THE EFFECT AND IMPORTANCE OF EXTRAHEPATIC BILE DUCT ANATOMY VARIATIONS IN THE ETIOLOGY OF CHOLEDOCHOLITHIASIS

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Abstract

Background: Biliary stone disease is a frequently encountered problem among the population with a variety of causes and resulting in a wide range of symptoms from vague abdominal discomfort to life-threatening conditions requiring urgent surgical intervention. Magnetic resonance cholangiopancreatography (MRCP) has become a noninvasive radiological diagnostic method extensively used in the evaluation of the biliary tract providing excellent anatomical detail. Apart from the classical causes widely described in the literature in stone etiology, the effect of anatomical variations of the bile tract is a subject that has been investigated recently. The present study aimed to manifest the effect of anatomical variations of the extrahepatic biliary tract on the etiology of choledocholithiasis.

Methods: The data of 182 patients who underwent MRCP in our hospital between 2016 and 2021 were retrospectively scanned. The patients were divided into two groups, asymptomatic patients and acute cholangitis. Cystic duct, common hepatic duct, choledochal lengths, and variations in cystic duct opening were analyzed by an experienced radiologist in MRCP.

Results: The relation was detected between the cystic choledochal variance of the patients (p<0.001). The cystic duct length of the patients showed statistically significant differences (p<0.05).

Conclusion: When the extrahepatic bile duct variations were evaluated, some notable values were found for the etiology, as well as being critical in acute cholangitis. There is a need for studies with larger sample sizes in the literature on this subject.

Keywords: anatomic variation, choledocholithiasis, bile ducts, MRCP
INTRODUCTION

Gallstones are formed by a variety of causes including cholesterol supersaturation in bile, insufficient bile salt levels, impaired bile salt function, and decreased contractility of the biliary walls due to the effects of diet, hormones, and genetic factors (1, 2). Bile duct stones, also known as choledocholithiasis, most commonly stem from the translocation of gallstones from the gallbladder into the biliary canals (3). It was shown that 10% to 20% of patients with symptomatic cholelithiasis have accompanying choledocholithiasis (4). The average age of bile duct stone patients is 67 years, whereas the mean age of patients with gallbladder stones is 56 years (5). Women are approximately twice as likely as men to form gallstones, while the ratio of women to men with bile duct stones is 0.89:1 (5, 6). Gallstones do not provoke any symptoms in most cases, but approximately 3% of patients with gallstones become symptomatic each year (5). Gallstones can be managed by follow-up only due to the benign natural course of the asymptomatic gallstone disease. However, bile duct stones must be removed owing to the increased probability of the development of severe complications, including biliary obstruction, acute pancreatitis, and cholangitis (7, 8). Although biliary duct stones can be suspected or diagnosed by imaging studies, as many as 25% of bile duct stones are still explored at the surgery in an unforeseen manner (9). The anatomy of the biliary tree has an abundance of variations that should be demonstrated before any interventional procedure in order not to cause unintentional damage to the bile ducts during the surgery (10). MRCP is the preferred radiologic study to reveal the detailed anatomy of the biliary tree owing to its excellent capability of delineation of stationary fluid, which is the bile in this situation. The cystic duct is around 2-4 cm in length and 1-5mm in diameter, providing the connection between the gallbladder and the common hepatic duct (10). Even though the insertion of the common bile duct (CBD) to the common hepatic duct (CHD) has many variations, the expected point of the entrance of CBD is the right lateral aspect at the midlevel of CHD (11). Some variations that are of great significance in terms of surgery are low insertion of the cystic duct, parallel course of the cystic duct with CHD, anterior or posterior spiral course with medial insertion, short cystic duct (length< 5 mm), aberrant drainage of cystic duct to the right hepatic or left hepatic duct, aberrant or accessory intrahepatic ducts draining into the cystic duct, and double cystic duct (12,13,14).

