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META-ANALYSIS

Is hand sewing comparable with stapling for anastomotic leakage after esophagectomy? A meta-analysis

Quan-Xing Liu, Jia-Xin Min, Xu-Feng Deng, Ji-Gang Dai

Quan-Xing Liu, Jia-Xin Min, Xu-Feng Deng, Ji-Gang Dai, Department of Thoracic Surgery, Xinqiao Hospital, Third Military Medical University, Chongqing 400037, China

Author contributions: Liu QX and Min JX contributed equally to this study; Min JX and Dai JG contributed substantially to conception and design of the study; Liu QX and Deng XF contributed to analysis and interpretation of all data and drafted the article; and Liu QX critically revised the article for important intellectual content.

Correspondence to: Ji-Gang Dai, MD, PhD, Department of Thoracic Surgery, Xinqiao Hospital, Third Military Medical University, No. 30 Gaotanyan Street, Shapingba District, Chongqing 400037, China. 691057831@qq.com
Telephone: +86-23-68774724 Fax: +86-23-68774724

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Abstract

AIM: To compare the outcome of hand sewing and stapling for anastomotic leakage after esophagectomy.

METHODS: A rigorous study protocol was established according to the recommendations of the Cochrane Collaboration. An electronic database search, hand search, and reference search were used to retrieve all randomized controlled trials that compared hand-sewn and mechanical esophagogastric anastomoses.

RESULTS: This study included 15 randomized controlled trials with a total of 2337 patients. The results revealed that there was no significant difference in the incidence of anastomotic leakage between the methods [relative risk (RR) = 0.77, 95% confidence interval (CI): 0.57-1.04; $P = 0.09$], but a subgroup analysis yielded a significant difference for the sutured layer and year of publication (Ps < 0.05). There was also no significant difference in the incidence of postoperative mortality (RR = 1.52, 95%CI: 0.97-2.40; $P = 0.07$). However, the anastomotic strictures rate was increased in the stapler group compared with the hand-sewn group (RR = 1.45, 95%CI: 1.11-1.91; $P < 0.01$) in the end-to-side subgroup, while the incidence of anastomotic strictures was decreased (RR = 0.34, 95%CI: 0.16-0.76; $P < 0.01$) in the side-to-side subgroup.

CONCLUSION: The stapler reduces the anastomotic leakage rate compared with hand sewing. End-to-side stapling increases the risk of anastomotic strictures, but side-to-side stapling decreases the risk.

Key words: Anastomotic leakage; Esophagectomy; Hand-sewn sutures; Mechanical sutures; Meta-analysis

Core tip: This was an important meta-analysis comparing the results of hand-sewn and stapling techniques for esophagogastric anastomosis after esophageal cancer resection. We performed some subgroup analyses that suggested some associations with anastomotic leakage: (1) the number of layers sutured (single or double); (2) year of publication (before 2003 *vs* 2003-2013); and (3) anastomotic sites (intrathoracic or cervical). A better understanding of this may yield a consensus for comparison of anastomotic leakage rate following the two methods of esophagogastric anastomosis after esophagogastrectomy for esophageal cancer.

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INTRODUCTION

Esophageal carcinoma is a multifaceted and complex disease process of rapidly rising incidence that exerts an increasing social and financial burden on global healthcare systems[1-3]. Currently, esophagectomy continues to be the standard treatment for esophageal cancer. After esophageal resection for carcinoma, the stomach is commonly used for restoring alimentary continuity. The success of esophagogastric anastomosis is closely correlated with the patient's outcome, including anastomotic leakage and stricture. Anastomotic leakage is a feared and frequent complication leading to increased hospital stay, and is a significant cause of early postoperative morbidity. Different anastomotic techniques have been described in order to minimize this risk.

Since the development of the mechanical stapler in the 1990s, there have been many reports showing that the stapler decreases the rate of leakage after esophagogastrostomy[4-7]. However, several meta-analyses recently conducted to compare hand-sewn and stapler anastomosis methods have revealed that there is no significant difference in the risk of developing anastomotic leakage, and the stapler method more frequently contributes to the development of anastomotic strictures[8-10]. These meta-analyses had some limitations: (1) they did not include all published randomized controlled trials (RCTs); and (2) the clinical heterogeneity among the included RCTs indicates that several subgroup meta-analyses are needed.

We conducted a systematic review and meta-analysis of RCTs that compared stapler and hand-sewn methods for esophagogastric anastomosis after esophagectomy, and examined the contribution of each method to the occurrence of anastomotic leakage, 30-d mortality, and anastomotic strictures. Subgroup analyses were also performed to evaluate the anastomotic leakage rate between the two methods related to the sutured layers, the anastomotic sites, and the year of publication. Through this pooled analysis, we hope to gain a consensus about treatment options for clinicians regarding esophagogastric anastomosis after esophagectomy.

MATERIALS AND METHODS

Study selection

The rigorous study protocol was established according to the recommendations of the Cochrane Collaboration. Before the meta-analysis, we pre-specified all the objectives, exclusion and inclusion criteria, major outcomes, and the methods used for synthesis to ensure the high quality of this meta-analysis.

Two investigators independently searched the Cochrane Library database Central, Medline, Embase, Chinese Biomedical Database and Chinese Scientific Journals Database (up to December 2013). All RCTs involving patients with esophageal cancer who underwent esophagogastric anastomosis after esophagectomy were included in the analysis. The search terms were "esophagectomy", "anastomosis", "esophagus", "hand-sewn", "manual", "stapled", "mechanical" and "gastric" and MeSH headings "anastomosis", "hand-sewn", "manual", "stapled", "mechanical" and "esophagectomy" were used in combination with the Boolean operators AND or OR. The electronic search was supplemented by a hand search of published abstracts from conference proceedings including the International Society for Diseases of the Esophagus, the China Esophageal Society Meeting, United European Gastroenterology Week, and some Surgery Associations. In reference searches, we scanned lists of trials that were selected from electronic searching to identify further associative trials. The two investigators independently obtained and reviewed copies of these full articles according to the inclusion criteria of this study. When disagreement occurred in the trial selection, it was discussed with another author to reach consensus.

