ÖZGÜN ARAŞTIRMA ORIGINAL RESEARCH

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MAGNETIC RESONANCE CHOLANGIO PANCREATICOGRAPHY (MRCP) DETECTION OF WHETHER THE JUNCTION OF THE CYSTIC DUCT TO THE COMMON BILE DUCT IS ASSOCIATED WITH THE DEVELOPMENT OF GALLSTONES AND/OR CHOLECYSTITIS

SİSTİK KANALIN ANA SAFRA KANALINA BİRLEŞME YERİNİN SAFRA TAŞI VE/VEYA KOLESİSTİT GELİŞİMİYLE İLİŞKİLİ OLUP OLMADIĞININ MRKP İLE SAPTANMASI

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Öz

Amaç
Safra taşı ve taşın neden olduğu inflamatuar süreçlerin gelişmesi çok sayıda biyolojik faktöre bağlıdır. Hem taş gelişmesi hem de bunun inflamasyona neden olması için yatkınlık oluşturan faktörlerin bilinmesi hastalığı öngörmede, takibini yapmada ve tedavisinde ve sonraki komplikasyonların yönetiminde oldukça önemlidir. Çalışmamızın amacı, sistik kanal (SK) uzunluğunun, sistik kanalın ana hepatik kanal (AHK) ile birleşme yeri düzeyinin ve yönünün, kolesistit ve kolelitiazis ile ilişkisi olup olmadığını saptamaktır.

Gereç ve Yöntem
Çalışmamıza, 2017 ocak ile 2020 aralık tarihleri arasında manyetik rezonans kolanjiopankteatikografi (MRKP) çekilen 172 hasta retrospektif olarak değerlendirilmek suretiyle dahil edildi. 1.5 Tesla MR cihazı ile (Signa HDI, General Electric, Milwaukee, WI, USA), HD 8 kanallı body array coil kullanılarak çekimler yapıldı. Elde edilen bulgular SPSS Versiyon 23 programı ile analiz edildi.

Bulgular
SK'nın ana AHK ile birleştiği düzeyin taş ve/veya kolesistit gelişimiyle anlamlı olarak korelasyon göstermediği saptandı (p>0.05). Benzer şekilde SK'nın AHK'ya açıldığı yön ile taş ve/veya kolesistit gelişimi arasında anlamlı ilişki saptanmadı(p>0,05). SK uzunluğu 2 cm'nin altında olan 27 (%15,7) olgunun 3(%11,1)'ünde yalnızca taş, 8 (%29,6)'inde ise kolesistit saptanmış olup 16 (%59,2)'u ise normaldir. 2-4 cm arasında 88 (%51,2) olgunun 43(%48,8)'ünde yalnızca taş, 19

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(%21,5)'unda ise taşlı kolesistit saptanmış olup 26 (%29,5) olgu ise normaldir. 4 cm'den daha uzun sistik kanalı olan 57 (%33,1) olgunun 31 (%54,3)'inde yalnızca taş, 16 (%28)'sında ise kolesistit saptanmış olup 10 (%17,5)'u ise normaldir. SK uzunluğu arttıkça taş ve/veya kolesistit gelişme sıklığı artmaktadır (p<0,05).

Sonuç

SK'nın AHK'ya açıldığı yön ve seviye taş ve/veya kolesistit gelişimine yatkınlık oluştururmazken, uzunluğundaki artış ise taş ve/veya kolesistit gelişimine yatkınlığı arttırmaktadır.

Anahtar Kelimeler: Kolelitiazis, Kolesistit, MRCP, Sistik kanal

Abstract

Objective

The development of gallstones and stone-induced inflammatory processes depends on a number of biological factors. Knowledge of the predisposing factors for both the development of stones and their inflammation is important in predicting, monitoring, and treating the disease and managing subsequent complications. The aim of our study was to determine whether the length of the cystic duct (CD), the level and direction of the junction of the cystic duct with the common hepatic duct (CHD) are associated with cholecystitis and cholelithiasis.

Material and Method

This retrospective study included 172 patients who underwent MRCP between January 2017 and December 2020. A 1.5 Tesla MR device (Signa HDI, General Electric, Milwaukee, WI, USA) was used with an HD 8-channel body array coil. The findings were analyzed using SPSS version 23 software.

