

Comparative analysis of manual vs. mechanical suturing techniques in esophagectomy: A propensity score-matched study of long-term outcomes

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Abstract. Esophageal cancer, particularly esophageal squamous cell carcinoma (ESCC), is a major health concern worldwide, particularly in China. Surgical resection is still considered the primary curative treatment for this disease. However, the effect of different surgical methods-traditional hand-sewn anastomosis and modern mechanical anastomosis-remains controversial. A retrospective study was thus performed to elucidate how these two techniques affected the clinical prognosis of patients. Data were retrospectively collected from the comprehensive Esophageal Cancer Case Management Database of Sichuan Cancer Hospital and

Institute (Chengdu, China), covering the period from 2010 to 2017. The cohort consisted of patients who underwent esophagectomy for ESCC, divided into two groups based on the suturing technique used: Manual suturing (MS) and mechanical suturing (MeS). A total of four causal inference methods for retrospective studies, namely inverse probability of treatment weighting, standardized mortality ratio weighting, overlap weighting and propensity score matching analysis, were used to minimize potential selection bias. The primary outcome evaluated was overall survival (OS), allowing for a direct comparison of the long-term efficacy of the two suturing methods. In a retrospective analysis of 2,510 patients undergoing esophagectomy, significant differences in OS were observed between the MeS group and the MS group (hazard ratio: 0.84; 95% confidence interval: 0.75-0.95; P=0.004). However, after matching or weighting based on causal inference analyses, no significant differences in survival outcomes between groups were obtained. The equivalence in outcomes suggests that either suturing method may be equally viable in clinical practice, offering flexibility in surgical decision-making without compromising OS.

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Abbreviations: ESCC, esophageal squamous cell carcinoma; LN, lymph node; OS, overall survival; TNM, tumor-node-metastasis; HR, hazard ratio; CI, confidence interval; PSM, performing propensity score matching; KPS, Karnofsky performance status; IPTW, inverse probability of treatment weighting; OW, overlap weighting

Key words: esophageal squamous cell carcinoma, manual suturing, mechanical suturing, esophagectomy, overall survival

Introduction

Esophageal cancer is recognized as one of the most aggressive types of malignancy, with a poor prognosis and low overall survival rate, making it a significant global health concern. The main histological type of this cancer, particularly common in East Asian populations, is esophageal squamous cell carcinoma (ESCC) (1-3). Patients with ESCC still have high risks of lymph node (LN) metastasis and poor long-term overall survival (OS) outcomes (4-6). Depending on the clinical stage, patients often undergo preoperative neoadjuvant chemotherapy, chemoradiotherapy or chemotherapy immunization, followed by postoperative immunotherapy maintenance.

Despite advancements in treatment strategies, esophagectomy remains the primary treatment approach for ESCC within multimodal therapy (7-10).

Surgical outcomes in esophagectomy are influenced by various patient-specific factors, underscoring the necessity for personalized treatment approaches tailored to individual clinical scenarios (11-13). While manual suturing (MS) has traditionally been the method of choice (14-16), the emergence of mechanical suturing (MeS) as a viable alternative has garnered interest (17,18). MS, also known as hand-sewn anastomosis, is a traditional surgical technique used to join the two ends of the esophagus following resection. This method provides greater flexibility in tailoring the anastomosis to the specific anatomical and physiological conditions of the patient; however, it is typically more time-consuming. By contrast, MeS, or stapled anastomosis, is a more modern technique that employs a mechanical stapler to connect the esophageal tissues. This approach creates a secure and uniform anastomosis, ensuring consistency in tissue approximation while reducing operative time. Additionally, the use of a stapler requires specific equipment and may incur higher costs compared to manual suturing. MeS was first reported by Sugimura *et al* (15), and later improved by Orringer *et al* (19). Both MS and MeS techniques have their specific advantages and disadvantages. Studies by Kondra *et al* (20), Singhal *et al* (21) and Singh *et al* (22) suggest that MeS significantly reduces the incidence of postoperative anastomotic leaks and strictures in esophageal cancer surgeries, considering it a safe and effective technique. When MeS is difficult or fails, MS becomes an important alternative (23). Initial comparisons between MS and MeS have indicated similar immediate postoperative outcomes and complication rates, hinting at a potential shift in surgical techniques (24). However, controversy remains over which suturing method is better and long-term survival data comparing these techniques in esophagectomy are lacking. Such research is essential for refining surgical practices and enhancing the long-term prognosis of patients undergoing esophagectomy for ESCC.