Data collection and outcomes

Data were extracted by the two investigators using standardized forms. The quality of all selected articles was ranked in accordance with the Jadad composite scale[11]. According to this scale, low quality studies had a score $\leqslant$ 2 and high quality studies had a score $\geqslant$ 3.

The primary outcome measure for the meta-analysis was anastomotic leakage. The secondary outcome measures were 30-d mortality and anastomotic strictures (developing within 6 mo of operation and requiring endoscopy).

Statistical analysis

Statistical analysis was performed by RevMan version 5.2.9 (provided by the Cochrane Collaboration, Oxford, United Kingdom). The data extracted from the included trials were combined and the relative risk (RR) was calculated with 95% confidence intervals (CIs). The Cochran's Q statistic (χ^2 test) and the Higgins I^2 statistic were used to determine the percentage of total variations across studies due to heterogeneity. If the I^2 statistic was $\leqslant$ 50%, the fixed effect model was used to pool studies, otherwise, the random effects model was used. To examine clinical heterogeneity, the following subgroup analyses were conducted to evaluate the anastomotic leakage: (1) the site of anastomosis (intrathoracic *vs* cervical); (2) year of publication (2003-2013 *vs* before 2003); and (3) double or single suture layer for the hand-sewn method. For obvious clinical heterogeneity, we performed two subgroup analyses (side-to-side stapler *vs* hand-sewn, and end-to-side stapler *vs* hand-sewn) to evaluate the anastomotic stricture.

RESULTS

Characteristics of included trials

Fifteen RCTs (2337 patients) that met the inclusion criteria were identified; all were performed between 1990 and 2013[5,12-26] (Figure 1). Table 1 shows the details for each trial, including baseline characteristics, year of publication, anastomotic method, and Jadad score.

Anastomotic leakage

All 15 trials reported the incidence of anastomotic leak-

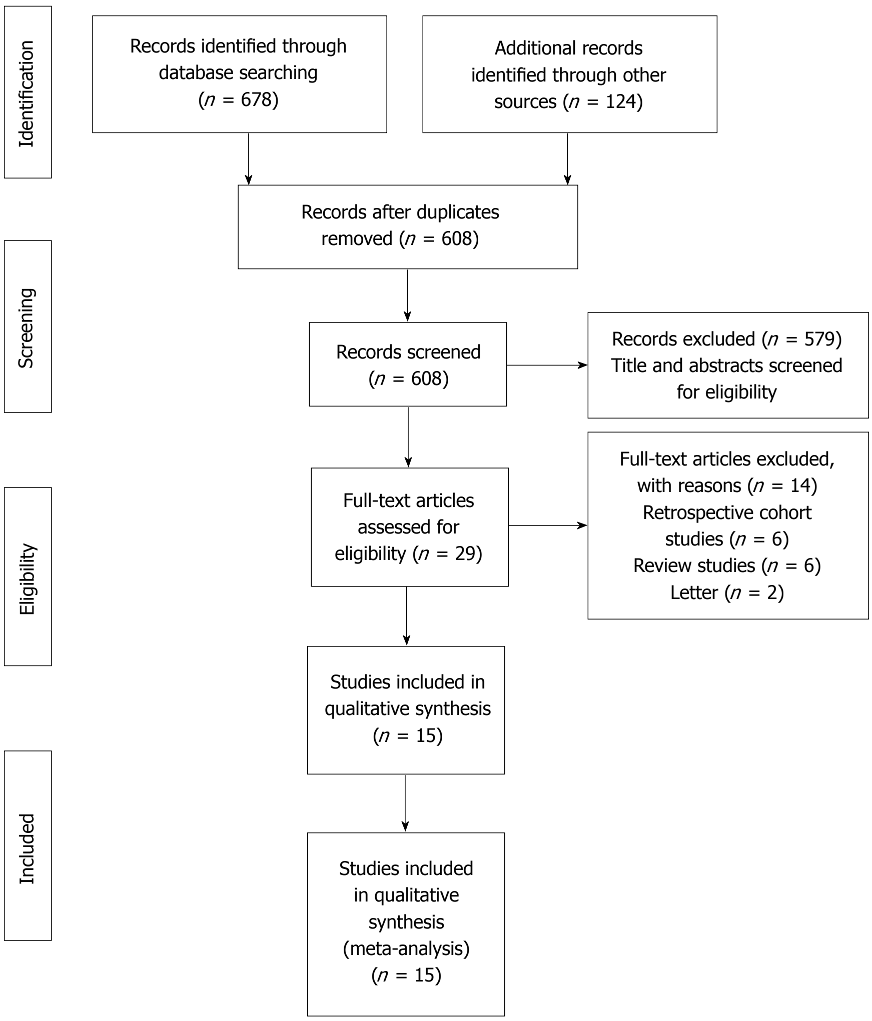


Figure 1 Flow chart of the literature search according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.

age following surgery. There was no significant difference in anastomotic leakage between the two groups (RR = 0.77, 95%CI: 0.57-1.04; P = 0.09) (Figure 2). Statistical heterogeneity was not detected (I^2 = 17%, χ^2 = 16.8, df = 14; P = 0.27). The subgroup analyses yielded significant differences for the number of suture layers for the hand-sewn method and the year of publication (Figure 3). One subgroup analysis found that the stapler method had an obvious benefit over the single-layer hand-sewn method in reducing the incidence of postoperative anastomotic leakage (RR = 0.37, 95%CI: 0.18-0.76; P < 0.01); however, there was no benefit when compared with the double-layer hand-sewn method (RR = 1.01, 95%CI: 0.66-1.53; P = 0.98). Another subgroup analysis showed that during the latest decade, the stapler method was superior to the hand-sewn method in preventing anastomotic leakage (RR = 0.66, 95%CI: 0.45-0.96; P = 0.03). The subgroup analysis of anastomotic site yielded no significant difference in anastomotic leakage between the two groups (RR = 1.23, 95%CI: 0.70-2.18; P = 0.47).

