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The effect of morphometric and anatomic relationship of gallbladder to the liver on standard laparoscopic cholecystectomies and proposal of a new anatomical classification

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Abstract. – OBJECTIVE: Anatomical variations of the extrahepatic biliary tree are frequently seen and may cause challenging conditions for surgeons. We aimed to investigate the morphological variations of the gallbladder in patients who underwent cholecystectomy and their effects during and after the surgery, by using a new anatomical classification.

PATIENTS AND METHODS: Dissection time, perioperative bleeding, perioperative/postoperative complication rates, the difference between preoperative/postoperative hematocrit and leukocyte levels of 164 symptomatic cholelithiasis patients who underwent laparoscopic cholecystectomy were evaluated. The patients' gallbladders were categorized in "seven" different types regarding their anatomical positions and morphometric relations with the liver's acute margin and fossa of the gallbladder. Relations between these gallbladders types and perioperative/postoperative parameters were also examined.

RESULTS: The median time to complete the dissection of the gallbladder from the fossa was 375.5 seconds. The mean length of the fossa was 68.06 ± 15.08 mm, the average size of the gallbladder was 92.10 ± 18.79 mm. A positive correlation was found between dissection time and length of fossa vesica and also in the size of the gallbladder ($p = 0.003$, $p = 0.034$). Moreover, a positive correlation was found between the dissection time and the perioperative perforation risk of the gallbladder ($p = 0.005$). The most common type of gallbladder was type I and III (23.2%). The least common gallbladder type among the patients assessed as part of the study was type VI (6.7%). When the gallbladder types were compared, the perioperative perforation rate of the gallbladder wall was found to be significantly higher in morphological type V ($p = 0.014$).

CONCLUSIONS: The perioperative perforation rate of the gallbladder wall was found significantly higher in morphological type V. To perform a safe cholecystectomy, surgeons should be aware of anatomical variations of the gallbladder and its relations with the liver parenchyma, which are important for surgical strategies.

Key Words:
Gallbladder, Liver, Anatomical variations, Cholelithiasis, Cholecystectomy, Classification.

Introduction

The gallbladder is responsible for storing, concentrate, secrete the bile and aid the digestion of the lipid, soluble compounds in humans – located beneath the visceral surface of the liver's right lobe and its fundus commonly projects anteriorly and contacts with the anterior abdominal wall at the transpyloric plane[1,2]. A ventral outgrowth of the distal/caudal end of the foregut differentiates to liver and gallbladder buds at the fourth week of the fetal development. These buds form the liver primordium, gallbladder, and biliary duct in the later phases of development [3].

Anatomical features and variations of the gallbladder and its ductal system have been discussed in several studies. Anatomical variations of the extrahepatic biliary tree are more frequent[4]. Furthermore, different variations about the gallbladder and its fossa such as left-sided gallbladder, floating abdominal gallbladder, large gallbladder, accessory/duplication, triplication

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and the agenesis of the gallbladder are rarely seen and can be observed in both children and adults[5-11].

Normal appearance of the gallbladder in the human can be basically pear, rectangular, fusiform or circular shaped[3]. Previously defined morphological differences of the intrahepatic or extrahepatic structures related to the biliary system are also ranging from rare to common in the literature. They can cause some pathological conditions such as perioperative duct injuries and torsion or volvulus that might require emergency surgery[4,7,10]. There may be many reasons for variable incidences of the gallbladder anomalies. Differences in surgical approaches, inattentive explorations and asymptomatic cases in the population are the possible reasons for this variability. Also, they may be omitted due to various reasons[9-11]. It must be noted that the combination of the endoscopic retrograde cholangiopancreatography (ERCP) with the ultrasonography (USG) or as a non-invasive technique the magnetic resonance cholangiopancreatography (MRCP) alone may give more accurate results for the intrahepatic or extrahepatic anomalies[12].