Results

The level at which the CD merged with the main CHD was not significantly correlated with the development of calculi and/or cholecystitis (p>0.05). Similarly, there was no significant correlation between the direction of the CD opening into the CHD and the development of calculi and/or cholecystitis (p>0.05).Of 27 (15.7%) cases with CD length less than 2 cm, 3(11.1%) had only stones, 8 (29.6%) had cholecystitis and 16 (59.2%) were normal. Of 88 (51.2%) cases between 2 and 4 cm, 43 (48.8%) had only calculi, 19 (21.5%) had cholecystitis with calculi and 26 (29.5%) were normal. Of 57 (33.1%) patients with cystic duct longer than 4 cm, 31 (54.3%) had only stones, 16 (28%) had cholecystitis and 10 (17.5%) were normal. As CD length increased, the frequency of stone and/or cholecystitis increased (p<0.05).

Conclusion

The direction and level of CD involvement in CHD does not predispose to the development of stones and/or cholecystitis, whereas an increase in its length predisposes to the development of stones and/or cholecystitis.

Keywords: Cholecystitis, Cholelithiasis, Cystic duct, MRCP

Introduction

Excluding variations, the anatomy of the biliary system is simple. The bile duct from the right lobe of the liver (right hepatic duct; RHD) and bile duct from the left lobe (left hepatic duct, LHD) join to form the common bile duct (CHD). Subsequently, the cystic duct joins them to form the choledochal duct (ChoD). Knowing the anatomy and physiology of the gallbladder and biliary tract is very important for understanding biliary diseases, especially gallstones and stone diseases such as cholecystitis, which represents a global health issue of considerable magnitude and is capable of giving rise to a variety of complications. The primary determinants behind the emergence of gallstones include a spectrum of risk factors, including advanced age, female sex, pregnancy, utilization of oral contraceptives, obesity, rapid and substantial weight loss, total parenteral nutrition, extended periods of fasting, familial predisposition, cirrhosis, and conditions affecting the ileum, such as diseases and surgical resections (1, 2)

Conversely, certain authors have attributed the development of gallstone formation to distinct environmental factors. A study conducted on Chileans and North American Indians, both populations with a significant incidence of cholelithiasis, provided an intriguing perspective. Nervi F et al. postulated that the consumption of legumes could potentially pose a risk factor for the onset of cholesterol gallstone disease (3). It is categorized into three distinct groups based on its chemical composition: cholesterol gallstones, comprising a minimum of 80% cholesterol and forming in tandem with bilirubin and calcium salts; pigment gallstones, also known as black pigment stones, encompassing less than 20% cholesterol and 70% calcium bilirubinate; and the amalgam-type gallstone, recognized as a brown pigment stone, characterized by a composition of 20-80% cholesterol, bilirubin, and bile salts (1, 4, 5). Notably, cholesterol-type gallstones tend to predominate in Western societies, while the pigment-type is more prevalent in East Asian communities (6). Causative factors contributing to the formation of cholesterol gallstones include an increase in both cholesterol synthesis and secretion, a reduction in bile salt synthesis and secretion, impaired intestinal absorption of cholesterol and bile salt, and gallbladder motility disorders. In contrast, black pigment stones exhibit a strong correlation with hemolytic diseases and cirrhosis5, conditions stemming from elevated unconjugated bilirubin levels, consequently leading to the accumulation of excessive bilirubin deposits (5-11).

Magnetic resonance MRCP has emerged as a noninvasive and reliable diagnostic tool for assessing gallbladder and bile duct disorders. There are many variations of extrahepatic bile ducts. In our study, we focused on the possible effects of CD positioning relative to CHD positioning on the development of calculi and cholecystitis.

MRCP offers a reliable alternative, providing accurate insights without the necessity for invasive procedures. While the clinical implications have not yet been fully elucidated, a multitude of anatomical variations exist within both the intra- and extra-bile ducts. These variations hold crucial importance in surgical interventions as they warrant meticulous consideration to avert potential inadvertent injuries (12). Furthermore, the role of anatomical variations in the bile ducts in the context of gallstone formation is yet to be explored and discussed in depth. As with many anatomical structures in the human body, there are many variations in the biliary tract. The cystic duct connects the gallbladder to the common bile duct and has many variations in terms of its attachment site, level, and length.

Our study aimed to determine whether there is a relationship between these anatomical variations and the development of cholelithiasis and cholecystitis.

