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Original Article

# Cost-effectiveness analysis of neoadjuvant chemoradiotherapy followed by surgery versus surgery alone for locally advanced esophageal squamous cell carcinoma based on the NEOCRTEC5010 trial

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ABSTRACT

*Background and purpose:* The phase 3 NEOCRTEC5010 trial demonstrated that neoadjuvant chemoradiotherapy (NCRT) plus surgery for locally advanced esophageal squamous cell carcinoma (ESCC) had significantly greater efficacy than surgery alone did, but at the same time, the addition of NCRT places an economic burden on patients. This study assessed the cost-effectiveness of NCRT followed by surgery based on the NEOCRTEC5010 trial.

*Materials and methods:* A three-state Markov model (disease-free survival, relapse and death) based on data from the NEOCRTEC5010 trial was used to estimate the incremental cost-effectiveness ratio (ICER) of NCRT plus surgery versus surgery alone for ESCC. The model evaluates the outcomes from the perspective of Chinese society. Costs, quality-adjusted life-years (QALYs), and the ICER in terms of 2019 US$ per QALY gained, were calculated. Model robustness was evaluated with one-way and probabilistic sensitivity analyses.

*Results:* Compared with surgery alone, NCRT plus surgery increased costs by $14933.57, while gaining 3.08 QALYs, resulting in an ICER of $4848.56 per QALY. The ICER was far below the commonly accepted willingness-to-pay threshold ($26,157 per QALY). The duration of disease-free survival (DFS) for the group that received NCRT was the crucial factor in determining the ICER.

*Conclusion:* Compared with surgery alone, NCRT followed by surgery for locally advanced ESCC can be cost-effective because of significant clinical benefits.



Esophageal cancer is a highly lethal disease, especially in developing countries. China has been a high-incidence area of esophageal cancer for many years and accounts for over 50% of the global morbidity and mortality [1]. The two major histological types of esophageal cancer are squamous cell carcinoma (ESCC) and adenocarcinoma, and there is a striking geographical variation in the incidence of the esophageal cancer subtypes. In China, approximately 90% of patients with esophageal cancer are diagnosed with ESCC [2]. Surgery has been the standard treatment for patients with esophageal cancer, but the long-term survival after surgery for esophageal cancer remains poor [3]. Neoadjuvant strategies have been prompted to improve survival; however, the results have been inconsistent [4–7]. The latest phase 3 clinical trial was the NEOCRTEC5010 trial conducted in China, and we performed cost-effectiveness analysis based on it [6].

The NEOCRTEC5010 trial was conducted to compare neoadjuvant chemoradiotherapy (NCRT) followed by surgery versus surgery alone in patients with potentially resectable thoracic ESCC, and it demonstrated a significant 33.6-month improvement of overall survival (OS) in the NCRT group (100.1 vs. 66.5 months; HR = 0.71; $P = 0.025$) [6]. The statistically significant improvements in DFS and OS demonstrated the benefit of NCRT in the treatment of ESCC. However, preoperative chemoradiotherapy may have a profound financial consequence due to the costs of treatment. Despite the proven effectiveness of neoadjuvant chemoradiotherapy, much concern has been dedicated to the costs associated with the treatments before surgery. Hence, this study aims to provide an economic assessment of NCRT based on the phase III trial from the perspective of Chinese society.

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## Materials and methods

### *Patients and regimens*

We extracted the clinical information from the NEOCRTEC5010 study. This trial recruited patients with histologically confirmed, potentially curable ESCC clinically staged as T1-4N1M0/T4N0M0 (stage IIB or III). Patients were randomly assigned to treatment with NCRT followed by surgery (the NCRT group) or surgery alone (the S group). In the NCRT group, vinorelbine was administered at 25 mg/m$^2$ as an intravenous bolus on days 1 and 8, and intravenous cisplatin 75 mg/m$^2$ within 3 h on day 1 or intravenous cisplatin 25 mg/m$^2$ within 2 h on days 1–4 was administered every 3 weeks for two cycles. A total radiation dose of 40.0 Gy was given in 20 fractions of 2.0 Gy each, five fractions per week, starting on the first day of the first chemotherapy cycle. Surgery was performed 4–6 weeks after completion of chemoradiotherapy. Surgery was performed as soon as possible after random assignment for patients in the S group.

