

Is magnetic resonance cholangiopancreatography the new gold standard in biliary imaging?

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Abstract. The timing and technique of perioperative biliary imaging in relation to laparoscopic surgery remains controversial. This study assessed the predictive value of magnetic resonance cholangiopancreatography (MRCP) in the diagnosis of biliary pathology. Clinical, laboratory and investigational data were evaluated from 374 patients undergoing MRCP at two hospital sites over a 5-year period. MRCP findings were compared with endoscopic retrograde cholangiopancreatography (ERCP) or operative findings and appropriate clinical endpoints. Complete data were available for 351 of the 374 patients (94%), of whom 232 (66%) were female. Median age was 64 years. The predominant presentation was abdominal pain ($n=190$). Features of pancreatitis were present in 59, cholangitis in 26 and jaundice in 109 patients. Ultrasound was the initial investigation in 312 (89%) (176-gallstone positive). Common duct dilatation was evident in 114 patients and ductal calculi in 31. ERCP was successful in 212/283 (75%) patients. Significant ERCP induced pancreatitis occurred in 12 (5.6%). Comparison between MRCP and ERCP was not possible in 85 due to failure of either technique. Nine patients underwent other investigations including intraoperative cholangiogram (IOC), percutaneous transhepatic cholangiogram (PTC) and were included. Of the 221 patients with full comparative data available the MRCP showed a sensitivity of 97.98% and specificity of 84.4%. MRCP is highly sensitive and specific for choledocholithiasis and avoids the need for invasive imaging in most patients with suspected choledocholithiasis.

This study has evaluated the longitudinal experience of magnetic resonance cholangiopancreatography (MRCP) in two large UK hospitals reporting largest series of cases comparing endoscopic retrograde cholangiopancreatography (ERCP) with MRCP.

The magnitude of the clinical problem of gallstones in Europe is considerable with an estimated prevalence of 5–20% [1] in the general population, rising with age. The prevalence of gallstones in women aged 60–70 years is 20–40%, and 10% in men of the same age group. The incidence of gallstones is three times more common in women than in men and rises with age irrespective of sex [2] giving a prevalence of 31% in women between 61 years and 70 years and 52% between 71 years and 90 years [3]. It is reported that at the time of cholecystectomy for symptomatic cholelithiasis, 8–15% of patients less than 60 years and 15–60% of patients over 60 years have common bile duct (CBD) stones [4]. Choledocholithiasis may be asymptomatic; or symptomatic with potential complications including pancreatitis, cholangitis and obstructive jaundice [5] adding further to the burden of management in gallstone disease. This is particularly the case in older patients with the additional attendant risks of invasive intervention associated with increased cardio-respiratory morbidity and diminished physiological reserve. Consequently, the European Association for Endoscopic Surgery (EAES) consensus development conference committee recommends common bile duct

investigation to rule out choledocholithiasis in all patients with symptomatic cholelithiasis [4].

Various clinical, biochemical and investigative procedures may be used to identify the ductal calculi [6]. Biochemical tests carry poor sensitivity and specificity. Ultrasound is an easily available, non-invasive and low cost investigation with no requirement for ionizing radiation. However, it is highly operator dependent [4], misses two in three patients with common bile duct stones and is subject to interference from bowel gas. It is particularly poor in detecting smaller partially obstructing calculi. The distal CBD may not routinely be examined if there is no extrahepatic biliary dilatation and this may further diminish the sensitivity.

Endoscopic ultrasound (EUS) facilitates better visualization of the entire extrahepatic biliary tree with high sensitivity (88%) and specificity (96%) [7, 8]. Despite the fact that both ERCP and EUS requires specialized expertise to perform, limited availability of EUS restricts its routine use at present for CBD evaluation. ERCP, intraoperative cholangiogram (IOC), percutaneous transhepatic cholangiography (PTC) and operative CBD exploration are considered as the gold standard procedures in the diagnosis of choledocholithiasis. The invasive nature of CBD exploration, IOC and PTC carries a significant morbidity and mortality. Furthermore, a high level of expertise is required in their performance.

ERCP is highly sensitive and specific, but invasive and inconvenient for the patient, requiring sedation and contrast (with minimal risk of allergic reaction), and associated with significant morbidity (5–10%) and mortality (<1%) [4]. MRCP is non-invasive for studying the biliary tree and requires no ionizing radiation or iodinated

Received 30 November 2004 and in final form 19 April 2005, accepted 6 May 2005.

