# Use of Resector Balloon Desobstruction in Patients With Severe Chronic Obstructive Pulmonary Disease

## A Pilot Feasibility Study on a Novel Desobstruction Technique

*Yalcin Karakoca, MD,\* Guler Karaagac Gogus, MD,†*
*and Ozlem Yapicier, MD‡*

***Background:*** **Inflammation of the small airways (bronchiolitis) contributes to airflow limitation by narrowing and obliterating the airway lumen in patients with chronic obstructive pulmonary disease (COPD). Although currently available treatments provide satisfactory disease control in most patients, a significant number of patients do not respond. This study presents the outcomes of Karakoca resector balloon desobstruction in patients with severe COPD who did not respond to medical treatment.**

***Methods:*** **Ten COPD patients classified as stage IV by the Global Initiative for Obstructive Lung Disease (GOLD) and unsuccessfully treated with high-dose bronchodilators and corticosteroids, oral corticosteroids, oxygen, and NIMV therapy underwent therapeutic bronchoscopy, including balloon desobstruction for segmental and subsegmental bronchi. Exercise capacity and $SpO_2$ levels were measured and lung function tests and bronchoscopic biopsies performed before and after the intervention.**

***Results:*** **After Karakoca resector balloon desobstruction, improvements were noted in the effort capacity, $SpO_2$ and forced expiratory volume in 1 second levels of all patients. None of the patients developed preoperative complications or complication or exacerbation within the postoperative 1 to 3 months of follow-up.**

***Conclusion:*** **Satisfactory results were achieved in all patients, warranting study of Karakoca resector balloon desobstruction in larger patient cohorts.**

**Key Words:** chronic obstructive pulmonary disease, stage IV, Karakoca resector balloon desobstruction

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Despite optimal pharmacological therapy and pulmonary rehabilitation, patients with chronic obstructive pulmonary disease (COPD) remain significantly disabled. Various bronchoscopic techniques have been used to treat emphysema, but proper patient selection is required for endoscopic lung volume reduction.[1–3] The pathologic hallmarks of COPD include inflammation of the small airways (bronchiolitis) and destruction of lung parenchyma (emphysema), which limits airflow. Bronchiolitis especially contributes to airflow limitation by narrowing and obliterating the airway lumen and actively constricting the airways.[4,5] Although endoscopic lung volume reduction has been used successfully in patients with severe emphysema, no bronchoscopic treatment approach is yet available for patients with COPD, even those with bronchiolitis dominant COPD.[6] Recently, desobstruction of submucosal bronchial tumors using Karakoca resector balloon has been shown to be successful in lung cancer patients.[7] Herein we present our clinical experience with Karakoca resector balloon desobstruction in patients with severe COPD (chronic bronchitis).

## PATIENTS AND METHODS

### Study Population

Of 60 patients with severe COPD admitted to our clinic in 2014, 10 patients (7 were males, all were smokers) with very severe (stage IV) COPD based on Global Initiative for Obstructive Lung Disease (GOLD) classification were included in the present study. Severely dyspneic patients with predominantly chronic bronchitis findings other than emphysema and bullous changes on respiratory function tests, high-resolution thorax CT, and quantitative ventilation and perfusion scintigraphy, with complaint of sputum expectoration leading to symptomatic relief and without indication of volume reduction therapy were included in the study provided

that they were considered to be appropriate for balloon desobstruction intervention during their evaluation by preintervention diagnostic fiber-optic bronchoscopy in terms of lack of bleeding risk during bronchoscopy-assisted therapeutic aspiration and finding of goblet cell (GC) hyperplasia indicating appropriate GC mucous secretion on bronchoscopic biopsy evaluation. Accordingly, of 60 patients initially enrolled, after exclusion of overall 50 patients due to the presence of acute exacerbation and infection at admission (n = 12), predominantly emphysema findings, and bullous changes on high-resolution thorax CT (n = 16) and findings positive for air trapping suggestive of emphysema in quantitative ventilation and perfusion scintigraphy (n = 2) along with lack of complaint of sputum expectoration (n = 16), lack of GC hyperplasia in bronchoscopic biopsy evaluation (n = 2), and no consent to participate in study (n = 2), the remaining 10 patients composed the final study population (Fig. 1).

Written informed consent was obtained from each subject following a detailed explanation of the objectives and protocol of the study that was conducted in accordance with the ethical principles stated in the "Declaration of Helsinki" and approved by the institutional ethics committee (September 30, 2014; no. 2014-5).

