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# Long-term survival of esophageal squamous cell carcinoma after surgical treatment in a large-scale retrospective study from a single cancer center

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## Abstract

**Purpose** To analyze the long-term overall survival (OS) and influencing factors of patients with esophageal squamous cell cancer (ESCC) under surgical treatment.

**Method** We collected patients with ESCC who received surgical treatment in Sichuan Cancer Hospital & institute from January 2010 to December 2017, and selected 2,766 patients with thoracic esophageal carcinoma with relatively complete follow-up results as the objects of this study. We analyzed the characteristics, postoperative complications and long-term OS results of those patients.

**Results** Of the 2766 patients, 81.6% were male, midthoracic esophageal cancer accounted for 53.5%. McKeown was used in 72.0% of patients and Ivor-Lewis was used in 26.4% of patients. About 47.8% of patients received minimally invasive esophagectomy (MIE). The overall complication rate was 25.8%. The 1-year, 3-year and 5-year OS rates were 86.2%, 57.5% and 46.8%, respectively. McKeown had a better long-term OS rate than Ivor-Lewis (49.5% vs 41.2%,  $P < 0.001$ ), and MIE is superior to open surgery (51.8% vs 42.5%,  $P < 0.001$ ).

**Conclusion** McKeown has advantages over Ivor-Lewis. MIE results in better long-term survival outcomes for patients. But more prospective randomized controlled trials with large samples are needed.

**Keywords** Esophageal squamous cell carcinoma, Minimally invasive esophagectomy, Open surgery, McKeown, Ivor-Lewis, Overall survival rate

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## 1 Introduction

Esophageal cancer is one of the most common digestive tract tumors. According to GLOBOCAN 2020, the incidence rate of esophageal cancer ranks tenth in the world, and the mortality rate ranks seventh [1]. In China, as of 2015, there were 61,732 newly diagnosed cases of esophageal cancer (44,067 in males and 17,667 in females), with a crude incidence of  $19.24/10^5$ , 6.69% of new cancer cases and 47,373 deaths (34,262 in males and 13,111 in females). The crude mortality rate was  $14.76/10^5$ , accounting for 8.39% of the total cancer deaths [2]. The histological subtypes of esophageal cancer are mainly squamous cell carcinoma and adenocarcinoma. In China, esophageal squamous cell carcinoma (ESCC) is the majority, accounting for about 90% of the incidence of esophageal cancer. The 5-year survival rate of esophageal cancer in China is 20.9% [3, 4]. In recent years, the multidisciplinary treatment of esophageal cancer has developed rapidly. For resectable ESCC, surgical treatment is still the core. Tumor stage, surgical method, number of lymph nodes dissection and postoperative complications are all factors affecting the long-term survival of postoperative patients. However, at present, there are very few related studies about minimally invasive esophagectomy (MIE) and open surgery, and most of them are retrospective studies with small sample, especially in China. Sichuan Province has a large population and several areas with high incidence of esophageal cancer. In 2015, the incidence rate of esophageal cancer in Sichuan Province was  $29.29/10^5$  and the mortality rate was  $22.20/10^5$ , much higher than the average level in China [5]. Sichuan Cancer Hospital & Institute carried out MIE earlier in China. Therefore, we analyzed the survival status and operative approaches of patients with ESCC in Sichuan Cancer Hospital & Institute from January 2010 to December 2017, hoping to supplement relevant data on surgical treatment of esophageal cancer in China.

## 2 Method

### 2.1 Patients

In this study, Sichuan Cancer Hospital & Institute Esophageal Cancer Case Management Database (SCCH-ECCM Database) was queried, and 3014 patients with esophageal cancer who received surgical treatment in Sichuan Cancer Hospital from 2010.01 to 2017.10 were collected. Among them, 117 patients with non-squamous cell carcinoma and 77 patients with primary multiple carcinomas were excluded. Besides, 35 cases of cervical esophageal cancer and 11 cases of esophageal cancer in the gastroesophageal junction area were excluded, and 2766 cases of thoracic esophageal cancer with complete long-term survival follow-up results were selected as the objects of this study. All patients' pathological stages were adjusted

according to the 8th edition of the TNM classification of the AJCC/UICC. We reviewed follow-up data on patients, examining their characteristics, postoperative complications, and long-term overall survival outcomes.

### 2.2 Statistical analyses

SPSS 26.0 (IBM, NY, America) was used for statistical processing of patient data, Kaplan–Meier method was used for survival analysis, and Log-rank test was used for comparison between groups. The test level  $\alpha$  was set at 0.05. A *P* value of less than 0.05 was considered statistically significant.

