

BURSECTOMY IN GASTRIC CANCER SURGERY: A META-ANALYSIS

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ABSTRACT

Background: Bursectomy consists of surgically removing the peritoneal lining covering the pancreas and the anterior plane of the transverse mesocolon during gastrectomy. However, there are little data to indicate whether bursectomy has a clinical benefit. **Objective:** The objective of this study was to study the effect of bursectomy on complications, recurrence, and overall survival of patients with gastric cancer. **Methods:** The publicly available literature published from January 2000 to July 2017 concerning gastrectomy with bursectomy and standard gastrectomy for gastric cancer was retrieved by searching the national and international online databases. Meta-analysis was performed after the data extraction process. **Results:** Eight studies were finally included for a total of 1644 patients, of whom 644 underwent bursectomy and 1000 received standard gastrectomy without bursectomy. As shown by the meta-analysis results, there were no statistically significant differences in the presence of total post-operative complications (odds ratio [OR] = 1.06, 95% confidence interval [CI] [0.83-1.35], $p = 0.63$), overall recurrence (OR = 1.07, 95% CI [0.77-1.50], $p = 0.68$), 3-year overall survival (OR = 1.30, 95% CI [0.82-2.07], $p = 0.26$), and 5-year overall survival (OR = 0.91, 95% CI [0.66-1.27], $p = 0.58$). **Conclusion:** Although application of bursectomy in radical gastrectomy did not increase post-operative complications, it offered no benefit to control tumor recurrence or improve overall survival. (REV INVEST CLIN. 2019;71:98-105)

Key words: Bursectomy. Complications. Recurrence. Overall survival. Gastric cancer. Meta-analysis.

INTRODUCTION

Bursectomy is defined as the removal of the peritoneal lining covering the pancreas and the anterior plane of the transverse mesocolon during gastrectomy. The rationale for en bloc resection of the post-gastric cavity includes the presence of free cancer cells, retrogastric lymphatic vessels, and micrometastases¹. Moreover, bursectomy removes some retrogastric lymphatic vessels. This procedure is recommended

in the Japanese gastric cancer treatment guidelines as part of the radical surgery for gastric cancer to remove micrometastases disseminated into the bursa omentalis².

On the other hand, there are questions arising from the anatomy, as the bursa omentalis is not actually a closed cavity, being connected to the free abdominal cavity through the foramen of Winslow. Moreover, a bursectomy causes some surgical stress when

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performed in addition to a D2 lymph node dissection. Among various adverse events, the most feared complication of this therapy is a leak from an injury site to the anterior surface of the pancreas with consequent development of a pancreatic fistula. Another concern is the possibility of the formation of bursectomy-related adhesions to the intestinal obstruction³.

Several factors may influence the effect of bursectomy including the location of the primary lesion, peri-operative chemotherapy, and post-operative radiotherapy. Hirao et al.⁴ in a randomized controlled trial (RCT) found that the overall survival was similar in the bursectomy and non-bursectomy groups when the tumor was located in the upper one-third of the stomach. On the contrary, in tumors in the middle or lower third of the stomach, overall survival for the bursectomy group was significantly longer than that in the non-bursectomy group. This may be due to differences among the relapse patterns of tumors in the upper versus middle or lower third of the stomach. Moreover, adjuvant S-1 therapy after curative gastrectomy for advanced gastric cancer has been established, which implicates that chemotherapy can eliminate micrometastatic disease to a greater degree than surgical intervention. Up to now, few studies demonstrate the efficiency of radiotherapy after bursectomy.

To the best of our knowledge, only one meta-analysis⁵ has compared the outcomes between bursectomy and non-bursectomy. However, this meta-analysis included a small number of studies and was published 3 years ago. In addition, the authors did not mention the patterns of recurrence, which were classified as peritoneal, hematogenous, and locoregional.

To elucidate the recurrence, safety, and survival benefits of bursectomy in gastric cancer surgery, we conducted a systematic review and meta-analysis of RCTs and non-randomized controlled trials (NRCTs).

METHODS

Search strategy

Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, PubMed, Web of Knowledge, Medline, and Ovid's database were searched

from January 2005 to July 2017 in the English language. The search terms used were "gastric cancer," "bursectomy," "complication," "recurrence," and "survival rate." The reference lists of relevant studies were checked manually to locate any missing studies.