The present study aimed to account for various potential confounders in order to ensure an unbiased and precise comparison of the long-term outcomes linked to each technique. This will be achieved through a comprehensive causal inference analysis to compare the long-term outcomes of MS and MeS following esophagectomy.

Materials and methods

Patients and methods. This retrospective study examined data from 2,510 patients diagnosed with ESCC who underwent esophagectomy at Sichuan Cancer Hospital (Sichuan, China) between January 2010 and December 2017. The data were obtained from the Esophageal Cancer Case Management database of Sichuan Cancer Hospital and Institute. The study aimed to compare the long-term OS outcomes between MS and MeS techniques used in esophagectomy. Patients included in the study had undergone esophagectomy for ESCC within the specified period and met the criteria of thoracic ESCC staging according to the 8th edition TNM staging system by the Union for International Cancer Control/American Joint Committee on Cancer (25). Exclusion criteria encompassed non-squamous

cell carcinoma histology in a surgical specimen, tumors located outside the thoracic esophagus, evidence of distant metastasis, R1/R2 resection (indicative of incomplete tumor removal), stage pTis/T1a, receipt of preoperative neoadjuvant therapy and missing data (Fig. 1).

Outcome measures. Demographic data, smoking and alcohol consumption history, clinical stage and tumor characteristics were collected for each patient. Clinical staging was reviewed by multiple experts and pathological findings were confirmed by two pathologists, with a third pathologist's review for accuracy. Patients were followed up every 3 months for the first 2 years post-surgery and then every 6 months for the next 3-5 years. OS, defined as the time from surgery to death from any cause or last known follow-up, served as the primary endpoint.

Statistical analysis. Categorical variables were presented as percentages and analyzed using chi-square or Fisher's exact test, as appropriate. The Kaplan-Meier method was used to generate survival curves and differences were assessed using the log-rank test. Univariate and multivariate logistic regression using the Cox proportional hazards model identified independent predictors of OS, providing hazard ratios (HRs) and 95% confidence intervals (CIs). To minimize selection bias and balance baseline characteristics between the MS and MeS Groups, four causal inference methods was performed. Propensity scores were calculated using logistic regression based on age, sex and other relevant baseline characteristics [propensity score matching (PSM)]. A 1:1 nearest-neighbor matching algorithm without replacement and a caliper width of 0.25 times the standard deviation of the logit of the propensity score were used. Sensitivity analyses with inverse probability of treatment weighting (IPTW), overlap weighting (OW) and standardized mortality ratio weighting (SMRW) validated the findings. Statistical significance was set at a two-sided P-value of <0.05. Analyses were conducted using SPSS version 23.0 (IBM Corp.) and RStudio software with R 4.3 (The R Foundation).

Results

Demographic data. The initial dataset included 2,957 patients diagnosed with ESCC who underwent esophagectomy at Sichuan Cancer Hospital between January 2010 and December 2017. After applying the exclusion criteria, 440 patients were excluded from the analysis. Specifically, 109 patients were excluded due to non-squamous cell carcinoma histology, 56 for tumor locations outside the thoracic region, 148 for R1/R2 resections indicating incomplete tumor removal, 5 for metastases to other organs, 122 for early-stage (pTis/T1a) disease and 7 for missing data. Consequently, a total of 2,510 patients were eligible for the study, as shown in the study flowchart in Fig. 1. A total of 82.1% of the patients (n=2,060) were male and 17.9% (n=450) were female. Approximately 57.5% of the patients (n=1,443) were above stage III, with 5.8% of the patients (n=212) aged >75 years (Table I). Before PSM, there were statistically significant differences between the MS and MeS groups in terms of sex, KPS, smoking history, tumor location, thoracic surgery, abdominal surgery, surgical approach and clinical treatment modality. However, after PSM,