### *Markov model*

A Markov model was constructed using Treeage software (Treeage, Williamstown, MA, USA, 2011) to perform a cost-effectiveness analysis of NCRT plus surgery versus surgery alone for locally advanced ESCC. The Markov model of three health states, DFS, relapse and death, evaluated the outcomes over a 30-year time horizon (after which >99% of patients have died) using monthly transitions. DFS defined as the state after resection without either disease recurrence or death. All simulated patients started in the DFS health state and were stay in the original health state or move to the relapse in the next month, according to transition probabilities. The patients who progress to the state of relapse can only stay in the state of relapse or move to the state of death. The model diagram is shown in Fig. 1. The cycle length was set as one month, which was short enough to reflect quality of life impact and facilitate to calculate parameters. We calculated the ICER of NCRT followed by surgery compared with surgery alone, and the results are described using costs per QALY. The formula used to calculate the ICER as following: $ICER = (Cost_{[the\ NCRT\ group]} - Cost_{[the\ S\ group]})/(QALY_{[the\ NCRT\ group]} - QALY_{[the\ S\ group]})$. QALYs was estimated by weighting the time each patients spend in different Markov state, using utility values as weights. In the model, costs and benefits were discounted at 3% annually, and cost effectiveness was calculated from the perspective of Chinese society.

### *Survival estimates and utilities*

Efficacy and grade 3–4 adverse events (AEs) related to costs derived from the NEOCRTEC5010 study are shown in Table 1. The time and survival probabilities was derived by digitizing the Kaplan–Meier curves of DFS and OS from the NEOCRTEC5010 study using Web-PlotDigitizer. We use the survival probabilities at intermediate times to improve the curve fits and the method described by Hoyle and Henley [8]. The Weibull distribution was used to simulate the DFS and OS curves. Table 2 presents the input parameters of the Weibull. Fig. 2 shows the survival curve simulation results. We use formula $S(t) = P(T \geq t) = \exp(-\lambda t^{\gamma})$ to calculate the survival probability at time t and formula $P(t) = 1 - \exp[(\lambda(t-1)^{\gamma} - \lambda t^{\gamma}]$ to calculate the transition probability at a given cycle $t$. Survival was adjusted to quality-adjusted life-years (QALYs) using utility values derived from previously published studies. As a result, the utility values were 0.80 for the DFS state and 0.41 for the relapse state [9], as 0 was used for death. In the Markov model, $QALY = \sum_1^{\text{cycle number}} \sum_1^{\text{state number}} Utility(state) \times Probability(state)$.

**Table 1**
Clinical efficacy and grade 3–4 adverse events.

| Variable | Base case value | |
|---|---|---|
| | The NCRT group | The S group |
| *Clinical efficacy* | | |
| OS (Months) | 100.1 | 66.5 |
| (95 % CI) | 74.6–125.6 | 39.7–93.3 |
| DFS (Months) | 100.1 | 41.7 |
| (95 % CI) | 49.7–150.6 | 19.0–64.4 |
| *Probability of grade 3–4 AEs (%)* | | |
| Anemia | 4.0 | / |
| Leukopenia | 48.8 | / |
| Neutropenia | 45.7 | / |
| Thrombocytopenia | 7.2 | / |
| Anorexia | 2.2 | / |
| Vomiting | 4.0 | / |
| Radiation esophagitis | 2.7 | / |

NCRT: neoadjuvant chemoradiotherapy; S: surgery; OS: overall survival; DFS: disease-free survival; AE adverse event.

### *Cost estimates*

Cost was calculated from the perspective of Chinese society and thus included the following medical costs: drug acquisition, radiotherapy, necessary tests, therapy administration, treatment of major AEs and surgery costs. Each of these costs is based on the price in West China Hospital. Doses administered were calculated using the reported median body surface area (1.63 kg/m$^2$) in China [10]. AEs used to calculate the costs were those rated at a severity of grade 3 or higher and must have occurred in at least 1% of patients in the NCRT group from the NEOCRTEC5010 study. Moreover, the patients who received NCRT needed to take off more work, so time costs (the absenteeism fees) were applied to the time for chemoradiotherapy, which was $29.99 per day based on the average salary of China's urban employees. Current studies showed that NCRT did not significantly increase the risk of major postoperative complications [6,7,11], so we hypothesized that the cost for postoperative complications was the same in both groups and that the cost for postoperative complications was included in surgery costs. Surgery costs included all hospitalization expenses during operation. The cost information for each input variable is presented in Table 3. All costs were adjusted to US dollars, using an exchange rate of $1 = ¥6.79 (22 Jan 2019). In the Markov model, total $cost = \sum_1^{\text{cycle number}} \sum_1^{\text{state number}} Cost(state) \times Probability(state)$

