ORIGINAL ARTICLE





Preoperative MRCP Can Rule Out Choledocholithiasis in Acute Cholecystitis with a High Negative Predictive Value: Prospective Cohort Study with Intraoperative Cholangiography

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Abstract

Background Magnetic resonance cholangiopancreatography (MRCP) provides a noninvasive and fast modality for imaging the biliary tree when choledocholithiasis is suspected. Guidelines suggest that MRCP is recommended when strong or moderate signs of common bile duct (CBD) stones are present. Well-performed prospective studies are scarce regarding the sensitivity and specificity of preoperative MRCP in patients with acute cholecystitis in comparison with intraoperative cholangiography, ERCP, or choledochoscopy.

Methods We performed a prospective, observational population-based feasibility study in Central Finland Hospital Nova between January 2019 and December 2019. We examined the diagnostic performance of preoperative MRCP on consecutive patients with acute cholecystitis scheduled for index admission cholecystectomy. The accuracy of MRCP was verified with IOC, choledochoscopy, or ERCP. The interobserver reliability of the image quality of MRCP and the sensitivity and specificity of choledocholithiasis were observed independently by three experienced radiologists.

Results A total of 180 consecutive patients diagnosed with acute cholecystitis followed by index admission cholecystectomy were identified. MRCP was performed in 113/180 (62.8%) patients, and complementary perioperative imaging of the bile ducts was performed in 72/113 (63.7%) patients. The incidence of choledocholithiasis was high (29.2%). In acute cholecystitis, the sensitivity (76.2–85.7%) and specificity (84.3–92.2%) of MRCP were equally compared to the literature with unselected patient groups. The best visibility was observed in the common hepatic duct, the inferior CBD, and the central hepatic duct. The interobserver reliability was excellent for determining the size and quantity of CBD stones.

Conclusion In acute cholecystitis, MRCP yields high negative predictive value regarding detection of choledocholithiasis. If CBD stones were discovered, the interobserver reliability was excellent when measuring the size and number of CBD stones. The best-visualized area was the distal part of the biliary tract, which provides good preoperative workup if choledocholithiasis is present.

Keywords Magnetic resonance cholangiopancreatography · Choledocholithiasis · Acute cholecystitis · Sensitivity

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Introduction

Cholecystitis is a common disease with a significant amount of patients admitted to surgical emergency units globally. The treatment of choice for acute cholecystitis is cholecystectomy performed as soon as possible after the onset of symptoms.¹ The high prevalence (9–25%) of choledocholithiasis in acute cholecystitis advocates preoperative risk stratification with biliary imaging^{2,3} as the consequences of untreated choledocholithiasis can lead to severe complications, such as acute pancreatitis and acute cholangitis. Additionally, early preoperative diagnosis of choledocholithiasis facilitates adequate planning of common bile duct (CBD) stone removal, preferably performed as a single-stage procedure.⁴ Magnetic resonance cholangiopancreatography (MRCP) provides a noninvasive and fast modality with 80–95% sensitivity and 93–100% specificity for imaging the biliary tree.^{5–9} Guidelines suggest that MRCP is recommended when strong or moderate signs of CBD stones are present.^{1,10} However, there is a paucity of well-performed studies regarding the sensitivity and specificity of preoperative MRCP in patients with acute cholecystitis, especially in comparison with intraoperative cholangiography.³

This present study focused on the radiologists' evaluation in the quality of the MRCP images and interobserved agreement. Furthermore, predictive value of MRCP regarding CBD stones was studied and compared to IOC.

