

## Obliteration of the Biliary System after Administration of an Oral Contrast Medium Is Probably due to Regurgitation: A Pitfall on MRCP

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**Purpose:** We retrospectively evaluated the incidence and related factors of obliteration of the lower bile duct after oral administration of contrast medium (OCM) probably resulting from its regurgitation into the biliary system (OCMRB) as observed on images of MR cholangiopancreatography (MRCP).

**Methods:** We retrospectively analyzed 305 MRCP images in 278 patients obtained between February 2010 and March 2011 using negative OCM with 1.0- and 1.5-tesla clinical units. OCMRB was defined as positive when visualization of the common bile duct was clear on precontrast 2-dimensional (2D) MRCP but obliterated on postcontrast 3-dimensional (3D) MRCP. Two abdominal radiologists reviewed all images in consensus. The incidence of OCMRB was correlated to various clinicoradiological factors.

**Results:** We observed OCMRB on 11 MRCP images in 10 patients (3.6%). Among various clinicoradiological factors, the presence of juxtapapillary diverticula, pneumobilia, and history of intervention to the papilla were suggested as significant factors related to positive OCMRB with multivariate analysis ( $P < 0.05$ ).

**Conclusion:** OCMRB occurs in about 4% of the patients who undergo MRCP, typically in those with juxtapapillary diverticula, pneumobilia, and history of papillary intervention. Acquisition of MRCP images before OCM may secure visualization of the common bile duct in these patients.

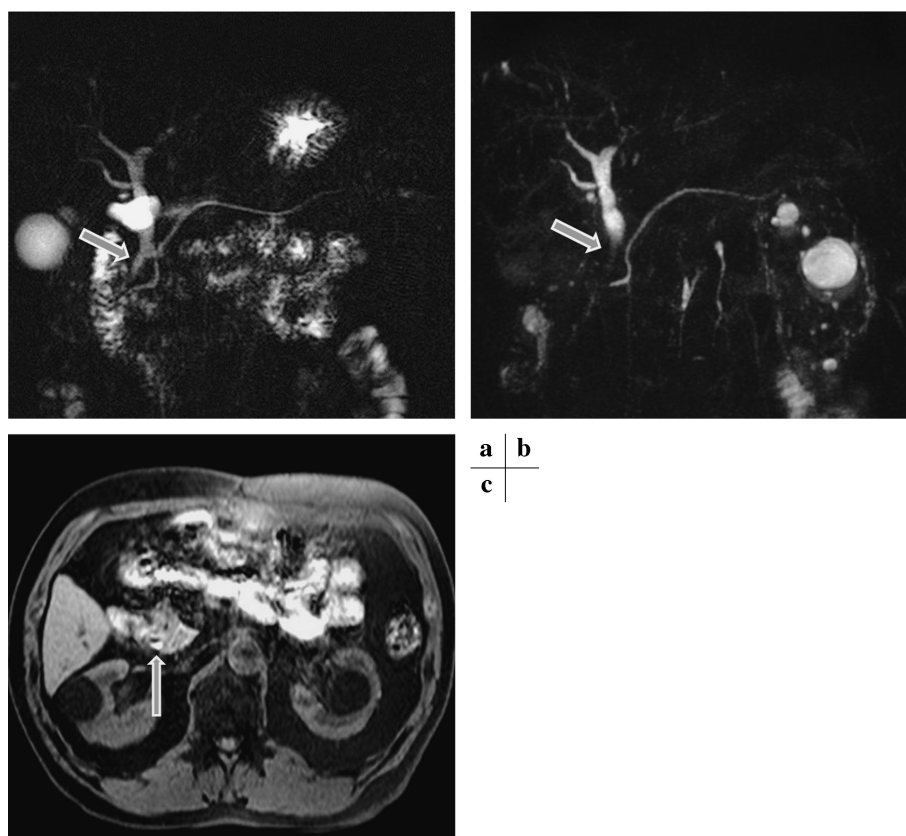
**Keywords:** *biliary system, MR cholangiopancreatography, negative oral contrast medium, regurgitation*

### Introduction

The usefulness of oral contrast medium (OCM) for magnetic resonance (MR) cholangiopancreatography (MRCP) is widely accepted because its excellent  $T_2$  and  $T_1$  shortening properties permit efficient suppression of signals from intestinal fluid that may hamper delineation of the biliary or pancreatic duct system.<sup>1,2</sup> However, one case report describes reflux of OCM into the biliary system that obscured visualization of the common bile duct (CBD) and the presence of CBD stones.<sup>3</sup> We experienced such cases in daily clinical practice and therefore changed our MRCP protocol in 2010.

