Original Article

Cost and effectiveness of video-assisted thoracoscopic surgery for clinical stage I non-small cell lung cancer: a population-based analysis

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Background: Video-assisted thoracoscopic surgery (VATS) is a minimally invasive alternative to conventional surgery (CS). We aimed to estimate the short-term cost-effectiveness of VATS *vs.* CS for clinical stage I non-small cell lung cancer (NSCLC-c-stage-I) patients from the payer's perspective (National Health Insurance).

Methods: We identified NSCLC-c-stage-I patients diagnosed and received surgery within 2007-2009 through a comprehensive population-based database containing cancer and death registries, and reimbursement data. The duration of interest was 1 year. We included potential confounding covariables through literature searching and our own experience, and used a propensity score to construct a 1:1 population for adjustment.

Results: Our study population constituted 966 patients. The mean hospital stay [days, standard deviation (SD)] were 14.4 [7] and 16.1 (7.7) for VATS and CS respectively (P=0.002). The mean cost (2013 USD) and survival (year) was $22,316 *vs.* $21,976 and 0.98 *vs.* 0.974 for VATS *vs.* CS. The probability for VATS to be cost-effective (i.e., positive net benefit) was 0.49 & 0.56 at willingness-to-pay (WTP) 50,000 & 100,000 USD/life-year, respectively.

Conclusions: We provide the first empirical evidence that when compared to CS, VATS was potentially cost-effective in the short term (1 year) within the common WTP levels in Taiwan.

Keywords: Cost-effectiveness analysis; video-assisted thoracoscopic surgery (VATS); clinical stage I non-small cell lung cancer (NSCLC-c-stage-I)

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Introduction

Surgery is the cornerstone of curative treatment for early stage non-small cell lung cancer (NSCLC) (1). Lobectomy is the usual approach but the role of sublobectomy is also debated (1,2). Video-assisted thoracoscopic surgery (VATS) is a minimally invasive alternative to open thoracotomy and may lead to better survival outcome (1,3). Due to its minimally invasive nature, VATS is also associated with less surgical trauma, less use of narcotics, and fewer complications (4,5).

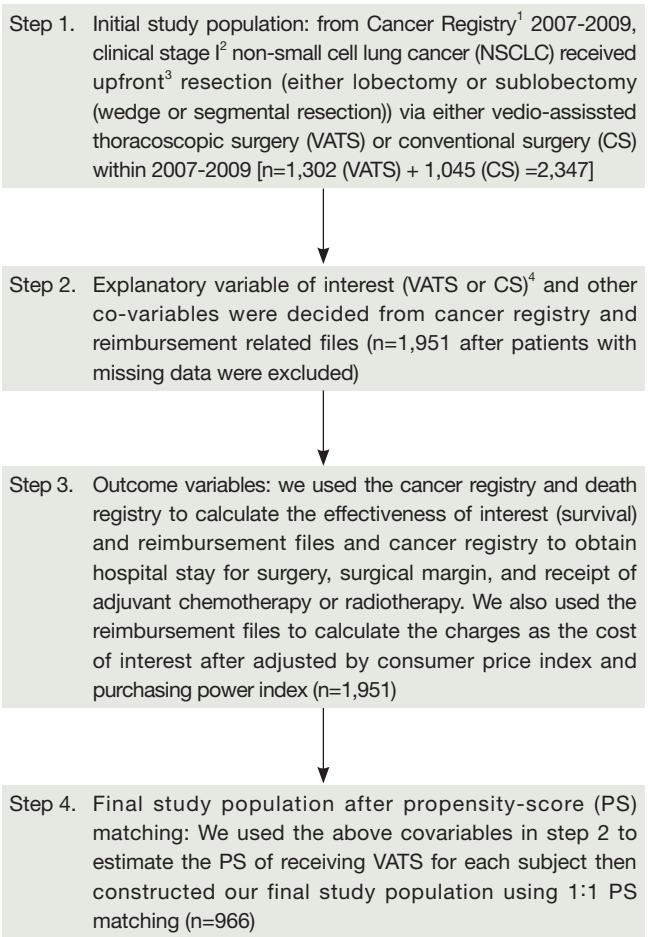

Figure 1 Study flow chart. [1], we only included those treated (class 1-2) by any single institution to ensure data consistency; [2], 6thAmerican Joint Committee on Cancer staging; [3], those who received neoadjuvant therapy were excluded; [4], for each institute, we excluded those cases received CS before 1st VATS case to ensure accessibility to VATS.

However, VATS is associated with a higher initial cost and may be overall more costly (6,7). Cost-effectiveness is an important issue nowadays (8). In an era when affordable cancer care is a worldwide issue, the cost-effectiveness of VATS should also be considered because this consideration will possibly affect patients' access to cancer treatment (9).

