長庚大學醫學院臨床醫學研究所
畢業生研究成果

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畢業論文題目（中文）：嚴重異質性肺氣腫患者使用Endobronchial valve和Intrabronchial valve的系統性回顧、網路統合分析與成本效益分析

畢業論文題目（英文）：Systematic Review, Network Meta-analysis, and Cost-effectiveness Analysis of Endobronchial Valve and Intrabronchial Valve in Patients with Severe Heterogeneous Emphysema

Background

Emphysema is one of the subtypes of chronic obstructive pulmonary disease (COPD). It results in hyperinflation because of destruction in the alveolar wall and bronchioles. Recently, the endobronchial valve (EBV) and intrabronchial valve (IBV) have been developed for relieving hyperinflation. However, these two valves have not been introduced to Taiwan. In this study, we conducted a systematic review and network meta-analysis (SR/NMA) to evaluate the efficacy and safety of both valves in COPD with severe heterogeneous emphysema and absence of collateral ventilation (CV). Microsimulation model was adopted to evaluate the cost and effectiveness of EBV, IBV, and SoC from the perspective of National Health Insurance Administration (NHIA) in Taiwan.

Methods

We searched PubMed and Embase in January 2022 for RCTs in COPD with severe heterogeneous emphysema and absence of CV. The primary outcome was the forced expiratory volume in one second in liter (FEV_1 in liter) at 3, 6, and 12 months. We also evaluated risk ratio (RR) of pneumothorax (PTX) and acute exacerbation of COPD (AECOPD) within 6 months after receiving valves. The R package “netmeta” was used to conduct NMA under random-effects model. In addition, CEA was conducted from the NHIA’s perspective to evaluate the cost and effectiveness of EBV, IBV and SoC by using microsimulation model. Subjects were COPD patients with severe heterogeneous emphysema and absence of CV. Information of treatment effects, utilities, and clinical events was obtained from our SR/NMA and clinical studies. Costs were obtained from the National Health Insurance (NHI) claims data and studies in other countries. The cycle length was 6 months, and the time horizons were 5 and 10 years. The outcome was quality-adjusted life years (QALYs) shown in the incremental cost-effectiveness ratio (ICER). A discount rate of 3% was applied to both costs and effectiveness.

Results

We included five trials of the EBV and IBV. Compared with the SoC, from 3 to 12 months after receiving valves, the EBV could improve in FEV_1 of 0.106 L to 0.230 L, the IBV improved 0.099 to 0.130 L. At 6-month, the EBV had the better efficacy than the IBV [MD 0.124 L (95% CI, 0.026 to 0.222)]. Compared with the SoC, RR of PTX in the EBV was 9.75 (95% CI, 2.11 to 44.93); the IBV was 5.12 (95% CI, 1.63 to 16.08). There was no difference between both valves. For RR of AECOPD, there was no difference between these treatments. In CEA, compared with the SoC at 5-year, the incremental costs of EBV were NT 347,280, and incremental QALYs were 0.28. The ICER was NT 1,232,658.43 per QALY. At 10 years, incremental costs were NT 352,183, and incremental QALYs were 0.70. The ICER was 503,257.60 per QALY. IBV was dominated by EBV at both 5- and 10-year time horizon.

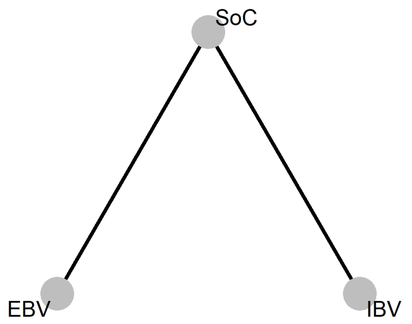

Figure 1 The network diagram

Table 1 Network meta-analysis results of FEV_1 (liter) at 3-month

EBV	-	**0.186 (0.123; 0.250)***
0.056 (-0.020; 0.132)	IBV	**0.130 (0.089; 0.172)***
0.186 (0.123; 0.250)*	**0.130 (0.089; 0.172)***	SoC

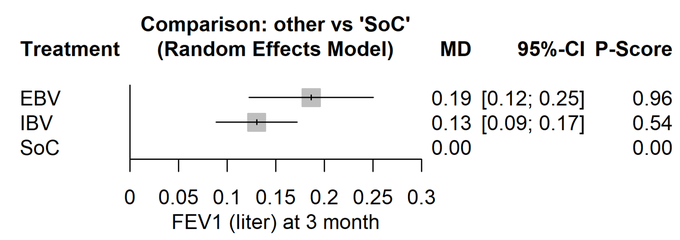

Figure 2 The forest plot for NMA of valves comparing with the SoC for FEV_1 (liter) at 3-month

Table 2 Network meta-analysis results of FEV_1 (liter) at 6-month

EBV	-	**0.230 (0.140; 0.320)***
0.124 (0.026; 0.222)*	IBV	**0.106 (0.068; 0.144)***
0.230 (0.140; 0.320)*	**0.106 (0.068; 0.144)***	SoC

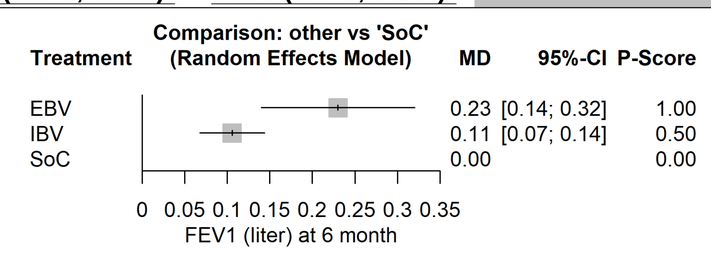

Figure 3 The forest plot for NMA of valves comparing with the SoC for FEV_1 (liter) at 6-month

