

Original Article

Meta-analysis of stapled versus hand-sewn esophagogastric anastomosis

Xuefei Zhang^{1,2}, Qian Yu¹, Hui Tian², Desheng Lv¹

¹Department of Thoracic Surgery, The Second Hospital of Dalian Medicine University, Dalian 116023, China;

²Department of Thoracic Surgery, Qilu Hospital of Shandong University, Ji'nan 250012, China

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Abstract: Background: Esophagogastric anastomosis can be performed using a hand-sewn or stapled technique. To compare clinical outcomes of hand-sewn and stapled esophagogastric anastomosis for patients with esophageal and cardiac disease, this meta-analysis was conducted. Patients and methods: A literature search was performed. Meta-analysis of fourteen randomized studies was carried out and statistical analysis was performed using Rev-Man 5.1 software. The primary endpoint was anastomotic leaks. Secondary endpoints were anastomotic stricture, operating time (OT), time of anastomosis, blood loss, hospital stay, median duration of stay in intensive care unit, hospital mortality and complications. Results: Fourteen randomized controlled trials, including 2,260 patients, were selected. Meta-analysis results were as follows. There were statistically significant differences in anastomotic leaks, anastomotic stricture, the OT, time of anastomosis, blood-borne infections, and recurrent laryngeal nerve palsy between stapled and hand-sewn anastomosis groups. Conclusion: Compared to hand-sewn anastomosis, stapled anastomosis can reduce the rate of anastomotic leaks, shorten the OT and time of anastomosis, and reduce the rate of anastomotic stricture, while also reducing the rate of the blood-borne infections and recurrent laryngeal nerve palsy.

Keywords: Esophageal carcinoma, cardiac carcinoma, benign esophageal disease, stapled esophagogastric anastomosis, hand-sewn esophagogastric anastomosis

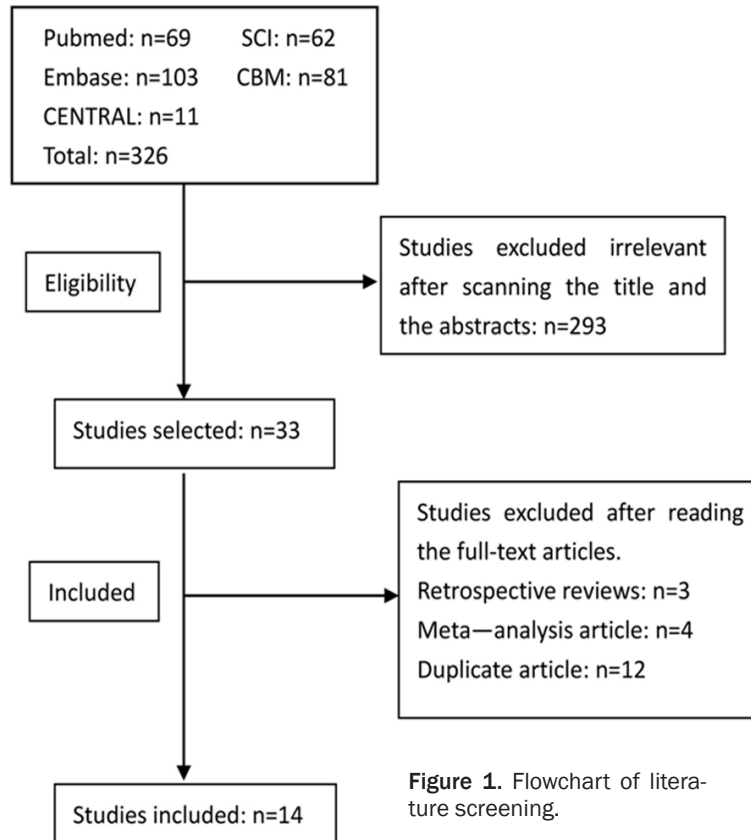
Introduction

Esophageal carcinoma, with incidence rapidly rising, is a multifaceted and complex disease [1-3]. The standard treatment for esophageal carcinoma is esophagogastric resection. It is performed with three main goals, cure of cancer, dysphagia palliation, and avoidance of complications after the operation [4, 5]. In most cases, alimentary tract reconstruction after esophagectomies is achieved through gastric transposition and esophagogastric anastomosis. However, esophagogastric anastomosis involves complicated techniques and is associated with various postoperative complications, of which leakage might cause significant mortality after esophagectomies [6]. In recent studies, leakage rates have ranged from 0% to 24% [7-12], with anastomotic leaks among the main causes of postoperative mortality, contributing to almost 90% of deaths after esophagectomies [13-16]. Late anastomotic complications,

such as stricturing, can negate the palliative benefits of esophagectomies [17]. Stricture rates range from 13.6% to 40% following esophageal reconstruction [18-20], while anastomotic strictures may lead to a recurrence of symptoms, off-setting the benefits [17, 21].

Two different methods are involved in esophagogastric anastomosis, stapling and hand-sewing. The circular and linear stapler are two different types of generally used staplers. Since the development of the circular stapler in 1977 [22], staplers have been more and more widely applied in esophagogastric anastomosis. They are convenient to use and an expert operator is not essential. Some studies have reported that the circular stapler has contributed to reduced leakage and increased anastomotic strictures [19, 23-27]. This meta-analysis of randomized controlled trials (RCTs) was carried out to compare the two anastomotic techniques aiming to guide clinical practice.

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Patients and methods

Inclusion and exclusion criteria

Inclusion criteria: All included trials must be randomized controlled clinical trials (regardless of publication or language status); Multiple reports of the same study were considered as one publication and only the most recent article was included; Abstracts or unpublished data would be included only under the condition that sufficient information was provided.