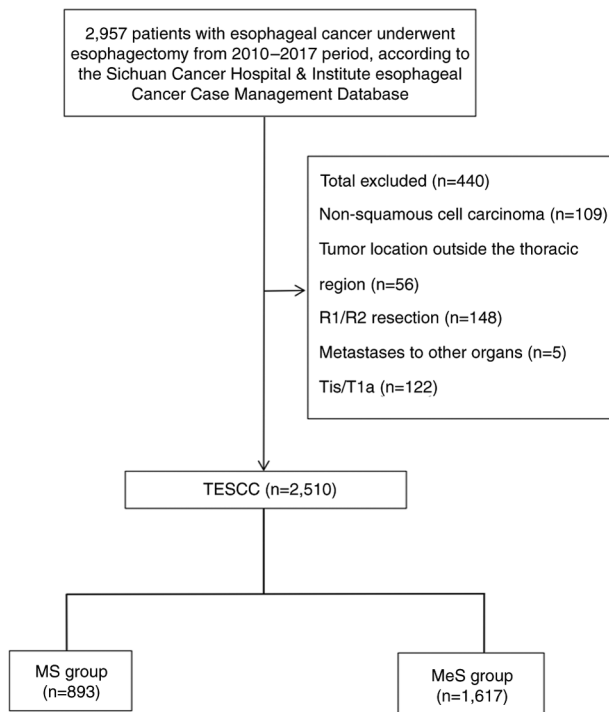


Figure 1. Consolidated Standards of Reporting Trials flow chart of patient selection. TESCC, thoracic esophageal squamous cell carcinoma; MS, manual suturing; MeS, mechanical suturing.

these baseline characteristics were well-balanced between the two groups, ensuring comparability for subsequent analyses.

OS. The study included 1,617 (64.4%) patients in the MeS group and 893 (35.6%) patients in the MS group. The median follow-up duration was 63.97 months. Patients in the MeS group had a median OS of 42.67 months (95% CI: 38.55-46.78), while those in the MS group had a median OS of 56.47 months. The 1-, 3- and 5-year OS rates were 86, 54 and 43% for patients in the MeS group, and 87, 60 and 50% for patients in the MS group, respectively [MeS vs. MS hazard ratio (HR): 0.84; 95% CI: 0.75-0.95; $P=0.004$; Fig. 2]. Following 1:1 PSM, the analysis showed no significant differences between the MeS and MS groups (HR: 0.88; 95% CI: 0.75-1.03; $P=0.099$; Fig. 3A). Similar results were observed after applying the IPTW, OW and SMRW methods (HR: 0.89; 95% CI: 0.89-1.13; $P=0.107$; Fig. 3B/HR: 0.91; 95% CI: 0.88-1.13; $P=0.102$; Fig. 3D and HR: 0.91; 95% CI: 0.91-1.11; $P=0.207$; Fig. 3E). Fig. 3C illustrates that for the 1:1 PSM, IPTW and OW methods, the standardized mean difference for all variables is <0.1 .

Risk factors. Factors significantly affecting OS after esophagectomy were identified through univariate analyses. These factors included drinking ($P<0.01$), smoking ($P<0.01$), age ($P<0.01$), Karnofsky performance status (KPS) scores ($P<0.01$), sex ($P<0.01$), thoracic surgical type ($P<0.01$), abdominal surgical type ($P=0.02$), surgical approach ($P<0.01$), tumor grade ($P<0.01$), lymphovascular invasion ($P<0.01$), nerve invasion ($P<0.01$), method of anastomosis ($P<0.01$), pathological T category ($P<0.01$), pathological N category ($P<0.01$) and TNM stage according to the eighth edition ($P<0.01$; Fig. 4). Multivariate analyses indicated that drinking

