Endobronchial Valve as Treatment of Emphysema Compared with Standard Medical Care: an Evidence-based Case Report

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ABSTRAK

Tujuan: *menilai efektivitas penggunaan endobronchial valve sebagai tatalaksana pasien dengan emfisema dibandingkan dengan tatalaksana medikal.* ***Metode:*** *pencarian kepustakaan mengenai perbandingan pengunaan endobronchial valve dan tatalaksana medikal pada emfisema di PubMed database. Kualitas dari kepustakaan yang didapat dinilai dengan menggunakan daftar tilik dari Center of Evidence-Based Medicine, University of Oxford.* ***Hasil:*** *dua randomized controlled trial (RCT) didapatkan dari pencarian kepustakaan. Didapatkan bahwa terapi dengan endobronchial valve meningkatkan kualitas pasien emfisema derajat sedang hingga sangat berat secara bermakna dibandingkan dengan tatalaksana medikal. Akan tetapi, peningkatan bermakna tersebut terjadi pada pasien emfisema dengan heterogenitas tinggi, fissura interlobar lengkap, dan ketiadaan ventilasi kolateral.* ***Kesimpulan:*** *endobronchial valve merupakan terapi yang lebih efektif pada pasien emfisema dengan keheterogenan tinggi, fissura interlobar lengkap, dan ketiadaan ventilasi kolateral. Pemeriksaan dengan High Resolution CT-scan (HRCT) harus dilakukan untuk memutuskan apakah terapi dengan endobronchial valve cocok untuk dilakukan pada seorang pasien dengan emfisema.*

Kata kunci: *endobronchial valve, talalaksana medikal, emfisema.*

ABSTRACT

Aim: *to determine the effectiveness of endobronchial valve placement as treatment of emphysema compared to medical care.* ***Methods:*** *literature searching regarding comparison of endobronchial valve and medical care as treatment of emphysema on PubMed database. The quality of the literatures found was appraised by using critical appraisal sheet from Center of Evidence-Based Medicine, University of Oxford.* ***Results:*** *two randomized controlled trials (RCT) were obtained from literature searching. It was revealed that endobronchial valve placement improved quality of patients with moderate to very severe as compared to medical treatment significantly. However, these significant improvements occurred in patients with high heterogeneity emphysema, complete interlobar fissure, and absence of collateral ventilation.* ***Conclusion:*** *endobronchial valve placement was a more effective treatment in patients with high heterogeneity emphysema, complete interlobar fissure, and absence of collateral ventilation. Assessment by using High Resolution CT-scan (HRCT) must be conducted prior to valve placement to determine suitability of this approach in emphysema patients.*

Keywords: *endobronchial valve, medical care, emphysema.*

INTRODUCTION

Emphysema one of the manifestation of chronic obstructive pulmonary disease (COPD) characterized by airway walls destruction causing increased size of distal airways further than terminal bronchioles, leads it to parenchymal destruction.[1,2] COPD has become a global burden with about 65 million people predicted to suffer from moderate to severe COPD.[3] Furthermore, this condition also accounted for about 3 million deaths in 2005 worldwide.[3] In Indonesia, it was estimated that the prevalence of COPD was 3.7% according to Result of National Basic Health Research (RISKESDAS) 2013.[4]

Medical care of emphysema involves use of bronchodilators, anti-cholinergics, corticosteroids, or a combination of bronchodilator-corticosteroid.[1] Another option directed for severe emphysema treatment is endobronchial valve placement.[1] Endobronchial valve is a one-way valve placed at the targeted lobe through a bronchoscope.[5] This one-way valve prevents inspired air entering while allowing exhaled air to pass leading to atelectasis in targeted lobe.[5]

CLINICAL QUESTION

A 56 years old man was diagnosed with emphysema 4 years ago. He had two exacerbations this year which occurred two and nine months ago. His last post-bronchodilator spirometry results after the second exacerbation were FEV1/FVC 55% and FEV1 35% of predicted value. Regular medications he received consisted of combination of inhaled long β2 agonist + corticosteroid (salmeterol 50 μg + fluticasone propionate 500 μg) twice a day and long acting anticholinergic (tiotropium bromide 18 μg) once a day. We aim to determine whether endobronchial valve placement is more effective than medical care and suitability of this approach for this patient.

In patients with emphysema, does endobronchial valve placement result in better outcomes compared to medical care?

METHODS

The eligible studies were searched from PubMed database on 26th December 2015. The limitation criteria of literature searching were: (1) Therapy studies regarding comparison of endobronchial valve and medical care exclusively in patients with emphysema, (2) Exclusion of review articles, (3) Studies published in English or Indonesian. The keywords used for literature searching were: endobronchial valve, medical care, and emphysema. Literature searching was conducted through combination of these three keywords which used Boolean operator "AND". The selected studies were then appraised using Center of Evidence-Based Medicine, University of Oxford critical appraisal sheet for therapy study or systematic review to check their validity.[6,7]

RESULTS

From the literature searching, two studies were found (**Figure 1**). These eligible studies were critically appraised using Center of Evidence-Based Medicine, University of Oxford critical appraisal sheet for therapy study (**Table 1**).[6] The summary of each study was described in **Table 2**.