Patients of any age and gender were eligible if they had undergone esophagectomy and esophageal reconstruction and had any histological type of cardiac cancer. There was no restriction on the path of reconstruction or the anastomotic site, such as: (1) Any patient diagnosed with an esophageal or gastric cardia carcinoma staging T1-T3 or N0-N1 fitting for operative resection from computed tomography scanning was eligible; (2) Patients with benign esophageal lesions where esophagectomy was considered necessary were also eligible for inclusion. In patients with corrosive stricture,

anastomosis was done in the healthy cervical esophagus.

Trials comparing mechanic anastomosis and manual esophagogastric anastomosis for patients with esophageal carcinoma and cardiac carcinoma.

Trials in which the primary outcome was rate of anastomotic leaks of each treatment arm. Secondary endpoints were the rate of anastomotic stricture, operating time, diameter of anastomosis, time of anastomosis, blood loss, hospital stay, the median duration of stay in intensive care unit, hospital mortality, complications, 30-day mortality, and 5-year survival rate.

Exclusion criteria: Patients were excluded from analysis if they were on advanced tumor stage (T4 disease), having poor pulmonary reserve (50% forced expiratory volume of

normal), having advanced involvement of lymph node or distant metastasis (M1 lymph or M1 disease), having had prior gastric surgery, or with increased cardiac risk (cardiac insufficiency grade IV NYHA or postmyocardial infarction).

Patients were not eligible if they required gastric pull up, or poor performance status (ECOG status 3 or 4), or patients with serious pharyngeal strictures that required pharyngogastric anastomosis.

Literature search

Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, Pubmed, Embase, Web of Science, and Chinese Biomedical Literature databases were searched for randomized controlled trials comparing stapled with hand-sewn esophagogastric anastomosis for patients with esophageal carcinoma and cardiac carcinoma, without language restriction. Moreover, references of all included studies were searched to obtain additional reports. If any information was not available, contact with the authors was initiated by e-mail or telephone. The search strategy used major

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Table 1. Characteristics of included studies

| Included studies | Study sites | No. of patients | Cases | | Male/Female (n/n) | | Age (years) | | Follow-up | Operation method | Anastomotic position | Stapler type |
|-----------------------------|-------------|-----------------|-------|-----|-------------------|---------|--------------|--------------|-------------|--|------------------------------------|---|
| | | | S | H | S | H | S | H | | | | |
| Walther B 2003 [19] | Sweden | 83 | 42 | 41 | 29/13 | 28/13 | 66 (42-82) | 68 (47-80) | 12 M | Right thoracotomy+upper abdomen+left cervical/no | Cervical/Intrathoracic Anastomosis | Circular stapler |
| Yong Fan 2011 [33] | China | 67 | 34 | 33 | 22/12 | 20/13 | 48.2 ± 3.5 | 48.5 ± 3 | | Right thoracotomy+upper abdomen+left cervical | Cervical Anastomosis | Circular stapler |
| Cayi R 2012 [34] | China | 227 | 102 | 125 | 79/23 | 92/33 | 59 (45-78) | 56 (43-76) | 6 M | Right thoracotomy+upper abdomen+left cervical | Cervical Anastomosis | Circular stapler |
| Jixing Zhao 2015 [35] | China | 100 | 68 | 32 | 36/32 | 18/14 | 51.2 ± 4.8 | 52.7 ± 4.5 | 3 M | Left thoracotomy | Intrathoracic Anastomosis | Circular stapler |
| Okuyama M 2007 [36] | Japan | 32 | 14 | 18 | 13/1 | 16/2 | 63.6 (57-72) | 64.3 (46-73) | 5 Y | Right thoracotomy+upper abdomen+left cervical/no | Cervical/Intrathoracic Anastomosis | Circular stapler |
| WP Wang 2013 [37] | China | 99 | 47 | 52 | 41/6 | 40/12 | 61.4 ± 7.7 | 58.9 ± 7.3 | 3 M | Left thoracotomy | Intrathoracic Anastomosis | Circular stapler |
| HH Hsu 2004 [38] | Taiwan | 63 | 31 | 32 | 30/1 | 27/5 | 61 ± 12 | 63 ± 10 | 88 M | Right thoracotomy+upper abdomen+left cervical | Cervical Anastomosis | Circular stapler |
| Laterza E 1999 [39] | Italy | 41 | 20 | 21 | 3/17 | 4/17 | 51.9 | 50.9 | 21 (6-34) M | Right thoracotomy+upper abdomen+left cervical | Cervical Anastomosis | Circular stapler |
| Valverde A 1996 [40] | France | 152 | 78 | 74 | 71/7 | 67/7 | 61 ± 12 | 61 ± 12 | 9-36 M | Right thoracotomy+upper abdomen+left cervical/no | Cervical/Intrathoracic Anastomosis | Circular stapler/linear mechanical stapler. |
| Luechakietis-ak P 2008 [41] | Thailand | 117 | 58 | 59 | 48/10 | 50/9 | 62 (45-74) | 63.6 (47-76) | | Right thoracotomy+upper abdomen | Intrathoracic Anastomosis | Circular stapler |
| QX Liu 2015 [42] | China | 467 | 235 | 232 | 180/55 | 170/62 | 62 ± 8 | 61 ± 9 | 5 Y | Right thoracotomy+upper abdomen+left cervical/no | Cervical/Intrathoracic Anastomosis | Circular stapler |
| SS Saluja 2012 [43] | India | 174 | 87 | 87 | 61/26 | 54/33 | 51.4 ± 12 | 50.9 ± 14 | 5 Y | Right thoracotomy+upper abdomen+left cervical | Cervical Anastomosis | Linear mechanical stapler. |
| Law S 1997 [18] | Hong-Kong | 122 | 61 | 61 | 53/8 | 54/7 | 63 ± 1 | 64 ± 1.2 | 20 M | Right thoracotomy+upper abdomen | Intrathoracic Anastomosis | Circular stapler |
| YS Zhang 2010 [44] | China | 516 | 272 | 244 | 158/144 | 142/102 | 59 ± 1.2 | 60 ± 1.3 | > 12 M | Left thoracotomy | Intrathoracic Anastomosis | Circular stapler |

Abbreviations: S = the stapled esophagogastric anastomosis group; H = the hand-sewn esophagogastric anastomosis group; M = months; Y = years.