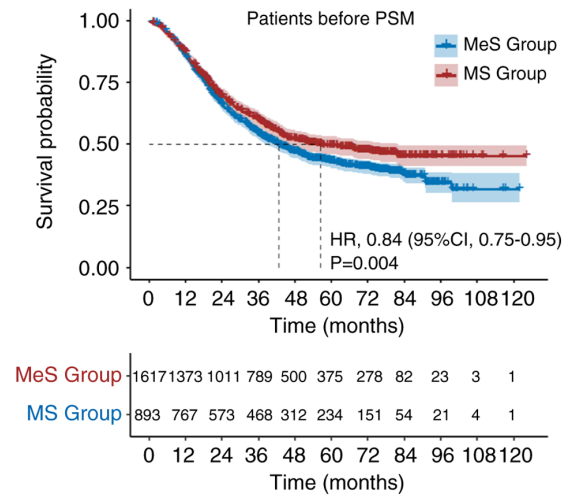


Figure 2. Overall survival curves of participants. MS, manual suturing; MeS, mechanical suturing; PSM, performing propensity score matching; HR, hazard ratio.

($P<0.01$), age ($P<0.01$), sex ($P=0.03$), method of anastomosis ($P=0.03$), lymphovascular invasion ($P=0.04$), pathological T3 category ($P=0.06$), pathological N2 category ($P<0.01$) and pathological N3 category ($P=0.03$) were independent influencing factors for OS after esophagectomy compared with other factors (Fig. 4).

Discussion

The impact of mechanical vs. manual suturing techniques on OS in patients undergoing esophagectomy is a critical consideration. In the present study, initially, patients in the MS group showed a superior median OS compared to the MeS group, suggesting a significant influence of the suturing technique on postoperative outcomes. However, subsequent analysis following PSM revealed that the differences between groups were not statistically significant. This implies that when matched for similar baseline characteristics, the choice of suturing technique may not be as crucial for OS as previously thought. The similarity in survival outcomes between MS and MeS provides surgeons with the flexibility to select a technique based on other factors, such as their proficiency, patient-specific anatomical or physiological considerations, and resource availability. Further investigation through univariate and multivariate analyses highlights other factors that have a more substantial impact on survival outcomes. Lifestyle factors like the drinking and smoking status, as well as clinical indicators, such as age, KPS scores, sex, tumor grade and the presence of lymphovascular and nerve invasion, emerge as significant predictors of OS. These results were also confirmed in corresponding studies and emphasized the multifaceted nature of survival following esophagectomy (26), where the surgical technique is just one of several variables influencing patient outcomes.

The ongoing discussion and evolution of treatment strategies for esophageal cancer emphasize a comprehensive approach that combines surgery with various adjuvant therapies to improve patient outcomes (26-29). Surgical resection remains crucial in esophageal cancer treatment, but the complexity of

Table I. Demographic characteristics of the MeS group and the MS group.