To our knowledge, the cost-effectiveness (regarding cost per life year saved) of VATS has not been reported in the literature except our previous preliminary report (10). Therefore, the aim of our study is to compare the cost and effectiveness of VATS *vs.* conventional surgery (CS) for clinical stage I NSCLC via this updated population-based propensity score (PS) matched analysis.

Materials and methods

Data source

The Collaboration Center of Health Information Application (CCHIA) database is a set of databases with complete information regarding cancer and death registration, and reimbursement data from National Health Insurance (NHI) for the whole Taiwanese population. The cancer registry within CCHIA provides details regarding individual demographics, tumor histology, cancer primary sites, stage of disease, and primary surgical, radiation, and systemic therapy. NHI is a single compulsory payer with universal coverage in Taiwan and provides a comprehensive services package "All medically necessary services are covered. The package covers inpatient, outpatient, dental services, traditional Chinese medicine, and maintains a very long list of nearly 20,000 items of prescription drugs". NHI's reimbursement data files at the CCHIA provide information regarding the income of the insured, details of treatment received, and the characteristics of health care providers.

Study population and study design

Our study flow chart is depicted in *Figure 1*. Our target populations were clinical stage I NSCLC patients received either VATS or CS within 2007-2009. In brief, the date of admission for surgery was used as the index date. We set the duration of interest as one year within the index date. We then decided the explanatory variable of interest (VATS *vs.* CS) based on the reimbursement coding. We also collected other covariables for the adjustment of potential non-randomized treatment selection and cost and effectiveness data from the CCHIA (see next sub-section "other explanatory covariables"). Finally, we constructed a PS matched sample based on PS estimated through the above covariables to compare the cost and effectiveness of VATS *vs.* CS within the duration of interest. In PS analysis, we modeled the use of VATS (*vs.* CS) as the dependent variable and the covariables as independent variables, and used non-conditional logistic regression to model the probability of receiving VATS as commonly used in the literatures (11,12). We then used the logit of the probability as the PS, as commonly used in the literature (12). This study had been approved by Research Ethics Committee in our institute [CMUH103-REC-005].

Other explanatory covariables

Firstly, we searched the literature regarding potential factors

that might influence the cost of VATS. We used the following balanced search filters regarding costs or economics in the PubMed "['costs and cost analysis' (MeSH) OR costs (Title/Abstract) OR cost effective* (Title/Abstract)] OR [cost* (Title/Abstract) OR 'costs and cost analysis' (MeSH:noexp) OR cost benefit analysis* (Title/Abstract) OR cost-benefit analysis (MeSH) OR health care costs (MeSH:noexp)]" as in the literatures (13,14). We combined the above keywords with "(cancer) AND (VATS OR thoracoscopic)" and found that social economic status (SES), surgeons' case load, and tumor location might influence the cost after VATS (15-17). Secondly, we collected other factors that were not reported in the literature but that might affect the cost of VATS based on our clinical and research experiences. In this regard, we also included patient demographic factors (age, gender, and residency region), patient characteristics (comorbidity), disease characteristics (histology and pathological stage), treatment pattern (surgical type), and health service provider characteristics (treating hospital preference) based on our clinical experiences and prior NHI and CCHIA related studies (18-24). Age was classified as ≥65 years old or not. Patient residency was classified as northern Taiwan or elsewhere. SES was classified as high (income greater than minimal wage) or not. Histology was classified as adenocarcinoma or others. Pathological stage was classified as early or advanced (beyond stage I). Tumor location was classified as lower *vs.* upper/middle. Surgical type was classified as lobectomy or sublobectomy. Surgeons' case load was classified as high *vs.* low (split at the median in our study sample). Treating hospital preference was classified as high (at least half of their patients were treated by VATS) or low.

Cost and effectiveness assessment

We included the following issues in effectiveness assessment: hospital stay for surgery, pathological stage, surgical margin, receipt of adjuvant chemotherapy or radiotherapy, survival within duration of interest, and overall survival. We obtained survival status according to the death registry, hospital stay from reimbursement files, and the other issues from cancer registry. The cost and cost-effectiveness were conducted from a Taiwan NHI perspective (i.e., charges to NHI). The cost was limited to the duration of interest then converted to 2013 USD by purchasing the power parity and consumer price indexes. The cost within our duration of interest was further broken down into four quarters (i.e., every 3 months) to illustrate the cost in different disease phrases. We then applied various thresholds of willingness-to-pay (WTP) to calculate the net benefit (NB) when VATS was compared to CS by applying the following equation (25):

NB = effectiveness * WTP – cost.