## Balloon Desobstruction Procedure

Karakoca resector balloon is an equipment developed by Professor Yalcin Karakoca for the first time for cancer patients and has been manu-factured in Turkey after its introduction in a Congress for Bronchology. It is a sterilized product available in 6 dimensions (40 × 25, 50 × 30, 10 × 10, 10 × 15, 15 × 20, and 15 × 30 mm) designed to enable interventions at the tracheal level and for the small bronchi at the discretion of bronchoscopy expert. It is single-use equipment and resterilization is not recommended. On an average 2 to 3 balloons are required for a treatment session in a single patient.

Before the operation, all patients were eval-uated by a cardiologist and an anesthesiologist. Patients were placed under general anesthesia, and interventions were performed using a flexi-ble therapeutic bronchoscope (Olympus model BF-XT, Tokyo, Japan), with a channel diameter of 3.2 mm. The resector balloon consisted of a latex balloon mounted onto the distal end of a 120 cm long single-lumen polyethylene tube of outer diameter 2 mm. The balloon length could vary between 10 and 50 mm, and its maximum inflated diameter between 10 and 25 mm. The balloon was covered with a mesh structure made of 0.2-mm thick polyurethane or lycra fibers. The minimum deflated balloon diameter with the mesh structure was 2.8 mm.

In this technique, the balloon is inserted into the bronchial lumen so that the mucosal obstruc-tion covers the balloon. The balloon is repeatedly inflated and deflated until lumen patency is estab-lished. Balloon was operated by electronic pump in a regular pulse mode and the force applied directly to the bronchial mucosa with the balloon pressure of approximately 2.2 to 2.5 bar compressing the hyperplasic GCs. Most of the resector balloons used was 10 mm in diameter. Although the balloon pressure that thins the mucosal hyperplasia does not cause any lacerations or bleeding, the egested mucous material flows into the bronchial lumen and is aspirated, resulting in complete
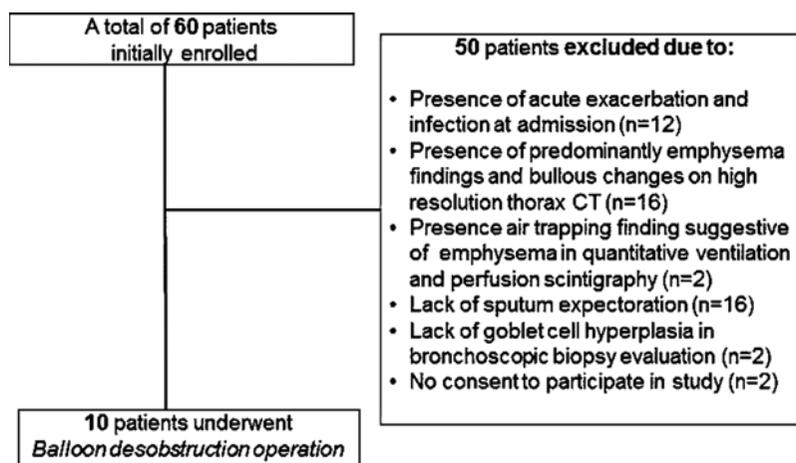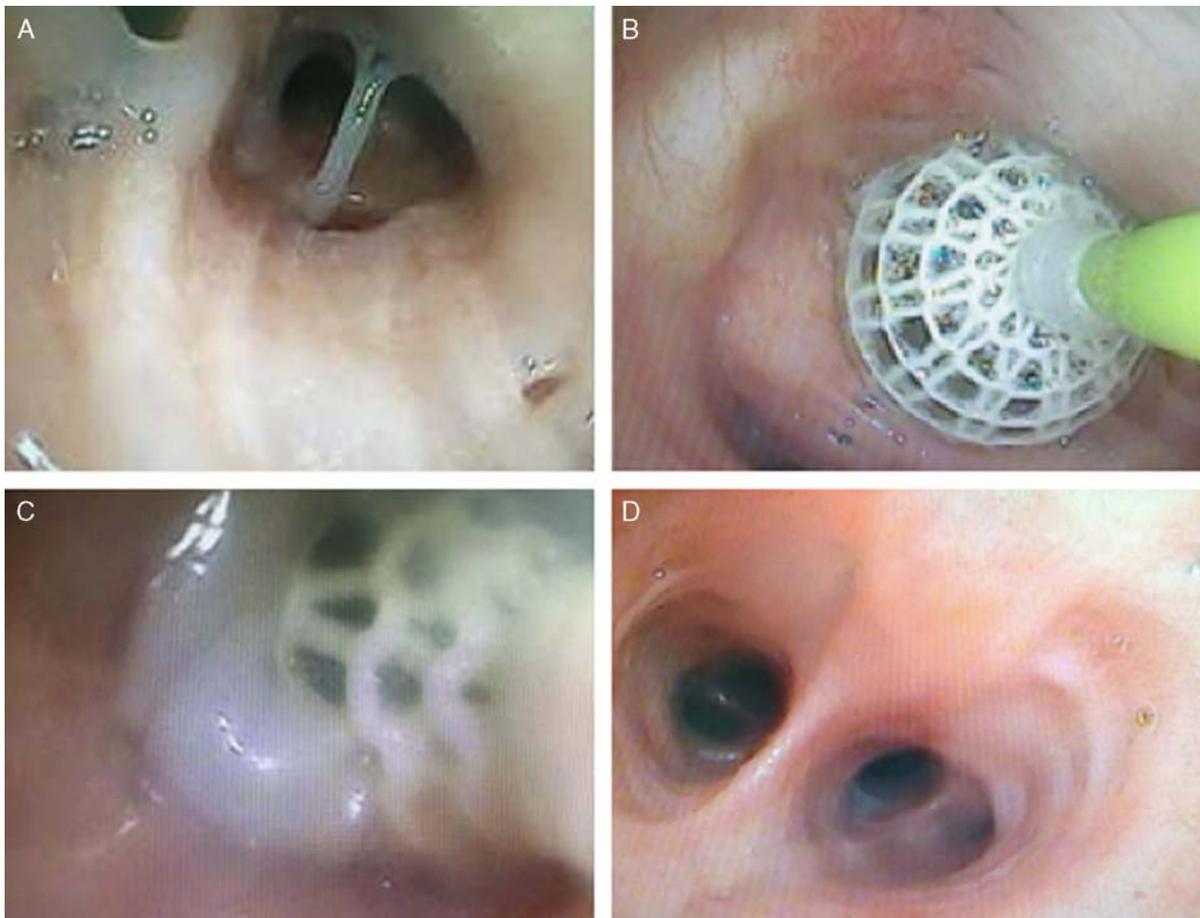


