

Cost-effectiveness analysis of positron-emission tomography-computed tomography in preoperative staging for nonsmall-cell lung cancer with resected monometastatic disease

Xiaohui Zeng, PhD^a, Liubao Peng, BS^b, Chongqing Tan, PhD^b, Yunhua Wang, MD^{a,*}

Abstract

Background: The aim of this study was, from the Chinese healthcare perspective, to assess the cost-effectiveness of positron-emission tomography-computed tomography (PET-CT) with ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) in preoperation staging for nonsmall-cell lung cancer (NSCLC) with resected monometastatic disease based on a retrospective study. This study was conducted from January 2017 to February 2019 at an academic hospital.

Methods: A Markov model and 3 decision-tree models were designed to calculate the long-term medical costs, outcomes, and incremental cost-effectiveness ratios (ICERs) of the 2 diagnostic strategies (PET-CT and conventional CT). Model robustness was assessed in sensitivity analyses.

Results: For the base-case analysis, preoperative PET-CT evaluation for NSCLC with resected monometastatic disease provided an additional 1.475, 2.129, and 2.412 life-years (LYs), in the time horizon of 10-, 20-, and 30-year, respectively, and the ICERs for the PET-CT group compared with the conventional CT group were \$1153, \$1393, and \$1430 per LY, separately. The acceptability curves demonstrated that when the willingness-to-pay (WTP) thresholds ranged from \$500 to \$3000/LY, the probability of cost-effectiveness changed varied dramatically, and at WTP > \$3000, the probability that the PET-CT group achieved cost-effectiveness was 100%. Sensitivity analyses suggested that the models we designed were robust.

Conclusion: Compared with conventional CT scan, preoperative ¹⁸F-FDG PET-CT evaluation for patients with resected monometastatic NSCLC is cost-effective from the Chinese healthcare perspective. Preoperative ¹⁸F-FDG PET-CT evaluation should be popularized for patients with resected monometastatic NSCLC.

Abbreviations: CI = confidence interval, CT = computed tomography, DFIs = disease-free intervals, EGFR = epidermal growth factor receptor, ¹⁸F-FDG = ¹⁸F-fluorodeoxyglucose, ICER = incremental cost-effectiveness ratio, LY = life-year, MRI = magnetic resonance imaging, NSCLC = nonsmall-cell lung cancer, OS = overall survival, PET = positron-emission tomography, RMB = Renminbi, USD = US dollars, WBRT = whole-brain radiation therapy, WTP = willingness-to-pay.

Keywords: cost-effectiveness analysis, decision tree, Markov model, nonsmall-cell lung cancer, positron-emission tomography

1. Introduction

Lung cancer, as one of the frequent types of cancer, occupies one-quarter of the 1st leading cause of cancer-related death.^[1] About 80% of lung cancers are nonsmall-cell lung cancer (NSCLC).^[2] In

the past, the standard imaging modalities for NSCLC staging include chest scan with X-radiograph or computed tomography (CT), upper abdomen scan with CT, liver ultrasonography, radionuclide bone scan, and central nervous system scan with magnetic resonance imaging (MRI).^[3] Because accurate staging allows for more appropriate treatment, the life expectancy of patients with NSCLC may be extended through accurate staging.^[4] As one of the 1st approved indications, positron-emission tomography (PET) scans were used for NSCLC staging based on the biological activity of euplastic cells but were rapidly replaced by combined PET and CT (PET-CT).^[5,6] An overview of PET-CT for different types of lung cancer indicated that integrated PET and CT improved the diagnostic accuracy, and overcome the limits of patients repositioning when the two image scans were acquired independently and fused afterwards.^[7] A recent retrospective study showed that, for patients with NSCLC with resected monometastatic disease, the overall survival (OS) rates of 5 years after preoperation staging by PET-CT with ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) and by traditional CT were 0.58 and 0.33, separately.^[8]

Although many studies have indicated that PET-CT is superior to conventional CT, the standard diagnostic work-up in clinical practice in China is still based on conventional CT scan. Evidence from cost-effectiveness analyses is limited in China, and PET-CT

Editor: Kou Yi.

This work was supported by the National Natural Science Foundation of China (nos: 81401547 and 81603081).

The authors have no conflicts of interest to disclose.

^a PET-CT Center, ^b Department of Pharmacy, The Second Xiangya Hospital of Central South University, Changsha, Hunan, China.

* Correspondence: Yunhua Wang, PET-CT Center, The Second Xiangya Hospital of Central South University, No 139 Renmin Middle Road, Changsha, Hunan 410011, China (e-mail: wangyunhua0801@csu.edu.cn).

Copyright © 2019 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

Medicine (2019) 98:33(e16843)

Received: 17 March 2019 / Received in final form: 21 July 2019 / Accepted: 24 July 2019

<http://dx.doi.org/10.1097/MD.00000000000016843>

has not been warranted coverage for any oncologic use.^[9] Through decision-tree analysis, many studies have demonstrated that PET-CT is likely to be cost-effective when added to the NSCLC current practice.^[9–12] However, it is unclear whether the preoperative PET-CT evaluation is cost-effective especially for patients with NSCLC with resected monometastatic disease.

We designed this study to assess the cost-effectiveness of ¹⁸F-FDG PET-CT in preoperation staging for NSCLC with resected monometastatic disease based on the recent retrospective study.

