following Molyork loading. In the case of nonconsecutive high intensity from the lower common bile duct to the duodenum, we did not regard the high intensity as bile flow. For statistical comparisons, repeated measurement of ANOVA (analysis of variance) was used. To determine the time required for the bile to be secreted following Molyork loading, the 40 min were divided into four segments of 10 min each and the frequency of bile secretion was counted in each segment.

To confirm indirectly that the high-intensity signal captured with the naked eye that emanates from the lower common bile duct and extends to the duodenum indeed represents the bile flow, an attempt was made to find a correlation between the frequency of the high-intensity signal and the total bilirubin content. A blood sample was collected within 24 hours of DMRC in order to measure this content.

For statistical analysis, Spearman’s rank correlation coefficient was used.

**Results**

1) Evaluation of cystic contractility

The cystic contractile ratios for the control, those with intracystic cholelithiasis, and those with choledocholithiasis were: 6.7 ± 17.7%, 0 ± 0%, and 6.9 ± 16.6% at 5 min; 11.4 ± 22%, 2.5 ± 5.1%, and 4.7 ± 12% at 10 min; 27 ± 27%, 7 ± 17%, and 6 ± 11% at 15 min; 31 ± 28%, 11 ± 20%, and 13 ± 15% at 20 min; 36 ± 25%, 12 ± 19%, and 16 ± 16% at 25 min; 47 ± 27%, 16 ± 21%, and 20 ± 18% at 30 min; 54 ± 20%, 24 ± 24%, and 19 ± 18% at 35 min; and 50 ± 20%, 19 ± 25%, and 17 ± 17% at 40 min, respectively.

The maximum contractile ratio for the gallbladder (mean ± standard deviation) was 54 ± 20% for the controls 35 min after Molyork loading; 24 ± 24% for those with intracystic calculi, also 35 min after Molyork loading; and 20 ± 18% for those with choledocholithiasis 30 min after Molyork loading (Figs. 1 and 2).

The cystic contractile ratio for those with cholelithiasis or choledocholithiasis was significantly reduced compared with the controls, starting 15 min after Molyork loading (P < 0.05).

2) Evaluation of the contractility of the common bile duct

Compared with those of the controls, the sequential changes in the mean contractile ratio of the common bile duct of the patients with intracystic cholelithiasis or choledocholithiasis were slight. No significant difference was noted between the two experimental groups in terms of the sequential changes in contractile ratios (Fig. 3).
3) Evaluation of bile flow

The frequency of bile secretion detected with the naked eye in the 40 min period was $13 \pm 2.4$ for the control, $6 \pm 2.2$ for those with intracystic cholelithiasis, and $4 \pm 1.3$ for those with choledocholithiasis (all mean $\pm$ standard deviation). Compared with the control, the frequency of bile secretion to the duodenum in those with intracystic cholelithiasis and choledocholithiasis was significantly reduced ($P<0.001$).

The frequency was also reduced in the group with choledocholithiasis, compared with those with intracystic cholelithiasis ($P<0.001$); however, all patients in the former group retained some bile secretory function.

During the sequential observations, the frequency of bile secretion for the control, those with intracystic cholelithiasis, and those with choledocholithiasis were, respectively, as follows: $2.30 \pm 0.48$, $1.0 \pm 0.82$, and $0.2 \pm 0.42$ between 0 and 10 min; $2.90 \pm 1.20$, $1.12 \pm 0.78$, and $0.40 \pm 0.52$ between 10 and 20 min; $3.70 \pm 0.68$, $1.60 \pm 0.65$, and $1.30 \pm 0.68$ between 20 and 30 min; and $4.50 \pm 1.50$, $2.20 \pm 0.82$, and $2.30 \pm 0.68$ between 30 to 40 min (Fig. 4).

A significant correlation was noted between the frequency of the high-intensity signals detected by the naked eye on DMRC and the total bilirubin level ($P<0.001$; Fig. 5).

**Discussion**

In the planning of treatment for cholelithiasis, the therapeutic choice has been determined by the presence (or absence) of recurrent upper abdominal pain, stone composition, and gallbladder functions (bile concentration capacity and gallbladder contractility). It has been reported that performing a cholecystectomy without evaluating gallbladder contractility, and no significant difference was evident in the sequential contractile ratios.

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Fig. 2. a and b are DMRC images for a healthy 35-year-old man; c and d, those for a 44-year-old woman with choledocholithiasis. a and c were prepared immediately after Molyork administration; b and d, 30 min later. For the healthy subject, satisfactory cystic contraction is noted (contractile ratio: 46%), while no change in the size of the gallbladder (cystic contractile ratio: 15%) was noted in the case with choledocholithiasis.

Fig. 3. No sequential changes were noted in the mean contractile ratio of the common bile duct in the controls or in those with cholelithiasis or choledocholithiasis. In addition, no significant difference was evident in the sequential contractile ratios.

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functions may risk changes in postoperative bile acid metabolism by the liver and biliary system and that an increased possibility of mucosal damage to the duodenum and small intestine may exist.\textsuperscript{13,14} Thus, preoperative evaluation of cystic contractility is highly significant. Even when an internal treatment is considered, it is equally important in order to preserve the gallbladder.\textsuperscript{8} As for MRCP, to date, the morphologic evaluation is of primary concern and its usefulness has been pointed out. However, in recent years, efforts to apply a functional evaluation have been reported, primarily exocrine functional evaluation of the pancreas with secretin. No functional evaluation of the biliary tract has been reported.

