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Changes in the recent three decades and survey on the current status of surgical treatment for esophageal cancer in China

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Abstract

Background: To review the changes and survey on status quo of the surgical treatment for esophageal cancer in China. The differences in diagnosis and treatment for esophageal cancer among hospitals in different regions across China were also investigated.

Methods: We sent questionnaires to 46 hospitals across China, investigating the volume of esophageal cancer surgeries, surgical procedures, and perioperative management under the guidance of esophageal surgery chiefs.

Results: A total of 46 questionnaires were sent out and collected. The survey results showed that in the past 5 years, the volume of surgeries for esophageal cancer remained stable by 23.9% of those hospitals, increased by 30.4%, and decreased by 45.7%. Of those patients treated by surgery, 19.1% were in the early stages, and 80.9% were in locally advanced stages. In terms of surgical procedures, 73.4% of the patients were treated by minimally invasive surgery and 85.7% of esophageal substitutes were a gastric conduit, 93.1% of the substitutes were pulled to the neck through the esophageal bed. For the lymph node dissection, 78.5% of the patients had a complete two-field lymph node dissection including the para-recurrent laryngeal nerve lymph nodes. Of the patients with neoadjuvant therapy, 53.5% received chemotherapy or chemotherapy plus immunotherapy (47.0%), and 43.5% had chemoradiation.

Conclusions: Currently, in China, minimally invasive surgery-oriented multimodality treatment, including complete two-field lymph node dissection, has become the

Yong Li, Wei-Xin Liu, and Ling Qi contributed equally to this work.

standard approach for esophageal cancer management. Over the past decade, this standardized approach has significantly improved prognosis compared to previous decades.

KEYWORDS
esophageal cancer, surgical treatment, questionnaire survey

INTRODUCTION

Esophageal cancer is one of the most common gastrointestinal tumors in China. According to China's cancer statistics released by the National Cancer Center in 2016, the number of patients with esophageal cancer was 253 000, ranking sixth in incidence rate among all malignancies; the number of deaths was 194 000, ranking fifth in the mortality among all malignancies.[1] There has been a significant difference in the quantity and quality of esophageal surgery due to a huge difference in the incidence of esophageal cancer and medical services among different regions across China. Historically, the treatment for esophageal cancer in China can be roughly divided into three phases: open esophagectomy with hand-sewing anastomosis (1940–1990), open esophagectomy with instrumental anastomosis (1990–2010), and minimally invasive esophagectomy (2010 to).[2] Since professor Yingkai Wu successfully completed the first case of esophageal cancer radical resection and esophagogastrostomy via left thoracotomy in Peking Union Medical College Hospital in 1940, almost all Chinese thoracic surgeons have received training of esophagectomy with an esophagogastric anastomosis through left thoracotomy for middle and lower thoracic esophageal cancers except a small portion of patients with upper thoracic esophageal cancers who underwent esophagectomy with a cervical esophagogastric anastomosis through right thoracotomy by three incisions. However, whether a left or right thoracotomy approach was taken during the open esophagectomy phase (1940–2010), the extent and degree of lymph node dissection were insufficient due to unfamiliarity with the anatomy of the recurrent laryngeal nerves and the patterns of lymph node metastasis in esophageal cancers. Chemotherapy and radiotherapy were rarely administered in esophageal cancer patients before 1990, because of a lack of effective chemotherapy agents and immature radiation technology. Therefore, the overall 5-year survival rate of surgically treated esophageal cancer patients has been at about 30% from the 1970s to the 1990s.[2] After China opened to the Western world, some hospitals in the coastal cities began to learn the experience from Western and Japanese colleagues. Since the 1990s, a few hospitals have attempted to perform esophagectomy with esophagogastric anastomosis through right thoracotomy and laparotomy, while a few surgeons attempted to perform the McKeown esophagectomy with cervical-thoracic-abdominal three-field lymph node dissection. Hand-sewn anastomosis was replaced by instrumental anastomosis in most hospitals, and gastric conduit instead of whole stomach was adopted as a substitute for the resected esophagus.[3] Meanwhile, some surgeons started to perform thoracoscopic/laparoscopic esophagectomy for esophageal cancer.[4] The introduction of these advanced concepts and technologies not only reduced complications such as anastomotic leakage but also improved the long-term survival of esophageal cancer patients in China.[5] However, most hospitals have adhered to the Sweet esophagectomy through left thoracotomy with an incomplete thoracoabdominal two-field lymph node dissection as their favorite surgical procedure until 2010. Most surgeons have not yet understood the lymph node metastasis patterns and mastered the methods of standardized lymph node dissection. During the second phase (1990–2010), the preoperative treatment for esophageal cancer was mainly radiotherapy to shrink the tumor for resection, and chemotherapy had not yet been administered for most patients with esophageal cancers. Because there were significant differences in the treatment concepts, surgical techniques, and outcomes for esophageal cancer among different regions across China, to promote standardized diagnosis and treatment for esophageal cancer, the Esophageal Cancer Committee of the China Anti-Cancer Association organized a group of famous esophageal cancer experts to deliver a series of academic lectures and demonstrate standardized minimally invasive esophageal cancer surgery across China annually since 2010. Therefore, significant changes in the surgical treatment for esophageal cancer gradually happened in China, which was from presurgical treatment mainly via left thoracotomy in the past decades to the current multimodality treatment with MIE plus complete two-field lymphadenectomy via right chest. These changes have significantly improved the treatment outcome of esophageal cancer. The overall 5-year survival rate of surgically treated esophageal cancer patients has been significantly improved from 30% to 40% in the past to over 60% at present.[6–9] Currently, surgery-oriented multimodality treatment has become the mainstay for resectable locally advanced esophageal cancer. Although the management and outcome of esophageal cancer in China have been significantly improved, there are still many hot and difficult issues that remain unresolved. For example, is the minimally invasive esophagectomy through the transmediastinal approach comparable with that through the right chest for the treatment of esophageal cancer? Could extended thoracoabdominal lymph node dissection during MIE avoid cervical lymph node dissection for most esophageal cancer patients? How to protect the structure and function of bilateral recurrent nerve (RLN) when dissecting the adjacent lymph nodes along the

