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Anatomical variations of cystic duct insertion and their relationship with choledocholithiasis: an MRCP study

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Abstract

Background: The frequency of insertion variations of cystic duct (CD) is inconsistent between studies caused to some extent by the way they give the relative frequency of the variations. Moreover, certain insertion variations have been reported to be associated with choledocholithiasis. This study aimed to assess the frequency of CD insertion variations with a comprehensive way of classification in an unselected population in whom MRCP was performed. Moreover, the relationship between the types of variant insertions and choledocholithiasis using MRCP was also assessed. Patients undergoing magnetic resonance cholangiopancreatography (MRCP) were reviewed retrospectively by two radiologists who were blinded to the clinical data. The normal insertion was defined as the union through middle one third of the lateral border of the extrahepatic bile duct. The transverse site (lateral, medial, anterior, and posterior) and the craniocaudal level (high, mid and low) of insertions and their intersections were assessed using axial and coronal slices, respectively. In addition, the frequencies of the CD insertion variations were compared between choledocholithiasis and control (no-choledocholithiasis) groups.

Results: A total of 307 patients (124 with choledocholithiasis and 183 controls) were analyzed. A true variant insertion was found in 149 (48.5%) cases. The insertion variations were less frequent in the choledocholithiasis group [50 (40.3%) vs. 99 (54.1%), respectively, $p = 0.018$]. The frequencies of craniocaudal level of insertion differed significantly between groups ($p = 0.014$) that was driven by a lower rate of low medial insertion (1.6% vs. 9.8%, respectively) in the choledocholithiasis group. The frequencies of transverse site of insertion were similar between groups ($p = 0.314$). The low medial insertion was 80.7% less likely associated with choledocholithiasis even after adjustment for age (Odds ratio: 0.193, 95% Confidence interval: 0.039–0.954, $p = 0.044$). The interreader agreement for insertion assessment was good (Cohen's Kappa: 0.748, $p < 0.001$).

Conclusions: The prevalence of CD insertion variations in an unselected population undergoing MRCP is quite high and a mid-posterior insertion is the most common variant type. Insertion variations of CD, the low medial insertion in particular, are less common in patients with choledocholithiasis than controls.

Keywords: MRCP, Anatomical variation, Choledocholithiasis, Cystic duct insertion

Background

The so-called normal mid-lateral insertion of cystic duct (CD) to extrahepatic bile duct is seen in only 51–72% of population [1, 2]. The frequency of true insertion variations is inconsistent between studies caused to some extent by the way they give the relative frequency of

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the variations [2–5]. The variations in terms of origin, course, and insertion may overlap, but they are commonly reported separately which results in ambiguity of variation rates. For instance, parallel course is commonly reported in the frequency tables, but it is unclear whether these cases have either a normal or variant insertion [2]. Yet, parallel coursing, aberrant, and accessory cystic ducts are not true insertion variations, because they do not necessarily involve the union of CD with extrahepatic bile duct. The short cystic duct is also commonly reported in the distribution of variations table without mentioning the insertion pattern of these ducts [3]. Moreover, some studies provide the low and low-medial insertions separately, although the latter is a subgroup of the former [2]. Other studies have reported only the frequency of low-medial insertion with no information about low insertion [4, 5]. A CD inevitably should insert at a craniocaudal (high/mid/low) level through a transverse (anterior/posterior/lateral/medial) aspect of the extrahepatic bile duct. However, the craniocaudal insertion level was not provided for cases with anterior or posterior insertions in one study [4]. Hence, the frequencies of the insertion variation types of CD remain ambiguous. A standardization in the way of reporting the frequencies of CD insertion variations would be plausible.

An increased incidence of common bile duct (CBD) stone formation and recurrence in those with low insertion of cystic duct was proposed [6, 7]. Biliary tract stones were seen in one-quarter of cases with posterior and anterior insertions in a recent study [5]. The relationship between CD insertion variations and choledocholithiasis requires addressing.

