ΜΕΤΑΠΤΥΧΙΑΚΟ ΠΡΟΓΡΑΜΜΑ ΣΠΟΥΔΩΝ:

‘‘ΕΛΑΧΙΣΤΑ ΕΠΕΜΒΑΤΙΚΗ ΧΕΙΡΟΥΡΓΙΚΗ,

ΡΟΜΠΟΤΙΚΗ ΧΕΙΡΟΥΡΓΙΚΗ ΚΑΙ ΤΗΛΕΧΕΙΡΟΥΡΓΙΚΗ’’

ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ

ΙΑΤΡΙΚΗ ΣΧΟΛΗ

ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ

ΘΕΜΑ:

LAPAROSCOPIC VERSUS OPEN GASTRECTOMY WITH D2 LYMPH NODE DISSECTION FOR ADVANCED GASTRIC CANCER – A SYSTEMATIC REVIEW WITH META-ANALYSIS

ΜΕΤΑΠΤΥΧΙΑΚΟΣ ΦΟΙΤΗΤΗΣ:

ΜΗΤΡΟΥΣΙΑΣ ΑΠΟΣΤΟΛΟΣ

Α.Μ. : 20110797

ΑΘΗΝΑ, ΙΟΥΝΙΟΣ 2015

ΠΡΑΚΤΙΚΟ ΚΡΙΣΕΩΣ

ΤΗΣ ΣΥΝΕΔΡΙΑΣΗΣ ΤΗΣ ΤΡΙΜΕΛΟΥΣ ΕΞΕΤΑΣΤΙΚΗΣ ΕΠΙΤΡΟΠΗΣ

ΓΙΑ ΤΗΝ ΑΞΙΟΛΟΓΗΣΗ ΤΗΣ ΔΙΠΛΩΜΑΤΙΚΗΣ ΕΡΓΑΣΙΑΣ

Του μεταπτυχιακού φοιτητή ΜΗΤΡΟΥΣΙΑ ΑΠΟΣΤΟΛΟΥ

Εξεταστική Επιτροπή

- Ευάγγελος Φελέκουρας, Αναπληρωτής Καθηγητής Χειρουργικής **(Επιβλέπων)**
- Χρήστος Π. Τσιγκρής, Καθηγητής Χειρουργικής & Επιστημονικός Υπεύθυνος του Π.Μ.Σ.
- Θεόδωρος Διαμαντής, Καθηγητής Χειρουργικής

Η Τριμελής Εξεταστική Επιτροπή η οποία ορίσθηκε από την ΓΣΕΣ της Ιατρικής Σχολής του Παν. Αθηνών Συνεδρίαση της.....ης ..... 20.... για την αξιολόγηση και εξέταση του υποψηφίου κου Μητρούσια Απόστολου , συνεδρίασε σήμερα .../.../....

Η Επιτροπή διαπίστωσε ότι η Διπλωματική Εργασία του κου Μητρούσια Αποστόλου με τίτλο: *«Laparoscopic versus Open Gastrectomy with D2 Lymph Node Dissection for Advanced Gastric Cancer – A Systematic Review with Meta-analysis»*, είναι πρωτότυπη, επιστημονικά και τεχνικά άρτια και η βιβλιογραφική πληροφορία ολοκληρωμένη και εμπεριστατωμένη.

Η εξεταστική επιτροπή αφού έλαβε υπ' όψιν το περιεχόμενο της εργασίας και τη συμβολή της στην επιστήμη, με ψήφους ..... προτείνει την απονομή του Μεταπτυχιακού Διπλώματος Ειδίκευσης (Master's Degree), στον παραπάνω Μεταπτυχιακό Φοιτητή.

Στην ψηφοφορία για την βαθμολογία ο υποψήφιος έλαβε για τον βαθμό «ΑΡΙΣΤΑ» ψήφους ....., για τον βαθμό «ΛΙΑΝ ΚΑΛΩΣ» ψήφους ....., και για τον βαθμό «ΚΑΛΩΣ» ψήφους ..... Κατά συνέπεια, απονέμεται ο βαθμός «.....».

Τα Μέλη της Εξεταστικής Επιτροπής

- Ευάγγελος Φελέκουρας **(Επιβλέπων)** (Υπογραφή) _____
- Χρήστος Π. Τσιγκρής (Υπογραφή) _____
- Θεόδωρος Διαμαντής (Υπογραφή) _____

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INTRODUCTION

Despite the great improvements in the diagnosis and treatment of gastric cancer, it is the third most common cancer and the second leading cause of cancer-related deaths in the world[1]. In order to cure this type of cancer, it is essential to perform radical gastrectomy, with lymph node dissection[2][3]. Indeed, over the past decades radical gastrectomy has contributed to the improvement of the survival rates for the gastric cancer patients.

The Japanese Gastric Cancer Association (JGCA) guidelines recommend D2 gastrectomy for the treatment of advanced gastric cancer (AGC)[4][5] . According to the same guidelines, stations 12a or 10 D2 dissection is technically demanding due to an increasing risk of organ injury or leakage (bile or pancreatic)[6][7]. Laparoscopic approach is also recommended as treatment for clinical research (Figure 1).

The first reported laparoscopic gastrectomy came from Kitano et al, who chose the procedure (Billroth I) to treat early gastric cancer[8]. The first who reported LG with D2-extended lymph node dissection (LGD2) were Uyama et al, in 2000, for treatment of AGC[9]. In 2002, Coh et al reported laparoscopy-assisted D2 radical gastrectomy for advanced gastric cancer[10].

The evolution in the minimally invasive era led to the instant increase of the number of such procedures being performed laparoscopically worldwide. Currently, laparoscopic gastrectomy with D2 lymph node dissection for gastric cancer treatment has become an alternative choice to an open approach (Figures 2-8). However, its wider acceptance was always a matter of considerable concern. Reasons for this can be summarized as following: (1) oncological safety and adequacy, that is determined mainly through a R0 resection and the extent of lymph node dissection, (2) steep learning curve, especially the reconstruction of the alimentary tract, (3) no large-scale prospective randomized trial has been yet published to favor this procedure.

At this time, laparoscopic gastrectomy is the accepted treatment of choice for EGC due to the general advantages of a minimally invasive technique (postoperative pain, recovery, hospital stay, cosmetic outcome)[11][12][13][14], combined the with oncologic and long-term equivalency. However, in certain cases of EGC, EMR is the treatment of choice[15] [16]. Indeed, in recent years, numerous studies acknowledged the importance of laparoscopy-assisted gastrectomy (LAG), especially in the early gastric cancer patients, in terms of feasibility and safety, and showed efficient oncological outcomes and better postoperative quality of life when compared to the open procedure[17][18][19][20][21]. However, the application of laparoscopic techniques for AGC remains controversial, especially in terms of technical feasibility and curability of D2 gastrectomy.

The decision of choosing the open or laparoscopic approach is strongly influenced by surgeon's suggestion or patient's preference; cosmetic result, pain, recovery and cost are the major factors that patients care about[22][23][24][25][26]. Regardless laparoscopic or open, nodal dissection increases morbidity and mortality similarly[27][28][29].

Several studies concluded that LAG for AGC achieves oncologically equivalent resection, its 5-year survival rate does not differ from open gastrectomy (OG) groups and is technically feasible with comparable survival rates to open D2 gastrectomy[7][30][31][32][33][34][35].

Regardless the controversies that exist about the oncologic efficacy between D1 and D2 dissection[36][37][38], and the lack of long-term oncologic outcomes[7][34], a great number of surgeons all over the world, especially in Eastern countries, have adopted the latter as standard treatment for AGC[39][40][41][42][43]. Furthermore, a recent

prospective randomized trial concluded that D3 dissection predominates over D1 or less dissection in terms of patient survival[44]. Regardless the technique some theories proposed pneumoperitoneum and visceral manipulation as factors for port-site recurrence[45].