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Table 2. Risk of bias in included studies

| Study | Adequate Sequence Generation | Allocation concealment | Blinding | Incomplete outcome data | Free of selective reporting | Free of other bias |
|------------------------------|------------------------------|------------------------|----------|-------------------------|-----------------------------|--------------------|
| Walther B 2003 [19] | Unclear | Yes (envelope) | Unclear | Yes | Unclear | Unclear |
| Yong Fan 2011 [33] | Unclear | Unclear | Unclear | Yes | Unclear | Unclear |
| Cayi R 2012 [34] | Unclear | Unclear | Unclear | Yes | Unclear | Unclear |
| Jixing Zhao 2015 [35] | Unclear | Unclear | Unclear | Yes | Unclear | Unclear |
| Okuyama M 2007 [36] | Unclear | Yes (envelope) | Unclear | Yes | Unclear | Unclear |
| WP Wang 2013 [37] | No (at a ratio of 1:1) | Unclear | Unclear | Yes | Unclear | Unclear |
| HH Hsu 2004 [38] | Yes (chart number) | Unclear | Unclear | Yes | Unclear | Unclear |
| Laterza E 1999 [39] | Unclear | Yes (envelope) | Unclear | Yes | Unclear | Unclear |
| Valverde A 1996 [40] | Unclear | Yes (questionnaire) | Unclear | Yes | Unclear | Unclear |
| Luechakiettaisak P 2008 [41] | No (odd/even counter number) | Unclear | Unclear | Yes | Unclear | Unclear |
| QX Liu 2015 [42] | Yes (chart number) | Yes (envelope) | Unclear | Yes | Unclear | Unclear |
| SS Saluja 2012 [43] | Yes (computer) | Unclear | Unclear | Yes | Unclear | Unclear |
| Law S 1997 [18] | Unclear | Yes (envelope) | Unclear | Yes | Unclear | Unclear |
| YS Zhang 2010 [44] | Yes (chart number) | Unclear | Unclear | Yes | Unclear | Unclear |

key words such as “esophagectomy”, “Manual anastomosis OR hand-sewn anastomosis”, “stapled anastomosis OR mechanical anastomosis”, “esophageal carcinoma”, “cardiac carcinoma”.

Data extraction and quality assessment

Using the search strategy described above, titles and abstracts of relevant randomized controlled trials were obtained. Two reviewers, independently, assessed all identified studies to confirm conformity to the inclusion criteria. Data was extracted by two independent reviewers. Any points of disagreement in the process of searching, quality assessment, data extraction, or other relevant studies between the two reviewers was settled by discussion.

Risk of bias of included studies was evaluated by two independent reviewers using the Cochrane Handbook 5.0.2 [29]. It was determined according to these criteria: adequate sequence generation, blinding of participants, allocation sequence concealment, free of selective reporting, and other biases [28]. Each entry was decided by a definitive answer (Yes or No or Unclear), where “Yes” “No” “Unclear” indicated low risk of bias, high risk of bias, and unclear or unknown risk of bias, respectively [29]. Different opinions were settled by consultation with a third reviewer.

Statistical analysis

Cochrane software RevMan 5.1 (Cochrane Collaboration, Software Update, Oxford, UK) was used to analyze data [29]. According to

heterogeneity status, fixed-effects or random-effects models were applied to calculate odds ratio (OR) with 95% confidence interval (95% CI) (dichotomous variables) and standardized mean difference (SMD) with 95% CI (continuous variables) [30]. Heterogeneity among studies was evaluated by Chi-square test (χ^2 test), with $P < 0.10$ used to determine statistical significance. I^2 was used to assess heterogeneity quantity, where $I^2 > 50\%$ indicated significant heterogeneity [31]. The fixed-effects model was applied when no statistically significant heterogeneity existed ($P \geq 0.10$, $I^2 < 50\%$).

Otherwise, possible reasons were explored when significant heterogeneity ($P < 0.10$, $I^2 > 50\%$) existed. Sensitivity analysis was performed through omitting poor-quality studies with a high risk of bias. Intention-to-treat analysis was not carried out as information concerning missed follow-ups was insufficient. Length of wounds was assessed with descriptive analysis. Publication bias was analyzed using a funnel plot [32].

Results

Description of studies

The process of literature screening is detailed in **Figure 1**. A total of 326 potentially relevant studies were identified. After filtration of titles and abstracts, 293 irrelevant studies were excluded. After full-text review of the 33 remaining studies, another 19 studies were excluded, leaving 14 trials [18, 19, 33, 44] meeting the inclusion criteria.