nerves? Could chemotherapy plus immunotherapy replace chemoradiation in the future as the optimal preoperative neoadjuvant therapy for esophageal cancer and so on?[10] Furthermore, although the gap in treatment for esophageal cancer in various regions of China has been significantly narrowed in recent years, is there still a difference in the outcome of standardization and treatment? To answer the above questions, the Esophageal Cancer Committee of the China Anti-Cancer Association (CACA) launched a questionnaire survey on the current status of surgical treatment for esophageal cancer in China in 2022. This survey aimed to investigate the current status and differences in surgical treatment for esophageal cancer in big hospitals across the country. This questionnaire survey also investigated the requirement for technical training and academic exchanges of thoracic surgeons to improve the level and standardization of esophageal cancer management in China.

METHODS

Design of the questionnaires

1. Objectives: To investigate the status of diagnosis and treatment, complications, and perioperative treatment for esophageal cancer.
2. Method: The questionnaires were sent to the chiefs of thoracic surgery/esophageal cancer surgery in 46 centers from the following 21 provinces and municipalities area across China: Nanjing in Jiangsu Province, Shijiazhuang in Hebei Province, Taizhou in Zhejiang Province, Beijing, Guangzhou, Meizhou and Maoming in Guangdong Province, Harbin in Heilongjiang Province, Shenyang in Liaoning Province, Fuzhou, Xiamen and Putian in Fujian Province, Hefei in Anhui Province, Chengdu and Nanchong in Sichuan Province, Jinan and Jining in Shandong Province, Taiyuan and Changzhi in Shanxi Province, Yinchuan in Ningxia Province, Liangjiang New Area and Yuzhong District in Chongqing, Xuhui District in Shanghai, Zhengzhou and Anyang in Henan Province, Haikou in Hainan Province, Changsha in Hunan Province, Wuhan in Hubei Province, Changchun in Jilin Province, and Nanchang in Jiangxi Province.
3. Design and quality control of the questionnaire survey: Designing WeChat mini program for question survey, conducting online surveys. The questionnaire covered the volume of esophagectomy in the department, surgical procedures, perioperative treatment, requirements of young doctors in research and career development of, and so on. The chiefs of the departments responded to survey and were responsible for the accuracy of the data reported.
4. Statistics: The statistical data results are generated directly by questionstar, showing the composition percentages of various survey outcomes.

RESULTS

Current status of surgical treatment for esophageal cancer

In the past 5 years, the volume of esophageal surgeries in different hospitals has remained stable in 23.9%, increased in 30.4%, and decreased in 45.7%.

Regarding the stages of esophageal cancer patients underwent surgery, 19.1% were in the early stages, 80.9% were in locally advanced stages, including 6.2% with recurrent diseases (Table 1).

Among the patients with early staged esophageal cancers patients, for T1aN0M0 patients, 95.7% of doctors recommended endoscopic mucosal resection (EMR), while 4.3% would recommend MIE. For patients with T1bN0M0, 8.7% of doctors recommended endoscopic treatment, while 91.3% of doctors did not recommend endoscopic treatment.

Of the esophageal cancers treated by surgery, 16.7% were located in the upper thoracic or cervical esophagus, 66.3% in the lower thoracic esophagus, and 17.0% in the esophagogastric junction.

Regarding the surgical procedures: 73.4% were thoracoscopic and laparoscopic minimally invasive esophagectomies, 17.5% were open surgery, and 9.1% were hybrid surgery.

Of the surgical approaches: 16.1% were through left thoracotomy with or without cervical incision, and 72.8% were thoracoscopic/laparoscopic McKeown esophagectomies through the right chest and 11.1% were thoracoscopic/laparoscopic Ivor-Lewis esophagectomy through the right chest.

