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WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, *etc.*

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Case Control Study

Classification of anatomical morphology of cystic duct and its association with gallstone

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Abstract

BACKGROUND

Gallstones are common lesions that often require surgical intervention. Laparoscopic cholecystectomy is the treatment of choice for symptomatic gallstones. Preoperatively, the anatomical morphology of the cystic duct (CD), needs to be accurately recognized, especially when anatomical variations occur in the CD, which is otherwise prone to bile duct injury. However, at present, there is no optimal classification system for CD morphology applicable in clinical practice, and the relationship between anatomical variations in CDs and gallstones remains to be explored.

AIM

To create a more comprehensive clinically applicable classification of the morphology of CD and to explore the correlations between anatomic variants of CD and gallstones.

METHODS

A total of 300 patients were retrospectively enrolled from October 2021 to January 2022. The patients were divided into two groups: The gallstone group and the nongallstone group. Relevant clinical data and anatomical data of the CD based on magnetic resonance cholangiopancreatography (MRCP) were collected and analyzed to propose a morphological classification system of the CD and to explore its relationship with gallstones. Multivariate analysis was performed using logistic regression analyses to identify the independent risk factors using variables that were significant in the univariate analysis.

RESULTS

Of the 300 patients enrolled in this study, 200 (66.7%) had gallstones. The mean age was 48.10 ± 13.30 years, 142 (47.3%) were male, and 158 (52.7%) were female. A total of 55.7% of the patients had a body mass index (BMI) ≥ 24 kg/m². Based on the MRCP, the CD anatomical typology is divided into four types: Type I: Linear, type II: n-shaped, type III: S-shaped, and type IV: W-shaped. Univariate analysis revealed differences between the gallstone and nongallstone groups in relation to sex, BMI, cholesterol, triglycerides, morphology of CD, site of CD insertion into the extrahepatic bile duct, length of CD, and angle between the common hepatic duct and CD. According to the multivariate analysis, female, BMI (≥ 24 kg/m²), and CD morphology [n-shaped: Odds ratio (OR) = 10.97, 95% confidence interval (95%CI): 5.22-23.07, $P < 0.001$; S-shaped: OR = 4.43, 95%CI: 1.64-11.95, $P = 0.003$; W-shaped: OR = 7.74, 95%CI: 1.88-31.78, $P = 0.005$] were significantly associated with gallstones.

CONCLUSION

The present study details the morphological variation in the CD and confirms that CD tortuosity is an independent risk factor for gallstones.

Key Words: Cystic duct; Gallstone; Classification; Anatomy; Magnetic resonance cholangiopancreatography; Risk factor

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Core Tip: We propose a novel classification system for the morphology of cystic duct (CD) based on magnetic resonance cholangiopancreatography to guide clinical practice. We also found that CD tortuosity is an independent risk factor for gallstones, which provides a theoretical basis for the construction of predictive models and prevention in high-risk patients.

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INTRODUCTION

Gallstone disease is the most common inpatient digestive diagnosis and carries substantial costs for health care services[1, 2]. There are three types of gallstones depending on the major constituents: Pure cholesterol, pure pigment, and mixed gallstones, of which cholesterol gallstones account for 80%-90% of all gallstones[3]. The formation of gallstones is a complex process involving interactions between the environment and genes. Major risk factors include age, sex, race, parity, obesity, and family history of gallstones[4,5]. Some scholars believe that the formation of gallstones is related to anatomical variation in the cystic duct (CD)[6,7]. The angle between the CD and common bile duct (CBD) junction (sistocholedochal angle: SCA) affects gallstone formation, and as the SCA increases, the incidence of gallstone formation increases[6]. The number of gallstones, the angle between the long axis of the gallbladder and the CD, and the diameter of the CD are significantly related to gallstone-related biliary events[7]. However, few scholars have focused on the relationship between the morphological variation in CDs and gallstones. The relationship between the two needs to be further explored and refined.

Currently, laparoscopic cholecystectomy (LC) has become the gold standard operation for treating symptomatic gallbladder stones[8,9]. According to relevant studies, during LC, the incidence of bile duct injury (BDI) was 0.86% from 1995 to 2002[10], 0.46% from 2000 to 2011[11], and 0.19% from 2012 to 2016[12]. With the improvements in preoperative examination and the refinement of intraoperative techniques, the incidence of BDI has decreased, but this condition has always existed. BDI is a constant topic, and how to reduce the occurrence of BDI is an area of study. Reducing the occurrence relies on our accurate identification of the anatomy of the CD before LC, especially when there are anatomical variations in the CD. We believe that the morphology of the CD deserves our attention. During LC, a tortuous gallbladder duct is more likely to cause misjudgment, which can lead to BDI.