Characteristic	Total	Before PSM		P-value	After PSM		P-value
		MeS group (n=1,617)	MS group (n=893)		MeS group (n=643)	MS group (n=643)	
Sex				0.017			0.783
Male	2,060 (82.1)	1,349 (83.4)	711 (79.6)		508 (79.0)	512 (79.6)	
Female	450 (17.9)	268 (16.6)	182 (20.4)		135 (21.0)	131 (20.4)	
Age, years				0.916			0.900
<75	2,365 (94.2)	1,523 (94.2)	842 (94.3)		610 (94.9)	609 (94.7)	
≥75	145 (5.8)	94 (5.8)	51 (5.7)		33 (5.1)	34 (5.3)	
KPS				<0.001			0.908
≥90	1,419 (56.5)	798 (49.4)	621 (69.5)		410 (63.8)	408 (63.5)	
≤80	1,091 (43.5)	819 (50.6)	272 (30.5)		233 (36.2)	235 (36.5)	
Smoker				<0.001			0.954
No	1,340 (53.4)	724 (44.8)	616 (69.0)		411 (63.9)	412 (64.1)	
Yes	1,170 (46.6)	893 (55.2)	277 (31.0)		232 (36.1)	231 (35.9)	
Drinker				0.157			0.852
No	1,841 (73.3)	1,171 (72.4)	670 (75.0)		467 (72.6)	464 (72.2)	
Yes	669 (26.7)	446 (27.6)	223 (25.0)		176 (27.4)	179 (27.8)	
Pathologic differentiation grade				0.204			0.755
Well G1	455 (18.1)	279 (17.3)	176 (19.7)		120 (18.7)	128 (19.9)	
Moderate G2	1,046 (41.7)	691 (42.7)	355 (39.8)		270 (42.0)	258 (40.1)	
Poor or undifferentiated G3	1,009 (40.2)	647 (40.0)	362 (40.5)		253 (39.3)	257 (40.0)	
Lymphovascular invasion				0.147			1.000
No	442 (17.6)	1,319 (81.6)	749 (83.9)		529 (82.3)	529 (82.3)	
Yes	2,068 (82.4)	298 (18.4)	144 (16.1)		114 (17.7)	114 (17.7)	
Nerve invasion				0.133			0.945
No	487 (19.4)	1289 (79.7)	734 (82.2)		513 (79.8)	514 (79.9)	
Yes	2,023 (80.6)	328 (20.3)	159 (17.8)		130 (20.2)	129 (20.1)	
Tumor location				<0.001			0.951
Upper	587 (23.4)	330 (20.4)	257 (28.8)		169 (26.3)	166 (25.8)	
Middle	1,367 (54.5)	893 (55.2)	474 (53.1)		364 (56.6)	363 (56.5)	
Lower	556 (22.2)	394 (24.4)	162 (18.1)		110 (17.1)	114 (17.7)	
Pathological T category				0.260			0.987
T1	202 (8.0)	120 (7.4)	82 (9.2)		62 (9.6)	66 (10.3)	
T2	509 (20.3)	333 (20.6)	176 (19.7)		124 (19.3)	123 (19.1)	
T3	1,584 (63.1)	1,033 (63.9)	551 (61.7)		392 (61.0)	389 (60.5)	
T4	215 (8.6)	131 (8.1)	84 (9.4)		65 (10.1)	65 (10.1)	
Pathological N category				0.272			0.903
N0	1,084 (43.2)	702 (43.4)	382 (42.8)		280 (43.5)	282 (43.9)	
N1	761 (30.3)	505 (31.2)	256 (28.7)		190 (29.5)	197 (30.6)	
N2	450 (17.9)	281 (17.4)	169 (18.9)		111 (17.3)	109 (17.0)	
N3	215 (8.6)	129 (8.0)	86 (9.6)		62 (9.6)	55 (8.6)	
8th TNM stage				0.182			0.927
I	202 (8.0)	120 (7.4)	82 (9.2)		61 (9.5)	62 (9.6)	
II	865 (34.5)	573 (35.4)	292 (32.7)		215 (33.4)	218 (33.9)	
III	1,152 (45.9)	746 (46.1)	406 (45.5)		284 (44.2)	288 (44.8)	
IV	291 (11.6)	178 (11.0)	113 (12.7)		83 (12.9)	75 (11.7)	
Thoracic surgery				0.022			0.695
MIE	1,199 (47.8)	745 (46.1)	454 (50.8)		359 (55.8)	352 (54.7)	
OE	1,311 (52.2)	872 (53.9)	439 (49.2)		284 (44.2)	291 (45.3)	

Table I. Continued.