FIGURE 1. Patients' disposition.

**FIGURE 2.** Bronchoscopic views in a patient with chronic obstructive pulmonary disease undergoing Karakoca resector balloon desobstruction. A, View before the intervention. B, Balloon desobstruction in segmental bronchi. C, Mucous material overlaying the balloon. D, View after the intervention.

patency of the obstructed airways. On the basis of the recommended operating time decided by the preoperative cardiac evaluation, the number of segmental bronchi that could be accessed over 60 minutes ranged from 60 to 90 during the desobstruction in our case series. The procedure is performed using 3.2-mm bronchoscope that revealed access to 8up to 3 mm bronchi, the ones with most extensive GC accumulation, along with use of resector balloon maneuvers in 3-mm bronchi that could not be reached by bronchoscope. Segmental and subsegmental bronchi were viewed during fiberoptic bronchoscopy, whereas therapeutic aspiration applied to patients with mucous layer lining the entire mucosa and bronchoscopic biopsies were taken from right inferio-posterior segment to compare preoperative and postoperative pathologic findings based on GCs and mucous accumulation. Lung function tests and clinical findings before and 1 week and 1 month after the intervention were also compared. The

bronchoscopic views of a patient at different stages of the intervention are presented in Figure 2.

## RESULTS

All cases were on high-dose nebuliser treatment, continuous oxygen replacement support, and oral corticosteroid treatment due to frequent exacerbation history, while 8 patients were on noninvasive mechanical ventilation therapy. After the operation, there was a significant reduction in oxygen need of patients. Routine inhaler and nebulizer treatments were maintained along with no need for oral corticosteroid treatment. In 1 patient who had been taken to ICU due to respiratory failure before operation, mechanical ventilation support was discontinued in the postoperative period and the patient was stabilized with no history of exacerbations in the past year.

Demographic and clinical characteristics of the patients are listed in Table 1.