Anastomosis: 13.1% were conducted by hand-sewing, 83.4% by circular stapler, and 3.5% by linear stapler.

Regarding the route of reconstruction: 93.1% were through the esophageal bed, 0.7% through the subcutaneous route in front of sternum, and 6.2% through the retrosternal route.

Substitution organ in the reconstruction of digestive tract: 85.7% of the hospitals chose gastric conduit, 8.5% chose part of the stomach, 4.1% chose jejunum and 1.8% chose colon.

For lymph node dissection, 78.5% of the hospitals chose complete two-field lymph node dissection (including RLN lymph nodes), 11.8% chose standard two-field lymph node dissection (without dissection of RLN lymph nodes), 8.1% chose three-field lymph node dissection and 1.8% chose lymph node sampling.

For the number of lymph nodes dissected: 5–10 lymph nodes accounted for 2.2%, 10–20 lymph nodes 30.4%, and ≥30 lymph nodes 17.4%.

As for robotic surgery: 47.8% of the hospitals have carried out robotic-assisted esophagectomy, while 52.2% have not yet. Of the hospitals already practiced robotic-assisted esophagectomy, 22.7% performed less than 10 cases, 40.9% between 20 and 50 cases, and 18.2% exceeded 50 cases.

TABLE 1 Current status of surgical treatment for esophageal cancer.

Questions	Number of hospitals/ average score	Percentages
Trends in the total volume of esophageal cancer surgeries in the past 5 years		
Stable	11	23.9%
Increased (<20%)	9	19.6%
Increased (>20%)	5	10.9%
Decreased (<20%)	18	39.1%
Decreased (>20%)	3	6.5%
Stages of surgically treated esophageal cancer		
Early stages	19.1	19.1%
Locally advanced stages	74.7	74.7%
Recurrent	6.2	6.2%
EMR/ESD recommended for T1aN0M0 lesion		
Yes	44	95.7%
No	2	4.4%
EMR/ESD recommended for T1bN0M0 lesion		
Yes	4	8.7%
No	42	91.3%
Locations of esophageal cancer		
Upper /cervical	16.7	16.7%
Middle/lower	66.3	66.3%
Esophagogastric junction	17.0	17.0%
Surgical procedures		
Thoracoscopic/laparoscopic	73.4	73.4%
Open	17.5	17.5%
Hybrid	9.1	9.1%
Robotic-assisted esophagectomy		
Yes	22	47.8%
No	24	52.2%
Cases of robotic-assisted esophagectomy each year		
<10	5	22.7%
10–20	4	18.2%
20–50	9	40.9%
>50	4	18.2%
Surgical approaches		
Left thoracotomy	10.6	10.6%
Left thoracotomy with cervical	5.5	5.5%
Minimally invasive McKeown esophagectomy	72.8	72.8%
Minimally invasive Ivor-Lewis	11.1	11.1%
Instrument used during esophagectomy		
Ultrasonic knife alone	9.3	9.3%
Electric hook alone	3.8	3.8%
Hybrid, mainly ultrasonic knife	40.2	40.2%
Hybrid, mainly hook alone	46.8	46.8%
Anastomosis		
Hand-sewn	13.1	13.1%
Circular stapler	83.4	83.4%
Linear stapler	3.5	3.5%
Substitution position		
Esophagus bed	93.1	93.1%
Subcutaneous (antesternal)	0.7	0.7%
Retrosternal	6.2	6.2%
Substitution for resected esophagus		
Gastric conduit	85.7	85.7%
Part of the stomach	8.5	8.5%
Jejunum	4.1	4.1%
Colon	1.8	1.8%
Lymph node dissection		
Complete two-field (with RLN lymph nodes)	78.5	7 8.5%
Standard two-field (without RLN lymph nodes)	11.8	11.8%
Three-field	8.1	8.1%
Lymph node sampling	1.8	1.8%
Numbers of lymph nodes dissected		
<5	0	0%
5–10	1	2.2%
10–20	14	30.4%
20–30	23	50.0%
>30	8	17.4%

Abbreviations: EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; RLN, recurrent laryngeal nerve.

Preoperative treatment

The survey on preoperative treatment of esophageal cancer showed that 53.5% of the hospitals chose chemotherapy alone, 3.2% chose radiation alone, 43.5% chose chemoradiation. Immunotherapy was involved in the preoperative treatment of 47% hospitals (Table 2).

With regard to preoperative nutritional support, 35% of the hospitals chose medical nutrients, 45.7% chose preoperative nutritional guidance, and 19.4% chose no nutritional support.

Before esophageal cancer surgery, 71.7% of doctors routinely placed gastrointestinal decompression tubes, while 28.3% of doctors did not routinely place gastrointestinal decompression tubes.

As for preoperative bowel preparation, 71.7% of the hospitals routinely asked patients to fast the night before surgery, 21.7% only 4 h before surgery, and 6.6% prohibited drinking water only 2 h before surgery. Preoperatively,

TABLE 2 Preoperative treatment.

