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Incidence and risk factors of gallstone formation after bariatric surgery

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ABSTRACT

Introduction: The primary aim of this research was to investigate the incidence and potential risk factors associated with gallstone formation following bariatric surgery.

Materials and Methods: A retrospective analysis was conducted on 478 patients who underwent bariatric and metabolic procedures between January 2017 and June 2021. After applying specific inclusion and exclusion criteria, 254 patients were deemed suitable for the study. Data, including age, gender, pre-operative body weight, body mass index (BMI), weight loss, familial history of gallstones, and duration of follow-up, were meticulously recorded and analyzed.

Results: Out of the 254 patients, 31.1% (79 patients) developed gallstones postoperatively. Notable differences were identified between patients with and without post-operative gallstones in terms of age, pre-operative body weight, BMI, and total weight loss percentage (TWL%). In addition, a familial history of gallstones emerged as a potential risk factor. However, regression analyses pinpointed only the total duration of post-operative follow-up as a significant predictor of gallstone formation. Interestingly, the longer the follow-up duration, the lower the risk of gallstone development.

Conclusion: While bariatric surgery offers numerous health benefits, there is a notable risk of gallstone formation post-surgery. Factors such as rapid weight loss, high TWL%, and familial history of gallstones were identified as potential risk indicators. However, the study's most significant finding was the inverse relationship between the duration of post-operative follow-up and the risk of gallstone formation. This emphasizes the importance of extended monitoring and follow-up for patients' post-bariatric surgery to mitigate gallstone-related complications.

Keywords: Bariatric surgery, Gallstone formation, Post-operative follow-up, Risk factors, Total weight loss

Introduction

Bariatric surgery is performed primarily to provide weight loss; however, it also provides benefits with regard to diabetes mellitus (DM), hypertension, dyslipidemia, obstructive sleep apnea syndrome, and quality of life.[1]

Obesity, rapid weight loss, age, female gender, genetic pre-disposition, pregnancy, improper dietary habits and lifestyles, insulin resistance, and dyslipidemia have been reported as risk factors for the development of gallstones, also known as cholelithiasis.[2]

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It has been reported that bariatric surgery may increase the incidence of cholelithiasis due to the rapid weight loss it causes. Thus, gallstones are considered a complication that should be followed up after bariatric surgeries. As a matter of fact, it has been reported that approximately 10% of bariatric surgery patients require cholecystectomy.[3,4]

The increase in biliary cholesterol concentration following rapid weight loss, development of hypomotility in the gallbladder secondary to vagal nerve resection, decreased secretion of cholecystokinin, increased secretion of calcium and biliary mucin, and impaired enterohepatic circulation of biliary salts may explain the mechanism of gallstone formation after bariatric surgery.[5]

In this context, this study was carried out to evaluate the incidence and risk factors of post-operative gallstone formation in patients undergoing bariatric surgery.

Materials and Methods

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the local ethics committee (Approval Date and Number: May 08, 2023 and HNEAH-KAEK 2023/92). Because the study was designed retrospectively, no written informed consent form was obtained from patients.

The population of this retrospective study consisted of 478 patients who underwent bariatric and metabolic surgery by a single surgeon between January 2017 and June 2021. Patients, who underwent laparoscopic sleeve gastrectomy (LSG) and laparoscopic mini gastric bypass (LGB), were included in the study, whereas patients who underwent revision surgery, pre-operative cholecystectomy, simultaneous cholecystectomy, and different surgical procedures were lost to follow-up, and whose data could not be accessed from hospital records were excluded from the study. The remaining 254 patients constituted the study group. Of these patients, 79 patients who developed gallstones in the post-operative period constituted Group 1 (study group), and 175 patients who did not develop gallstones in the post-operative period constituted Group 2 (control group).

The patients had not been given ursodeoxycholic acid postoperatively. They had been routinely called for follow-up visits at the 3rd, 6th, 12th, 18th, and 24th months. Patients' pre-operative and post-operative data were obtained from the hospital records and patients over the phone.