Study selection

The full papers identified were assessed for eligibility for inclusion in the review by scanning the titles, abstracts, and keywords of every record retrieved. Clinical studies concerning comparisons of outcomes between a bursectomy group and a non-bursectomy group for gastric cancer were included regardless of whether they were RCTs or non-randomized controlled trials (NRCTs). Studies were restricted to those published in English.

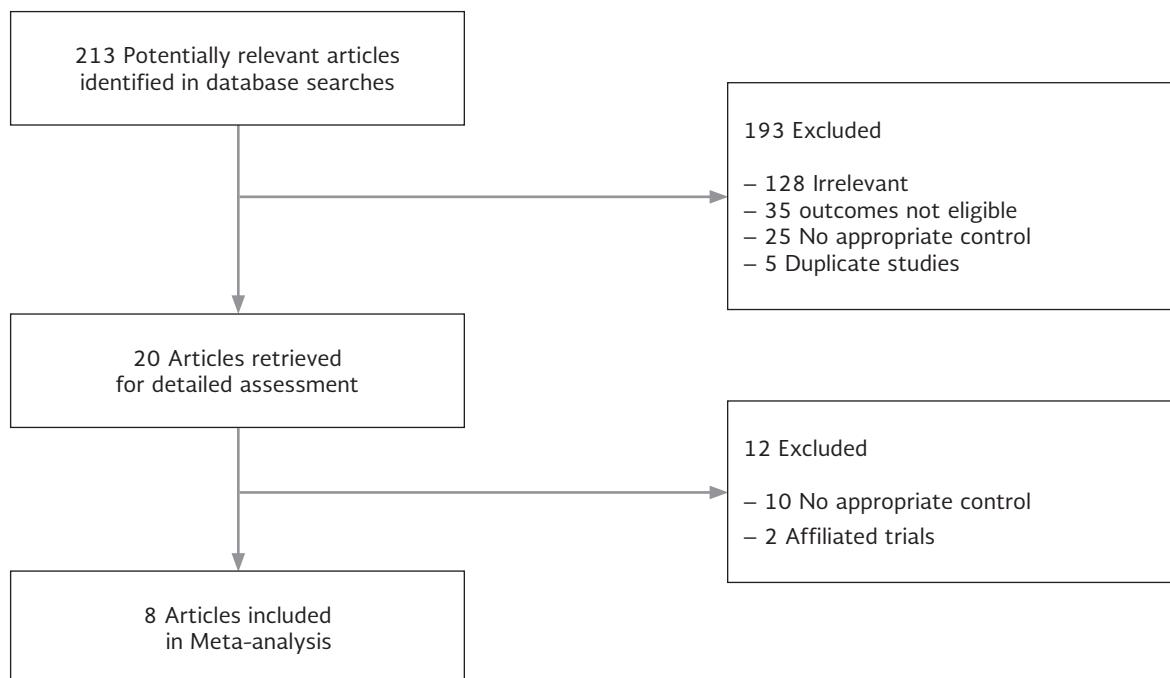
Data extraction

Two coauthors (Yangjun Li and Yujie Li) independently selected studies for inclusion and exclusion and reached consensus when they did not agree in the initial assignment. The following variables were recorded: authors, journal and year of publication, number of patients, age, median tumor size, histological type, surgical procedure, complications, recurrence, and overall survival. If necessary, the corresponding authors of studies were contacted to obtain supplementary information. The Jadad et al.⁶ assessed the methodological quality of the eligible RCTs, and the methodological index assessed that of the NRCTs for non-randomized studies (MINORS)⁷.

Quality assessment

The Jadad scoring system was used for the randomized clinical trials (RCTs)⁶. The scale consists of three items, randomization, blinding, and description of the withdrawals and dropouts. Studies with a score of 3-5 were considered to be of high quality. Correspondingly, the Newcastle-Ottawa scale⁷ was used to assess the quality of non-randomized studies based on the following nine questions: (1) representativeness of the exposed cohort; (2) selection of the non-exposed cohort; (3) ascertainment of exposure; (4) demonstration that the outcome was not present at the outset of the study; (5) comparability; (6) assessment of outcome; (7) sufficient length of follow-up; (8) adequacy of participant follow-up; and (9) total number

Figure 1. Flowchart of the results of literature search.



of “stars.” Maximum score on this scale is a total of 9. “Good” was defined as a total score of 7-9; “fair,” a total score of 4-6; and “poor,” a total score of < 4.