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contrast. It gives high-resolution projectional images of the CBD with no known hazards, in the absence of incompatible foreign bodies. Our study aimed at evaluating predictive value of MRCP in assessing symptomatic patients prior to cholecystectomy or further biliary intervention with particular reference to laparoscopic surgery. We also evaluated the potential for additional benefit including the diagnoses of other hepatobiliary and pancreatic pathology.

Patients and methods

Study design and inclusion criteria

This was a retrospective cohort study of a consecutive group of patients who underwent MRCP. Referral for the investigation was based on clinical, bio-chemical and ultrasound suspicion of CBD stone. Patients were identified from two large UK hospitals over a total period of 57-months. Data collected included: clinical presentation, liver function test results, ultrasound, ERCP and MRCP findings, and procedure related complications (ERCP/MRCP) were recorded. ERCP was the reference imaging technique for comparison of the results of MRCP in the detection of CBD stones. Where ERCP failed, PTC and IOC and per-operative CBD exploration were the reference standards.

Patients who were claustrophobic to MRCP and in whom ERCP had failed were excluded from the predictability calculation. Patients who underwent MRCP (true negative for CBD stone) but without a comparable reference procedure were also excluded.

Imaging technique

MRCP at Kirkcaldy hospital was performed using a 0.5 Tesla Elscint Privilege MRI scanner with two sequences; axial T_2 weighted for liver and multislice RARE sequence (10 mm slice thickness, three-dimensional (3D) maximum intensity projection to reconstruct the bile duct). MRCP at Aberdeen was performed using a 1 Tesla Siemens Magnetom impact MRI scanner with three sequences; axial T_2 weighted turbo spin echo breath hold (slice thickness 10 mm, repetition time (TR) 2054, echo time (TE) 128), coronal and coronal oblique thick slab RARE and thin slice (6 mm) coronal HASTE (TR 11, TE 87). No oral or intravenous contrast medium was used.

Statistical analysis

The data were entered in a Microsoft Excel database. Statistical calculations were performed using Fisher's exact test, supported by StatsDirect® statistical software version 2.3.8 for Windows, to predict the association between the variables (ERCP and MRCP) following appropriate statistical advice. A p -value of <0.05 was considered statistically significant. The results of MRCP were analysed against ERCP or other invasive imaging for the entire study population. Detailed subgroup analysis was also carried out for ERCP following MRCP ($n=176$), ERCP prior to MRCP ($n=107$) and MRCP following ERCP in whom ERCP was subsequently repeated ($n=13$). Where ERCP was unavailable but an alternative form of

invasive imaging was carried out (IOC or PTC) ($n=9$), this was used as reference standard. Sensitivity, specificity, positive and negative predictive values were individually calculated in the usual manner.

Results

374 patients underwent MRCP and were eligible for further evaluation during the 57-month period studied. Complete data were available for 351 (94%) patients of whom 232 (66%) were female with median age of 64 years (range 16–92 years). Abdominal pain was the predominant symptom at presentation ($n=190$) with 84 having associated jaundice. 18 patients presented with painless jaundice. Pancreatitis ($n=59$) and cholangitis ($n=26$) were the other most common features. Atypical presentations occurred in 24 patients: weight loss ($n=16$), altered bowel habit ($n=4$), retrosternal pain ($n=3$) and abdominal distension ($n=1$).

Ultrasound

Ultrasound scan of the hepatobiliary system was the primary investigation in 312 patients of whom 29 had previously undergone cholecystectomy. 196 (63%) showed evidence of cholelithiasis and 13 biliary sludge. Other abnormalities seen were stricture, duplication of gall bladder, cholesterol polyp (one each) and choledochal cyst in two patients. No abnormality was observed in 98 patients.

The CBD was dilated (more than 7 mm) in 114 (36.5%). Ultrasound evidence of choledocholithiasis was seen in 31 (31%) of the 99 patients subsequently diagnosed by ERCP. In 37 (12%) studies, visualization of the CBD was obscured by gas.

MRCP

Of 351 patients referred, MRCP was successfully performed in 337 (96%). 14 study failures were due to claustrophobia, lack of co-operation (inability to lie still) or excessive body mass.

ERCP

ERCP was attempted in 283 (84%) of the 337 patients who underwent MRCP. In 163 (58%) of cases ERCP was performed subsequent to MRCP, before MRCP in 107 (37%) and both before and after MRCP in 13 (5%). ERCP was successful in 212 (75%) patients with a maximum of four attempts (81 failures occurred after the first attempt, 12 after the second and one failure after the third and fourth attempts, respectively). It was a common practice to perform sphincterotomy and balloon trawl in cases with a strong suspicion of biliary calculus despite reasonable contrast imaging for choledocholithiasis. However, there has been a general change in the practice recently with the aim of avoiding additional morbidity associated with sphincterotomy. In our study, 158 patients underwent sphincterotomy and balloon trawl. The most common reasons for unsuccessful ERCP were: failure to identify the ampulla, mobile ampulla, duodenal diverticulum, agitated or uncooperative patient, pyloric stenosis, duodenal

stricture and previous gastrectomy. 12 (5.7%) patients developed clinically significant pancreatitis following ERCP.