## 3 Results

### 3.1 Patient characteristics

Of the 2766 patients collected, 2256 (81.6%) were male, and the mean age of the patients was  $(61.57 \pm 8.3)$  years. The middle thoracic of the tumor was the most common location (1479 cases, 53.5%), followed by the upper thoracic (693 cases, 25.1%) and the lower thoracic (594 cases, 21.5%). The pathological stages of 0, IA, IB, IIA, IIB, IIIA, IIIB, IVA and IVB were 68(2.5%), 32(1.2%), 227(8.2%), 437(15.8%), 448(16.2%), 180(6.5%), 1042(37.7%), 324(11.7%) and 8(0.3%) respectively. Only 52 patients (1.9%) received neoadjuvant therapy (Table 1).

### 3.2 Intraoperative and postoperative indexes

During the study period, 1444 cases (52.2%) underwent open surgery (including 44 cases conversion to open surgery), and 1322 cases (47.8%) underwent MIE. McKeown (72.0%) was the most commonly used three-incision surgical approach, followed by Ivor-Lewis (26.4%). The average operation time was  $(236.5 \pm 66.2)$  min. The proportion of R0 esophagectomy was 94.7%. The average number of intraoperative lymph node dissected were  $(21.8 \pm 12.0)$ , and the average number of lymph node metastasis were  $(2.1 \pm 3.5)$ . In terms of the degree of tumor differentiation, grade1(G1), G2 and G3 accounted for 18.8%, 39.8% and 38.4%, respectively. In situ carcinoma and basal cell carcinoma accounted for 0.5% and 2.5%, respectively (Table 2).

### 3.3 Postoperative complications

The overall incidence of postoperative complications was 25.8%, of which pulmonary infection was the most common (8.6%), anastomotic leakage was 7.5%, pleural effusion needing treatment was 2.5%, and incision infection was 2.2% (Table 3).

### 3.4 Survival status

The 1-, 3- and 5-year OS of all patients were 86.2%, 57.5% and 46.8% (Fig. 1). 5-year OS was significantly better in female patients than in male patients (62.0% vs 43.3%

**Table 1** Baseline characteristics of patients

Characteristic	Total
Gender, n (%)	
Male	2256(81.6%)
Female	510(18.4%)
Age (years), ( $\bar{X}\pm s$ )	61.57 $\pm$ 8.3
Location, n (%)	
Upper	693(25.1%)
Middle	1479(53.5%)
Lower	594(21.5%)
pT, n (%)	
Tis	68(2.5%)
T1a	59(2.1%)
T1b	206(7.4%)
T2	527(19.1%)
T3	1645(59.5%)
T4a	209(7.6%)
T4b	52(1.9%)
pN, n (%)	
N0	1237(44.7%)
N1	810(29.3%)
N2	480(17.4%)
N3	239(8.6%)
pM, n (%)	
M0	2758(99.7%)
M1	8(0.3%)
pSt, n (%)	
0	68(2.5%)
IA	32(1.2%)
IB	227(8.2%)
IIA	437(15.8%)
IIB	448(16.2%)
IIIA	180(6.5%)
IIIB	1042(37.7%)
IVA	324(11.7%)
IVB	8(0.3%)
Differentiation degree, n (%)	
G1	519(18.8%)
G2	1101(39.8%)
G3	1063(38.4%)
Neoadjuvant therapy, n (%)	52(1.9%)

**Table 2** Surgical procedure and outcomes

Characteristic	Total
Mean operative time(min) ( $\bar{X}\pm s$ )	236.5 $\pm$ 66.2
Surgical approach, n (%)	
McKeown	1991(72.0%)
Ivor-Lewis	729(26.4%)
Sweet	46(1.7%)
Surgical method, n (%)	
MIE	1322(47.8%)
Open surgery	1444(52.2%)
No. of resected lymph nodes, ( $\bar{X}\pm s$ )	21.8 $\pm$ 12.0
No. of positive lymph nodes, ( $\bar{X}\pm s$ )	2.1 $\pm$ 3.5
R0 esophagectomy, n (%)	2620(94.7%)