2. Materials and methods

Through TreeAge Pro Suit 2009 (TreeAge Software Inc, Williamstown, MA), we developed a Markov model to evaluate the cost-effectiveness of ¹⁸F-FDG PET-CT (PET-CT group) vs conventional CT (CT group) as a preoperative evaluation for patients with NSCLC with resected monometastatic disease based on a retrospective study.^[8] The model was used to calculate the total costs and long-term life-years (LYs), on the basis of the clinical practice in the published research.

The direct medical costs associated with the clinical practice were calculated in this evaluation, including imaging examinations, physical examination, bronchoscopy, operative treatment, adjuvant treatment with chemotherapy, and radiotherapy, the epidermal growth factor receptor (EGFR) mutation test, routine follow-up for patients after operative and adjuvant treatment, and the terminal 3-month healthcare cost. Three decision-tree models were used to calculate the costs of operative treatment, adjuvant chemotherapy, and radiotherapy for NSCLC on account of different lymph node involvement, metastatic sites, and disease-free intervals (DFIs, interval between pneumonectomy and recognition of oligometastatic disease), respectively. The costs of the brain MRI scan and adjuvant whole-brain radiation therapy (WBRT) for brain metastases were also calculated by the decision-tree model of operative treatment. All costs were

discounted at 5% annually and adjusted to 2018 US dollars (USD) with an exchange rate of 1 USD to 6.6174 Renminbi (RMB).

Effectiveness were estimated as LYs based on the OS curves of the retrospective study,^[8] in which whether the preoperative PET-CT evaluation influenced survival in patients with NSCLC with resected monometastatic disease was investigated.

The total costs and outcomes in the time horizon of 10, 20, and 30 years were evaluated in baseline analyses. By means of sensitivity analyses, uncertainty of the input variables was addressed to assess the model robustness. In the analyzed, the willingness-to-pay (WTP) threshold was equaled the cost-effectiveness ratio of the CT group.

2.1. Model structure

As shown in Figure 1A, the Markov model structure included 2 health states (survival after operation and death). During each Markov model cycle (3 months), patients after operation may still be in “survival,” or in “death” until time horizon termination of 30 years (more than 90% of the patients died). A 2-parametric log-logistic distribution analysis was fitted to the OS curves of the retrospective study using R software (<https://www.r-project.org/>). The estimated parameters (theta and kappa) of log-logistic distribution are displayed in Table 1. The mortality rates in each cycle were calculated with the following formula:

$$M(t_u) = 1 - \frac{1 + \exp(\theta) (t - \mu)^\kappa}{1 + \exp(\theta)t^\kappa}$$

where the *u* is the cycle of Markov model and *t_u* defines the arrival at state *t* after *u* Markov cycles, *θ* and *κ* represent the parameters of log-logistic distribution.

The structures of 3 decision-tree models are shown in Figure 1B–D. These models were used to calculate the different costs due to different lymph node involvement, metastatic sites,

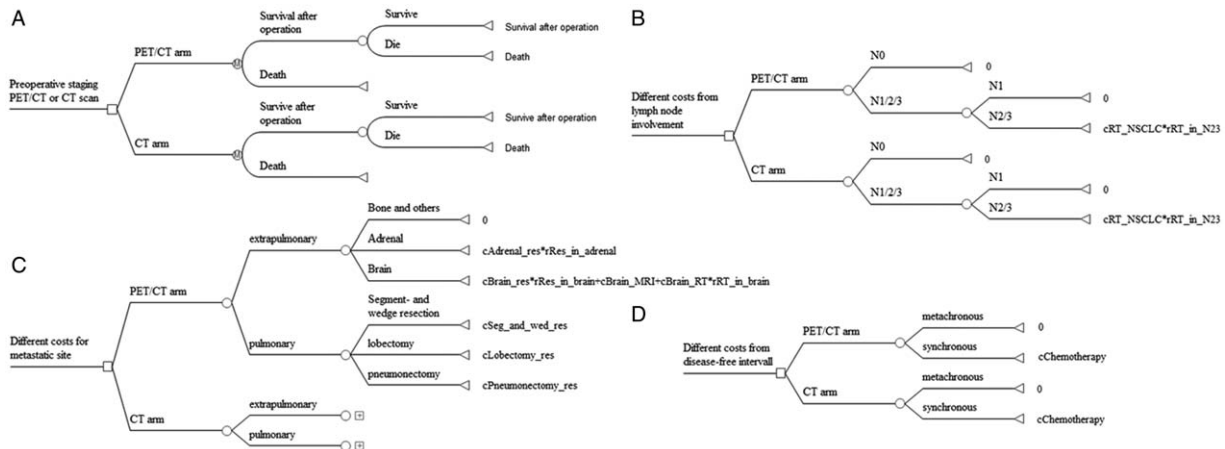


Figure 1. The Markov model and 3 decision-tree models used to evaluate the cost-effectiveness and to calculate the different costs. (A) The Markov model for non-small-cell lung cancer with resected monometastatic disease. (B) Decision-tree model used to calculate the differences in costs due to lymph node involvement. (C) Decision-tree model used to calculate the differences in costs due to different metastatic sites and types. (D) Decision-tree model used to calculate the differences in costs due to different disease-free intervals. cAdrenal_res=cost of adrenalectomy, cBrain_MRI=cost of brain magnetic resonance imaging, cBrain_res=cost of brain metastasectomy, cBrain_RT=cost of whole-brain radiation therapy, cChemotherapy=cost of adjuvant chemotherapy, cLobectomy_res=cost of lobectomy, cPneumectomy_res=cost of Pneumectomy, cRT_NSCLC=cost of adjuvant radiotherapy for non-small-cell lung cancer, cSeg_and_wed_res=cost of segment and wedge resection, rRes_in_adrenal=risk of adrenalectomy for patients with adrenal metastasis, rRes_in_brain=risk of brain metastasectomy for patients with brain metastasis, rRT_in_Brain=risk of adjuvant whole-brain radiation therapy for patients with brain metastasis, rRT_in_N23=proportion of patients with pN/3 received adjuvant radiotherapy.