Characteristic	Total	Before PSM		P-value	After PSM		P-value
		MeS group (n=1,617)	MS group (n=893)		MeS group (n=643)	MS group (n=643)	
Abdominal surgery				<0.001			0.822
MIE	964 (38.4)	674 (41.7)	290 (32.5)		285 (44.3)	281 (43.7)	
OE	1,542 (61.4)	939 (58.1)	603 (67.5)		358 (55.7)	362 (56.3)	
None		4 (0.2)	0 (0.0)				
Surgical approach				<0.001			0.631
McKeown	1,779 (70.9)	1,009 (62.4)	770 (86.2)		528 (82.1)	534 (83.0)	
Iovr-Lewis	691 (27.5)	583 (36.1)	108 (12.1)		109 (17.0)	106 (16.5)	
Sweet	4 (0.2)	4 (0.2)	0 (0.0)				
Left thoracotomy and laparotomy	36 (1.4)	21 (1.3)	15 (1.7)		6 (0.9)	3 (0.5)	
Clinical treatment modality				<0.001			0.939
Preoperative CT or RT/CRT plus surgery	46 (1.8)	24 (1.5)	22 (2.5)		16 (2.5)	18 (2.8)	
Surgery alone	1,269 (50.6)	687 (42.5)	582 (65.2)		395 (61.4)	395 (61.4)	
Surgery plus postoperative CT or RT/CRT	1,195 (47.6)	906 (56.0)	289 (32.4)		232 (36.1)	230 (35.8)	

Values are expressed as n (%). PSM, performing propensity score matching; MS, manual suturing; MeS, mechanical suturing; KPS, Karnofsky performance status; CRT, chemoradiotherapy; CT, chemotherapy; MIE, minimally invasive esophagectomy; OE, open esophagectomy; RT, radiotherapy.