The CD connects the gallbladder to the extrahepatic bile duct (EHBD). The CD usually measures 2-4 cm in length and enters the EHBD from the right lateral aspect in 49.9% of patients[13]. Anatomic variants of CD are common and many researchers have proposed their own anatomical classification according to the CD insertion site to the EHBD[14-16]. A new classification system for EHBD according to the percentile distribution of the length ratio between CD insertion and the duodenal papilla (CDDP)/EHBD was designed, and the following categories were obtained: Type 1 (below the 25th percentile) for a CDDP/EHBD ratio $\leq 50\%$; type 2 (25th to 75th percentile) for a CDDP/EHBD ratio 51%-75%; and type 3 (above the 75th percentile) for CDDP/EHBD ratio $> 75\%$ [14]. According to the angle and morphology of the convergence of the CD into the EHBD, CD patterns were divided into 3 patterns: Type I (85.4%), located on the right and angled up; type II (3.1%), located on the right and angled down; and type III (11.5%), located on the left and angled up[15]. Several researchers have also broadly classified the configuration of the CD into four types: Angular (44%), linear (40%), spiral (11%) and complex (5%)[16]. However, not all CDs insert into the EHBD, and some CDs insert into the left hepatic duct (LHD) or right hepatic duct (RHD)[17]. We should not focus only on the insertion of the CD to classify its anatomical

variants. Perhaps we can start from the morphology of the CD and propose new classification criteria.

Magnetic resonance cholangiopancreatography (MRCP) is a well-established and noninvasive diagnostic technique for visualizing the pancreatic and biliary duct systems without the adverse effects of injecting a contrast agent[18,19]. MRCP has excellent overall sensitivity and specificity for demonstrating the severity and presence of biliary obstruction[20]. MRCP can clearly show the anatomy of the intrahepatic and EHBDs. The alignment and morphology of CDs can be determined *via* MRCP. At present, MRCP has become a routine examination before LC.

Therefore, the primary aim of this study was to propose a new classification system for the morphology of CD for improved clinical application. The secondary aim was to explore the relationship between anatomic variants of the CD and gallstones.

MATERIALS AND METHODS

Study population

We retrospectively collected data from patients who underwent MRCP for disease diagnosis and treatment between October 2021 and January 2022 at our hospital. The observation group (gallstone group) met the following criteria for inclusion: (1) Had preoperative MRCP and abdominal ultrasonography confirmed gallstones or postoperative pathology suggested gallstones; and (2) Had CD anatomy that was completely and clearly visualized *via* MRCP. Patients who met the following criteria were excluded: (1) Had other gallbladder diseases, such as gallbladder polyps, gallbladder adenomyosis, or gallbladder cancer; (2) Had CBD stones, stricture or obstruction; (3) Had their gallbladder removed; and (4) Had incomplete clinical information. The control group (nongallstone group) met the following criteria for inclusion: (1) Had MRCP or pathology suggesting hepatic hemangioma, hepatocellular carcinoma, or pancreatic tumor; and (2) Had MRCP clearly revealing the structure and morphology of the intrahepatic and EHBDs. Patients who met the following criteria were excluded: (1) Had gallbladder diseases such as gallstones, gallbladder polyps, gallbladder adenomyosis, or gallbladder cancer; and (2) Had the remaining exclusion criteria detailed in (2) to (4) of the exclusion criteria for the gallstone group. The following data were collected for each patient: Age, sex, body mass index (BMI), cholesterol, and triglycerides. This study was approved by the ethics committee of our hospital and was conducted in accordance with the Declaration of Helsinki.

Imaging technique and analysis

All magnetic resonance imaging (MRIs) were performed on a 1.5 T MRI superconductive scanner (Siemens Sonata) by using an abdominal coil. The imaging parameters for T2W-TSE slices: TR 4500 ms, TE 985 ms, 150 flip angle, 256 × 512 matrix, 28 cm × 28 cm field of view, 265 Hz bandwidth, and 60 mm slice thickness. The collection of evaluation indicators for CD was performed by 2 researchers who were proficient in MRCP. When disagreements arose, a third researcher participated in the discussion, and a consensus was finally reached. The following data were collected for each MRCP examination: The morphology of the CD, the site of CD insertion into the EHBD, the length of the CD, and the angle between the common hepatic duct and the CD (< CHD) (Figure 1). In addition, the anatomy of the intrahepatic bile ducts was also observed and documented in the present study.

Statistical analysis

The statistical analyses were performed using SPSS version 25.0 (Chicago, IL, United States). Continuous variables are expressed as the mean ± SD or median and interquartile ranges (IQRs). Categorical variables are expressed as counts and percentages. The Mann-Whitney U test was performed to compare continuous variables. Categorical variables were compared using the chi-square test or Fisher's exact test. Multivariate analysis was performed using the logistic regression analyses to identify the independent risk factors using variables significant in the univariate analysis. $P < 0.05$ was considered to indicate statistical significance.