Questions	Number of hospitals/average score	Percentages
Preoperative nutritional therapy program selection for esophageal cancer		
Preoperative supportive treatment with medical nutritional supplements	35.0	35.0%
Enhanced nutritional support through preoperative dietary counseling	45.7	45.7%
No nutritional support provided	19.4	19.4%
Gastrointestinal decompression		
Yes	33	71.7%
No	13	28.3%
Preoperative fasting		
Fasting the night before surgery	33	71.7%
Fasting 4 h before surgery	10	21.7%
Prohibiting drinking 2 h before surgery	3	6.5%
Bowel preparation (enema or oral laxatives)		
Yes	26	56.5%
No	20	43.5%
Psychological counseling		
Yes	34	73.9%
No	12	26.1%
Psychological counseling personnel		
Professional psychologists	2	5.9%
Chief surgeons	4	11.8%
Nurses	17	50.0%
Attendings/residents	11	32.3%
Preoperative treatment		
Chemotherapy/chemotherapy	53.5	53.5%
Radiation alone	3.2	3.2%
Chemoradiation	43.5	43.5%

56.5% of hospitals routinely provided bowel preparation for patients, while 43.5% did not. A total of 73.9% of hospitals gave patients preoperative psychological counseling, while 26.1% did not provide it. Among the personnel who offered psychological counseling, 5.9% were professional psychologists, 11.8% were chief surgeons, 50.0% were nurses, and 32.3% were other medical personnel (such as attendings and residents).

DISCUSSION

Importance of early diagnosis and early treatment of esophageal cancer

With the development of China's economy and society, the lifestyles and dietary structures of the Chinese people are gradually moving towards the West, and their nutritional status has also greatly improved. The incidence of lung cancer, colorectal cancer, and breast cancer are increasing on an annual basis. However, according to the cancer registration data in China from 2000 to 2016, the incidence rate and mortality of esophageal cancer have been decreasing at an average rate of 4.6% annually due to continuous improvement of life quality,[1] and ongoing program of prevention, and early diagnosis treatment of esophageal cancer across China. This questionnaire survey showed that the volume of esophageal cancer surgeries within 5 years was decreasing, and the volume in 45.7% of the hospitals decreased, indicating the decrease in incidence and the effect of early diagnosis and treatment. The survey also showed that esophageal cancer surgery tends to be concentrated in large medical centers. Meanwhile, the number of hospitals and doctors to perform esophageal cancer surgery is gradually shrinking due to a decrease in patients.

Patients with locally advanced esophageal cancer mainly receive surgery-oriented multimodality treatment. Perioperative treatment, including radiotherapy, chemotherapy, and immunotherapy may bring serious side effects to patients, meanwhile, the esophagectomy itself is also a highly traumatic procedure that changes the structure and function of the gastrointestinal tract greatly. Therefore, the quality of life of esophageal cancer patients after surgery-oriented multimodality treatment is usually very poor. Unfortunately, most patients may still have recurrence/metastasis postoperatively after considerable suffering. Therefore, early diagnosis and early treatment such as EMR/ESD are important strategies for preserving the structure and function of the patient's esophagus, which will help patients live longer and better. This survey showed that the proportion of early esophageal cancer underwent surgery increased but accounted for only about 1/5 (19.1%) of all surgically treated patients. Most of the patients (74.7%) still had locally advanced esophageal cancers at diagnosis, indicating there is still a long way to go in screening, early diagnosis, and treatment for esophageal cancer in China. Therefore, regular screening for populations in high-risk areas and high-risk populations, as well as opportunistic screening in other regions, needs to be strengthened. Meanwhile, opportunistic screening covered by medical insurance for high-risk populations may be a wise policy in the future to improve early diagnosis and treatment of esophageal cancer.

Changes and status of surgical treatment for esophageal cancer in China

Before 2010, esophagectomy for middle and lower thoracic esophageal cancers in China was mainly through left thoracotomy except for upper thoracic esophageal cancers. Surgeons did not have a clear understanding of the metastatic patterns through lymph nodes for esophageal cancer, and there was no consensus on the range and extent of lymphadenectomy in esophagectomy. After persistent academic

tour speeches on standardized management and live demonstrations of minimally invasive esophagectomy for esophageal cancer across China over the past decade, the level of standardized management for esophageal cancer in China has significantly been promoted.[6] Chinese surgeons have completed the transition from open esophagectomy through a left thoracotomy to minimally invasive esophagectomy through the right chest for esophageal cancer. The survey showed that over 90% of the doctors currently can select a rational treatment for T1aN0M0 and T1bN0M0 esophageal cancer, 72.8% of surgeons can performed right thoracoscopic/laparoscopic McKeown esophagectomy with complete two-field lymph node dissection 85.7% of the hospitals have adopted gastric conduit as the substitute of resected esophagus, and 83.4% of the surgeons use a circular stapler to make anastomosis. All these changes improved the outcome of esophageal cancer patients after surgical treatment.