Materials and Methods

A prospective, observational population-based feasibility study was conducted in Central Finland Hospital Nova between January 2019 and December 2019. Inclusion criteria were as follows: all consecutive patients diagnosed with acute cholecystitis followed by preoperative MRCP and complementary perioperative imaging of the bile ducts (intraoperative cholangiography (IOC), intraoperative choledochoscopy, and intra- or postoperative endoscopic retrograde cholangiopancreatography (ERCP)) and operated during index admission. Patients with nonoperative management or delayed operation were excluded. Diagnostic imaging of the acute abdomen included an ultrasound examination of the upper abdomen or computed tomography (CT) primarily. MRCP was scheduled after the diagnostic criteria of acute cholecystitis according to Tokyo guidelines were filled.¹¹ Routinely intended MRCP has been implemented in our hospital for all patients diagnosed with acute cholecystitis since January 2019. Before the study period, preoperative MRCP was only scheduled for clinical or radiological suspicion of common bile duct stones or a rise in liver laboratory markers. The final study cohort constituted of patients with performed MRCP and complimentary visualization of the biliary ducts (IOC, choledochoscopy, intra-or postoperative ERCP). Three radiologists (with five, nine, and 25 years of experience) interpreted the MRCP images. All readings of MRCP were performed independently by three radiologists without information on the surgical findings. All readers underwent a training session for 10 patients not included in the study prior to the first reading session.

The acquisition of individual patient data from hospital records was approved by the local hospital districts. The study was registered in the ClinicalTrials.gov identifier: NCT04059601.

Data Collection

The onset of symptoms, hospital arrival, time from arrival to operation, time from arrival to MRCP imaging, reasons for MRCP refusal, usage of oral contrast agent, laboratory values, operative details, 30-day morbidity, and postoperative outcome were registered.

Qualitative Evaluation of MRCP

Undisputed stones in MRCP, high suspicion of CBD stones, and sludge were interpreted as choledocholithiasis in preoperative MRCP images. The image quality of MRCP was evaluated using a 5-point scale adopted and modified from Asbach et al.¹² The depiction of predefined segments of the biliary and pancreatic ductal tree was scored independently by the three radiologists on a 5-point scale (1 = perfect visualization)of the entire ductal structure; 2 = most of the ductal structure visualized; 3=ductal structure partially visible; 4=detection of the ductal structure almost impossible; 5 = ductal structure not visible). The ductal segments were assessed as follows: (1) inferior part of the common bile duct (CBD); (2) the common hepatic duct (CHD); (3) the central hepatic ducts; (4) the peripheral intrahepatic bile ducts (PID); (5) the pancreatic duct at the level of the head, the body, and the tail; and (6) the cystic duct. The total score of the ductal segments was also calculated. The presence of common bile duct stones and sludge was collected, as the stone size and number of observed stones.

Magnetic Resonance Cholangiopancreatography

Subjects were scanned using 1.5T Siemens Symphony Tim or GE Discovery MR450 clinical MR systems with 6- or 8-channel phased-array coil (Siemens Healthcare, Erlangen, Germany and GE Healthcare, Illinois, USA).

Imaging protocol comprised T2-weighted axial TRUFI/ FIESTA (6 mm; 0.6 mm/8 mm; 1 mm (thickness; gap)), fatsaturated coronal TRUFI/FIESTA (7 mm; 0.7 mm/8 mm; 1 mm (thickness; gap)), fat-saturated thick slab (40 mm/50 mm) 2D MRCP, and coronal 3D MRCP (1.5 mm/1.4 mm (thickness)) sequences.

Commercially available blueberry juice was used as a negative contrast agent if the patient did not have nausea, or the examination was evaluated not to impede the consequent surgery. In other cases, the imaging was performed without any oral contrast agent.

Operative Approach

Laparoscopic or open cholecystectomy was scheduled according to the patient's clinical scenario. Intraoperative

cholangiography (IOC) was performed if feasible. IOC's quality, technical success, and c-arm cholangiography were documented and stored in the hospital database. In the case of common bile duct stones, the operating surgeon decided on the policy of stone removal. Methods for CBD clearance included laparoscopic transcystic or transductal choledochoscopy, open CBD exploration, intra- or post-operative ERCP, or a combination of formerly mentioned methods.