Table 1

Log-logistic parameters of model estimated to overall survival curves of resected monometastatic nonsmall-cell lung cancer with preoperative ¹⁸F-FDG PET-CT scan or conventional CT scan.

Technique	Theta, mean (SE)	Kappa, mean (SE)	Adjusted R ²	Correlation coefficient
PET-CT Scan	-4.5380 (0.2765)	1.4804 (0.1127)	0.9613	-0.9995
CT Scan	-3.1414 (0.0702)	1.2529 (0.0252)	0.9941	-0.9996

CT=computed tomography, ¹⁸F-FDG=¹⁸F-fluorodeoxyglucose, PET=positron-emission tomography, SE=standard error.

and DFIs, respectively. The risks of metastatic sites, types of resection for oligometastatic disease, DFIs, and lymph node involvement were all derived or calculated from the details of the retrospective study (Table 2).^[8]

2.2. Medical costs

The medical costs of the 2 staging strategies are presented in Table 3, on the basis of the Chinese healthcare perspective. The aggregate medical costs of the terminal 3 months, and the prices of a chest spiral CT, bone scans, and MRI were obtained from our previous study.^[13] Prices of brain CT, chest roentgenographs, FDG PET-CT, and bronchoscopy were derived from the public network of local prices.^[14] The medical costs of the physical examination, operative treatment, adjuvant treatment with chemotherapy, adjuvant mediastinal radiotherapy for primary NSCLC, adjuvant WBRT, and EGFR mutation test were estimated according to case records in the local hospital and the local Chinese charges^[14]; the 95% confidence intervals (CIs) of these costs obtained through bootstrapping were evaluated using the R software (<https://www.r-project.org/>). The study of case records was received ethics approval by the ethics Committee of the Second Xiangya Hospital of Central South

University, and the informed consent was allowed by the patients for their information to be saved in the electronic health records system and used for research. Because in the study, 29 patients in the PET-CT group were tested for EGFR mutations,^[8] the price of the EGFR mutation test was multiplied by the calculated probability of 0.439 (29/66) to populate the model analysis for the PET-CT arm. The treatment cost of routine follow-up in the health state of survival after the operation was obtained from the published study.^[15]

2.3. Incremental cost-effectiveness ratio and WTP threshold

Incremental cost-effectiveness ratio (ICER) was used to confirm the cost-effectiveness of the 2 groups, which was estimated using the following formula:

$$\text{ICER} = \frac{\text{COST}_{\text{PET-CT}} - \text{COST}_{\text{CT}}}{\text{LY}_{\text{PET-CT}} - \text{LY}_{\text{CT}}}$$

where COST_{PET-CT}, COST_{CT}, LY_{PET-CT}, and LY_{CT} indicated the long-term costs and the LYs for the PET-CT and CT groups, respectively. When the calculated ICER was less than the WTP

Table 2

Base cases, ranges, and distributional assumptions of the risk or proportion derived from the retrospective study^[8].

Variables	Base case	Range*	Distribution
Risk of pulmonary metastasis			
PET-CT group	0.697	0.558/0.836	Beta
CT group	0.60	0.48/0.72	Beta
Risk of metastases for patients with extrapulmonary metastasis			
Brain	0.44	0.35/0.53	Dirichlet
Adrenal	0.24	0.19/0.29	Dirichlet
Bone and other locations	0.32 [†]	–	Dirichlet
Risk of adrenalectomy for patients with adrenal metastasis	0.688	0.550/0.826	Beta
Risk of brain metastasectomy for patients with brain metastasis	0.621	0.497/0.745	Beta
Risk of adjuvant WBRT for patients with brain metastasis	0.793	0.634/0.952	Beta
Proportion for pulmonary metastasis resection types			
Lobectomy	0.061	0.0488/0.0732	Dirichlet
Pneumonectomy	0.087	0.0696/0.1044	Dirichlet
Segment and wedge resection	0.852 [‡]	–	Dirichlet
Percentage of patients with synchronous monometastatic disease			
PET-CT group	0.727	0.582/0.872	Beta
CT group	0.722	0.578/0.866	Beta
% of patients with N1/2/3 lymph node involvement			
PET-CT group	0.364	0.291/0.437	Beta
CT group	0.464	0.371/0.557	Beta
Percentage of patients with pN2/3 in pN1/2/3	0.60	0.48/0.72	Beta
Percentage of patients with pN2/3 who received AMRT	0.36	0.29/0.43	Beta
Percentage of patients who received the EGFR mutation test in the PET-CT group	0.439	0.352/0.527	Beta

AMRT=adjuvant mediastinal radiotherapy, CT=computed tomography, EGFR=epidermal growth factor receptor, PET=positron-emission tomography, WBRT=whole-brain radiation therapy.