Though postoperative reflux has been reduced due to the application of gastric conduit and circular stapler, the proportion of postoperative anastomotic stenosis was still high (9.5%). Therefore, it is necessary to conduct a comparative study on anastomosis methods among end-to-side anastomosis by circular stapler, T-shaped anastomosis by linear cutting stapler, and hand-sewing anastomosis in the future.

Regarding the lymph node dissection, 78.5% of the surgeons routinely perform complete two-field lymph node dissection (including lymph node dissection adjacent to RLN) with ≥20 lymph nodes dissected in 67.4% of the patients survey results indicated that the current concept and technology of surgical treatment for esophageal cancer in China have tended to be consistent in different regions.[10] Complete two-field lymphadenectomy is an essential procedure in esophagectomy and has been proven to improve the prognosis of esophageal cancer patients in China in recent years.[9]

Because esophageal cancer surgery is complex and laborious, robotic-assisted minimally invasive esophagectomy is becoming popular in China for reducing the labor intensity of surgeons and improving lymph node dissection.[11] The questionnaire survey showed that about half of high-volume hospitals in China currently could carry out robotic-assisted minimally invasive esophagectomy. However, there is still significant room for the application of robotic-assisted minimally invasive esophagectomy for esophageal cancer in China in the future.

In terms of postoperative complications, the survey results showed that the incidence of pneumonia was about 25.0%, hoarseness about 16.0%, anastomotic stenosis about 9.5%, immunotherapy-related side effects about 8.6%, anastomotic fistula about 7.2%, severe cardiovascular and cerebrovascular events about 5.0%, chylothorax about 2.9%, reoperation caused by bleeding about 1.6%, and gastro-tracheal/bronchial fistula about 1.2%. The major surgery-related complications were still pneumonia, recurrent laryngeal nerve paralysis, anastomotic stenosis, and fistula. Minimally invasive technology may reduce complications somewhat but cannot avoid complications; therefore, careful intraoperative manipulations are still required. In addition, with the increase of preoperative neoadjuvant immunotherapy, the immune-related adverse effects are gradually increasing. Detection and treatment of these immune-related side effects, in the beginning, are very important to avoid severe immunotherapy-related complications. Moreover, the postoperative unplanned transfer to the ICU was less than 5% in 87.0% of the hospitals. Overall, the incidence of complications after esophagectomy in China is relatively lower.[12]

Regarding postoperative oral intake, survey results showed that 2.2% of the surgeons likely advised the patients to start oral intake on Day 1 postoperatively, 11.1% on Day 2 to Day 5, 86.7% on Day 7 or thereafter, indicating that postoperative early oral intake remains controversial and more prospective randomized controlled clinical studies are required.

Changes in neoadjuvant treatment

Regarding the perioperative treatment for locally advanced esophageal cancer, the results of the 11th Five-Year Plan database of esophageal cancer in China established from 2009 to 2014 showed that 20.1% of the patients received preoperative chemoradiation, 1.3% received preoperative chemotherapy alone, and 4.5% received preoperative radiotherapy alone.[8] The results of the current questionnaire survey showed that preoperative chemotherapy or chemoimmunotherapy accounted for 53.5%, preoperative chemoradiation accounted for 43.5%, and preoperative radiation alone accounted for 3.2%. Surprisingly, the results showed that approximately 47.0% of the patients received chemoimmunotherapy in their neoadjuvant treatment, indicating that immunotherapy has developed rapidly over the past 5 years. Since the prospective randomized controlled study (CROSS Trial) reported the 5-year survival of preoperative neoadjuvant chemoradiotherapy followed by surgery versus surgery alone for locally advanced esophageal cancer in 2015,[13] physicians in China have gradually recognized the effectiveness and benefits of preoperative chemoradiotherapy. In 2018, Yang et al. from Zhongshan Cancer Prevention and Treatment Center in China reported survival data of locally advanced esophageal squamous cell carcinoma patients treated with preoperative neoadjuvant chemoradiotherapy followed by surgery compared to surgery alone (5010 trial).[14] The results of this study further confirmed the effectiveness of preoperative neoadjuvant chemoradiotherapy in improving patient survival, thereby preoperative chemoradiation was recommended as standard neoadjuvant therapy for locally advanced esophageal cancer in the guidelines. In recent years, preoperative chemotherapy combined with immunotherapy has also achieved favorable results with a relatively high PCR rate in esophageal squamous cell