RESULTS

Among the 300 patients enrolled in this study, 200 patients (66.7%) were in the gallstone group, and 100 patients (33.3%) were in the nongallstone group. The mean age was 48.1 ± 13.3 years; 142 (47.3%) were male and 158 (52.7%) were female. A total of 55.7% of the patients had a BMI over 24 kg/m². In addition, in the study population, cholesterol and triglyceride levels were 4.8 mmol/L (IQR: 4.1-5.4 mmol/L) and 1.6 mmol/L (IQR: 1.1-2.2 mmol/L), respectively. These results are detailed in Table 1.

We found that the anatomical variations in the intrahepatic bile ducts were mainly in the right posterior duct (RPD). We classified the different locations at which the RPD converged into the intrahepatic and EHBDs into 4 types (Figure 2): Type A, the right RPD converges into the RHD (Figure 2A); Type B, the right RPD converges into the junction of the right and LHDs (Figure 2B); and Type C, the right RPD converges into the LHD (Figure 2C); and Type D, the right RPD converges into the EHBD (Figure 2D). The typical anatomy of intrahepatic bile ducts (type A) was observed in patients (66.7%), and the atypical anatomy (type B, type C, and type D) was observed in 30 patients (33.3%) (Table 1).

Classification of the morphology of CD

A novel classification system for CD based on the anatomical morphology of the CD was proposed. It is classified into

Table 1 Clinical and demographical characteristics of the study population

Variables	Study population (n = 300)
Sex, n (%)	
Male	142 (47.3)
Female	158 (52.7)
Age, mean ± SD, years	48.1 ± 13.3
BMI, kg/m ² , n (%)	
< 24	133 (44.3)
≥ 24	167 (55.7)
Cholesterol, median (IQR), mmol/L	4.8 (4.1-5.4)
Triglyceride, median (IQR), mmol/L	1.6 (1.1-2.2)
Morphology of CD, n (%)	
Linear	117 (39)
Tortuosity	183 (61)
Site of the CD insertion into the EHBD, n (%)	
Right	265 (88.3)
Nonright	35 (11.7)
Length of CD, median (IQR), mm	23.4 (17.3-29.8)
< CHD, median (IQR), degrees	31.6 (21.8-45.7)
Intrahepatic biliary anatomy, n (%)	
Typical	270 (66.7)
Atypical	30 (33.3)
Group, n (%)	
Gallstone	200 (66.7)
Nongallstone	100 (33.3)

BMI: Body mass index; CD: Cystic duct; EHBD: Extrahepatic bile duct; < CHD: The angle between the common hepatic duct and the cystic duct.

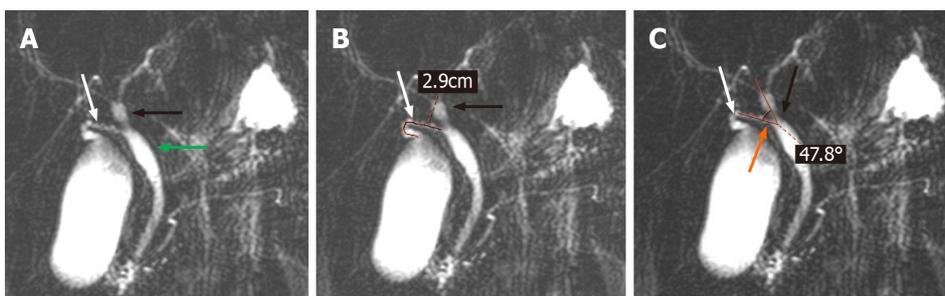


Figure 1 The length of cystic duct and < common hepatic duct were measured on magnetic resonance cholangiopancreatography images. A: Measure relevant anatomy: Cystic duct (CD) (white arrow), common hepatic duct (CHD) (black arrow), common bile duct (green arrow); B: Length of CD: Measurements are taken from the beginning of the cystic duct and along the trajectory of the CD until it reaches the point of confluence of the CD (white arrow) into the CHD (black arrow); C: < CHD: The angle between the common hepatic duct (black arrow) and the cystic duct (white arrow).

four types (Figure 3): (1) Type I: Linear, the CD is straight and enters straight into the EHBD with no tortuosity (Figure 3A and E); (2) Type II: n-shaped, the CD has a bend in the shape of an n (Figure 3B and F); (3) Type III: S-shaped, the CD converges in an S-shape into the EHBD (Figure 3C and G); and (4) Type IV: W-shaped, the CD converges into the EHBD in a W-shape (Figure 3D and H).