Moreover, the worldwide increasing incidence of adenocarcinoma in the middle and proximal thirds of the stomach raised concerns whether laparoscopic-assisted total gastrectomy (LATG) is feasible, safe and oncologically effective[46][47][48][49]. D2 dissection seems to be a more appropriate treatment for patients with advanced disease[50]. Moreover, D2 dissection showed the benefits for fit patients with early-, as well as intermediate-stage disease[51][52][53][54] due to the potential of removing more positive nodes than D1 dissection, which is necessary to moderate the stage migration[55]. It is essential to underline that standardized lymph nodes dissection according to tumor location is more important than only the number of removed nodes.

Regarding to the inclusion criteria used to select studies, many of the reports contained a mixed patient population with EGC and AGC. Only few reports analyze the efficacy of LAG with D2 lymph node dissection for AGC. However, many of them contain a great proportion of stage Ib disease.

Therefore, in order to conclude to more accurate results regarding the short- and long-term outcomes, we performed this literature search and selected studied that not only did not contained EGC, but also the proportion of Ib disease was <1/3 of the whole patients.

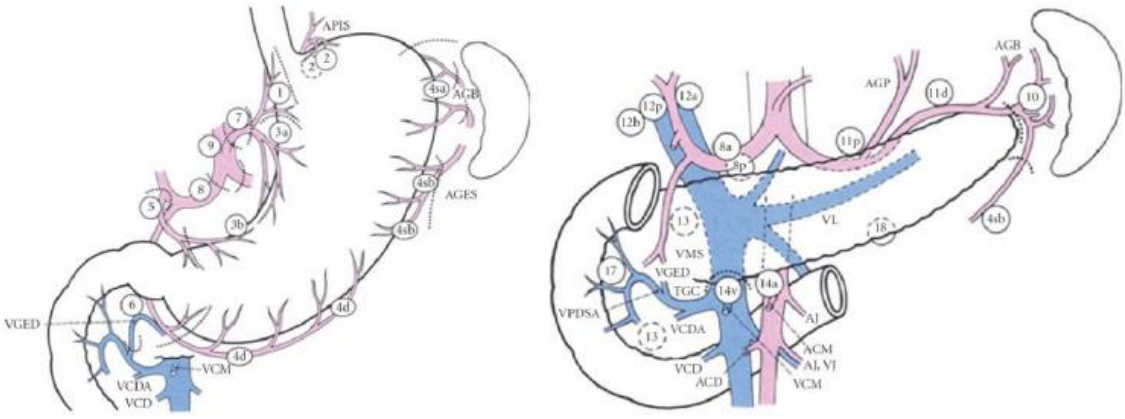

Figure 1 Lymph Node stations according to the Japanese classification. From Japanese Gastric Cancer Association, Japanese Classification of Gastric Cancer, Kanehara & Co., Ltd, Tokyo, Japan, 14th edition, 2010

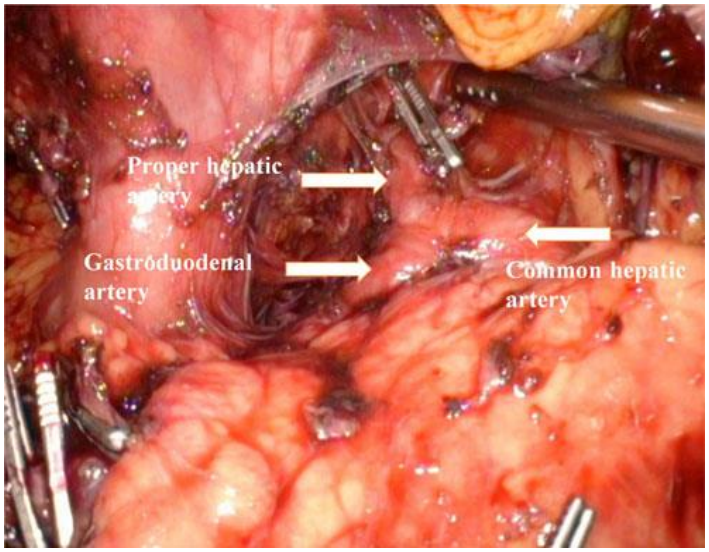

Figure 2 Laparoscopic image around the proper hepatic artery, common hepatic artery, and gastroduodenal artery after lymph node dissection

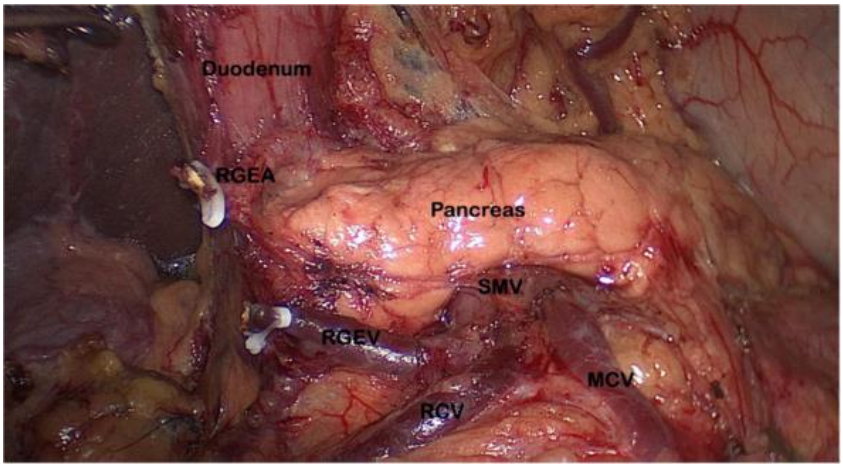

Figure 3 Dissection of the lymph node numbers 6 and 14v. MCV: middle colic vein; RCV: right colic vein; REGV: right gastroepiploic vein; RGEA: right gastroepiploic artery; SMV: superior mesenteric vein.

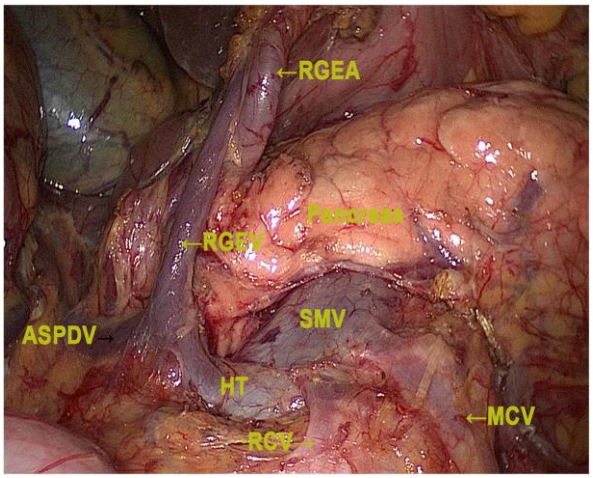

Figure 4 Dissection of lymph node number 6. RGEV, right gastroepiploic vein; RGEA, right gastroepiploic artery; ASPDV, anterior superior pancreaticoduodenal vein; SMV, superior mesenteric vein; RCV, right colic vein; HT, Herne's trunk; MCV, middle colic vein

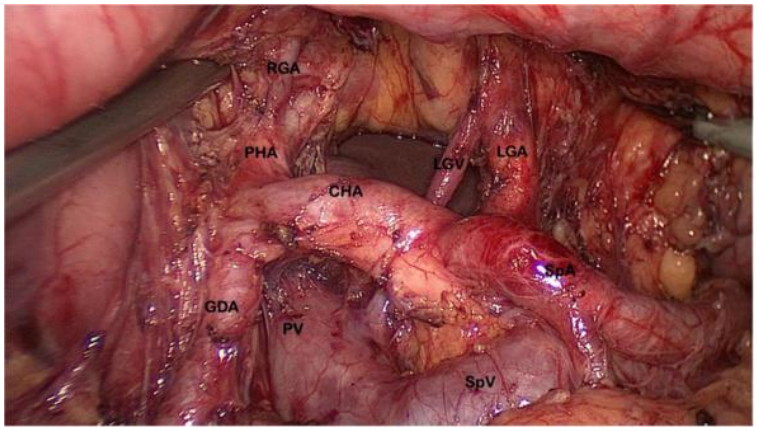

Figure 5 Dissection of the lymph node numbers 7, 8, 9, 11p and 12a. CHA: common hepatic artery; GDA: gastroduodenal artery; LGA: left gastric artery; LGV: left gastric vein; PHA: portal hepatic artery; PV: portal vein; SpA: splenic artery; SpV: splenic vein