Statistical analysis

A formal meta-analysis was carried out for all included studies comparing the results from the bursectomy group with the non-bursectomy group for gastric cancer. The outcomes in our study were complications, recurrence, and overall survival. A fixed effects model was used to calculate a pooled odds ratio (OR) with its 95% confidence interval (CI). Heterogeneity was explored using I^2 statistics, a measure of how much the variance between studies, rather than chance, can be attributed to inter study differences. $I^2 > 50\%$ was regarded to indicate strong heterogeneity. The Cochrane Collaboration’s Review Manager Software (Revman version 5.0) was utilized for the data analysis.

RESULTS

Study selection

A total of 213 potentially relevant titles and abstracts were obtained (Fig. 1). After exclusion of duplicate

references, non-relevant literature, and those that did not satisfy the inclusion criteria, 20 candidate articles were considered for the meta-analysis. After careful review of the full text of these articles, eight studies fulfilled the eligibility criteria. The reports by Fujita et al., Hirao et al., and Imamura et al., which provide different results of RCTs from the same institute, were regarded as one study. Other five papers were retrospective clinical trials. Details of the included studies are summarized in tables 1 and 2.

The publication dates ranged from January 2010 to July 2017. Study sizes ranged from 108 to 470 patients.

Outcome measures

A total of 644 patients who underwent bursectomy and 1000 patients who did not undergo bursectomy were analyzed. The total post-operative complications were 23.9% for patients with bursectomy and 23.6% for non-bursectomy patients according to the six included studies; the non-bursectomy group had fewer complications, but no significant difference was found (OR = 1.06, 95% CI [0.83-1.35], $p = 0.63$) (Fig. 2). The overall prevalence of recurrence was 24.60% in the bursectomy

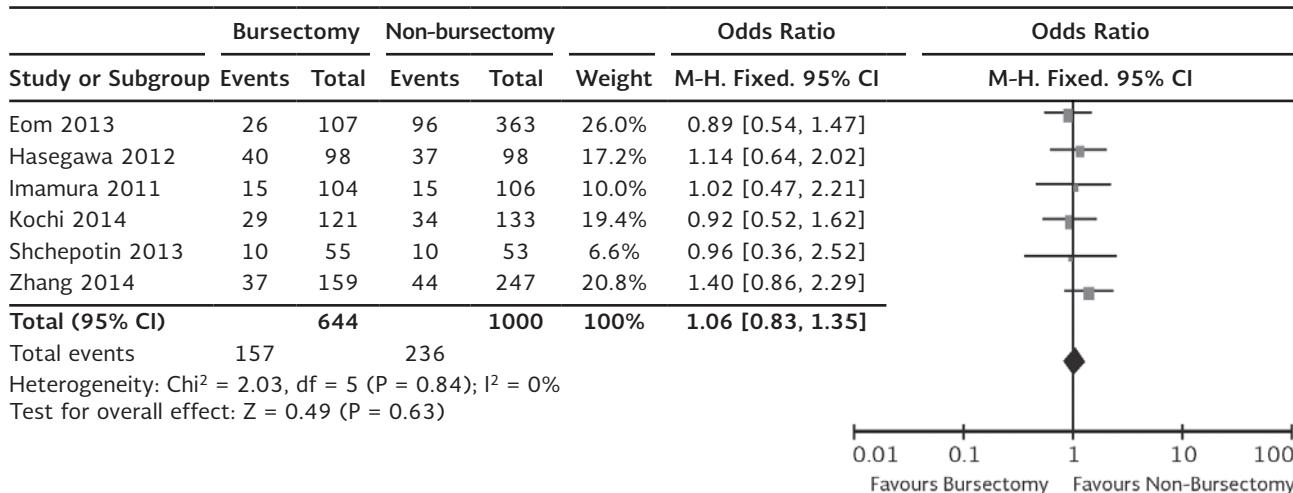
Table 1. Summary and comparison of baseline characteristics between bursectomy and non-bursectomy patients.