In the study conducted by Sciurba et al[8], standard medical care was defined according to the Endobronchial Valve for Emphysema Palliation Trial (VENT) design.[9-10] In VENT, standard medical care was based on GOLD 2001 guidelines.[11] Study conducted by Klooster et al (2015) defined standard medical care according to GOLD 2006 guideline.[9,12]

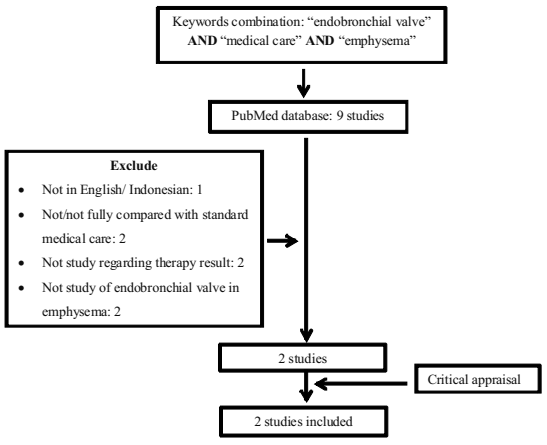

Figure 1. Flow chart of literature searching process.

DISCUSSION

From literature searching, only two studies compared the treatment of emphysema using endobronchial valve to medical care were found. These two studies were randomized controlled

Table 1. Critical appraisal of two randomized controlled studies

Study	Year	N	Study design	Validity					Level of Evidence+
				Randomization	Similarity at trial start	Equal treatment outside allocated treatments	Intention to treat	Double Blinded	
Sciurba, et al.[8]	2010	321	RCT	+	+	+	+	-	2
Klooster, et al.[9]	2015	68	RCT	+	+	+	+	-*	2

N: number of participants; RCT: randomized controlled trial; *blinding was conducted for outcome assessors only; +: level of evidence as determined by Center of Evidence-Based Medicine, University of Oxford.[10]

Table 2. Summary of two randomized controlled trials included

Study	Patient Characteristic	Results	Complications
Sciurba, et al.[8]	Age: 40-75 years old; FEV1: 15-45% predicted value; TLC >100% predicted value; RV >150% predicted value	3.8 valves/patient were placed on average	Major adverse events in 90 days: Two deaths occurred in endobronchial valve group but not significantly different compared to medical care group (p-value=1.00)
	BMI ≤31.1 kg/m2 (male), ≤32.3 kg/m2 (female); PaCO2 <50 mmHg, PaO2 >45 mmHg; 6-minute walk test ≥140 meter.	**6 months follow up period:** Improvement of FEV1 (%): 4.3% (endobronchial valve) vs -2.5% (medical care), p-value=0.005	
	Patients with heterogeneous emphysema as revealed by HRCT.	Improvement of 6-minute walk test (meter): 9.3 meter (endobronchial valve) vs -10.7 meter (medical care), p-value=0.02	No significant difference in major adverse events such as respiratory failure, massive hemoptysis, pneumothorax >7 days, and others between endobronchial valve group and medical care group (p-value>0.05)
	No significant difference of baseline characteristics between endobronchial valve and medical care group	Improvement of FEV1 (% difference: 10.7%, p-value=0.004) and 6-min walk test (distance difference: 12 meter, ¬p-value=0.002) in patients with high heterogeneity* was significantly higher in endobronchial valve compared to medical care but not in low heterogeneity patients (% FEV1 improvement difference: 2.5%, p-value=0.38; 6-min walk test difference: -1.0 meter, p-value=0.80).	
		Improvement of in patients with complete fissure† was significantly higher in endobronchial valve compared to medical care FEV1 (% difference: 16.2%, p-value<0.001) but not in incomplete fissure patients (% difference: 2.0%, p-value=0.51)	

Table 2. Summary of two randomized controlled trials included

Study	Patient Characteristic	Results	Complications
Klooster, et al.[9]	Age >35 years old; FEV1 post-bronchodilator <60% predicted; TLC >100% predicted value; RV >150% predicted value; mMRC scale >1	4 valves/patient were placed on average	**Serious adverse events in 6 months follow up period:** One death found in endobronchial valve group but not significantly different compared to medical care group (p-value=1.00)
	Patients with complete or near complete fissure as revealed by HRCT	**6 months follow up period: Improvement of FEV1 (%):** 20.9% (endobronchial valve) vs 3.1% (medical care), p-value=0.002	
	Absence of collateral ventilation as assessed by using Chartis system (Pulmonx)	Improvement of FVC (%): 18.3% (endobronchial valve) vs 4.0% (medical care), p-value=0.005	Incidence of pneumothorax was higher in endobronchial valve group (18% vs 0%, p-value=0.02)
	No significant difference of baseline characteristics between endobronchial valve and medical care group	Improvement of 6-minute walk test (meter): 60 meter (endobronchial valve) vs -14.0 meter (medical care), p-value<0.001	