Material and Method

Ethics and Study Population

The study was conducted in compliance with the Declaration of Helsinki 1975, as revised in 2008, and was approved by the Health Science University İstanbul Gaziosmanpaşa Training and Research Hospital Scientific Research Ethics Committee (date:20.10.2021, no:346). As the study had a retrospective design and re-examination of images was performed anonymously, the requirement for written informed consent was waived. All research steps were carried out at the Department of Radiology of Health Science University İstanbul Gaziosmanpaşa Training and Research Hospital. This retrospective study included 172 patients who underwent MRCP between January 2017 and December 2020.

A total of 172 patients who underwent MRCP between January 2017 and December 2020 at the Department of Radiology, University of Health Sciences, Istanbul Gaziosmanpaşa Training and Research Hospital were retrospectively analyzed. The exclusion criteria were age < 18 years, previous cholecystectomy, carcinoma of the biliary system, liver or pancreas, previous liver operation, biliary tract abnormalities such as choledochal cyst, periampullary region pathologies, presence of metallic stent, and inappropriate examination in terms of evaluation.

MRCP Technic and Image Assessment

All MRCP examinations were conducted using 1.5 Tesla magnetic resonance imaging system (Signa HDI, GE Medical Systems, Milwaukee, ABD). A phased-array torso coil was employed to enhance the signal reception. The initial unenhanced axial sequences were acquired through the liver with a slice thickness of 8 mm and a 2-mm gap. These sequences encompassed breath-hold in-phase and opposed-phase T1-weighted sequences, specifically T1 fast multiplanar spoiled gradient-recalled echo (T1 FMPSPGR) with steady-state precession or T1 fast low-angle shot (T1 FLASH 2D), as well as fat-saturated signal-averaged T2-weighted sequences, such as respiratory-triggered T2 fast spin-echo (T2 FSE) or non-respiratory-gated T2 turbo spin-echo (T2 TSE). The implementation of these techniques has contributed to the acquisition of more accurate imaging data.

MRCP images were acquired through breath-holding using heavily T2-weighted sequences, specifically T2 single-shot fast spin-echo (T2 SSFSE) or T2 half-Fourier acquisition single-shot turbo spin-echo (T2 HASTE). These sequences were obtained in both the axial and coronal planes, featuring contiguous thin sections with thicknesses ranging from 3 to 5 mm. Additionally, we conducted T2 SSFSE or T2 HASTE (or T2 turbo spin-echo with a high echo train length [T2 TSE with high ETL]) for coronal thick-section slabs measuring 5 cm and 7 cm, as well as rotating (coronal and oblique coronal) thin-section slabs measuring 3 cm.

Initially, the common duct and bifurcation plane were localized using coronal thick-section slabs. Subsequently, employing the vertical axis of the common hepatic duct as the center of rotation, we obtained thin (3 cm) slab images in the sequential coronal and coronal oblique planes at 20-degree rotational increments. The following MR sequence parameters were applied (Table 1):

No intravenous contrast agent was administered during the procedure. Subsequently, thin-section MRCP images were utilized to generate maximum-intensity-projection (MIP) views of the bile ducts, providing comprehensive visualization of the anatomical structures of interest. MRCP images were evaluated on heavy T2 sequences and 3-dimensional (3D) images by a radiologist with more than five years of experience in MRCP. Data were obtained by noting the level at which the CD merged with the CHD, direction of merging with the CHD, and length of the CD.

We employed a combination of multiple rotating perspectives and slabs of varying thicknesses to optimize the clarity of biliary structures while minimizing any potential interference from other high T2 signal sources. Prior to the study, the patients were instructed to refrain from consuming any food or liquids for a minimum of six hours. Overall, although certain images exhibited some gastric superimposition, this did not impede the visualization of the bifurcation in any patient. Notably, an excessive presence of gastroduodenal fluid overlay could potentially obscure the bifurcation area and lead to confusion in certain projections. To mitigate this, the use of an oral negative contrast agent has been suggested as a means to reduce signal interference and overlay originating from gastroduodenal fluid. Implementing this approach could prove beneficial in diminishing any overlay stemming from gastroduodenal fluid.