Table 3 Network meta-analysis results of FEV_1 (liter) at 12-month

EBV	-	**0.106 (0.045; 0.167)***
0.007 (-0.076; 0.090)	IBV	**0.099 (0.042; 0.156)***
0.106 (0.045; 0.167)*	**0.099 (0.042; 0.156)***	SoC

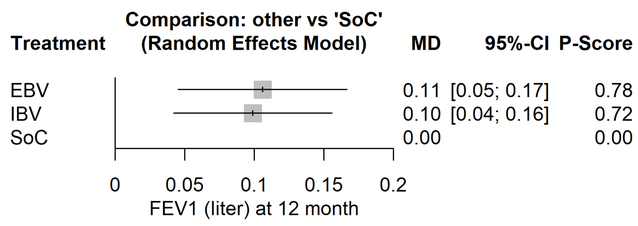

Figure 4 The forest plot for NMA of valves comparing with the SoC for FEV_1 (liter) at 12-month

Table 4 Risk ratio of PTX in 6 months after the procedure

EBV	-	**9.75 (2.11; 44.93)***
1.90 (0.28; 12.84)	IBV	**5.12 (1.63; 16.08)***
9.75 (2.11; 44.93)*	**5.12 (1.63; 16.08)***	SoC

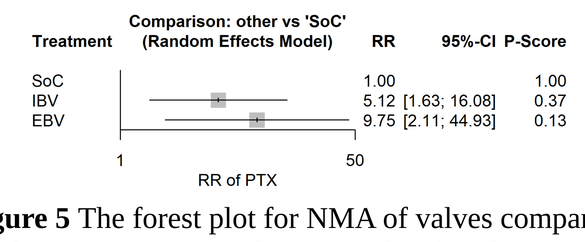

Figure 5 The forest plot for NMA of valves comparing with the SoC for PTX within 6 months after the procedure

Table 5 Risk ratio of AECOPD in 6 months after the procedure

EBV	-	1.13 (0.94; 1.36)
0.69 (0.35; 1.38)	IBV	1.64 (0.84; 3.20)
1.13 (0.94; 1.36)	1.64 (0.84; 3.20)	SoC

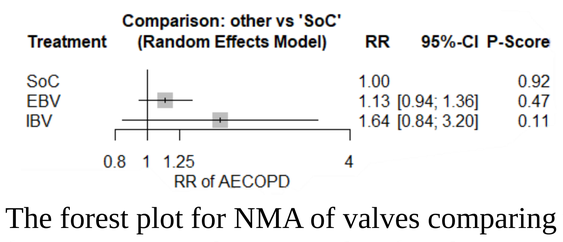

Figure 6 The forest plot for NMA of valves comparing with the SoC for AECOPD within 6 months after the procedure

Table 6 Base case results

Treatment	Life years	Life expectancy	Total costs	Incremental cost	Total QALYs	Incremental QALYs	ICER
5-year							
SoC	3.16	3.72	$177,450		2.36		
EBV	3.32	3.92	$524,730	$347,280	2.64	0.28	$1,232,658.43
IBV	3.26	3.85	$565,020	$40,290	2.57	-0.07	Dominated
10-year							
SoC	4.32	5.09	$251,681		3.17		
EBV	4.85	5.76	$603,864	$352,183	3.87	0.70	$503,257.60
IBV	4.74	5.62	$642,379	$38,514	3.74	-0.13	Dominated

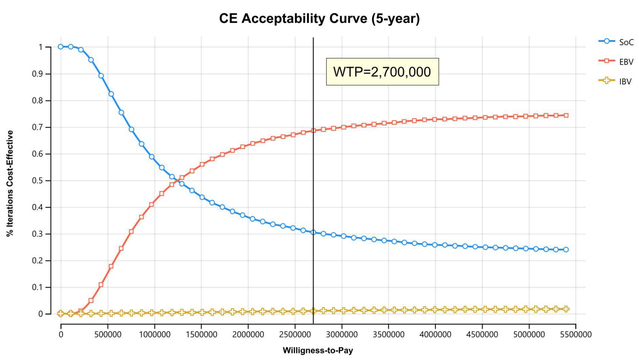

Figure 7 Cost-effectiveness acceptability curve at 5-year time horizon

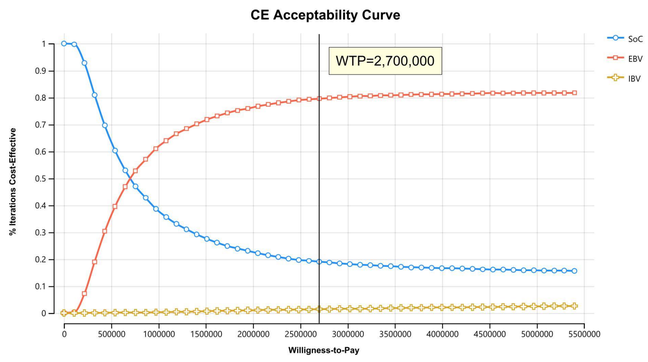

Figure 8 Cost-effectiveness acceptability curve at 10-year time horizon

Conclusion

Despite the limitation of few included studies, we concluded that the EBV and IBV could improve lung function. However, PTX should be noticed after the procedure. From the NHIA’s perspective, EBV dominated IBV, and EBV was cost-effective compared to SoC at the threshold of three GDPs.