Further imaging

In an additional nine patients where ERCP was failed, comparator imaging data were available from other invasive procedures (IOC, PTC).

Accuracy of MRCP

A total of 221 patients with complete comparative data were considered for detailed analysis. The overall sensitivity and specificity of MRCP was 97.98% (95% CI, 92.19–99.64, $p < 0.0001$) and 84.43% (95% CI, 76.49–90.13, $p < 0.0001$), respectively. The positive predictive value (has the disease) of MRCP for all biliary pathology was 83.62%. The negative predictive value of MRCP (truly disease free) was 98.10% (Table 1).

Subgroup analysis

Subgroup 1: MRCP compared with subsequent invasive imaging (n=186)

ERCP was attempted after MRCP in 163 patients and successful in 144. Choledocholithiasis was confirmed in 52. A further 13 patients with an initial ERCP failure followed by MRCP underwent successful therapeutic ERCP. Nine patients with a failed ERCP in whom MRCP had indicated choledocholithiasis were confirmed as having CBD stones (true positive for MRCP) during other invasive procedures [IOC (n=6), CBD exploration (n=2), PTC (n=1)]. In this subgroup of 185 patients who had undergone MRCP comparable data were available (with ERCP, IOC, PTC) for 166. The median interval between MRCP and ERCP (or IOC/PTC) was 8.5 days (ranging from same day to 127 days). Sensitivity and specificity was analysed for these 166 patients (Table 1).

Subgroup 2: ERCP before MRCP (n=107)

The ERCP was attempted before MRCP in 107 patients and was successful in 55. The median interval between the procedures was 11 days (range 2–71 days). 52 test failures were further investigated with MRCP and subsequently managed either conservatively or underwent operative intervention based on the MRCP results. No comparable data were available for these 52 patients and were excluded from the sensitivity and specificity calculation. The

Table 2. Different diagnoses among true positive and false negative results of magnetic resonance cholangiopancreatography

Diagnosis	Number
True positive	
CBD stones	74
Stricture	6
Malignant growth	14
Congenital anomalies	3
False negative	
CBD stone	2
Total	99

CBD, common bile duct.

comparative results available from the 55 patients are given in Table 1. There were 76 choledocholithiasis among various positive diagnoses, based on all investigations (Table 2).

Of the 71 patients with unsuccessful ERCP but negative (for CBD stone) on MRCP, 51 were managed conservatively and remained symptom free at the time of the review; 20 patients were lost to follow-up.

Discussion

Since the advent of laparoscopic cholecystectomy, preliminary evaluation of the biliary tree has assumed even greater importance in patients at risk of choledocholithiasis and may help to avoid intraoperative difficulty, particularly with “forced conversion” to open surgery due to lack of skills, equipment or unsuccessful attempts at laparoscopic bile duct exploration. The need for a time consuming and potentially hazardous intraoperative cholangiogram may also be reduced or eliminated if a confident prior assessment and appropriate pre-operative clearance of the CBD is carried out.

In spite of different diagnostic modalities available for detecting choledocholithiasis, currently no single method is both risk free and with high sensitivity and specificity. Intraoperative cholangiogram, when used routinely, increases operating time [9] significantly. Disposable equipment adds to the cost of treatment and the procedure offers limited benefit to patients, particularly if the specialist skills and equipment required for laparoscopic duct exploration are unavailable. Hence such imaging is not advocated routinely in laparoscopic cholecystectomy [9, 10].