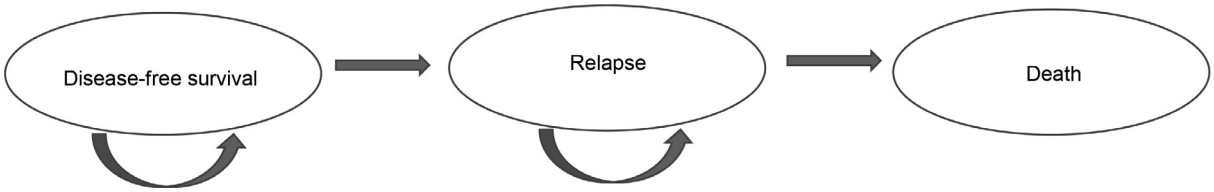


**Fig. 1.** Model diagram. Two groups of patients were analysed: those treated with neoadjuvant chemoradiotherapy followed by surgery with surgery alone. The Markov model simulated three health states: DFS, Relapse and death. DFS: disease-free survival; NCRT: neoadjuvant chemoradiotherapy, S: surgery.

**Table 2**
Key model input parameters.

| | Parameter | | | |
|---|---|---|---|---|
| Weibull survival model of DFS of the NCRT group | Intercept | 4.87895 | Lambda | 0.013 |
| | log(scale) | 0.12369 | Gamma | 0.884 |
| Weibull survival model of DFS of the S group | Intercept | 4.26726 | Lambda | 0.033 |
| | log(scale) | 0.22658 | Gamma | 0.797 |
| Weibull survival model of OS of the NCRT group | Intercept | 4.96279 | Lambda | 0.017 |
| | log(scale) | 0.20239 | Gamma | 0.817 |
| Weibull survival model of OS of the S group | Intercept | 4.36183 | Lambda | 0.010 |
| | log(scale) | −0.04428 | Gamma | 1.045 |

NCRT: neoadjuvant chemoradiotherapy; S: surgery; DFS: disease-free survival; OS: overall survival.