There has been a shift from endoscopic retrograde cholangiopancreatography and intraoperative cholangiography to preoperative magnetic resonance cholangiopancreatography (MRCP) for the assessment of biliary anatomy [8]. The MRCP is noninvasive and its diagnostic accuracy to detect gallstones, choledocholithiasis and visualize the anatomy of biliary tree preoperatively is comparable to endoscopic retrograde cholangiopancreatography or intraoperative cholangiography [9].

This study aimed to assess the frequency of CD insertion variations with a comprehensive way of classification in an unselected population in whom MRCP was performed. Moreover, the relationship between the types of variant insertions and choledocholithiasis using MRCP was also assessed.

Methods

Study population

This single center retrospective study comprised patients who underwent MRCP in our tertiary referral center between July 2019 and July 2020. Overall 379 (150 with

choledocholithiasis and 229 without choledocholithiasis) subjects who were imaged with MRCP were identified from the institutional database. The MRI images were reloaded from the Picture Archiving Communication System of our Institute. Patients whose cystic duct insertion to common hepatic duct could not be clearly identified were excluded (26 from choledocholithiasis group and 46 from control group). The remaining 307 eligible subjects (124 choledocholithiasis and 183 controls) constituted the final study population. The inclusion criteria for choledocholithiasis group were adequate MRCP allowing for the clear assessment of CD insertion and visible gallstone in common bile duct. The inclusion criteria for the control group were absence of choledocholithiasis [Normal MRCP findings ($n=161$), non-biliary pancreatitis ($n=10$), malignant biliary strictures ($n=2$), perampullary masses ($n=5$), biliary injuries ($n=3$), pancreatic divisum ($n=2$)]. The only exclusion criteria for both groups was inadequate MRCP that was not allowing for thorough assessment of CD insertion [72 (19%) of 379 reviewed patients]. Institutional Ethics Committee approval was obtained. Patients' age, gender, a previous history of and the elapsed time since cholecystectomy, presence and the type of cystic duct variations were recorded into a database.

MRCP scanning and interpretation

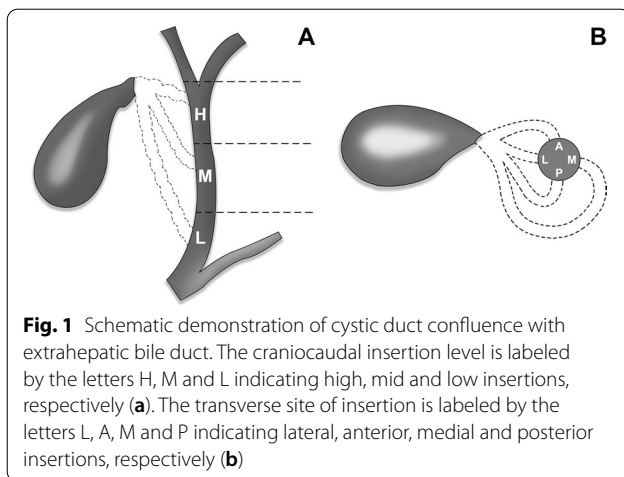
The patients were scanned using the 1.5 Tesla GE Optima MR450w (General Electric, Chicago, Illinois, USA) system. The MRCP protocol used in our Institute is shown in Table 1.

Two radiologists experienced in abdominal cross-sectional imaging (10 and 3 years, respectively) who were blinded to the clinical data reviewed all of the MRCP images on separate sessions for interrater agreement analysis. An additional session was performed

Table 1 MRCP protocol and sequences used for the current study

	T2W SS-FSE	T2W SS-FSE	3D MRCP
Plane	Axial	Coronal	Coronal
Fat suppression	+ and –	–	+
Flip Angle (°)	160	90	90
Slice thickness (mm)	4	4	1.4
FOV	40	40	36
Matrix (mm × mm)	320 × 320	320 × 320	512 × 224
TR/TE (ms)	4000/84	3500/100	3000/720
Scan time (ms)	59	59	176

T2W T2 weighted, SS-FSE single-shot fast spin echo, MRCP magnetic resonance cholangiopancreatography, FOV field of view, TR/TE repetition time and echo time



for eliminating the discrepancies between readers by consensus.