**TABLE 1.** Demographic and Clinical Characteristics of the 10 Patients in This Study

| Patient | Sex | Age (y) | Smoking (Pack-Year) | Additional Diseases | FEV$_1$ (L) | mBorg Dyspnea Scale | Resting SpO$_2$ (%) |
|---|---|---|---|---|---|---|---|
| A.Y. | M | 72 | 30 | DM, HT | 0.69 | 9 | 85 |
| V.P. | M | 83 | 80 | HF, BPH | 1.17 | 7 | 90 |
| R.O. | M | 56 | 35 | CAD | 0.55 | 10 | 82 |
| I.M. | M | 82 | 30 | SVO, CAD | 0.71 | 10 | 89 |
| K.O. | M | 51 | 40 | DM | 0.99 | 7 | 89 |
| O.E. | M | 51 | 40 | HT | 1.16 | 7 | 91 |
| K.O. | M | 57 | 20 | HT | 0.98 | 9 | 88 |
| A.Y. | F | 57 | 80 | SCLC | 0.91 | 10 | 87 |
| N.N.G. | F | 67 | 50 | Operated bladder Ca, operated lung Ca | 0.99 | 7 | 88 |
| F.O. | F | 61 | 45 | DM | 0.70 | 10 | 88 |

BPH indicates benign prostatic hyperplasia; Ca, cancer; CAD, coronary artery disease; DM, diabetes mellitus; F, female; HF, heart failure; HT, hypertension; M, male; mBorg, modified Borg; SCLC, small cell lung cancer; SpO$_2$, oxygen saturation; SVO; small vessel occlusion.

None of the patients developed intraoperative or postoperative complications. One of the female patients had a newly diagnosed small cell lung cancer, as shown by computed tomography–guided transthoracic needle aspiration biopsy, with a $28 \times 20$ mm peripheral mass observed on chest x-ray and PET scan. Her modified Borg dyspnea scale score was 10; and her resting oxygen saturation (SpO$_2$) in room air was 87% to 88%; due to her performance status, she was not administered chemotherapy.

Comparisons of lung function tests 1 week and 1 month after the procedure with results before the procedure showed improvements in forced expiratory volume in 1 second (FEV$_1$) (Table 2), Borg dyspnea scale (Table 3), and SpO$_2$ levels (Table 3).

Patients with dyspnea on minimal exertion before intervention were determined to be able to walk at least 250 meters (1000 m in some patients) 2 days after the operation. None of the patients developed complications or exacerbation within the postoperative 1 to 3 months of follow-up.

### Histopathologic Examination

Biopsies obtained before the intervention showed GC hyperplasia, as shown by higher than normal ratios of GCs to ciliated cells in the upper and middle bronchial system (normal ratio 1:4) (Fig. 3). Mucus-containing GCs was more evident in periodic acid Schiff/alcian blue pH 2.5 (PAS/AB) stained sections (Fig. 3).

Biopsies after the intervention were taken from the area of the initial biopsies. Scattered GCs were observed in these H + E-stained sections (Fig. 4). Use of PAS/AB stains clearly showed decreases, relative to baseline, in the number of GCs and mucus-containing GCs (Fig. 4). The GC/ciliated cell ratios of these biopsies had decreased to 1:4.

**TABLE 2.** FEV$_1$ Results Before and 1 Week and 1 Month After the Procedure

| Patient | Procedure Date | FEV$_1$ (L) Before | After 1 wk | After 1 mo |
|---|---|---|---|---|
| A.Y. | 15.4.2014 | 0.69 | 1.19 | 1.52 |
| V.P. | 11.6.2013 | 1.17 | 1.33 | 1.31 |
| R.O. | 18.11.2013 | 0.55 | 0.61 | 0.78 |
| I.M. | 22.10.2013 | 0.71 | 0.74 | 1.06 |
| K.O. | 8.5.2014 | 0.99 | 1.06 | 1.21 |
| O.E. | 17.5.2013 | 1.16 | 1.41 | 1.59 |
| K.O. | 11.11.2013 | 0.98 | 1.19 | 1.21 |
| A.Y. | 17.5.2013 | 0.91 | 1.06 | 1.05 |
| N.N.G. | 2.10.2012 | 0.99 | 1.00 | 1.37 |
| F.O. | 22.5.2013 | 0.70 | 1.06 | 1.00 |

