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Oncologic Effectiveness and Safety of Bursectomy in Patients with Advanced Gastric Cancer: A Systematic Review and Updated Meta-Analysis

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ABSTRACT

Purpose/Aim: In the past few decades some researchers have questioned whether bursectomy for gastric cancer is essential from an oncological point of view and no consistent recommendations have been proposed. The aim of this systematic review with meta-analysis is to investigate the oncologic effectiveness and safety of bursectomy for the treatment of advanced gastric cancer patients. *Materials and Methods*: We planned and performed this systematic review and meta-analysis in accordance with Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement and Cochrane Handbook for Systematic Reviews of Intervention. *Results*: Overall, four studies with a total of 1,340 patients met inclusion criteria. The pooled hazard ratio for overall survival between the bursectomy versus nonbursectomy groups was [HR = 0.85, 95% CI 0.66–1.11, p = .252]. Interestingly, the pooled HR between the two groups in serosa-positive cases subgroup, showed a significant improvement of overall survival rate in favor of bursectomy [HR = 0.72, 95% CI 0.73–0.99, $p < .05$]. *Conclusions*: Bursectomy represents a surgical procedure that might be able to improve overall survival in serosa positive gastric cancer patients. However, a definitive conclusion could not be made because of the studies' methodological limitations. This meta-analysis points to the urgent need of high quality, large-scaled, clinical trials with short- as well as long-term evaluation comparing bursectomy with non bursectomy procedures, in a controlled randomized manner, helping future researches and establishing a modern and tailored approach to gastric cancer.

Keywords: gastric cancer; bursectomy; D2 lymphadenectomy; prognosis; gastrectomy; meta-analysis

INTRODUCTION

Gastric cancer (GC), despite its decreasing incidence, is the fifth most common type of malignancies, remaining the third leading cause of cancer-related deaths worldwide [1]. Although recent progresses in diagnostic and therapeutic modalities can improve outcome of GC patients, surgery remains the only curative therapy [2–4]. Currently, surgical resection with extended lymph node dissection is considered the optimal curative treatment for non-metastatic gastric cancer, while neoadjuvant and adjuvant chemotherapies, as well as chemoradiation, can improve the outcomes aimed at the reduction of recurrence and extension of survival [5].

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Nevertheless, many issues regarding the surgical technique are still debated, such as the extension of lymphadenectomy [6–9], the opportunity of associating a multivisceral resection (MVR) of adjacent organs in patients with locally advanced disease [5, 10–17], and the role of bursectomy as an essential component of radical surgery for advanced gastric carcinoma [18–22]. As what concerns the latter question, total resection of the bursa omentalis (including the removal of the peritoneal lining covering the pancreas and the anterior plane of the transverse mesocolon) along with a total omentectomy has been advocated as an essential part of radical gastrectomy with extended lymphadenectomy at the beginning of the 1960s in Japan by Jinnai [23] with the rationale to reduce peritoneal recurrences by eliminating micrometastatic disease in the lesser sac of peritoneal cavity [24, 25] and to complete resection of the subpyloric lymph nodes.

Initially, even if in absence of any supporting evidence, the Japanese Gastric Cancer Treatment Guidelines recommended the bursectomy as part of complete radical gastrectomy [26]. Three years later, the Japanese Gastric Cancer Association revised the gastric cancer treatment guidelines recommending bursectomy only for tumors with invasion of the serosa [27] and, more recently, they changed the guidelines again limiting the indication of bursa omentalis resection only to tumors penetrating the serosa of posterior gastric wall [7, 28].

Since considerable evidence exists that removing the peritoneum of the lesser sac does not provide an increase in the incidence of intraoperative as well as postoperative complications (hemorrhage, pancreatic fistula, and intestinal obstruction) [20–22, 29], in the past few decades a number of surgeons have continued to perform D2 lymphadenectomy with bursectomy as the conventional operation for advanced gastric cancer [18, 30, 31[. Contrarily, some researchers have questioned whether bursectomy is essential from an oncological point of view [22, 32]. To this address, very few studies with no large sample size have compared bursectomy with nonbursectomy surgery, in terms of efficacy and safety, and no consistent recommendations have been proposed since the results are ambiguous from one side with very good prognosis and with conflicting results from the other [18, 21, 22].

To the best of our knowledge, only one meta-analysis by Shen et al. [33] concluded that there were no survival benefits for the bursectomy when compared with nonbursectomy surgery for gastric cancer patients. However, since the search strategy was conducted until October 2013, additional data has become available.