MRC is an approach in which strongly T\textsubscript{2}-weighted images are used to depict the bile, which is identified by its high-intensity signal. In the actual image, the fluid content of the stomach and duodenum is also imaged from a high-intensity signal, which results in overlapping of the two signals (one from the bile and the other from the gastric and duodenal content), making it difficult to distinguish the anatomical features of these organs and negat-
duct.18 However, MRCP, a form of hydrography, and raising the pressure within the pancreatic reducing the pressure within the duodenal papilla pancreatic juice secretion to the duodenum by believed that secretin loading enhances the bile and cholithiasis exhibited low cystic contractile ratios, patients with intracystic cholelithiasis or choledo- more than 40 reported that the normal cystic contractility was conditions than conventional methods. Inoue et al. that, if the main thrust of a study was to examine the duodenal papilla, DMRC under secretin loading, rather than with bile secretion caused by Molyork loading, would be more efficient. It was believed that secretin loading enhances the bile and pancreatic juice secretion to the duodenum by reducing the pressure within the duodenal papilla and raising the pressure within the pancreatic duct. However, MRCP, a form of hydrography, does not depict the actual movement of the papilla; instead, it indirectly serves to detect any signal that links the bile and pancreatic ducts to the duode- num. This method is sufficient for indirect observation of the contraction-relaxation of Oddi’s sphinc- ter, and the basic concept—that the presence of an intensified signal emanating from the lower common bile duct and shifting to the duodenum attests to valid bile secretion—is observed. Secretin loading results in the generation of those signals not only for the bile directed to the duodenum but also for the signals mixed with those of the pancreatic juice, which is not suitable for the current method. Our method is intended mainly to evaluate the biliary stasis caused by cholelithiasis.

During rest, about 70% of the bile that has been formed in the liver flows into the gallbladder, while the remaining 30% is secreted directly into the duode- num via the bile duct. When one consumes food rich in fats, cholecystokinin is secreted from the duodenal wall, which causes cystic contraction and relaxation of Oddi’s sphincter via the actions of the vagus nerve, resulting in bile secretion. In the present study, Molyork, a dry egg yolk preparation, was used in place of a fatty meal and MR cholangiography was conducted in an attempt to evaluate the dynamics of bile secretion in a manner that is less invasive and closer to the physiological conditions than conventional methods. Inoue et al. reported that the normal cystic contractility was more than 40%. In the current study, those patients with intracystic cholelithiasis or choledo- cholithiasis exhibited low cystic contractile ratios, suggesting a compromised gallbladder function.

A cystic contraction does not occur immediately after Molyork administration because the amount of this agent secreted into the duodenum depends on the state of peristalsis. Inoue et al. pointed out that an immediate need exists for innovation to expedite the gastric secretory process into the duode- num through methods such as shifting one’s posture. According to the results of our study, however, the time required to reach the maximum cystic contractile ratio was from 30 to 35 min, which was approximately equal to that observed in the controls and those groups with biliary diseases. This finding may be explained by the fact that the subjects of the current study were intentionally limited to those with no history of vagotomy or complications such as diabetes mellitus, which may cause delays in gastric motility. In other words, it was indicated that when the test was conducted on patients having only cholelithiasis but without a history or the complications cited above (as in the current study), MRC is quite adequate for the evaluation of cystic contractility.

The common bile duct diameter fluctuated little, indicating no significant difference associated with sequential contraction. Reports on US indicate that the significance level for changes in the diameter of the common bile duct is around 2 mm. The MRC conducted in the current study was at a disadvan- tage in comparison with US because the former is affected by spatial resolution and respiratory shift. Therefore, the procedure should be undertaken with breath-holding at the minimum.

DMRC combined with Molyork loading entails the following problem: As the test progresses, more gastric juice is secreted, so it is possible that the high-intensity signal may not necessarily represent pure bile (i.e., the high-intensity signal representing the secretion from the lower common bile duct and continuing to the duodenum during 40 min, start- ing immediately after Molyork loading, may not actually indicate the excretion of pure bile). Therefore, for indirect proof that the visually counted frequency of the high-intensity signals represents bile secretion, the correlation between the count and the total bilirubin level was examined. This substantiated the correlation, thus indicating a strong possibility that the findings did represent the expression of bile secretion. It was confirmed that bile secretion is poor in those patients with biliary calculi, especially those with choledochocholithiasis. A future objective will be to determine how to trans- late the extent of the bile secretion observed by DMRC into therapeutic approaches.

Another problem associated with the current
method is the time required for the test. According to our data, the gallbladder contractile ratio and the mean high-intensity signals were highest between 30 and 40 min for all subjects (inclusive of the controls and those with intracystic or choledocholithiasis) during the 40 min period following Molyork administration. To shorten the testing time and maintain the efficacy of the test, it may be logical to conduct imaging prior to Molyork administration, allow the patients to leave the laboratory temporarily, and bring them back 30 to 40 min after Molyork loading for further imaging.

An acute stage of a cholelithiasis attack may be cited as a contraindication of DMRC following Molyork loading. In this stage, DMRC may exacerbate inflammation and intensify the pain. It is mandatory that, before the test is conducted, the patient be examined to confirm that the fever and pain have abated and that the inflammatory reactions indicated by the biochemical tests have subsided. None of our patients experienced abdominal pain or shock symptoms during the test; however, if abdominal pain is recognized in a patient in the subacute or chronic stage during the test, the procedure should be interrupted and pain control measures should be taken immediately.

**Conclusion**

It was concluded that DMRC with Molyork loading enables an evaluation of the biliary system, integrating its morphological and functional characteristics.

**References**