Patients' data, including age, gender, pre-operative body weight, body mass index (BMI), weight loss, percentage total weight loss (TWL%), DM history and familial history of gallstones, time of onset of gallstone formation, the presence of dyslipidemia, the surgical method used in their treatment, and total duration of follow-up were compared between the groups. In addition, the complaints of patients who developed post-operative gallstones at the time of admission and their emergency operation requirements were evaluated.

Surgical Technique

As a standard, 38-F bougie-guided surgical resection was performed from 3 cm to 4 cm proximal to the pylorus in LSG, and anastomosis was performed at 200th cm from the Treitz ligament after creating a gastric tube between 15 cm and 20 cm in LGB.

Statistical Analysis

The descriptive statistics obtained from the collected data were tabulated as mean±standard deviation or median with minimum and maximum values in the case of continuous (numerical) variables depending on their normal distribution characteristics and as numbers and percentage values in the case of categorical variables. Normal distribution characteristics of the numerical variables were analyzed with Shapiro–Wilk, Kolmogorov–Smirnov, and Anderson–Darling tests.

In the comparison of differences between categorical variables according to groups, Pearson's Chi-square and Fisher's exact tests were used in 2 × 2 tables with expected frequencies of 5 and above and below 5, respectively.

In the comparison of two independent groups, the independent samples t-test was used where numerical variables showed normal distribution, and the Mann–Whitney U-test was used where numerical variables did not show normal distribution.

Cox regression analysis was used to determine the risk factors for post-operative gallstone formation. To this end, univariate and multivariate Cox regression analyses were performed.

The Kaplan–Meier curve was used to visualize the effects on cumulative gallstone formation, and differences between the groups were evaluated with the log-rank test.

Jamovi project 2.3.24.0 (Jamovi, version 2.3.24.0, 2023, retrieved from https://www.jamovi.org) and JASP 0.17.1 (Jeffreys' Amazing Statistics Program, version 0.17.1, 2023, retrieved from https://jasp-stats.org) software packages were used in the statistical analyses. Probability (P) statistics of ≤0.05 were deemed to indicate statistical significance.

Results

Of the 254 patients included in the study, 79 (31.1%) patients who developed gallstones in the post-operative period constituted Group 1 (study group), and 175 patients (68.9%) who did not develop gallstones in the post-operative period constituted Group 2 (control group).

The mean age of Groups 1 and 2 was 38.0 years and 41.5 years, respectively, indicating a significant difference between the groups (p=0.035). Pre-operative body weight and BMI values were significantly higher in Group 1 patients than in Group 2 (p=0.002 and p=0.010, respectively) (Table 1). There was no significant difference between the groups in DM history (p=0.605). The rate of patients who had a family member with gallstones was significantly higher in Group 1 than in Group 2 (59.5% vs. 20.6%, p<0.001) (Table 1). The pre-operative cholesterol level was significantly higher in Group 2 than in Group 1 (p=0.008). On the other hand, there was no significant difference between the groups in triglyceride levels (p=0.791) (Table 1).

Fifty-six (31.6%) and 23 (29.9%) patients developed gallstones in the LSG and LGB groups, respectively (p=0.895) (Table 2). The median duration of surgery was 70 (range: 40–140) min in the LSG group and 120 (range: 75–190) min in the LGB group. The median length of stay in the hospital was 2 (range: 2–6) days in the LSG group and 3 (range: 3–8) days in the LGB group (Table 2).

The median total duration of follow-up was 42–44 months in Group 1 and Group 2, respectively (p=0.256) (Table 3).