We no longer give OCM routinely but choose its use only when initial 2-dimensional (2D) MRCP suggests the presence of a significant amount of gastric or intestinal fluid that may hinder delineation of the pancreaticobiliary system, after which we obtain 3-dimensional (3D) MRCP. Thus, acquisition of 2D MRCP before administration of OCM allows us to secure delineation of the lower CBD or parapapillary region even if administered medium is later regurgitated into the biliary system (OCMRB). Further, this new protocol has permitted comparison of images of MRCP obtained before and after OCM administration for the systematic observation of OCMRB. Thus, clear visualization of the CBD on MRCP images obtained prior to contrast administration that becomes obliterated or disappears on images obtained after contrast is

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**Fig. 1.** A 58 year-old man with a history of papillotomy for papillary tumor. Magnetic resonance (MR) examination was performed in a 1.5-tesla clinical unit. (a) Two-dimensional (2D) MR cholangiopancreatography (MRCP) obtained before administration of oral contrast medium (OCM) clearly shows lower common bile duct (arrow). (b) Three-dimensional (3D) MRCP obtained after administration of OCM. The lower part of the common bile duct (CBD) is not visualized (arrow). (c) Transverse  $T_1$ -weighted image with fat suppression through the level of the CBD. High signal intensity at the dorsal aspect of the CBD (arrow) suggests air-OCM level, direct evidence of OCM reflux into the CBD.

administered would reasonably suggest the presence of OCMRB.

Little regarding the details of OCMRB has been studied systematically, so we undertook this retrospective investigation to elucidate the incidence and relevant clinicoradiological factors of OCMRB.

## Materials and Methods

Our institutional review board waived the requirement for informed consent for this retrospective study.

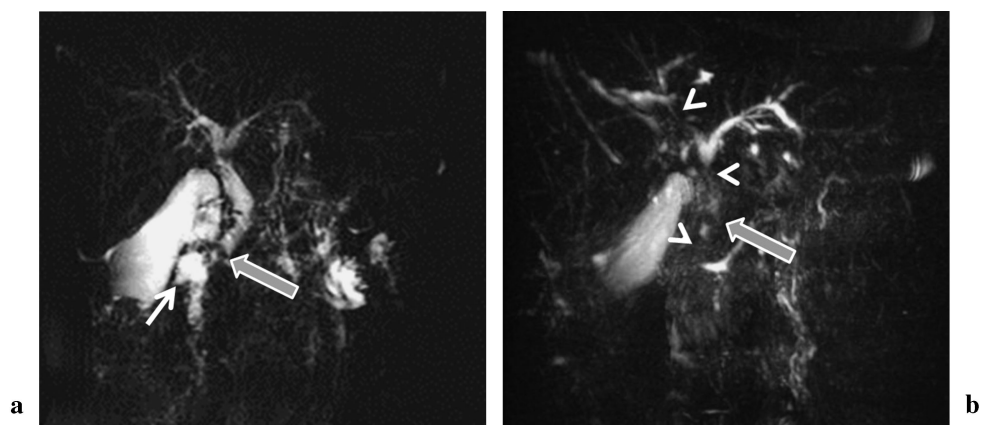
### Subjects

Between February 1 2010 and March 31 2011, 427 patients underwent 466 consecutive MRCP imaging studies in our institution. Patients fasted 6 hours before examination. At the examination, we first obtain 2D MRCP images in 3 directions, and when we observe a significant amount of gastric or

intestinal fluid that may obscure delineation of the pancreaticobiliary ducts, we administer 250 mL of negative OCM (Bothdel Oral Solution 10, Meiji Co., Ltd., Tokyo); when we observe little or no gastrointestinal fluid, we proceed and complete the examination without administering OCM. Thus, during the study period, we obtained 315 MRCP images with OCM in 288 patients, who became our study population, and 151 MRCP images without OCM in 139 patients.