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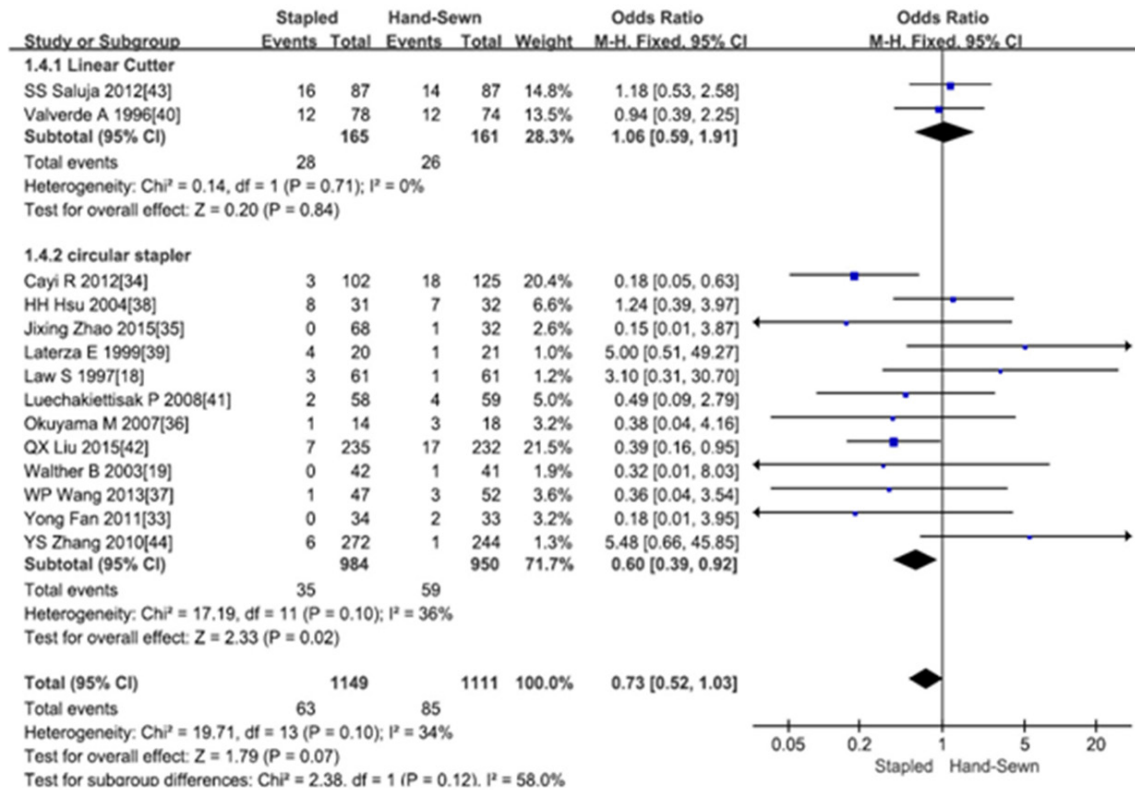


Figure 2. Meta-analysis of the rate of anastomotic leaks.

Characteristics of included studies

Specific characteristics of included studies are demonstrated in **Table 1**. Six trials [33-35, 37, 42, 44] were performed in China, while other trials [18, 19, 36, 38-41, 43] were performed in India, Sweden, Japan, Taiwan, Italy, France, Thailand, and Hong Kong. According to the information in all trials, the two groups were well matched at baseline.

Risk of bias in included studies

Risk of bias in included trials is shown in **Table 2**. All trials were randomized, one [43] was randomized by computer-generated numbers, three [38, 42, 44] were randomized by chart number, one [41] was randomized by odd/even counter number, and one [37] was randomized by a ratio of 1:1. Allocation concealment was reported in six trials [18, 19, 36, 39, 40, 42]. Allocation concealment was used by envelope and questionnaires, while blinding was not reported in any trials.

Rate of anastomotic leaks

PFS was reported in fourteen trials [18, 19, 33, 44]. A fixed-effects model was used, as no sig-

nificant heterogeneity existed among trials ($I^2 = 34\%$, $P = 0.10$). The meta-analysis results of overall rate of anastomotic leaks demonstrated no statistically significant differences between the two groups [OR = 0.73; 95% CI (0.52, 1.03), $P = 0.07$] (**Figure 2**). According to subgroup analysis of the circular stapler, stapled esophagogastric anastomosis obviously decreased the rate of anastomotic leaks over hand-sewn esophagogastric anastomosis [OR = 0.60; 95% CI (0.39, 0.92), $P = 0.02$]. In subgroup analysis of the linear cutter, a fixed-effects model was used, as explained above. Analysis results of the rate of anastomotic leaks showed no statistically significant differences between the two groups in the linear cutter group [OR = 1.06; 95% CI (0.59, 1.91), $P = 0.84$].

Rate of anastomotic stricture

Rate of anastomotic stricture was reported in thirteen trials [18, 33, 44]. There existed significant heterogeneity among trials ($I^2 = 63\%$, $P = 0.001$). Subgroup analysis of anastomotic stricture was performed according to site of anastomosis. Compared to hand-sewn anastomotic, anastomotic stricture was significantly reduced

