

A novel approach for differentiating etiology of gallstone formation: Sistocholedochal angle

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Abstract. – OBJECTIVE: Many etiological factors such as gall bladder motility disorders, chemical component of bile and chemical content of bile have been accepted on gallstone formation; but anatomic variations of bile duct has been never discussed before. The aim of this study was to assess whether the anatomical measurements of cystic canal length, common bile duct length, choledoc length and the angle between the cystic duct and common bile duct junction (sistocholedochal angle: SCA) affects the gallstone formation.

PATIENTS AND METHODS: MRI data of patients who had undergone magnetic resonance cholecysto pancreatography (MRCP) due to any reason, were collected retrospectively. A total of 126 patients was divided into two groups as without (group I; n=38) and with (group II; n=88) gallstone formation. The cystic canal, choledoc and common bile duct length and SCA measurements were obtained.

RESULTS: There was no significant difference between two groups on the means of cystic canal, choledoc and common bile duct lengths ($p > 0.05$) but SCA measurements were significantly higher in group II compared with group I, statistically ($p < 0.05$); showing that as the SCA increases, the incidence of gallstone formation increases.

CONCLUSIONS: Higher SCA values can be indictable on gallstone formation.

Key Words:

Gallstone, Extrahepatic bile duct, Magnetic resonance cholecystography.

Introduction

As the gallstone formation is a worldwide health problem which can cause several complications, the incidence of cholecystectomy operation is 700.000 per year with a cost of 6.5 billion dollars¹. The main risk factors of gall-

stone formations are advanced age, female gender, pregnancy, oral contraceptive use, obesity, fast weight loss, total parenteral nutrition, prolonged fasting, family history, cirrhosis, ileal disease and ileal resection²⁻⁵. On the other hand, some authors blamed different environmental factors on development of gallstone formation. In a study which is performed on Chileans and North American Indians with the major incidence of cholelithiasis, Nervi F et al pointed that the legume intake is a potential risk factor for cholesterol gallstone disease⁶. It is divided into three groups according to their chemical composition as; cholesterol gallstones that include at least 80% cholesterol and forms with bilirubin and calcium salt, pigment gallstones with the synonym name of black pigment stones; that include less than 20% cholesterol, 70% calcium bilirubinate and the mix type gallstone (brown pigment stone) which is a compound of 20-80% cholesterol, bilirubin and bile salt³. The ethnicity is an important risk factor in both its incidence and type². The incidence of gallstone formation vary from societies to societies as it is 0-10% in Africa, 73% in North American Hindu's and is 5.9-21.9% in European countries²⁻⁴. While the cholesterol type gallstone is common in western societies, the pigment type is frequent in East Asian societies^{1,2}. The etiological factors for the cholesterol gallstones formation are increment in cholesterol synthesis and secretion, decrement in bile salt synthesis and secretion, degradation intestinal absorption of cholesterol and bile salt and motility disorders of gallbladder. Black pigment stones are well associated with hemolytic diseases and cirrhosis⁵ that is caused by the increment of unconjugated bilirubin resulting deposition of high bilirubin³⁻¹¹. Brown pigment stones forms with the effect of some

Table I. The measurements of anatomical structures.

		N	Mean	StD
Group I	cystic canal length (mm)	34	14.588	6.0897
	common bile duct length (mm)	38	29.874	9.6464
	choledoc length (mm)	38	57.574	10.5613
	sisto-choledochal angle (degrees)			
Group II	cystic canal length (mm)	55	12.958	4.1473
	common bile duct length (mm)	88	27.768	7.5221
	choledoc length (mm)	88	99.394	22.9545
	sisto-choledochal angle (degrees)			
Overall	cystic canal length (mm)	89	13.581	5.0096
	common bile duct length (mm)	126	28.403	8.238
	choledoc length (mm)	126	55.898	10.3244
	Sisto-choledochal angle (degrees)	126	96.03	22.9025

parasitic diseases such as *opisthorchis viverrini* and *Ascaris lumbricoides* or after the bile stasis combined with *Escherichia coli* and *Klebsiella* infection^{5,6}.

Recent studies showed that there is a significant effect of some gene polymorphisms such as cholecystokinin receptor A (CCK-AR), cholesterol 7- α -hydroxylase (CYP7A1) on gallstone formation^{7,8}. As the lack of mucin secretion; which is originated from the epithelia of the neck of the gallbladder; causes cholesterol crystal nucleation and the formation⁵, it is shown that some polymorphisms on encoding the mucin secretion causes gallbladder stone formation, also^{9,10}.