WTP refers to the amount of money the payer is willing to pay for an outcome. The commonly cited WTP threshold [50,000-100,000 USD/life year (LY)] means that the payer is generally willing to pay 50,000-100,000 USD to gain a year of life and this was considered a threshold to decide whether an intervention was cost-effective or not (26,27). This WTP range also covers the World Health Organization (WHO) criteria (3 times gross domestic product per capita) regarding cost-effectiveness in Taiwan [around 58,042 (19,347.329*3)] (28). When the incremental NB (INB) of an intervention is positive at a specific WTP level, this means that this intervention is associated with a positive net monetary gain, so it is also cost-effective at this specific WTP level.

Statistical analysis

Tabulation and standardized difference were used to assess the balance of covariates between PS-matched groups. We used a stratified log-rank test to compare the survival of VATS versus CS for the entire follow-up period (censored on 1 January 2012) (12). Other outcomes between VATS and CS were compared with McNemar test or paired *t*-test (12). We used the paired *t*-test to evaluate the statistical significance of the INB, and then constructed the cost-effectiveness acceptability curve (CEAcC) (25). SAS 9.3 (SAS Institute, Cary, NC, USA) was used for all the analysis.

Results

Identification of the study cases (Figure 1, Table 1)

As revealed in *Figure 1*, 2,347 clinical stage I NSCLC patients treated with either VATS or CS were identified as the initial study population. After exclusion of those with missing data and matching by PS, the final study population included 966 patients. The characteristics of these patients are described in *Table 1*. A good balance of covariables and small standardized differences (<0.1) were seen for all covariables.

Cost and effectiveness

The mean hospital stay (in days, with standard deviation (SD)) were 14.4 [7] and 16.1 (7.7) for VATS and CS respectively (P=0.002). The distribution regarding

Table 1 Patient characteristics of the propensity-score matched final study population

Covariables	VATS number	(%, rounded)	CS number	(%, rounded)	Standardized difference (rounded)
Age					0.01
<65 y/o	233	[48]	235	[49]	
≥65 y/o	250	[52]	248	[51]	
Gender					0.06
Male	254	[53]	240	[50]	
Female	229	[47]	243	[50]	
Residency					0.02
North	241	[50]	245	[51]	
Non-north	242	[50]	238	[49]	
Social-economic status					0.01
High	253	[52]	251	[52]	
Low	230	[48]	232	[48]	
Comorbidity					0.03
Without	170	[35]	176	[36]	
With	313	[65]	307	[64]	
Histology					0.05
Adenocarcinoma	365	[76]	375	[78]	
Non-adenocarcinoma	118	[24]	108	[22]	
Stage					0.03
Early	407	[84]	401	[83]	
Advanced	76	[16]	82	[17]	
Location					0.01
Upper/middle	316	[65]	318	[66]	
Lower	167	[35]	165	[34]	
Surgery					0.07
Lobectomy	424	[88]	412	[85]	
Sublobectomy	59	[12]	71	[15]	
Hospital preference					0.05
High	243	[50]	231	[48]	
Low	240	[50]	252	[52]	
Surgeon case load					0.06
High	241	[50]	255	[53]	
Low	242	[50]	228	[47]	

CS, conventional surgery; VATS, video-assisted thoracoscopic surgery; y/o, years old.

surgical margin and receipt of adjuvant chemotherapy or radiotherapy were similar between VATS and CS without statistical significance. For the entire follow-up period, the survival rate of VATS was better than CS (2 years: 92% *vs.* 90%, P=0.8), but was not of statistical significance. The Kaplan-Meier survival curve is depicted in *Figure 2*. The mean cost (2013 USD) and survival (year) within one year after surgery were higher for VATS versus CS ($22,316 *vs.* $21,976; 0.98 *vs.* 0.974). Given the above incremental cost $340 (=22,316 – 21,976) and incremental effectiveness 0.06 (=0.98 – 0.974) LY, the net benefit if WTP equals $50,000/LY would be negative $40 (=0.006*50,000 – 340) but positive $260 (=0.006*100,000 – 340) if WTP equals $100,000/LY. The incremental cost-effectiveness ratio (ICER) when VATS was compared to CS was 56,667 (=340/0.006) (USD/LY). The above results were also tabulated in *Table 2*. Although VATS is associated with higher initial cost (in the 1st quarter after surgery), the difference

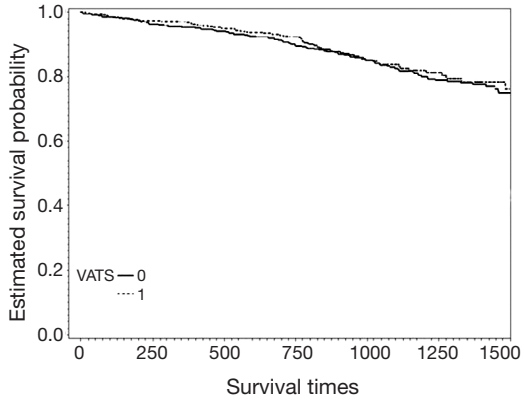

Figure 2 Kaplan-Meier survival curve (in days). Video-assisted thoracoscopic surgery (VATS =1 in dotted line) *vs.* conventional surgery (VATS =0 in solid line); P=0.8.