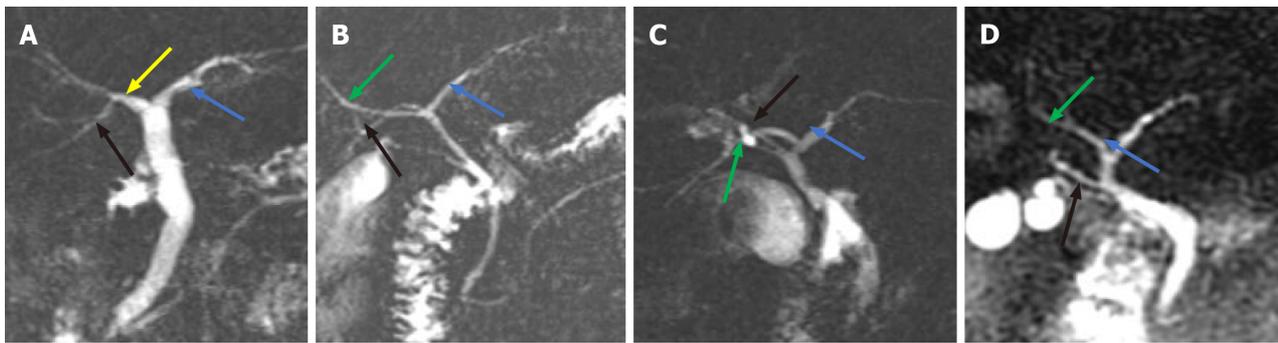


Figure 2 The classification of intrahepatic bile duct anatomy. A: Type A: The right posterior duct (RPD) (black arrow) converges into the right hepatic duct (yellow arrow); B: Type B: The RPD (black arrow) converges into the junction of the right and left hepatic ducts, and the three show a three-fork type; C: Type C: The RPD (black arrow) converges into the left hepatic duct (blue arrow); D: Type D: The RPD (black arrow) converges into the extrahepatic bile duct.

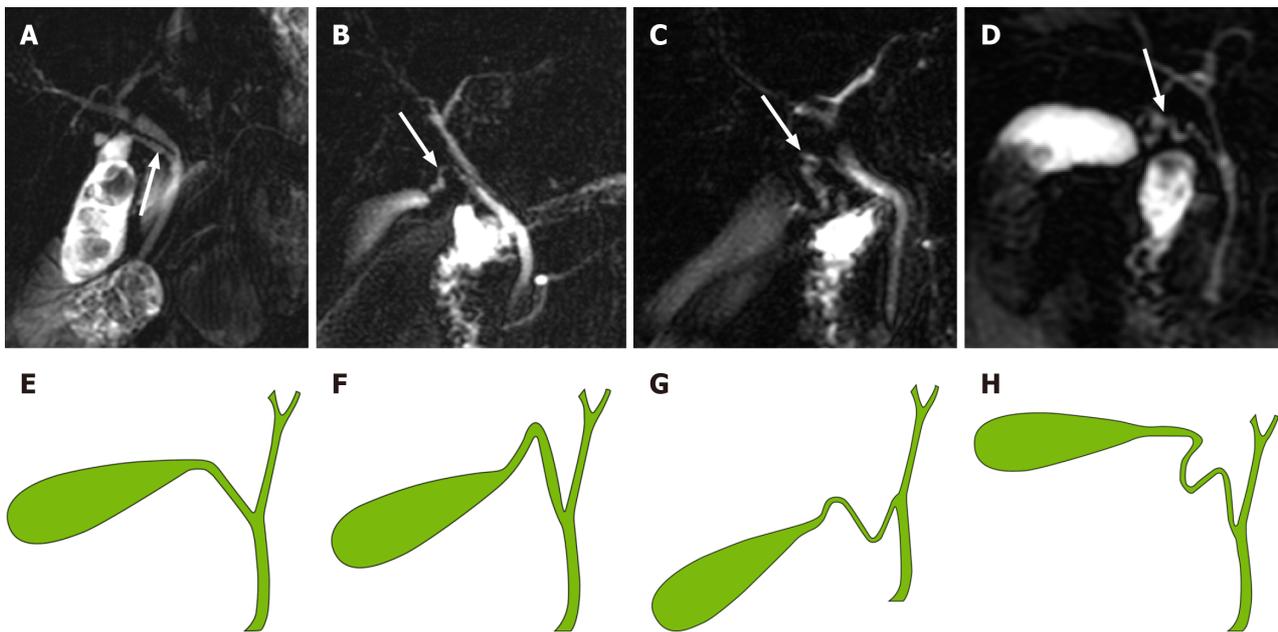


Figure 3 The classification of the morphology of cystic duct and model diagram. A: Type I: Linear, cystic duct (CD) (white arrow) straight into extrahepatic bile duct (EHBD) with no tortuosity; B: Type II: n-shaped, CD (white arrow) has a bend in the shape of an n; C: Type III: S-shaped, CD (white arrow) converges in an S-shape into the EHBD; D: Type IV: W-shaped, CD (white arrow) converges into the EHBD in a W-shape; E: Type I: Linear; F: Type II: n-shaped; G: Type III: S-shaped; H: Type IV: W-shaped.