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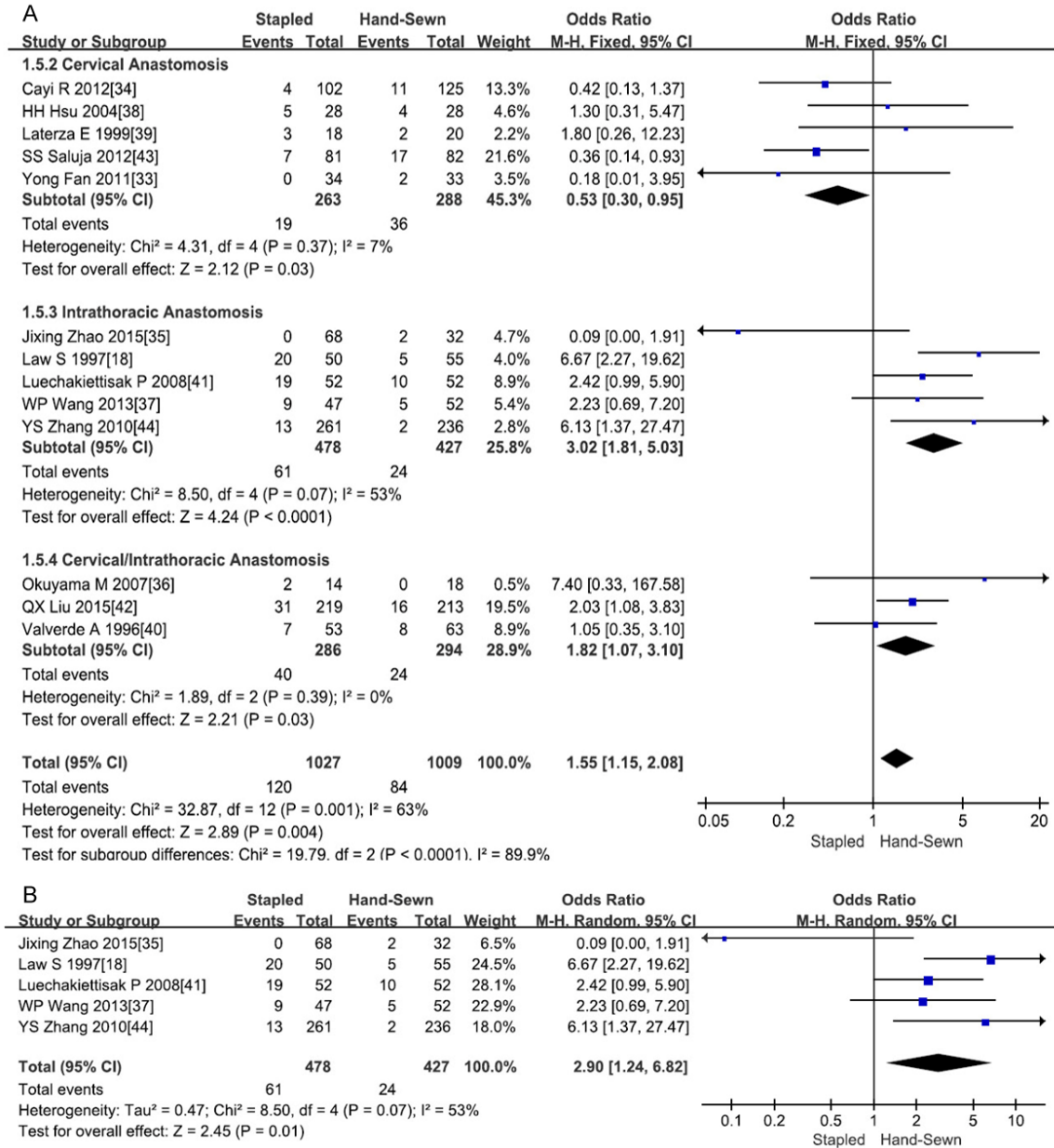


Figure 3. A. Meta-analysis of the rate of anastomotic stricture; B. Meta-analysis of the rate of anastomotic stricture in intrathoracic anastomosis group.

in the neck in the stapled anastomotic group [OR = 0.53, 95% CI (0.30, 0.95), P = 0.03] (Figure 3A). A fixed-effects model was used in the subgroup analysis of cervical/intrathoracic anastomosis group, as there was no statistically significant heterogeneity between trials (I² = 0%, P = 0.39). Meta-analysis results of the rate of anastomotic stricture showed statistically significant differences between the two groups in the cervical/intrathoracic anastomosis group [OR = 1.82, 95% CI (1.07, 3.10), P = 0.03] (Figure 3A). In intrathoracic anastomosis subgroup analysis, a random-effects model

was applied because of the significant heterogeneity between trials (I² = 53%, P = 0.07). Results of the rate of anastomotic stricture showed statistically significant differences between the two groups in the intrathoracic anastomosis group [OR = 2.90, 95% CI (1.24, 6.82), P = 0.01] (Figure 3B).

Operating time (OT)

OT was reported in ten trails [18, 19, 35, 36, 38, 40, 41-44]. A random-effects model was adopted due to significant heterogeneity among

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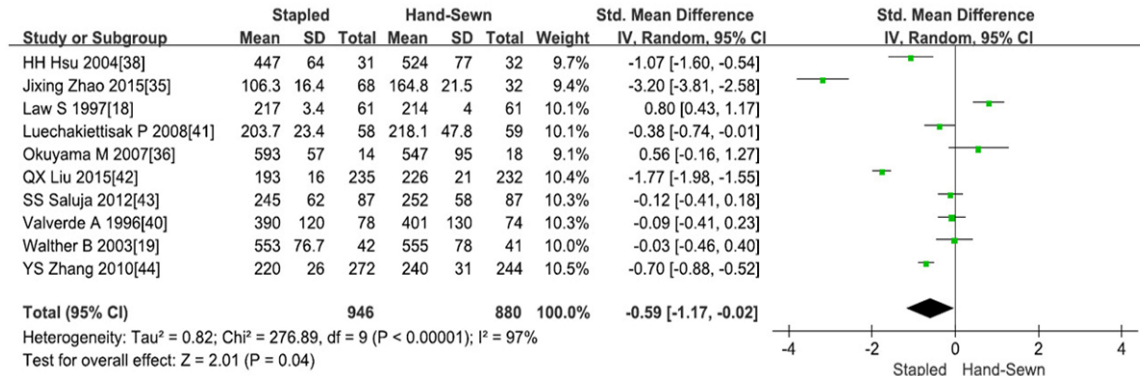


Figure 4. Meta-analysis of operating time (OT).

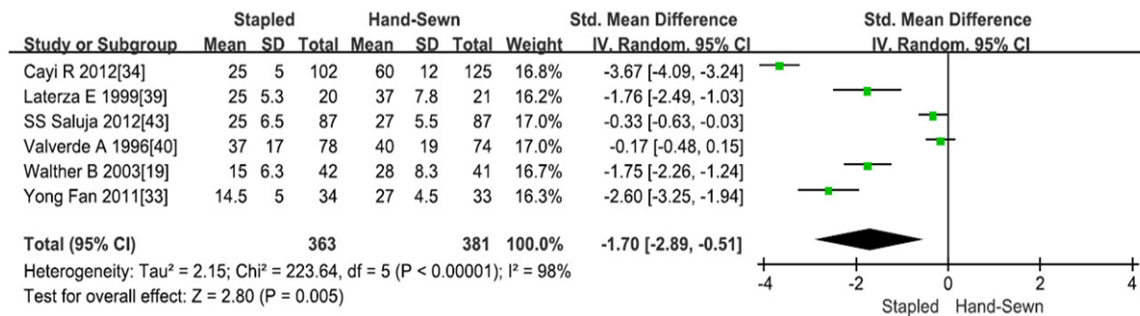


Figure 5. Meta-analysis of time of anastomosis.