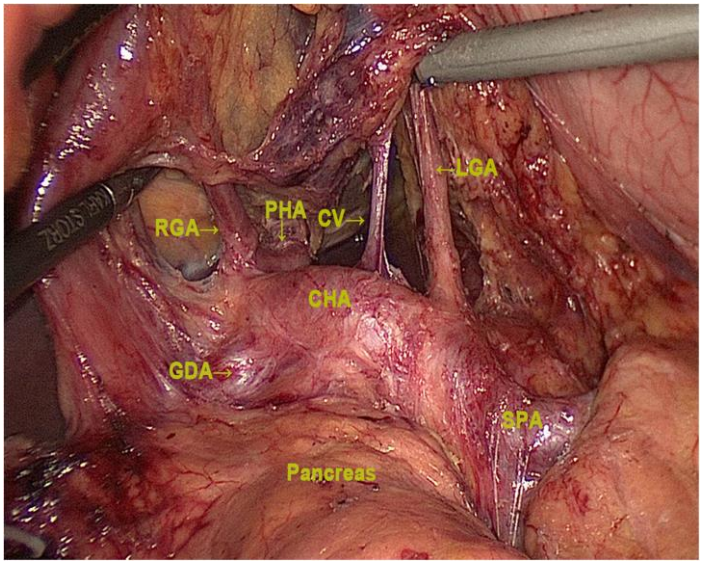

Figure 6 Dissection of lymph nodes numbers7, 8a, 9, 12a, 11p. LGA, left gastric artery; RGA, right gastric artery; CV, coronary vein; CHA, common hepatic artery; PHA, proper hepatic artery; GDA, gastroduodenal artery; SPA, splenic artery.

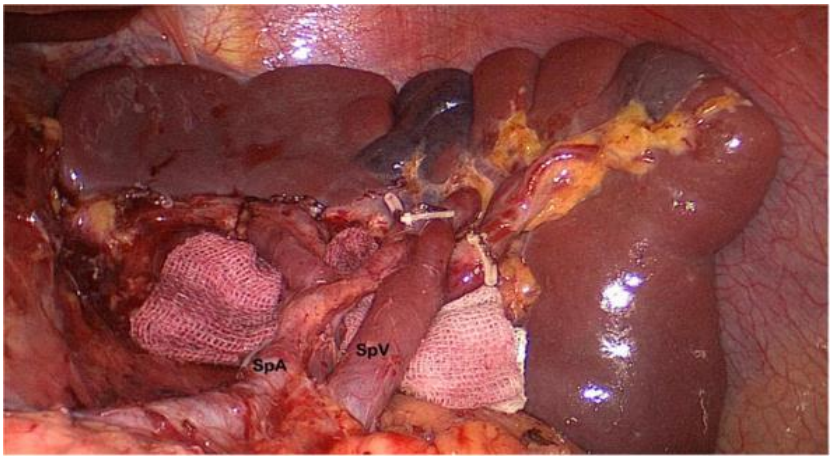

Figure 7 Dissection of the lymph node numbers 11d and 10. SpA: splenic artery; SpV: splenic vein.

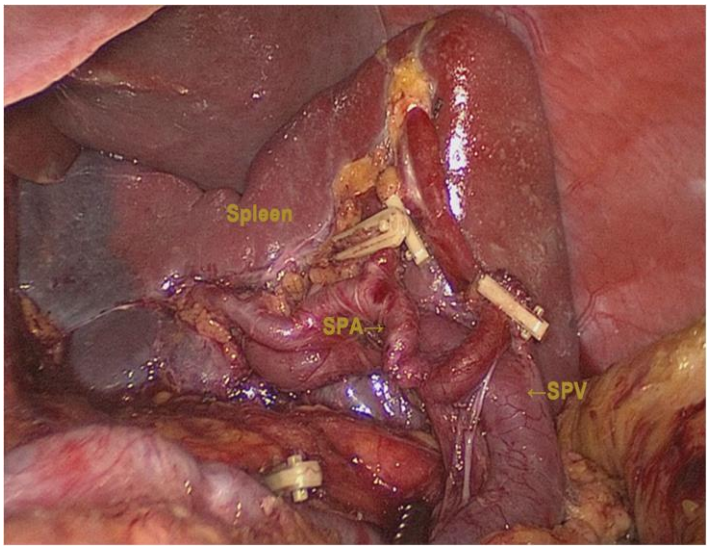

Figure 8 Dissection of the splenic hilum preserving the splenic artery and vein. SPA, splenic artery; SPA, splenic vein.

MATERIALS AND METHODS

Literature search

All trials (RCTs and non-RCTs) and meta-analyses were identified by searching the Pubmed, EMBASE and Cochrane Library databases for studies published between 1 January 2000 to 31 December 2014. Only articles published in English were included in this study. The search strategy was based on the following medical subject heading terms: stomach neoplasms; stomach cancer; gastric cancer; laparoscopy; laparoscopic; laparoscopy-assisted gastrectomy; laparoscopic-assisted gastrectomy; minimally invasive; open gastrectomy; conventional gastrectomy; D2 lymph node dissection; D2 gastrectomy; extended; radical. Logical combinations of these and related terms were used to maximize sensitivity. Additional relevant articles were identified using references of relevant articles and previous meta-analyses.

Method of review

One reviewer (AM) evaluated all retrieved studies to determine if they met the criteria, to assess study quality and extract data. The extracted information comprised: study features, clinical, surgical and pathological parameters (sample size, age, BMI, tumor size, extend of lymphadenectomy, type of GI reconstruction, conversion rate, tumor stage). The following outcome parameters were collected: operative time, intraoperative bleeding, number of resected and positive lymph nodes, time to first flatus, time to liquid diet, postoperative hospital stay, complications, morbidity and mortality. The study team resolved all of their disagreements through discussion to reach a consensus.

Inclusion criteria

Study design: RCTs and non-RCTs
Target population: LGD2 with OGD2 in patients with AGC (stage Ib-III), no evidence of local and distant metastasis, no neoajuvant therapy
Stage: Ib < 1/3 of all cases
Main purpose: comparing short and long-term outcomes of LADG and ODG with D2 dissection
Recorded the majority of the following: age, BMI, tumor size, serosa invasion status, number of HLNs, positive LN rate
Outcomes: short and long-term outcomes
Language: English

Exclusion criteria

Included EGC cases, malignant stromal tumors
Combined D1-D3 lymphadenectomy
>1/3 of cases be stage Ib
Hand-assisted, robotic surgery, emergency operations
Neoadjuvant therapy
Recurrent gastric cancer or palliative resection cases
Insufficient data; duplicate publications

Quality Assessment of Literature

The (modified) Newcastle-Ottawa Quality Assessment star scoring system was used to evaluate the quality of all the included studies. The scale is comprised of seven elements that assess patient population and selection, study comparability, follow-up and outcome of interest. In assessing comparability between groups, focus was on the variables that might affect primary endpoints such as, patient age and sex, pathologic tumor-node-metastasis stage, type of gastrectomy, resection margin, tumor size, histologic type, reconstruction, and adjuvant treatment.Studies were scored using an ordinary star scale so as to compare their quality, with higher scores representing higher quality. A maximum of one star was awarded to a study for each numbered item within the selection and outcome assessment. A maximum of two stars was awarded for the comparability of the two groups. The total score was 9 stars and the quality of each article was graded as level 1/low quality (0-5 stars) or level 2/high quality (6-9 stars).
RCTs were evaluated by the Jadad composite scale. High-quality trials scored more than 2 out of a maximum possible score of 5.