Association between the anatomic variants of the CD and gallstones

In 300 patients, the CD length was 23.4 mm (IQR: 17.3-29.8 mm), 88.3% of the CDs converged to the right of the EHBD, the $<$ CHD was 31.6 degrees (IQR: 21.8-45.7 degrees), and only 117 (39%) CDs converged to the EHBD in a straight line (Table 1). Univariate analysis revealed a correlation between gallstone formation and anatomical variation in the CD (Table 2). Among all the anatomical factors, there were significant differences in the morphology of CDs between the gallstone group and the non-gallstone group [linear: 43 (21.5%) *vs* 74 (74%); n-shaped: 108 (54%) *vs* 15 (15%); S-shaped: 28 (14%) *vs* 8 (8%); W-shaped: 21 (10.5%) *vs* 3 (3%), $P < 0.001$]. The gallstone group had a significantly longer CD length [24.5 (19.6-32.4) mm *vs* 18.9 (13.5-27.1) mm, $P < 0.001$]. There was also a significant difference in the site of CD insertion into the EHBD between the two groups [gallstone *vs* nongallstone: Right: 177 (88.5%) *vs* 99 (99%); left: 16 (8%) *vs* 1 (1%); front: 2 (1%) *vs* 0 (0%); back: 5 (2.5%) *vs* 0 (0%), $P = 0.011$]. There was no difference in $<$ CHD between the gallstone and nongallstone groups [31.0 (21.9-44.9) degrees *vs* 33.4 (21.2-50.8) degrees, $P = 0.576$]. Moreover, there was no difference in intrahepatic biliary anatomy in the gallstone and the nongallstone groups [typical: 178 (89.0%) *vs* 22 (11.0%), $P = 0.414$]. In addition, there were significant differences in sex distribution, BMI, cholesterol, and triglyceride levels between the two groups. The gallstone group had more women than nongallstone ($P < 0.001$), and the gallstone group had larger BMI ($P = 0.002$), higher cholesterol [4.9 (4.4-5.4) mmol/L *vs* 4.5 (3.8-5.3) mmol/L, $P = 0.01$], and higher triglyceride [1.7 (1.2-2.3) mmol/L *vs* 1.5 (1.0-2.0) mmol/L, $P = 0.025$] (Table 2).

According to our multivariate analysis, female [odds ratio (OR) = 3.32, 95% confidence interval (95% CI): 1.77-6.21; $P < 0.001$], BMI (≥ 24 kg/m²) (OR = 2.51, 95% CI: 1.35-4.66; $P = 0.004$), and CD morphology were found to be independent risk factors for gallstone formation. The odds ratios for the n-shaped, S-shaped, and W-shaped variables were 10.97 (95% CI:

Table 2 Univariate analysis and multivariate logistic regression analysis of the risk factors for gallstones

Variables	Univariate		Multivariate		
	Gallstone group (n = 200)	Nongallstone group (n = 100)	P value	OR (95%CI)	P value
Sex, n (%)					
Male	79 (39.5)	63 (63)	< 0.001		
Female	121 (60.5)	37 (37)		3.32 (1.77-6.21)	< 0.001
Age, median (IQR), years	49.00 (38-59)	48 (41.00-56.8)	0.857		
BMI, kg/m ² , n (%)					
< 24	76 (38)	57 (57)	0.002		
≥ 24	124 (62)	43 (43)		2.51 (1.35-4.66)	0.004
Cholesterol, median (IQR), mmol/L	4.9 (4.3-5.4)	4.5 (3.8-5.3)	0.01		
Triglyceride, median (IQR), mmol/L	1.67 (1.2-2.3)	1.5 (1.0-2.0)	0.025		
Morphology of CD, n (%)					
Linear	43 (21.5)	74 (74)	< 0.001		
n-shaped	108 (54)	15 (15)		10.97 (5.22-23.07)	< 0.001
S-shaped	28 (14)	8 (8)		4.43 (1.64-11.95)	0.003
W-shaped	21 (10.5)	3 (3)		7.74 (1.88-31.78)	0.005
Site of the CD insertion into the EHBD, n (%)					
Right	177 (88.5)	99 (99)	0.011		
Left	16 (8)	1 (1)			
Front	2 (1)	0 (0)			
Back	5 (2.5)	0 (0)			
Length of CD, median (IQR), mm	24.5 (19.6-32.4)	18.9 (13.5-27.1)	< 0.001		
< CHD, median (IQR), degrees	31.0 (21.9-44.9)	33.4 (21.2-50.8)	0.576		
Intrahepatic biliary anatomy, n (%)					
Typical	178 (89)	92 (92)	0.414		
Atypical	22 (11)	8 (8)			