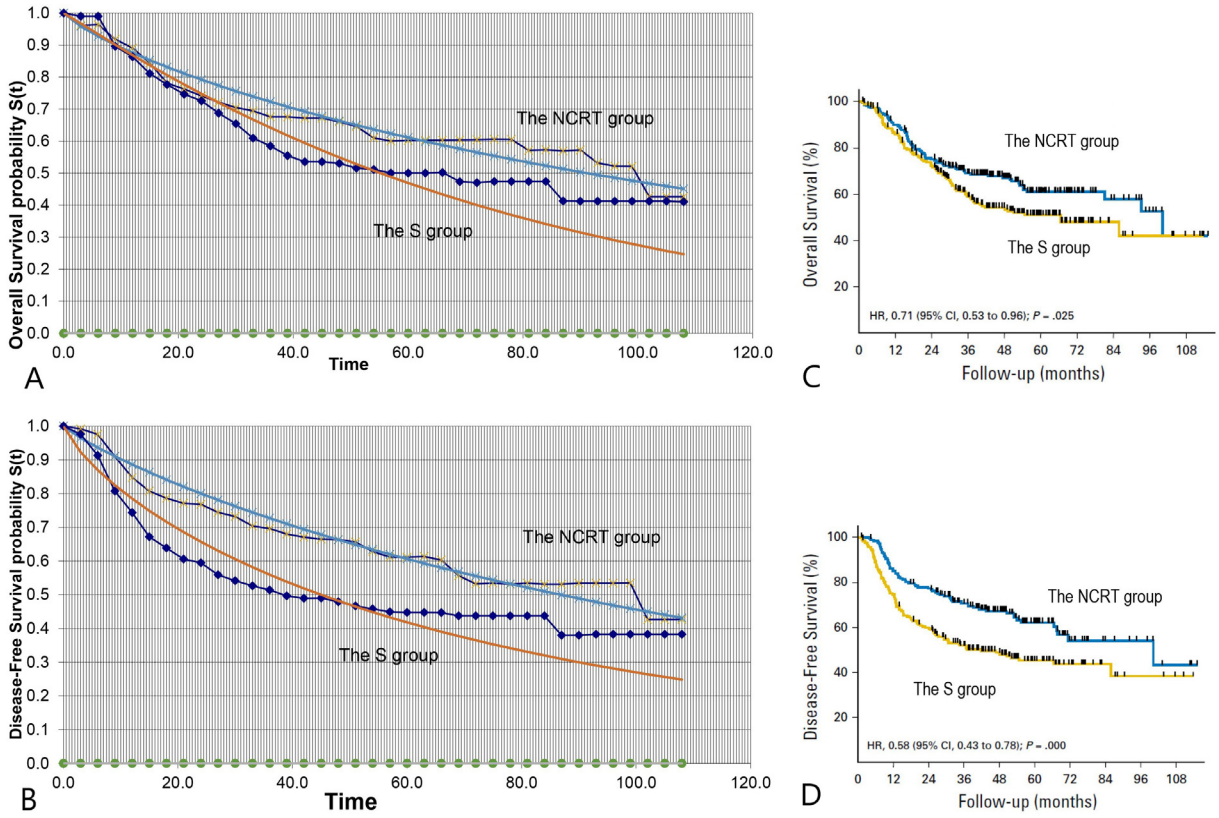


**Fig. 2.** (A) Simulate overall survival curve for the NCRT group and the S group. (B) Simulate disease-free survival curve for the NCRT group and the S group. (C) Kaplan–Meier curve of overall survival from the NEOCRTEC5010 study. (D) Kaplan–Meier curve of disease-free survival from the NEOCRTEC5010 study. NCRT: neoadjuvant chemoradiotherapy, S: surgery.

*Sensitivity analyses*

One-way sensitivity analysis was performed to estimate the potential influences of different variables by varying them by ±20%. We performed a probabilistic sensitivity analysis to assess uncertainty around the ICER estimate by conducting a Monte-Carlo simulation of 10,000 samples at different hypothetical willingness-to-pay (WTP) thresholds. According to the World Health Organization guidelines for cost-effective analysis [12,13], strategies are defined as cost-effective if the ICER is below three times the gross domestic product (GDP) per capita, which was $26,157 in China in 2018.

## Results

In the NEOCRTEC5010 study, compared with the S group, the NCRT group achieved a better median OS (100.1 months vs 66.5 months; hazard ratio, 0.71; 95% CI, 0.53–0.96; $P = 0.025$). The R0 resection rates in the NCRT and S groups were 98.4% and 91.2%, respectively. The median DFS was 100.1 months (95% CI, 49.7–150.6 months) in the NCRT group, while the S group had a median DFS of 41.7 months (95% CI, 19.0–64.4 months) (HR, 0.58; 95% CI, 0.43–0.78; $P < 0.001$). Overall, QALYs in the NCRT group were higher than those in the S group (9.08 QALYs vs 6.00 QALYs).

By model calculation, the NCRT group provided an additional 3.08 QALYs at an additional cost of $14933.57 (Table 3). In the base-case analysis, the ICER of the NCRT group compared with the S group was $4848.56 per QALY, which was much lower than the commonly accepted threshold for cost-effectiveness ($26,157 per QALY in China).

In one-way sensitivity analysis, the duration of DFS in the NCRT group was the factor that most altered the cost-effectiveness of the strategies within the model. When the duration of DFS varied from 80.08 months to 120.12 months, the ICER ranged from $ 3416.42 per QALY to $6990.24 per QALY. In addition, the costs of testing

**Table 3**
Results of the cost-effectiveness analysis.

| Parameters | The NCRT group | The S group |
|---|---|---|
| *Costs ($)* | | |
| DFS state ($) | 14925.69 | 8806.79 |
| cRadiotherapy ($/month) | 38.73 | 0.00 |
| cChemotherapy ($/month) | 8.36 | 0.00 |
| cHospital ($/month) | 0.59 | 0.00 |
| cAbsenteeism ($/month) | 8.39 | 0.00 |
| cAEs ($/month) | 3.71 | 0.00 |
| cSurgery ($/month) | 109.30 | 262.38 |
| cTest ($/month) | 169.80 | 180.91 |
| Relapse state ($/month) | 0.00 | 0.00 |
| Total Cost ($) | 33334.51 | 18400.94 |
| Incremental costs ($) | 14933.57 | / |
| *Effectiveness (QALYs)* | | |
| DFS state (QALYs) | 6.59 | 4.25 |
| Relapse state (QALYs) | 2.49 | 1.75 |
| Total effectiveness (QALYs) | 9.08 | 6.00 |
| Incremental effectiveness (QALYs) | 3.08 | / |
| ICERs compared with PC alone ($/QALY) | 4848.56 | |

