

Important risk factors for gallstones after laparoscopic gastrectomy: A retrospective study

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Abstract

Background: The frequency of gallstones is higher in patients who have undergone gastrectomy than in the general population. While there have been some studies of gallstone formation after open gastrectomy, there are few reports of gallstones after LG. This study aimed to evaluate the incidence of gallstones after laparoscopic gastrectomy.

Methods: We retrospectively reviewed the records of 184 patients who underwent laparoscopic gastrectomy between January 2011 and May 2016 at Saiseikai Utsunomiya Hospital. After gastrectomy, abdominal ultrasonography was generally performed every 6 months until 5 years later. Patients who underwent simultaneous cholecystectomy or with an observation period of < 24 months were excluded from the study. Ninety patients were ultimately analyzed. Laparoscopic cholecystectomy was performed whenever biliary complications occurred.

Results: Gallstones were detected after laparoscopic gastrectomy in 27 of the 90 (30%) cases. Multivariate analysis identified Roux-en-Y reconstruction and male sex as significant risk factors for gallstones after gastrectomy. Symptomatic gallstones after laparoscopic cholecystectomy were found in 6 cases (6/27, 22%), and all patients underwent laparoscopic cholecystectomy.

Conclusion: Roux-en-Y reconstruction was identified as a significant risk factor for gallstones after laparoscopic gastrectomy.

Background

Based on low-quality evidence, there is no difference in short-term mortality between laparoscopic and open gastrectomy, and there is no evidence for any differences between short-term or long-term outcomes. However, the data are sparse, and the confidence intervals were wide, suggesting that the significant benefits or harms of laparoscopic gastrectomy cannot be ruled out.

The frequency of gallstones is higher in patients who have undergone gastrectomy than in the general population (6.5–25% vs. 2.2–5.0%) [1–7]. Possible mechanisms associated with this increased incidence include vagotomy, the extent of gastrectomy, method of gastrointestinal reconstruction, and lymph node dissection [1, 8].

Preserving the hepatic branch of vagal nerves reduces the frequency of gallstones [4]. Laparoscopic gastrectomy (LG) can reliably preserve the vagal nerves by a magnification effect [9], so it may reduce the rate of gallstones. While there have been some studies of gallstone formation after open gastrectomy, there are few reports of gallstones after LG. Thus, our retrospective study analyzed the frequencies and risk factors for gallstones in patients who had undergone LG for gastric cancer.

Materials And Methods

We retrospectively reviewed data from 184 patients who underwent LG for gastric cancer at Saiseikai Utsunomiya Hospital between January 2011 and March 2016. All 184 cases involved either total gastrectomy or distal gastrectomy associated with systemic lymph node dissection. The patients had been treated by laparoscopic total gastrectomy (LTG) or laparoscopic distal gastrectomy (LDG) with lymph node dissection and TNM (tumor; node; metastasis) staging, following the guidelines of the Japanese Classification of Gastric Carcinoma (3rd English edition), and the Japanese Gastric Cancer Treatment Guidelines [10, 11].

In our institution, the LG procedure has been indicated for cT1-2, cN0 gastric cancer. Intestinal reconstruction was performed using the Roux-en-Y method for LTG, and Billroth I anastomosis or Roux-en-Y reconstruction for LDG. Our first choice of reconstructive procedure for LDG was Billroth I Roux-en-Y for patients with a small remnant stomach or tumor invasion to the duodenum, in which the anastomosis would be under tension, or for patients with a hiatal hernia. The hepatic branch of the vagal nerves was preserved in all patients regardless of the extent of lymph node dissection. We confirmed the vagal nerve's hepatic branch running across the hepatogastric ligament, and then divided this ligament just below the hepatic branch to preserve this nerve. The quality of vagal nerve preservation was confirmed by an expert surgeon who always participated in the operation as an operator or assistant. We did not preserve the celiac branch of the vagal nerve irrespective of clinical stage. If the preoperative examination detected gallbladder disease, we performed simultaneous cholecystectomy

Abdominal ultrasonography and computed tomography (CT) were generally performed every 6 months for 5 years after the operation. Among the 184 patients, we excluded five who underwent cholecystectomy before LG, 69 who underwent simultaneous cholecystectomy at the time of LG, 18 who were followed-up for less than 24 months, and two who did not undergo abdominal ultrasonography. The remaining 90 patients were analyzed in this study. After LG, if symptomatic gallstones, such as biliary colic, acute cholecystitis, or cholangitis occurred a cholecystectomy was performed.

Statistical analysis

The statistical analysis was performed with JMP (SAS Institute, Inc., Cary, NC, USA). Patient characteristics were compared using the two-tailed Fisher's exact test or the Chi-square test. Risk factors for postoperative gallstones were analyzed using logistic regression analysis. All p-values < 0.05 were considered statistically significant.