BMI: Body mass index; CD: Cystic duct; EHBD: Extrahepatic bile duct; < CHD: The angle between the common hepatic duct and the cystic duct.

5.22-23.07, $P < 0.001$), 4.43 (95%CI: 1.64-11.95, $P = 0.003$), and 7.74 (95%CI: 1.88-31.78, $P = 0.005$), respectively (Table 2).

DISCUSSION

Gallstones are a frequent health problem. The overall prevalence of gallstones ranges from 10% to 15% in adults in Europe and the United States[3], and from 4.2% to 12.1% in the Chinese population[21]. The incidence rate of gallstones in the general population was found to be 0.60% per year[2]. Gallstones can cause various complications, such as secondary choledocholithiasis, cholangitis, acute biliary pancreatitis, gallstone ileus, and even life-threatening complications including severe acute pancreatitis, gallbladder cancer, and recurrent pyogenic cholangitis, leading to an increased health care burden[22,23]. Currently, LC is the first treatment for symptomatic gallstones. Preoperatively, we need to accurately predict the morphology of CDs based on MRCP, especially those with anatomical variants, which are otherwise prone to BDI. However, the anatomical morphology of CD has not been adequately studied to date. Therefore, we formulated a classification system for the morphology of CD for improved clinical application.

Anatomic variations in the biliary system are highly prevalent and might be observed in more than 30% of cases[24]. Operative findings of LC revealed variations in 61 (20.33%) patients, mainly involving the cystic artery (10.67%), CD (4.33%), right hepatic artery (2.67%) and gallbladder (2%)[25]. Turner and Fulcher[13] indicated that variations in CD insertion are common, and occur in 18%-23% of cases[13]. Sureka *et al*[26] attempted to simplify the classification of CD anatomy and ultimately classified it into 8 types[26]. Al-Muhanna *et al*[24] found only four variants, Type (A), Type (B), Type (C), and Type (D), based on the classification system of Sureka *et al*[26]. Renzulli *et al*[14] proposed an anatomical

classification of CD based on the ratio of the length of the CDB to the length of the EHBD. According to the CD take-off, Cao *et al*[15] divided 226 CD patterns into 3 patterns, of which type I was divided into three subtypes: Line type, S type, and α type. Garg *et al*[16] broadly classified gliomas into four subtypes, angular, linear, spiral and complex, which were subsequently divided into numerous subtypes. On the one hand, these anatomical typologies are too complex for clinical application; on the other hand, some CD confluence flows into the intrahepatic bile duct (Figure 3), while our new classification focuses on the morphology of CD.

We believe that the residual CD length should be ≤ 0.5 cm when LC is performed. The long CDs may develop secondary or residual stones after LC, further leading to postcholecystectomy syndrome[27,28]. Patients in this group often require reoperation to remove the overlong CD. The incidence of residual gallstones following cholecystectomy is $< 2.5\%$ [29,30]. However, the pursuit of shorter CDs is usually accompanied by an increased risk of BDI. Moreover, the length of the residual CD is not always less than 0.5 cm each time LC is undertaken, especially when there are anatomical variants of the CD, such as convergence to the left side of the EHBD, or convergence to the intrahepatic bile duct, or if the classification of the morphology of CD is type II, III, or IV. The length of the residual CD should be further investigated and explored. Near-infrared imaging with indocyanine green (ICG) may be the answer to this contradiction. The use of near-infrared imaging with the ICG technique provides good overall visualization of the CD, CBD, CHD and CD junction regions prior to and following dissection of Calot's triangle[31,32]. Therefore, the use of near-infrared imaging with the ICG technique for cholecystectomy should be considered, especially in patients with anatomical variants of CD.