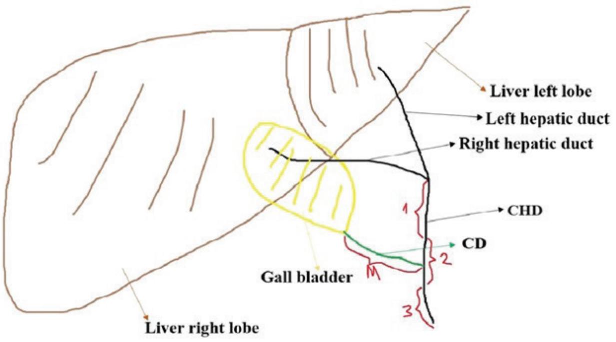

Figure 1
Diagrammatic representation depicting the interconnection between the liver, gallbladder, and biliary ducts. M (red letter): measure of CD. 1,2 and 3 parts of between starting CHD and termination ChoD (red numbers and sections 1/3 proximal, 1/3 medium, 1/3 distal respectively)

The position and junctional relationship of the CD with the CHD was evaluated on MRCP images, and Figures 1 and 3 illustrate this anatomical relationship. Figure 1 schematizes the coronal image and Figure 3 schematizes the axial excitation of the CHD and surrounding organs, with the CHD enlarged for easy understanding.

The basis for the assessment made here was as follows. The anatomical structure of the CHD formed by the fusion of the LHD and RHD is the anatomical structure of the CHD anatomical structure where the proximal part, marked in red as 1 in Figure 1, begins. 2 and 3, also marked in red, together with 1, represent

Table 1 Magnetic resonance imaging parameters

	For T2 SSFSE	For T2 HASTE	For T2 TSE
TR/TE	3000–5000/500–800 msec	Infinite/95 msec	2800/1100 msec
Matrix	256 × 256	240 × 256	240 × 256
FOV	24–36	27	24–36
NEX	0.5	1	1
RP	180^0	180^0 or 150^0	
FA			150^0

SSFSE :single-shot fast spin-echo sequence, HASTE: half-Fourier single-shot turbo spin-echo, TSE: turbo spin echo, TE: time to echo, TR: time to repetition, FOV field of view, RP: Refocusing pulse, FA: flip angle, msec.:milisecond the canal that continues to the ampulla after the CHD is formed by the LHD and RHD. The part of this duct before the CD is formed is anatomically called CHD and the part after the CD is formed is called ChoD. In our study, this anatomical relationship is what we mean when we express the level of fusion of the CD structure with the CHD.

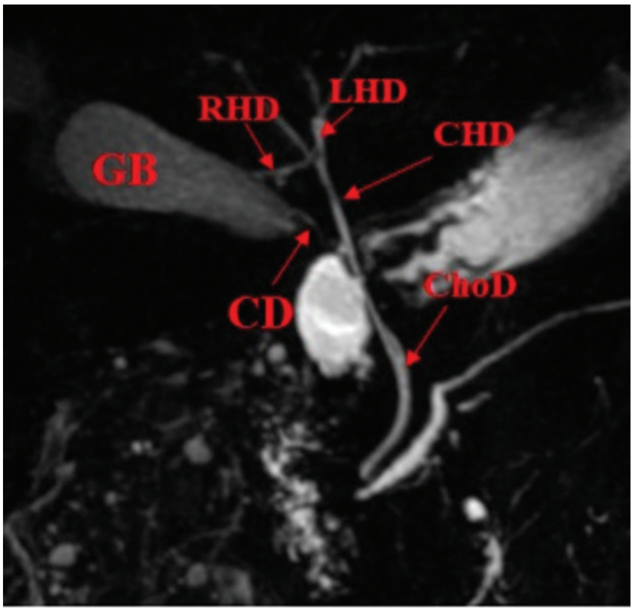

Figure 2
MRCP 3D coronal oblique image. This image shows a normal patient. GB, Gallbladder, RHD, right hepatic duct; LHD, hepatic duct; CHD, common hepatic duct; ChoD, choledochal duct (MIP; heavy T2 sequences and 3D images).

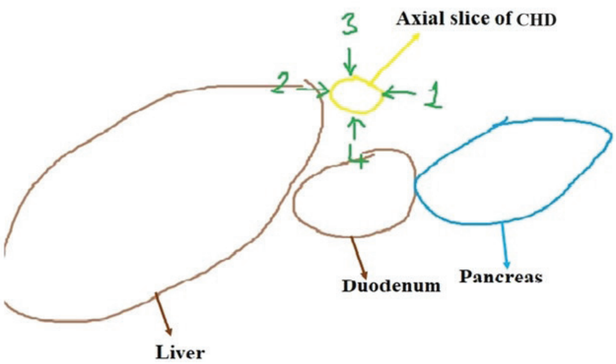

Figure 3
Diagrammatic representation depicting the interconnection between the liver, other organs, and CHD (yellow circles). Arrows and numbers show directions of CD connection to CHD: 1. lateral, 2. medial, 3. posterior, 4. anterior.