Statistical Analysis

The data are presented as means with standard deviations (SD), medians with interquartile range (IQR), or counts with percentages. The 95 percent confidence intervals (95% CI) are given for the most important outcomes. Confidence intervals for sensitivity, specificity, and accuracy are "exact" Clopper-Pearson confidence intervals. The groups were compared using the Mann–Whitney *U*-test, Kruskal–Wallis test, or the chi-square test as appropriate. Statistical analyses were performed using IBM SPSS 27.0 (IBM corp., Armonk, NY, USA).

Feasibility was reported as percentage of patients in which preoperative MRCP was possible.

Values < 0 indicate no agreement and 0–0.20 as slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as

substantial, and 0.81–1 as almost perfect agreement.¹³ Intraclass correlation coefficients (ICC) were calculated to assess agreement between raters through absolute agreement and 2-way random-effects model.

Results

Demographic Data

One hundred eighty patients were operated on during index admission for acute cholecystitis during the study period (Fig. 1). Preoperative emergency MRCP was performed in 113/180 (62.8%) patients. MRCP with consequent IOC was performed in 63/113 (55.8%) patients. Complementary bile duct evaluation (choledochoscopy, intra-or postoperative ERCP) without IOC was performed in 9/113 (8.0%) patients. Thus, in 72 (63.7%) patients, the biliary tree was evaluated with preoperative MRCP and additional imaging, which formed the final study cohort.

Reasons for MRCP withdrawal in 67 (37.2%) patients were logistic (nighttime, unavailability of MRCP service, quick access to the operative theater), 12 (6.7%) suspicion of gallbladder perforation, 12 (6.7%) unclear, 4 (2.2%) severe health problems, 3 (1.7%) incoherent mental status, 3 (1.7%) patient refusal, and 1 (0.6%) sepsis. The baseline

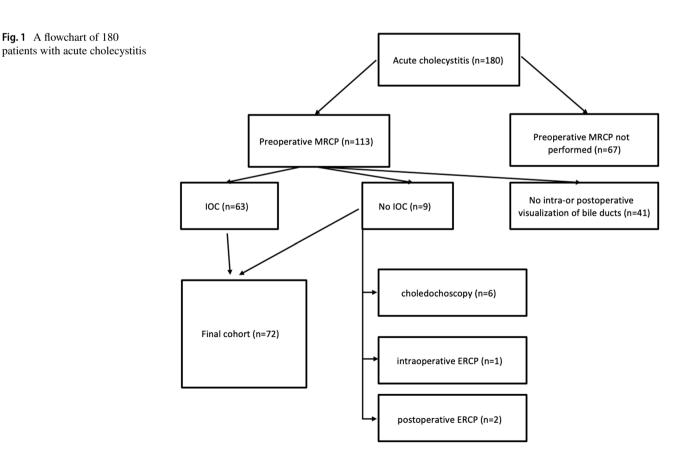


Table 1 The baseline characteristics between the study patients (MRCP and complimentary visualization of the biliary ducts (IOC, choledochoscopy, intra- or postoperative ERCP)) and the excluded patient population