Thirty-day mortality

Fourteen trials reported the incidence of 30-d mortality, with no significant difference observed following stapled *vs* hand-sewn anastomosis (RR = 1.52, 95%CI: 0.97-2.40; P = 0.07) (Figure 4). There was no evidence of statistical heterogeneity (I^2 = 0%, χ^2 = 8.17, df = 9; P = 0.52).

Anastomotic strictures

Fourteen studies reported the incidence of anastomotic stricture following surgery. Because there was obvious clinical heterogeneity present in these studies, we performed two subgroup-analyses. In one analysis, there was a significant increase in the incidence of anastomotic stricture following end-to-side stapled anastomosis compared with hand-sewn anastomosis (RR = 1.45, 95%CI: 1.11-1.91; P < 0.01) (Figure 5). However, in the other analysis, side-to-side stapled anastomosis contributed to reducing the incidence of anastomotic stricture compared with hand-sewn anastomosis (RR = 0.34, 95%CI: 0.16-0.76: P < 0.01).

DISCUSSION

Since the 1990s, the use of the stapler for esophagogastric anastomosis has become increasingly popular. How-

Table 1 Study characteristics

Ref.	Year	Anastomostic methods	No. of patients	Male/female	Mean age (yr)	Jadad score
Fok *et al*[4]	1991	Hand-sewn	25	Details unknown	63.7	2
		Stapler	27		65.3	
Valverde *et al*[26]	1996	Hand-sewn	74	67/7	59	3
		Stapler	78	71/7	59	
Craig *et al*[25]	1996	Hand-sewn	50	27/23	65	2
		Stapler	50	34/16	65	
Law *et al*[24]	1997	Hand-sewn	61	54/7	64	2
		Stapler	61	53/8	64	
Laterza *et al*[23]	1999	Hand-sewn	21	4/17	50.9	3
		Stapler	20	3/17	51.9	
Walther *et al*[22]	2003	Hand-sewn	41	28/13	68	3
		Stapler	42	23/13	66	
Hsu *et al*[21]	2004	Hand-sewn	32	27/5	63	2
		Stapler	31	30/1	61	
Okuyama *et al*[19]	2007	Hand-sewn	18	16/2	64.3	2
		Stapler	14	13/1	63.6	
Luechakiettisak *et al*[18]	2008	Hand-sewn	59	50/9	63.6	2
		Stapler	58	48/10	62	
Aquino *et al*[17]	2009	Hand-sewn	15	Details unknown	45.6	3
		Stapler	15		45.6	
Zhang *et al*[15]	2010	Hand-sewn	244	142/102	60	2
		Stapler	272	158/114	59	
Wu *et al*[20]	2005	Hand-sewn	154	122/32	54	3
		Stapler	162	116/46	55	
Saluja *et al*[13]	2012	Hand-sewn	87	54/33	50.9	3
		Stapler	87	61/26	51.4	
Cayi *et al*[14]	2012	Hand-sewn	125	92/33	56	2
		Stapler	102	79/31	59	
Wang *et al*[12]	2013	Hand-sewn	52	27/5	60.8	3
		Stapler	92	30/1	58.9	

Study or subgroup	Stapler Events	Stapler Total	Hand-sewn Events	Hand-sewn Total	Weight	Risk ratio M-H, fixed, 95%CI
Aquino 2009	1	15	5	15	5.7%	0.20 (0.03, 1.51)
Cayi 2012	3	102	18	125	18.4%	0.20 (0.06, 0.67)
Craig 1996	4	50	3	50	3.4%	1.33 (0.31, 5.65)
Hsu 2004	8	31	7	32	7.8%	1.18 (0.49, 2.86)
Law 1997	3	61	1	61	1.1%	3.00 (0.32, 28.04)
Luechakiettisak 2008	2	58	4	59	4.5%	0.51 (0.10, 2.67)
Okuyama 2007	1	14	3	18	3.0%	0.43 (0.05, 3.69)
Pernilla 2006	9	148	9	126	11.1%	0.85 (0.35, 2.08)
Salujaet 2012	16	87	14	87	15.9%	1.14 (0.59, 2.20)
Valverde 1996	12	78	12	74	14.0%	0.95 (0.46, 1.98)
Walther 2003	0	42	1	41	1.7%	0.33 (0.01, 7.77)
Wang 2013	1	47	3	52	3.2%	0.37 (0.04, 3.42)
WSHASG 1991	0	27	1	25	1.8%	0.31 (0.01, 7.26)
Wu 2005	2	162	6	154	7.0%	0.32 (0.06, 1.55)
Zhang 2010	6	272	1	224	1.2%	4.94 (0.60, 40.74)
Total (95%CI)		1194		1143	100.0%	0.77 (0.57, 1.04)
Total events	68		88			

Heterogeneity: χ^2 = 16.80, *df* = 14 (*P* = 0.27); I^2 = 17%

Test for overall effect: *Z* = 1.68 (*P* = 0.09)