Among the patients, seemingly insignificant and minor, metric or non-metric differences are commonly seen related to the gallbladder anatomy and they can presumably lead to different operational or post-operational results. We aimed to investigate the morphological relations between the gallbladder fundus and the inferior border of the liver and between the gallbladder corpus and the gallbladder fossa. Our other objective was to demonstrate the effects of these anatomical relations on the dissection time, perioperative bleeding and postoperative drainage parameters recorded during and 24th hours after laparoscopic cholecystectomy. We also emphasize a new morphometric classification to describe the anatomic position of the gallbladder regarding the liver's anatomical landmarks.

Patients and Methods

This prospective clinical comparative study was approved by the Ethics Committee of Sevket Yilmaz Training and Research Hospital (Approval Date/Number: 02.04.2014/07) and conducted in Department of General Surgery, Sevket Yilmaz Training and Research Hospital. Written informed consent was obtained from patients who participated in this study.

A total of 164 patients who had laparoscopic cholecystectomy due to symptomatic cholelithiasis were included in this prospective study. To ensure the homogeneity of the study, patients who have a history of acute or chronic cholecystitis, porcelain gallbladder, empyema of the gallbladder, intra-abdominal adhesions affecting the corpus of the gallbladder, previous upper abdominal surgery, an additional disease that may affect the biliary tract surgery, and bleeding-clotting problems were excluded. Patients with a provisional diagnosis of gallbladder cancer and those who have intra/extra-hepatic biliary tract anomalies and additional liver disorders (cirrhosis, etc.) were also excluded. Patients with a calculus of > 2.5 cm were excluded due to the difficulty of dissection and increased the occurrence of gallbladder cancer. All of the patients were examined with ultrasonography (USG) before the surgery, and normal gallbladder wall thickness and extra-hepatic biliary tract, lack of pericholecystic fluid was confirmed.

Standard 4-port laparoscopic cholecystectomy was performed in all patients at a single department by experienced surgeons, each of whom had performed > 250 cholecystectomies. The gallbladder was dissected from the fossa vesica fellea using laparoscopic hook and cautery. Single dose 1 gram of 1st generation cephalosporin intravenously applied to all patients for antibiotic prophylaxis. Once the gallbladder was removed outside the abdomen, a safe distance from the cystic duct was checked. Hemorrhagic fluid, coagulum, and bile accumulated on the site due to bleeding and occasional perforations, respectively were not irrigated but only aspirated. No drain was placed in the subhepatic area during surgery.

Antibiotic prophylaxis was continued up to 24-hour in patients who developed perioperative gallbladder wall perforation.

In our study, we categorized the gallbladders in seven different types regarding their anatomical positions and morphometric relations with the liver's acute margin and fossa of the gallbladder (Table I and Figure 1).

Before the cystic artery and cystic duct were clipped, length measurements were performed with a sterile measuring tape placed into the abdomen and categorized (Table II and Figure 1).

After the cystic artery and cystic duct had been clipped and cut, time was tracked and complete dissection time of the gallbladder from the fossa was recorded in seconds. In the meantime,

Table I. Classification of gallbladders by their anatomic and morphometric relationships to the liver.

Classification	Definition
Type I	The fundus extends beyond the margo anterior; the fossa vesica extends to the margo anterior
Type II	The fundus extends beyond the margo anterior; the fossa vesica does not extend to the margo anterior
Type III	The fundus and margo anterior are in alignment; the fossa vesica extends to the margo anterior
Type IV	The fundus and margo anterior are in alignment; the fossa vesica does not extend to the margo anterior
Type V	The fundus is below the level of the margo anterior; the apex of the fundus extends to the margin of the fossa vesica
Type VI	The fundus is below the level of the margo anterior; the apex of the fundus does not extend to the margin of the fossa vesica
Type VII	The gallbladder is completely free; it has no adjacency with the liver except a peritoneal connection