**Table 3** postoperative complications

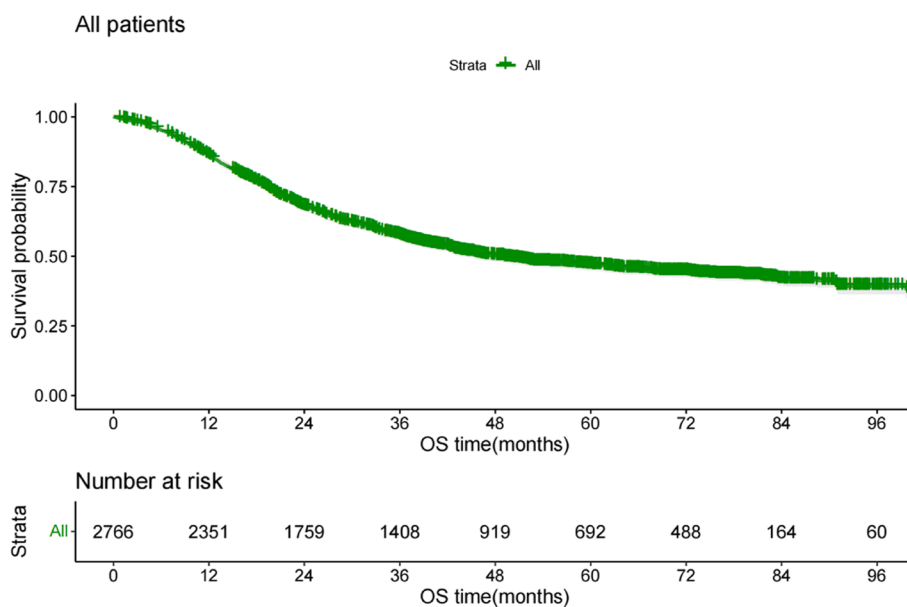
Complications, n (%)	Total
Overall complications	715(25.8%)
Pulmonary infection	238(8.6%)
Arrhythmia	24(0.8%)
Anastomotic leakage	207(7.5%)
Recurrent laryngeal nerve injury	32(1.2%)
Chylothorax	30(1.1%)
Postoperative bleeding	18(0.7%)
Pulmonary atelectasis	5(0.2%)
Pleural effusions requiring treatment	68(2.5%)
Incision fat liquefaction	25(0.9%)
Incision infection	60(2.2%)
Gastrointestinal dysfunction	23(0.8%)
Venous thrombus	11(0.4%)
Postoperative pneumothorax	12(0.4%)
Incisional hernia	2(0.1%)
Pyothorax	3(0.1%)
Pneumoderm	2(0.1%)
Respiratory failure	17(0.6%)
Anastomotic stenosis	3(0.1%)
Esophagotracheal fistula	6(0.2%)
Tracheal fistula	1(0.03%)
Postoperative death	4(0.14%)

$P < 0.001$ ) (Fig. 2). For different pathological stages, the 5-year OS of stage 0, I, II, III and IV patients are 95.6%, 76.4%, 61.4%, 35.6% and 14.5%, respectively ( $P < 0.001$ ) (Fig. 3). The 5-year OS of upper, middle and lower thoracic esophageal cancer patients was 49.5%, 46.7% and 44.1% ( $P = 0.20$ ). Patients who underwent McKeown and Ivor-Lewis had 5-year OS rates of 49.5% and 41.2%, respectively ( $P < 0.001$ ) (Fig. 4). MIE patients had better

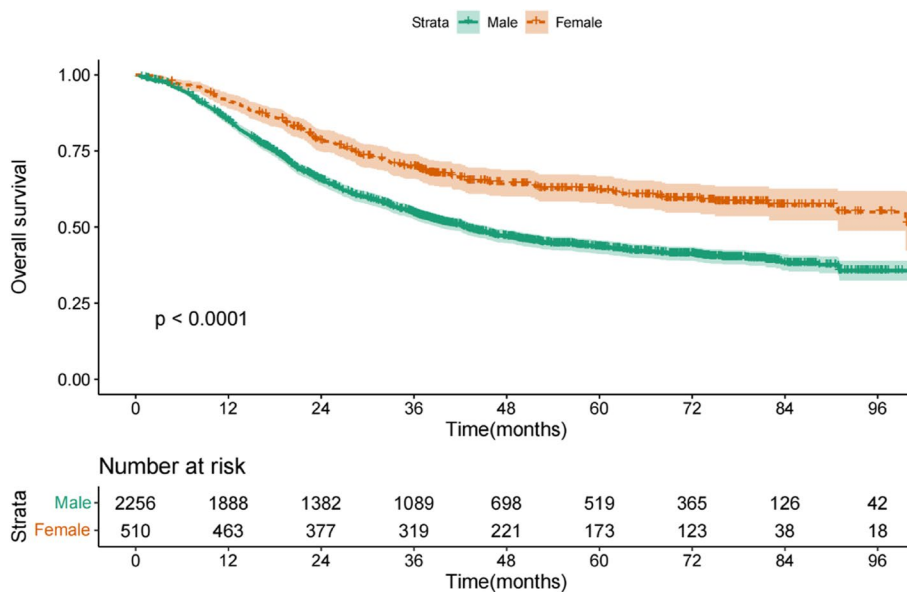
5-year OS than open surgery (51.8% vs 42.5%,  $P < 0.001$ ) (Fig. 5) (Table 4).