Based on a study of MRCP in 300 patients, we classified the anatomy of the intrahepatic bile ducts into 4 types: Type A, type B, type C, and type D. Type D was defined when the right RPD converged into the EHBD. For type D, we observed that the RPD converged into the common hepatic duct in our study (Figure 2D). Sarawagi *et al*[33] found that in 4% of subjects, the RPD drained into the common hepatic duct, whereas in 0.8% of subjects, the RPD drained into the CD in their MRCP-based study. Choi *et al*[34] intraoperative cholangiography of 300 liver transplant donors revealed that the anatomy of the intrahepatic bile ducts was typical in 63% of patients ($n = 188$), that of the RPD into the common hepatic duct in 6% ($n = 19$), and that of the RPD was anomalous into the CD in 2% ($n = 6$). In this study, we did not observe the convergence of the RPD into the CD, but this anatomical variation in the intrahepatic bile duct is not uncommon. Gupta *et al*[35] found it in 4.4% of MRCPs; Chaib *et al*[36] showed it in 6.1% of the study population based on endoscopic retrograde cholangiography and intraoperative cholangiography. In the present study, 22% of the patients with gallstones had anatomical variations in their intrahepatic bile ducts. When the anatomical classification of intrahepatic bile ducts is type D, especially when the RPD into the CD, we tend to misidentify the RPD as the CD, resulting in BDI. Accurate assessment of the anatomical variations in the intrahepatic bile ducts prior to LC is also essential for ensuring the safety of surgery. In our clinical practice, we sometimes observe a phenomenon in which the CD converges into the intrahepatic bile duct (Figure 4). Before LC, both the anatomical morphology of the CD and the anatomical variations in the intrahepatic bile ducts need to be considered.

Several studies have shown that advanced age, female gender, race, obesity, rapid weight loss, diet and a family history of gallstone disease are risk factors for the gallstone development[3-5,37,38]. Univariate analysis revealed that sex, BMI, triglycerides and cholesterol were associated with the formation of gallstones. Multivariable logistics analysis suggested that sex and BMI are independent risk factors for gallstones. A population-based study in China revealed that the risk of gallstones increases markedly with age[39]. Our study did not show that age is a risk factor for gallstones. With the awakening of health awareness, people undergo regular medical checkups, which can lead to an earlier age at gallstone diagnosis. BMI (≥ 24 kg/m²) is an independent risk factor for gallstones. A recent study revealed that there have been steady increases in the mean BMI among all age groups in China[40]. Rapid increases in BMI may accelerate the formation of gallbladder stones and thus weaken the correlation between gallbladder stones and age.

In addition, our study showed that the anatomical morphology of the CD is an independent risk factor for gallstone formation, which means that tortuous CD is an important cause of gallstone formation. When the gallbladder is not functioning properly, the components of the bile are supersaturated leading to the formation of solid crystals, called gallstones[41]. Gallbladders with tortuous CDs are prone to gallstone formation for the following reasons:

(1) Bile stasis: Bile stasis may cause cholesterol supersaturation and allow the formation of cholesterol stones[41]. Studies suggest that flow resistance is affected by CD morphology, which plays a dominant role[42,43]. Tortuous CDs can lead to increased flow resistance, resulting in bile stasis, which can promote the development of gallstones. From the aspect of conservation of energy, the gallbladder can be considered to be a pump, that pumps bile flow through the CD into the CBD. The pump function of the gallbladder provides bile with kinetic energy that enables the bile to flow. The tortuous CD increases the flow resistance, which eliminates some of the kinetic energy. With this reduction in kinetic energy, the bile cannot be completely drained, resulting in bile stasis, which contributes to the formation of gallstones.

(2) Increased bile viscosity: Increased viscosity of gallbladder bile plays an important role in the pathogenesis of gallstones[41]. The tortuous CD increases flow resistance, which leads to reduced bile flux. According to Poiseuille's law, bile flux through the CD is inversely correlated with bile viscosity[43]. A decrease in bile flux increases bile viscosity, which leads to the development of gallstone.

And (3) Mucous membrane repair: The bile flowing through the tortuous CD constantly impinges on the tortuous points of the duct, which may cause damage to the mucosa in CD. On the one hand, under the stimulation of inflammation and mucosal repair, gallstones may form by damaging the mucosa as an eruption point. On the other hand, repair of the mucosa may cause narrowing of the CD, possibly resulting in bile stasis[41,43].

Univariate analysis revealed that the length of the CD ($P < 0.001$) and nonright lateral confluence into the EHBD ($P = 0.011$) were risk factors for gallstone formation. The group with gallstones had a longer or narrower CD than those without calculi[44,45]. The longer the CD is, the more likely it is to become tortuous in a relative space. When the CD converges into the anterior, posterior or bypasses the anterior or posterior EHBD to the left side, the length of the CD increases, and the filling of the EHBD may squeeze the CD, causing relative narrowing and leading to bile stasis.

