



ORIGINAL ARTICLE

Gallstone formation after gastrectomy for adenocarcinoma of the stomach



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Abstract *Background/Introduction:* An increased incidence of gallstones after gastrectomy has been reported, but with varying risk factors.

Purposes/Aims: To delineate the incidence of and risk factors for gallstone formation after gastrectomy.

Methods: We retrospectively analyzed patients with Stages 0, I, and II adenocarcinoma of the stomach who had undergone curative gastrectomy with routine lymph node dissection between August 1996 and November 2010. We reviewed the clinical factors, radiographic presentation of the gallstones, and follow-up records.

Results: We included 215 patients (124 men and 91 women), with a median age of 53 years (range, 16–89 years). Gallstones were observed in 46 patients (21.4%) during follow-up periods of 6 months–14.5 years. Gallstones were diagnosed at a median of 2.3 years after gastrectomy. The cumulative incidence of gallstones at 5 years and 10 years was 18% and 20%, respectively. Total gastrectomy, Billroth II reconstruction (vs. Billroth I), age ≥ 60 years, and diabetes mellitus (multivariate odds ratios of 3.8, 3.3, 2.7, and 2.6, respectively) were the risk factors for gallstone formation. Complicated cholelithiasis was identified in seven patients (15.2% of patients with gallstones and 3.3% of all patients) and was more prevalent in patients who had undergone total gastrectomy (5 of 14; 35.7%) than in those who had undergone subtotal gastrectomy (2 of 32; 6.2%; $p = 0.02$). *Conclusion:* The incidence of gallstone formation was 21.4%. Total gastrectomy, Billroth II reconstruction, age ≥ 60 years, and diabetes mellitus were risk factors for gallstone formation. Total gastrectomy is also a risk factor for complicated gallstone.

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Conflicts of interest: The authors declare no conflicts of interest.

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1. Introduction

A cross-sectional study conducted in a rural Taiwanese village reported a 5.0% prevalence of gallstones, with a slight propensity for the female sex. Risk factors for gallstone disease in both sexes included age and fatty liver. In females, diabetes mellitus, a history of gallstone disease in first-degree relatives, and the use of oral contraceptives were additional risk factors.¹ Liu et al² reported a 5.3% prevalence of gallstones in a Taiwanese population that had undergone a paid health examination. In their study, older age, higher body mass index, and type 2 diabetes mellitus were associated with an increased prevalence of gallstone disease.²

A higher incidence of gallstones has been reported in gastrectomy patients than in the general population.^{3–8} Wu et al⁸ reported cholelithiasis in 30% of patients receiving radical gastrectomy. The pathophysiology remains unclear, but the current theories posit that the surgical dissection of the vagal trunk affects gallbladder contractility and that a nonphysiological reconstruction of the gastrointestinal tract, such as duodenal exclusion, results in increased gallstone formation. The present study evaluated the incidence of gallstone formation after gastrectomy for stomach cancer and identified risk factors for gallstones.

2. Methods

The medical records of patients who had undergone radical gastrectomy for gastric adenocarcinoma were reviewed, and clinical information was retrospectively collected. This study was approved by the Institutional Review Committee of Koo Foundation Sun Yat-Sen Cancer Center, Taipei, Taiwan.

In total, 657 patients had undergone gastrectomy with lymph node dissection between August 1996 and November 2010 at our cancer institute. Curative resection (R0) without microscopic or macroscopic residual diseases was achieved in 503 patients with Stage 0, I, or II cancer [pathologically staged according to the *American Joint Committee on Cancer (AJCC) Staging Manual, 7th Edition*]. Patients with Stage III and IV cancer were excluded owing to poor survival and early recurrence. Moreover, patients with previous cholecystectomy or cholecystectomy combined with gastrectomy ($n = 159$); gallstones diagnosed preoperatively or within 6 months of gastrectomy ($n = 29$); previous partial gastrectomy ($n = 7$); a history of cholecystitis and obstructive jaundice ($n = 3$); and insufficient clinical data, imaging, and follow-up ($n = 57$) and those who underwent reconstruction methods other than Billroth I, Billroth II, Roux-en-Y, and uncut Roux-en-Y ($n = 33$), were excluded.

In total, 215 patients (124 men and 91 women), with a median age at operation of 53 years (range, 16–89 years) were included. Pathological staging according to the seventh edition of the AJCC Manual showed Stages 0, I, and II for three patients, 142 patients, and 70 patients, respectively. Overall, 180 distal subtotal gastrectomies and 35 total gastrectomies were performed. All patients had undergone lymph node dissections [D1 or more (over D1), 197 patients; D0, 18 patients]. The extent of lymph node

dissection was classified according to the Japanese gastric cancer treatment guidelines 2010 (version 3).⁹ Lymph node dissection around the liver hilum was not routinely performed in our patients. Moreover, splenectomy was also not a routine procedure accompanying total gastrectomy. Thirty-seven patients received postoperative concurrent chemoradiation therapy; 24 patients had type 2 diabetes mellitus.

Gallstones were identified through abdominal ultrasonography or abdominal computed tomography. According to the in-house guidelines, radiographic imaging after radical gastrectomy for gastric cancer was performed every 6 months for the first 2 years and annually thereafter. Gallstone-related symptoms and complications include typical biliary colic, acute cholecystitis, common bile duct stones with obstructive jaundice, and gallstone pancreatitis.

Clinical factors—age at gastrectomy, sex, cancer stage, diabetes mellitus, method of gastrectomy, extent of lymph node dissection, method of reconstruction, and postoperative concurrent chemoradiation therapy—were recorded for analysis.

The cumulative incidence of gallstones after gastrectomy was evaluated using the Kaplan–Meier method. Univariate analysis of risk factors for gallstone formation was performed using the Chi-square and Fisher's exact tests for categorical variables and Student *t* test for numerical variables. Multivariate analysis was performed using a logistic regression model. A *p* value < 0.05 was considered statistically significant. Statistical analyses were performed using SAS software, version 9.3 (SAS Institute, Cary, NC, USA).

3. Results

Gallstones were detected in 46 of the 215 patients (21.4%) during a median follow-up period of 3.5 years (range, 0.5–14.5 years). Gallstones were diagnosed at a median of 2.3 years (range, 0.5–11.5 years) after gastrectomy. Half of the patients with gallstones were diagnosed within 2 years after surgery, mostly during routine abdominal ultrasonography. The incidence of new cases peaked 1–2 years after gastrectomy and then gradually decreased (Figure 1). The cumulative incidence of gallstones at 5 years and 10 years after gastrectomy was 18% and 20%, respectively (Figure 2). Furthermore, univariate and multivariate analyses revealed that an age at operation of ≥ 60 years, type 2 diabetes mellitus, total gastrectomy, and Billroth II reconstruction (vs. Billroth I) were independent risk factors for gallstone formation (Tables 1 and 2).

Seven patients with complicated gallstones, accounting for 3.3% of all gastrectomy patients and 15.2% of patients with newly diagnosed gallstones, were clinically diagnosed with acute cholecystitis. Three patients had undergone cholecystectomy soon after visiting the emergency department of other hospitals, three patients had undergone urgent operations in our hospital, and one patient refused surgery. Moreover, three patients had common bile duct stones with associated bile duct obstruction and infection. An episode of acute cholecystitis occurred at a median of 4.3 years (range, 1.7–6 years) after the initial surgery. This event was more

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