#### 4 Discussion

Through the data analysis of 2766 patients with thoracic ESCC, the 5-year OS was 46.8%, higher than the average level. Sichuan Cancer Hospital & Institute, the largest tertiary cancer hospital in southwest China, started total MIE as early as April 2010. From 2010 to 2017, surgery is



**Fig. 1** Kaplan–Meier curve of overall survival for patients



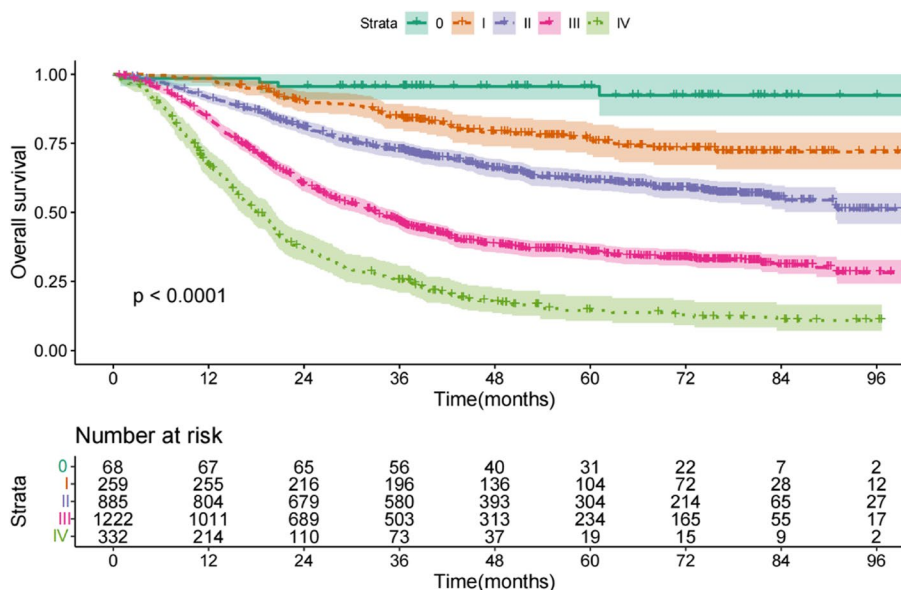
**Fig. 2** Kaplan–Meier curves of overall survival stratified by gender

still the main treatment for ESCC in China, and the proportion of neoadjuvant therapy is low. The results of this study represent the current status of surgical treatment for esophageal cancer in that period to a certain extent.

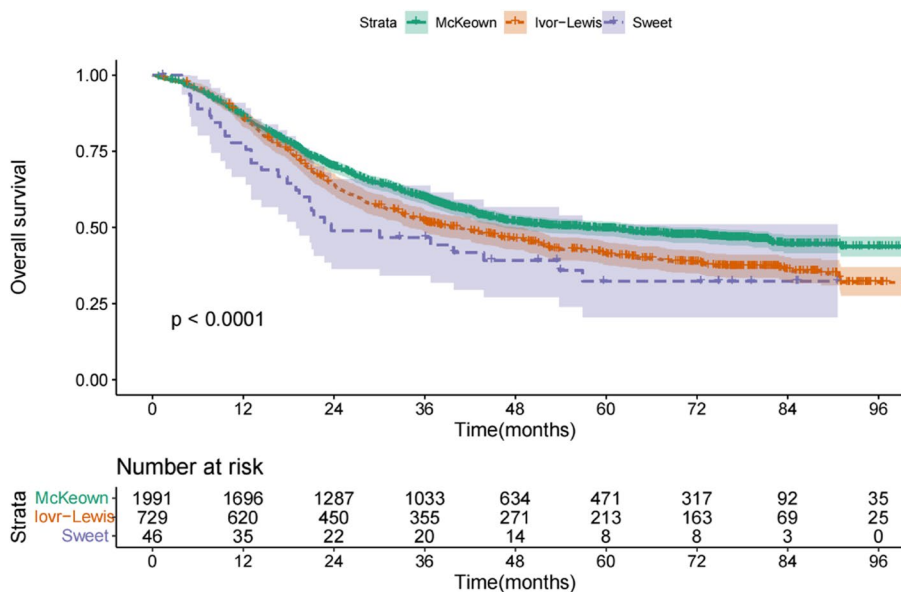
The results of survival analysis indicated that women had better long-term survival outcomes than men in patients with ESCC (62.0% vs 43.3%,  $P < 0.001$ ). Similar results can be found in most cancer-related studies. Haupt et al. also demonstrated a higher incidence and