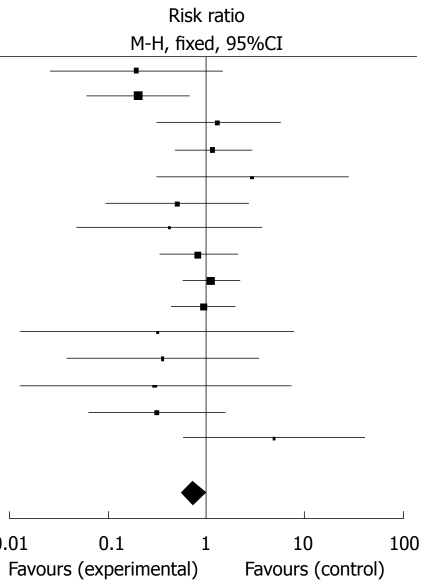
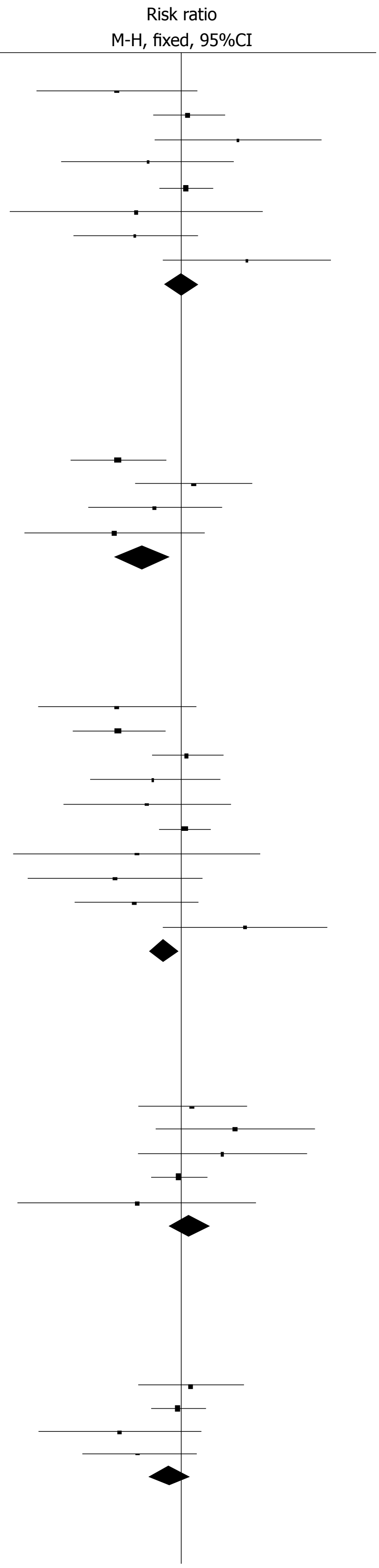


Figure 2 Forest plot for anastomotic leakage. Fifteen studies were included.

ever, compared with the routine hand-sewn method, the superiority of the stapler method is still controversial. Anastomotic leakage is one of the main postoperative complications that is associated with a high mortality rate. Since the development of the mechanical stapler, there have been many reports to show that the stapler can decrease the rate of leakage after esophagogastrostomy[6,7,27,28]. Also, several RCTs have shown that mechanical suturing is as adequate as manual suturing, leading to a lower incidence of anastomosis leakage.

The results of this study revealed that there is no significant difference between the hand-sewn and stapler groups in the incidence of developing anastomotic leakage. However, the subgroup analyses revealed two

Study or subgroup	Stapler Events	Stapler Total	Hand-sewn Events	Hand-sewn Total	Weight	Risk ratio M-H, fixed, 95%CI
1.1.1 anastomotic double layer						
Aquino 2009	1	15	5	15	2.4%	0.20 (0.03, 1.51)
Hsu 2004	8	31	7	32	3.4%	1.18 (0.49, 2.86)
Laterza 1999	4	20	1	21	0.5%	4.20 (0.51, 34.44)
Okuyama 2007	1	14	3	18	1.3%	0.43 (0.05, 3.69)
Salujaet 2012	16	87	14	87	6.8%	1.14 (0.59, 2.20)
Walther 2003	0	42	1	41	0.7%	0.33 (0.01, 7.77)
Wu 2005	2	162	6	154	3.0%	0.32 (0.06, 1.55)
Zhang 2010	6	272	1	244	0.5%	5.38 (0.65, 44.39)
Subtotal (95%CI)		643		612	18.7%	1.01 (0.66, 1.53)
Total events	38		38			
Heterogeneity: χ^2 = 10.05, *df* = 7 (*P* = 0.19); I^2 = 30%						
Test for overall effect: *Z* = 0.03 (*P* = 0.98)						
1.1.2 anastomotic single layer						
Cayi 2012	0	0	0	0		Not estimable
Craig 1996	3	102	18	105	7.9%	0.20 (0.06, 0.67)
Law 1997	4	50	3	50	1.5%	1.33 (0.31, 5.65)
Luechakiettisak 2008	2	58	4	59	1.9%	0.51 (0.10, 2.67)
Wang 2013	1	92	3	52	1.9%	0.19 (0.02, 1.77)
Subtotal (95%CI)		302		286	13.2%	0.37 (0.18, 0.76)
Total events	10		28			
Heterogeneity: χ^2 = 4.46, *df* = 3 (*P* = 0.22); I^2 = 33%						
Test for overall effect: *Z* = 2.72 (*P* = 0.008)						
1.1.3 anastomotic leakage (2003-2013)						
Aquino 2009	1	15	5	15	2.4%	0.20 (0.03, 1.51)
Cayi 2012	3	102	18	125	7.9%	0.20 (0.06, 0.67)
Hsu 2004	8	31	7	32	3.4%	1.18 (0.49, 2.86)
Luechakiettisak 2008	2	58	4	59	1.9%	0.51 (0.10, 2.67)
Okuyama 2007	1	14	3	18	1.3%	0.43 (0.05, 3.69)
Salujaet 2012	16	87	14	87	6.8%	1.14 (0.59, 2.20)
Walther 2003	0	42	1	41	0.7%	0.33 (0.01, 7.77)
Wang 2013	1	92	3	52	1.9%	0.19 (0.02, 1.77)
Wu 2005	2	162	6	154	3.0%	0.32 (0.06, 1.55)
Zhang 2010	6	272	1	244	0.5%	5.38 (0.65, 40.39)
Subtotal (95%CI)		875		827	29.9%	0.66 (0.45, 0.96)
Total events	40		62			
Heterogeneity: χ^2 = 15.68, *df* = 9 (*P* = 0.07); I^2 = 43%						
Test for overall effect: *Z* = 2.16 (*P* = 0.03)						
1.1.4 anastomotic leakage (-2003)						
Craig 1996	4	50	3	50	1.5%	1.33 (0.31, 5.65)
Laterza 1999	4	20	1	21	0.5%	4.20 (0.51, 34.44)
Law 1997	3	61	1	61	0.5%	3.00 (0.32, 28.04)
Valverde 1996	12	78	12	74	6.0%	0.95 (0.46, 1.98)
WSHASG 1991	0	27	1	25	0.8%	0.31 (0.01, 7.26)
Subtotal (95%CI)		236		231	9.2%	1.23 (0.70, 2.18)
Total events	23		18			
Heterogeneity: χ^2 = 3.15, *df* = 4 (*P* = 0.53); I^2 = 0%						
Test for overall effect: *Z* = 0.72 (*P* = 0.47)						
1.1.5 anastomotic site (Thoracic)						
Craig 1996	4	50	3	50	1.5%	1.33 (0.31, 5.65)
Valverde 1996	12	78	12	74	6.0%	0.95 (0.46, 1.98)
Wang 2013	1	92	3	52	1.9%	0.19 (0.02, 1.77)
Wu 2005	2	162	6	154	3.0%	0.32 (0.06, 1.55)
Subtotal (95%CI)		382		330	12.4%	0.73 (0.41, 1.27)
Total events	19		24			
Heterogeneity: χ^2 = 3.64, *df* = 3 (*P* = 0.30); I^2 = 18%						
Test for overall effect: *Z* = 1.12 (*P* = 0.26)						