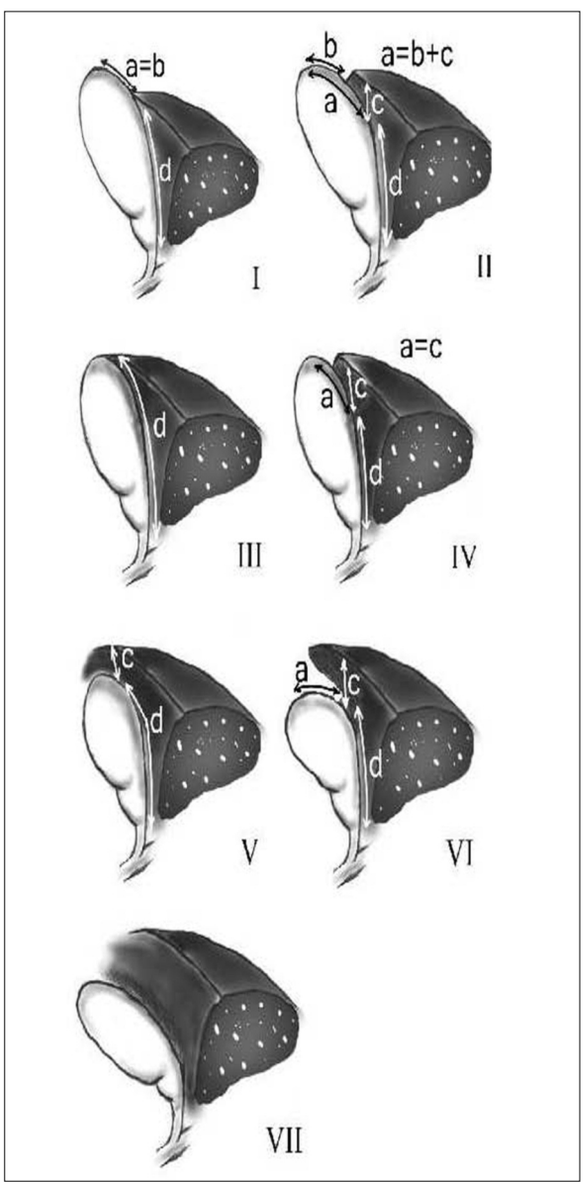

Figure 1. Classifications of the gallbladders regarding their anatomical positions and morphometric relations with the livers' acute margin and fossa vesica biliaris.

the amount of bleeding due to dissection was assessed visually and classified (Table III).

During the dissection of the gallbladder from the fossa, perforations of the gallbladder wall were also recorded.

No biliary tract injury was observed during and after operations in any of the patients. None of the patients developed early complications (massive bleeding requiring re-laparotomy, biliary leakage, surgical site infections, etc.).

Statistical Analysis

The statistical analyses were performed using SPSS (Statistical Package for the Social Sciences ver. 21.0, SPSS Inc, Chicago, IL, USA) computer program. The number of samples was less than 50 in each group; therefore, normality was analyzed using Shapiro-Wilk test. For analysis of the data from all subjects, normality was assessed using Kolmogorov-Smirnov test because the number of samples was more than 50. In descriptive analyzes, the median ± standard deviation was used for data that are normally distributed. However, for non-normally distributed data median and interquartile range (IQR) were used. Data for percentage changes, such as hematocrit, hemoglobin and leukocyte were evaluated by using the formula of "(final value – initial value) / initial value". For comparisons between groups, Kruskal-Wallis test was used in case of non-normally distributed variables. However, analysis of variation was used if the variables were normally distributed. Between groups, comparison of categorical variables was conducted using Fisher-Freeman-Halton test. Correlations between variables were analyzed with Spearman non-parametric correlation test. In all statistical tests conducted as part of the study, α value was taken as 0.05 and $p < 0.05$ was considered as statistically significant.

Table II. Morphometric measurements used in the classification.