NCRT: neoadjuvant chemoradiotherapy; S: surgery; DFS: disease-free survival; AE: adverse event; QALY: quality-adjusted life years; ICER incremental cost-effectiveness ratio.

for both group, the duration of DFS in the S group, the cost of surgery, radiotherapy for the NCRT group and the utility of DFS and relapse had impacts on ICER. Other parameters, such as absenteeism fee, the costs of chemotherapy, AEs and hospitalization for the NCRT group, the cost of surgery for the S group, had a minor impact on the robustness of the cost-effectiveness analysis. Changing individual parameters did not change the results (Fig. 3). Probabilistic sensitivity analysis showed that surgery alone had no possibility of being a cost-effective treatment unless the threshold of cost-effectiveness analysis sharply decreased to $5000 per QALY (Fig. 4). At present, it seems that there is no possibility for China's GDP to fall to this level.

## Discussion

In the process of economic evaluation, we set WTP thresholds at three times GDP per capita according to WHO, but different organizations have different cost-effectiveness threshold value. For example, the National Institute for Health and Clinical Excellence (NICE) use a threshold range of £20,000–£30,000 per QALY gained [14], meanwhile others may use implicit values in their decision making [15]. But the present analysis shows even if the WTP thresholds is set at GDP per capita ($8,719 per QALY), the ICER is still far below WTP.

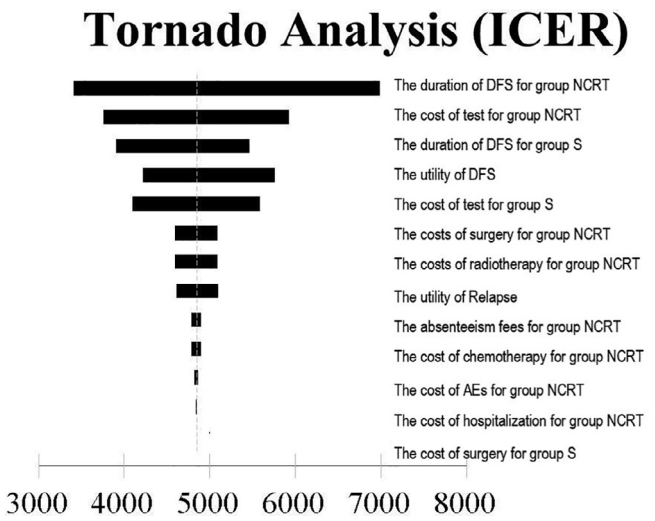


**Fig. 3.** Tornado diagram of one-way sensitivity analysis. This summarizes the results of one-way sensitivity analysis, listing influential parameters in descending order in which they affect the ICER over the variation of each parameter value. DFS: disease-free survival; AE adverse event; NCRT: neoadjuvant chemoradiotherapy, S: surgery, ICER: incremental cost-effectiveness ratio.