Table 1. Distribution of patients' demographic and clinical characteristics by the study and control groups

	Groups		p
	Group 1 (n=79)	Group 2 (n=175)	
Age (years)†	38.0±12.2	41.5±11.5	0.035***
Gender‡			
Male	21 (26.6)	35 (20.0)	0.314**
Female	58 (73.4)	140 (80.0)	
Preoperative body weight (kg)§	126.0 (84.0–220.0)	118.0 (87.0–190.0)	0.002*
Preoperative BMI (kg/m^2) §	46.6 (35.4–62.3)	43.1 (36.2–64.2)	0.010*
DM history, yes‡	22 (27.8)	56 (32.0)	0.605**
Familial cholelithiasis history, yes	47 (59.5)	36 (20.6)	<0.001**
Cholesterol Level (mg/dL)§	178.0 (87.0–343.0)	191.0 (87.0–317.0)	0.008*
Triglycerides Level (mg/dL)§	131.0 (34.0–479.0)	126.0 (46.0–521.0)	0.791*

‡n (%), †mean±standard deviation; §median (min–max). BMI: body mass index; DM: diabetes mellitus; *Mann–Whitney U-test; **Pearson's Chi-square or Fisher's exact test. ***Independent samples t-test.

Table 2. Distribution of intraoperative and post-operative findings by the type of surgery

	Type of surgery		p
	LSG (n=177)	LGB (n=77)	
Post-operative cholelithiasis‡			
Yes	121 (68.4)	54 (70.1)	0.895**
No	56 (31.6)	23 (29.9)	
Duration of surgery (min)§	70.0 (40.0–140.0)	120.0 (75.0–190.0)	<0.001*
Length of stay in hospital (days)§	2.0 (2.0–6.0)	3.0 (3.0–8.0)	<0.001*

‡n (%), †mean±standard deviation; §median (min–max); LSG: Laparoscopic sleeve gastrectomy; LGB: Laparoscopic mini gastric bypass; *Mann–Whitney U-test. **Pearson's Chi-square or Fisher's exact test.

There was no significant difference between the groups in body weight and BMI values obtained at the end of the follow-up period (p=0.451 and p=0.158, respectively). On the other hand, the decreases in body weight and BMI values were significantly greater in Group 1 than in Group 2 (p<0.001 for both cases). In addition, post-operative 3rd-month and 1st-year TWL% was significantly higher in Group 1 than in Group 2 (p<0.001 for both cases) (Table 3).

The median time of onset of gallstone formation in Group 1 was 12th (range: 3rd–26th) month postoperatively. Of the 79 patients, 53 (67.1%) developed gallstones between the post-operative 6th and 12th months (Table 4).

Analysis of patients' complaints at admission revealed biliary colic as the most common (60.8%) symptom, followed by other symptoms summarized in Table 4. Emergency cholecystectomy was required in only two (2.52%) patients (Table 4).

The Kaplan–Meier plot of the cumulative frequencies of the patients according to the time of onset of gallstone formation is shown in Figure 1. Accordingly, it was determined that gallstone formation was more prominent in the second 6-month follow-up period compared to other follow-up periods (Table 4).

The univariate Cox regression analysis indicated that pre-operative BMI, post-operative 3rd-month TWL%, and total duration of follow-up significantly predicted post-operative gallstone formation (p<0.005) (Table 5). Further analysis of these potential risk factors with the

Table 3. Distribution of post-operative bariatric surgery outcomes by the study and control groups

	Groups		p
	Group 1 (n=79)	Group 2 (n=175)	
Total duration of follow-up (months)§	42.0 (16.0–75.0)	44.0 (16.0–78.0)	0.256**
Post-operative body weight (kg)§	75.0 (45.0–125.0)	75.0 (49.0–170.0)	0.451*
Post-operative BMI (kg/m²)§	27.6 (18.3–38.6)	28.2 (19.0–56.0)	0.158*
TWL (%)§	-41.5 (-60.8–-16.0)	-35.9 (-55.6–-4.3)	<0.001*
TBMIL (%)§	-41.5 (-60.8–-16.0)	-35.9 (-54.7–-4.3)	<0.001*
3rd-month TWL (%)§	22.2 (10.8–37.9)	17.1 (8.5–30.4)	<0.001*
1st-year TWL (%)§	43.2 (31.5–74.8)	37.5 (15.9–61.0)	<0.001*

‡n (%); §: median (min–max); BMI: Body mass index; *Mann–Whitney U-test. **Pearson's Chi-square test. TWL: Total weight loss; TBMIL: Total body mass index loss.