Definitions

AGC was defined as malignant neoplasmatic growth beyond the submucosal layer of the stomach. Locally AGC is the subgroup which does not contain stage IV. LG was defined as total LG or laparoscopy-assisted gastrectomy. In all included studies, D2 lymph node dissection was performed according to the JGCA lymph node classification[56], which state that lymph node numbers 1, 3, 4sb, 4d, 5, 6, 7, 8a, 9, 11p and 12a should be dissected.
The evaluated endpoints were classified as operative outcomes (operative time, intraoperative blood loss, conversion rate), postoperative outcomes (postoperative analgesic consumption, time to first ambulation, time to first flatus, time to first oral intake, length of postoperative hospital stay, incidence of reoperation, postoperative morbidity and mortality) and oncologic outcomes (number of harvested LNs, tumor

recurrence and metastasis, disease-free and overall survival rates). The primary endpoints were postoperative morbidity and mortality and overall survival rates.
Morbidity is defined as the incidence of 30-day postoperative complications and the mortality as 30-day mortality. Postoperative complications were classified as organ injury, intra-abdominal bleeding, anastomotic leakage, duodenal stump fistula, lymporrhea, ileus, pancreatitis, intra-abdominal abscess, anastomotic stenosis, wound infection. Pneumonia, pleural effusion, cardiocerebral vascular complications were classified as nonsurgical.

RESULTS

Descriptive assessment and study characteristics

Of the publications identified in the initial litearture search, 11 trials (1 RCT, 10 non-RCTs) were included in the analyses, published between 2010 and 2014 [57][58][59][60][61][62][63][64][65][66][67]. A total of 1693 participants (883 in the LGD2 group and 810 in the OGD2 group) were included in the study (Figure 9, Table 1). 9 of the studies were conducted in China, 1 Korea and 1 in Italy. In the laparoscopic group, all of the procedures were laparoscopically-assisted performed. Of the 1693 gastrectomies, 906 were total, 699 were distal and 88 were proximal, almost equally distributed for either group.

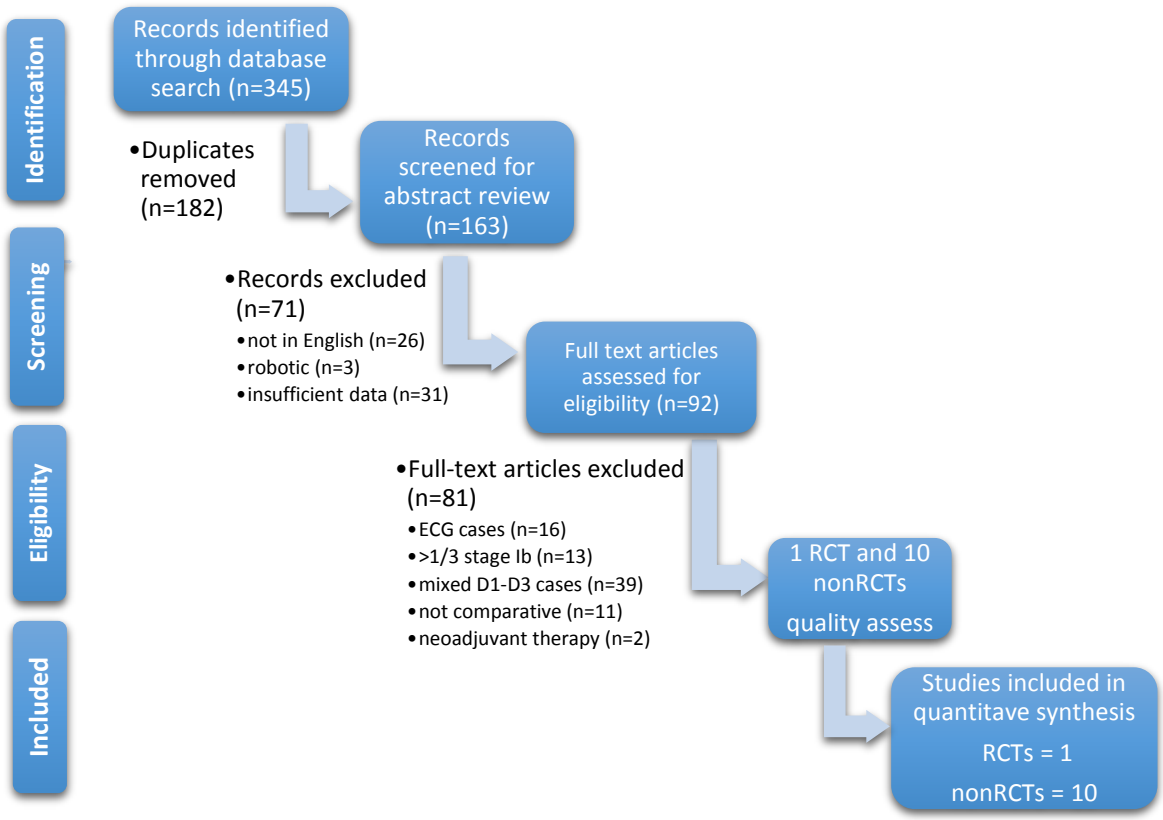

Figure 9 Flow chart of the identification and inclusion of studies

Publication	*Study design*	*Country*	*Journal Year*	*Study period*	*LADG2 ODG2*	*Type of gastrectomy*
Fang C[57]	nonRCT	China	Am J Surg 2014	2005-2009	87 - 87	46 / 46 Distal 41 / 41 Total
Lin J[58]	nonRCT	China	Chin Med J (Engl) 2014	2009-2011	58 - 58	58 / 58 Total
Cai J[59]	nonRCT	China	Hepatogastroenterology 2013	2008-2011	41 - 43	25 / 27 Total 16 / 16 Prox
Li ZX[60]	nonRCT	China	J BUON 2013	2009-2011	106 - 133	22 / 31 Distal 84 / 102 Total
Lin JX[61]	nonRCT	China	World J Surg Oncol 2013	2008-2010	83 - 83	37 / 37 Total 46 / 46 Distal
Chen QY[62]	nonRCT	China	World J Surg Oncol 2012	2008-2012	224 - 112	106 / 61 Total 118/ 51 Distal
Kim KH[63]	nonRCT	Korea	Dig Surg 2012	1999-2007	88 - 88	18 /30 Total 69 / 58 Distal 1 / 0 Proximal
J. Cai D[64]	RCT	China	Dig Surg 2011	2008-2009	49 - 47	4 / 1 Total 19 / 17 Distal 26 / 29 Prox
Scatizzi M[65]	nonRCT	Italy	Updates Surg 2011	2006-2009	30 - 30	30 / 30 Distal
Shuang J[66]	nonRCT	China	J Gastrointest Surg 2011	2005-2007	35 - 35	35 / 35 Distal
Du J[67]	nonRCT	China	Hepatogastroenterology 2010	2005-2009	82 - 94	82 / 94 Total
TOTAL					**1693 (883-810)**	**906 Total / 699 Distal / 88 Proximal**

Table 1 Study characteristics

Clinicopathological characteristics

The mean age was 60,9 for the LDG2 group and 60,6 for the OGD2 grou (Table 2). Ten studies reported the BMI status and all of them showed no significant difference between the two groups.

Two of the nine trials which recorded the tumor size, demonstrated that this was statistically different between the laparoscopic and open group.

Of the patients that were included in this review no one had EGC. The maximum percentage for Ib disease was 33,4 % for each study, and in seven out of the eleven studies this percentage was <20%. The mean proportion of Ib disease in our review was just below 15% for each group.

Study quality

The quality of all 10 non-RCTs was level 2 (6-9 stars) on the modified Newcastle-Ottawa scale and good for the RCT according to the Jadad composite scale (Table 3).