In the sensitivity analysis, the duration of DFS in the NCRT group had the highest impact on the ICER. However, the median OS or DFS reported in the NEOCRTEC5010 trial were significantly longer than those reported in previous studies [16–18]. A possible explanation is that the sample size of patients with ESCC in the previous study was relatively small. China has a high prevalence of ESCC, which is different from that in Western countries. The NEOCRTEC5010 study enrolled patients with squamous cell carcinoma and was conducted in China. The NEOCRTEC5010 study is the latest completed randomized trial that compared NCRT plus surgery with surgery alone. In choosing a phase III trial to perform a cost-effectiveness analysis, the NEOCRTEC5010 study was the best choice. We searched PubMed and found that pharmacoeconomic studies on esophageal cancer were limited, and many of them focused on screening or surgical techniques [19–22]. Furthermore, most studies were conducted in patients with Barrett's esophagus [23–25]. There were only two economic analyses of neoadjuvant chemoradiotherapy in esophageal cancer [26,27]. The latest study [26] was a population-based matched case-control study conducted in Taiwan, and their outcome variables were extracted from the database. Their study included 150 locally advanced ESCC patients and showed that neoadjuvant concurrent chemoradiotherapy was probably more cost-effective than was esophagectomy, at a $50,000–150,000 per QALY WTP threshold. The major limitation is that the duration of interest (three years) might be too short to adequately assess the cost-effectiveness of NCRT compared with esophagectomy. Other research was conducted in 1997 [27], when neoadjuvant chemoradiotherapy was not a standard treatment for patients with potentially curable ESCC. They found that despite the high cost of neoadjuvant chemoradiotherapy therapy, neoadjuvant multimodal therapy was a cost-effective alternative when the acceptable cost-effectiveness ratio was set at approximately $50,000 per life year gained. However, this cost-effectiveness analysis was based on a small-size controlled trial involving only 113 patients with esophageal adenocarcinoma. Their study population had a different composition than the general population based on the major pathological types of esophageal cancer in China. Although both studies revealed that neoadjuvant therapy would be cost-effective, their WTP threshold was higher because the GDPs of Taiwan and Italy are higher than that of mainland China. The WTP threshold remains controversial in China, and patients with esophageal cancer may be able to afford a relatively lower cost per QALY in China because the incidence rates for esophageal cancer in rural areas were approximately three times those in urban areas [1]. Therefore, we still need long-term, large sample studies to evaluate the cost-effectiveness of neoadjuvant chemoradiotherapy therapy. The NEOCRTEC5010 study that our cost-effectiveness analysis was based on is a long-term, multicenter, randomized trial that enrolled 451 patients with ESCC. Thus, our research was able to overcome the major drawbacks of the above two studies.

Our study inevitably had some limitations of data availability and assumptions because our analysis model primarily relied on the data from a phase III trial rather than real-world experience. First, the incidence of postoperative complications after esophagectomy was similar between the two groups, with the exception of arrhythmia. In addition, detailed data on the clinical and economic burden of complications of esophageal resection remain limited. Given the impact of cardiac complications on our

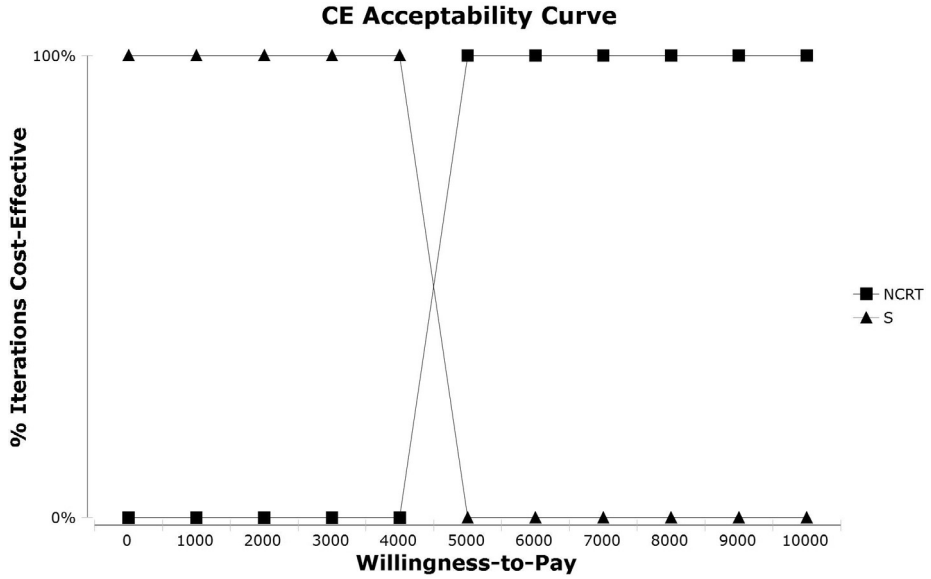


**Fig. 4.** Cost-effectiveness acceptability curves. Cost-effectiveness acceptability curves show the probability of each treatment strategy being cost-effective at different WTP thresholds. NCRT: neoadjuvant chemoradiotherapy, S: surgery.