No doubts exist that standardized knowledge about this entity is needed, so we prepared a systematic review of the literature with meta-analysis of updated available data to provide a more robust answer regarding the oncologic effectiveness and safety of bursectomy for the treatment of advanced gastric cancer.

METHODS

Searches

We planned and performed this systematic review and meta-analysis in accordance with Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement [34] and Cochrane Handbook for Systematic Reviews of Intervention [35]. A literature search in Pubmed, Cochrane and Ovid databases of all articles published, until January 31, 2017 with the medical subject headings (MeSH) and keywords "Stomach neoplasms," "Stomach carcinoma," "Stomach adenocarcinoma," "Stomach tumor," "Gastric carcinoma," "Gastric adenocarcinoma," "Gastric tumor," "Gastric cancer," "Bursectomy," "Omentum surgery," "Omentum removal," "Serosal removal" was independently carried out by two investigators. The key words were used in all possible combinations to obtain the maximal number of articles. We also reviewed the bibliographies of relevant articles to identify additional publications.

Selection

The articles were then assessed for the presence of the following defined eligibility criteria according to PICO format [36]: P-Population: all patients with diagnosis of gastric cancer submitted to surgical treatment; I-Intervention: D2 gastrectomy with bursectomy; C-Comparator: D2 gastrectomy without bursectomy; O-Outcomes of interest: prognostic characteristics and postoperative outcomes. Only published studies with full-text were included. Otherwise, experimental studies in animal models, single case reports, technical reports, reviews, abstracts, editorials and studies in other languages than English were excluded.

When the same population was included in multiple publications, only data from the most recent article were used for meta-analysis.

Data Extraction

Two of the authors (L.M. and A.P.) independently reviewed the formal published versions of all eligible studies for content according to the specified inclusion criteria using a data extraction form based on the Cochrane Consumers and Communication Review Group's data extraction template [35]. Disagreements were resolved by discussion or consultation with third author.

The following data were recorded: first author, type of study design, mono- or multicentricity, country of origin, year of publication, study period, number of patients, median/mean patient age, gender distribution, operative factors, intra- and postoperative complications, median or mean duration of follow-up, control and intervention groups for estimation of hazard ratio (HR), and the type of survival outcomes. The HR and 95% confidence interval (CI) were indirectly estimated from a Kaplan–Meier curve [37, 38] using WebPlotDigitizer version 3.10 (http://arohatgi.info/WebPlotDigitizer) if they were not available in a study. We contacted the Authors for more detailed data but no response was obtained. Additionally, whenever data in individual studies were expressed as a median and range, they were converted to estimated mean ± standard deviation (SD) before analysis using "Estimation of a sample's mean and variance from its median and range software" (VassarStats: Website for Statistical Computation, www.vassarstats.net, Richard Lowry, Poughkeepsie, NY, USA) on the basis of the sample's reported median and range according to the method devised by Hozo et al. [39].

This study did not require the ethical approval and informed consent due to all analyses were carried out based on the previous published data.

Summary Measures

The primary outcome was to analyze the influence of bursectomy on the prognostic outcomes of gastric cancer patients by comparing the prognosis of patients undergoing gastrectomy with bursectomy for gastric cancer with that of patients undergoing gastrectomy alone. Additionally, the mean difference in procedure time, length of hospital stay, blood loss, number of retrieved lymph nodes, the odds ratio of peritoneal recurrence as well as postoperative complications comparing bursectomy to non bursectomy were investigated as a secondary analysis.

Quality Assessment

All eligible studies were independently evaluated by two reviewers (K.P. and L.M.) for risk of bias according to Quality In Prognosis Study (QUIPS) tool [40]. Risk of bias was scored as low, moderate or high for each domain, answering to three to six prompting questions, of the following six items: study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding and statistical analysis. A final grading of low risk of bias was assigned when three or more of the six items were considered to be of "high" methodological quality, while high risk of bias was considered when three or more of the six items resulted to be of "low" methodological quality. Otherwise a moderate risk of bias was scored. Any reasons for disagreement on certain risk of bias items for a study were discussed and, if no consensus was reached, a third reviewer was involved in order to obtain a final agreement.