Results

The characteristics of the 90 patients are shown in Table 1. Gallstone formation after LG was observed in 27 of the 90 patients (30%) in this study. The median follow-up period after gastrectomy was 46.2 months (range, 24–60). The average time between gastrectomy and diagnosis of gallstones was 24.3 months (range, 6–48). The mean age of the 63 patients (36 men and 27 women) in the stone-

negative group was 64.4 years (range, 32–85) and that of the 27 patients (24 men and 3 women) in the stone-positive group was 67.9 years (range, 44–85).

Table 1
Characteristics of the gastric cancer patients and the laparoscopic gastrectomy procedures

Variables	Stone-negative		%	Stone-positive	
	n = 63			n = 27	
Age (years)	64.4 (32–85)			67.9 (44–85)	
Sex (M/F)	Male	36	60	24	40
	Female	27	90	3	10
Body mass index (kg/m ²)	23.2 (12.8–34.7)			24.1 (18.1–29.7)	
Type of gastrectomy	LTG	9	60	6	40
	LDG	54	72	21	28
pStage	□	53	68	25	32
	□	3	75	1	25
	□	1	100	0	0
	□	0	0	0	0
Extent of dissection	D1	15	71	6	29
	D1+	42	69	19	31
	D2	6	75	2	25
Reconstruction after LG	B-I	17	94	1	6
	R-Y	46	64	26	36
Operation time (min)	287			311	
Blood loss (mL)	43			63	
LG: laparoscopic gastrectomy, B-I: Billroth-I, R-Y: Roux-en-Y					

The findings of the risk factor analysis for gallstones after LG are shown in Table 2. Among the 75 patients who had undergone LDG, 21 developed gallstones. Six of the 15 patients who had undergone LTG also developed gallstones (28% vs 40%; $p = 0.36$). There were no significant statistical differences between the frequency of gallstone formation in the various types of LG. However, a significantly higher proportion of patients developed gallstones after a Roux-en-Y than after a Billroth I reconstruction (36% vs 6%; $p = 0.005$). The proportion of gallstones was higher in male than female patients (40% vs 10%; $p = 0.002$). Age, body mass index, and extent of lymph node dissection were not associated with gallstones.

Multivariate analysis identified Roux-en-Y reconstruction and male sex as significant risk factors for gallstones after LG.

Table 2

Univariate and multivariate analysis of risk factors associated with gallstones after laparoscopic gastrectomy

Variables		Stone-negative n = 63	Stone-positive n = 27	Univariate p-value	Multivariate Odds ratio	p-value
Age (years)	< 70	38	14	0.46		
	≥ 70	25	13			
Sex (M/F)	Male	36	24	0.002	0.17 (0.045– 0.65)	< 0.001
	Female	27	3			
Body mass index (kg/m ²)	< 23	32	9	0.12		
	≥ 23	31	18			
Type of gastrectomy	LDG	54	21	0.36	0.90 (0.27– 3.05)	0.86
	LTG	9	6			
Extent of dissection	D1/D1+	57	25	0.74		
	D2	6	2			
Reconstruction after laparoscopic gastrectomy	Billroth-I	17	1	0.005	5.83 (1.52– 22.3)	0.04
	Roux-en-Y	46	26			

LDG: laparoscopic distal gastrectomy, LTG: laparoscopic total gastrectomy

Among the 27 cases in whom gallstones were noted, 6 (22%) had gallstone symptoms (Table 3). One patient had biliary colic, three had acute cholecystitis, and two had common bile duct stones and cholangitis. The reconstruction method for these six patients was Roux-en-Y. Regarding acute cholecystitis management, percutaneous transhepatic gallbladder drainage was performed in one patient. Endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy using an enteroscope were performed in two patients who had common bile duct stones and cholangitis. All six patients underwent laparoscopic cholecystectomy.

Table 3
Treatment of symptomatic gallstones after laparoscopic gastrectomy

Symptoms	n = 6	%	Treatment
Biliary colic	1	17	Laparoscopic cholecystectomy
Acute cholecystitis	3	50	Laparoscopic cholecystectomy after PTGBD
CBD stone / cholangitis	2	33	Laparoscopic cholecystectomy after ERCP

CBD: common bile duct, PTGBD: percutaneous transhepatic gallbladder drainage, ERCP: endoscopic retrograde cholangiopancreatography

Discussion

Gallstone formation after LG was observed in 30% of the patients. Roux-en-Y reconstruction was identified as a significant risk factor for gallstones after gastrectomy. A possible reason is that exclusion of the duodenum during reconstruction was associated with gallstone formation. Food passage through the duodenum serves as a stimulus for cholecystokinin secretion, and this hormone causes the contraction of the gallbladder through the humoral regulation system. It is postulated that the exclusion of the duodenum leads to changes in the pattern of cholecystokinin secretion, resulting in decreased gallbladder contraction and an increased risk of gallstones [1]. In Roux-en-Y reconstruction, the bacterial count in the duodenum has been confirmed to significantly increase because of biliary stasis, dysfunction of the sphincter of Oddi, and hypoacidity in the duodenum. In this state, the incidence of bactibilia affects the formation of gallstones [12].