MATERIALS-METHODS

Data of patients
In the present study, the data of the patients who underwent Magnetic Resonance Cholangiopancreatography (MRCP) between 2016-2021 at the University of Health Sciences Kanuni Sultan Süleyman Training and Research Hospital were reviewed retrospectively. Patients older than 18 years of age were included in the study, and patients who had previous hepatopancreatic biliary surgery, patients with signs of tumors in the gastrointestinal tract, and pregnant women were excluded from the study. The patients were divided into two groups. Those who were asymptomatic were included in Group 1, and those who had choledocholithiasis were included in Group 2. Permission was obtained for the study from the Ethics Committee of Kanuni Sultan Süleyman Training and Research Hospital.

Magnetic Resonance Imaging method and evaluation

The Magnetic Resonance Cholangiopancreatography (MRCP) data were reviewed retrospectively. All Magnetic Resonance Imaging (MRI) examinations were performed with the whole body Siemens MagnetomAera Device using a 1.5 Tesla Unit Abdominal Coil. The imaging parameters of T2W-TSE parts were set at 1100ms/620ms/1 (Time of Repetition [TR]/Time of Echo [TE]/Number of Signals on Average [NSA]). MRCPad and MRCP 3D
images were also acquired. Cystic duct, common hepatic duct, and common hepatic duct lengths and variations in cystic duct opening were evaluated retrospectively in MRCP by an experienced radiologist. The variations of the junction of the cystic duct with the common bile duct were classified according to 6 anatomical localizations. The union of the cystic duct with the distal 1/3 of the extrahepatic bile duct was considered low, and the proximal 1/3 of the cystic duct was considered high. The normal insertion of CD was defined as the union through the middle one-third of the lateral border. The Clock Method was used in transverse MRCP sections. The anterior was taken as 9-3 o’clock, the medial as 1-5 o’clock, and the posterior as 5-9 o’clock.

**Statistical Evaluation of the Data**

When the findings obtained in the study were evaluated, the SPSS 22.0 Statistics Package Program was used for statistical analyses. The results of the patients were analyzed descriptively. The conformity of the quantitative values of the patients with normal distribution was tested with the Shapiro-Wilk Method (p<0.05). The comparisons were made using the Mann-Whitney U-Test because these variables were not suitable for normal distribution. The comparisons of the qualitative values were evaluated with the Pearson Chi-Square and Fisher’s Exact Test. The ROC Analysis was performed on cystic duct length, common hepatic length, and common hepatic length values of GROUP 1-GROUP 2, and the sensitivity, specificity, Positive Predictive Value, Negative Predictive Value, and Accuracy Ratios were given based on these values. The results of the comparisons were in the 95% and 99% Confidence Intervals, and p<0.05 or p<0.01 were evaluated at the level of significance.

**RESULTS**

**Table 1.** Descriptive statistics of the patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Frequency</th>
<th>Percent</th>
<th>Variables</th>
<th>Mean ± Standard Deviation</th>
<th>Standard Median (Min-Max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>116</td>
<td>63.74</td>
<td>Age</td>
<td>53.58 ± 18.43</td>
<td>50.50 (19-93)</td>
</tr>
<tr>
<td>Male</td>
<td>66</td>
<td>36.26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>182</td>
<td>100.0</td>
<td>Cystic Duct Length</td>
<td>30.93 ± 10.25</td>
<td>29 (4-70)</td>
</tr>
<tr>
<td>Cystic Variant</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>3</td>
<td>1.65</td>
<td>Common Length</td>
<td>31.65 ± 10.14</td>
<td>30 (5-67)</td>
</tr>
<tr>
<td>High</td>
<td>28</td>
<td>15.38</td>
<td>Hepatic Length</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>3</td>
<td>1.65</td>
<td>Cystocholedochal Angle</td>
<td>39.85 ± 11.71</td>
<td>39 (18-76)</td>
</tr>
<tr>
<td>Medial Normal</td>
<td>73</td>
<td>40.11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior</td>
<td>67</td>
<td>36.81</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>182</td>
<td>100.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient</td>
<td></td>
<td></td>
<td>Choledochal Length</td>
<td>41.79 ± 12.90</td>
<td>40 (14-79)</td>
</tr>
<tr>
<td>Group 1</td>
<td>67</td>
<td>36.81</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td>115</td>
<td>63.19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>182</td>
<td>100.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
In Table 1, when the characteristics of the patients are examined, it was found that gender was 63.74% women and 36.26% men. Cystic choledochal variance was 1.65% anterior, 15.38% high, 1.65% low, 4.40% medial, 40.11% normal, 36.81% posterior. Group1: 36.81%, and Group2: 63.19%. The mean age of the patients was 53.58 (± 18.43), the mean cystic duct length was 30.93 (± 10.25), the mean common hepatic length was 31.65 (±10.14), the mean choledochal length was 41.79 (± 12.90), mean cystocholedochal angle was 39.85 (± 11.71).