Author, Year	Country	Study design	Number of patients	Sex (male/female)	Mean age	Tumor location		Median tumor size (cm)	Quality score ^a
						U	M+L		
Hasegawa et al., 2012 ⁸	Japan	NRCT	196	BS: 72/26 NBS: 72/26	BS: 69 NBS: 68.7	–	–	–	7/9
Fujita et al., 2012 ⁹	Japan	RCT	210	BS: 73/31 NBS: 77/29	BS: 65 NBS: 63	BS: 15 NBS: 16	BS: 89 NBS: 90	BS: 4.3 NBS: 4.5	3/5
Imamura et al., 2010 ¹⁰	Japan	RCT	210	BS: 73/31 NBS: 77/29	BS: 65 NBS: 63	BS: 15 NBS: 16	BS: 89 NBS: 90	BS: 4.3 NBS: 4.5	3/5
Hirao et al., 2015 ⁴	Japan	RCT	210	BS: 73/31 NBS: 77/29	BS: 65 NBS: 63	BS: 15 NBS: 16	BS: 89 NBS: 90	BS: 4.3 NBS: 4.5	3/5
Kochi et al., 2014 ¹¹	Japan	NRCT	254	BS: 82/39 NBS: 97/36	BS: 67 NBS: 66	BS: 25 NBS: 24	BS: 96 NBS: 109	BS: 3.5 NBS: 3.5	7/9
Zhang et al., 2014 ¹²	China	NRCT	406	BS: 108/51 NBS: 160/87	BS: 57.3 NBS: 58.3	BS: 62 NBS: 28	BS: 97 NBS: 219	BS: 5.6 NBS: 5.7	6/9
Shchepotin et al., 2013 ¹³	Ukraine	NRCT	108	–	–	–	–	–	5/9
Eom et al., 2013 ²²	Korea	NRCT	470	BS: 65/42 NBS: 241/122	BS: 56.1 NBS: 57.1	BS: 13 NBS: 62	BS: 66 NBS: 242	BS: 6.7 NBS: 6.0	7/9

^aJadad score for RCTs, NOS score for NRCTs.

U: upper, M: middle, L: lower, BS: bursectomy, NBS: non-bursectomy. RCT: randomized controlled trial.

Figure 2. Meta-analysis of total complications for bursectomy group versus non-bursectomy group.



group versus 25.04% in the non-bursectomy group, without significant difference ($OR = 1.07$, 95% CI [0.77-1.50], $p = 0.68$). In the bursectomy group, each pattern of recurrence had similar proportions (range 4.21-7.77%); the same occurred for the non-bursectomy group (5.64-8.11%) (Fig. 3). Comparing the proportion of each pattern between the two groups, there were no significant differences ($p = 0.96$, 0.95 , and 0.52 , respectively). The

prevalence of 3-year overall survival was 86.07% in the bursectomy group versus 89.02% in the non-bursectomy group, and this difference was not significant ($OR = 1.30$, 95% CI [0.82-2.07], $p = 0.26$) (Fig. 4). The prevalence of 5-year overall survival was 73.54% in the bursectomy group versus 72.31% in the non-bursectomy group, and no significant difference was observed ($OR = 0.91$, 95% CI [0.66-1.27], $p = 0.58$) (Fig. 5).

Table 2. Summary and comparison of baseline characteristics between bursectomy and non-bursectomy patients.

Author, Year	Histological type (differentiated/ undifferentiated)	p-stage (Stage I~II/ Stage III~IV)	pT stage (T1~T2/ T3~T4)	pN stage (N0~N1/ N2~N3)	Surgical procedure (TG/DG)	Adjuvant chemotherapy	Follow-up (months)
Hasegawa et al., 2012 ⁸	BS: 61/37 NBS: 58/40	BS: 56/42 NBS: 57/41	BS: 43/137 NBS: 55/95	BS: 64/34 NBS: 64/34	BS: 46/52 NBS: 37/63	BS: 20 NBS: 34	108
Fujita et al., 2012 ⁹	–	–	BS: 79/25 NBS: 83/23	BS: 86/18 NBS: 84/22	–	–	54
Imamura et al., 2010 ¹⁰	BS: 47/57 NBS: 50/56	–	BS: 79/25 NBS: 83/23	BS: 86/18 NBS: 84/22	–	–	54
Hirao et al., 2015 ⁴	BS: 47/57 NBS: 50/56	–	BS: 79/25 NBS: 83/23	BS: 86/18 NBS: 84/22	–	–	54
Kochi et al., 2014 ¹¹	BS: 63/58 NBS: 64/69	–	–	–	BS: 36/85 NBS: 36/97	–	68
Zhang et al., 2014 ¹²	–	BS: 54/105 NBS: 86/161	BS: 20/139 NBS: 48/199	BS: 63/96 NBS: 111/136	BS: 86/73 NBS: 63/184	–	24
Shchepotin et al., 2013 ¹³	–	–	–	–	–	–	–
Eom et al., 2013 ²²	BS: 38/69 NBS: 137/226	BS: 33/73 NBS: 202/155	BS: 10/97 NBS: 79/284	BS: 59/48 NBS: 235/128	BS: 43/64 NBS: 147/216	BS: 68 NBS: 238	66