Table 4. Gallstone-related clinical features in patients with post-operative cholelithiasis

	Group 1 (n=79)
Time of onset of post-operative cholelithiasis (post-operative months)§	12.0 (3.0–26.0)
<6 months‡	4 (5.1)
Between 6 and 12 months‡	53 (67.1)
>12 months‡	22 (27.8)
Patients' complaints at admission‡	
Asymptomatic, yes	26 (32.9)
Biliary Colic, yes	48 (60.8)
Choledocholithiasis, yes	2 (2.5)
Acute Cholecystitis Attack, yes	5 (6.3)
Biliary Pancreatitis Attack, yes	3 (3.8)
Emergency cholecystectomy requirement, yes‡	2 (2.5)

‡n (%); §: median (min–max).

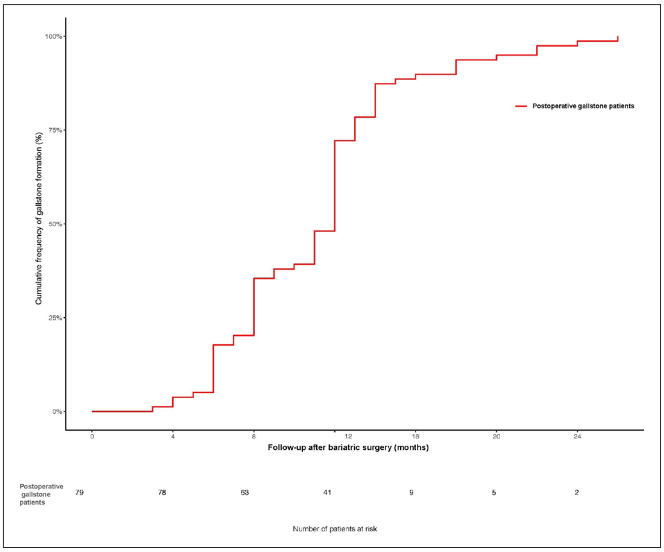

Figure 1. Kaplan–Meier curve representation of cumulative gallstone formation after bariatric surgery.

multivariate model indicated that only the total duration of follow-up significantly predicted post-operative gallstone formation (hazard ratio [HR]: 0.98, confidence interval [CI]: 0.97–1, p=0.039). Accordingly, post-operative gallstone formation decreased as the total duration of follow-up increased (Table 5).

The cumulative effect of TWL on post-operative gallstone formation was evaluated with the Kaplan–Meier curve analysis according to the grouping based on median 3rd-month and 1st-year TWL% values (18.27% and 39.48%). Consequently, it was found that 3rd-month and 1st-year TWL% did not significantly affect post-operative gallstone formation (p=0.073 and p=0.342, respectively) (Figs. 2 and 3).

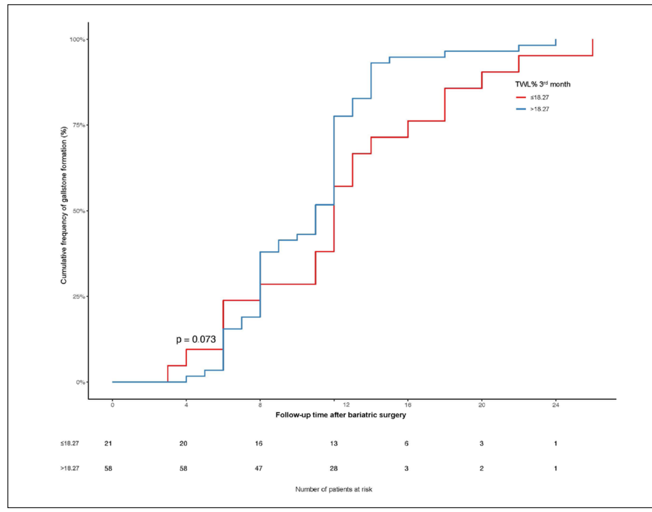

Figure 2. The relationship between 3rd-month total weight loss value and cumulative gallstone formation.