Statistical Analysis
The location and direction of the junction of the CD with the CHD and its level, as well as the length of the CD were statistically compared separately with the development of stones and/or cholecystitis. To compare different groups, Student's t-test, Mann-Whitney U test, and Kruskal-Wallis test were employed, as appropriate. Statistical significance was set at $P < 0.05$. Pearson's correlation test. Statistical analysis was performed using SPSS v.23.0 (IBM Corp., Armonk, NY, USA). Two-tailed values of $p < 0.05$ were regarded as statistically significant.

Results

Of the 172 cases included in our study, 99 were female (57.5 %) and 73 were male (42.5 %). The age range of our female patients was 18-87 years with a mean age of 48.76 ± 18.76 years, and the age range of our male patients was 18-85 years with a mean male age of 50.77 ± 16.07 years (Table 2). Stones and/or cholecystitis were not detected in 52 cases (30.2%). In 77 patients (44.8%), only stones were observed, and no cholecystitis was detected. Cholecystitis with calculi was detected in 43 patients (25%) (Table 3, Figure 4).

In 18(10.5%) of our cases, the CD was connected to the proximal 1/3 of the CHD (Figure 5), 132(76.7%) to the middle 1/3, and 22(12.8%) to the distal 1/3 (Table 4).

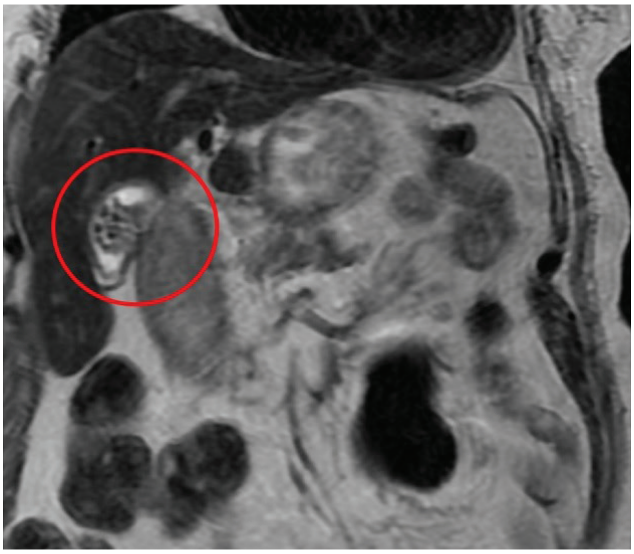

Figure 4
Gallbladder filled with stones (red circles). Coronal TSE T2 image.TR/TE:2800/1100 msec Matrix: 240 × 256 NEX: 1 Flip angle: 150 degrees FOV: 24–36

Table 2 Table showing the age and sex distributions of our patients.

Gender	Number of cases (%)	Age range	Average age
Female	99(%57,5)	18-87	48,76 ± 18,76
Male	73(%42,5)	18-85	50.77 ± 16,07

Table 3 Table showing the distribution of stone and cholecystitis status of our patients

Number of normal subjects without stones and/or cholecystitis-group 1(%)	Number of patients with calculous cholecystitis-group 2 (%)	Number of only stones detected-group 3 (%)
52 (%30,2)	43(%25)	77(%44,8)

Table 4 Table showing the distribution of stone and cholecystitis status of our patients

	Juncton localisation	Number of cases (%)
Group 1	CD 1/3 proximal	18(%10,5)
Group 2	CD 1/3 medium	132(%76,7)
Group 3	CD 1/3 distal	22(%12,8)

In 90(52.3%) of our cases, the CD was connected to the lateral aspect of the CHD, 31(18%) to the medial side, 49(28.5%) to the posterior side (Figure 5), and 2(1.2%) to the anterior side (Table 4).