TG: total gastrectomy, DG: distal gastrectomy, BS: bursectomy, NBS: non-bursectomy.

DISCUSSION

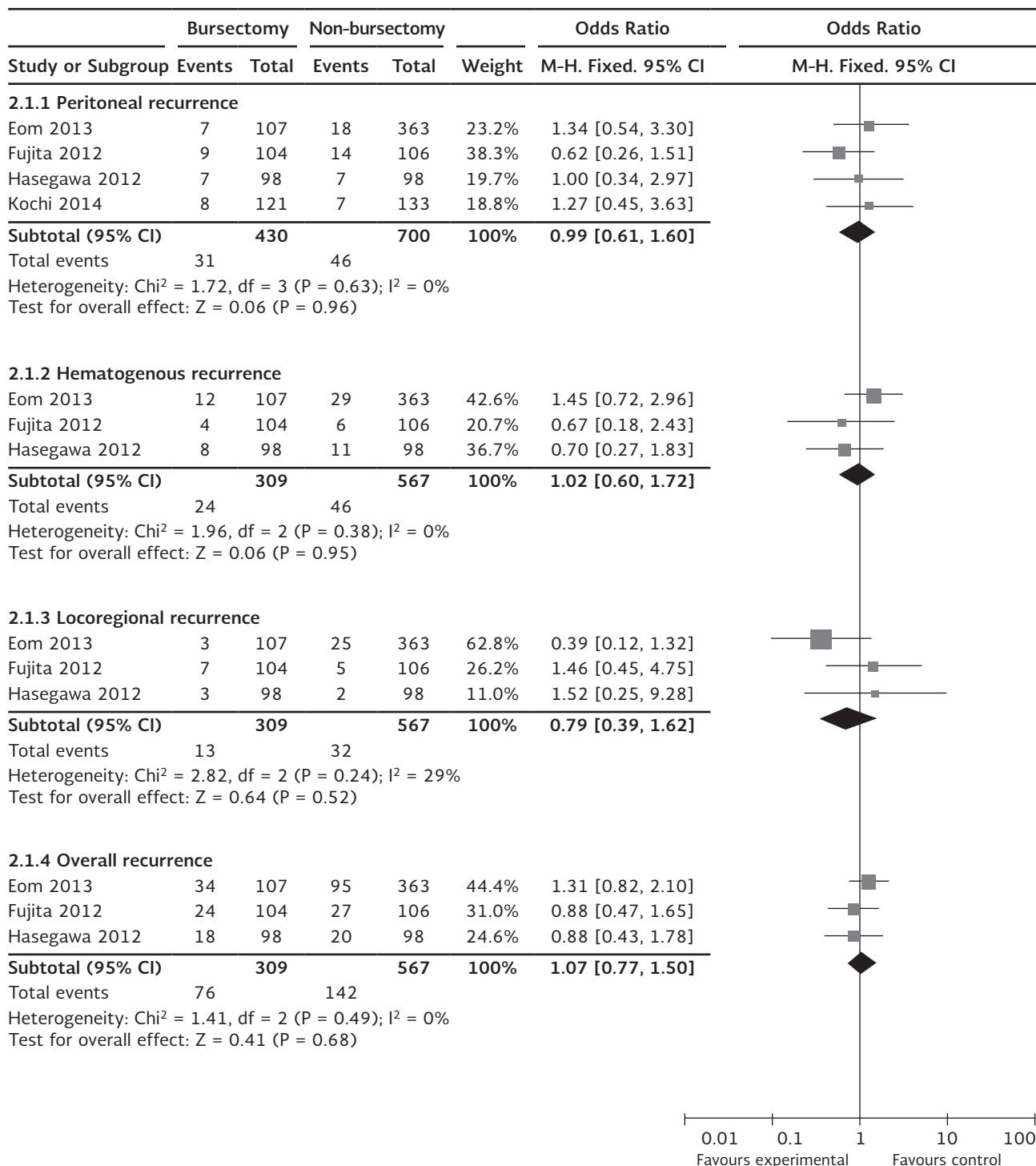
Several studies have led to radical gastrectomy with extended D2 removal of regional lymph nodes becoming the standard treatment for curable gastric cancer¹⁴⁻¹⁶. The effect of bursectomy on overall survival of patients with gastric cancer remains unclear. Considering the balance between the risk and benefit of each surgical procedure, some researchers have remained skeptical about prophylactic bursectomy. Two factors are necessary for bursectomy to be accepted as a standard treatment for advanced gastric cancer: safety and oncologic benefit. In the current study, we compared the total complications, recurrence, and long-term survival of patients with gastric cancer between the bursectomy and non-bursectomy groups.