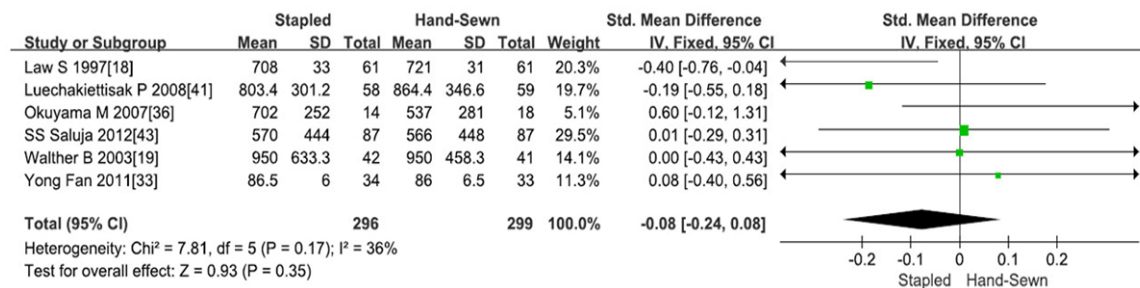


Figure 6. Meta-analysis of blood loss.

trials (I² = 97%, P < 0.00001). Results of the OT showed statistically significant differences between the two groups [SMD = -0.59; 95% CI (-1.17, -0.02), P = 0.04] (Figure 4).

Time of anastomosis

Time of anastomosis was reported in six trials [19, 33, 34, 39, 40, 43]. A random-effects model was used due to significant heterogeneity between trials (I² = 98%, P < 0.00001). Results of time of anastomosis showed statistically significant differences between the two

groups [SMD = -1.7; 95% CI (-2.89, -0.51), P = 0.005] (Figure 5).

Blood loss

Blood loss was reported in six trials [18, 19, 33, 36, 41, 43]. A fixed-effects model was applied as there was no statistically significant heterogeneity between trials (I² = 36%, P = 0.17). Results of blood loss showed no statistically significant differences between the two groups [SMD = -0.08; 95% CI (-0.24, 0.08), P = 0.35] (Figure 6).

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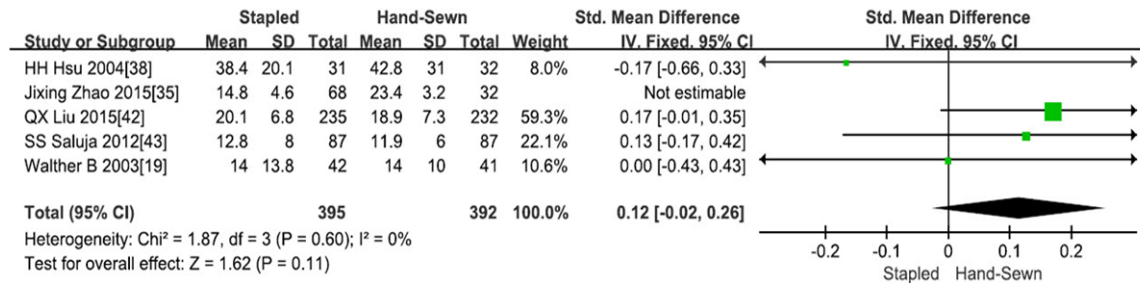


Figure 7. Meta-analysis of hospital stays.

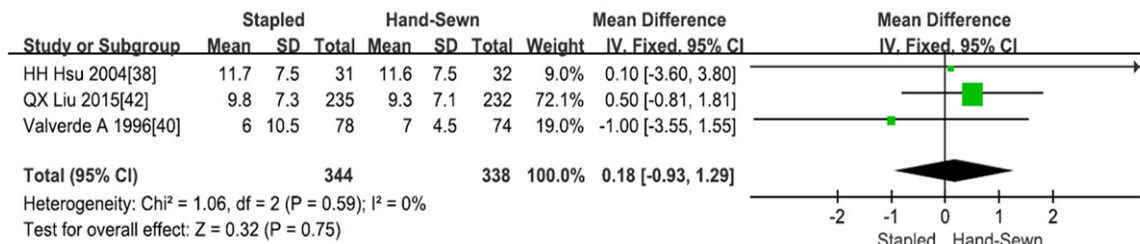


Figure 8. Meta-analysis of median duration of stays in intensive care units.

Table 3. Meta-analysis results of complications in included studies

| Complication | Stapled | Hand-Sewn | I ² (%) | Heterogeneity: P | OR (95% CI) | P |
|--|---------|-----------|--------------------|------------------|-------------------|------|
| Hospital mortality [18, 19, 38, 39, 43] | 17/241 | 16/242 | 0 | 0.92 | 1.08 (0.53, 2.20) | P |
| Blood-borne infection [38, 40] | 13/109 | 25/106 | 0 | 0.98 | 0.44 (0.21, 0.91) | 0.03 |
| Cardiac complication [18, 19, 38, 40-42] | 67/505 | 58/499 | 0 | 0.92 | 1.18 (0.80, 1.74) | 0.40 |
| Pulmonary complication [18, 19, 36, 38, 40-42] | 118/519 | 102/517 | 0 | 0.61 | 1.21 (0.88, 1.66) | 0.24 |
| Repeat operation [19, 40] | 15/120 | 12/115 | 0 | 0.43 | 1.22 (0.54, 2.75) | 0.63 |
| Recurrent laryngeal nerve palsy [19, 36] | 1/56 | 9/59 | 0 | 0.55 | 0.14 (0.02, 0.84) | 0.03 |

Hospital stays

Hospital stays were reported in five trails [19, 35, 38, 42, 43]. A fixed-effects model was used because no significant heterogeneity existed between trials (I² = 0%, P = 0.60). Result of hospital stays showed no statistically significant differences between the two groups [SMD = 0.12; 95% CI (-0.02, 0.26), P = 0.11] (Figure 7).