Table 2. Relation between the gender and cystic choledochal variance of the patients and the Groups

<table>
<thead>
<tr>
<th>Gender</th>
<th>Group 1</th>
<th>Group 2</th>
<th>χ²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>45 (67.16%)</td>
<td>71 (61.74%)</td>
<td>0.33</td>
<td>0.566</td>
</tr>
<tr>
<td>Male</td>
<td>22 (32.84%)</td>
<td>44 (38.26%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystic Choledoch Variance</td>
<td></td>
<td></td>
<td>14.801</td>
<td>0.005**</td>
</tr>
<tr>
<td>ANTERIOR</td>
<td>2 (2.99%)</td>
<td>1 (0.87%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIGH</td>
<td>10 (14.93%)</td>
<td>18 (15.65%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LOW</td>
<td>0 (0.00%)</td>
<td>3 (2.61%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEDIAL</td>
<td>5 (7.46%)</td>
<td>3 (2.61%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NORMAL</td>
<td>35 (52.24%)</td>
<td>38 (33.04%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>POSTERIOR</td>
<td>15 (22.39%)</td>
<td>52 (45.22%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**p<0.01; *p<0.05

After examining Table 2, no relations were detected between the gender of the patients and cystic choledochal variance. In this respect, it can be argued that the gender and cystic choledochal variance of the patients did not differ at statistical levels (p>0.05).

When Table 2 is examined, it is seen that no relation was detected between the gender of the patients. In this respect, it can be argued that the gender of the patients did not differ at statistical levels (p>0.05).

On the other hand, it is seen that relation was detected between the cystic choledochal variance of the patients. In this respect, it can be argued that the cystic choledochal variance of the patients differs at statistical levels (p<0.01). In this case, the highest cystic common bile duct variance rate was found to be normal among the patients in group 1, while the highest cystic common bile duct variance rate was determined as posterior among the patients in group 2.

Table 3. Relation between the Groups in terms of the Age, Cystic Duct Length, Common Hepatic Length, Choledochal Length, and Cystocholedochal Length of the Patients