* All ranges were varied by ±20%.

[†] 1-0.44-0.24.

[‡] 1-0.061-0.087.

threshold, preoperative PET-CT staging was deemed to be a cost-effective scan for resected monometastatic NSCLC; otherwise, it was viewed as unfavorable in light of cost-effectiveness.

In the current evaluation, the WTP threshold (WTP_{THR}) equaled to the cost-effectiveness ratio of the CT group, as shown with the following formula:

$$WTR_{THR} = \frac{COST_{CT}}{LY_{CT}}$$

where the indications of the $COST_{CT}$ and LY_{CT} were the same as those described earlier.

2.4. Sensitivity analysis

Sensitivity analyses were conducted to assess the model robustness and the uncertainty of input parameters. The ranges and distributions of each parameter used in our analyses are listed in Tables 2 and 3; these values were derived or calculated from the published literature or public networks of local prices or were estimated using local charges in China.^[8,13–15] All risk or proportion ranges were varied by $\pm 20\%$ (Table 2). The ranges of medical costs were estimated with 95% CIs or varied by $\pm 20\%$ (Table 3). Beta distributions were chosen as the input parameters for risks and proportions, except for the risk of metastases for patients with extrapulmonary metastasis and the proportions of resection types for pulmonary metastasis, for which Dirichlet distributions were used. We used log-normal distributions for all medical costs, and fixed the discount rate in the probabilistic sensitivity analyses (PSA). A tornado diagram was used to present the results of 1-way sensitivity analyses (OSA). Scatter plot of

incremental cost-effectiveness and acceptability curves of cost-effectiveness were performed to present the PSA results.

3. Results

As shown in Figure 2, the log-logistic distributions matched the OS curves satisfactorily. The 5-year OS rates gained by the model we designed were not significantly different from those of the published study.^[8] In the designed model, the 5-year OS rates of PET-CT and CT groups were 0.526 and 0.341, respectively. According to the published study, the 5-year OS rates were 0.58 and 0.33, for the PET-CT and CT groups, respectively.^[8] These results indicate that our method for estimating the missing OS time data was a practical solution.

3.1. Base-case results

Table 4 displays the base-case results of model analyses, which revealed that preoperative PET-CT evaluation for NSCLC with resected monometastatic disease provided an additional 1.475, 2.129, and 2.412 LYs, in the time horizon of 10, 20, and 30 years, respectively; and the ICERs for the PET-CT group compared with the conventional CT group were \$1153, \$1393, and \$1430 per LY, separately, all of which were less than the corresponding WTP threshold (cost-effectiveness ratio of the CT group, equaled to \$5714, \$4842, and \$4495, respectively).

3.2. One-way sensitivity analyses

To assess the uncertainty around the parameters, a series of 1-way sensitivity analyses were performed, and the results were shown in the tornado diagram (Fig. 3). The 2 most sensitive

Table 3
Base cases, ranges and distributional assumptions of the costs (\$) and discount rates.

Variables	Base case	Range	Basis of variables	Distribution
Imaging examinations				
¹⁸ F-FDG PET-CT ^[14]	1198	958.4/1437.6	$\pm 20\%$	Lognormal
Chest roentgenographs ^[14]	17	13.6/20.4	$\pm 20\%$	Lognormal
Spiral chest CT ^[13]	96	76.8/115.2 ^a	$\pm 20\%$	Lognormal
Brain CT ^[14]	39	31.2/46.8	$\pm 20\%$	Lognormal
Liver ultrasonography ^[13]	49	39.2/58.8	$\pm 20\%$	Lognormal
Bone scans ^[13]	87	69.6/104.4	$\pm 20\%$	Lognormal
Brain MRI ^[13]	134	107.2/160.8	$\pm 20\%$	Lognormal
Bronchoscopy ^[14]	129	103/155	$\pm 20\%$	Lognormal
Physical examination*	330	311/349	95% CI [†]	Lognormal
Operative treatment				
Lobectomy*	6648	6421/6882	95% CI [†]	Lognormal
Pneumonectomy*	6234	5843/6650	95% CI [†]	Lognormal
Segment and wedge resection*	5672	5157/6284	95% CI [†]	Lognormal
Brain metastasectomy*	11271	10791/11725	95% CI [†]	Lognormal
Adrenalectomy*	7513	6869/8170	95% CI [†]	Lognormal
Adjuvant chemotherapy (per course)*	2071	1976/2167	95% CI [†]	Lognormal
Adjuvant radiotherapy				
Radiotherapy for NSCLC*	5892	5032/6856	95% CI [†]	Lognormal
WBRT*	4226	3609/4918	95% CI [†]	Lognormal
EGFR mutation test*	603	482.4/723.6	95% CI [†]	Lognormal
Routine follow-up of patients per unit ^[15]	51.5	45.0/58.4	Low–high	Lognormal
Terminal phase in last 3 months ^[13]	7372	6109/8695	Low–high	Lognormal
Discount rate, %	5	0/8	Low–high	Fixed in PSA

CI=confidence interval, EGFR=epidermal growth factor receptor, NSCLC=non-small-cell lung cancer, PET=positron-emission tomography, PSA=probabilistic sensitivity analysis, WBRT=whole-brain radiation therapy.