At present, ERCP is considered the gold standard method for the diagnosis of the ductal calculus, but carries potential risk of complications including pancreatitis,

Table 1. Results and sensitivity/specificity for MRCP as evidenced against invasive gold standard procedures (confidence interval (CI))

Category	True positive	True negative	False positive	False negative	Sensitivity (CI) %	Specificity (CI) %	Positive predictive value (CI) %	Negative predictive value (CI) %
ERCP after MRCP	74	78	13	1	98.67 (91.79–99.93)	85.71 (76.45–91.88)	85.06 (75.44–91.49)	98.73 (92.18–99.93)
ERCP before MRCP	23	25	6	1	95.83 (76.88–99.78)	80.65 (61.94–91.88)	79.31 (59.74–91.29)	96.15 (78.41–99.80)
Overall	97	103	19	2	97.98 (92.19–99.64)	84.43 (76.49–90.13)	83.62 (75.35–89.61)	98.10 (92.61–99.67)

MRCP, magnetic resonance cholangiopancreatography; ERCP, endoscopic retrograde cholangiopancreatography.

bleeding particularly from sphincterotomy sites and duodenal perforation [11]. The procedure may not be successful with an attendant diagnostic and therapeutic dilemma in subsequent management. The incidence of such complications varies according to operator expertise and experience and once more the frail elderly patients are at greatest risk. In this study ERCP failed in 25% of procedures. As a total of six operators (all consultants with experience) were involved at the two sites studied we believe this is a reasonable reflection of real clinical practice and is within the published limits [12, 13]. This population also included a significant proportion of patients who had undergone previous biliary or gastric surgery which increase the technical difficulties of ERCP. These factors may have contributed to the finding of significant pancreatitis developed in 5.7% of our patients.

There were two sub-mucosal injections in this group requiring further cannulations or alternative investigation to confirm the ductal calculi, adding to the cost of the treatment and the morbidity.

MRCP approaches the ideal imaging modality and when used with proper indications, based on clinical suspicion and predictive scoring [6, 11], offers a safer and more acceptable alternative to diagnostic ERCP [14]. Moreover, MRI technology has progressed from the machines that were used in our study. Field strengths are higher; the gradient switching is faster, which makes better image resolution with improved accuracy. The use of MRCP for the initial "screening" of patients at risk of choledocholithiasis permits selection for more invasive procedures based on a high probability of therapeutic intervention. Very few patients are claustrophobic to the