Removing the mesocolon and pancreatic capsule is physically detrimental to patients and increases the risk of intraoperative and/or post-operative complications. A previous study reported that subclinical pancreatic fistula could occur in up to 10% of the patients with the resection of the pancreatic capsule¹⁷. However, other studies⁹⁻¹¹ indicated that the incidence of major post-operative complications

including pancreatic fistula, anastomotic leakage, abdominal abscess, bowel obstruction, and hemorrhage was not significant difference between the two groups. They also pointed out that pancreatic fistula may not be caused by the removal of the pancreatic capsule but by the lymph node dissection adjacent to the pancreas parenchyma. As the safety of surgical treatments strongly depends on the surgeon's experience, the literature suggests that bursectomy can safely be performed by experienced surgeons⁹. For our research, gastrectomy with bursectomy does not increase the risk of post-operative complications.

Locoregional recurrences in gastric cancer have been reported to be as high as 72%¹⁸. Radical resection of the bursa omentalis for gastric cancer, which may eliminate the majority of cancer cells seeded within the peritoneum¹⁹, has been advised for almost a century¹ as one of the strategies to reduce locoregional recurrence. Hasegawa et al.⁸ indicated that complete omentectomy and extensive lymph node resection during gastrectomy improved the survival of patients with peritoneal metastasis of gastric cancer. Nevertheless, our meta-analysis did not show any benefit on each pattern of recurrence. As Yamamura et al.

Figure 3. Meta-analysis of recurrences for bursectomy group versus non-bursectomy group.



pointed out, it is improbable that viable cancer cells disseminated into the bursa remain restricted to this cavity without migrating into the free abdominal cavity²⁰. Routine bursectomy may not be an essential procedure for resecting gastric cancer, from the

viewpoint of eliminating microscopic peritoneal deposits within the omental bursa.

There are little data to support bursectomy in improving the overall survival rates of patients. Only

Figure 4. Meta-analysis of 3-year overall survival for bursectomy group versus non-bursectomy group.