Statistical Analysis

Effect sizes for numerical variables were expressed as difference in means with 95% confidence interval (CI); while that of categorical data were expressed as odds ratio (OR) with 95% CI. The hazard ratio (HR) and 95% CI was retrieved from each article where possible (otherwise the estimated value according to Tierney et al. [38] was runned into analysis) to estimate the pooled effect size of overall survival. The between-study heterogeneity was tested with the Higgins I^2 measure [35]. Percentages of around 25% ($I^2 = 25$), 50% ($I^2 = 50$), and 75% ($I^2 = 75$) were considered at low, moderate, and high heterogeneity, respectively. A χ^2 based Q-test was also performed to check between-study heterogeneity. When a I^2 value higher than 50 indicated moderate heterogeneity between the studies, the effect size for each study was calculated by the random-effect model DerSimonian-Laird approach [35]. Otherwise, a fixed effect model was considered. With regard to outcomes when significant heterogeneity existed across studies, sensitivity analysis was performed by sequentially omitting each study to test the influence of each individual study on pooled data. We did not produce the Funnel plot to test the publication bias due to the limited number (below 10) of studies included in each analysis [34]. All analyses were performed using Comprehensive Meta-analysis software (Version 3.3.070 – November 21, 2014).

RESULTS

Study Selection and Characteristics

The initial search produced 592 studies, of which 450 were selected for eligibility assessment after exclusion of duplicates. By checking the relevant bibliography, one additional article was included. The titles and abstracts of the remaining 451 records were screened and seven studies fulfilled criteria for eligibility. 444 studies, that were not related to the comparison between bursectomy and nonbursectomy surgery for gastric cancer patients or that were either a review, editorial or case report, were excluded. Of the remaining seven records, only four fulfilled criteria for inclusion: papers by Fujita [41], Imamura [19], and Hirao [20] were included as one study, since they separately published complementary data from the same group of patients. Additionally, the study by Hasegawa et al. [42] was excluded because the Authors reported the comparison between greater omentum resection and greater omentum sparing and nonbursectomy conventional gastric surgery for gastric cancer patients. After these analyses, four studies, one randomized controlled trial and the three others published between 2013 and 2016, with a study period between 2001 and 2013, were included [20, 21, 29, 43]. The total number of included patients was 1,340 (491 in bursectomy group and 849 in nonbursectomy group) ranging from 210 to 470 patients per study. Only one study (210 patients, 15.7%) was multicentric (11 hospitals belonging to the Osaka University Clinical Research Group for Gastroenterological Surgery, Japan) [20], while the three others were performed in single centers in the Eastern populations (1,130 patients, 84.3%) (Japan [21], China [29], and South Korea [43]). The overall proportion of patients in bursectomy group was 36.6% (491 patients) ranging from 39.2% [20] to 49.5% [29] patients per study. Weighted mean age of the patients was 58.6 years in bursectomy group and 58.8 in nonbursectomy group. The proportion of female patients was 33.2% in bursectomy group and 32.3% in nonbursectomy group. The main characteristics of each study included in the meta-analysis are shown in Table 1. Since not all studies reported all variables examined in the meta-analysis, only studies reporting the variable of interest were included, in turn, for quantitative synthesis to investigate the association of bursectomy with that variable.

Bursectomy and Survival of Gastric Cancer Patients

Median follow-up period was 20–80 months; the study by Kochi et al. [21] did not clearly specify the follow-up duration for survival analysis. All selected studies did not find statistically significant prognostic difference, in terms of OS, between the bursectomy versus nonbursectomy groups. Furthermore, only two studies [21, 43] reported HR and 95% CI of the overall survival according to the bursectomy. We contacted the corresponding authors of the other sudies [20, 29] but no response was obtained. For this reason we performed an estimation of HR from a Kaplan-Meier curves. The pooled HR of bursectomy for OS from selected studies was [HR = 0.85, 95% CI 0.66–1.11, $p = 0.252$] in a fixed effect model [$I^2 = 0\%$, Cochran's Q = 0.536] (Figure 1).

Additionally, we assessed the relationship between bursectomy and non bursectomy in serosa-positive cases only, since the Japanese gastric cancer treatment guidelines 2014 (ver. 4) recommend the resection of bursa omentalis for tumors penetrating the serosa of the posterior gastric wall [7, 28]. The pooled HR showed a trend toward significant improvement of overall survival rate in favor of bursectomy compared to nonbursectomy group in serosa positive patients [HR = 0.72, 95% CI 0.73–0.99, $p < .05$] in a fixed effect model [$I^2 = 0\%$, Cochran's Q = 2.46] (Figure 2).