Neurological disorders caused by lymphadenectomy for gastrectomy are also considered the reason for gallstone formation; damage to the vagal nerve's hepatic branch induces a reduction in the contractile function of the gallbladder, which may lead to a stagnation of bile juice [4]. In our study, we considered that the magnification effect due to laparoscopic surgery could reliably preserve the hepatic branch of vagal nerves and reduce the incidence of gallstones. However, despite the preservation of the hepatic branch of vagal nerves, a high incidence of gallstones (30%) was noted. In a study of 10 cadavers, innervation of the gallbladder predominantly occurred through two routes [8]. One was from the anterior hepatic plexus containing the branches arising from the hepatic division of the vagal nerves and the celiac plexus. The other route was from the posterior hepatic plexus, containing the branches originating from the celiac branches of the posterior vagal trunk and the celiac plexus [8]. During fundoplication, cutting the hepatic branch of the anterior vagus nerve may reduce the size of gallbladder, but it has no effect on the ejection fraction [13]. A study found that the occurrence of gallstones after Roux-en-Y reconstruction following LDG was significantly less common in patients with the preservation of the celiac branch of the vagal nerve than in patients with resection of the celiac branch (16 vs. 33%, $p =$

0.035) [14]. However, LG with preservation of the celiac branch of the vagal nerve has limited adaptation, and it is not generally performed due to the complexity of the procedure.

Regarding the 27 cases of gallstones, six patients with symptoms of gallstones underwent laparoscopic cholecystectomy. However, Hashimoto et al. [15] performed laparoscopic cholecystectomy in patients with gallstones after gastrectomy, and for 26% of the patients, conversion to laparotomy was performed because of adhesions. If the cholelith falls into the common bile duct, it is necessary to perform ERCP. However, the use of enteroscopy is required in cases after Roux-en-Y reconstruction. The success rate of ERCP for common bile duct stone clearance was reported to be 81.2% in patients with Billroth I reconstruction but 23.7% in patients with non-Billroth I reconstruction [16]. The ERCP failures in those who underwent Roux-en-Y reconstruction were probably a result of the length and sharp angulation of the Roux limb, making it difficult to negotiate the scope's passage to the papilla [17]; many of these patients were referred for surgical or percutaneous interventions. Laparoscopic surgery for common bile duct stone is not common and is likely to result in laparotomy. Even if LG is performed, the merits of LG are decreased when laparotomy is performed for the common bile duct stones.

It is desirable to prevent gallstones after gastrectomy as much as possible. The need to conduct routine prophylactic cholecystectomy, at the same time as gastrectomy, has been widely discussed but remains controversial [12]. Those who received prophylactic cholecystectomy did not experience any additional perioperative complications related to biliary surgery. Moreover, no additional time and costs were associated with the gastrectomy because of the comparable duration of surgery and the length of postoperative stay [18]. In a randomized controlled trial of 130 patients, 65 underwent prophylactic cholecystectomy while another 65 underwent standard gastric surgery only for curable cancers; the cholelithiasis-free survival rate did not show statistical significance between the two groups ($p = 0.267$) [19]. Although the sample size was small, this result showed that prophylactic cholecystectomy was not required for all patients. However, prophylactic cholecystectomy may be considered for patients at higher risk for cholelithiasis, such as those who have undergone Roux-en-Y reconstruction. Younger patients with early gastric cancer whose life expectancy is high should also be considered for prophylactic cholecystectomy.

The limitations of this study require consideration. This was a single-center retrospective study with a small sample population. Further, there was no comparison between patients who underwent LG and those who underwent open gastrectomy. In our hospital, open gastrectomy was not performed by the same surgeon who performed the LG, so preservation of the hepatic branch of vagal nerves could not be ascertained with only operation records, thus making it difficult to make a simple comparison. In studies of 17 325 patients (laparoscopy 678 vs. open 16647) and 1284 patients (laparoscopy 980 vs. open 304), there were no significant differences between laparoscopic and open gastrectomy [20, 21]. A prospective investigation with a larger number of patients is needed to clarify the significance of prophylactic cholecystectomy.

In conclusion, Roux-en-Y reconstruction was identified as a significant risk factor for gallstones after LG.

Abbreviations

ERCP

Endoscopic retrograde cholangiopancreatography

LDG

laparoscopic distal gastrectomy

LG

laparoscopic gastrectomy

LTG

laparoscopic total gastrectomy

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the Institutional Review Board (IRB) of Saiseikai Utsunomiya Hospital (IRB No. 2020-17). This study was conducted in compliance with the Helsinki Declaration.

Consent for publication

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Shohei Fujita and Masaru Kimata: participated in the conception and design of the study, analysis and interpretation of data, drafting the article, revised it critically for important intellectual content, and approved the final version of the article. Kenji Matsumoto, Yuichi Sasakura, Toshiaki Terauchi, Junji Furukawa, Yoshiro Ogata, Kenji Kobayashi, and Hiroharu Shinozaki: participated in the analysis and interpretation of data, drafting the article, and approved the final version of the article.

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