economic model, we conducted sensitivity analyses using the additional costs of cardiac complications derived from a previously published study [28]. The ICER remained far lower than the WTP threshold of $5580.63 per QALY. Second, our analysis did not take into account costs for subsequent anticancer therapy after disease progression because no information was available in the NEOCRTEC5010 study. According to the NCCN guidelines, when the disease relapsed after surgery, the patients who were treated with surgery alone could receive chemoradiotherapy, and the patients who received neoadjuvant chemoradiotherapy may accept palliative management. If the S group received chemoradiotherapy, the cost for relapse in the S group might be higher than that in the NCRT group. In other words, calculating the cost for subsequent anticancer therapy after relapse would not alter our conclusion. Furthermore, the cost for postoperative chemoradiotherapy was uncertain and difficult to estimate. For the reasons given above, we did not calculate the cost for the relapse state. Third, because no data on the quality of life were available from the NEOCRTEC5010 study, the utilities for the state of DFS and relapse were referenced from previously published research. In addition, the utilities for DFS had a higher impact on the model outcomes, but even if the utility for DFS varied from 0.41 to 1, the ICER ranged from $7742.68 per QALY to $ 4101.89 per QALY, which was still far below the WTP. Fourth, because the DFS was calculated only for the patients who received R0 resection, the OS was calculated for all patients who were enrolled and randomly assigned. However, the rates of R0 resection were high in both groups (98.4%, 91.2%), especially for the NCRT group (98.4%). According to one-way sensitivity analysis, when the duration of DFS varied by ±20%, the ICER remained far below the WTP. Developing countries such as China have a higher incidence of esophageal cancer, and the economics of treatments require more concern. The NEOCRTEC5010 regimen can provide significantly greater efficacy, a tolerable safety profile and acceptable cost-effectiveness. There are three alternative chemotherapy regimens based on clinical research, including the Dutch CROSS trial [18] using carboplatin plus paclitaxel, CALGB 9781 [17] using cisplatin plus fluorouracil (FU) and NEOCRTEC5010 [6] using cisplatin plus vinorelbine. Preoperative chemoradiotherapy was recommended, which is the optimal regimen as a neoadjuvant approach for ESCC, but has not been definitively established. Therefore, further studies are required.

## Conclusions

In conclusion, our results showed that NCRT followed by surgery was very cost-effective compared with surgery alone. Based on the existing research results, we suggest neoadjuvant chemoradiotherapy with surgery rather than resection alone for patients with ESCC. Although ICERs are influenced by many factors, sensitivity analysis was performed to reduce uncertainty. The present results is potentially useful to healthcare systems making decisions, However, real-world studies are needed to verify the efficacy, safety and economics of these regimens for neoadjuvant therapy of ESCC.

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## Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors

## Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References

[1] Chen W, Zheng R, Baade PD, Zhang S, Zeng H, Bray F, et al. Cancer statistics in China, 2015. CA Cancer J Clin 2016;66:115–32.