Secondary Analysis

The mean difference in procedure time, length of hospital stay, blood loss, number of retrieved lymph nodes, the odds ratio of peritoneal recurrence as well as postoperative complications comparing bursectomy to non bursectomy were investigated as a secondary analysis (Table 2).

Operative Time and Hospital Stay

All selected studies were pooled in the analysis as regard the operative time, resulting in a lower operative time of nonbursectomy compared with bursectomy [MD = 0.64, 95% CI 0.38–0.90, $p < .001$]. Significant heterogeneity was found among the included studies ($I^2 = 79.4\%$, $p < .05$), and a random-effect analysis model was used. Sensitivity analysis was repeated sequentially omitting each study without primary outcome alteration.

The same studies, with the exclusion of the study by Hirao et al. that has not reported that information, were pooled in the analysis as regard to the length of hospital stay, resulting in no significant difference between bursectomy and nonbursectomy [MD = –0.07, 95% CI –0.39 to 2.40, $p = .64$]. Significant heterogeneity was found among the included studies ($I^2 = 84.1\%$, $p = .002$), and a random-effect analysis model was used.

Blood Loss

Three studies reported intraoperative blood loss data [20, 21, 29] and the estimated effect size indicated no significant difference between groups (MD 0.27; 95% CI –0.09 to 0.64, $p = .142$). Significant heterogeneity was found among the included studies ($I^2 = 86\%$, $p = .001$), and a random-effect analysis model was used. Sensitivity analysis was repeated sequentially omitting each study without primary outcome alteration.

Number of Retrieved Lymph Nodes

All selected studies with a total of 1,340 patients presented data of retrieved lymph nodes and the estimated effect size indicated no significant difference between groups (MD 0.34; 95% CI –0.29 to 0.99, $p = .290$). A significant heterogeneity was found among the included studies ($I^2 = 96.6\%$, $p < .001$), and a random-effect analysis model was used. Sensitivity analysis was repeated sequentially omitting each study without primary outcome alteration.

Peritoneal Recurrence

Two studies reporting peritoneal recurrence data [21, 22] highlighted no statistically differences between the bursectomy and nonbursectomy groups, with a pooled analysis resulting in [OR = 3.68, 95% CI 0.47–

TABLE 1 Characteristics of included studies

Author	Study period	Country of origin	Type of study	Sample size (M/F ratio)		Age in years[a]		Type of surgery (TG/DG)		TNM stage	OS[b]	Follow up[c]
				Bursectomy	Nonbursectomy	Bursectomy	Nonbursectomy	Bursectomy	Non bursectomy			
Eom BW et al. [22]	2001–2006	Korea	NRCT	107 (65/42)	363 (241/122)	107 (65/42)	363 (241/122)	43/64	147/216	I - IV	0,98 [0,62–1,55]	75 (0,3–126,3)
Hirao M et al. [20]	2002–2007	Japan	RCT	104 (73/31)	106 (77/29)	104 (73/31)	106 (77/29)	22/82	27/79	T1 – T3	0,75 [0,38–1,47]	80 (NR)
Kochi M et al. [21]	2004–2010	Japan	NRCT	121 (82/39)	133 (97/36)	121 (82/39)	133 (97/36)	36/85	36/97	IA - IIIC	0,82 [0,37–1,74]	NR
Zhang WH et al. [29]	2012–2013	China	NRCT	159 (108/51)	247 (160/87)	159 (108/51)	247 (160/87)	86/73	63/184	IB - IIIC	0,82 [0,54–1,23]	20 (2–35)

NRCT, Nonrandomized Controlled Trial; RCT, Randomized Controlled Trial; OS, overall survival; NR, not reported; TG, total gastrectomy; DG, distal gastrectomy.
[a]Either mean (standard deviation) or median (range).
[b]Hazard ratio [95% confidence interval].
[c]Median.