* Estimated according to local charges in China.

[†] Evaluated through bootstrapping with the R software.

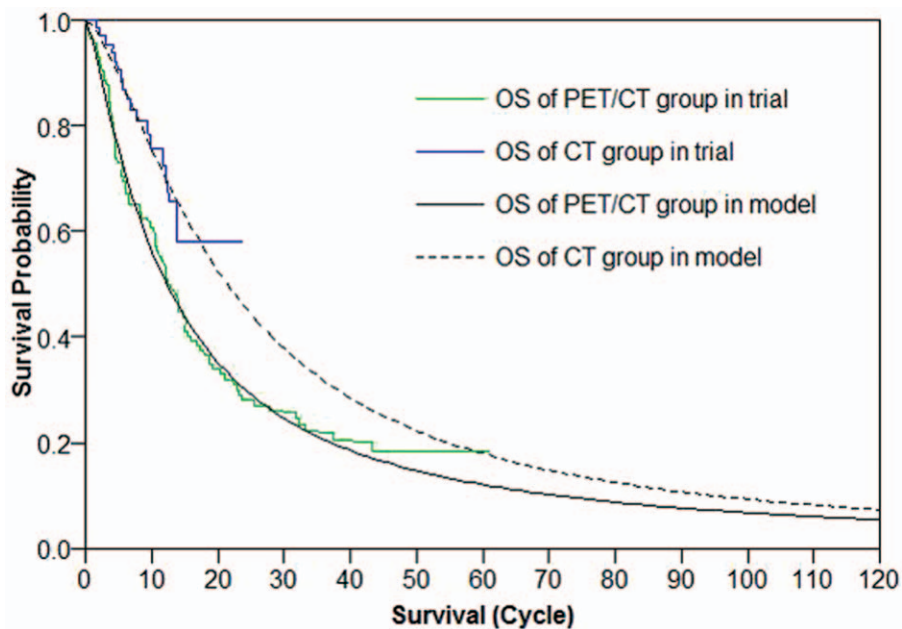


Figure 2. Overall survival (OS) curves in the patients with preoperative positron-emission tomography-computed tomography (PET-CT) scan or conventional CT scan.

variables were the proportions of patients with DFIs of synchronous monometastatic disease in the PET-CT and CT groups. The other sensitive variables included the discount rate, the treatment cost of routine follow-up, and cost of FDG PET-CT. None of the populated variables had sensitivity impact upon the ICER (all achieved ICERs were still below the value of WTP threshold, which equaled to the cost-effectiveness ratio of the CT group).

3.3. Probabilistic sensitivity analysis

The scatter plot of incremental cost-effectiveness showed that all dots of 1000 simulations were below the WTP threshold of \$4495/LY (Fig. 4). In other words, the probability of achieving cost-effectiveness with preoperative ¹⁸F-FDG PET-CT evaluation for NSCLC with resected monometastatic disease was 100%. The acceptability curves (Fig. 5) indicated that the likelihood of cost-effectiveness in the PET-CT group increased with the increasing WTP thresholds and that the sensitivity range was

approximately \$500 to \$3000/LY. At WTPs >\$3000, the probability that the PET-CT group achieved cost-effectiveness was 100%.

4. Discussion

For the cancer staging, the diagnostic accuracy and sensitivity has been significantly improved with the development of PET-CT. Due to more-reasonable treatment options after the accuracy staging, preoperative ¹⁸F-FDG PET-CT evaluation was a favorable predictor of survival for patients with resected monometastatic NSCLC.^[8] However, the economic influence of preoperative ¹⁸F-FDG PET-CT evaluation for NSCLC with resected monometastatic disease must be considered before it is widely generalized, especially in developing countries, such as China, where the population is more than 13.9 billion and the resources of healthcare system are insufficient.^[16-18]

Mathematical models are useful tools to estimate the cost-effectiveness of optional techniques or strategies.^[13,19] In the present study, a Markov model and 3 decision-tree models with a 2-parametric distribution were designed and selected to calculate the time-dependency mortality rates and to estimate the total costs and long-term effectiveness based on the clinical practice of a retrospective study.^[8] The main focus of this study from the Chinese healthcare perspective was an economic evaluation of preoperative ¹⁸F-FDG PET-CT evaluation for NSCLC with resected monometastatic disease. According to base-case results, the ICERs of the 10-, 20-, and 30-year time horizons were \$1153, \$1393, and \$1430 per LY gained, respectively, all of which were less than the corresponding WTP threshold. Both the OSA and PSA demonstrated that the models we designed were robust.

In this study, the WTP threshold we used equaled to the cost-effectiveness ratio of the CT group, which was based on an assumption that the traditional evaluation technology itself was accredited of cost-effectiveness. As a recommended strategy for resected NSCLC in the clinical guidelines, conventional CT

Table 4
Base-case analysis results for LYs, costs, WTP thresholds, and ICERs.

Arm	LYs, yrs	Cost, \$	WTP, \$/LY	ICER, \$/LY
10 yr				
PET-CT arm	5.835	26,614	-	1153
CT arm	4.360	24,913	5714	-
20 yr				
PET-CT arm	7.728	30,076	-	1393
CT arm	5.599	27,110	4842	-
30 yr				
PET-CT arm	8.681	31,567	-	1430
CT arm	6.269	28,117	4495	-

CI=confidence interval, ICER=incremental cost-effectiveness ratio, LY=life-year, LYs=life-years, PET=positron-emission tomography, WTP=willingness-to-pay.