### MR protocols

We used 1.0- (Gyroscan-NT Intera, Philips Medical Systems, Best, The Netherlands) and 1.5-tesla (Intera Achieva Nova Dual, Philips) clinical MR imaging units. Table 1 outlines our MRCP protocols. Initial 2D MRCP was obtained with a turbo spin-echo (TSE) sequence,  $256 \times 256$  matrix, 5- or 6-cm slice thickness, parallel imaging factor of 2, and one excitation, in 3 directions (coronal, right



**Fig. 2.** A 62 year-old woman with a history of endoscopic sphincterotomy for choledocholithiasis. Magnetic resonance (MR) examination was performed in a 1.0-tesla clinical unit. **(a)** Two-dimensional (2D) MR cholangiopancreatography (MRCP) obtained before oral contrast medium (OCM) administration shows a recurrent stone (arrow) within the lower common bile duct along with a juxtapaillary diverticulum (small arrow). **(b)** Three-dimensional (3D) MRCP obtained after OCM administration. Poor visualization of the majority of the common bile duct and proximal right duct (arrowheads) as well as the juxtapaillary diverticulum is attributable to regurgitation of OCM into the biliary system. A stone of the common bile duct is vaguely appreciated (arrow).

**Table 1.** Outlines of the magnetic resonance cholangiopancreatography (MRCP) protocols

Protocol for 1T unit

	Sequence	TR/TE (ms)
1	Thick-slice 2D MRCP with breath holding/3 directions	2000/825
Oral contrast medium administration		
2	Balanced turbo field-echo/coronal	6.7/3.4
3	T <sub>2</sub> -weighted image/axial	8000/250
4	T <sub>1</sub> -weighted image with fat suppression/axial	243/4.3
5	Diffusion-weighted image/axial	2500/130
6	3D T <sub>1</sub> -weighted fast field-echo/axial	6.3/3.6
7	3D MRCP with respiratory triggering	1610/1000

Protocol for 1.5T unit

	Sequence	TR/TE (ms)
1	Thick-slice 2D MRCP with breath holding/3 directions	3000/800
Oral contrast medium administration		
2	Balanced turbo field-echo/coronal	3.8/1.92
3	T <sub>2</sub> weighted image/axial	1000/320
4	T <sub>1</sub> weighted image with fat suppression/axial	235/5.5
5	Diffusion-weighted image/axial	5000/65
6	3D T <sub>1</sub> -weighted fast field-echo (eTHRIVE)/axial	4.4/2.1
7	3D MRCP with respiratory triggering	1264/650

eTHRIVE, enhanced T<sub>1</sub>-high resolution isotropic volume excitation; TE, echo time; TR, repetition time; 2D, 2-dimensional; 3D, 3-dimensional

oblique coronal, and left oblique coronal), with acquisition time of 2 to 3 s and under breath holding. Three-dimensional MRCP was obtained with a TSE sequence, 512 × 512 in-plane matrix, one-mm thickness and 96 partitions, parallel imaging factor of 2, and one excitation, in coronal direction, with acquisition time of 3 to 5 min and under respiratory triggering.

#### *Image interpretation and analysis*

Two experienced abdominal radiologists (K.S. and Y.S.) retrospectively reviewed all 315 MRCP images in 288 patients and CT images obtained within one year from MRCP, when available, and recorded the presence of OCMRB, juxtapapillary diverticula, pneumobilia, and biliary stones in consensus. For 3D MRCP, they reviewed the original source images as well as maximum intensity projection images. OCMRB was considered positive when the CBD was seen clearly on initial 2D MRCP, its visualization was obliterated on 3DMRCP obtained after OCM administration, and pneumobilia was excluded as a cause of this obliteration, according to its definition below. Juxtapapillary diverticulum was defined as an air-containing cavitory structure located medially and outside of the second portion of the duodenum. Pneumobilia was defined as the presence of air, visualized as signal void on any MR imaging sequence, located at the ventral aspect of the ducts on axial images and with low density, around -1000 HU, on CT, within any part of the biliary system. Stones were defined as nodule-shaped signal voids on MRCP or areas of low or high signal on T<sub>1</sub>-weighted images (T<sub>1</sub>WI)<sup>4</sup> located at the dorsal aspect of the bile ducts on axial images or as structures of high density on plain CT. One radiologist (K.S.) reviewed medical records of all patients and recorded relevant clinical information.