**TABLE 3.** Borg Dyspnea Scale and SpO$_2$ Levels Before and 1 Week and 1 Month After the Procedure

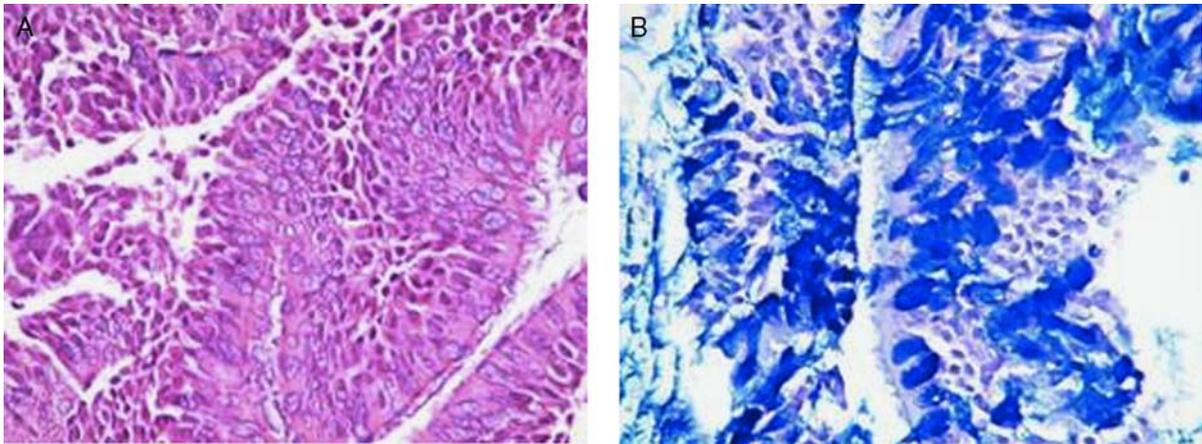| Patient | Modified Borg Dyspnea Scale Before | After 1 wk | After 1 mo | Resting Oxygen Saturation (%) Before | After 1 wk | After 1 mo |
|---|---|---|---|---|---|---|
| A.Y. | 9 | 3 | 3 | 85 | 93 | 94 |
| V.P. | 7 | 3 | 3 | 90 | 95 | 94 |
| R.O. | 10 | 7 | 7 | 82 | 90 | 91 |
| I.M. | 10 | 3 | 3 | 89 | 95 | 97 |
| K.O. | 7 | 4 | 3 | 89 | 96 | 95 |
| O.E. | 7 | 3 | 3 | 91 | 96 | 96 |
| K.O. | 9 | 9 | 9 | 88 | 92 | 91 |
| A.Y. | 10 | 3 | 3 | 87 | 93 | 93 |
| N.N.G. | 7 | 3 | 3 | 88 | 94 | 93 |
| F.O. | 10 | 3 | 3 | 88 | 94 | 96 |

**FIGURE 3.** Histopathologic results of biopsies obtained before the procedure. A, H&E staining ($\times$400), showing goblet cell hyperplasia. B, PAS/AB pH 2.5 staining ($\times$400), showing increased acidic mucin contents of hyperplastic goblet cells. *a+*

## DISCUSSION

COPD is a major cause of mortality worldwide. It is characterized by progressive airflow limitations associated with a chronic inflammatory process in the airways and lung parenchyma. Small airways disease and parenchymal destruction are the main structural abnormalities, although there is increasing evidence that large airways are also inflamed in patients with COPD (4-6). A lower $FEV_1$ has been associated with an increased volume of tissue in the walls, and the accumulation of mucous exudates in the lumen, of the small airways.[8] Epithelial abnormalities, including epithelial proliferation, squamous metaplasia, and GC hyperplasia, likely contribute to narrowing of the lumen of the 8 to 3 mm airways by increasing in wall thickness.[9,10] Peribronchiolar fibrosis is also responsible for narrowing the small airways in patients with COPD. Accumulation of mucous exudates within the lumen of 8- to 3-mm conducting airways further aggravates airflow limitations. Interestingly, squamous metaplasia promotes peribronchiolar fibrosis, and mucins secreted by airway epithelial GCs contribute to the accumulation of mucous exudates in airway lumen, suggesting that the epithelium may be a major target for therapeutic intervention.[11–13] However, therapeutic bronchoscopic options are limited in these patients.