1.1.6 anastomotic site (Cervical)						
Aquino 2009	1	15	5	15	2.4%	0.20 (0.03, 1.51)
Cayi 2012	3	102	18	125	7.9%	0.20 (0.06, 0.67)
Hsu 2004	8	31	7	32	3.4%	1.18 (0.49, 2.86)
Laterza 1999	4	20	1	21	0.5%	4.20 (0.51, 34.44)
Law 1997	3	61	1	61	0.5%	3.00 (0.32, 28.04)
Luechakiettisak 2008	2	58	4	59	1.9%	0.51 (0.10, 2.67)
Subtotal (95%CI)		287		313	16.6%	0.63 (0.38, 1.06)
Total events	21		36			

Heterogeneity: χ^2 = 11.62, *df* = 5 (*P* = 0.04); I^2 = 57%

Test for overall effect: *Z* = 1.73 (*P* = 0.09)

Test for subgroup differences: χ^2 = 9.42, *df* = 5 (*P* = 0.09); I^2 = 46.9%

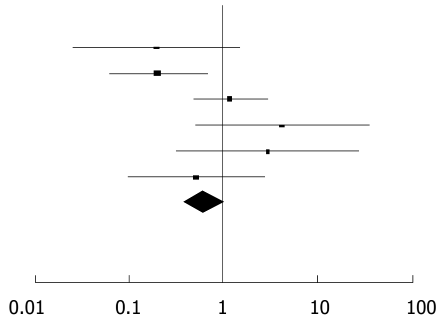


Figure 3 Subgroup analyses for anastomotic site, number of suture layers in the hand-sewn method, and year of publication.

	Stapler		Hand-sewn			Risk ratio
Study or subgroup	Events	Total	Events	Total	Weight	M-H, fixed, 95%CI
Aquino 2009	0	15	0	15		Not estimable
Cayi 2012	0	102	0	125		Not estimable
Craig 1996	4	50	1	50	3.5%	4.00 (0.46, 34.54)
Hsu 2004	2	31	1	32	3.4%	2.06 (0.20, 21.63)
Laterza 1999	1	20	2	21	6.7%	0.53 (0.05, 5.35)
Law 1997	3	61	0	61	1.7%	7.00 (0.37, 132.70)
Luechakiettisak 2008	6	58	7	59	24.0%	0.87 (0.31, 2.44)
Okuyama 2007	0	14	0	18		Not estimable
Salujaet 2012	6	87	5	87	17.3%	1.20 (0.38, 3.79)
Valverde 1996	12	78	5	74	17.7%	2.28 (0.84, 6.15)
Walther 2003	1	42	0	41	1.7%	2.93 (0.12, 69.92)
Wang 2013	0	47	0	52		Not estimable
WSHASG 1991	0	0	0	0		Not estimable
Wu 2005	1	162	4	154	14.2%	0.24 (0.03, 2.10)
Zhang 2010	7	244	3	272	9.8%	2.60 (0.68, 9.95)
Total (95%CI)		1011		1061	100.0%	1.52 (0.97, 2.40)
Total events	43		28			

Heterogeneity: χ^2 = 8.17, *df* = 9 (*P* = 0.52); I^2 = 0%

Test for overall effect: *Z* = 1.82 (*P* = 0.07)

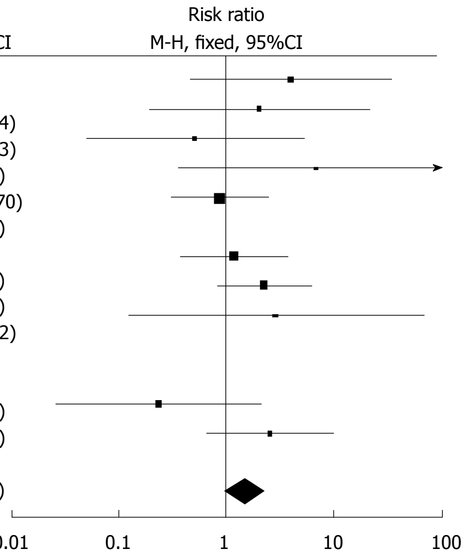


Figure 4 Forest plot for 30-d mortality. Fifteen studies were included.

important findings. First, the use of a stapler method contributed to a reduced anastomotic leakage rate over the last decade. Second, the stapler was superior to the single-layer hand-sewn method in preventing postoperative anastomotic leakage.