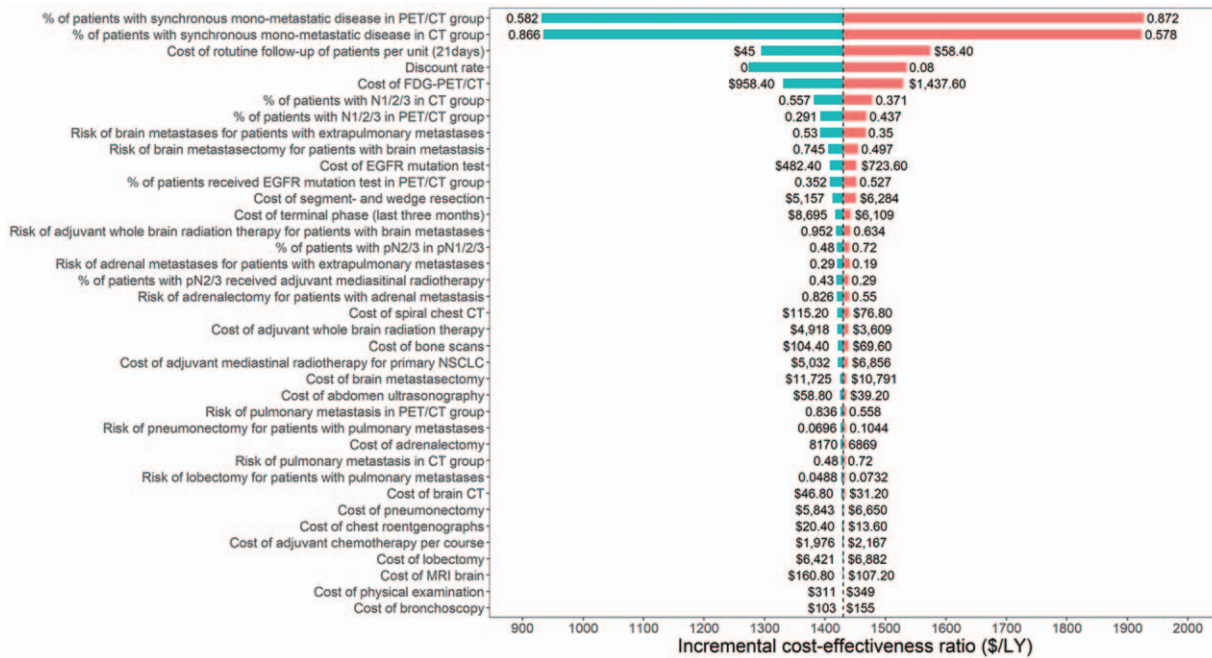


Figure 3. Tornado diagram for the results of 1-way analyses. CT=computed tomography, EGFR=epidermal growth factor receptor, ¹⁸F-FDG=¹⁸F-fluorodeoxyglucose, LY=life-year, PET=positron-emission tomography.

evaluation is a standard diagnostic work-up in Chinese clinical practice.^[9,20] Therefore, the WTP threshold applied in our analyses was reasonable for evaluation of the cost-effectiveness of a preoperative ¹⁸F-FDG PET-CT evaluation for NSCLC with resected monometastatic disease.

As far as we know, our study is the 1st assessment of cost-effectiveness for preoperative PET-CT evaluation for particular patients with resected monometastatic NSCLC, although 2 other studies have evaluated the cost-effectiveness of PET-CT for

operative or potentially operative NSCLC.^[9,21] Due to imparities in healthcare organizations and reimbursements (e.g., governments, social security funds, and insurance companies), generalizing the economic evaluation results from 1 country to another is not appropriate. Thus, the study from Wang and Huang, which was also conducted from the Chinese healthcare system perspective, is comparable to our study.^[9] The baseline analyses in their study reported that the ICER of PET-CT staging was 23,800RMB/LY (approximately \$3500/LY [year 2010 value])