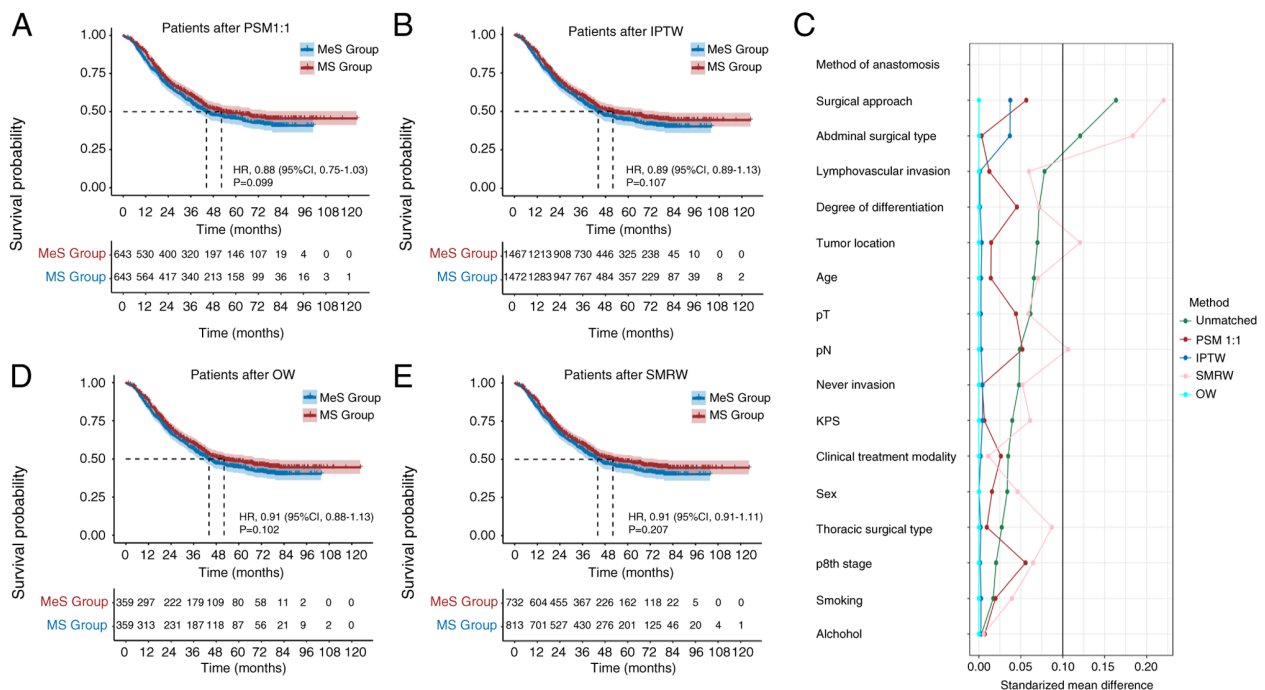


Figure 3. OS curves of participants. (A) OS curve of MeS and MS groups after PSM; (B) OS curve of MeS and MS groups after IPTW. (C) Standardized mean difference among the subjects stratified by characteristic. (D) OS curve of MeS and MS groups after OW; (E) OS curve of MeS and MS groups after SMRW. OS, overall survival; MS, manual suturing; MeS, mechanical suturing; HR, hazard ratio; PSM, performing propensity score matching; IPTW, inverse probability of treatment weighting; OW, overlap weighting; SMRW, standardized mortality ratio weighting; KPS, Karnofsky performance status.

the disease necessitates a comprehensive strategy involving neoadjuvant chemoradiotherapy, chemotherapy, combined

chemotherapy and immunotherapy, as well as postoperative immunotherapy maintenance (7,29-32).