[2] Tran GD, Sun XD, Abnet CC, Fan JH, Dawsey SM, Dong ZW, et al. Prospective study of risk factors for esophageal and gastric cancers in the Linxian general population trial cohort in China. Int J Cancer 2005;113:456–63.
[3] Herskovic A, Russell W, Liptay M, Fidler MJ, Al-Sarraf M. Esophageal carcinoma advances in treatment results for locally advanced disease: review. Ann Oncol 2012;23:1095–103.
[4] Bosset JF, Gignoux M, Triboulet JP, Tiret E, Mantion G, Elias D, et al. Chemoradiotherapy followed by surgery compared with surgery alone in squamous-cell cancer of the esophagus. N Engl J Med 1997;337:161–7.
[5] Mariette C, Dahan L, Mornex F, Maillard E, Thomas PA, Meunier B, et al. Surgery alone versus chemoradiotherapy followed by surgery for stage I and II esophageal cancer: final analysis of randomized controlled phase III trial FFCD 9901. J Clin Oncol 2014;32:2416–22.
[6] Yang H, Liu H, Chen Y, Zhu C, Fang W, Yu Z, et al. 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;36:2796–803.
[7] Shapiro J, van Lanschot JJB, Hulshof M, van Hagen P, van Berge Henegouwen MI, Wijnhoven BPL, et al. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (CROSS): long-term results of a randomised controlled trial. Lancet Oncol 2015;16:1090–8.
[8] Hoyle MW, Henley W. Improved curve fits to summary survival data: application to economic evaluation of health technologies. BMC Med Res Method 2011;11:139.
[9] de Boer AG, Stalmeier PF, Sprangers MA, de Haes JC, van Sandick JW, Hulscher JB, et al. Transhiatal vs extended transthoracic resection in oesophageal carcinoma: patients' utilities and treatment preferences. Br J Cancer 2002;86:851–7.
[10] Xie Q, Wen F, Wei YQ, Deng HX, Li Q. Cost analysis of adjuvant therapy with XELOX or FOLFOX4 for colon cancer. Colorectal Dis 2013;15:958–62.
[11] Kidane B, Coughlin S, Vogt K, Malthaner R. Preoperative chemotherapy for resectable thoracic esophageal cancer. Cochrane Database Syst Rev 2015: Cd001556.
[12] Eichler HG, Kong SX, Gerth WC, Mavros P, Jonsson B. Use of cost-effectiveness analysis in health-care resource allocation decision-making: how are cost-effectiveness thresholds expected to emerge?. Value Health 2004;7:518–28.
[13] Murray CJ, Evans DB, Acharya A, Baltussen RM. Development of WHO guidelines on generalized cost-effectiveness analysis. Health Econ 2000;9:235–51.
[14] McCabe C, Claxton K, Culyer AJ. The NICE cost-effectiveness threshold: what it is and what that means. Pharmacoeconomics 2008;26:733–44.
[15] Wang S, Gum D, Merlin T. Comparing the ICERs in medicine reimbursement submissions to NICE and PBAC-does the presence of an explicit threshold affect the ICER proposed?. Value Health 2018;21:938–43.
[16] Burmeister BH, Smithers BM, Gebski V, Fitzgerald L, Simes RJ, Devitt P, et al. Surgery alone versus chemoradiotherapy followed by surgery for resectable cancer of the oesophagus: a randomised controlled phase III trial. Lancet Oncol 2005;6:659–68.
[17] Tepper J, Krasna MJ, Niedzwiecki D, Hollis D, Reed CE, Goldberg R, et al. Phase III trial of trimodality therapy with cisplatin, fluorouracil, radiotherapy, and surgery compared with surgery alone for esophageal cancer: CALGB 9781. J Clin Oncol 2008;26:1086–92.
[18] van Hagen P, Hulshof MC, van Lanschot JJ, Steyerberg EW, van Berge Henegouwen MI, Wijnhoven BP, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med 2012;366:2074–84.
[19] Lee L, Sudarshan M, Li C, Latimer E, Fried GM, Mulder DS, et al. Cost-effectiveness of minimally invasive versus open esophagectomy for esophageal cancer. Ann Surg Oncol 2013;20:3732–9.
[20] Yang J, Wei WQ, Niu J, Liu ZC, Yang CX, Qiao YL. Cost-benefit analysis of esophageal cancer endoscopic screening in high-risk areas of China. World J Gastroenterol 2012;18:2493–501.
[21] Gordon LG, Hirst NG, Mayne GC, Watson DI, Bright T, Cai W, et al. Modeling the cost-effectiveness of strategies for treating esophageal adenocarcinoma and high-grade dysplasia. J Gastrointest Surg 2012;16:1451–61.
[22] Wei WQ, Yang CX, Lu SH, Yang J, Li BY, Lian SY, et al. Cost-benefit analysis of screening for esophageal and gastric cardiac cancer. Chin J Cancer 2011;30:213–8.
[23] Hur C, Choi SE, Rubenstein JH, Kong CY, Nishioka NS, Provenzale DT, et al. The cost effectiveness of radiofrequency ablation for Barrett's esophagus. Gastroenterology 2012;143:567–75.
[24] Yang Y, Chen HN, Wang R, Tang YJ, Chen XZ. Cost-effectiveness analysis on endoscopic surveillance among western patients with Barrett's esophagus for esophageal adenocarcinoma screening. Medicine 2015;94:e1105.
[25] Sanchez A, Reza M, Blasco JA, Callejo D. Effectiveness, safety, and cost-effectiveness of photodynamic therapy in Barrett's esophagus: a systematic review. Dis Esophagus 2010;23:633–40.
[26] Lin CY, Fang HY, Feng CL, Li CC, Chien CR. Cost-effectiveness of neoadjuvant concurrent chemoradiotherapy versus esophagectomy for locally advanced esophageal squamous cell carcinoma: A population-based matched case-control study. Thorac Cancer 2016;7:288–95.
[27] Davini I, Becagli P, Pani M, Trippoli S, Peverini D, Messori A, et al. Cost-effectiveness of neoadjuvant multimodal therapy in patients with esophageal adenocarcinoma. Oncol Rep 1997;4:1033–7.
[28] Goense L, van Dijk WA, Govaert JA, van Rossum PS, Ruurda JP, van Hillegersberg R. Hospital costs of complications after esophagectomy for cancer. Eur J Surg Oncol 2017;43:696–702.