For this study, we made attempts wherever possible to follow the recommendations of the Cochrane Collaboration. A rigorous study protocol was pre-specified and several electronic databases, references, and international conference abstracts for relevant trials, were searched without restrictions on language. Several pooled analyses on this topic have demonstrated a similar incidence of anastomotic leakage between the two groups[8,9,29,30]. These pooled analyses either did not attempt to produce subgroup analyses or they did not include an adequate number of publications. The largest number of RCTs to date was included in the present study, and through subgroup analyses, we also examined the contribution of the site of anastomosis, the number of suture layers for the hand-sewn method, and the year of publication as effect modifiers. A major merit of this study was that we performed the analyses by the pre-specified protocol that closely adhered to the Cochrane Collaboration. Therefore, repeating the meta-analysis might achieve a consensus with statistically greater power and better quality of analysis for surgeons with regard to the method of esophagogastric anastomosis after esophagectomy.

Although all the studies met our inclusion criteria, to some extent, this meta-analysis showed heterogeneity; the suture materials and the surgical techniques varied among the studies. We specifically selected three main factors that were suspected as effective modifiers. First, despite the methods of esophagogastric anastomosis, there was no consensus on whether the site of anastomosis (intrathoracic or cervical) affected the outcome of esophagectomy. Second, it is still controversial whether the stapler method is more effective in preventing anastomotic leakage than either single-layer or double-layer suturing methods. Third, although stapler technology has improved over the past 20 years, and has matured during the current decade, and whether year of publication affects the outcome is unclear[14,24]. To make these potential problems clear, we performed subgroup analyses that were stratified by such techniques.

Study or subgroup	Stapler Events	Stapler Total	Hand-sewn Events	Hand-sewn Total	Weight	Risk ratio M-H, fixed, 95%CI
1.10.1 Stapler (side to side) *vs* Hand-sewn						
Wang 2013	0	45	5	52	5.4%	0.10 (0.01, 1.84)
Salujaet 2012	7	81	17	82	17.7%	0.42 (0.18, 0.95)
Subtotal (95%CI)		126		134	23.1%	0.34 (0.16, 0.76)
Total events	7		22			
Heterogeneity: χ^2 = 0.87, *df* = 1 (*P* = 0.35); I^2 = 0%						
Test for overall effect: *Z* = 2.65 (*P* = 0.008)						
1.10.2 Stapler (end to side) *vs* Hand-sewn						
Zhang 2010	13	261	2	236	2.2%	5.88 (1.34, 25.77)
Wu 2005	3	162	7	154	7.5%	0.41 (0.11, 1.55)
Walther 2003	12	42	8	41	8.5%	1.46 (0.67, 3.21)
Valverde 1996	7	53	8	63	7.7%	1.04 (0.40, 2.68)
Okuyama 2007	2	14	0	18	0.5%	6.33 (0.33, 122.21)
Luechakiettisak 2008	19	52	10	52	10.5%	1.90 (0.98, 3.68)
Law 1997	20	50	5	55	5.0%	4.40 (1.79, 10.84)
Laterza 1999	3	18	2	20	2.0%	1.67 (0.31, 8.87)
Hsu 2004	5	28	4	28	4.2%	1.25 (0.37, 4.17)
Craig 1996	13	46	13	49	13.2%	1.07 (0.55, 2.05)
Cayi 2012	4	102	11	125	10.4%	0.45 (0.15, 1.36)
Aquino 2009	3	15	5	15	5.2%	0.60 (0.17, 2.07)
Subtotal (95%CI)		843		856	76.9%	1.45 (1.11, 1.91)
Total events	104		75			
Heterogeneity: χ^2 = 22.00, *df* = 11 (*P* = 0.02); I^2 = 50%						
Test for overall effect: *Z* = 2.70 (*P* = 0.007)						
Subtotal (95%CI)		969		990	100.0%	1.20 (0.93, 1.54)
Total events	111		97			
Heterogeneity: χ^2 = 31.93, *df* = 13 (*P* = 0.002); I^2 = 59%						
Test for overall effect: *Z* = 1.41 (*P* = 0.16)						
Test for subgroup differences: χ^2 = 11.47, *df* = 1 (*P* = 0.0007); I^2 = 91.3%						

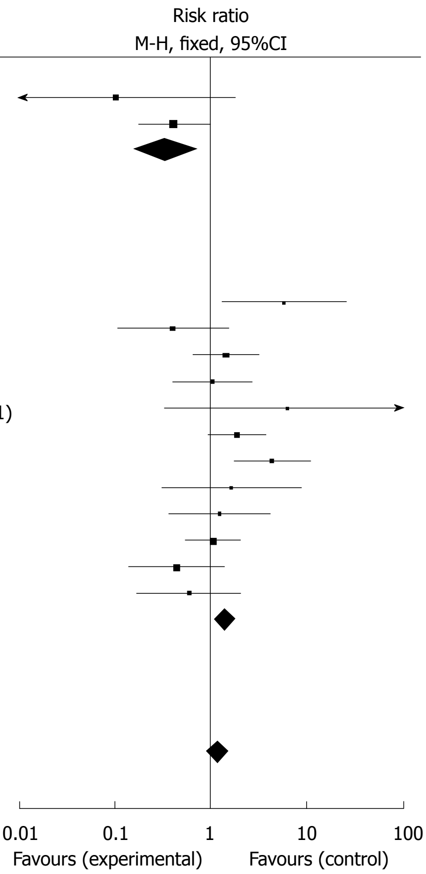


Figure 5 Forest plot for anastomotic strictures including two subgroup analyses.

The primary outcome measures from our meta-analysis demonstrated that there was no significant difference between the two groups for anastomotic leakage. However, in one subgroup analysis, there was a significantly decreased incidence of anastomotic leakage compared with hand-sewn anastomosis in 2003-2013. In another subgroup analysis, stapling was significantly superior to the single-layer hand-sewn method in reducing anastomotic leakage. For secondary outcome measures, the difference identified between the hand-sewn and stapler groups was increased anastomotic stricture in the end-to-side stapling group, while there was decreased anastomotic stricture in the side-to-side stapling group.