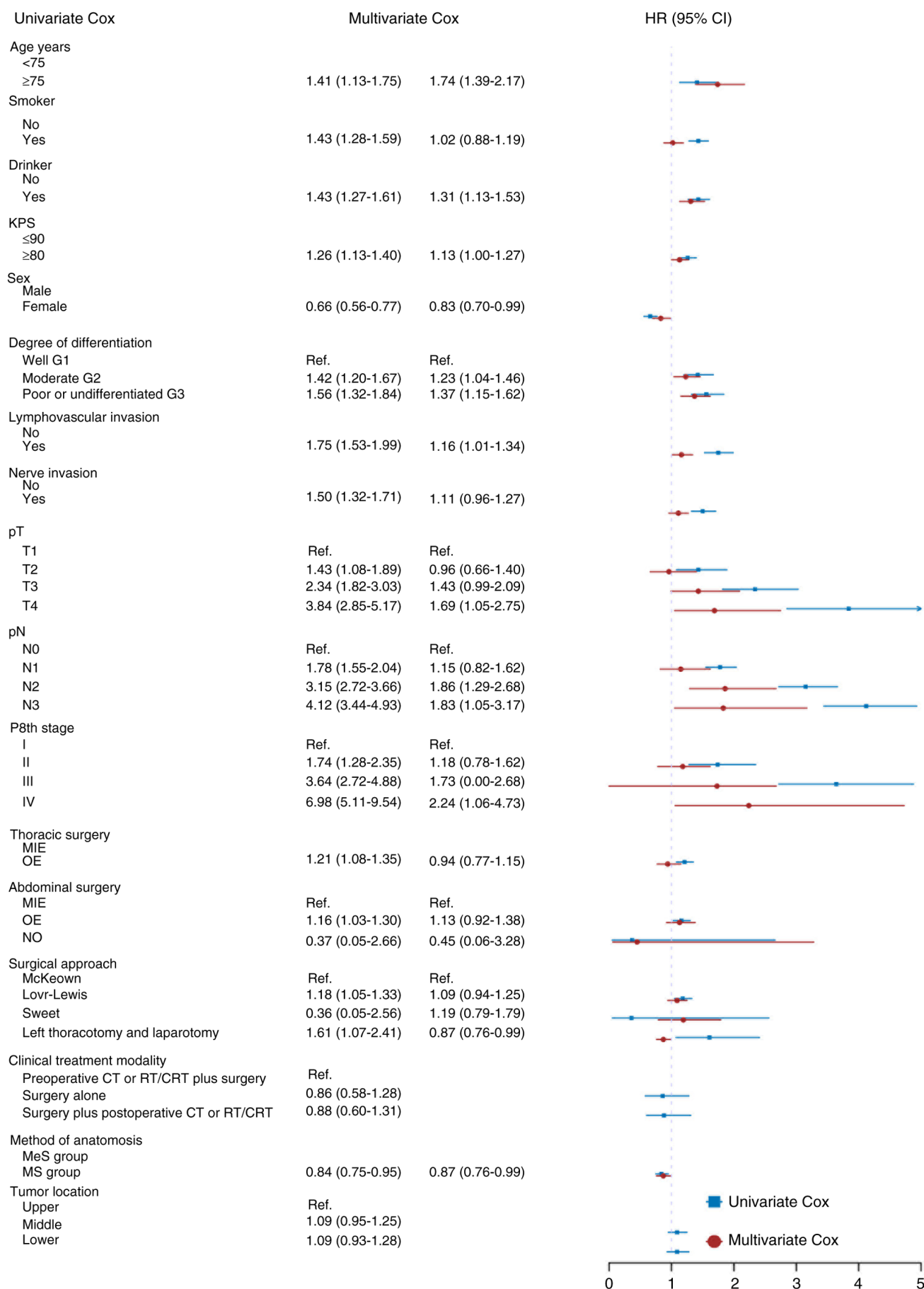


Figure 4. Univariate and multivariate Cox regression analyses regarding factors affecting patient survival. OS, overall survival; MS, manual suturing; MeS, mechanical suturing; HR, hazard ratio; KPS, Karnofsky performance status; CRT, chemoradiotherapy; CT, chemotherapy; MIE, minimally invasive esophagectomy; OE, open esophagectomy; RT, radiotherapy.

The debate among surgical experts revolves around the extent of LN dissection and the decision on thoracic duct resection, both crucial in treating esophageal cancer (33-35). LN involvement is a key factor in predicting adverse outcomes (4,5). The present study showed that there is no statistically significant difference in long-term survival between traditional manual anastomosis and mechanical anastomosis, suggesting both are viable options. The choice should be personalized based on the patient's condition and the surgeon's skill. As we delve deeper into treatment combinations, surgical techniques like LN dissection and thoracic duct management will continue to play a pivotal role. Future research should focus on not just the technical aspects of esophageal cancer surgery but also on integrating these techniques with other treatments to enhance survival, quality of life and patient-centered outcomes.

There are several limitations that should be acknowledged in the present study. The retrospective design of the study, despite using propensity score matching to minimize bias, inherently limits the ability to establish causality. Prospective randomized controlled trials are necessary to definitively compare the efficacy and safety of MS and MeS techniques. The data were collected from a single institution, which may limit the generalizability of the findings. Multi-center studies could provide a more representative overview of outcomes and potentially validate the applicability of these results across different surgical settings and populations. The study focused on OS as the primary endpoint, neglecting other important outcomes such as post-operative recovery, quality of life and complication rates. Furthermore, while the significance of preoperative neoadjuvant therapy, particularly for patients with T2/T3N0-1 ESCC, has been highlighted in studies like CROSS (8) and NEOCRTEC5010As the founder of the Department of Thoracic Surgery, he gave guidance and suggestions for the design and data collection of this study, and also gave guidance on each clinical technical issue at the discussion meeting

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

Study conception and design: SLu, KL, LJ, JX, SLi, ZW, HC, WH, CW, KW, HL, QZ, HZ, QF, QW, YH, LP and XL. Acquisition, analysis or interpretation of data: SLu, KL, LJ, JX, SLi, ZW, HC, WH, CW, KW, HL, QZ, HZ, QF, QW, YH, LP and XL. Drafting of the article: KL. Revising the article critically for important intellectual content: SLu, KL, LJ, JX, SLi, ZW, HC, WH, CW, KW, HL, QZ, HZ, QF, QW, YH, LP and XL. Statistical analysis: SLu. Obtained funding: XL. Administrative, technical or material support: YH and LP. Study supervision: XL, LP. SLu and XL confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee for Medical Research and New Medical Technology of Sichuan Cancer Hospital (Chengdu, China; approval no. SCCHEC-02-2022-050).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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