Length (mm)	Definition
a	Length of the free fragment of the gallbladder
b	Length of the portion of the gallbladder extending to the level of the margo anterior
c	Distance between the fossa vesica fellea and margo anterior
d	Length of the fossa vesica fellea
e	Distance between the fundus and collum - measured after the gallbladder has been removed outside the abdomen

Table III. Visual evaluation of parenchymal bleeding during the dissection of the gallbladder from the fossa vesica fellea.

Amount of blood loss (visual evaluation)	
Minimally	< 5 mL
Few	5-15 mL
Medium	16-24 mL
High	> 25 mL

Results

The mean age of 164 patients (26 male (15.9%) and 138 (84.1%) female) was 49.86 ± 13.61 (iqr = 22-88) in the study population (Table IV).

After assessment of all patients, independent from the morphometric types, median complete dissection time was 375.5 seconds (iqr = 40-1660). No statistically significant difference was found between the different types of gallbladders in terms of dissection time ($p = 0.258$) (Table V).

Also, the analysis demonstrated that perioperative bleeding was commonly minimal (n = 94; 57.3%) independent from classification. Additionally, major bleeding was observed only in 2 patients (1.2%) during the dissection of the gallbladder. However, no significant difference was found between different types of gallbladders in terms of the amount of bleeding ($p = 0.567$).

During dissection of the gallbladder, 29 patients' gallbladders (17.7%) were perforated. Perioperative perforation rate of the gallbladder was found significantly higher in type V ($p = 0.014$) (Table V). No statistical difference was found for pre- and postoperative hemoglobin and hematocrit level changes between gallbladder types ($p = 0.746$; $p = 0.334$) (Table VI).

Furthermore, the most common type of gallbladder was type I and type III (for both, n = 38; 23.2%). Twenty-nine patients (17.7%) had morphometric characteristics consistent with type II, 27 (16.4%) with type V and 21 (12.8%) with type IV. Type VI was found the least common type among the patients (n = 11; 6.7%). Otherwise, Type VII was not observed in any of the cases (Table IV).

The mean length of the fossa vesica fellea (d) was 68.06 ± 15.08 millimeters. (iqr = 32 = 115), the average size of the gallbladder (e) was 92.10 ± 18.79 millimeters. (iqr = 49-167). In the analysis of morphometric types positive correlation was found between dissection time and length of fossa vesica (length "d") and the size of gallbladder (length "e") ($r = 0.228$, $p = 0.003$; $r = 0.166$,

Table IV. The distribution of morphometric gallbladder types by age and sex of patients.

	Total number n = 164	Age	Gender	
			Male n = 26 (15.9%)	Female n = 138 (84.1%)
Type I	38 (23.2%)	54 ± 12.57	7 (4.3%)	31 (18.9%)
Type II	29 (17.7%)	52.86 ± 14.49	2 (1.2%)	27 (16.5%)
Type III	38 (23.2%)	47.92 ± 14.05	7 (4.3%)	31 (18.9%)
Type IV	21 (12.8%)	46.71 ± 13.59	4 (2.4%)	17 (10.4%)
Type V	27 (16.4%)	47.81 ± 13.58	5 (3%)	22 (13.4%)
Type VI	11 (6.7%)	45.36 ± 10.34	1 (0.6%)	10 (6.1%)
	p-value	0.123	0.736	

Table V. Comparison of dissection time, perioperative blood loss and perioperative perforation rate between morphometric types.