We correlated the incidence of OCMRB with clinicoradiological information, including patient factors of sex, age, history of intervention to the papilla, and history of gastrectomy with nodal dissection; imaging findings, including the presence of pneumobilia, juxtapapillary diverticula, and biliary tract stones; and MR equipment used for imaging (1.0 versus 1.5T). We included gastrectomy with nodal dissection as one patient factor based on a previous report that suggested it may cause autonomous nervous dysfunction of the sphincter of Oddi.<sup>5</sup> Univariate and multivariate analyses were applied for these factors, and factors related to OCMRB were elucidated. We analyzed statistics using JMP software (Version 11; SAS Institute, Cary, NC, USA).  $P < 0.05$  or 0.1 was considered

significant.

## **Results**

After excluding 10 MRCP images of 10 patients from evaluation due to poor image quality secondary to inadequate breath holding or inconsistent breathing, we assessed 305 MRCP images of 278 patients. Among these, we observed OCMRB on 11 MRCP images of 10 patients (3.6%). Six 3DMRCP images of 5 of these patients obtained after administration of OCM revealed high signal intensity on T<sub>1</sub>WI (as high as OCM) at the dorsal aspect of the CBD that showed fluid level that strongly suggested the presence of OCM in the CBD. Table 2 details the 10 cases.

CT images were available for all 278 patients for diagnosis of the presence of juxtapapillary diverticula and pneumobilia. Among the various clinicoradiological factors tested, univariate analysis indicated history of intervention to the papilla, presence of juxtapapillary diverticula, and presence of pneumobilia as significant (Table 3). Sex, age, when divided into high and low groups at the median value of 67 years, history of gastrectomy with nodal dissection, presence or absence of biliary stones, and MR equipment used were revealed to be insignificant. Papillary intervention included papillectomy (n = 2), sphincterotomy with CBD stent placement (n = one), and pylorus-preserving pancreaticoduodenectomy (PpPD) (n = 2) in cases positive for OCMRB and papillectomy (n = 3), papilloplasty (n = one), sphincterotomy (n = 3), CBD stent placement (n = 14), PpPD (n = 8), and choledochojejunostomy (n = 4) in cases negative for OCMRB (Table 3). Multivariate (nominal logistic) analysis also showed these 3 factors to be significant, with odds ratios of 3.8 for history of intervention to the papilla, 3.3 for presence of juxtapapillary diverticula, and 4.8 for presence of pneumobilia (Table 4).

Representative cases are shown in Figs. 1 and 2.

## **Discussion**

Our data indicated the occurrence of OCMRB in approximately 4% of MRCP examinations obtained with OCM. Patients with pneumobilia, history of intervention to the papilla, and juxtapapillary diverticula were suggested to be more likely to have OCMRB compared to those without, and all these conditions may represent dysfunction of the sphincter of Oddi.

Only one case report of a patient who had undergone endoscopic sphincterotomy (EST) has de-

**Table 2.** Details of the 10 patients with regurgitation of oral contrast medium into the biliary system

Patient number	MRCP number	Age (years)	Sex	T <sub>1</sub> high	JPD	PnB	Clinical diagnoses
1	1	88	F	N	N	N	abdominal pain, unknown etiology
2	2	80	M	N	P	N	pancreas cancer
3	3, 10	58	M	P	P	P	papillectomy for papillary tumor
4	4	78	F	P	N	P	PpPD for papillary cancer
5	5	65	F	P	N	P	PpPD for pancreas head cancer
6	6	78	F	N	N	N	Pancreas neuroendocrine tumor
7	7	75	F	P	N	N	RUQ pain, unknown etiology
8	8	83	F	N	N	N	pancreas cystic lesion
9	9	68	F	N	N	N	main pancreatic duct dilatation
10	11	62	F	P	P	N	EST for choledocholithiasis