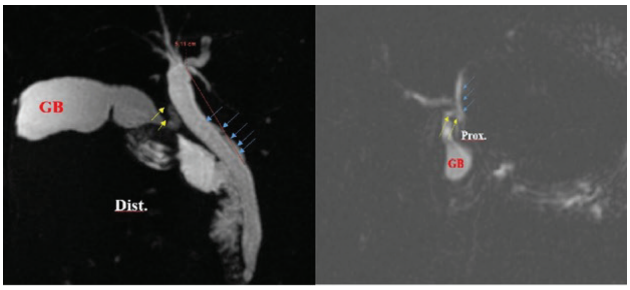

Figure 5
3D MRCP image.GB: Gallbladder, yellow arrows CD, blue arrows CHD. On te left picture long CD connecting to the distal part, and on the right proximal.

Cases were categorized according to the location where the cystic duct merged with the common bile duct to form choledoc duct. Of the 18 cases (10.5%) that opened into the proximal 1/3 of the common bile duct, seven (4%) had only cholelithiasis, five (2.9%) had cholecystitis with calculi, and six (3.5%) had no calculi and/or cholecystitis. Of the 132 (76.7%) cases that joined the middle 1/3, 58 (33.7%) had cholelithiasis only, 30 (17.4%) had calculous cholecystitis, and 44 (26.6%) were normal. Of the 22 (12.8%) cases that opened to the distal part, 12 (7%) had only cholelithiasis, 8 (4.6%) had cholecystitis with calculi, and 2 (1.2%) were normal. The level of CD combined with CHD was not significantly correlated with the development of calculi and cholecystitis (p = 0.213)

Of the two (1.2%) cases in which the cystic duct joined the common bile duct anteriorly, only one (1.1%) had cholecystitis and one (1.1%) had stones without cholecystitis. Of the 49 (28.5%) cases that opened posteriorly, 19 (11%) had cholecystitis, 23 (13.3%) had only stones, and seven (4.6%) were normal. Of the 31(18%) medially joined cases, 16(9.3%) had stones only, 8(4.7%) had cholecystitis, and

Table 5 Table showing the direction of the CD-CHD junction in patients divided into groups.

	Number of cases (%)
Lateral	90(%52,3)
Medial	31(%18)
Posterior	49(%28,5)
Anterior	2(%1,2)

Table 6 Table showing the direction of the CD-CHD junction in patients divided into groups.

	Normal	Only stones	Cholecystitis	p value
less than 2cm (n:27)	16 (59.2%)	3(11,1%)	8 (29,6%)	0.01
between 2-4 cm (n:88)	43(48,8%)	19(21,6%)	26 (29.5%)	
greater than 4 cm (n:57)	31(54,3%)	16(28%)	10(17,5%)	

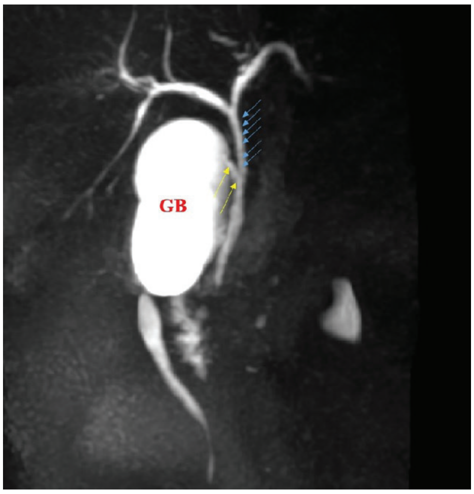

Figure 6
3D MRCP image. GB: Gallbladder, yellow arrows CD, blue arrows CHD.CD connecting posterior side.

7(4.6%) were normal. Of the 90(52.3%) cases, 15(8.7%) had cholecystitis, 37(21.5%) had only stones, and 38(22%) were normal. There was no significant correlation between the side from which the CD joined the CHD and the development of calculi or cholecystitis (p=0.09).

Of the 27(15.7%) cases with cystic duct length less than 2 cm, 3(11,1%) had only stones, 8(29,6%) had cholecystitis, and 16(59.2%) were normal. Of the 88(51.2%) cases with a length between 2 and 4 cm, 43(48,8%)) had only calculi, 19(21,6%) had cholecystitis with calculi, and 26(29.5%) were normal. Of 57(33.1%) patients with cystic ducts longer than 4 cm, 31(18%) had only stones, 16(9.3%) had cholecystitis, and 10(5.8%) were normal. CD size is a predisposing factor for the development of calculi and cholecystitis, and the frequency of calculi and cholecystitis increases with increasing length (p=0.01) (Table 6).

Discussion

Our study was based on investigating the anatomical relationship between CD and CHD and the development of cholelithiasis and/or cholecystitis without considering any other factors.