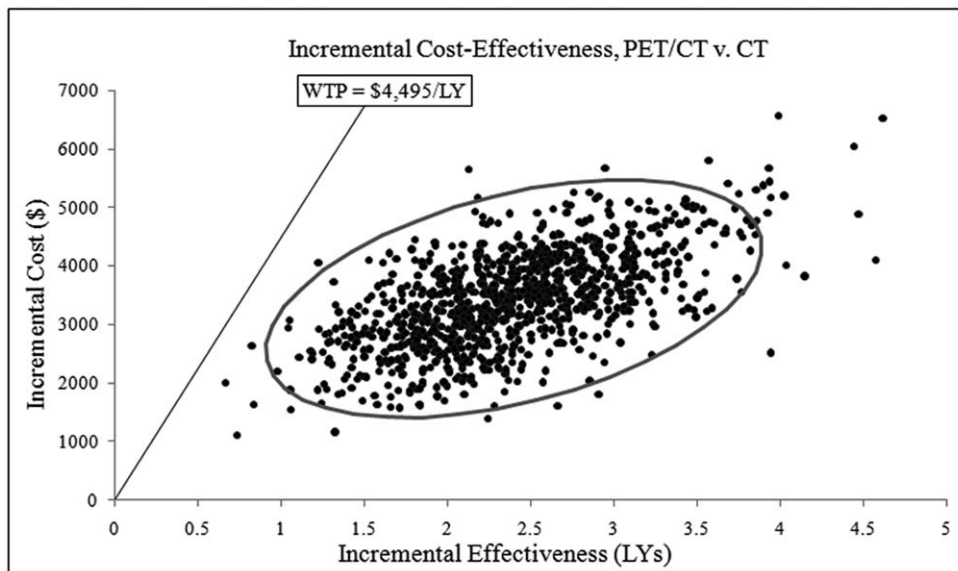


Figure 4. Scatter plot of incremental cost-effectiveness for the result of probabilistic sensitivity analysis. CT = computed tomography, LY = life-year, LYs = life-years, PET = positron-emission tomography, WTP = willingness-to-pay.

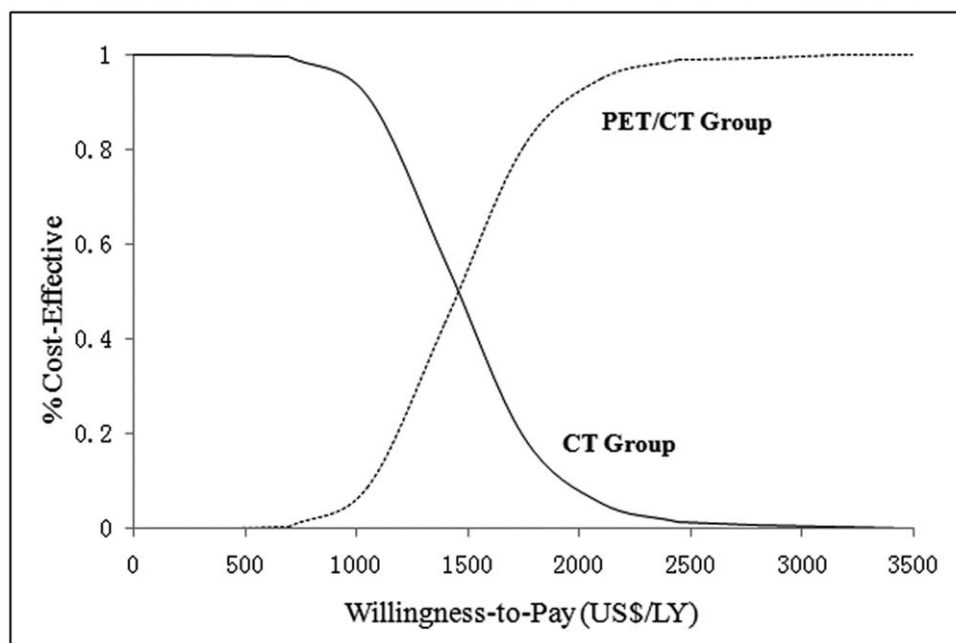


Figure 5. Acceptability curves for the positron-emission tomography-computed tomography (PET-CT) and CT groups. LY=life-year.

compared with a conventional CT scan. Obviously, this value is higher than our estimated ICERs. There are 2 possible explanations for this result. First, the evaluation we completed was aimed at patients with resected monometastatic NSCLC rather than all potentially operative NSCLC cases. Second, as a limitation stated in that article, the recent study of potentially operative NSCLC did not adequately estimate the medical costs for bronchoscopy, bone scan, brain MRI, and other programs for staging.^[9] To some extent, our study has bridged that gap, and thus generally the total costs are higher. However, according to clinical practice, some of these programs (e.g., bone scan) were only added in the CT group in our study, which resulted in lower incremental costs and ICERs.

Our study has 3 main limitations. First, although the comparison of the 5-year OS rates between the model and the study suggested that the estimation method employed in this study minimized this bias, using the selected distribution to prolong the OS datum beyond the retrospective study completion was an inevitable limitation.^[19,22] Second, because no progression-free survival data and no detailed quality of life information were available from the study, quality-adjusted LYs were not estimated in the present study. Finally, the use of high/low ranges, which originated from the practice trial, our previous study, the published paper and local charges in China, might be arbitrary. Nevertheless, all model input parameters of costs we used stemmed from the Chinese healthcare perspective, which echoed the purpose of our study.

Despite the limitations mentioned earlier, the results of our simulation are still justified. Our analysis was based on reasonable assumptions and adhered to the recommendations of *Decision Modeling For Health Economic Evaluation*.^[2,3] Nevertheless, a series of sensitivity analyses were conducted to assess the uncertainty of the input parameters, and revealed that the models we established were robust. In addition, as the 1st economic evaluation of preoperative PET-CT evaluation for

patients with resected monometastatic NSCLC, we believe that our study represents the common clinical conditions of resected monometastatic NSCLC and provides a feasible method for further economic analyses of PET-CT for specific groups. Our results supplied crucial information for healthcare funders and providers.

5. Conclusion

Compared with conventional CT scan, preoperative ¹⁸F-FDG PET-CT evaluation for patients with resected monometastatic NSCLC is cost-effective from the Chinese healthcare perspective. Preoperative ¹⁸F-FDG PET-CT evaluation must be popularized for patients with resected monometastatic NSCLC.

Acknowledgment

The authors thank Ping Chen, Xi Chen, and Changming Yu for their help in guiding the data collection.