<table>
<thead>
<tr>
<th>N</th>
<th>Mean ± Standard Deviation</th>
<th>Median (Min-Max)</th>
<th>Z</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Group 1 67</td>
<td>47.48 ± 14.15</td>
<td>46 (19-78)</td>
<td>-3.233</td>
</tr>
<tr>
<td></td>
<td>Group 2 115</td>
<td>57.14 ± 19.72</td>
<td>55 (19-93)</td>
<td></td>
</tr>
<tr>
<td>Cystic Duct Length</td>
<td>Group 1 67</td>
<td>28.42 ± 9.21</td>
<td>28 (4-63)</td>
<td>-2.386</td>
</tr>
<tr>
<td></td>
<td>Group 2 115</td>
<td>32.40 ± 10.58</td>
<td>31 (11-70)</td>
<td></td>
</tr>
<tr>
<td>Common Hepatic Length</td>
<td>Group 1 67</td>
<td>31.19 ± 8.28</td>
<td>31 (17-56)</td>
<td>-0.098</td>
</tr>
<tr>
<td></td>
<td>Group 2 115</td>
<td>31.92 ± 11.12</td>
<td>30 (5-67)</td>
<td></td>
</tr>
<tr>
<td>Choledochal Length</td>
<td>Group 1 67</td>
<td>39.45 ± 8.47</td>
<td>38 (24-60)</td>
<td>-1.615</td>
</tr>
<tr>
<td></td>
<td>Group 2 115</td>
<td>43.17 ± 14.76</td>
<td>42 (14-79)</td>
<td></td>
</tr>
</tbody>
</table>
After examining Table 3, it can be argued that the common hepatic length and choledochal length of the patients did not show statistically significant differences ($p>0.05$). On the other hand, it can also be argued that the age of the patients showed statistically significant differences ($p<0.01$). In this case, the mean age of the patients in GROUP 2 ($X=57.14$) was found to be higher than the mean age of the patients in GROUP 1 ($X=47.78$). It can be argued that the cystic duct length of the patients showed statistically significant differences ($p<0.05$). In this case, the mean cystic duct length of the patients in GROUP 2 ($X=32.40$) was found to be higher than the mean cystic duct length of the patients in GROUP 1 ($X=28.42$). It can be argued that the cystic duct length of the patients showed statistically significant differences ($p<0.05$). In this case, the mean Cystocholedochal Angle of the patients in GROUP 1 ($X=42.12$) was found to be higher than the mean of the patients in GROUP 2 ($X=38.53$). It can be argued that the Cystocholedochal Angle of the patients showed statistically significant differences ($p<0.01$).

**Figure 1.** ROC Curve.

As a result of the ROC analysis given in Figure 1, the prevalence rate was found to be 63.2% according to classification. The cystic duct length cut-off value was determined as 32. Specificity value was determined as 73.1%, sensitivity value 46.1%, PPV value 74.6%, NPV value 44.1, Accuracy value 60.6% (CI=53.1%-67.8%), $p=0.011$. **Figure 1.** ROC Curve.
Common hepatic length cut off value was found to be 41, specificity value 91.1%, sensitivity value 20.9%, PPV value 88.0%, NPV value 40.1%, Accuracy value 50.4% (CI=42.9%-57.9%), and p=0.919. Also, Choledoch length cut off value was found to be 49, Specificity value 88.1%, Sensitivity value 30.4%, PPV value 81.4%, NPV value 42.4%, Accuracy value 57.2% (CI= 50.4%-63.7%), and p=0.087 (Figures 2-5).

Figure 2. Choledoch length measurement.

Figure 3. Cystocholedochal angle.
DISCUSSION

In this study, we aimed to reveal the effect of anatomical variations of the extrahepatic biliary tract on the etiology of choledocholithiasis. It was shown that among these variations, especially cystic choledochal variance, cystic duct length and cystocholedocal angle play an important role in the etiology. In the etiology of choledocholithiasis, the relation between posterior insertion of cystic duct variance and cholelithiasis was found to be more significant than the cystic choledochal variance. There is an inverse relationship between cystocholedochal angle and choledocholithiasis, and the less the angle, the higher the probability of stone formation. The mean cystic duct length was longer in patients with choledocholithiasis. It also found that
the average age of patients with choledocholithiasis was higher than patients without choledocholithiasis.