	Type I n = 38	Type II n = 29	Type III n = 38	Type IV n = 21	Type V n = 27	Type VI n = 11	*p*-value
Dissection time (sec)	385.5	382	364.5	324	450	376	0.258
375.5 (40-1660)	(140-1380)	(78-927)	(110-1370)	(72-1084)	(40-1660)	(42-485)	
Blood loss							
Minimally n = 94 (57.3%)	26 (68.4%)	13 (44.8%)	24 (63.2%)	11 (52.4%)	13 (48.1%)	7 (63.6%)	0.567
Few n = 53 (32.3%)	9 (23.7%)	14 (48.3%)	10 (26.3%)	8 (38.1%)	8 (29.6%)	4 (36.4%)	
Medium n = 15 (9.1%)	3 (7.9%)	2 (6.9%)	3 (7.9%)	2 (9.5%)	5 (18.50%)	0 (0%)	
High n = 2 (1.2%)	0 (0%)	0 (0%)	1 (2.6%)	0 (0%)	1 (3.7%)	0 (0%)	
Perforation ratio n = 29 (17.7%)	5 (13.2%)	1 (3.4%)	6 (15.8%)	4 (19%)	**11 (40.7%)**	2 (18.2%)	**0.014**

Table VI. Comparison of percentage change in hemoglobin and hematocrit between morphometric types.

	Change in hemoglobin (percentage change)	Change in hematocrit (percentage change)
Type I	-0.05 (-0.16;2.08)	-0.04 (-0.15;2.02)
Type II	-0.06 (-0.14;0.01)	-0.07 (-0.15;-0.04)
Type III	-0.06 (-0.19;2.11)	-0.04 (-0.20;2.04)
Type IV	-0.08 (-0.28;0.13)	-0.07 (-0.27;0.08)
Type V	-0.05 (-0.14;0.05)	-0.06 (-0.18;0.07)
Type VI	-0.05 (-0.13;-0.03)	-0.06 (-0.27;2.04)
p-value	0.746	0.334

$p = 0.034$). Also positive correlation was found between dissection time and perioperative perforation risk of gallbladder wall ($r = 0.221$, $p = 0.005$) (Table VII).

Discussion

Cholelithiasis is one of the most common gastroenterological pathologies and its prevalence is up to 20% in western societies[13]. Regarding the meta-analysis about cholecystectomies published by Hua et al[14], similar to our findings, cholelithiasis is much more common in the female population with a mean age range of 40 to 60. More than 50% of the patients with cholelithiasis have no symptoms and their gallstones have been detected incidentally due to the eas and widely usage of abdominal USG, that has a sensitivity of 81% and specificity of 83%[13,15]. Thus, the majority of the patients with asymptomatic cholelithiasis do not require any surgical interventions. However, patients with symptomatic and/or complicated cholelithiasis such as biliary colic, cholecystitis, cholangitis, biliary pancreatitis, need surgical treatment. Therewithal, since late

Table VII. The median values of length for all morphometric types.

	Length a (mm)	Length b (mm)	Length c (mm)	Length d (mm) 68.06 ± 15.08 (32-115)	Length e (mm) 92.10 ± 18.79 (49-167)
Type I	21.50 (5-54)	21.50 (5-54)	–	69.45 ± 15.02	99.89 ± 17.32
Type II	25 (8-60)	15 (3-50)	10 (3-26)	61.24 ± 13.99	97.76 ± 21.68
Type III	–	–	–	76.84 ± 14.68	93.34 ± 18.70
Type IV	18 (5-30)	–	18 (5-30)	61.76 ± 13.32	84.67 ± 13.29
Type V	–	–	16 (5-55)	70.15 ± 13.33	83.52 ± 17.80
Type VI	12 (8-28)	–	20 (16-32)	57.91 ± 8.43	81.27 ± 9.26
p-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0 .001

80's, laparoscopic cholecystectomy was recognized as the "gold standard" procedure for benign gallstone diseases[13,16]. Shorter hospitalization, more rapid recovery, and much fewer wound complications are the advantages of laparoscopic approach when compared to open cholecystectomy[16].