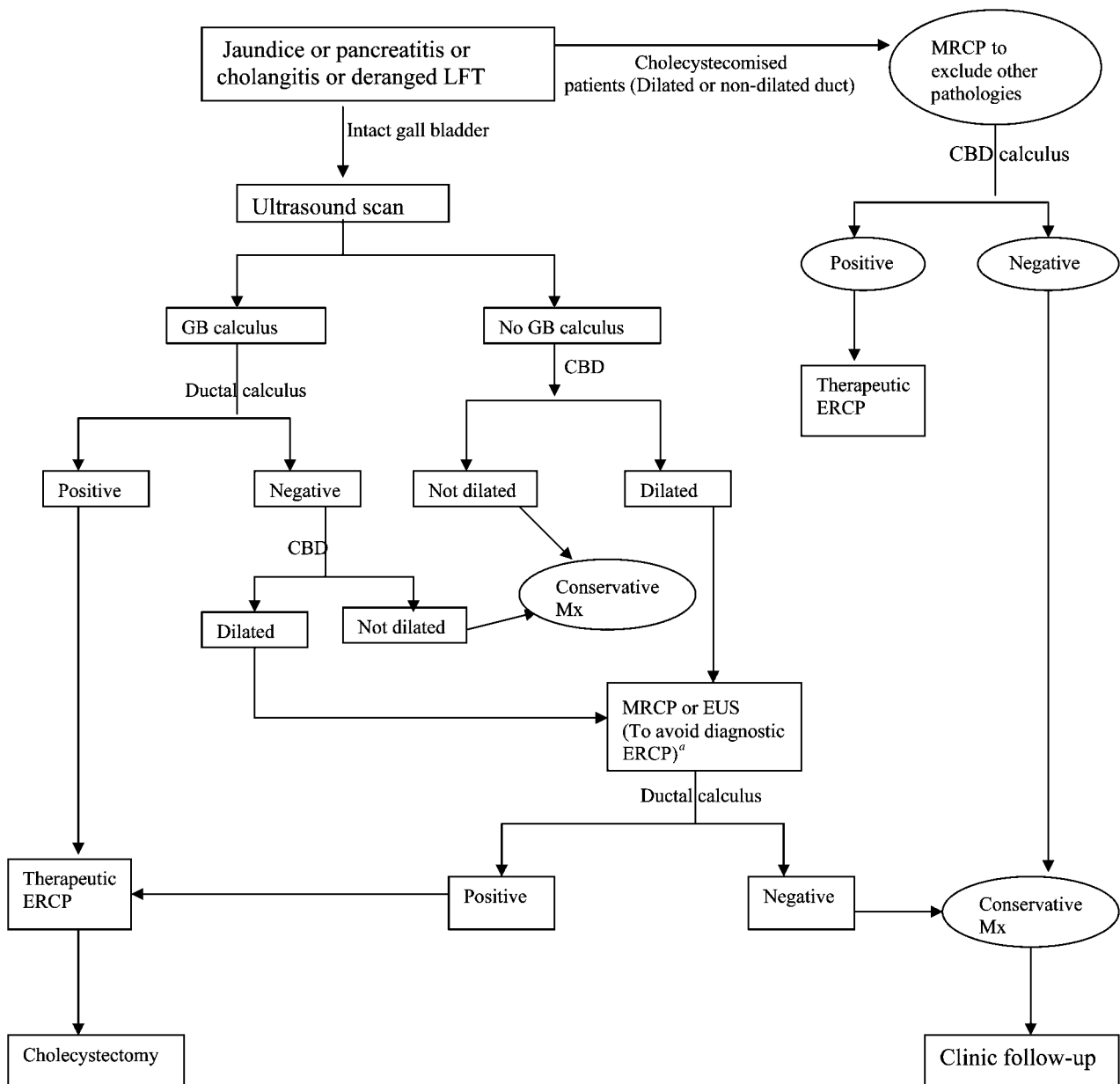


Figure 1. Algorithm for the management of biliary calculus to reduce number of diagnostic ERCP. ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography; EUS, endoscopic ultrasound; GB, gallbladder; CBD, common bile duct; LFT, liver function test. *Based on the degree of suspicion and availability.

machine for the brief period required for a biliary study. A few studies may be of reduced quality because of excess body mass or poor cooperation (movement artefact) that frequently complicates ERCP is generally less problematic. The 4% failure for MRCP in our study compares unfavourably with 25% for ERCP, and none of the complications seen with ERCP occurred. MRCP carries an additional advantage of diagnosing abnormalities of the biliary tree including duplication, choledochal cyst, pancreas divisum and cholangiocarcinoma. The superior sensitivity of MRCP over ERCP in diagnosing primary sclerosing cholangitis [15, 16] and intrahepatic calculi [17] has been well documented. A disadvantage of MRCP is that currently no therapeutic options are available for the management of common duct calculi. Sugiyama et al reported a sensitivity of 100% from their series of 101 patient [18], but Mendler et al found MRCP less sensitive for smaller stones (less than 3 mm) [19, 20]. Such small stones tend to pass and are of dubious clinical significance.

This study reported the largest consecutive series of patients undergoing MRCP for suspected extrahepatic biliary pathology yet presented. The sensitivity for the diagnosis is extremely high (97.98%). It is also evident that 78 (true negative) in subgroup 1 and 25 (true negative) in subgroup 2 underwent ERCP without therapeutic indication. In a further 51 patients, ERCP was performed unsuccessfully, whereas MRCP in the same group of patients did not show evidence of ductal calculi. This cohort of patients were managed conservatively and recovered without sequelae. This implies that invasive ERCP could have been potentially avoided in 157 patients (of 283), and in some patients more than once. Avoiding these examinations would have effectively resulted in considerable resource release. However, this reduction in the number of ERCP examinations, particularly diagnostic, will have some impact on training. This can be overcome by the centralization of ERCP service with structured training patterns.

We believe that the small false positive rate for MRCP is comfortably outweighed by the incidence of the hazards of "unnecessary" ERCP where this is confined to patients in whom the probability of operative intervention is high. Clearly, further longitudinal follow-up data must be awaited for patients with negative MRCP results with transient jaundice or pancreatitis in whom a decision is made not to undertake ERCP. Based on the results of the comparative data from two imaging modalities, as has been shown in this study, we believe the likelihood of such problems recurring is low, particularly if cholecystectomy is undertaken. British Society of Gastroenterology guidelines on the management of acute pancreatitis recommends endoscopic sphincterotomy as the definitive management for medically unfit patients presenting with gall stone pancreatitis [21] and following this algorithm ERCP would largely be confined to those with a high probability of therapeutic intervention. The average clinical workload of ERCP in our institution grossly outnumbers MRCP with an average of 430 procedures each year. Based on our findings we have developed a practical algorithm for the management of biliary calculus in different clinical situations (Figure 1).

In conclusion, MRCP can be considered as the new gold standard for the investigation of CBD stones and permits reservation of ERCP to patients with a high probability of

therapeutic intervention. Such a change in practice would have implications for allocation of resources and service design.

Acknowledgments

We are grateful to Ms Caroline Gault, Clinical audit analyst, Grampian Health Board, Aberdeen, for the statistical help and Rona Allan, medical records assistant, for retrieval of medical notes.

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