Karakoca resector balloon desobstruction is a new technique in therapeutic bronchoscopy that has been used in lung cancer patients. We previously showed that Karakoca resector balloons are very useful for submucosal and endoluminal tumoral obstructions.[7] We hypothesized that narrowing of the small airways in some COPD patients is similar to mucosal tumoral obstructions.
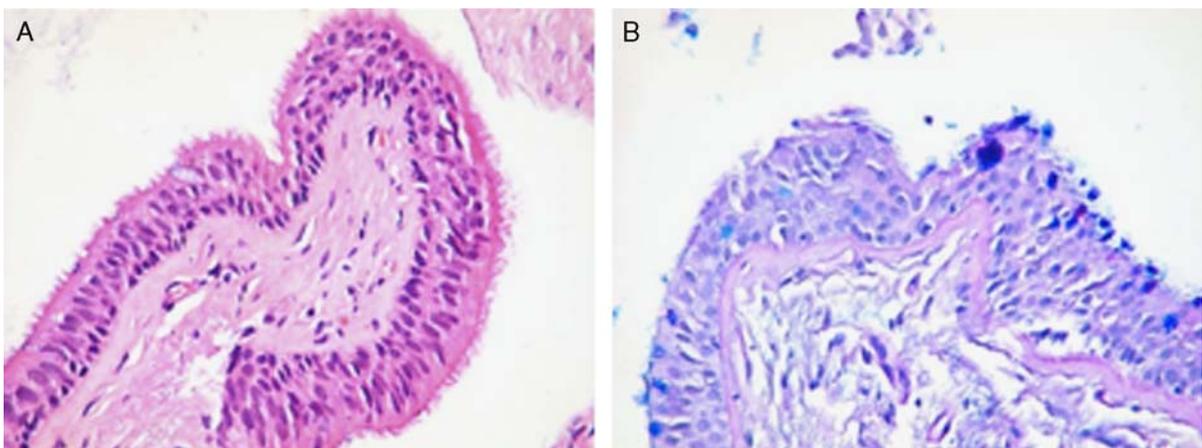


**FIGURE 4.** Histopathologic results of biopsies obtained after the procedure. A, H&E staining ($\times$400), showing a marked reduction in the number of goblet cells. B, PAS/AB pH 2.5 staining ($\times$400), showing scattered goblet cells and a reduction in their acidic mucin content. *a+*

As a pilot feasibility study on a novel desobstruction technique, our findings regarding use of the Karakoca desobstruction technique in 10 COPD patients yielded satisfactory results, including improvements not only in $SpO_2$ levels and lung function tests but also in effort capacity accompanied with rapid relief of symptoms. Moreover, patients with dyspnea on minimal exertion before intervention were determined to be able to walk at least 250 meters (1000 m in some patients) 2 days after the operation. None of the patients developed complications or exacerbation within the postoperative 1 to 3 months of follow-up. Exacerbation frequency and life quality was also markedly improved in the postoperative period.

One of the female patients had a newly diagnosed small cell lung cancer, as shown by computed tomography–guided transthoracic needle aspiration biopsy, with a $28 \times 20$ mm peripheral mass observed on chest x-ray and PET scan. Her modified Borg dyspnea scale score was 10; and her resting oxygen saturation ($SpO_2$) in room air was 87% to 88%; due to her performance status, she was not administered chemotherapy. After this procedure, she was given her oncological therapy.

Given the recommended operating time decided by the preoperative cardiac evaluation, 60 to 90 segmental bronchi could be reached during the desobstruction in our case series. Nonetheless it should be noted that the number of accessed segments within the operating time will increase with the experience.

It should be noted that unlike to a smooth balloon, Karakoca resector balloon is equipped with a specific curettage/resection function that enables removal of GC layer. Moreover, the balloon is operated by electronic pump in a regular pulse mode at 2.2 to 2.5 bars operating pressure that also enables revealing of a resection effect on the GCs. Therefore, pathologic changes observed in our cases are associated with the mechanical force applied to GC layer leading to removal of the cell layer by means of physical properties of the Karakoca resector balloon. Our findings seem to indicate the association reduction in $FEV_1$ with the GC hyperplasia that causes luminal obliteration predominantly at 8 to 3 mm segmental and subsegmental bronchi. Hence, significant clinical improvement obtained after the treatment seems to be associated with the fact that Karakoca resector balloon desobstruction is based principally on the elimination of GC layer. Thus, the actual pathology treated by this technique seems to be the GC hyperplasia at 8 to 3 mm bronchi in patients with chronic bronchitis phenotype.

The success of the Karakoca desobstruction technique in these patients warrants further studies in large patient cohorts.

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