Table 2 Cost-effectiveness analysis results*

Outcomes	VATS	CS
Cost (2013 USD)	22,316	21,976
Effectiveness (lift-year)	0.980	0.974
Incremental cost	340	Reference
Incremental effectiveness	0.006	Reference
ICER	56,667	Reference
INB (at WTP 50,000)	–40	Reference
INB (at WTP 100,000)	260	Reference

CS, conventional surgery; ICER, incremental cost-effectiveness ratio; INB, incremental net benefit; VATS, video-assisted thoracoscopic surgery; WTP, willingness-to-pay (unit: USD/life-year); *, cost round at integral; life-year rounded at 3rd decimal.

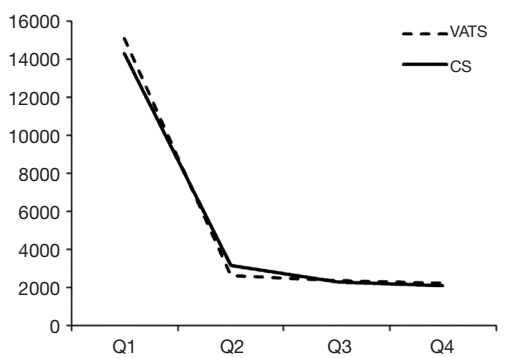

Figure 3 Time trend of cost. Vertical axis: 2013 USD; transverse axis: 1st-4th quarter after surgery; video-assisted thoracoscopic surgery (in dotted line) *vs.* conventional surgery (in solid line).

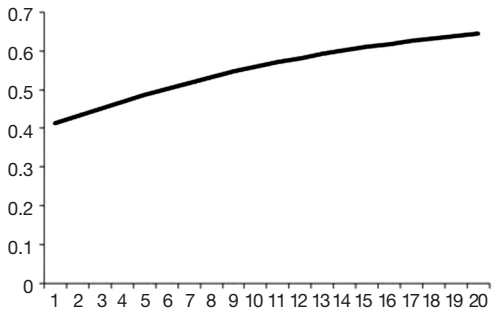

Figure 4 Cost-effectiveness acceptability curve. Vertical axis: probability of video-assisted thoracoscopic surgery to be cost-effective; Transverse axis: willingness-to-pay (unit: 10,000 US dollars/life-year).

is not obvious in the end of follow-up (*Figure 3*). When we changed the WTP level, the corresponding probability of VATS to be cost-effective (i.e., positive net benefit) as estimated by paired *t*-test was shown in *Figure 4*. For example, the probability was 0.49 & 0.56 at WTP 50,000 & 100,000, respectively.

Discussion

In this population-based propensity-score matched cost-effectiveness analysis, we provide the first empirical evidence that VATS is potentially cost-effective versus CS in the short-term (1 year) within the common WTP levels from a payer's perspective since our estimated ICER ($56,667 USD/LY) was below either the common criteria ($100,000 USD/LY) or the WHO criteria ($58,042 USD/LY).

Our results were compatible with the literatures in that VATS provides better survival (1,3). The higher cost for VATS might partly be due to the higher operation fee for VATS *vs.* CS (dereferences in operation fee: $399 for VATS lobectomy *vs.* CS lobectomy whereas $224 for VATS sublobectomy *vs.* CS sublobectomy, both in USD 2013). Our estimated cost within 1 year after surgery was also higher for VATS as ever reported by other study (8), although conflict results had also been reported (7,15,29-31). Our updated estimates were also in line with our previous preliminary estimates but were more representative now given the much larger sample size (10).

Although the interpretation of our results is that VATS is potentially cost-effective within the common WTP levels in the short term, we could not specify to specific VATS due to data limitation. For example, we could not define whether VATS was complete or assisted (32). There were also some

other limitations in our study. Firstly, there is always concern in potential unobserved confounding bias although we had performed comprehensive literature searching and used our own clinical and research experiences to include potential confounders we suspected. Secondly, although the long term outcome of early stage NSCLC was quite good, whether our duration of interest (1 year) was long enough to fully capture the cost-effectiveness of VATS versus CS might deserve further studies although longer follow-up might make VATS more favorable given the slightly improved survival and similar cost in the end of our follow-up period (as revealed in *Figures 2,3*).

Conclusions

In this population-based propensity-score matched cost-effectiveness analysis, we provide the first empirical evidence that when compared to CS, VATS was potentially cost-effective in the short term (1 year) within the common willingness-to-pay levels from a payer's perspective in Taiwan. Further studies would be helpful to see the long term results and whether the same results could be obtained in other health care systems.

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Disclosure: The authors declare no conflict of interest.

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