EST, endoscopic sphincterotomy; F, female; JPD, juxtapaillary diverticulum; M, male; MRCP, magnetic resonance cholangiopancreatography; N, negative; P, positive; PnB, pneumobilia; PpPD, pylorus-preserving pancreaticoduodenectomy; RUQ, right upper quadrant; T<sub>1</sub> high, high signal within bile ducts on T<sub>1</sub>-weighted imaging

**Table 3.** Correlation between clinicoradiological factors and regurgitation of oral contrast medium into the biliary system): univariate analysis in 11 magnetic resonance cholangiopancreatography (MRCP) studies

		Regurgitation of oral contrast medium into the biliary system		P value
		Positive (P)	Negative (N)	
Sex	M	3	132	NS
	F	8	162	
Age (years)	H	7	131	NS
	L	4	163	
PapIV	P	5	33	0.006
	N	6	261	
GastND	P	0	7	NS
	N	11	287	
JPD	P	4	32	0.029
	N	7	262	
PnB	P	4	17	0.004
	N	7	277	
Stone	P	4	119	NS
	N	7	175	
MR equipment	1.0T	8	203	NS
	1.5T	3	91	

F, female; GastND, gastrectomy with nodal dissection; H, higher age (>67 years); JPD, juxtapaillary diverticulum; L, lower age (≤67); M, male; NS, not significant; PapIV, intervention to the duodenal papilla; PnB, pneumobilia; T, tesla

**Table 4.** Correlation between clinicoradiological factors and regurgitation of oral contrast medium into the biliary system: multivariate analysis

	Chi-square	P value	Odds ratio
History of intervention to the papilla	3.14	0.05	3.8
Juxtapaillary diverticulum	2.77	0.09	3.3
Pneumobilia	4.01	0.04	4.8

scribed disappearance of the signal of the common bile duct on MRCP as a result of reflux of negative OCM.<sup>3</sup> Dysfunction of the papilla of Vater is reported in patients with choledochoduodenostomy, choledochoduodenal or choledochocolic fistula, biliary dyskinesia, endoscopic sphincterotomy, papilloyplasty, liver transplantation, gastrectomy with nodal dissection, juxtapaillary diverticula, and complete absence of sphincter function is reported in patients with pancreaticoduodenectomy, PpPD, and choledochojejunostomy.<sup>5-7</sup> Observation of pneumobilia on upright abdominal plain-film X-ray has been reported in 85.7% and reflux of barium into the bile duct in 69.2% of upper gastrointestinal studies of patients after papilloyplasty for cholelithiasis.<sup>6</sup> Our data (Table 3) showed OCMRB in 13% (5/38) of patients with history of papillary intervention, the incidence of which is low compared to that in the previous report. Although the exact reason for this discrepancy is unknown, it may be partly attributable to the fact that regurgitation may be a transient phenomenon, so some

cases could have been missed on MRCP even if it was present during the examination. Another possibility may be that papillary intervention in our series included various procedures other than papiloplasty, each of which may have different impact on the function of the sphincter of Oddi. The use of another recently available type of negative OCM for MRCP that contains ferric ammonium citrate (FerriSeltz<sup>®</sup> powder, Otsuka Pharmaceutical, Co., Ltd., Tokyo, Japan) could theoretically result in OCMRB, but we are unaware of such report. This could be partly attributable to the smaller dosage (150 mL) compared to that of our OCM (250 mL).

The presence of juxtapapillary diverticula has been reported to lower the basal and contraction pressure of the sphincter of Oddi and to increase the incidence of retrograde contraction, which may lead to duodenobiliary reflux and resultant stone formation.<sup>7–10</sup> Our data indicated the presence of juxtapapillary diverticula as a significant factor for the incidence of OCMRB both at univariate and multivariate analyses, which supports a positive relationship between the presence of juxtapapillary diverticula and papillary dysfunction. The third condition suggested to be related to OCMRB, pneumobilia, is also considered a consequence of dysfunction of the muscle of Oddi.<sup>11</sup> It is therefore reasonable that patients with positive OCMRB were associated with the presence of pneumobilia.

