

Rafal Krenke

Department of Internal Medicine, Pneumology and Allergology, Medical University of Warsaw, Poland

Change is in the air: bronchial valves to improve quality of life in heterogeneous emphysema

The author declare no financial disclosure

Pneumonol Alergol Pol 2015; 83: 415–417

Chronic obstructive lung disease (COPD) is a major healthcare problem. It is not only an important cause of chronic morbidity but also the fourth leading cause of mortality worldwide [1]. Moreover, due to population aging and exposure to risk factors, the global burden of COPD is projected to further increase in the nearest future [2].

Although COPD has been characterized as preventable and treatable disease, most experts agree that both COPD prevention and treatment are challenging. While the number of smokers in well developed countries is decreasing, the percentage of young people who begin to smoke is still alarmingly high in many poor developing countries. The management of COPD should be based on multidirectional approach, that includes lifestyle changes (smoking cessation), education, pharmacotherapy, pulmonary rehabilitation, vaccinations, oxygen therapy, and others. It must be admitted, however, that the efficacy of pharmacological treatment is unsatisfactory. In clinical trials that applied lung function as a primary or secondary outcome, none of the medications has been shown to significantly modify the long term decline in lung function [2]. On the other hand, the advances in COPD management that were made in last decades should also be emphasized and appreciated. One of the most important changes in the approach to COPD studies was the application of the new outcome measures in clinical trials evaluating the efficacy of different therapies.

The need for redefining of the outcome measures has become evident in the first years of the 21st century. Until that time, the only outcome that was recognized by different international agencies evaluating medical products was improvement in lung function, particularly in the forced expiratory volume in 1 second (FEV₁). However, it has been realized that the use of such a specific outcome which in fact reflects only a single biological variable could result in missing other potential beneficial effects of therapeutic interventions [3]. Therefore, numerous new outcome measures have been widely applied in further studies assessing the efficacy of COPD management. These include: dyspnea score, health status, frequency and severity of exacerbations, exercise capacity, quality of life (QOL), cognitive function, the multi-dimensional symptom scores, mortality and other. The use of these outcomes clearly showed that some relevant therapeutic effects can be achieved in COPD patients even when there is no significant improvement in lung function assessed by spirometry. One of the most important tools to assess health status in COPD patients is the St. George's Respiratory Questionnaire (SGRQ). This questionnaire has been originally designed to measure and quantify the health-related quality of life in patients with chronic airflow limitation [4]. Later, a COPD specific version had also been developed [5]. Since then, the SGRQ has been widely used in clinical trials to measure the effect

of various therapies. Currently, it is regarded as a quasi standard in clinical trials [3]. The minimal important difference (MID) in SGRQ score has been evaluated by different methods, and changes of 2 to 8 points were considered clinically significant. A decline in SGRQ score ≥ 4 points is generally accepted as the minimal difference indicating a significant improvement in quality of life [3].

In the last two decades, several novel therapeutic interventions were developed for patients with COPD, particularly for those with predominating emphysema. These include different bronchoscopic techniques referred to as bronchoscopic lung volume reduction (BLVR) or endoscopic lung volume reduction (ELVR). The common denominator for all these methods is the use of the fiberoptic bronchoscope to reduce lung hyperinflation and improve the distribution of lung ventilation. This can be achieved by endobronchial (intra-bronchial) valve implantation, placement of lung coils or bronchoscopic thermal vapor ablation (BTVA) of emphysematous lung regions [6, 7]. Studies on endobronchial valves started more than ten years ago, that is before the concepts of lung coils or BTVA arose [8]. Therefore, till now significantly more patients have been treated with valves than with lung coils and BTVA. In consequence, more data are available on the efficacy and safety of endobronchial valves than on other bronchoscopic therapies applied in COPD. In the recent meta-analysis by Iftikhar et al. the authors were able to identify 8 studies on endobronchial valves as compared to two small studies on lung coils and only one study on BTVA [9]. It must be admitted, however, that there has been growing interest in the treatment with lung coils and there are some interesting recent results [10] as well as ongoing studies on this technique [e.g. Lung Volume Reduction Coil Treatment in Patients With Emphysema (RENEW) Study, NCT01608490].

In this issue of “Polish Pneumonology and Allergology” a paper by Szlubowska et al. presenting the effect of treatment with intrabronchial valves (IBV) in patients with severe emphysema has been published [11]. The authors showed that the mean difference between the SGRQ score measured before and after three months from treatment was -12.8 ± 11.9 points and that in 13/20 patients this difference was greater than 4 points. These results suggest significant improvement of quality of life in 70% of patients treated with IBV. However, the true impact of treatment with IBVs on health related quality of life should be interpreted with caution. This is because in severe COPD the MID

in SGRQ score may be higher than 4 points. Recently, Welling et al. proposed alternative SGRQ MID values for patients with severe COPD treated with BLVR. These values are -8.3 units at 1 month and -7.1 units at 6 months follow-up after intervention [12]. If those MID values were used in the study by Szlubowska et al. the significant improvement in quality of life would be found in smaller number of patients. The above study also has other limitations. These include short-term follow up, and lack of criteria defining heterogeneous emphysema. Also, comparative analysis of responders and non-responders could have added some important data. Nevertheless, the paper is interesting, particularly for Polish readers as this is the first, prospective study on the relationship between IBV treatment and health related quality of life in our country.