The CD insertions were classified in terms of craniocaudal level and transverse site of the union of cystic duct with extrahepatic duct (Fig. 1). The craniocaudal level of union was subclassified as high, middle, and low. The whole length of the extrahepatic bile duct was divided into three thirds subjectively. The beginning of this length was accepted as the union of the right and left hepatic ducts where they form the common hepatic duct. The ending point of this length was accepted as the opening of common bile duct into the ampulla of Vater. The transverse site of the union was subclassified as lateral, medial, anterior, and posterior. The transverse site of union of the CD was assessed according to clock method. The lateral union corresponded to 7–11 o'clock, the anterior union corresponded to 11–1 o'clock, the medial union corresponded to 1–5 o'clock, and posterior union corresponded to 5–7 o'clock.

The normal insertion of CD was defined as the union through middle one third of lateral border. All other insertions were recorded as variant.

Statistical analysis

Statistical analysis was performed with SPSS 19.0. The normality of continuous variables was analyzed by Shapiro–Wilk test. Descriptive statistics were reported as median with quartiles (25th–75th percentile) for continuous variables since the data distributions were not normal. Categorical variables were reported as frequencies with percentages. Independent two-group comparisons for continuous variables were tested using Mann–Whitney U test. The proportions were compared between the groups using Pearson's Chi-square test in case the assumptions were met. Otherwise, Fisher's exact test was used. Interobserver agreement was

also assessed using Kappa statistics. The CD insertion variants that are significant univariate predictors of choledocholithiasis were entered into a logistic regression model to adjust for age. Significance level was accepted at $p < 0.05$ for all statistical analyses.

Results

Overall 307 (156 males, 151 females) patients (124 with choledocholithiasis and 183 controls) constituted the final study population. Out of 124 choledocholithiasis patients, 61 (49.2%) were males and 63 (50.8%) were females, and the median age was 66.5 (54.25–66.5) years. Out of 183 controls, 95 (51.9%) were males and 88 (48.1%) were females, and the median age was 56 (43–69) years. The gender rate ($p = 0.64$) did not differ between the groups but the controls were younger ($p < 0.001$).

In the whole cohort, the CD insertion was normal in 158 (51.5%) and variant in 149 (48.5%) subjects. Substantial inter-reader agreement for assessment of variation types was observed (Cohen's Kappa 0.748, $p < 0.001$).

The craniocaudal insertion level was high in 18 (5.9%), mid in 269 (87.6%) and low in 20 (6.5%) cases. The site of insertion in the transverse plane was lateral in 176 (57.3%), medial in 55 (17.9%), posterior in 70 (22.8%), anterior in 6 (2%) cases. Among the intersections of craniocaudal insertion level and transverse insertion site, the most common variation type was mid-posterior [70 (22.8%)]. All intersections of insertion planes are demonstrated in Table 2. The normal insertion and all variant insertions of CD encountered in the current study are demonstrated in Fig. 2

A total of 38 CDs had a parallel course, with 7 of them having normal mid-lateral insertion. Among the remaining 31 cases with variant insertions, the most common variant insertion pattern was low-medial [14 (36.8%)] followed by mid-medial [10 (26.3%)], mid-posterior [7 (18.4%)].