Publication	*Age*	*BMI*	*Tumor size*	*Pathological stage (Ib:II:III)*	*% Ib*	*Adjuvant therapy*	*Follow-up (months)*	*Follow-up rate*
Fang C	57 (33-82) / 56 (33-79) [p NS]	23,3 (18,3-31,6) / 22,9 (18,3-31,6)	NR	19:**38**:30 / 19:**29**::39	21,8% / 21,8%	NR	44 (1-82)	96,6% / 94,8%
Lin J	61,4 ± 9,2 / 60,9 ± 9,4 [p 0,853]	22,0 ± 2,6 / 22,0 ± 2,7 [p 0,981]	5,3 ± 1,9 / 5,4 ± 2,7 [p 0,896]	7:**21**:30 / 9:**21**:28	12,1% / 15,5%	NR	24,0 (2-50)	NR
Cai J	61,9 ± 9,1 / 60,1 ± 9,2 [p 0,362]	22,2 ± 3,0 / 23,0 ± 2,7 [p 0,215]	3,3 ± 1,1 / 3,7 ± 1,2 [p 0,135]	3:**15**:23 / 1:**25**:17	7,3% / 2,3%	YES	24 (4-54)	NR
Li ZX	62,3 ± 8,4 / 63,0 ± 8,8 [p 0,252]		4,1 ± 2,5 / 4,4 ± 2,6 [p 0,185]	NR	≤17,9% / ≤15,8%	NR	15 (3 -39)	92,1%
Lin JX	61,6 ± 10,3 / 61,1 ± 10,5 [p 0,777]	22,3 / 21,5 [p 0,113]	4,6 ± 2,1 / 4,4 ± 2,2 [p 0,631]	16:**26**:31 / 16:**38**:30 [p 0,958]	19,3% / 19,3%	YES	23,0 (12 - 50)	96,40%
Chen QY	61,6 ± 10,6 / 60,8 ± 10,2 [p 0,525]	22,3 / 22,0 [p 0,498]	4,7 ± 2,0 / 4,4 ± 2,0 [p 0,631]	40:**109**:85 / 25:**51**:36 [p 0,958]	17,9% / 22,3%	NR	19,0 (1 - 48)	94,6% / 92,9%
Kim KH	56,0 ± 13,5 / 59,0 ± 13,1 [p 0,147]	22,9 ± 3,0 / 22,5 ± 3,0 [p 0,414]	3,8 ± 2,2 / 5,2 ± 2,7 [p 0,0001]	32:**35**:13 / 28:**33**:27	33,4%/31,8%	YES	53,7 (8,3-138,1) / 58,1 (0,3-106,2) [p 0,212]	NR
J. Cai D	60,16 ± 9,78 / 60,27 ± 10,18 [p 0,956]	21,99 ± 3,29 / 22,88 ± 2,76 [p 0,162]	4,2 ± 2,0 / 4,3 ± 1,8 [p 0,671]	14:**13**:22 / 11:**17**:19 [p 0,733]	28,5% / 23,4%	YES	22,1 (4-36)	NR
Scatizzi M	70 (39-87) / 69 (43-86) [p 0,861]	22 (17-21) / 24 (16-42) [p 0,316]	7,2 (25-115) / 5,6 (10-130) [p 0,651]	0:**12**:18 / 0:**10**:20 [p 0,620]	0% / 0%	NR	18 (2-37) / 18 (7-42)	NR
Shuang J	58 (36-78) / 59 (24-78)	21 (18-30) / 23 (16-28)		10:**15**:10 / 9:**13**:13	28,6% / 25,7%	NR	36,5 (23-50) / 38,5 (27-50)	NR
Du J	60,4 ± 18,5 / 57,8 ± 17,2 [p 0,336]	22,3 ± 2,6 / 22,5 ± 2,4 [p 0,589]	5,4 ± 1,4 / 5,9 ± 1,6 [p 0,030]	3:**36**:43 / 6:**31**:57	3,7% / 6,4%	YES	22,5 (2-44)	96,3% / 95,7%

Table 2 Clinicopathological characteristics (LADG2 / ODG2)

	Selection[a]			Combarability[b]		Outcomes[c]		
Publication	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***Total score***
Fang C[57]	*	*	*	**	**	*		8*
Lin J[58]	*	*	*	**	*	*	*	8*
Cai J[59]	*	*	*	**	**	*		8*
Li ZX[60]	*	*	*	*	*	*	*	7*
Lin JX[61]	*	*	*	**	*	*	*	8*
Chen QY[62]	*	*	*	**	**	*	*	9*
Kim KH[63]	*	*	*	**	**	*	*	9*
Scatizzi M[65]	*	*	*	**	*	*	*	8*
Shuang J[66]	*	*	*	**	*	*		7*
Du J[67]	*	*	*	**	**	*	*	9*

	Randomization		Blinding			
Publication	***Mentioned***	***Appropriated***	***Mentioned***	***Appropriated***	***An account of all patients***	***Total score***
J. Cai D[64]	1	0	0	0	1	2

Table 3 Modified Newcastle-Ottawa scale and Jadad composite scale for quality assessment of nonRCTs and RCTs respectively

***a*Selection**: (1) Assignment for treatment: One star was assigned if details of criteria for assignment of patients to treatments provided. (2) One star was assigned if the laparoscopic-assisted distal gastrectomy group was representative of patients for gastric cancer; no star was assigned if groups of patients were selected or selection of the group was not described. (3) One star was assigned if the open distal gastrectomy group was representative of patients for gastric cancer; no star was assigned if groups of patients were selected or selection of the group was not described.

***b*Comparability:** Comparability variables were as follows: 1, age; 2, sex; 3, depth of tumor invasion on preoperative diagnosis; 4, extent of lymphadenectomy; 5, median or mean follow-up; 6, American Society of Anesthesiologists status; 7, tumor size; 8, postoperative pathologic stage; and 9, histological type. (4) Two stars were assigned if the groups were all comparable for the variables 1–5; 1 star was assigned if one of these five characteristics was not reported, even if there were no other differences between the groups, and other characteristics had been controlled for; and no star was assigned if the two groups differed. (5) Two stars were assigned if the groups were all comparable for the variables 6–9; 1 star was assigned if one of these four characteristics was not reported, even if there were no other differences between the groups, and other characteristics had been controlled for; and no star was assigned if the two groups differed.

***c*Outcomes:** (6) One star was assigned if primary outcome parameters were clearly defined. (7) One star was assigned if more than 90% of patients were followed up.

Analyses of operative outcomes

Operative time has been provided by all of the studies. Seven of them showed significant longer operative times in the laparoscopic group, with an mean difference of 67,66 minutes (Table 4).

Blood loss was found in 9 studies. Eight of them revealed significant lower blood loss in the laparoscopic group, with a mean amount of 124,65 ml less loss (Table 5). The number of transfused patients was recorded in 4 studies, three of which have shown significant difference against the OGD2 group (Table 6).

Conversion rates were documented in four studies, ranging from 0,0% to 6,67% with an average of 3,19%. The authors reported the following reasons for converting to open procedures: uncontrolled bleeding (n=2); overlarge tumor (n=1); lack of pneumoperitoneum (n=1); technical difficulties (n=1); hardly distinguished posterior stomach wall from the pancreas (n=1); hard to dissect no. 7,8 and 11 lymph nodes (n=1) (Table 7).

Publication	***LADG2***	***ODG2***	***p***
Fang C	337 (240-650)	224 (145-500)	<0,01
Lin J	235,7 ± 67,2	245,4 ± 54,5	0,118
Cai J	269,2 ± 49,2	188,7 ± 44,4	0,001
Li ZX	268 ± 51	261 ± 49	0,142
Lin JX	212,7 ± 57,2	226,4 ± 63,5	0,214
Chen QY	207,2 ± 137,3	213,0 ± 54,7	0,667
Kim KH	228,3 ± 49,4	183,6 ± 42,7	<0,0001
J. Cai D	270,51 ±55,27	187,66 ± 40,18	<0,0001
Scatizzi M	240 (160-90)	180 (120-240)	0,001
Shuang J	320 (260-570)	210 (138-300)	<0,01
Du J	275 ± 78	212 ± 51	<0,001

Table 4 Operative time (min)

Publication	*LADG2*	*ODG2*	*p*
Fang C	220 (50-400)	310 (100-600)	<0,05
Lin J	74,0 ± 80,1	218,4 ± 195,2	0,000
Cai J	219,5 ± 125,4	303,3 ± 163,6	0,010
Li ZX	134,0 ± 66	289 ± 139	0,000
Lin JX	78,4 ± 77,9	200,4 ± 218,3	0,000
Chen QY	82,7 ± 101,3	213,0 ± 54,7	0,000
J. Cai D	293,67 ± 164,49	344,47 ± 219,65	0,205
Shuang J	200 (100-600)	300 (100-1100)	<0,05
Du J	156 ± 112	339 ± 162	<0,001

Table 5 Blood loss (ml)

Publication	*LADG2*	*ODG2*	*p*
Lin J	2	3	0,648
Li ZX	5	19	0,000
Lin JX	3	11	0,025
Chen QY	4	8	0,029

Table 6 Number of transfused patients

Publication	*Conversion*
Li ZX	2,80%
J. Cai D	3,28% (2)
Scatizzi M	6,67% (2)
Du J	0%

Table 7 Conversion rates

Analyses of post-operative outcomes

Analgesic administration duration was reported in four articles included in this study. All of them showed a significantly shorter duration of analgesic use in the laparoscopic group compared to the open group, with an average of 1,9 days (Table 8).