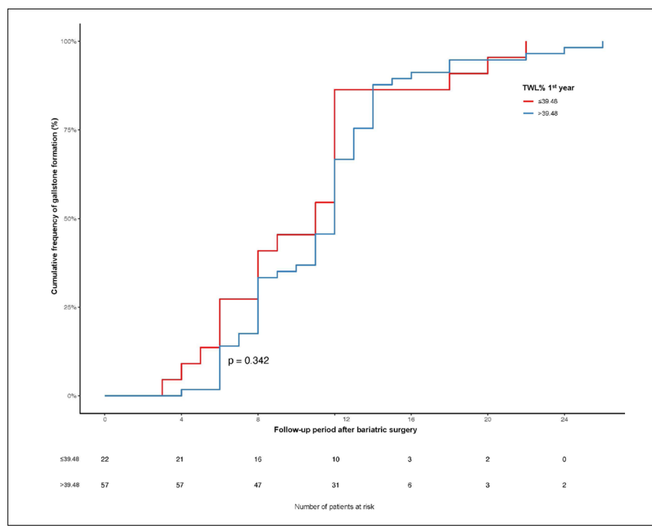

Figure 3. The relationship between 1st-year total weight loss value and cumulative gallstone formation

Table 5. Results of univariate and multivariate cox regression analyses of potential risk factors affecting post-operative gallstone formation

	Univariate analysis		Multivariate analysis	
	HR (%95 CI)	p	Adjusted HR (%95 CI)	Adjusted p
Age	0.99 (0.98–1.01)	0.570	--	--
Familial cholelithiasis history: Yes vs. No	0.92 (0.58–1.45)	0.713		
Pre-operative BMI (kg/m^2)	0.96 (0.92–1.01)	0.042	0.96 (0.92–1.01)	0.097
Type of Surgery: LSG vs. LGB	1.08 (0.66–1.78)	0.753	--	--
3rd-month TWL (%)	1.04 (1.01–1.08)	0.048	1.03 (0.99–1.07)	0.147
1st-year TWL (%)	1.01 (0.96–1.04)	0.923	--	--
Total duration of follow-up (months)	0.98 (0.97–1.01)	0.032	0.98 (0.97–1.01)	0.039

HR: Hazards ratio; CI: Confidence of interval; BMI: Body mass index; LSG: Laparoscopic sleeve gastrectomy; LGB: Laparoscopic mini gastric bypass.

Discussion

Gallstone formation increases with age.[6] However, in a retrospective cross-sectional Asian study, it was reported that individuals younger than 50 years of age are at higher risk of gallstones if they are obese and have metabolic syndrome.[7] While some studies report that the risk of gallstone formation and gallbladder disease decreases with age after bariatric surgery, there are also studies reporting the opposite.[8,9]

In comparison, in this study, the mean age of the patients who developed gallstones postoperatively was significantly lower than those who did not (38.0 vs. 41.5 years, p=0.035). This finding may be explained by the fact young patients lost more weight and also more rapidly. However, univariate and multivariate regression analyses did not reveal a significant relationship between weight loss parameters and the development of gallstones.

Although there are publications reporting that female gender is a risk factor for gallstone formation after bariatric surgery,[3] Aldriweesh et al. reported no relationship.[10] In line with Aldriweesh et al.'s study, no significant difference was found between the patients who developed gallstones postoperatively and those who did not in terms of gender.