carcinoma.[15–28] Li and colleagues[29] collected data from 15 large medical centers across China and conducted a retrospective analysis. The results showed that after neoadjuvant chemotherapy plus immunotherapy, the overall PCR rate was 25.8%, which is comparable to that of chemoradiotherapy. However, the combination of chemotherapy and immunotherapy may bring long-term side effects to patients, and further prospective randomized controlled studies to confirm the effectiveness of chemoimmunotherapy are still needed in the future. More evidence is still needed as to whether chemoimmunotherapy could replace the role of chemoradiotherapy in the preoperative treatment for locally advanced esophageal cancer in the future. T3–T4a/N0-1 locally advanced esophageal cancer patients, preoperative neoadjuvant therapy including chemoradiotherapy or chemoimmunotherapy, are becoming a trend.[30] In terms of postoperative adjuvant therapy, the results from the 11th Five-Year Plan database showed that patients with lymph node metastasis, poor differentiation, vascular cancer cell emboli, or nerve invasion tended to receive postoperative treatment. For patients undergoing curative resection, the current evidence for postoperative treatment, such as chemotherapy, radiation, chemoradiotherapy, and immunotherapy, is still insufficient. Nevertheless, for the patients who underwent R0 resection but still had residual diseases after neoadjuvant chemoradiotherapy, postoperative maintenance immunotherapy was recommended.[31] In the future, further studies are still needed to determine whether postoperative chemotherapy or chemoimmunotherapy is necessary or not for patients with lymph node metastasis, poor differentiation, vascular tumor emboli, or nerve invasion.

A previous study has reported that 90% of esophageal cancer patients are at risk of malnutrition.[32] Therefore, preoperative nutritional support for esophageal cancer patients also needs to be taken seriously. Regarding postoperative enhanced recovery, intestinal preparation, and gastrointestinal decompression tubes were not routinely carried out perioperatively. Patients were also allowed to drink water just 4 h before surgery.[33,34] However, further studies are still needed to improve the practices of enhanced recovery measures.

In summary, in the past decade, with the promotion of standardized surgery-oriented multimodality treatment by academic tour speech and live MIE demonstration on esophageal cancer across China, organized by the Esophageal Cancer Committee of CACA, the quality of surgical treatment for esophageal cancer in China has gradually been improved. Compared with the status before 2010, the transition from left thoracic approach to right thoracic approach, from open esophagectomy to minimally invasive surgery, from incomplete two-field lymphadenectomy to extended two-field lymphadenectomy, and from surgical treatment alone to multimodality therapy has almost been realized. Currently, the minimally invasive esophagectomy with extended two-field lymphadenectomy through the right thoracic approach has become the mainstay, and neoadjuvant therapy such as chemoradiation or chemoimmunotherapy have become a trend. The prognosis of esophageal cancer has also been significantly improved. On the other hand, complications and side effects of neoadjuvant therapy still deserve to be paid more attention in our clinical practice.

AUTHOR CONTRIBUTIONS

You-Sheng Mao contributed to the conception of the study and review the manuscript; Yong Li, Wei-xin Liu and Ling Qi contributed significantly to analysis and write the original manuscript; Yin Li, Jun-Feng Liu, Jian-Hua Fu, Yong-Tao Han, Wen-Tao Fang, Zhen-Tao Yu, Ke-Neng Chen contributed to organize the investigation and analyze data. Zhen-Tao Yu and Jun-Feng Liu contributed to review the manuscript and helped perform the analysis with constructive discussions.

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CONFLICT OF INTEREST STATEMENT

All authors declare they have no competing interests.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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REFERENCES

1. Zheng RS, Zhang SW, Sun KX, Chen R, Wang SM, Li L, et al. Cancer statistics in China, 2016. Zhonghua Zhong Liu Za Zhi. 2023 Mar 23; 45(3):212–20. Chinese. https://doi.org/10.3760/cma.j.cn112152-20220922-00647
2. Mao YS, He J, Cheng GY. Current status of surgical management of esophageal cancer in China and the future strategy. Zhonghua Zhong Liu Za Zhi. 2010 Jun;32(6):401–4. Chinese.
3. Mao Y, Yang D, Gao S, Xue Q, He J. Consensus and controversies of surgical approach selection in the treatment for thoracic esophageal cancers. Zhonghua Wei Chang Wai Ke Za Zhi. 2016 Sep 25;19(9): 961–4. Chinese.
4. Qu JQ, Hou WP, Gao X. Preliminary report on eight cases of television-assisted thoracoscopy esophagectomy for esophageal cancer. Zhonghua Zhong Liu Za Zhi. 1996;34(2):84–6. Chinese.
5. Ma M, Jiang H, Tang P, Duan X, Gong L, Yu Z. Retrospective comparative study of preoperative complications and lymphadenectomy