Median duration of stays in intensive care unit

Median duration of stays in intensive care units was reported in three trails [38, 40, 42]. A fixed-effects model was applied since no significant heterogeneity existed between trials (I² = 0%, P = 0.59). Results of median duration of stays in intensive care units demonstrated no statistically significant differences between the two groups [SMD = 0.18; 95% CI (-0.93, 1.29), P = 0.75] (Figure 8).

Complications

Complications were reported in seven trails [18, 19, 36, 38, 40-42]. Complications in included trials are summarized in Table 3. Results showed that stapled anastomosis can decrease the rate of the blood-borne infections and recurrent laryngeal nerve palsy. However, results showed no increase in the rate of hospital mortality, pulmonary and cardiac complications, and repeat operations.

30-day mortality

Reports regarding 30-day mortality were shown in seven trails [18, 36, 38, 40-42, 44]. A fixed-effects model was applied since no significant heterogeneity existed between trials (I² = 0%, P > 0.1). Results of 30-day mortality showed no statistically significant differences between the two groups [OR = 1.59; 95% CI (0.95, 2.66), P = 0.08] (Figure 9).

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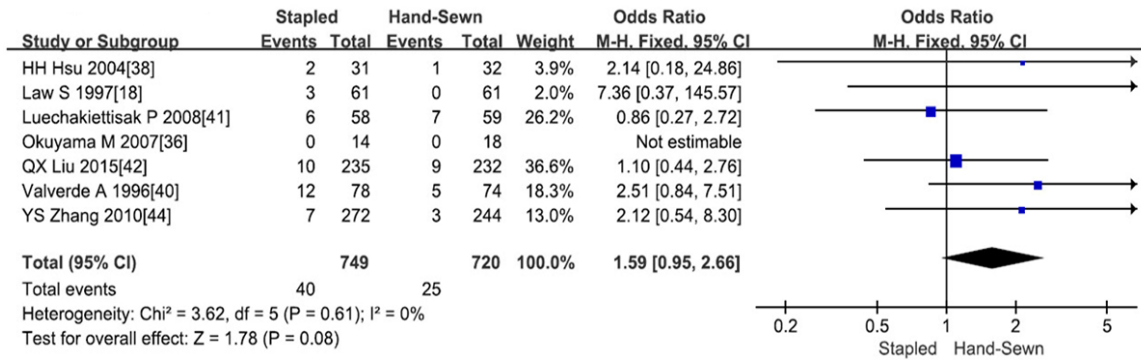


Figure 9. Meta-analysis of 30-day mortality.

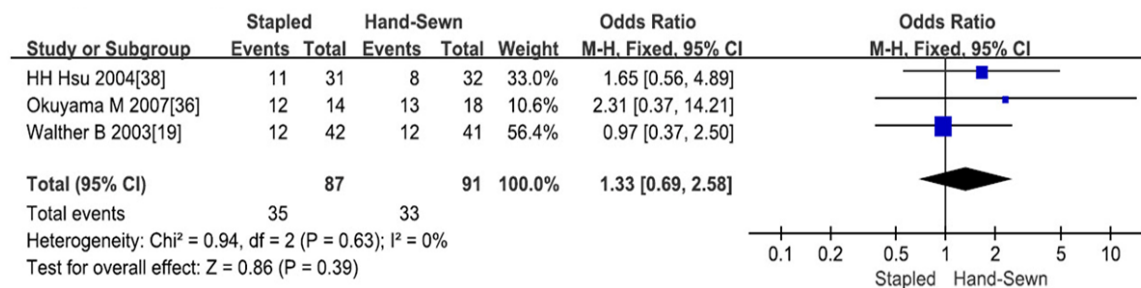


Figure 10. Meta-analysis of 5-year survival rate.

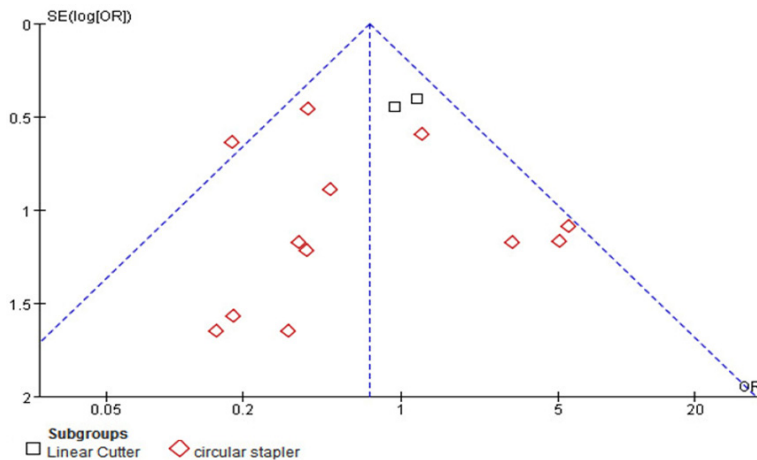


Figure 11. Funnel plot analysis of 14 studies.

5-year survival rate

The 5-year survival rate was reported in three trails [19, 36, 38]. A fixed-effects model was adopted as there was no significant heterogeneity between trials (I² = 0%, P > 0.1). Results of the 5-year survival rate showed no statistically significant differences between the two groups [OR = 1.33; 95% CI (0.69, 2.58), P = 0.39] (Figure 10).

Publication bias

Publication bias of included studies was analyzed by a funnel plot. The symmetry of the funnel plot was better, so publication bias may be less (Figure 11).