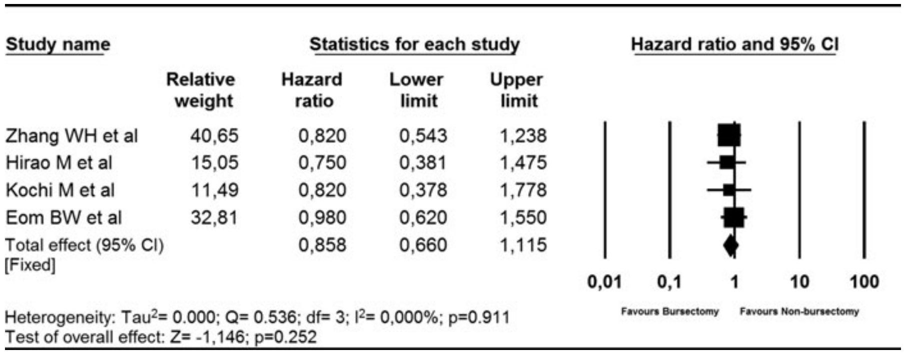


FIGURE 1 Forest plot of hazard ratio with 95% confidence interval (CI) for the effect of bursectomy on overall survival (OS).

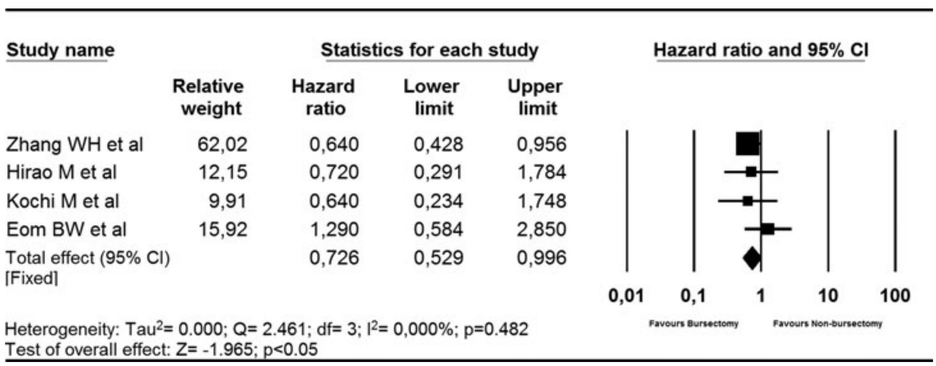


FIGURE 2 Forest plot of hazard ratio with 95% confidence interval (CI) for the effect of bursectomy on overall survival (OS) in serosa-positive patients.

28.5, $p = .212$] in a random effect model [$I^2 = 88.6\%$, $p = .003$].

Postoperative Complications

All studies reporting overall morbidity data highlighted no statistically differences between the bursectomy and nonbursectomy groups, with a pooled analysis resulting in [OR = 1.05, 95% CI 0.80–1.39, $p = .698$] in a fixed effect model [$I^2 = 0\%$, $p < .001$].

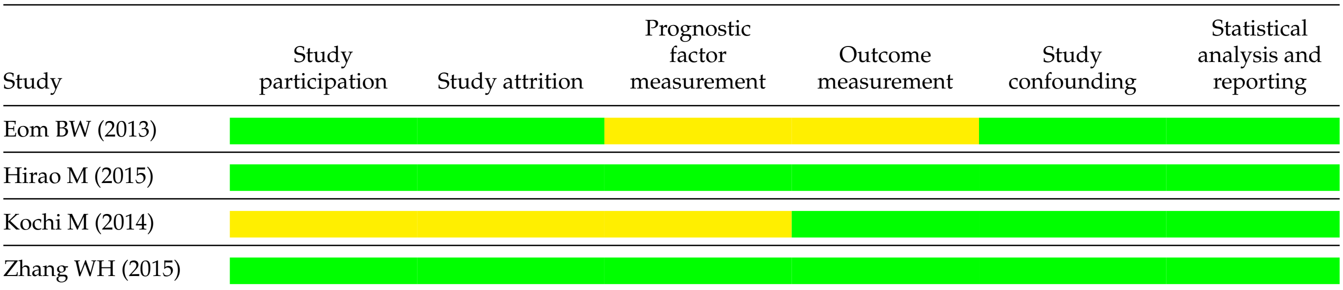
Furthermore, we performed an independent meta-analysis for surgical site infections (SSIs) (with the exclusion of the study by Hirao et al. [20] that has not reported that data), pancreatic fistula (with the exclusion of the study by Eom et al. [22] that has not reported that information), intraperitoneal infections, anastomotic leakage as well as postoperative ileus, and