Table 2 The distribution of all CD insertion patterns in the whole cohort

Whole cohort	Horizontal insertion site [n (%)]				Total
	Lateral	Medial	Posterior	Anterior	
Craniocaudal insertion level, <i>n</i> (%)					
High	18 (5.9)	0 (0)	0 (0)	0 (0)	18 (5.9)
Mid	158 (51.5)	35 (11.4)	70 (22.8)	6 (2)	267 (87.6)
Low	0 (0)	20 (5.5)	0 (0)	0 (0)	20 (6.5)
Total	176 (57.4)	55 (16.9)	70 (22.8)	6 (2)	307 (100)



Fig. 2 The 3D volume rendering MRCP images demonstrate the high-lateral (a), mid-anterior (b), mid-posterior (c), mid-medial (d), mid-lateral (e), and low-medial (f) insertions of the cystic duct

Comparison of CD insertion variations between choledocholithiasis and control groups

The rate of total CD insertion variations was significantly lower in choledocholithiasis group than controls [50 (40.3%) vs. 99 (54.1%), respectively, $p=0.018$]. The frequencies of transverse plain insertion site were similar ($p=0.314$) between groups (Table 3). The frequencies

of craniocaudal insertion level were different between groups ($p=0.003$) driven by a significantly a lower rate of low insertion [2 (1.6%) vs. 18 (9.8%), respectively] and a higher rate of mid insertion [118 (95.2%) vs. 151 (82.5%), respectively] in choledocholithiasis group (Table 3).

The frequencies of each intersections of the variations in the craniocaudal and transverse plains in

Table 3 Intergroup differences of CD insertion variants

CD insertion	Choledocholithiasis (n = 124)	Controls (n = 183)	P
Variation [n (%)]			0.018
Present	50 (40.3)	99 (54.1)	
Absent	74 (59.7)	84 (45.9)	
Craniocaudal insertion level [n (%)]			0.003
High	4 (3.2)	14 (7.7)	
Mid	118 (95.2)	151 (82.5)	
Low*	2 (1.6)	18 (9.8)	
Horizontal insertion site [n (%)]			0.294
Lateral	78 (62.9)	98 (53.6)	
Medial	17 (13.7)	38 (19.1)	
Posterior	26 (21)	44 (25.7)	
Anterior	3 (2.4)	3 (1.6)	

The p values of comparisons with significant ($p < 0.05$) intergroup difference are represented as bold and italics

*Post hoc analysis revealed a significant difference ($p < 0.05$) for only low insertion pattern. High and mid insertions remained similar ($p > 0.05$ for all) between groups

choledocholithiasis and control groups are demonstrated in Table 4. A normal lateral insertion was more common in the choledocholithiasis group (Fig. 3). The only insertion variation that significantly differed between groups was the low-medial insertion as per the post hoc analyses.

A parallel course was less frequent in the choledocholithiasis group than controls [9 (7.3%) vs. 29 (15.8), respectively, $p = 0.025$].

A binary logistic regression analysis model including the low-medial insertion, parallel course and age was constructed for prediction of choledocholithiasis. The low-medial insertion was 80.7% less likely associated with choledocholithiasis (Odds ratio: 0.193, 95% Confidence interval: 0.039–0.954, $p = 0.044$), the age (Odds ratio: 1.035, 95% Confidence interval: 1.02–1.05, $p < 0.001$) also independently predicted choledocholithiasis, but the parallel course did not show a significant association (Odds ratio: 0.515, 95% Confidence interval: 0.211–1.25, $p = 0.144$).

Table 4 Comparison of CD insertion patterns between choledocholithiasis and control groups

CD insertion pattern	Choledocholithiasis (n = 124)	Controls (n = 183)	P
High lateral	4 (3.2)	14 (7.7)	0.019
<i>Mid lateral*</i>	<i>74 (59.7)</i>	<i>84 (45.9)</i>	
Mid medial	15 (12.1)	20 (10.9)	
Mid posterior	26 (21)	44 (24)	
Mid anterior	3 (2.4)	3 (1.6)	
<i>Low medial*</i>	<i>2 (1.6)</i>	<i>18 (9.8)</i>	

The p values of comparisons with significant ($p < 0.05$) intergroup difference are represented as bold and italics