Imaging of the gallbladder and bile ducts is important for predicting and detecting stone disease and its complications, as well as some early and late complications that may develop after surgery. There are many variations of the extrahepatic bile ducts, and knowledge of these structural variations can predispose patients to possible diseases and provide important data for the management of patients during and after surgery. MRCP is the most optimal non-invasive radiologic method to visualize the extrahepatic bile ducts.

Magnetic resonance cholangiopancreatography (MRCP) is a noninvasive imaging method used to assess the structure of the bile ducts and pancreas. It relies heavily on T2-weighted images, which display prominent signal intensity from stationary fluid structures while minimizing the background signal. Various MRCP techniques have been documented in scientific literature. Our study used these breath-hold techniques. ERCP-mimicking images were generated through maximal-intensity-projection (MIP) three-dimensional rendering, involving contiguous axial and coronal thin-section raw data, or by employing rotating thick-slab images.

Many studies have examined the anatomy of the biliary tract using MRCP, and these studies mainly included preoperative and postoperative evaluations and were mostly based on preoperative planning and postoperative complications. Studies advocate the necessity of MRCP for preoperative planning (13-15)

Therefore, it is important to examine the anatomic type and variations in the biliary tract as a cause of stone and/or cholecystitis. One of the most important studies on this subject was that by Sipahi et al. In this study, it was found that the cystocholedochal angle predisposes to stone development (16). In Taştemur's study, cystic duct variations were found to predispose patients to stone development (17). Bird et al. concluded that the structure within the lumen played a role in stone development (18). This result can be considered a result of the predisposition of excessive CD length to the development of stones and/or cholecystitis in our study because increased length in the intralumen structure can also be considered as conditions that cause bile stasis. Another study concluded that CD length had no direct effect on stone development and that other factors were needed for predisposition to occur (19). In the study conducted by Castelian et al. it was found that increasing CD diameter increased the rate of choledocholithiasis in patients with sac calculi (20). In the study of Ojo et al. it was revealed that the presence of aberrant extrahepatic bile duct increased the risk of stone development (21).

Limitations

If the CD terminates distally, it does not mean that it has a long course; if it terminates proximally, it does not mean that it has a short course. It may terminate distally, have a short course, terminate proximally, and have a long course. The lengths of those that terminate distally or proximally were not analyzed individually, and the effect of both distal termination and long course on the development of stones and/or cholecystitis was not determined, which is also a limitation of our study. The difficulty in identifying the exact location of the junction of CD with CHD directionally using MRCP is also a limitation. Another limitation of our study is that patients with cholesis and cholelithiasis were evaluated in the same category, and no separate analysis was performed for either condition. The most important limitation is that no other cause of stone development other than the anatomy of the patients was examined. The other limitation of our study is related to patient selection; all individuals were selected from patients referred to the Radiology Department due to various biliary complaints, which may not accurately represent a uniform population. However, additional research involving extensive quantitative assessments of intraluminal flow rates and encompassing larger patient cohorts are necessary to validate our hypothesis.

Conclusion

In our study, it was concluded that long CD increased the frequency of stone and/or cholecystitis development, whereas the location and direction of attachment did not create a statistically significant predisposition for stone and/or cholecystitis development. We believe that further studies in large patient series with the inclusion of other clinical and laboratory parameters will reduce the limitations and provide more valuable data.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Ethical Approval

The study was conducted in compliance with the Declaration of Helsinki 1975, as revised in 2008, and was approved by the Health Science University İstanbul Gaziosmanpaşa Training and Research Hospital Scientific Research Ethics Committee (date:20.10.2021, no:346). All research steps were carried out at the Department of Radiology of Health Science University İstanbul Gaziosmanpaşa Training and Research Hospital. This retrospective study included 172 patients who underwent MRCP between January 2017 and December 2020.

Consent to Participate and Publish

As the study had a retrospective design and re-examination of images was performed anonymously, the requirement for written informed consent was waived.

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Availability of Data and Materials
Data available on request from the authors.

Authors Contributions
LK: Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing-original draft. Writing-original draft.

OG: Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing-original draft. Writing-original draft.

EMY; Investigation; Visualization; Writing-original draft.

EOY; Investigation; Visualization; Writing-original draft.

SCU; Investigation; Visualization; Writing-original draft.

MFK; Investigation; Visualization; Writing-original draft.

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