Author contributions

Conceptualization: Yunhua Wang.

Data curation: Xiaohui Zeng.

Funding acquisition: Xiaohui Zeng, Chongqing Tan.

Investigation: Chongqing Tan.

Methodology: Xiaohui Zeng.

Project administration: Liubao Peng, Yunhua Wang.

Software: Chongqing Tan.

Supervision: Liubao Peng, Yunhua Wang.

Visualization: Xiaohui Zeng, Chongqing Tan.

Writing – original draft: Xiaohui Zeng.

Writing – review & editing: Xiaohui Zeng, Yunhua Wang.

Xiaohui Zeng orcid: 0000-0001-6050-4137.

References

- [1] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin* 2019;69:7–34.
- [2] Fehrenbach U, Kahn J, Boning G, et al. Spectral CT and its specific values in the staging of patients with non-small cell lung cancer: technical possibilities and clinical impact. *Clin Radiol* 2019;74:456–66.
- [3] Suga JM, Nguyen DV, Mohammed SM, et al. Racial disparities on the use of invasive and noninvasive staging in patients with non-small cell lung cancer. *J Thorac Oncol* 2010;5:1772–8.
- [4] National Comprehensive Cancer Network. Non-small cell lung cancer (version 5.2019). Available at <https://www.nccn.org>. Accessed July 20, 2019.
- [5] McCann J. PET scans approved for detecting metastatic non-small-cell lung cancer. *J Natl Cancer Inst* 1998;90:94–6.
- [6] Silvestri GA, Gonzalez AV, Jantz MA, et al. Methods for staging non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2013;143:e211S–50S.
- [7] Ambrosini V, Nicolini S, Caroli P, et al. PET/CT imaging in different types of lung cancer: an overview. *Eur J Radiol* 2012;81:988–1001.
- [8] Tönnies S, Tönnies M, Kollmeier J, et al. Impact of preoperative 18F-FDG PET/CT on survival of resected mono-metastatic non-small cell lung cancer. *Lung Cancer* 2016;93:28–34.
- [9] Wang YT, Huang G. Is FDG PET/CT cost-effective for pre-operation staging of potentially operative non-small cell lung cancer? – from Chinese healthcare system perspective. *Eur J of Radiol* 2012;81:903–9.
- [10] Han Y, Xiao H, Zhou Z, et al. Cost-effectiveness analysis of strategies introducing integrated 18F-FDG PET/CT into the mediastinal lymph node staging of non-small-cell lung cancer. *Nucl Med Comm* 2015; 36:234–41.
- [11] Cao JQ, Rodrigues GB, Louie AV, et al. Systematic review of the cost-effectiveness of positron-emission tomography in staging of non-small-cell lung cancer and management of solitary pulmonary nodules. *Clin Lung Cancer* 2012;13:161–70.
- [12] Hou C, Siva S, Haas M, et al. Cost-effectiveness of post-therapy pet and telephone interview in the clinical follow-up of patients treated with locally advanced cervical cancer. *Value Health* 2014;17:A736–7.
- [13] Zeng XH, Karnon J, Wang SY, et al. The cost of treating advanced non-small cell lung cancer: estimates from the Chinese experience. *PLoS One* 2012;7:e48432.
- [14] Development and Reform Commission of Hunan Province [in Chinese]. Available at <http://www.hnfgw.gov.cn/>. Accessed July 20, 2019
- [15] Wu B, Chen H, Shen J, et al. Cost-effectiveness of adding rh-endostatin to first-line chemotherapy in patients with advanced non-small-cell lung cancer in China. *Clin Ther* 2011;33:1446–55.
- [16] Babar ZU, Scahill S. Is there a role for pharmacoeconomics in developing countries? *Pharmacoeconomics* 2010;28:1069–74.
- [17] National Bureau of Statistics of China. China statistical year book 2018. Available at <http://www.stats.gov.cn/tjsj/ndsj/2018/indexeh.htm>. Accessed July 20, 2019
- [18] Shi J, Yao Y, Liu G. Modeling individual health care expenditures in China: evidence to assist payment reform in public insurance. *Health Econ* 2018;27:1945–62.
- [19] Zhang Y, Zeng X, Deng H, et al. Cost-effectiveness analysis of adding palbociclib as a second-line endocrine therapy for HR(+)/HER2(-) metastatic breast cancer from the US and Chinese perspectives. *Clin Ther* 2019;41:1175–85.
- [20] National Comprehensive Cancer Network. The Chinese edition of NCCN clinical practice guidelines in oncology: non-small-cell lung cancer guideline (version 7.2015) [in Chinese]. Available at <http://www.nccnchina.org/nccn-guidelines-china.aspx>. Accessed July 20, 2019
- [21] Søgaard R, Fischer BM, Mortensen J, et al. Preoperative staging of lung cancer with PET/CT: cost-effectiveness evaluation alongside a randomized controlled trial. *Eur J Nucl Med Mol Imaging* 2011;38:802–9.
- [22] Wan X, Zhang Y, Tan C, et al. First-line nivolumab plus ipilimumab vs sunitinib for metastatic renal cell carcinoma: a cost-effectiveness analysis. *JAMA Oncol* 2019;5:491–6.
- [23] Briggs A, Claxton K, Sculpher M. *Decision Modelling for Health Economic Evaluation*. New York: Oxford University Press Inc; 2006.