Standardized laparoscopic intervention is defined by using two 10 mm and two 5 mm trochars. On the other hand, technical improvements allow the surgeon to perform less invasive procedures such as 3-port-laparoscopic cholecystectomy or even single-access-surgery[16]. The following process after the trocars' placement is a direct vision for a complete dissection of Calot's triangle that its boundaries comprise cystic duct, right liver lobe, and common hepatic duct. It provides a clear anatomical demonstration of the cystic duct and cystic artery to the surgeon which is mandatory for a safe cholecystectomy[17]. After the ligation of cystic artery and cystic duct, gallbladder dissection from the fossa composes the second step of the cholecystectomy. In this study, standardized 4-port-laparoscopic retrograde cholecystectomy was chosen for all patients to ensure the uniformity of the procedures.

The illustrated anatomical textbooks describe a similar anatomical relation between the gallbladder and the liver[1,18-21]. Nevertheless, in clinical practice, the natural presentation of gallbladder's anatomical position varies and from time to time, these variations may becloud its dissection. Although many articles about the anatomical variation of intra- and extrahepatic biliary tree and its vascular support can be found in literature, still there is no clinical study designed to evaluate the effect of this challenging condition. Thus, there is no scientific evidence about the relation between the anatomical position of the gallbladder and the efficiency of laparoscopic cholecystectomy.

Fetal gallbladder measurements and relations with the gestational age or hepatic markers were worked extensively in the literature commonly in adults. Previously, Alpay et al[3], Moon et al[22], and Having et al[23] measured fetal gallbladder dimensions and they found a significant positive relationship between gestational age and gallbladder length, width, height and volume parameters. Haffajee[24] performed microdissection to the 89 formalin-embalmed fetuses of 10 to 36 weeks gestational age. They investigated the relation between the fatal gallbladders and the umbilical vein, anterior hepatic margin and their protrusion below the inferior surface of the liver. He found fundus protrusion beyond the hepatic margin only in two fetuses. He also showed that the ratio of the length of the fetal gallbladder to the midsagittal liver width is a fairly constant ratio (0.2-0.3) in most of the fetuses. Alpay et al[3] also pointed out the gallbladder projection from the inferior border of the liver in their study. They reported that this protrusion occurs 8% in the first trimester, 19% after in the second trimester and 20% in the third trimester (12% total). Another result of this study was about gallbladder types. They revealed that the rectangular shaped gallbladder was most common type in full-term fetuses followed by circular shape type (pear shaped 20%, rectangular shaped 40%, fusiform shaped 10%, circular shaped 30%, n = 118).

Although several correlations were found between measurements and investigated parameters for each type of gallbladders, in our opinion, their effects were practically unobservable during the surgical interventions. So, further researches are needed to interpret their clinical importance.

There is no satisfactory information on morphometric measurements of the adult gallbladder in literature. Mean lengths of the gallbladder were reported 3-7 cm in older children, more than 7 cm in adolescents, 7-10 cm in adults and width of the gallbladder was 2-3.5 cm[25,26]. The mean length of the fossa vesica fellea (d) was 68.06 ± 15.08 mm (iqr = 32-115), the average size of the gallbladder (e) was 92.10 ± 18.79 mm (iqr = 49 = 167) in our series. These results were similar to data reported in the literature.

In our investigation, a positive correlation was found between dissection time and length of fossa vesica and the size of the gallbladder, as expected. Additionally, a positive correlation was found between dissection time and perioperative perforation risk of the gallbladder wall. However, no other relation was found between the measurements and the other perioperative and postoperative parameters evaluated during the study. For example, there was no correlation between the size of the gallbladder and perioperative bleeding. Probably, surgeons are much more careful when they dissect a longer gallbladder to avoid the perioperative parenchymal hemorrhage.