mortality in males compared with females in non-reproductive system tumors, this may be related to the fidelity of the genetic code [6].

In China, the choice of esophageal cancer surgery has long been controversial, especially between Sweet and Ivor-Lewis. To date, few studies have investigated the overall survival outcome of esophagectomy in China, and most of them are retrospective low volum studies. Sweet procedure is generally considered to be easier to perform



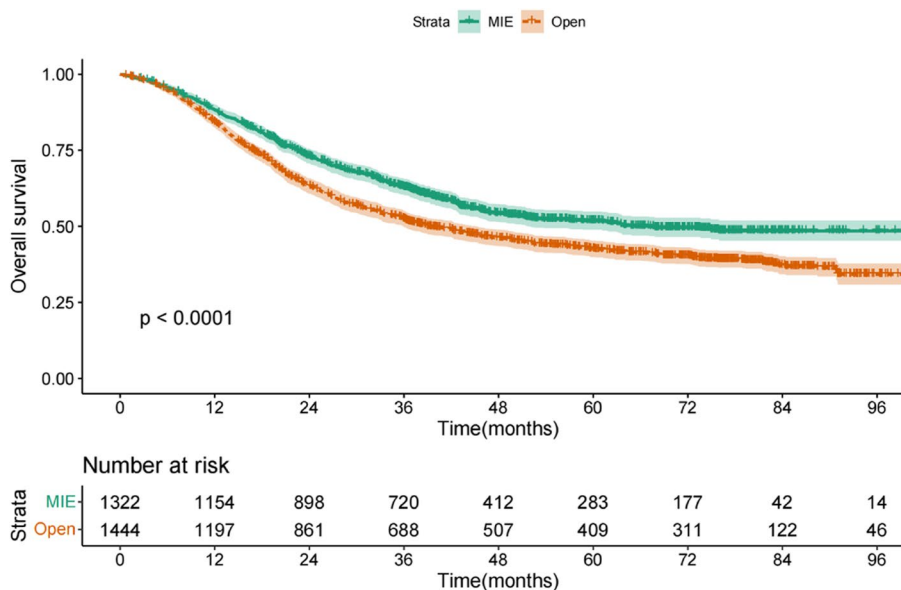
**Fig. 3** Kaplan–Meier curves of overall survival stratified by TNM stage



**Fig. 4** Kaplan–Meier curves of overall survival stratified by surgical approach

with shorter operation time and better tolerance from patients. Ivor-Lewis can offer better visualization of the thoracic esophagus, and has advantages in lymph node dissection, but it will cause more postoperative complications [7, 8]. But a randomized clinical trial demonstrated that, patients in the Ivor-Lewis group experienced a lower incidence of in-hospital morbidity and shorter hospital stay compared with those in the Sweet group [8]. Therefore, we need more prospective clinical trials. Our

study, a retrospective study with large sample sizes shows that McKeown is by far the most commonly performed esophagectomy and in terms of long-term survival, there was an advantage over Ivor-Lewis (49.5% vs. 41.2%,  $P < 0.001$ ). In this period, the proportion of neoadjuvant therapy and comprehensive treatment is low, and surgery is still the main treatment, so the number of lymph node dissection is closely related to the survival and prognosis of patients. In this study,  $(22.4 \pm 12.3)$  lymph nodes had