The time to first ambulation was documented in 7 studies. Only two of them revealed significant difference between the two controls, with the patients in the OGD2 group ambulating on average 1,65 days after the LGD2 (Table 9).

The time to first flatus was reported in nine studies. All but two showed significantly shorter time in the LGD2 than in the OGD2 group, i.e. an average of 1,1 days (Table 10).

The time to first oral intake was found in 7 seven papers. Five of them demonstrated this time significantly shorter in the LGD2 group than in the OGD2 patients. Indeed, the former began liquid intake in a mean 4,66 days after surgery, whereas the former began 5,64 days postoperatively (Table 11).

The number of days during which the body temperature was over 37 ^{o}C was recorded in three studies. All of them showed statistically different advantage of 2,2 days for the laparoscopic group (average 3,3 days compared to 5,5 days in the open group) (Table 12).

The length of postoperative hospital stay was reported in 10 articles. Seven of them revealed significant advantage over the laparoscopic group, i.e. an average of 3,67 days less hospitalization. Furthermore, one of the remainder 3 studies showed no statistical difference between the two groups when complications postoperatively occurred, but with a significant advantage over the LAGD2 group when the postoperative was uncomplicated (Table 13).
The postoperative morbidity rates were reported in all eleven studies and all of them showed no statistical difference regarding the complication rates between the two groups. However, the subgroup analyses in three of the trials demonstrated significantly lower incidence rates of nonsurgical (cardiovascular, pulmonary) complications after LADG2. No difference in the incidence rate of major surgical site complications, such as anastomosis stenosis, anastomotic leakage, duodenal stump leakage, pancreatic fistula, pancreatitis and intra-abdominal bleeding, was found between the two groups.
The reoperation incidence was reported in only one article with the LDG2 group having a slight higher rate compared to the ODG2 group (2,3% vs 1,1%) (Table 14).
The postoperative in-hospital mortality rates were reported in 8 studies with no significant difference in the rate between the LGD2 and OGD2 groups (Table 15).

Publication	***LADG2***	***ODG2***	***p***
Lin JX	3,1 ± 1,2	5,8 ± 2,0	0,006
Scatizzi M	3 (1-10)	4,5 (3-11)	0,048
Shuang J	3 (0-5)	4 (1-6)	<0,01
Du J	1,3 ± 1,2	3,8 ± 1,4	<0,001

Table 8 Duration of analgesic administration (days)

Publication	***LADG2***	***ODG2***	***p***
Lin J	2,7 ± 1,0	2,8 ± 1,1	0,458
Cai J	4,2 ± 1,5	5,0 ± 1,1	0,014
Lin JX	2,6 ± 1,1	2,7 ± 1,1	0.577
Chen QY	2,7 ± 1,2	2,9 ± 1,2	0.099
J. Cai D	4,78 ± 2,09	4,89 ± 1,54	<0,753
Scatizzi M	1 (0-3)	1 (1-5)	0,659
Du J	2,4 ± 1,1	4,9 ± 1,4	<0,001

Table 9 Time to first ambulation (days)

Publication	***LADG2***	***ODG2***	***p***
Lin J	2,6 ± 1,1	3,7 ± 1,1	0,028
Cai J	3,9 ± 1,5	4,3 ± 1,1	0,118
Li ZX	3,4 ± 0,9	5,0 ± 1,4	0,000
Lin JX	2,9 ± 1,2	2,9 ± 1,2	0,038
Chen QY	2,6 ± 1,1	3,2 ± 1,1	0,000
Kim KH	3,2 ± 0,9	3,7 ± 0,9	<0,0001
J. Cai D	3,89 ± 1,65	4,21 ± 1,25	0,293
Scatizzi M	2 (1-4)	3 (2-5)	0,036
Du J	3,5 ± 0,8	5,3 ± 1,3	<0,001

Table 10 Time to first flatus (days)

Publication	*LADG2*	*ODG2*	*p*
Lin J	4,2 ± 1,5	5,5 ± 2,3	0,031
Cai J	7,0 ± 1,7	7,2 ± 2,0	0,692
Li ZX	7,3 ± 1,3	8,1 ± 1,4	0,031
Lin JX	4,1 ± 1,5	5,5 ± 2,3	0,041
Chen QY	4,7 ± 1,5	5,1 ± 1,8	0,034
J. Cai D	6,85 ± 1,81	6,47 ± 1,67	<0,277
Scatizzi M	3 (1-5)	4 (1-10)	0,020

Table 11 Time to first oral intake (days)

Publication	*LADG2*	*ODG2*	*P*
Cai J	3,4 ± 1,5	6,0 ± 3,4	0,001
J. Cai D	3,55 ± 1,62	6,11 ± 3,42	<0,0001
Du J	2,8 ± 0,7	4,4 ± 0,8	<0,001

Table 12 Days with body T >37 ºC

Publication	*LADG2*	*ODG2*	*P*
Fang C	12 (5-36)	18 (7-45)	<0,01
Lin J	14,2 ± 6,9	18,1 ± 5,3	0,012
Cai J	12,2 ± 3,3	11,8 ± 2,2	0,463
Li ZX	12,8 ± 6,9	14,5 ± 3,1	0,000
Lin JX	14,2 ± 7,2	17,2 ± 5,0	0,000
Chen QY	13,3 ± 5,7	17,4 ± 5,0	0,000
Kim KH	uncomplicated 7,0 ± 1,3	uncomplicated 10,4 ± 7,1	<0,0001
	complicated 9,5 ± 14,7	complicated 10,3 ± 6,9	0,618
J. Cai D	11,63 ± 2,95	11,43 ± 1,17	0,65
Scatizzi M	7 (6-50)	9 (6-23)	0,029
Shuang J	12 (5-36)	17 (8-45)	<0,01

Table 13 Length of postoperative hospital stay (day)

Publication	*LADG2*	*ODG2*	*p*
Fang C	6,9%	5,7%	NSD
Lin J	12,1%	15,5%	0,744
Cai J	14,6%	23,3%	0,314
Li ZX	non-surgical complications 14,2%	non-surgical complications 24,8%	0,029
	surgical complications NSD	surgical complications NSD	NSD
Lin JX	12%	14,4%	0,819
Chen QY	11,1%	15,3%	0,266
Kim KH	8%	8%	0,605
J. Cai D	non-surgical complications 4,1%	non-surgical complications 17,0%	0,038
	surgical complications 12,24 %	surgical complications 19,15%	0,357
Scatizzi M	non-surgical complications 0%	non-surgical complications 20%	0,048
	surgical complications 6,67%	surgical complications 6,67%	1,0
Shuang J	5,7%	8,6%	NSD
Du J	9,8%	24,5%	0,214

Table 14 Postoperative morbidity

Publication	*LADG2*	*ODG2*	*P*
Fang C	0%	0%	
Lin J	0%	1,7%	1,000
Cai J	0%	0%	
Li ZX	0%	0%	
Lin JX	1,2%	2,4	1,000
Chen QY	0,9%	1,8%	0,859
Kim KH	0%	0%	
Du J	0%	2,1%	NSD

Table 15 Postoperative in-hospital mortality

Analyses of oncologic outcomes

The number of lymph nodes harvested was reported in 10 studies and no significant difference has been shown in this parameter (Table 16).