*Post hoc tests revealed significant difference between groups only for mid-lateral and low-medial insertions

Discussion

The main findings in the current study were: (1) The prevalence of CD insertion variations in an unselected population undergoing MRCP is quite high (49.2%); (2) Mid-posterior insertion is the most common (22.8%) variant type; (3) A CD with high insertion joins exclusively through the lateral aspect of extrahepatic bile duct; (4) A CD with low insertion joins exclusively through medial aspect of extrahepatic bile duct; (5) A variant insertion is less frequent in patients with choledocholithiasis than controls; (6) A low-medial insertion independently predicts the absence of choledocholithiasis (Fig. 4).

The relatively high rate of CD insertion variations in current study is close to that observed in a previous report which included an unselected MRCP population [2]. The prevalence of CD anatomical variations has been reported between 8.3 and 24% in surgical series [10–12] which is lesser than the rate observed in current or previous MRCP cohorts.

Three most common variations of cystic duct have been previously described as low insertion, medial insertion and insertion after a parallel course in earlier studies [13, 14]. More recent studies have reported that the posterior insertion was the most common anomaly of the cystic duct [2, 15]. A mid-posterior insertion was also the most frequent [(70 (22.8%))] variation type in the current study followed by mid-medial insertion. For this study, a parallel course ($n = 34$) was not considered a CD insertion anomaly, yet 20% of them showed normal mid-lateral insertion. Since a more than 2-cm long proximal-to-distal extension is required for a parallel course, it is not surprising that none of the CDs with a parallel course had a high insertion. All showed either a mid or low insertions.

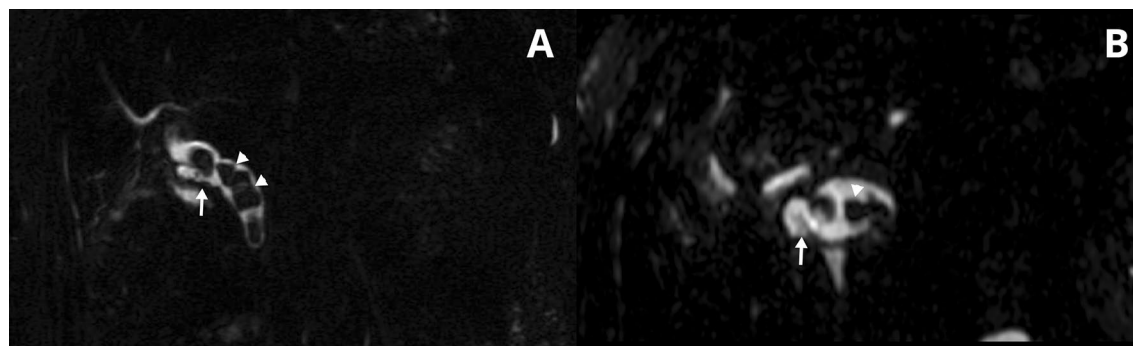


Fig. 3 A patient with mid-lateral insertion of cystic duct and choledocholithiasis. The coronal **a** MRCP image depicts the mid insertion level, and the axial **b** MRCP image shows the lateral insertion site. Note the insertion point (arrows) and the multiple stones (arrowheads) in the common bile duct