Choledocholithiasis is a relatively common problem recorded in more than 10% of patients planning cholecystectomy (15). Although bile duct stones may be asymptomatic, they can present as biliary colic, cholangitis, pancreatitis, or jaundice in the vast majority of patients. In patients with a high suspicion of choledocholithiasis, abdominal sonography is the preferred initial valuation due to the low cost, high accuracy, and lack of ionizing radiation, however, it is a procedure that is highly dependent on the operator. In patients with equivocal symptoms by means of vague abdominal pain, computed tomography is usually performed, but the mainstay of the noninvasive diagnosis is MR cholangiopancreatography (15). MRCP is the favored imaging modality to reveal the biliary anatomy with all relationships and variations via delineating the entire biliary tract (10).

Excessive variability is detected in the route of the cystic duct and its union with the extrahepatic bile duct. The expected anatomy of the cystic duct connecting the CHD at its middle third from the lateral aspect is encountered in 58%-75% of patients (16). In our study, this anatomy has been seen in 40% of our patients. In this study, we identified risk factors for choledocholithiasis including posterior insertion of cystic duct along with cystocholedochal angle.

Our study was conducted retrospectively in a single center without considering the diameters of biliary canals contributing to the limitations of the study.

In conclusion, our findings suggest that high and posterior insertion of the cystic duct along with the cystocholedochal angle were risk factors for choledocholithiasis, however owing to the retrospective nature of our study, future prospective studies are needed to confirm the clinical significance of these three mentioned risk factors related to the increased probability of choledocholithiasis.

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Sažetak

DEJSTVO I ZNAČAJ VARIJACIJA ANATOMIJE EKSTRAHEPATIČNIH ŽUĆNIH KANALA U ETIOLOGIJI HOLEDOHOLITIAZE

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Uvod: Bolest žučnih kamenaca je čest problem među populacijom sa različitim uzrocima, koji rezultira širokim spektrom simptoma od nejasne nelagodnosti u stomaku do stanja opasnih po život koji zahtevaju hitnu hiruršku intervenciju. Holangiopankreatografija magnetnom rezonancom (MRCP) je postala neinvazivna radiološka dijagnostička metoda koja se uveliko koristi u proceni bilijarnog trakta dajući odlične anatomske detalje. Pored klasičnih uzroka koji su u literaturi naširoko opisani u etiologiji kamena, efekat anatomskih varijacija žučnih puteva je tema koja se u poslednje vreme istražuje. Ova studija je imala za cilj da pokaže uticaj anatomskih varijacija ekstrahepatičnog bilijarnog trakta na etiologiju holedoholitijaze.

Metode: Retrospektivno su analizirani podaci 182 pacijenta koji su podvrgnuti MRCP-u u našoj bolnici u periodu od 2016. do 2021. godine. Pacijenti su podeljeni u dve grupe, asimptomatski bolesnici i oni sa akutnim holangitisom. D. cysticus (žučni kanal), ductus hepaticus communis (zajednički jetreni vod), dužina holedoha i varijacije u otvaranju žučnih kanala analizirao je iskusni radiolog za MRCP.

Rezultati: Utvrđena je veza između cistične i holedohalne varijanse kod pacijenata (p<0,001). Dužina žučnog kanala pacijenata je pokazala statistički značajne razlike (p<0,05).

Zaključak: Kada su procenjene varijacije ekstrahepatičnog žučnog kanala, utvrđene su neke značajne vrednosti za etiologiju, kao i da su kritične kod akutnog holangitisa. Postoji potreba za studijama sa većim uzorcima u literaturi na ovu temu.

Ključne reči: anatomska varijacija, holedoholitijaza, žučni kanali, MRCP

REFERENCES

*Accepted papers are articles in press that have gone through due peer review process and have been accepted for publication by the Editorial Board of Sanamed. The final text of the article may be changed before the final publication. Accepted papers can already be cited using the year of online publication and the DOI, as follows: the author's last name and initial of the first name, article title, journal title, online first publication month and year, and the DOI. When the final article is assigned to volumes/issues of the journal, the Article in Press version will be removed and the final version will appear in the associated published volumes/issues of the journal. The date the article was made available online first will be carried over.

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