It has been shown that increased body weight and high BMI are risk factors for gallstone formation and are associated with the risk of symptomatic cholelithiasis.[11] It has been shown that the risk of gallstone formation increases 8 times in individuals with a BMI of >40 kg/m^2 compared to those with a normal BMI.[12]

It has been suggested that abdominal adiposity increases hepatic cholesterol secretion and that increased body weight and decreased gallbladder motility contribute to gallstone formation.[13]

In our study, there were statistically significant differences between the patients who developed gallstones post-operatively significantly lower than those who did not in pre-operative body weight and BMI, suggesting that high pre-operative body weight and BMI values potentially lead to post-operative gallstone formation, in line with the literature findings. Of these two factors, a high BMI value was found to be a significant risk factor in the univariate Cox regression analysis, whereas none of the two factors was found to be a significant risk factor in the multivariate Cox regression analysis.

Bariatric surgery has curative effects on underlying diseases, and many randomized controlled studies have shown that surgical treatment is superior to medical treatment with regard to DM.[14]

DM is an independent risk factor for the formation of gallstones larger than 1 cm and for cholecystectomy.[15] A meta-analysis of 11 articles describing DM exposure as the presence of pre-operative DM and the absence of post-operative DM concluded that having pre-operative DM is neither a risk nor a protective factor after bariatric surgery.[16]

Similarly, DM exposure was defined as the presence of pre-operative DM and the absence of post-operative DM in this study, and no significant correlation was found between pre-operative DM and post-operative gallstone formation, consistent with the literature.

High serum triglyceride levels and low-density lipoprotein have been reported as risk factors in the pathophysiology of gallstone formation.[17] However, a meta-analysis reported that dyslipidemia is neither a risk factor nor a protective factor in the formation of gallstones after bariatric surgery.[16]

In our study, unlike the literature, in terms of dyslipidemia, cholesterol levels were found to be significantly higher in patients without gallstones, whereas triglyceride levels were found to be comparable between the groups. Based on these findings, dyslipidemia is not a risk factor for gallstone formation.

Familial history of gallstone formation has been reported as a risk factor in the literature.[4] In our study, the rate of patients with a familial history of gallstones was 59.5% in Group 1 and 20.6% in Group 2, indicating a statistically significant difference between the groups, consistent with the literature findings (p<0.001). However, further analysis of the familial history of gallstone formation by regression analyses did not reveal any evidence that familial history of gallstone formation is a risk factor for gallstone formation after bariatric surgery.

While there are publications reporting that gallbladder stone formation is more common in patients who underwent bypass due to the change in enterohepatic circulation and gallbladder physiology, Elgohary et al. reported that there was no statistically significant difference between the patients who underwent bypass due to the change in enterohepatic circulation and gallbladder physiology and the patients who underwent other surgical procedures in terms of post-operative gallstone formation.[18,19] Sneineh et al. reported that 14.5%, 4.4%, and 7.5% of the patients who had roux-en-y gastric bypass, LSG, and LGB had post-operative symptomatic gallstone formation, respectively.[20]

Similarly, in our study, there was no significant difference in the rate of patients who developed gallstones after LSG and LGB procedures (31.6% vs. 29.9%).

It has been suggested that weight loss after bariatric surgery is a factor contributing to gallstone formation.[16,17] In contrast, a meta-analysis reported that TWL% is not a risk factor for gallstone formation after bariatric surgery.[16] On the other hand, Li et al.[21] found that TWL% >25 was associated with symptomatic gallstone formation.

In comparison, in this study, the TWL% and TBMIL% values of the patients in Group 1 were significantly higher than those in Group 2 ($p<0.001$ for both cases).

Rapid weight loss after bariatric surgery is a known risk factor. Gallstones may occur in approximately one-third of the patients undergoing bariatric surgery, and cholecystectomy may be required in 10–15%.[22]

Alsaif et al.[3] found a strong relationship between rapid weight loss and gallstone formation, whereas Aridi et al. did not.[23]