between thoracoscopic esophagectomy and open procedure. Chin J Thorac Cardiovasc Surg. 2015;31(5):260–3. Chinese.
6. Mao YS, He J, Xue Q, Shao K, Su K, Li N, et al. Nationwide speaking tour of standardized diagnosis and treatment for esophageal cancer. Zhonghua Wei Chang Wai Ke Za Zhi. 2013 Sep;16(9):801-4. Chinese.
7. Zhang DW, Cheng GY, Huang GJ, Zhang RG, Liu XY, Mao YS, et al. Operable squamous esophageal cancer: current results from the east. World J Surg. 1994;18:347–54.
8. Mao YS, Gao SG, Wang Q, Shi XT, Li Y, Gao WJ, et al. Analysis of a registry database for esophageal cancer from high-volume centers in China. Dis Esophagus. 2020 Aug 3;33(8): doz091. https://doi.org/10.1093/dote/doz091
9. Mao Y, Gao S, Li Y, Chen C, Hao A, Wang Q, et al. Minimally invasive versus open esophagectomy for resectable thoracic esophageal cancer (NST 1502): a multicenter prospective cohort study. J Natl Cancer Center. 2023a;3:106–14. https://doi.org/10.1016/j.jncc.2023.02.002
10. Mao Y, Gao SG, Li Y, Xue Q, Li F, Jin DH, et al. Hotspots and prospects of esophageal cancer research in China. Wei Chang Wai Ke Za Zhi. 2023b Apr 25;26(4):307–11. Chinese. https://doi.org/10.3760/cma.j.cn441530-20221222-00535
11. Yang Y, Li B, Yi J, Hua R, Chen H, Tan L, et al. Robot-assisted versus conventional minimally invasive esophagectomy for resectable esophageal squamous cell carcinoma: early results of a multicenter randomized controlled trial: the RAMIE trial. Ann Surg. 2022a Apr 1;275(4):646–53. https://doi.org/10.1097/SLA.0000000000005023
12. Low DE, Alderson D, Cecconello I, Chang AC, Darling GE, D'Journo XB, et al. International consensus on standardization of data collection for complications associated with esophagectomy: esophagectomy complications consensus group (ECCG). Ann Surg. 2015 Aug;262(2):286–94. https://doi.org/10.1097/SLA.0000000000001098
13. Shapiro J, van Lanschot JJB, Hulshof MCCM, van Hagen P, van Berge Henegouwen MI, et al, CROSS study group. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial. Lancet Oncol. 2015 Sep;16(9):1090–8. https://doi.org/10.1016/S1470-2045(15)00040-6
14. Yang H, Liu H, Chen Y, Zhu C, Fang W, et al, AME thoracic surgery collaborative group. neoadjuvant chemoradiotherapy followed by surgery versus surgery alone for locally advanced squamous cell carcinoma of the esophagus (NEOCRTEC5010): a phase III multicenter, randomized, open-label clinical trial. J Clin Oncol. 2018 Sep 20;36(27):2796–803. https://doi.org/10.1200/JCO.2018.79.1483
15. Liu J, Yang Y, Liu Z, Fu X, Cai X, Li H, et al. Multicenter, single-arm, phase II trial of camrelizumab and chemotherapy as neoadjuvant treatment for locally advanced esophageal squamous cell carcinoma. J Immunother Cancer. 2022a Mar;10(3):e004291. https://doi.org/10.1136/jitc-2021-004291. Erratum in: J Immunother Cancer. 2022 Jun;10(6):e004291corr1.
16. Yang W, Xing X, Yeung SJ, Wang S, Chen W, Bao Y, et al. Neoadjuvant programmed cell death 1 blockade combined with chemotherapy for resectable esophageal squamous cell carcinoma. J Immunother Cancer. 2022b Jan;10(1):e003497. https://doi.org/10.1136/jitc-2021-003497
17. Liu J, Li J, Lin W, Shao D, Depypere L, Zhang Z, et al. Neoadjuvant camrelizumab plus chemotherapy for resectable, locally advanced esophageal squamous cell carcinoma (NIC-ESCC2019): as multicenter, phase 2 study. Int J Cancer. 2022b Jul 1;151(1):128–37. https://doi.org/10.1002/ijc.33976. Epub 2022 Mar 21.
18. Wang Z. Neoadjuvant camrelizumab combined with chemotherapy and apatinib for locally advanced thoracic esophageal squamous cell carcinoma (ESCC): a single-arm, open-label, phase Ib study. JCO. 2021;39:4047–4047. https://doi.org/10.1200/JCO.2021.39.15_suppl.4047
19. Ma J, Zhang J, Yang Y, Zheng D, Wang X, Liang H, et al. 65P camrelizumab combined with paclitaxel and nedaplatin as neoadjuvant therapy for locally advanced esophageal squamous cell carcinoma (ESPRIT): a phase II, single - arm, exploratory research[J]. Ann. Oncol. 2021;32(Suppl 7):S1400. https://doi.org/10.1016/j.annonc.2021.10.083
20. Yang P, Zhou X, Yang X, Wang Y, Sun T, Feng S, et al. Neoadjuvant camrelizumab plus chemotherapy in treating locally advanced esophageal squamous cell carcinoma patients: a pilot study. World J Surg Oncol. 2021 Nov 22;19(1):333. https://doi.org/10.1186/s12957-021-02446-5