The variations and abnormalities of the extrahepatic biliary tract can lead the surgeon to injure the common bile duct. Kocaoglu et al[27] pointed out to the frequency of the "normal" biliary

anatomy was the case in only 58% of the population. Hence, especially for surgeons, it is important not only to have a normal biliary anatomy but also to know possible variations and malformations. On the other hand, there were not many authors who pointed out the importance of the gallbladder variations. Faure at al[28] mentioned about gallbladder abnormalities including volvulus due to an abnormally long mesentery suspension -which was classified as type VII gallbladder in our study-, ectopia, retroposition, duplication, triplication, multiseptated and agenesis in their review. All of them have potential injury risk that may increase the operational time, blood loss and, moreover, the morbidity and mortality. In our study population, we did not meet any type VII gallbladder morphology.

The mean duration of four-port laparoscopic cholecystectomy varied between 30 and 60 minutes in studies [29,30]. The operation may end longer in the presence of a variation or an abnormality. However, in our study, no statistical difference was found between overall variational types of the gallbladder in point of the dissection time. We did not evaluate the whole operational time, yet the median time of the gallbladder dissection from the liver bed was found as 375.5 seconds (± 6.25 min).

Zanghì et al[31] evaluated 164 laparoscopic cholecystectomies and reported the rate of perioperative gallbladder perforation as 17.07% (n=28), the mean intraoperative blood loss volume as < 30 ml and the mean amount of postoperative drainage as < 20 ml. In 1997, Huang et al[32] reported one of the largest series for laparoscopic cholecystectomy with 39,238 patients. In this study, the rate of bile duct injury was found as 0.3%, the rate of postoperative bile leak was 0.2%, the rate of postoperative hemorrhage was 0.1% and the rate of mortality was 0.04%.

We showed that preoperative hemorrhage was less than 5 ml in 94 patients (57.3%) and between 5-15 ml in 53 patients (32.3%). Only in two patients' blood loss amount during the dissection were higher than 25 ml (1.2%) which was considered the as high amount of perioperative hemorrhage. We observed 29 gallbladder perforations in 164 operations (17.7%) which could be accepted as a minor perioperative complication. Our perforation rate was acceptable regarding the literature[29,31,32]. Whereas the rate of common bile duct injury and postoperative bile leak were found 0% in our study. In addition, no mortality was observed.

In 1898, Wendel[33] firstly described the gallbladder volvulus due to "floating gallbladder" which was classified as type VII gallbladder in our study. It is a very rare condition and its true incidence is unclear[34]. There are slightly more than 500 cases reported[35,36]. In such cases, an urgent surgery should be performed otherwise the prognosis may be fatal[36]. Although, no type VII was observed among the patients included in our study, our surgical team operated a patient with a "floating gallbladder". This 42-year-old female patient was excluded from the study because she admitted to the hospital with an acute abdomen due to gallbladder torsion and underwent an urgent open surgery. However, this case was reported in the literature as a case report[37].

We had some study limitations. The amount of perioperative parenchymal hemorrhage due to gallbladder dissection from the fossa was evaluated semi-subjectively. A precise quantitative evaluation could not be carried out. Another limitation was the leak of "single-surgeon experience". Despite the high experienced surgeon team, the data may be more accurate if the surgeries were performed by a single surgeon. Also, preoperative ultrasonographic estimation of gallbladders' morphological classification should be investigated in future studies in term of preoperative awareness about variations. Additionally, the number of patients is limited and not enough to estimate the real prevalence. Further investigations should be planned with larger series to figure out the accurate ratio of the gallbladder types in populations.

Conclusions

Regarding our results, during the laparoscopic cholecystectomy, gallbladder perforation rate found higher in morphological type V gallbladders. Considering that the cholecystectomy is one of the most common surgical interventions, anatomical variations of the gallbladder and its relations with the liver parenchyma might be important for the surgeon to calculate the surgical strategies. Variations of the gallbladder may be positional, locational and/or in terms of size. Anyhow, to perform a safe cholecystectomy, surgeons should also be aware of these variations; knowing that, in practice, anatomy may differ from the illustrated textbooks.

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Conflict of Interest

The Authors declare that there are no conflicts of interest.

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