Post-operative 3rd-month and 1st-year TWL% values of the patients in Group 1 were significantly higher than those in Group 2 ($p<0.001$ for both cases), indicating that higher weight loss values in the first 1-year period after the surgery are associated with a higher risk of gallstone formation. The univariate Cox regression analysis revealed 3rd-month TWL% as a significant variable in predicting post-operative gallstone formation ($p<0.005$), whereas the results of the multivariate Cox regression analysis did not support this finding (Table 5). The cumulative effect of TWL on post-operative gallstone formation was evaluated with the Kaplan–Meier curve analysis according to the grouping based on median 3rd-month and 1st-year TWL% values (18.27% and 39.48%). Consequently, it was found that the 3rd-month and 1st-year TWL% did not significantly affect post-operative gallstone formation ($p=0.073$ and $p=0.342$, respectively) (Figs. 2 and 3). This paradoxical finding may be attributed to this study's relatively small sample size. Therefore, it is likely that further studies with larger samples will reveal significant relationships between post-operative gallstone formation and rapid weight loss, high TWL% rate, and familial history of gallstones.

The incidence of the formation of gallstones after bariatric surgery is around 30%. Most patients who develop gallstones after bariatric surgery develop gallstones during the first 2 years post-operatively, particularly in the 1st year.[22] Keilani et al. reported the incidence of gallstone formation as 33.8% and 21.6% in the first and second 6-month periods postoperatively. They attributed the higher incidence of gallstone formation during the first 1-year postoperatively to rapid weight loss.[24] Guzman et al. reported the incidence of gallstone formation during the first 12 months after bariatric surgery as 33%.[5]

In parallel with the literature, the incidence of post-operative gallstone formation in this study was 31.1%. The median onset time of gallstone formation was 12th (range: 3rd–26th) month post-operatively. Of the 79 patients, 53 (67.1%) developed post-operative gallstones between the 6th and 12th months (Table 4).

The univariate Cox regression analysis revealed the total duration of follow-up as a significant variable in predicting post-operative gallstone formation ($p<0.005$), a finding supported by the results of the multivariate Cox regression analysis (HR: 0.98, CI: 0.97–1, $p=0.039$). Accordingly, as the total duration of follow-up increased, the risk of gallstone formation decreased (Table 5).

A study, which reported the incidence of gallstone formation after bariatric surgery as 28.9%, found that 15.7% of the patients with post-operative gallstones were symptomatic.[25] The most common symptom seen in these patients was biliary colic, followed by other complications such as acute cholecystitis, acute cholangitis, acute pancreatitis, and choledocholithiasis.[26]

In comparison, in this study, 53 of the 79 patients with post-operative gallstones were symptomatic (67.1%), and the most common symptom seen in these patients was biliary colic, consistent with the literature findings. In addition, calculi extraction with endoscopic retrograde cholangiopancreatography was performed, followed by laparoscopic cholecystectomy in two (2.52%) patients who developed choledocholithiasis after LSG. In addition, acute cholecystitis was observed in five patients, whereas emergency cholecystectomy was required in only two (2.52%) patients (Table 4).

The primary limitation of this study was its retrospective design.

Conclusion

This study was carried out to evaluate the incidence and risk factors of post-operative gallstone formation in patients undergoing bariatric and metabolic surgery. The comparisons between the patients who developed gallstones in the post-operative period and those who did not develop post-operative gallstones revealed age, high pre-operative body weight, BMI, TWL%, and TBMIL% values, familial history of gallstones, rapid weight loss as significant variables in predicting post-operative gallstone formation. However, further analysis of these variables with univariate and multivariate regression models cumulatively revealed only the total duration of follow-up as a significant variable in predicting post-operative gallstone formation. A higher sample size would likely reveal significant correlations between post-operative gallstone formation and rapid weight loss, high TWL% rate, and familial history of gallstones. Therefore, large-scale studies are needed to shed more light on this subject.

Disclosures

Ethichs Committee Approval: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the local ethics committee (Approval Date and Number: May 08, 2023 and HNEAH-KAEK 2023/92).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – G.Ç.O.; Design – G.Ç.O.; Supervision – G.Ç.O.; Materials – G.Ç.O.,A.S.; Data collection and /or production – G.Ç.O.,A.S.; Analysis and/or interpretation – G.Ç.O.; Literature search – G.Ç.O., A.S.; Writing – G.Ç.O.

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