Discussion

The first-line treatment for esophageal cancer is still esophagectomy, with chemotherapy and/or radiation therapy combined or not [45]. Techniques involved in esophagectomy are complex and diversified, and having been associated with many postoperative complications [46]. Two prevalent and serious complications are anastomotic leakage and anastomotic stricture. These are responsible for postoperative morbidity and other complications, drawing much attention to the method of anastomosis [47, 48]. Hand-sewing and stapling with a mechanical device are two different methods used in esophagogastric anastomoses. Many debates have arisen regarding the

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advantages and negative aspects of these methods [49].

This present meta-analysis was based on fourteen RCTs, including 2,260 patients. All patients were well-matched for sex, age, and type of disease. All trials were randomized. Out of the 14 included studies, only six trials [37, 38, 41-44] mentioned adequate sequence generation, possibly producing selective bias. Allocation concealment was reported in six trials [18, 19, 36, 39, 40, 42], which might result in unclear risk of selection bias as it was possible for physicians to alter their assignment when recruiting participants if allocation was concealed.

Meta-analysis results showed that, comparing the stapled anastomosis and hand-sewn anastomosis groups, statistically significant differences were observed in anastomotic leaks of the circular stapler subgroup [OR = 0.60; 95% CI (0.39, 0.92), P = 0.02] and anastomotic stricture of the neck anastomotic subgroup [OR = 0.53, 95% CI (0.30, 0.95), P = 0.03], cervical/intrathoracic anastomosis subgroup [OR = 1.82, 95% CI (1.07, 3.10), P = 0.03], and intrathoracic anastomosis subgroup [OR = 2.90, 95% CI (1.24, 6.82), P = 0.01]. Operating time (OT) [SMD = -0.59; 95% CI (-1.17, -0.02), P = 0.04], time of anastomosis [SMD = -1.7; 95% CI (-2.89, -0.51), P = 0.005], blood-borne infections [OR = 0.44, 95% CI (0.21, 0.91), P = 0.03], and recurrent laryngeal nerve palsy [OR = 0.14, 95% CI (0.02, 0.84), P = 0.03] were also significantly different compared with the hand-sewn esophagogastric anastomosis group. There were no statistically significant differences between the two groups with respect to overall rate of anastomotic leaks [OR = 0.73; 95% CI (0.52, 1.03), P = 0.07], rate of anastomotic leaks of the liner cutter subgroup [OR = 1.06; 95% CI (0.59, 1.91), P = 0.84], blood loss [SMD = -0.08; 95% CI (-0.24, 0.08), P = 0.35], hospital stay [SMD = 0.12; 95% CI (-0.02, 0.26), P = 0.11], median duration of stay in intensive care unit [SMD = 0.18; 95% CI (-0.93, 1.29), P = 0.75], hospital mortality [OR = 1.08; 95% CI (0.53, 2.20), P = 0.83], cardiac complications [OR = 1.18; 95% CI (0.80, 1.74), P = 0.40], pulmonary complications [OR = 1.21; 95% CI (0.88, 1.66), P = 0.24], repeat operations [OR = 1.22; 95% CI (0.54, 2.75), P = 0.63], 30-day mortality [OR = 1.59; 95% CI (0.95, 2.66), P = 0.08], and 5-year survival rate [OR = 1.33; 95% CI (0.69, 2.58), P = 0.39].

Subgroup analyses revealed that, following stapled anastomosis, incidence of anastomotic stricture significantly increased in the intrathoracic anastomotic subgroup, while significantly decreasing in the neck anastomotic subgroup, compared with hand-sewn anastomosis. This might be due to necrosis of tissue beyond the staple line and the type and size of stapler, while hand-sewn anastomoses could avoid risk of tissue strangulation. Time of operation and anastomosis were slightly reduced for stapled anastomoses. The higher rate of blood-borne infections in the hand-sewn group could be a result of longer operation times. In addition, prolonged surgery time can be associated with a lot of postoperative complications [50, 51]. However, the rate of hospital mortality, rate of repeat operations, rate of 30-day mortality, and 5-year survival rates were not different, indicating that no matter what anastomotic method is used, it will not affect long-term effects.

There were some limitations that should be noted and improved in future studies. (1) Blinding was not reported in any trial, which may have led to a high risk of performance or detection bias. Future research should specify the process of implement blinding. Even after a comprehensive literature search, it is still possible to miss clinical studies, published or unpublished, resulting in nonpublication bias. Also, none of the trials were multicenter studies. (2) In fourteen trials, the site of esophageal anastomosis was different, possibly influencing meta-analysis results. (3) In fourteen trials, the type of stapler was different, such as circular stapler and liner cutter stapler. Surgical experience also differed. (4) Rigorous test designs should be conducted to reduce bias.

Conclusion

In summary, this meta-analysis, comparing stapled and handsewn esophagogastric anastomoses, showed that stapled anastomosis decreased the rate of anastomotic leaks in circular and liner cutter stapler subgroup, shortened the operating time and time of anastomosis, decreased the rate of anastomotic stricture in the neck anastomotic subgroup, and reduced the rate of the blood-borne infections and recurrent laryngeal nerve palsy and in the circular stapler subgroup. Blood loss, hospital stays, median duration of stays in intensive care units, rate of other complications (hospital mor-

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tality, cardiac complication, pulmonary complication, and repeat operations), and long-term treatment effects (30-day mortality and the 5-year survival rate) were similar between the two groups. Stapled anastomosis achieves different results regarding the rate of anastomotic stricture for different anastomosis sites. Furthermore, the stapled technique is easy to use and is standardized, while the hand-sewn method requires expertise. Therefore, this study concludes that stapled anastomosis should be recommended over the hand-sewn anastomosis method. Although existing evidence confirms the present results, large-sample, multi-center, and randomized controlled trial outcomes are still needed.

Disclosure of conflict of interest

None.

Address correspondence to: Desheng Lv, Department of Thoracic Surgery, The Second Affiliated Hospital of Dalian Medical University, Dalian 116023, China. E-mail: dslvts@126.com

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