Gastrectomy with nodal dissection has been reported to cause dysfunction of the sphincter of Oddi and delay bile flow as a result of denervation during the procedure, which results in a high incidence of cholelithiasis following gastrectomy for gastric cancer.<sup>5</sup> Our data showed no correlation between the incidence of OCMRB and history of gastrectomy with nodal dissection. This may be attributable to the small number of positive cases in our study, which we mention as a limitation. Another possibility is that the effect of denervation of the sphincter of Oddi may be insufficient to cause regurgitation of the intestinal fluid into the bile duct.

Review of medical records of 6 of 10 OCMRB-positive patients clarified no significant etiologies to cause OCMRB (Table 2). However, OCMRB in these patients might have resulted from any sub-clinical condition that might impair function of the sphincter of Oddi, for example, biliary stones that had already passed through the papilla at the time of MRCP or compression of the papilla due to tumor or distended intestine nearby.

As mentioned, we do not routinely give OCM to all patients who undergo MRCP but decide on its administration depending upon the amount of intestinal fluid present that may hamper visualization

of the pancreaticobiliary duct system. Our approach may be justified, not only because it may solve the issue of OCMRB, as presented in this study, but also because it avoids unnecessary administration of OCM in patients with a sufficiently small amount of intestinal fluid. Furthermore, it would facilitate diagnosis of pathologies at the papillary or parapapillary regions, such as papillary tumors, duodenal stenosis, and anomalous junction of the pancreaticobiliary duct, because some fluid around the papilla may improve visualization of these areas. We therefore believe it would be beneficial to obtain MRCP images before OCM administration to secure visualization of the lower CBD or papillary and parapapillary regions, particularly when pathologies are clinically suspected around these areas in patients with known juxtapapillary diverticula, pneumobilia, and history of papillary intervention. When 3D MRCP images obtained after OCM administration are degraded due to poor respiratory triggering, we can then arbitrarily add 2D MRCP with breath holding, which takes only a few seconds. Another possible approach would be to perform meticulous surveys before MRCP, reviewing medical records or previous images regarding the presence of juxtapapillary diverticula, pneumobilia, and history of papillary intervention, and to obtain MRCP images before OCM administration for those with these factors.

Our study has several limitations in addition to its retrospective design. Our small number of positive cases among the large number of overall participants would underpower this study. A larger multicenter study may be required to solve this issue. Another limitation is the different MRCP sequences used before (2D) and after (3D) OCM administration, each of which may yield different image quality and signal intensity profile. Ideally, OCMRB should have been evaluated using the same sequence, and this usage of two different sequences could have affected our results. In general, 3D MRCP may be superior to 2DMRCP in terms of image quality and delineation of minute anatomy of the duct system if respiratory navigation or triggering functions adequately,<sup>12,13</sup> but if it does not, 2D MRCP would provide more information than 3D MRCP<sup>14</sup>; thus, the two work complementarily. For delineation of a large duct system such as that of the CBD, however, both work well, without significant difference, and we believe this inconsistency of the MRCP sequences may have had little influence on our results. A third limitation is possible bias in our study population because we studied only 288 patients who received OCM and excluded 139 patients who underwent MRCP without OCM.

Therefore, strictly speaking, our result of a 4% incidence of OCMRB may not be generalized. Fourth, some bias may have resulted because we assessed images by consensus interpretation of 2 radiologists and not independently. However, we believe any bias may be minimized by the relatively easy and straightforward identification of OCMRB, juxtapapillary diverticula, and pneumobilia according to our definitions. Finally, because the appearance of pneumobilia may be inconsistent and change according to the time course, we might have underestimated the incidence of pneumobilia on MRCP or computed tomography.

## Conclusion

Radiologists should be aware that OCMRB may be observed in about 4% of patients who undergo MRCP, the presume etiology of which is the dysfunction of the sphincter of Oddi. Acquisition of MRCP images before OCM administration may secure visualization of the lower CBD or parapapillary regions, particularly in patients with juxtapapillary diverticula, pneumobilia, and history of papillary intervention, for whom pathologies are clinically suspected around these areas.

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