Since the computed tomography (CT) and ultrasonography (USG) are most used imaging tools, they have some disadvantages on image quality such as motion artifacts or gas superposition. Endoscopic retrograde cholangio pancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC) are used on only selected cases because of its potential complication risks. MRCP is a noninvasive and reliable diagnostic tool in gallbladder and bile duct diseases¹².

Although the clinical significance is not demonstrated yet, there are many anatomic variations on both intra and extra bile ducts which are important in surgical procedures to avoid possible injuries¹². Additionally, the significance of anatomic variations of bile duct on the formation of gallstone never discussed before. Therefore, we aimed to assess whether the anatomical measurements of cystic canal length, common bile duct length, choledoc length and SCA affects the gallstone formation.

Patients and Methods

Study Population

MRI data of patients, who had undergone MRCP due to any reason in one year period (January-December 2014), were collected, retrospectively. The evidence of gallstone formation in patients without cholecystectomy was evaluated with their MRI and ultrasonographic data. Patients with a history of cholecystectomy operation were analyzed with their postoperative pathology report or preoperative radiological archives by the means of gallstone formation. A total of 126 patients was divided into two groups as without (group I; n=38) and with (group II; n=88) gallstone formation. The ethical approval and patients' consent form each patient obtained for the study and the investigation was performed with obeying the principles outlined in the Declaration of Helsinki.

Assessment of Measurement with MRCP

All MRI examinations were performed on a whole-body 1.5 T unit (Ingenia, Philips, Germany) by using a 32-channel sensitivity-encoding (SENSE) abdominal coil. The imaging parameters for T2W-TSE slices were 3810 ms/114 ms/1 (repetition time [TR]/echo time [TE]/number of signal average [NSA]), 150 flip angle, 259 x 118 matrix, 800-cm field of view (FOV), 130 kHz bandwidth, and 13 echo train length, slice thickness 0.9 mm, with an acquisition time of 4 minutes 26 seconds. Additionally the SSF, MCPrad and MRCP 3D HR images were also obtained. The cystic canal, choledoc and com-