FEV1: forced expiratory volume in 1 second; HRCT: high resolution CT-scan; mMRC scale: Modified Medical Research Council scale (range: 0-4, higher value represented more uncompromising dyspnea); RV: residual volume; TLC: total lung capacity; *high heterogeneity was described percentage of emphysema heterogeneity >15%. Percentage of emphysema heterogeneity was counted as proportion of pixels < -910 HU between targeted lobe and ipsilateral adjacent targeted lobe as shown by HRCT; †complete fissure was described as present of >90% fissure on thin slice HRCT on at least one axis.

trials conducted by Sciurba et al[8] and Klooster et al[9], respectively. Three point eight until four valves were placed for every patient on average.

The characteristics of recruited patients between these two studies were almost similar. Subjects in the study conducted by Sciurba et al[8] included patients with severe to very severe emphysema while Klooster et al[9] also included patients with moderate emphysema.[1] Both studies revealed that improvement of the FEV1 and 6-minute walk test was significantly higher in the endobronchial valve group at 6 months follow up period for patients with moderate to very severe emphysema.[8,9] Furthermore, occurrence of adverse events in endobronchial valve group was similar compared to medical treatment group at 90 days and 6 months follow up.[8,9] Mortality occurrence was found in the endobronchial valve group but not statistically difference compared to the medical care group.[8,9] Interestingly, there were three important features that must be considered to determine suitability for endobronchial valve placement. These three features were emphysema heterogeneity, interlobar fissure integrity, and absence of collateral ventilation.[8,9]

According to quantitative densitometry from HRCT, emphysema was determined as presence of density value which was less than -910 HU (Hounsfield Units).[13] Sciurba et al[8] found that improvement of both FEV1 and 6-minute walk test from endobronchial valve placement occurred in subjects with high heterogeneity emphysema.[8] In this study, high heterogeneity was defined as percentage of pixels less than -910 HU between targeted lobe and its adjacent lobe was more than 15%.[8] This indicated that heterogeneity of emphysema determined effectiveness of endobronchial valve placement hence heterogeneity assessment by HRCT prior to valve placement was crucial.

The second important feature was interlobar fissure integrity. Sciurba, et al defined an interlobar fissure to be complete if presence of fissure was more than 90% on at least one axis in thin slice HRCT.[8] Incomplete interlobar fissure signified presence of collateral ventilation which passed across this incomplete fissure.[14] Collateral ventilation, the third important feature, was described as ventilation that occurs through

passages which bypass the normal airways.[15] Sciurba et al[8] found that improvement of FEV1 was significantly higher in subjects with complete interlobar fissure but not in incomplete interlobar fissure.[8]

Klooster et al[9] determined the presence of collateral ventilation by using Chartis system (Pulmonx). From their study which only recruited patients with absence of interlobar collateral ventilation, improvement of FEV1, FVC, and 6-min walk test were significantly higher in endobronchial valve group.[9] In this system, an inflated balloon was placed on target airway through catheter hence expired air would pass only from the catheter.[16] Absence of collateral ventilation would be marked by continuous decrease of expired air.[16] It was reported that Chartis system (Pulmonx) had similar diagnostic performance as compared to HRCT fissure analysis.[17] This system might be used as an alternative approach instead of HRCT in determining presence of collateral ventilation.

As for the patient in the case illustration, treatment by endobronchial valve might be considered. Assessment by HRCT should be conducted prior to valve placement to determine emphysema heterogeneity and fissure completeness. Endobronchial valve placement would be suitable if the HRCT result reveals complete fissure which indicates absence of collateral ventilation and high heterogeneity emphysema. Since we did not find studies that compared use of medical care after valve placement and valve placement only, we could not determine whether the use of medical treatment gives additional benefits after valve placement.

Currently, the endobronchial valve is not available in Indonesia. However, the possibility of using this novel approach in the future should be considered by physicians due to its high efficacy in managing severe emphysema. Regarding the cost of treatment, Pietzsch et al[18] mentioned that it would cost EUR 9,581 for average 3.08 valves placement for every procedure. This study also predicted that endobronchial valve placement would increase quality-adjusted life year (QALY) by 0.41 point with an extra cost of EUR 10,425 over 10 years as compared to medical treatment.[18]

CONCLUSION

Endobronchial valve placement is more effective compared to medical care in patients with high heterogeneity emphysema, complete fissure, and absence of collateral ventilation. Assessment by HRCT should be conducted prior to valve placement to determine suitability for valve placement. Further studies are needed to determine whether use of medical care after valve placement gives additional benefits.

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