Tumor recurrence was documented in four studies, which all demonstrated no significant difference in this rate (Table 17).

One study involving 176 patients provided 5-year disease-free survival rates and another one with 174 patients provided DFS rates during a mean follow-up of 44 months. The two groups showed no significant difference among these rates (Table 18).

One trial involving 176 patients provided 5-year overall survival rates and two trials 156 patients provided. 3-year overall survival rates. Three further studies including 174, 84 and 239 patients with 44, 24 and 15 months follow-up respectively, provided overall survival rates. None of these studies demonstrated significant differences between the two groups regarding the overall survival rates (Table 19).

Publication	***LADG2***	***ODG2***	***P***
Lin J	30,8 ± 10,6	29,0 ± 8,3	0,114
Cai J	23,3 ± 2,9	22,3 ± 1,5	0,051
Li ZX	29,1 ± 6,1	30,2 ± 7,0	0,100
Lin JX	30,2 ± 10,1	28,0 ± 8,1	0,103
Chen QY	30,6 ± 10,1	30,3 ± 8,6	0,786
Kim KH	38,3	41,8	NSD
J. Cai D	22,98 ± 2,70	22,87 ± 2,43	0,839
Scatizzi M	31 (16-60)	37 (8-89)	0,174
Shuang J	35 (7-63)	38 (6-66)	NSD
Du J	34,2 ± 13,5	36,4 ± 19,1	0,331

Table 16 Number of harvested lymph nodes

Publication	***LADG2***	***ODG2***	***P***
Fang C	41,4%	51,7%	NSD
Lin J	NSD	NSD	NSD
Kim KH	17,1%	14,8%	0,837]
Du J	23,2%	24,5%	NSD

Table 17 Tumor recurrence

5-year				44-month		
Publication	***LADG2***	***ODG2***	***p***	***LADG2***	***ODG2***	***p***
Fang C				59%	48%	0,205
Kim KH	84,6%	81,1%	0,415			

Table 18 Disease free survival rates

5-year				3-year			2-year		
Publication	***LADG2***	***ODG2***	***p***	***LADG2***	***ODG2***	***p***	***LADG2***	***ODGG2***	***p***
Cai J							58,5%	60,5%	NSD
Kim KH	85,9%	83,1%	0,463						
J. Cai D				67,1%	53,8%	0,911			
Scatizzi M				70,91%	56,77%	0,449			

44-month				15-month		
Publication	***LADG2***	***ODG2***	***p***	***LADG2***	***ODG2***	***P***
Fang C	59%	54%	0,525			
Li ZX				100%	99,3%	>0,05

Table 19 Overall survival rates

DISCUSSION

At this time LDG for GC has gained acceptance for the clinical benefits that are offered, and numerous studies demonstrate the superiority over conventional open surgery such as less blood loss, less postoperative pain, accelerated recovery, shorter hospital stay, reduced postoperative morbidity[11][12][23][68][69][70][71]. LADG with limited lymphadenectomy (D1 or D1+) has been adopted worldwide as operation of choice in patients with EGC. Furthermore, with the development of the laparoscopic instruments and techniques in complex gastric surgery, more surgeons prefer to perform total gastrectomy laparoscopically, and some studies indicated even the superiority of LTG over the open procedure[72][73][74]. Nevertheless, debate on oncological adequacy and postoperative outcomes render the use of LGD2 for AGC still controversial and it remains questionable regarding the difficulty of D2 lymph node dissection. Therefore, we performed this systematic review to assess the value of LAGD2 for AGC. In order to achieve more accurate results regarding the survival rates we only included studies that had no ECG cases and a maximum proportion of 33,3% of stage Ib disease.

Our literature review identified 1 RCT and 10 non-RCTs that met our criteria and examined whether LGD2 is an acceptable alternative to OGD2 for AGC from a clinical perspective. Only one study was carried out by the scholars in Italy and the remainder were conducted in Eastern countries. No significant difference of characteristics such as age, BMI and tumor size found between the two groups, indicating the fact that the two groups were comparable. The results suggest that despite LGD2 being a technically demanding and time-consuming procedure with longer operative times and acceptable conversion rates, it can be used to achieve short- and long-term prognosis.

Indeed, this comparison between LGD2 and OGD2 revealed similar numbers of harvested lymph nodes, tumor recurrence and disease-free and overall survival rates. Moreover, LGD2 provides better short-term prognoses with lower postoperative pain, faster recovery and shorter hospital stays. There was also a lower postoperative non-surgical related morbidity associated with LDG2.

Main reasons for long operative times that can be seen in LADG2 include long learning curve, time for setting up the laparoscopic equipment, lack of tactile sensation, the extent of lymphadenectomy and the postresectional gastrointestinal tract reconstruction. Longer procedures mean prolonged anesthesia and pneumoperitoneum, which may have a negative impact on the mortality and morbidity rates, especially in elderly patients with comorbidities[24]

The less the operative blood loss is, as well as the less blood is transfused, the lower the postoperative mortality is due to acute or late adverse effects (ALI, hypothermia, volume overload, etc)[75]. Less pain during the postoperative period suggests not only earlier recovery and better quality of life, but also less patient cost. The postoperative pain the patients suffered was evaluated by counting the rate of analgesic use, because the feeling of pain is difficult to measure due to its subjectivity. Time to first flatus, which is mainly affected by the extent of surgical trauma, is thought to be an ideal objective indicator for alimentary tract recovery, when compared to postoperative feeding. Earlier passage of flatus represents quicker return of the bowel function, which leads to faster administration of liquid diet and an earlier discharge from the hospital. Shorter hospital stay is cost-effective and reduces the pressure on hospital beds.

The postoperative complication rate is usually used to assess the safety of such procedures. All the prementioned advantages come undoubtedly as a result of the minimal invasiveness and the use of small incision, which is responsible for the reduction of the surgical stress and the consequent decrease of the generalized inflammatory reaction, that may leads to minimalization of the postoperative morbidity.

To estimate the quality of oncological adequacy and assess the long-term outcome the number of HLN is a fundamental subject. Cancer recurrence and long-term survival rates are of critical importance when evaluating such interventions in oncological therapy. Laparoscopic surgeons must overcome the complexity of the technique and focus on the quality of the D2 lymph node dissection in order to fulfill the aspects of an oncologically safe D2 surgery[76][77]. Indeed, the majority of clinical studies correlate the quality of the procedure with the number of the HLN and many of them compare D2 lympadenectomy between LADG and ODG[78][79][80][81][82][83][84][85]. An accepted D2 lymph node dissection should harvest a minimum of 15 nodes for pathologic examination, but usually an average number of 25 nodes is harvested. Most studies were collected from eastern countries due to the preference of the majority of the Asian surgeons to perform D2 dissection. It is important to highlight that compared with the patients in Western countries, Asian patients are considered to be younger, slimmer and healthier[86], factors that are associated with better postoperative outcomes of the latter after open gastrectomy[43][87][88].

Lymph node stations 12a and 14v are rated as the most difficult anatomical positions for laparoscopic surgery. In order to reduce the chance of local recurrence and increase the survival rates many surgeons perform additional removal of lymph nodes around splenic artery and the hilus of the spleen, and those located in hepatoduodenal ligament. It is widely accepted that at least 30 cases of LADG with D1 resection should be performed in order for a surgeon to overcome the learning curve[89][90][91]. Yoo et al[92] concluded that after completing 50 LADG cases the operative time improved, without analogous reduction in complications. Laparoscopic D2 surgery is considered to be much more difficult for beginners, particularly when it comes to control the instruments, regulate the operation field, skeletonize major vascular structures and control intraoperative bleeding. Thus, LGD2 is not recommended in small volume centers. There is a nebulous relationship between the surgeon's experience and patients' safety; while some studies indicate that a high frequency of postoperative complications mainly occur in the very early learning period[93][94]. Indeed, training for laparoscopic second-tier lymph node dissection under a two-dimensional video is demanding in terms of selecting a reasonable surgical approach and achieving en bloc resection[91][95]. There are various ways for determining whether the learning curve has been overcome, with measures such as reaching a consistent operative time, confining the operative complications rate or retrieving a more than adequate number of lymph nodes. In order to overcome the complexity of this operation it is essential for a surgeon to accumulate cases, familiarize with the laparoscopic instruments and cooperate efficiently with the therapeutic team[90]. Through proficiency in laparoscopic technique and constant equipment enhancement, the time for performing a laparoscopic-assisted gastrectomy will be shortened[96].