When therapy with bronchial valves is considered several practical comments might be useful for the readers who are unfamiliar with BLVR. First, there are two major types of valves: Spiration intrabronchial valves and Zephyr endobronchial valves. Although the construction of both valves is different, there are neither significant differences between the sites of their placement in the airways (even though one is referred as intrabronchial valve and the second as endobronchial valve) nor their effectiveness and safety. In the study by Szlubowska et al. Spiration IBVs were used but the authors did not include data on the average number of valves applied per patient and the sites of their placement. In earlier studies, the median number of valves implanted to one patient ranged from 3 to 6.7 [13–16]. Second, based on the results of previous studies three major prerequisites for effective treatment have been identified. These include: heterogeneous emphysema, lack of collateral ventilation and successful lobar exclusion [6, 7]. Thus, in all COPD patients who are potential candidates for bronchial valve treatment the use of appropriate diagnostic methods to demonstrate whether the first two criteria are met is indispensable. The third determinant of good clinical response is proper technique of valve placement to produce complete lobar exclusion (and in consequence — desired reduction of the lobe volume) [17]. Third, the long-term effects of valves are largely unknown and this particularly refers to the durability of improvement. Most of the studies published to date evaluated the effects of treatment after 3, 6 and 12 months. Fourth, there is no reimbursement for severe COPD treatment with bronchial valves in Poland. The treatment is

relatively expensive with the approximate cost of one valve 1,000 EUR (4,300 PLN). In view of this fact, the authors should be congratulated that they were able to perform the study with no external financial support. The lack of external funds for the study may explain the relatively small study group. Regarding the small number of involved patients it should also be remembered that, contrary to some previous studies that reported larger study groups, this was a single center study.

In summary, BLVR is one of the therapeutic options for patients with advanced emphysema. This therapy may improve both pulmonary function and health related quality of life. As BLVR is a rapidly growing area of knowledge that utilizes novel exciting technologies we will certainly hear about it again in the near future.

Conflict of interest

The author declare no conflict of interest.

References:

- World Health Report. Geneva: World Health Organization. Available from URL: http://www.who.int/whr/2000/en/whr00_en.pdf?ua=1; 2000.
- Global Strategy for the Diagnosis, Management and Prevention of COPD. Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2015. Available from: <http://www.goldcopd.org/>.
- Glaab T, Vogelmeier C, Buhl R. Outcome measures in chronic obstructive pulmonary disease (COPD): strengths and limitations. *Respir Res* 2010; 11: 79. doi: 10.1186/1465-9921-11-79.
- Jones PW, Quirk FH, Baveystock CM, Littlejohns P. A self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. *Am Rev Respir Dis* 1992; 145: 1321–1327.
- Meguro M, Barley EA, Spencer S, Jones PW. Development and validation of an improved, COPD-specific version of the St. George Respiratory Questionnaire. *Chest* 2007; 132: 456–463.
- Gompelmann D, Eberhardt R, Herth F. Endoscopic volume reduction in COPD — a critical review. *Dtsch Arztebl Int* 2014; 111: 827–833. doi: 10.3238/arztebl.2014.0827.
- Mineshita M, Slebos DJ. Bronchoscopic interventions for chronic obstructive pulmonary disease. *Respirology* 2014; 19: 1126–1137. doi: 10.1111/resp.12362.
- Snell GI, Holsworth L, Borill ZL et al. The potential for bronchoscopic lung volume reduction using bronchial prostheses: a pilot study. *Chest* 2003; 124: 1073–1080.
- Iftikhar IH, McGuire FR, Musani AI. Efficacy of bronchoscopic lung volume reduction: a meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2014; 9: 481–491. doi <http://dx.doi.org/10.2147/COPD.S69148>.
- Zoumot Z, Kemp SV, Singh S et al. Endobronchial coils for severe emphysema are effective up to 12 months following treatment: medium term and cross-over results from a randomised controlled trial. *PLoS One* 2015; 10: e0122656. doi: 10.1371/journal.pone.0122656.
- Szłubowska S, Zalewska-Puchała J, Majda A et al. The influence of a lung volume reduction with intrabronchial valves on the quality of life of patients with heterogeneous emphysema — a prospective study. *Pneumonol Alergol Pol* 2015; 83: 418–423. doi: 10.5603/PiAP.2015.0069.
- Welling JB, Hartman JE, Ten Hacken NH, Klooster K, Slebos DJ. The minimal important difference for the St George's Respiratory Questionnaire in patients with severe COPD. *Eur Respir J* 2015. doi: 10.1183/13993003.00535-2015.
- Sterman DH, Mehta AC, Wood DE et al. A multicenter pilot study of a bronchial valve for the treatment of severe emphysema. *Respiration* 2010; 79: 222–233. doi: 10.1159/000259318.
- Sciurba FC, Ernst A, Herth FJ et al. A randomized study of endobronchial valves for advanced emphysema. *N Engl J Med* 2010; 363: 1233–1244. doi: 10.1056/NEJMoa0900928.
- Wood DE, Nader DA, Springmeyer SC et al. IBV Valve trial: a multicenter, randomized, double-blind trial of endobronchial therapy for severe emphysema. *J Bronchology Interv Pulmonol* 2014; 21: 288–297. doi: 10.1097/LBR.0000000000000110.
- Davey C, Zoumot Z, Jordan S et al. Bronchoscopic lung volume reduction with endobronchial valves for patients with heterogeneous emphysema and intact interlobar fissures (the BeLieVeR-HiFi study): a randomised controlled trial. *Lancet* 2015; 386: 1066–1073. doi: 10.1016/S0140-6736(15)60001-0.
- Eberhardt R, Gompelmann D, Schuhmann M, Heussel CP, Herth FJ. Complete unilateral vs partial bilateral endoscopic lung volume reduction in patients with bilateral lung emphysema. *Chest* 2012; 142: 900–908.