21. Duan H, Wang T, Luo Z, Wang X, Liu H, Tong L, et al. A multicenter single-arm trial of sintilimab in combination with chemotherapy for neoadjuvant treatment of resectable esophageal cancer (SIN-ICE study). Ann Transl Med. 2021 Nov;9(22):1700. https://doi.org/10.21037/atm-21-6102
22. Zhang Z, Hong ZN, Xie S, Lin W, Lin Y, Zhu J, et al. Neoadjuvant sintilimab plus chemotherapy for locally advanced esophageal squamous cell carcinoma: a single-arm, single-center, phase 2 trial (ESONICT-1). Ann Transl Med. 2021 Nov;9(21):1623. https://doi.org/10.21037/atm-21-5381
23. Lv H, Tian Y, Huang C, Sun B, Gai C, Li Z, et al. 110P neoadjuvant PD-1 blockade combined with chemotherapy for patients with resectable locally advanced esophageal squamous cell carcinoma (ESCC): a real world data analysis[J]. Annals of Oncology. 2021;32(Suppl 7):S1423. https://doi.org/10.1016/j.annonc.2021.10.128
24. Shang X, Zhang C, Zhao G, Zhang W, Liu L, Duan X, et al. LBA3 safety and efficacy of pembrolizumab combined with paclitaxel and cisplatin as a neoadjuvant treatment for locally advanced resectable (stage III) esophageal squamous cell carcinoma (keystone - 001): interim analysis of a prospective, single - arm, single - center, phase II trial[J]. Annals of Oncology. 2021;32(Suppl 7):S1428–9. https://doi.org/10.1016/j.annonc.2021.10.218
25. Huang B, Shi H, Gong X, Yu J, Xiao C, Zhou B, et al. Comparison of efficacy and safety between pembrolizumab combined with chemotherapy and simple chemotherapy in neoadjuvant therapy for esophageal squamous cell carcinoma. J Gastrointest Oncol. 2021 Oct;12(5):2013–21. https://doi.org/10.21037/jgo-21-610
26. Yan X, Duan H, Ni Y, Zhou Y, Wang X, Qi H, et al. Tislelizumab combined with chemotherapy as neoadjuvant therapy for surgically resectable esophageal cancer: A prospective, single-arm, phase II study (TD-NICE). Int J Surg. 2022 Jul;103:106680. https://doi.org/10.1016/j.ijsu.2022.106680
27. Xing W, Zhao L, Zheng Y, Liu B, Liu X, Li T, et al. The sequence of chemotherapy and toripalimab might influence the efficacy of neoadjuvant chemoimmunotherapy in locally advanced esophageal squamous cell cancer-A phase II study. Front Immunol. 2021 Dec 6;12:772450. https://doi.org/10.3389/fimmu.2021.772450
28. Gu Y, Chen X, Wang D, Ding M, Xue L, Zhen F, et al. 175P a study of neoadjuvant sintilimab combined with triplet chemotherapy of lipo - paclitaxel, cisplatin, and S - 1 for resectable esophageal squamous cell carcinoma (ESCC) [J]. Ann. Oncol. 2020;31(Suppl 6):S1307–8. https://doi.org/10.1016/j.annonc.2020.10.196
29. Yang Y, Tan L, Hu J, Li Y, Mao Y, Tian Z, et al. Esophageal cancer committee of chinese anti-cancer association. safety and efficacy of neoadjuvant treatment with immune checkpoint inhibitors in esophageal cancer: real-world multicenter retrospective study in China. Dis Esophagus. 2022c Nov 15;35(11):doac031. https://doi.org/10.1093/dote/doac031
30. Leng XF, Daiko H, Han YT, Mao YS. Optimal preoperative neoadjuvant therapy for resectable locally advanced esophageal squamous cell carcinoma. Ann N Y Acad Sci. 2020 Dec;1482(1):213–24. https://doi.org/10.1111/nyas.14508
31. Kelly RJ, Ajani JA, Kuzdzal J, Zander T, Van Cutsem E, Piessen G, et al. CheckMate 577 Investigators. Adjuvant Nivolumab in Resected Esophageal or Gastroesophageal Junction Cancer. N Engl J Med. 2021 Apr 1;384(13):1191–203. Erratum in: N Engl J Med. 2023 Feb 16;388(7):672. https://doi.org/10.1056/NEJMoa2032125
32. Cao J, Xu H, Li W, Guo Z, Lin Y, Shi Y, et al. Investigation on nutrition status and clinical outcome of common cancers (INSCOC) group, chinese society of nutritional oncology. Nutritional assessment and risk factors associated to malnutrition in patients with esophageal

cancer. Curr Probl Cancer. 2021 Feb;45(1):100638. https://doi.org/10.1016/j.currproblcancer.2020.100638
33. Pachella LA, Mehran RJ, Curtin K, Schneider SM. Preoperative carbohydrate loading in patients undergoing thoracic surgery: a quality-improvement project. J Perianesth Nurs. 2019 Dec;34(6):1250–6. https://doi.org/10.1016/j.jopan.2019.05.007
34. Findlay JM, Gillies RS, Millo J, Sgromo B, Marshall RE, Maynard ND. Enhanced recovery for esophagectomy: a systematic review and evidence-based guidelines. Ann Surg. 2014 Mar;259(3):413–31. https://doi.org/10.1097/SLA.0000000000000349

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