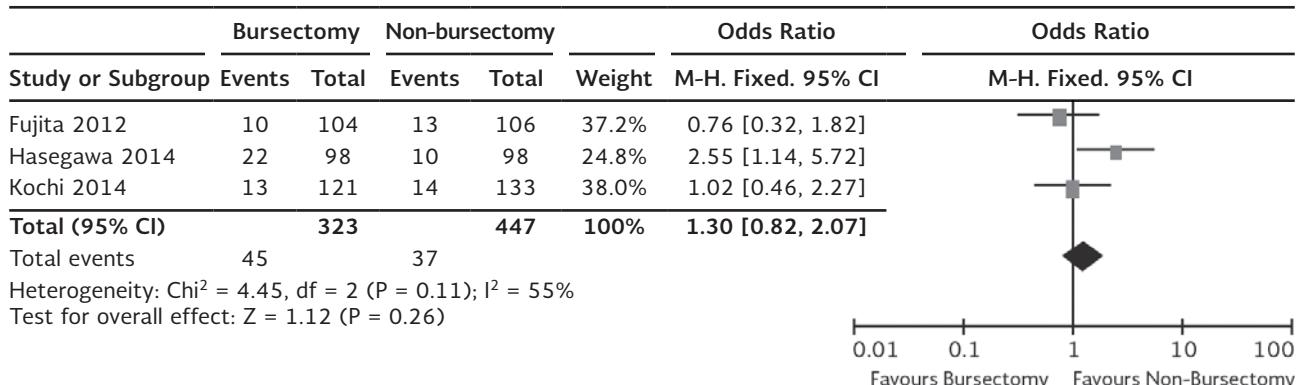
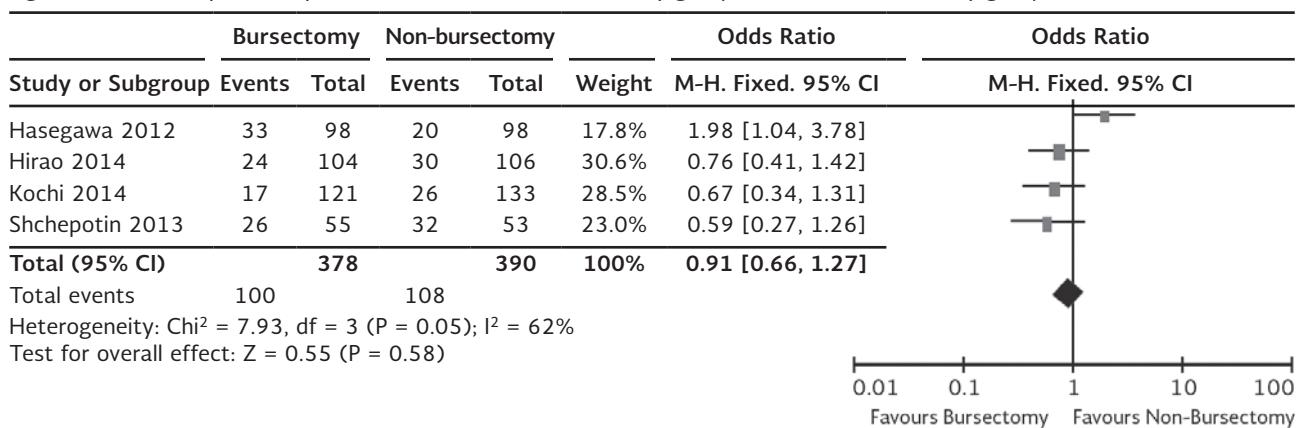


Figure 5. Meta-analysis of 5-year overall survival for bursectomy group versus non-bursectomy group.



Shchepotin et al.¹³ pointed out that bursectomy was associated with a better 5-year survival. Other retrospective studies failed to show any survival advantage of bursectomy^{8,11,21}. In a randomized controlled study, bursectomy was not an important prognostic factor in the multivariate analysis¹⁰. Although they demonstrated a potential effect of bursectomy on survival among the patients with serosa-positive gastric cancer, it was too weak to reach a clear conclusion. Two included studies^{8,22} mentioned the use of perioperative chemotherapy; however, they did not explain the effect of chemotherapy on patients.

The lack of survival benefit of bursectomy in our study may be explained by several factors. First, the cavity of the bursa omentalis is not a closed space, but remains open to the abdominal cavity, as suggested by Yamamura et al.²⁰ In this work, carcinoembryonic antigen or cytokeratin 20 mRNA was

detected not only in the bursa omentalis but also in other parts of the abdominal cavity in most cases. Hence, all disseminated free cancer cells cannot be eliminated by bursectomy. Second, it is possible that bursectomy was not performed completely in most cases on account of a highly technical experience required. Especially, fat amount and fat density of the omentum are principal factors of surgical quality. Completeness of the bursectomy may be different based on the number and nature of the patient's mesenteric fat and degree of bleeding tendency.

There are some limitations in our study. First, most of the included studies were retrospective chart reviews with inherent limitations such as selection bias and inaccurate or missing data reports. Second, our analysis included only studies published in English. Finally, the sample size of the included studies was too small to exclude beta error. Hence, our findings must be interpreted with caution.

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