CONCLUSION

The results of our meta-analysis suggest that stapler anastomosis should remain the first option, because it can significantly reduce the anastomotic leakage. Furthermore, application of the stapler is usually easy and standardized, such that it should not increase the incidence of technical errors. In contrast, hand-sewn methods require surgical expertise and may not be practicable everywhere. Although in this meta-analysis the end-to-side stapler method was associated with the risk of postoperative anastomotic stricture, several new mechanical anastomosis methods (including side-to-side stapling) have been used to resolve this problem[30,31].

COMMENTS

Background

Currently, the standard treatment for esophageal cancer continues to be esophagectomy. Hand-sewn and stapler anastomosis are two major methods for esophagogastric anastomosis after esophagectomy. The purpose of this meta-analysis was to compare the outcomes from hand-sewn and stapler methods for esophagogastric anastomosis after esophagectomy by pooling all data from relevant randomized controlled trials (RCTs), to reach a consensus for comparison of anastomotic leakage.

Research frontiers

Several meta-analyses undertaken to compare hand-sewn and stapler anastomosis methods revealed that there was no significant difference in the risk of developing anastomotic leakage, and that stapler anastomosis contributed more frequently to the development of anastomotic strictures.

Innovations and breakthroughs

Previous meta-analyses did not include all published RCTs, and there is clinical heterogeneity among the ones that were included, indicating that several subgroup meta-analyses are needed. The study presented here is believed to be the first meta-analysis to include subgroup analyses, which indicate an association between anastomotic leakage and: (1) the number of layers sutured; (2) year of publication; and (3) the anastomotic site.

Applications

The results suggest that the stapler method reduces the anastomotic leakage rate compared with the single-layer hand-sewn method. In addition, although the end-to-side stapler method increased the risk of anastomotic strictures, the side-to-side stapler was associated with a decreased rate.

Terminology

Hand-sewn anastomosis is the esophagogastric anastomosis performed by hand with interrupted absorbable monofilament sutures. Stapler anastomosis means that the esophagogastric anastomosis is performed using circular or linear staplers.

Peer review

This is a nicely written manuscript and the analyses seem to be well performed. The topic of the esophagogastric anastomosis is not really new, but it is still one of the mainly important problems in esophageal surgery.

REFERENCES

1 **Biere SS**, van Berge Henegouwen MI, Maas KW, Bonavina L, Rosman C, Garcia JR, Gisbertz SS, Klinkenbijl JH, Hollmann MW, de Lange ES, Bonjer HJ, van der Peet DL, Cuesta MA. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. *Lancet* 2012; **379**: 1887-1892 [PMID: 22552194 DOI: 10.1016/S0140-6736(12)60516-9]

2 **Jemal A**, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin* 2011; **61**: 69-90 [PMID: 21296855 DOI: 10.3322/caac.20107]

3 **Siegel R**, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. *CA Cancer J Clin* 2014; **64**: 9-29 [PMID: 24399786 DOI: 10.3322/caac.21208]

4 **Fok M**, Ah-Chong AK, Cheng SW, Wong J. Comparison of a single layer continuous hand-sewn method and circular stapling in 580 oesophageal anastomoses. *Br J Surg* 1991; **78**: 342-345 [PMID: 2021852 DOI: 10.1002/bjs.1800780323]

5 Suturing or stapling in gastrointestinal surgery: a prospective randomized study. West of Scotland and Highland Anastomosis Study Group. *Br J Surg* 1991; **78**: 337-341 [PMID: 2021851 DOI: 10.1002/bjs.1800780322]

6 **Kondra J**, Ong SR, Clifton J, Evans K, Finley RJ, Yee J. A change in clinical practice: a partially stapled cervical esophagogastric anastomosis reduces morbidity and improves functional outcome after esophagectomy for cancer. *Dis Esophagus* 2008; **21**: 422-429 [PMID: 19125796 DOI: 10.1111/j.1442-2050.2007.00792.x]

7 **McManus KG**, Ritchie AJ, McGuigan J, Stevenson HM, Gibbons JR. Sutures, staplers, leaks and strictures. A review of anastomoses in oesophageal resection at Royal Victoria Hospital, Belfast 1977-1986. *Eur J Cardiothorac Surg* 1990; **4**: 97-100 [PMID: 2184859 DOI: 10.1016/1010-7940(90)90222-L]

8 **Honda M**, Kuriyama A, Noma H, Nunobe S, Furukawa TA. Hand-sewn versus mechanical esophagogastric anastomosis after esophagectomy: a systematic review and meta-analysis. *Ann Surg* 2013; **257**: 238-248 [PMID: 23001084 DOI: 10.1097/SLA.0b013e31826d4723]

9 **Markar SR**, Karthikesalingam A, Vyas S, Hashemi M, Winslet M. Hand-sewn versus stapled oesophago-gastric anastomosis: systematic review and meta-analysis. *J Gastrointest Surg* 2011; **15**: 876-884 [PMID: 21271360 DOI: 10.1007/s11605-011-1426-9]

10 **Markar SR**, Arya S, Karthikesalingam A, Hanna GB. Technical factors that affect anastomotic integrity following esophagectomy: systematic review and meta-analysis. *Ann Surg Oncol* 2013; **20**: 4274-4281 [PMID: 23943033 DOI: 10.1245/s10434-013-3189-x]

11 **Jadad AR**, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, McQuay HJ. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996; **17**: 1-12 [PMID: 8721797 DOI: 10.1016/0197-2456(95)00134-4]

12 **Wang WP**, Gao Q, Wang KN, Shi H, Chen LQ. A prospective randomized controlled trial of semi-mechanical versus hand-sewn or circular stapled esophagogastrostomy for prevention of anastomotic stricture. *World J Surg* 2013; **37**: 1043-1050 [PMID: 23381675 DOI: 10.1007/s00268-013-1932-x]

13 **Saluja SS**, Ray S, Pal S, Sanyal S, Agrawal N, Dash NR, Sahni P, Chattopadhyay TK. Randomized trial comparing side-to-side stapled and hand-sewn esophagogastric anastomosis in neck. *J Gastrointest Surg* 2012; **16**: 1287-1295 [PMID: 22528571 DOI: 10.1007/s11605-012-1885-7]