TABLE 2 Results of meta-analysis of the secondary outcomes

				Heterogeneity		
Outcomes	Effect size	95% CI	*p* Value	I^2 (%)	*p* Value	Effect model
Operative time	MD: 0.64	0.38–0.90	<.001	79.4	<.05	Random
Hospital stay	MD:-0.07	– 0.39–2.40	.64	84.1	.002	Random
Blood loss	MD: 0.27	– 0.09–0.64	.142	86	.001	Random
Retrieved lymph nodes	MD: 0.34	– 0.29–0.99	.290	96.6	<.001	Random
Peritoneal recurrence	OR: 3.68	0.47–28.5	.212	88.6	.003	Random
Postoperative complications:	OR: 1.05	0.80–1.39	.698	0	<.001	Fixed
SSIs	OR: 0.94	0.43–2.98	.890	0	<.001	Fixed
Pancreatic fistula	OR: 0.77	0.33–1.76	.209	0	<.001	Fixed
Intraperitoneal infections	OR: 0.85	0.40–1.80	.342	0	<.001	Fixed
Anastomotic leakage	OR: 0.99	0.31–3.15	.996	0	<.001	Fixed
Postoperative ileus	OR: 0.83	0.32–2.11	.698	0	<.001	Fixed

MD, mean difference; OR, odds ratio; CI, confidence interval; SSIs, surgical site infections.

TABLE 3 Quality assessment of studies using the quality in prognosis studies (QUIPS) assessment tool[a]



Risk of bias: ■ Low Risk ■ Moderate Risk ■ High Risk

[a]The included studies were assessed on items of methodological quality using the QUIPS assessment tool [40].
"high" methodological quality: on three or more items "low risk" of bias,
"low" methodological quality: on three or more items "high risk" of bias,
All other studies: "moderate" methodological quality.

no significant differences between non bursectomy and bursectomy groups was highlighted.

Quality Assessment

All included studies were scored to be of "high" methodological quality according to Quality In Prognosis Study (QUIPS) tool [40] (Table 3).

DISCUSSION

Results from our meta-analysis clearly show that there is not statistically significant prognostic difference, in terms of OS, between the bursectomy versus nonbursectomy groups. Conversely, the resection of bursa omentalis is associated with better overall survival than nonbursectomy surgery in serosa positive gastric cancer patients. The omental bursa (or lesser peritoneal sac) represents a posterior peritoneal space between the liver, stomach and omentum, anteriorly, and the pancreas, left adrenal gland and kidney, posteriorly. Since it is connected with the main peritoneal cavity only through the foramen of Winslow, it is considered an anatomical barrier against the spillage of cancer cells adhering at the posterior gastric wall [24, 25]. According to this anatomical as well as oncological consideration, the bursectomy (mainly defined as a dissection of the peritoneal lining covering the pancreas and the anterior plane of the transverse mesocolon with an omentectomy [24, 30]) represents a procedure performed to: (1) eliminate cancer cells and/or micrometastasis trapped in the lesser sac of peritoneal cavity; (2) improve the resection of the subpyloric and peripancreatic lymph nodes [24, 25, 44–47]. Interestingly, this surgical technique has been recommended as part of complete radical gastrectomy since the 1960s in Japan exclusively based on traditional acceptance. However, recent changes of Japanese Gastric Cancer Treatment Guidelines recommended bursectomy only for tumors with invasion of the serosa of posterior gastric wall [7, 28]. Nevertheless, the therapeutic efficacy of bursectomy is still controversial because the survival benefit is uncertain. The unique randomized controlled trial on 210 patients with cT2–3 gastric adenocarcinoma indicated the bursectomy as an independent prognostic factor of good OS [20]. The five-year OS resulted in 77.5% for the bursectomy group and 71.3% for the non bursectomy group, while the subgroup analysis showed a trend toward improved survival after bursectomy for tumors in the middle or lower third of the stomach and for pathologically serosa-positive tumors [20]. Similar results were reported in the retrospective study by Zhang et al. [29]. Converesely, other studies showed totally opposite results, finding no survival benefits of bursectomy when compared with nonbursectomy surgery [21, 33, 43]. Furthermore, a recent meta-analysis by Shen et al. [33] concluded that there was no statistically significant survival benefits for the bursectomy when compared with nonbursectomy surgery for gastric cancer patients and for subgroup of serosa-positive patients as well. These results, however, may be unreliable since the study by Shen et al. [33] was affected by selecting bias due to the inclusion of the paper by Hasegawa et al. [42], investigating the impact of greater omentum resection rather than bursectomy for advanced gastric cancer patients.