	Study patients $n = 72$	Preoperative MRCP not performed n = 67	MRCP without intra- or postoperative visualization of bile ducts n=41	<i>p</i> -value
Age, mean (SD) (years)	58.9 (18.6)	67.2 (14.7)	56.7 (20.2)	0.01
Female sex, n (%)	41 (56.9)	27 (40.3)	23 (56.1)	0.105
BMI (kg/m ²), mean (SD)	30.0 (5.4)	30.4 (5.7)	30.3 (7.2)	0.785
ASA I-II, <i>n</i> (%)	48 (66.7)	27 (40.3)	22 (53.7)	0.005
ASA III-IV, <i>n</i> (%)	24 (33.3)	40 (59.7)	19 (46.3)	
Comorbidities, n (%)				
Diabetes	15 (20.8)	19 (28.4)	2 (4.9)	0.012
Cerebrovascular disease	5 (6.9)	7 (10.4)	4 (9.8)	0.75
Peripheral vascular disease	0 (0)	3 (4.5)	0 (0)	0.076
Chronic obstructive pulmonary disease	0 (0)	3 (4.5)	0 (0)	0.076
Onset of symptoms before hospital, hours, mean (SD)	40 (35)	50 (43)	60 (56)	0.231
Triage time, hours, mean (SD) ^a	48 (24)	28 (25)	45 (26)	< 0.001
Tokyo severity grade, n (%)				
Ι	31 (43.1)	34 (50.7)	12 (29.3)	0.091
Π	40 (55.6)	28 (41.8)	29 (70.7)	0.013
III	1 (1.4)	5 (7.5)	0 (0)	0.055
Laboratory values				
CRP (mg/l), mean (SD)	62 (77)	129 (120)	73 (83)	0.002
WBC $(10^{9}/l)$, mean (SD)	11 (3.7)	13 (4.9)	13 (4.3)	0.063
ALAT (U/l), mean (SD)	149 (191)	45 (74)	91 (261)	< 0.001
AFOS (U/l), mean (SD)	129 (92)	90 (74)	83 (41)	< 0.001
Bilirubin (µmol/l), mean (SD)	26 (27)	18 (17)	17 (17)	0.721
Operation time, min, mean (SD)	100 (43)	107 (41)	90 (30)	0.197
Intraoperative bleeding (ml), mean (SD)	74 (136)	256 (310)	140 (232)	< 0.001
Laparoscopy, n (%)	64 (88.9)	27 (40.3)	21 (51.2)	< 0.001
Open, <i>n</i> (%)	1 (1.4)	29 (43.3)	6 (14.6)	
Conversion, <i>n</i> (%)	7 (9.7)	11 (16.4)	14 (34.1)	
Intraoperative cholangiography, n (%)	63 (87.5)	34 (50.7)	NA	
CBD stone clearance, n (%)	21 (29.2)	6 (9.0)	NA	
LCBDE	11 (15.3)	2 (3.0)	NA	
LC + postoperative ERCP	6 (8.3)	3 (4.5)	NA	
Open CBDE	2 (2.8)	0 (0)	NA	
LC + intraoperative ERCP	1 (1.4)	1 (1.5)	NA	
Open cholecystectomy + postoperative ERCP	1 (1.4)	0 (0)	NA	
Postoperative Clavien-Dindo complications, n (%)	6 (8.3)	12 (17.9)	3 (7.3)	0.08
I	2 (2.8)	1 (1.5)	1 (2.4)	
П	1 (1.4)	1 (1.5)	0 (0)	
IIIa	1 (1.4)	2 (3.0)	0 (0)	
IIIb	1 (1.4)	6 (9.0)	0 (0)	
IVa	1 (1.4)	2 (3.0)	2 (4.9)	
IVb	0 (0)	0 (0)	0 (0)	
Postoperative length of stay (days), mean (SD)	2.1 (1.4)	4.1 (4.5)	2.2 (1.4)	0.008

^aWaiting time from emergency to operation theater

characteristics between the study patients (MRCP and complimentary visualization of the biliary ducts (IOC, choledochoscopy, intra- or postoperative ERCP)) and the excluded patient population are presented in Table 1.

Blueberry juice was used in 63/72 (87.5%) patients as an oral contrast before MRCP. The mean time from emergency room to MRCP was 18.1 h (SD 12.3). IOC or intraoperative endoscopy confirmed the incidence of CBD stones in 21 (29.2%) patients. The median CBD stone size was 5.0 mm (IQR 4.25–6). There were no adverse events related to MRCP imaging or bile duct exploration. All postoperative ERCPs were performed during the index admission without any complications. All patient data for further contact concerning biliary symptoms were checked from the patient registry. The follow-up data of the total patient cohort with a median follow-up time of 30 months. No stone-related residual symptoms were observed during the follow-up.¹⁴

Sensitivity and Specificity

When IOC, intraoperative choledochoscopy, and intra- or postoperative ERCP were used as the reference standard, radiologist A correctly identified choledocholithiasis in 61/72 cases with 18 true-positive and 43 true-negative cases, with 8 false-positive and 3 false-negative cases. Radiologist B correctly identified choledocholithiasis in 63/72 cases with 16 true-positive and 47 true-negative cases, with 4 false-positive and 5 false-negative cases. Radiologist C correctly identified choledocholithiasis in 63/72 cases with 16 true-positive and 47 true-negative cases, with 4 falsepositive and 5 false-negative cases. Table 2 summarizes the performance.