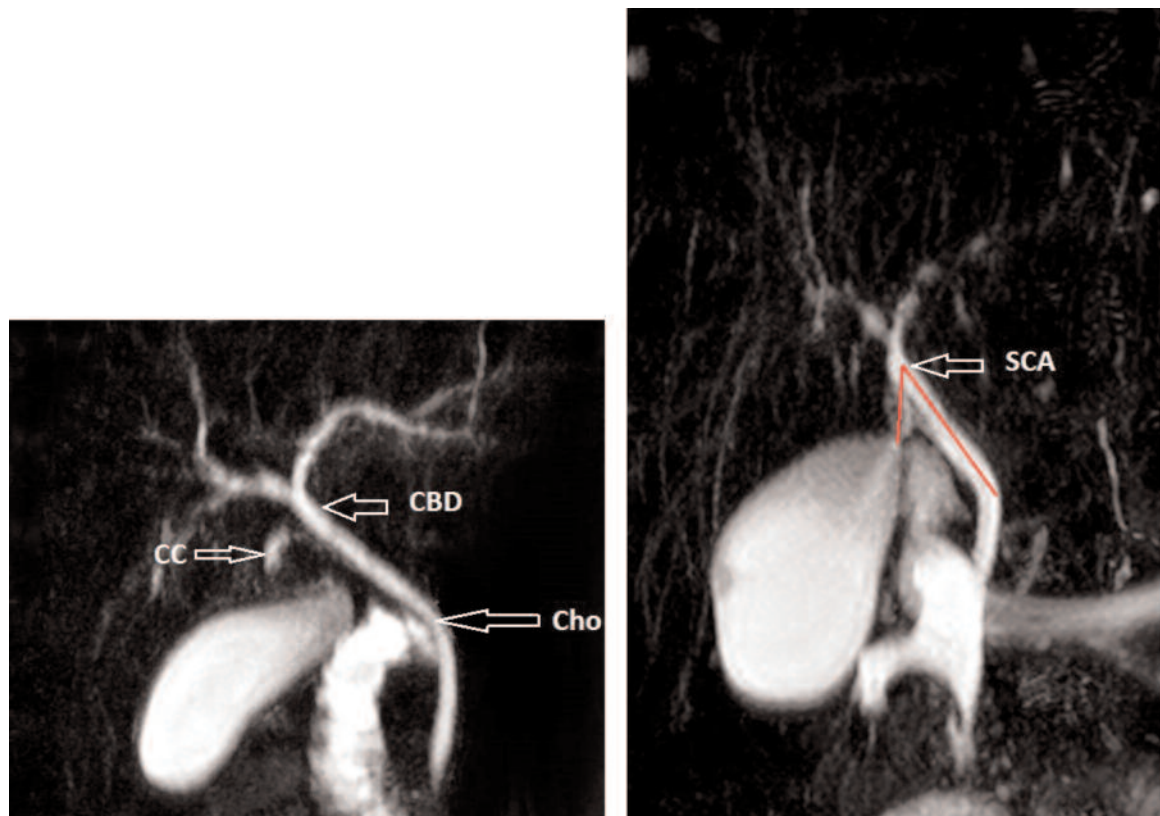


Figure 1. The region of interests used to obtain the measurements on MRCP image.

mon bile duct lengths and SCA measurements were obtained (Figure 1). The SCA was accepted as the angle between the two crossing lines extending into cystic canal and choledoc. As the cystic canal excises preoperatively, we could not measure the cystic canal length and SCA of cholestectomy patients ($n = 37$).

Statistical Analysis

All statistical analyses were carried out using the SPSS software program. Student's *t* test, Mann-Whitney U test and Kruskal-Wallis tests were performed to compare groups accordingly. A *p* value of less than 0.05 was considered to show statistically significant result.

Results

There was 50 male (39.68%) and 76 females (60.32%) subjects with the mean age 55 ± 12 and 58 ± 14 respectively. The mean age of the group I was 55 years (58 ± 16.10); and was 57 years (55.55 ± 16.32) in group II. The incidence of gall-

stone formation was 66% in men and was 30.2% in women. The overall mean cystic canal length was 13.58 mm (without cholestectomy patients, $n=89$), choledoc length was 55.9 mm, common bile duct length was 28.4 mm and the SCA was 96.03 degrees. These results are summarized in Table I.

There was no significant difference between two groups on the means of common bile duct length, statistically ($p=0.189$). Although the mean choledoc length was higher in group II compared with group I; the results cannot meet any statistical significance ($p=0.233$). Since the mean cystic canal length was 14.588 mm in group I, and was 12.958 in group II; there was no significant statistical difference between the groups ($p=0.353$).

It was found that the SCA was significantly greater in group II, compared with group I ($p=0.012$); and when the patients are calcified as greater and less than 90 degrees according to their SCA's; the incidence of gallstone formation was 78.8% and 54.3% respectively; proving that; as the SCA increases, the incidence of gallstone

Table II. The statistical comparison results of groups.

	Group I (mean)	Group II (mean)	Significance (2-tailed)
Cystic canal length (mm)	15.588	12.958	P=0.353
Common bile duct length (mm)	29.874	27.768	p=0.189
Choledoc length (mm)	57.574	55.175	p=0.233
Sisto-choledochal angle (degrees)	88.239	99.394	p=0.012

formation increases accordingly. The comparison results of two groups are shown in Table II.

Discussion

The gallstone formation is a worldwide health problem which can cause several complications and the incidence of cholecystectomy operation increases day by day. CT and USG have some limitations on diagnosis of bile duct diseases. With the injection of contrast agent into the bile ducts, the most reliable diagnostic tool for assessment of normal anatomy and variations is PTK and ERCP, but these techniques have some disadvantages¹². Some of the complications can be summarized as duodenal perforation, pancreatitis, and it has a significant radiation exposure^{13,14}. With these limitations, PTK or ERCP generally used on selected patients to whom bile drainage, sphincterectomy or gallstone extraction have been programmed already. MRCP is a noninvasive and reliable diagnostic tool in the diagnosis of gallbladder or bile duct diseases, as well as the anatomical variations. Although the clinical significance is not demonstrated yet, there are many anatomic variations on both intra and extra bile ducts. The most important value of such variations is to alert the surgeons to analyze the bile ducts variations correctly preoperatively and to avoid from bile duct injury¹². Although there are many etiological factors including environmental and genetic effects are reported on gallstone formation, the main mechanism is defined as biliary cholesterol supersaturation, excess pronucleating proteins, or shortage of nucleation inhibiting proteins, and factors related to the gallbladder, such as hypomotility and bile stasis¹⁵. But, the significance of the effect of variation and anatomical characteristic of bile ducts to the motility and stasis is still unknown. We found no significant difference between the groups on the measurements of cystic canal length, common bile duct length and choledoc length opposite to the