**Fig. 5** Kaplan–Meier curves of overall survival stratified by surgical method

**Table 4** Overall survival rates

5-year OS, (%)	Total
1-year OS	86.2%
3-year OS	57.5%
5-year OS	46.8%
pSt, (%) ( $P < 0.001$ )	
0	95.6%
I	76.4%
II	61.4%
III	35.6%
IV	14.5%
Gender, (%) ( $P < 0.001$ )	
Female	62.0%
Male	43.3%
Location, (%) ( $P = 0.20$ )	
Upper	49.5%
Middle	46.7%
Lower	44.1%
Surgical method, (%) ( $P < 0.001$ )	
McKeown	49.5%
Ivor Lewis	41.2%
Surgical method, (%) ( $P < 0.001$ )	
MIE	51.8%
Open surgery	42.5%

been removed by McKeown and ( $20.3 \pm 10.8$ ) by Ivor-Lewis. Obviously, the McKeown allowed for a more thorough dissection of the lymph nodes. However, minimally invasive McKeown did not show a significant survival

advantage in our patients (52.1% VS 51.1%,  $P = 0.94$ ), which may be due to the small number of minimally invasive Ivor-Lewis cases in our patients (82 cases). In addition, previous relevant studies have shown that the prognosis of patients with minimally invasive Ivor-Lewis is even better than that of minimally invasive McKeown, because the former has shorter operation time and hospital stay and a lower incidence of postoperative complications [9–12]. But there are still doctors preferring the minimally invasive McKeown because they believe that a neck anastomotic leakage is easier to cure than a chest anastomotic leakage [13].

MIE has become the mainstay treatment for esophageal cancer, and MIE showed an advantage over open surgery in our study (51.8% vs. 42.5%,  $P < 0.001$ ). A multicenter randomized controlled trial in Japan showed that MIE surgery had advantages in terms of intraoperative blood loss, length of stay, and complication rate. This conclusion was also confirmed in our patients, who had a significantly lower incidence of postoperative complications with MIE (22.7 vs 28.7,  $P < 0.001$ ). Japanese surgeons even argued that MIE’s greatest advantage was not its low invasiveness, but its more thorough and meticulously lymphadenectomy lymphadenectomy. However, none of these studies showed significant benefits of MIE in long-term survival [14–16]. The JCOG1409 currently being carried out in Japan is a multi-center clinical study on open surgery versus MIE. This study is still in progress, while there is no similar prospective clinical study in China. Therefore, it remains to be concluded whether minimally invasive surgery or open surgery can bring

better long-term benefits to patients with ESCC. Therefore, the results of this study have significant instruction for clinical practice.

There are still many shortcomings in this study, including: 1. The database is retrospective. From 2010 to 2017, the economy of Sichuan region was still underdeveloped, and the process of follow-up and data input were still flawed. A large number of esophagectomies were performed each year, but there were only 2766 patients with complete follow-up data, so that the data related to DFS, clinical stage and recurrence and metastasis are lacking. 2. The proportion of neoadjuvant therapy is too low. Chinese Society of Clinical Oncology (CSCO) and Chinese Anti-cancer Association (CACAA) published their esophageal cancer diagnosis and treatment guidelines in 2019 and 2022, respectively, and the first prospective multi-center clinical trial of neoadjuvant chemoradiotherapy in China was only published in 2018, these factors account for the low percentage of patients who received neoadjuvant therapy in our data.

In summary, based on this large-sample single-center retrospective study, it is well confirmed that MIE can bring more radical lymph node dissection and better long-term survival compared with open surgery in the real world. McKeown also shows its advantage in OS. The results have important significance for the selection of ESCC esophagectomy, and also add clinical evidence to the data of ESCC surgery in China. With the continuous development of minimally invasive techniques and treatment concepts, we believe, minimally invasive McKeown and robot-assisted minimally invasive McKeown can bring more surgical benefits to patients.

#### Abbreviations

OS	Overall survival
ESCC	Esophageal squamous cell cancer
MIE	Minimally invasive esophagectomy

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None.

#### Authors' contributions

YH, XL, LJ and QW conceived the study and approved the database construction. KN designed the study, analyzed the data, and wrote the paper. ZL, WH, CW, KW, QZ, HL, JL, GL, WX, QF and LP provided suggestions for paper writing. KN, ZL, KL, CL, KD, XN, KL, YH and SL developed the database. ZL contributed to the statistical analyses. All authors reviewed the results and approved the final version of the manuscript.

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#### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### Declarations

##### Ethics approval and consent to participate

The study was approved by the Ethics Committee for Medical Research and New Medical Technology of Sichuan Cancer Hospital (SCCHEC-02-2022-050). The data are anonymous and retrospective, and the requirement for informed consent was therefore waived.

##### Consent for publication

Not applicable.

##### Competing interests

The authors declare that they have no competing interests.

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