The current meta-analysis involved four studies compared the bursectomy with nonbursectomy surgery for gastric cancer patients with 1,340 (491 in bursectomy group and 849 in nonbursectomy group) ranging from 210 to 470 patients per study. All included studies were scored to be of "high" methodological quality according to Quality In Prognosis Study (QUIPS) tool [40].

The oncologic effectiveness, in terms of OS, was the primary outcome of this study. According to our results, even though the bursectomy did not affect patient survival compared to nonbursectomy surgery, the pooled HR showed a trend toward statistically significant improvement of overall survival rate in favor of bursectomy compared to nonbursectomy group in serosa positive patients. However, the complete removal of the peritoneal lining of bursa omentalis per se, does not condition the harvest of a large number of additional lymph nodes [32]. Accordingly, since in our analysis no differences were highlighted in the total number of dissected lymph nodes between the two groups, it could be postulated that survival benefit of bursectomy was attributable not to more accurate lymphadenectomy, but to the en bloc removal of free cancer cells or micrometastases contained in the bursa omentalis. However, a fascinating study on 136 potentially curable gastric cancer patients investigating the effect of bursectomy in the resection of micrometastases trapped within the bursa omentalis of gastric cancer patients using the cytologic examination as well as the real-time reverse transcriptase-polymerase chain reaction analysis of the peritoneal washes obtained from the Douglas pouch, left subphrenic cavity, and inside the omental bursa questioned this hypothesis [31]. The results showed that in only two of 14 patients with positive carcinoembryonic antigen (CEA) mRNA from the omental bursa, the free cancer cells were found uniquely in the lesser peritoneal sac. It could be argued that free cancer cells from the primary tumor are rarely found confined to the bursa omentalis and they are eliminated or migrate rapidly into the other parts of the abdominal cavity. Interestingly, in our analysis no differences were observed in the peritoneal recurrence between the two groups. On these basis we can speculate that bursectomy may not have a direct role in the inhibition of the tumor cells spreading into the bursa omentalis, offering only a contribution on the entire more complex surgical procedure.

With regard to the safety of bursectomy, we found that blood loss and hospital stay were equivalent between the two groups. On the other hand, a significant increase in operative time was registered for the bursectomy surgery. The extra time consuming of the operations was mainly due to the meticulous en bloc dissection of the peritoneal lining that covers the lesser peritoneal sac. Interestingly, the long surgical duration did not appear unsafe for the bursectomy procedures since the overall postoperative complication rate resulted similar between groups. Of the postoperative complications, in details, we were concerned about the increased incidence of pancreatic fistulas after bursectomy, hypothetically due to pancreatic parenchyma injury during the dissection of the pancreatic capsule [19]. Previous studies [20, 21, 29, 43] did not observe a significant increase in the incidence of pancreatic fistula between the bursectomy group and nonbursectomy group. Overall, our pooled outcomes on post-procedure complications confirmed the data. On these basis we can theorize that pancreatic fistula may not be caused as much by the removal of the pancreatic capsule but rather by the dissection of peripancreatic lymph nodes.

Our study was affected by some limitations. No randomization of patients certainly constituted the weak point of the four included studies. Additionally, it would be of immense interest to evaluate the relationship between bursectomy and nonbursectomy in the subgroup of serosa-positive cases involving the posterior gastric wall. Unfortunately, only in the study by Zhang et al. [29] is this detailed information reported. Lastly, one of the most important limitation is surgical methodology. Because to this day there is not a standardized quality control of the complete en-bloc resection, it is postulated that bursectomy was not performed completely in all cases because it requires high technical experience and is strictly dependent on patient's mesenteric fat [19, 32, 43].

CONCLUSIONS

In conclusion, bursectomy represents a surgical procedure that might be able to improve overall survival in serosa positive gastric cancer patients. However, a definitive conclusion could not be made because of the studies' methodological limitations. Our results may help in planning tailored treatment for different subgroups of patients and we suppose that especially patients with serosa positive as well as posteriorly extruded cancers has to be taken into account for future studies. This meta-analysis points to the urgent need of high quality, large-scaled, clinical trials with short- as well as long-term evaluation comparing bursectomy with non bursectomy procedures, in a controlled randomized manner, helping future researches and establishing a modern and tailored approach to gastric cancer. To this address, a large-scale multicentric Phase III trial is currently underway for macroscopically subserosa or serosa-positive gastric cancer in Japan (JCOG 1001) [48] and we are waiting for the results that will provide important information about the role of bursectomy at radical gastrectomy.

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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