The present study has several limitations. First, it is not a meta-analysis in order to reveal more accurate conclusions. Second, all but one of the included trials were observational. Third, most of the included studies were conducted at tertiary centers and major institutions in East Asia (9 China, 1 Korea and 1 in Italy). Hence, the included patients might not reflect general patient populations. Finally, this analysis was performed at the study level and did not address or incorporate individual factors at patient level.

In conclusion, although LGD2 is a technically demanding and time-consuming procedure, the results of this study suggest it may be an acceptable alternative to OGD2 for locally AGC. The procedure may yield comparable oncologic results and better short-term prognoses than OGD2. Through additional clicical trials that will evaluate this procedure, it remains to be confirmed whether laparoscopic D2 gastrectomy can guarantee the advantage of minimal invasion, in which way affects perioperative mortality and whether it can achieve the same degree of radicality as open surgery.

Abstract

AIM: Review of the literature collecting trials comparing laparoscopic (LGD2) and open D2 gastrectomies (OGD2) for the treatment of advanced gastric cancer (AGC).

METHODS: Randomized control trials (RCTs) and non-RCTs comparing LGD2 with OGD2 for AGC treatment, published between 1 January 2000 to 31 December 2014 were identified by searching the Pubmed, EMBASE and Cochrane Library databases. Primary endpoints included operative outcomes (operative time, intraoperative blood loss, number of transfused patients and conversion rates), postoperative outcomes (postoperative analgesic consumption, time to first ambulation, time to first flatus, time to first oral intake, duration of body temperature >37 ºC, length of postoperative hospital stay, postoperative morbidity, incidence of reoperation and postoperative in-hospital mortality), and oncologic outcomes (number of harvested lymph nodes, tumor recurrence, disease-free rates and overall survival rates). The modified Newcastle-Ottawa scale was used to assess the quality of RCTs and non-RCTs in the study.

RESULTS: One RCT and 10 non-RCTs with a total of 1693 patients were included in the review. LGD2 when compared to OGD2 demonstrated significant lower intraoperative blood loss [8 out of 9 studies; mean difference (MD) = 124,65 ml], shorter duration of analgesic administration (4 out of 4 studies; MD = 1,9 days), shorter times to first ambulation (2 out 7 studies; MD = 1,65 days), flatus (7 out of 9 studies; MD = 1,1 days), and oral intake (5 out of 7 studies; MD = 0,98 days), shorter length of body temperature > 37 ºC (3 out of 3 studies; MD = 2,2 days), shorter postoperative hospital stay (7 out 10 studies; MD = 3,67 days), lower incidence of nonsurgical complications (3 out of 3 studies). No significant differences were observed between LGD2 and OGD2 for the following criteria: postoperative in-hospital mortality, number of harvested lymph nodes, tumor recurrence, 5-year disease-free survival rates and five- or three-year overall survival rates. However, LGD2 had longer operative times (7 out of 11 studies; MD = 67,66 min).

CONCLUSION: Although a technically demanding and time-consuming procedure, LGD2 offers the advantages of minimal invasion and can achieve the same degree of radicality, harvested lymph nodes and short- or long-term prognosis for the treatment of locally AGC.

Περίληψη

ΣΚΟΠΟΣ: Ανασκόπηση της βιβλιογραφίας ώστε να συλλεχθούν μελέτες οι οποίες συγκρίνουν τη λαπαροσκοπική (LGD2) και ανοιχτή D2 γαστρεκτομὴ (OGD2) για την αντιμετώπιση του προχωρημένου γαστρικού καρκίνου (AGC).

ΜΕΘΟΔΟΣ: Με αναζήτηση στις βάσεις δεδομένων Pubmed, EMBASE, Cochrane Library αναγνωρίσθηκαν τυχαιοποιημένες (RCTs) και μη τυχαιοποιημένες μελέτες (non-RCTs) που δημοσιεύθηκαν μεταξύ 1 Ιανουαρίου 2000 και 31 Δεκεμβρίου 2014 και συνέκριναν τη LGD2 και OGD2 για την αντιμετώπιση του AGC. Στις βασικές παραμέτρους περιλαμβάνονταν εγχειρητικά αποτελέσματα (χρόνος επέμβασης, διεγχειρητική απώλεια αίματος, αριθμός μεταγγιζόμενων ασθενών και ποσοστά μετατροπής), μετεγχειρητικά αποτελέσματα (μετεγχειρητική χρήση αναλγητικών, χρόνος πρώτης κινητοποίησης, χρόνος πρώτων αερίων, χρόνος πρώτης δίαιτας, διάρκεια θερμοκρασίας >37 ºC, συχνότητα επανεπέμβασης και μετεγχειρητική εντός νοσοκομείου θνητότητα), και ογκολογικά συμπεράσματα (αριθμός λεμφαδένων, υποτροπή νόσου, διάστημα ελεύθερο νόσου και συνολική επιβίωση). Η τροποποιημένη κλίμακα Newcastle-Ottawa χρησιμοποιήθηκε για την εκτίμηση της ποιότητας των RCTs και non-RCTs της μελέτης.

ΑΠΟΤΕΛΕΣΜΑΤΑ: Μία τυχαιοποιημένη (RCT) και 10 μη τυχαιοποιημένες μελέτες (non-RCTs) με ένα σύνολο 1693 ασθενών συμπεριελήφθησαν στη μελέτη. Η LGD2 συγκριτικά με την OGD2 κατέδειξε σημαντικά λιγότερη διεγχειρητική απώλεια αίματος [8 από τις 9 μελέτες / μέση διαφορά (MD) = 124,65 ml], μικρότερη διάρκεια χορήγησης αναλγησίας (4 από τις 4 μελέτες / MD = 1,9 ημέρες), μικρότερους χρόνους πρώτης κινητοποίησης (2 από τις 7 μελέτες / MD = 1,65 ημέρες), αερίων (7 από τις 9 μελέτες / MD = 1,1 ημέρες), δίαιτας (5 από τις 7 μελέτες / MD = 0,98 ημέρες), μικρότερη διάρκεια θερμοκρασίας σώματος > 37 ºC (3 από τις 3 μελέτες / MD = 2,2 ημέρες), μικρότερη μετεγχειρητική παραμονή στο νοσοκομείο (7 από τις 10 μελέτες / MD = 3,67 ημέρες), μικρότερη συχνότητα μη χειρουργικών επιπλοκών (3 από τις 3 μελέτες). Μη στατιστικά σημαστική διαφορά παρατηρήθηκε μεταξύ LDG2 και ODG2 για τις ακόλουθες παραμέτρους: εντός νοσοκομείου θνητότητα, αριθμός συλλεχθέντων λεμφαδένων, υποτροπή νόσου, 5ετές διάστημα ελεύθερο νόσου και 5ετής ή 3ετής συνολική επιβίωση. Παρ'ολα αυτά, LDG2 είχε μεγαλύτερους χειρουργικούς χρόνους (7 από τις 11 μελέτες / MD = 67,66 λεπτά).

ΣΥΜΠΕΡΑΣΜΑ: Αν και τεχνικά απαιτητική και χρονοβόρα επέμβαση, η LDG2 προσφέρει τα πλεονεκτήματα της ελάχιστα επεμβατικά τεχνικής και μπορεί να επιτύχει τον ίδιο βαθμό ριζικότητας, συλλεχθέντων λεμφαδένων και βραχυ- ή μακροπρόθεσμης πρόγνωσης για την αντιμετώπιση του AGC.

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