14 **Cayi R**, Li M, Xiong G, Cai K, Wang W. [Comparative analysis of mechanical and manual cervical esophagogastric anastomosis following esophagectomy for esophageal cancer]. *Nanfang Yike Daxue Xuebao* 2012; **32**: 908-909 [PMID: 22699083]

15 **Zhang YS**, Gao BR, Wang HJ, Su YF, Yang YZ, Zhang JH, Wang C. Comparison of anastomotic leakage and stricture formation following layered and stapler oesophagogastric anastomosis for cancer: a prospective randomized controlled trial. *J Int Med Res* 2010; **38**: 227-233 [PMID: 20233534 DOI: 10.1177/147323001003800127]

16 **Ma RD**, Zhang WT, Xu QR, Chen LQ. [Esophagogastrostomy by side-to-side anastomosis in prevention of anastomotic stricture: a randomized clinical trial]. *Zhonghua Waike Zazhi* 2010; **48**: 577-581 [PMID: 20646472]

17 **Aquino JL**, Camargo JG, Said MM, Merhi VA, Maclellan KC, Palu BF. [Cervical esophagogastric anastomosis evaluation with a mechanical device versus manual suture in patients with advanced megaesophagus]. *Rev Col Bras Cir* 2009; **36**: 19-23 [PMID: 20076864 DOI: 10.1590/S0100-69912009000100006]

18 **Luechakiettisak P**, Kasetsunthorn S. Comparison of hand-sewn and stapled in esophagogastric anastomosis after esophageal cancer resection: a prospective randomized study. *J Med Assoc Thai* 2008; **91**: 681-685 [PMID: 18672632]

19 **Okuyama M**, Motoyama S, Suzuki H, Saito R, Maruyama K, Ogawa J. Hand-sewn cervical anastomosis versus stapled intrathoracic anastomosis after esophagectomy for middle or lower thoracic esophageal cancer: a prospective randomized controlled study. *Surg Today* 2007; **37**: 947-952 [PMID: 17952523 DOI: 10.1007/s00595-007-3541-5]

20 **Wu YS**, Ye M, Ma LY. Mechanical compared with hand-sewn Esophagogastric Anastomosis after esophagectomy for esophageal cancer. *Zhonghua Weichang Waike Zazhi* 2005; **8**: 367-368

21 **Hsu HH**, Chen JS, Huang PM, Lee JM, Lee YC. Comparison of manual and mechanical cervical esophagogastric anastomosis after esophageal resection for squamous cell carcinoma: a prospective randomized controlled trial. *Eur J Cardiothorac Surg* 2004; **25**: 1097-1101 [PMID: 15145015 DOI: 10.1016/j.ejcts.2004.02.026]

22 **Walther B**, Johansson J, Johnsson F, Von Holstein CS, Zilling T. Cervical or thoracic anastomosis after esophageal resection and gastric tube reconstruction: a prospective randomized trial comparing sutured neck anastomosis with stapled intrathoracic anastomosis. *Ann Surg* 2003; **238**: 803-812; discussion 812-814 [PMID: 14631217]

23 **Laterza E**, de' Manzoni G, Veraldi GF, Guglielmi A, Tedesco P, Cordiano C. Manual compared with mechanical cervical oesophagogastric anastomosis: a randomised trial. *Eur J Surg* 1999; **165**: 1051-1054 [PMID: 10595609 DOI: 10.1080/110241599750007883]

24 **Law S**, Fok M, Chu KM, Wong J. Comparison of hand-sewn and stapled esophagogastric anastomosis after esophageal resection for cancer: a prospective randomized controlled trial. *Ann Surg* 1997; **226**: 169-173 [PMID: 9296510 DOI: 10.1097/00000658-199708000-00008]

25 **Craig SR**, Walker WS, Cameron EW, Wightman AJ. A prospective randomized study comparing stapled with hand-sewn oesophagogastric anastomoses. *J R Coll Surg Edinb* 1996; **41**: 17-19 [PMID: 8930036]

26 **Valverde A**, Hay JM, Fingerhut A, Elhadad A. Manual versus mechanical esophagogastric anastomosis after resection for carcinoma: a controlled trial. French Associations for Surgical Research. *Surgery* 1996; **120**: 476-483 [PMID: 8784400 DOI: 10.1016/S0039-6060(96)80066-3]

27 **Ercan S**, Rice TW, Murthy SC, Rybicki LA, Blackstone EH. Does esophagogastric anastomotic technique influence the outcome of patients with esophageal cancer? *J Thorac Cardiovasc Surg* 2005; **129**: 623-631 [PMID: 15746747 DOI: 10.1016/j.jtcvs.2004.08.024]

28 **Urschel JD**, Blewett CJ, Bennett WF, Miller JD, Young JE. Handsewn or stapled esophagogastric anastomoses after esophagectomy for cancer: meta-analysis of randomized controlled trials. *Dis Esophagus* 2001; **14**: 212-217 [PMID: 11869322 DOI: 10.1046/j.1442-2050.2001.00187.x]

29 **Kayani B**, Garas G, Arshad M, Athanasiou T, Darzi A, Zacharakis E. Is hand-sewn anastomosis superior to stapled anastomosis following oesophagectomy? *Int J Surg* 2014; **12**: 7-15 [PMID: 24239928 DOI: 10.1016/j.ijsu.2013.11.001]

30 **Takemura M**, Yoshida K, Fujiwara Y. Modified triangulating stapling technique for esophagogastrostomy after esophagectomy for esophageal cancer. *Surg Endosc* 2013; **27**: 1249-1253 [PMID: 23093236 DOI: 10.1007/s00464-012-2586-8]

31 **Okushiba S**, Kawarada Y, Shichinohe T, Manase H, Kitashiro S, Katoh H. Esophageal delta-shaped anastomosis: a new method of stapled anastomosis for the cervical esophagus and digestive tract. *Surg Today* 2005; **35**: 341-344 [PMID: 15815856 DOI: 10.1007/s00595-004-2943-x]

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