Interobserver Agreement

The interobserver reliability for total score of image quality in all six evaluated areas was almost perfect (ICC average 0.827, 95% CI 0.721 to 0.893). Almost perfect agreement was observed when measuring the presence or absence of choledocholithiasis (stones and sludge together) (ICC average 0.885, 95% CI 0.830 to 0.925). When dividing sludge and CBD stones into separate groups, substantial agreement was observed (ICC average 0.782, 95% CI 0.678 to 0.857). Almost perfect agreement was observed when measuring the CBD stone number (ICC average 0.952, 95% CI 0.857 to 0.986) and CBD stone size (ICC average 0.923, 95% CI 0.796 to 0.976). Mean scored levels of the image quality on MRCP are presented in Table 3.

Discussion

In this study, we evaluated prospectively the diagnostic accuracy of preoperative MRCP in detecting CBD stones on population-based patients with acute cholecystitis during the index admission. The diagnostic accuracy of MRCP within the framework of acute cholecystitis has not been well described in the literature. The relevance of the accuracy of MRCP interpretation in this study is highlighted by the immediate confirmation of the reference imaging with IOC, choledochoscopy, or ERCP. According to a recent

 Table 2
 Performance of the preoperative MRCP to detect choledocholithiasis when IOC, intraoperative choledochoscopy, and intra- or postoperative ERCP were used as the reference standard

	Sensitivity, % (95% CI)	Specificity, % (95%CI)	Accuracy, % (95% CI)	Positive predictive value, % (95% CI)	Negative predictive value, % (95% CI)
Radiologist A	85.7 (64–97)	84.3 (71–93)	84.7 (74–92)	69.2 (54–81)	93.5 (83–98)
Radiologist B	76.2 (53–92)	92.2 (81–98)	87.5 (78–94)	80.0 (60-91)	90.4 (81–95)
Radiologist C	76.2 (53–92)	92.2 (81–98)	87.5 (78–94)	80.0 (60-91)	90.4 (81–95)

Table 3Mean scored levels ofthe image quality on MRCP(graded on scale from 1 (best)to 5 (worst)

	Radiologist A mean (SD)	Radiologist B mean (SD)	Radiologist C mean (SD)	ICC	95% CI
Inferior CBD	1.1 (0.3)	1.1 (0.4)	1.1 (0.4)	0.605	0.416 to 0.740
Common hepatic duct	1.0 (0.2)	1.2 (0.5)	1.1 (0.5)	0.614	0.432 to 0.745
Central hepatic duct	1.2 (0.6)	1.3 (0.8)	1.1 (0.5)	0.822	0.736 to 0.883
Peripheral hepatic ducts	2.6 (0.6)	2.3 (1.0)	1.9 (0.9)	0.680	0.463 to 0.806
Pancreatic ducts	2.3 (0.8)	1.8 (1.0)	1.7 (1.0)	0.854	0.752 to 0.917
Cystic duct	2.2 (1.1)	2.2 (1.2)	1.9 (1.1)	0.832	0.750 to 0.889

meta-analysis,³ the main findings in our study are that the sensitivity (76.2–85.7%) and specificity (84.3–92.2%) of preoperative MRCP regarding CBD stones in acute cholecystitis are equal compared to the literature with unselected patient groups with sensitivities ranging from 77 to 100% and specificities from 73 to 99%.^{7,8,5,15}

The incidence of choledocholithiasis in acute cholecystitis varies between 9 and 25%, depending on whether selective or routine biliary imaging is practiced.^{3,16} Our study's high incidence of choledocholithiasis was in line with previous results. In our study, the incidence of choledocholithiasis was high despite the small size (median 5 mm) of detected CBD stones. Even small CBD stones could be ruled out with a high negative predictive value (90.4–93.5%).