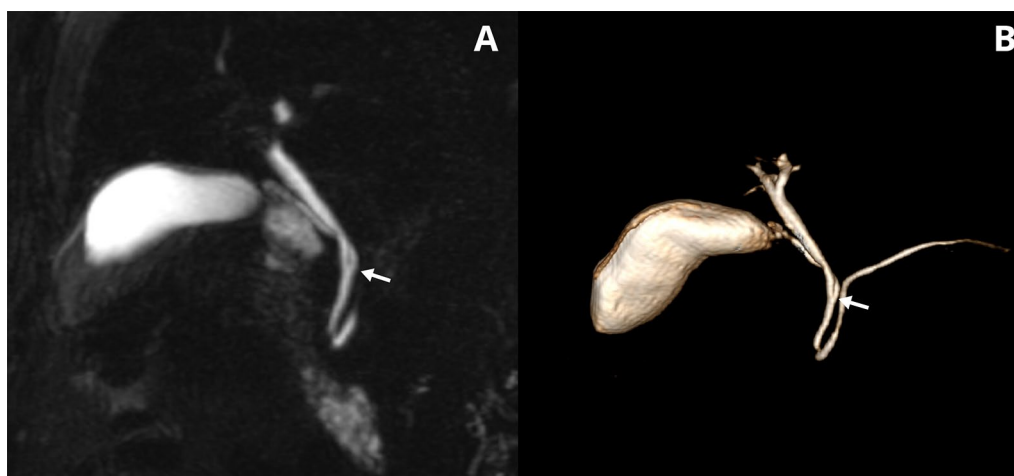


Fig. 4 A patient with low-medial insertion of cystic duct with no choledocholithiasis. The Coronal (a) and 3D volume rendering (b) MRCP images demonstrate the low medial insertion (white arrow) of cystic duct with no stone in the common bile duct

Of note, CDs with a high insertion were exclusively lateral, and those with a low insertion were exclusively medial in the current study.

A recent study has found an association between intra-pancreatic low insertion cystic duct and choledocholithiasis [16]. However, a plausible underlying mechanism for how low insertion may trigger stone formation in the common bile duct was not provided. A low insertion has been associated with biliary stones in previous studies. The stagnation of biliary flow in CD's with low-insertion has been proposed that would produce the formation of biliary stone. However, this hypothesis is not evidence based. Moreover, expecting stagnation of bile flow in CD's would be more plausible in those with long parallel or spiral course variations, rather than in those with insertion variations. Indeed, a low medial insertion was less commonly associated with choledocholithiasis even after adjustment for age and presence of parallel course, in the current work. This observation is contradictory to previous reports, and may be explained by the differences between populations studied in terms of biochemical and clinical contributors to stone formation. However, investigating all of the biological triggers of gallstone formation was beyond the scope of our study and was not evaluated. Although the genesis of gallstone due to stagnation of bile in patients with variant insertion of CD is common sense, this does not automatically mean that the stone will subsequently travel to common bile duct. We argue that, the reduced flow may even slow or preclude the movement of the gallstone through the CD, which may explain the relatively lower frequency of choledocholithiasis in patients with variant CD insertions in the current study.

The main limitation of our study is that our results are derived from an unselected MRCP population with or without choledocholithiasis and may not be extrapolated to the general population. The lack of surgical confirmation of CD insertions may be considered another limitation.

The strengths of our study are the relatively large sample size, presence of control group and standardized definitions of CD insertion variations. The CD variations including the size or course were not considered as insertion variations and the relative frequencies in our study reflect the exact insertion patterns.

Conclusions

The prevalence of CD insertion variations in an unselected MRCP population is quite high and a mid-posterior insertion is the most common variant type. The CDs with high insertion joins exclusively through the lateral aspect and those with low insertion joins exclusively through the medial aspect of extrahepatic bile duct. A low-medial insertion independently predicts the absence of choledocholithiasis.

Abbreviations

CD: cystic duct; CBD: common bile duct; MRCP: magnetic resonance cholangiopancreatography.

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Authors' contributions

NG (corresponding author) was responsible for project development and final approval of the manuscript. NG (corresponding author), MBD, MA and MY collected the data. NG (corresponding author) and UPOS were involved in manuscript writing. NG (corresponding author), UPOS and BA were involved

in critical review. BA was involved in manuscript editing. MBD analyzed the data. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

"Istanbul Medeniyet University Goztepe Prof. Dr. Süleyman Yalcin City Hospital Ethics Committee" approval was obtained. Decision Number: 2020/0068.

Consent for publication

No clinical photographs; not applicable.

Competing interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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