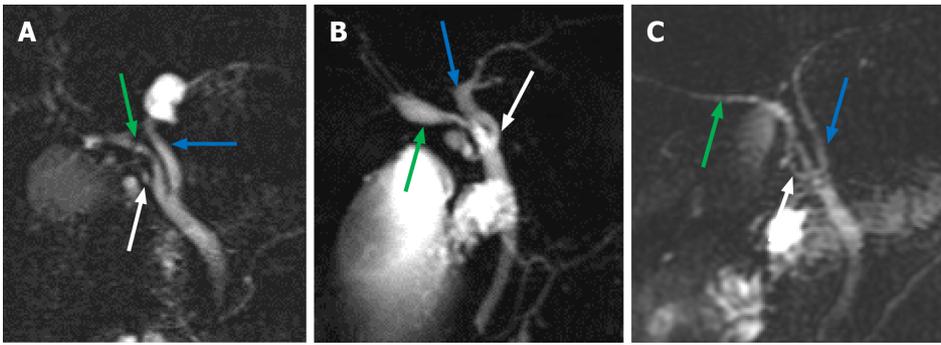


Figure 4 The cystic duct converges into the intrahepatic bile duct. A: The cystic duct (CD) (white arrow) converges into the right hepatic duct (green arrow); B: The CD converges into the left hepatic duct (blue arrow); C: The CD converges into the confluence of the right and left hepatic ducts.

There are certain limitations of our study. First, this study is retrospective and may need further validation by prospective studies. Second, we excluded patients who were unable to undergo MRCP, which could have led us to miss certain rare CD morphologies. Third, we performed only an imaging study, and we can use near-infrared imaging with the ICG technique for further in-depth study and validation in LC.

CONCLUSION

In conclusion, our study provides comprehensive knowledge of the spatial anatomical morphology of CDs and suggests a better clinically applicable classification of the morphology of CDs. It has also been confirmed that CD tortuosity is an independent risk factor for gallstones. In the future, we will construct predictive models based on the risk factors for gallstones identified in our study to provide individualized follow-up strategies for high-risk patients.

ARTICLE HIGHLIGHTS

Research background

At present, there is no optimal classification of the morphology of the cystic duct (CD) applicable to clinical practice, and the relationship between anatomical variation of the CD and gallstone remains to be explored.

Research motivation

Classification of anatomical morphology of CD can be applied to clinical practice to reduce the occurrence of bile duct injury, and we also found that CD tortuosity is an independent risk factor for gallstone. In the future, we will construct predictive models based on the risk factors for gallstone identified in our study to provide individualized follow-up strategies for high-risk groups.

Research objectives

To create a more comprehensive clinically applicable classification of the morphology of the CD and to explore the correlations between anatomic variants of the CD and gallstone.

Research methods

This was a case-control study. We retrospectively collected data on patients underwent magnetic resonance cholangiopancreatography with (without) gallstones at the Second Affiliated Hospital of Kunming Medical University, Yunnan, China. 300 patients with (without) gallstones identified by abdominal ultrasound and magnetic resonance cholangiopancreatography were enrolled from October 2021 to January 2022. They were divided into two groups: The gallstone group and the non-gallstone group. Data such as sex, age and body mass index were collected.

Research results

Of the 300 patients enrolled in this study, 200 (66.7%) of them had gallstones. The mean age was 48.10 ± 13.30 years, of which 142 (47.3%) were male and 158 (52.7%) were female. 55.7% of the patients had a body mass index (BMI) ≥ 24 kg/m². Based on the magnetic resonance cholangiopancreatography, the CD anatomical typology is divided into four types: Type I: Linear, type II: n-shaped, type III: S-shaped, and type IV: W-shaped. Univariate analysis showed differences between the gallstone and non-gallstone groups in relation to sex, BMI, cholesterol, triglyceride, morphology of CD, site of the CD insertion into the extrahepatic bile duct, length of CD, the angle between the common hepatic duct and CD. In the multivariate analysis, female, BMI (≥ 24 kg/m²), and morphology of CD [n-shaped: Odds ratio (OR) = 10.97, 95% confidence interval (95%CI): 5.22-23.07, $P < 0.001$; S-shaped: OR = 4.43, 95%CI: 1.64-11.95, $P = 0.003$; W-shaped:

OR = 7.74, 95%CI: 1.88-31.78, $P = 0.005$] were significantly associated with gallstone.

Research conclusions

This present study details the morphological variation of the CD and confirms that CD tortuosity is an independent risk factor for gallstones.

Research perspectives

Basic and clinical research of diseases in hepatopancreatobiliary surgery.

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FOOTNOTES

Author contributions: Zhu JH, Kang Q, Zhu Y, Liu LX, Zhao SL and Zou H designed the research study; Zhu JH, Kang Q, Zhu Y, and Liu LX performed the research; Zhu JH, Zhao SL and Zou H analyzed the data and wrote the manuscript; All authors have read and approve the final manuscript.

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