There was almost perfect interobserver reliability of the total quality scores and the verification of choledocholithiasis in MRCP images between the three radiologists. However, when divided into subgroups, almost perfect interobserver reliability was observed only in the areas of the pancreatic ducts, the cystic duct, and the central hepatic duct. Substantial interobserver reliability was found in the inferior CBD and the common hepatic and the peripheral hepatic ducts. Furthermore, the visibility of the common hepatic duct, the inferior CBD, and the central hepatic duct was evaluated to be perfect by all three radiologists. In addition, the cystic duct and the pancreatic duct were graded to be mostly visible. Interestingly, the visibility of the peripheral hepatic ducts was categorized as the weakest of the areas studied. However, even in these parts of the biliary tract, the visibility was evaluated as "partially or most of the ductal structure visualized." The high quality of the MRCP images in the distal part of the biliary tract enables good preoperative workup if choledocholithiasis is present, which is of utmost importance if cholecystectomy is performed during the same index admission. Overall, if CBD stones were discovered, the interobserver reliability was excellent when measuring the size and number of CBD stones.

In a recent review, oral contrast agents for gastrointestinal signal suppression in MRCP was recommended.¹⁷ In our study, the use of commercially available blueberry juice was possible in 87.5% of examinations. Additionally, the use of oral contrast agent did not cause any delay to surgery, as the median triage time from emergency to surgery was only 44 h.

In our hospital, routinely intended MRCP has been used in patients with acute cholecystitis since 2019. According to a recent meta-analysis, routine biliary imaging is recommended in acute cholecystitis due to the high incidence of choledocholithiasis.³ However, according to the World Society of Emergency Surgery (WSES) and the American Society for Gastrointestinal Endoscopy (ASGE) guidelines, MRCP is recommended only when the probability of CBD stones is moderate or strong. Low-risk patients could be operated on directly, and moderate- and high-risk patients need pre-, intra-, or postoperative confirmation and therapeutics for possible choledocholithiasis.^{1,10,18} Recently, we have also shown in a feasibility study that the routine use of IOC offers no additional benefit over the selective use in acute cholecystitis.¹⁴ Intraoperative cholangiography is sometimes technically demanding and risky in patients with severe cholecystitis. MRCP could be used as an alternative imaging method for ruling out choledocholithiasis. However, the potential risk of dropping stones into CBD with surgical manipulation has to be taken into consideration. Taken together, the need for preoperative MRCP is still controversial.³

In addition to the relatively small sample size, some other limitations should be acknowledged. The high number of different surgeons performing IOC may have affected the interpretation of the images. Some selection bias may have occurred when performing IOC. It is possible that in patients with higher suspicion of CBD stones, IOC could be less often abandoned in case of difficulties. However, the routine protocol was IOC in all patients and therefore, this effect should be limited. Preoperative MRCP could only be performed in a moderate number of acute cholecystitis patients mainly due to logistic reasons and patients' comorbid sickness not allowing immediate imaging. To evaluate the accuracy of preoperative MRCP, complementary intraoperative verification of the biliary tree was accomplished in 63.7%. However, the time frame from emergency MRCP to surgery in this study was narrow. Thus, the issue of migrating stones from the gallbladder to the CBD or from the CBD to the duodenum can be minimized in the sensitivity and specificity analysis.⁸

Conclusion

In acute cholecystitis, MRCP yields high negative predictive value in choledocholithiasis. If CBD stones were discovered, the interobserver reliability was excellent when measuring the size and number of CBD stones. The distal part of the biliary tract is best visualized thus enabling preoperative planning of CBD clearance if choledocholithiasis is present.

Declarations

Conflict of Interest The authors declare no competing interests.

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