knowledge that as the lengths of these structures increases, the intraluminal pressure increases and cause a risk factor in gallstone formation. According to our results as the SCA increases, the incidence of gallstone formation increases accordingly. As it is known that there are many plica spiralis and spiral folds in the lumen of cystic canal which acts as a valve¹⁶, we postulate that the increment in SCA causes a resistance to bile flow and results with longer duration of residue saturated bile in the gallbladder with a decrement of bile drainage from cystic canal through the choledoc and these factors effects the gallstone formation. Our study has some limitations in selecting the participants: all of them were selected from the patients who were referred to the Radiology Department with a complaint of any biliary disorder, and do not reflect a homogenized population. But further studies based on quantitative intraluminal flow rate measurements and with a large numbers of patients are needed to confirm our hypothesis.

Conclusions

The higher SCA values are a potential risk factor on gallstone formation with the cause of probable decrement of bile drainage.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

- 1) SHAFFER EA. Gallstone disease: epidemiology of gallbladder stone disease. *Best Pract Res Clin Gastroenterol* 2006; 20: 981-996.
- 2) GALLAGHER TK, PARKS RW. Gallstones. *Surgery* 2014; 1: 512-516.
- 3) AERTS R, PENNINGCKX F. The burden of gallstone disease in Europe. *Aliment Pharmacol Ther* 2003; 3: 49-53.

- 4) BAR DY, VILKIN A, NIV Y. Gallbladder mucin plays a role in gallstone formation. *Eur J Intern Med* 2004; 7: 411-414
- 5) CHOWDHURY AH, LOBO DN. Gallstones. *Surgery (Oxford)* 2011; 29: 610-617.
- 6) NERVI F, COVARRUBIAS C, BRAVO P, VELASCO N, ULLOA N, CRUZ F, FAVA M, SEVERIN C, DEL POZO R, ANTEZANA C. Influence of legume intake on biliary lipids and cholesterol saturation in young Chilean men. Identification of a dietary risk factor for cholesterol gallstone formation in a highly prevalent area. *Gastroenterology* 1989; 3: 825-830.
- 7) SRIVASTAVA A, PANDEY SN, DIXIT M, CHOUDHURI G, MITTAL B. Cholecystokinin receptor A gene polymorphism in gallstone disease and gallbladder cancer. *J Gastroenterol Hepatol* 2008; 6: 970-975.
- 8) NAKAMOTO K, WANG S, JENISON RD, GUO GL, KLAASSEN CD, WAN YJ, ZHONG XB. Linkage disequilibrium blocks, haplotype structure, and htSNPs of human CYP7A1 gene. *BMC genet* 2006; 7: 29.
- 9) LAMMERT F, SAUERBRUCH T. Mechanisms of disease: the genetic epidemiology of gallbladder stones. *Nat Clin Pract Gastroenterol Hepatol* 2005; 9: 423-433.
- 10) CHUANG SC, JUO SHH, HSI E, WANG S-N, TSAI P-C, YU ML, LEE KT. Multiple mucin genes polymorphisms are associated with gallstone disease in Chinese men. *Clin Chim Acta* 2011; 7: 599-603.
- 11) STRASBERG SM. The pathogenesis of cholesterol gallstones—a review. *J Gastrointest Surg* 1998; 2: 109-125.
- 12) DUSUNCELI E, ERDEN A, ERDEN . Biliyer sistemin anatomik varyasyonları: MRKP bulguları. *Tani Girişim Radyol* 2004; 10: 296-303.
- 13) KOCAMAN O, SİPAHI M, CUBUKCU A, BAYKARA ZN, HÜLAGÜ S. Porous diaphragm syndrome after ER-CP in a patient with bile duct stricture. *Turk J Gastroenterol* 2009; 2: 157.
- 14) TURNER M, FULCHER A. Gallbladder and biliary tract: normal anatomy and examination techniques. *Textbook of Gastrointestinal Radiology* 2000; 2: 1250-1276.
- 15) VENNEMAN NG, VAN ERPECUM KJ. Pathogenesis of Gallstones. *Gastroenterol Clin North Am* 2010; 2: 171-183.
- 16) DOWLING RH. Review: pathogenesis of gallstones. *Aliment Pharmacol Ther* 2000; 2: 39-47.