Bronchoscopic Biological Lung Volume Reduction Therapy for Patients with Emphysema

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Abstract

Background: Emphysema is a worldwide leading cause of disability and death. The current standard maximal medical treatment allows improvement in exercise capacity and quality of life. Also lung volume reduction is important in management of emphysema and one of this procedures is using using autologous blood and gelfoam by the bronchoscope and evaluation of this method is important.

Aim of the Work: The aim of this work is to evaluate the safety and efficacy of bronchoscopic biological lung volume reduction using autologous blood and gel foam in patients with emphysema and/or emphysematous bullae.

Patients and Methods: This study was carried out in Bronchoscopy Unite, Chest Department, Al-Azhar University Hospitals in the period from April 2013 to July 2016. And a written informed consent was taken from the patients before the start of the research.

Thirty patients with heterogeneous emphysema or bullae were recruited in this study. The patients were divided into two groups: The first group: Seventeen patients with emphysematous bullae. The second group: Thirteen patients with heterogeneous emphysema. All patients underwent the following: Full history taking, clinical examination, pre and one month post bronchoscopic pulmonary function tests (FEV1, FVC, FEV1/FVC and RV), pre and one month post bronchoscopic arterial blood gases, pre and one month post bronchoscopic radiological assessment by plain chest X-ray and high resolution CT chest, pre and one month post bronchoscopic evaluation of dyspnea grade according to Modified Medical Research Council (MMRC) score, Echocardiography for assessment of pulmonary artery pressure before the procedure and Fiberoptic bronchoscopy under local anesthesia and light sedation, in which injection of 10ml of autologous blood, 5ml of tranexamic acid and 10ml of prepared gel foam in the feeding bronchus (first group) and in the most affected four subsegments in each side (second group).

Results: This study include 30 patients male with emphysema age ranged (59.6 ± 8.3) years, FEV1 (% of predicted) (32.9 ± 8.8), RV (% of predicted) 156.0 ± 23.2, 6 MWT (m) 275.7 ± 85.3, PaO2 (mmHg) on room air 66.0 ± 6.0, size of bullae by chest CT (cm) 10.9 ± 2.8 and the outcomes post BLVR shows FEV1 (% of predicted) (50.6 ± 15.5), with p-value <0.0001 RV (% of predicted) 144.3 ± 22.9 with p-value <0.0001, 6 MWT (m) 343.2 ± 83.1 with p-value <0.0001, PaO2 (mmHg) on room air 70.9 ± 4.7 with p-value <0.0001, size of bullae by chest CT (cm) 9.1 ± 2.5 with p-value <0.0002.

Conclusion: Bronchoscopic biological lung volume reduction therapy using autologous blood and gelfoam was well tolerated and safe in patients with advanced emphysema especially in heterogeneous type.

Key Words: Biological lung volume reduction therapy – BLVR – Emphysema.

Introduction

EMPHYSEMA is a worldwide leading cause of disability and death affecting about 1.8% of the global population [1]. The current standard maximal medical treatment includes smoking cessation, administration of bronchodilators, pulmonary rehabilitation and long-term oxygen therapy; it allows improvement in exercise capacity and quality of life. However, it shows some limitations in the case of advanced disease [2].

For this reason, according to radiological, functional details and the clinical status of the patients, a number of surgical procedures have been proposed historically, these include: Bullectomy, single and double lung transplantation and, more recently, Lung Volume Reduction Surgery (LVRS) [3].

In fact, when target areas of hyper-inflated lungs are resected, the residual lung and chest wall mechanics are significantly improved with consequent symptomatic relief [2].

Some authors have speculated that similar results could be achieved by less invasive broncho-
Bronchoscopic Biological Lung Volume Reduction in Emphysema

Bronchoscopic approaches, isolating and deflating the most hyperinflated parts of the emphysematous lungs. Several bronchoscopic alternatives have been proposed: Endobronchial valves, occluders, sealants, coils, steam and airway by-pass [4].

Aim of the work:
The aim of this work is to evaluate the safety and efficacy of bronchoscopic biological lung volume reduction using autologous blood and gel foam in patients with emphysema and/or emphysematous bullae.

Patients and Methods
This study was carried out in Bronchoscopy Unite, Chest Department, Al-Azhar University Hospitals in the period from April 2013 to July 2016. Thirty patients with heterogeneous emphysema or bullae were recruited in this study. The patients were divided into two groups:
The first group: Seventeen patients with emphysematous bullae.
The second group: Thirteen patients with heterogeneous emphysema.

All patients underwent the following:
1- Full history taking.
2- Clinical examination.
3- Pre and one month post bronchoscopic pulmonary function tests (FEV₁, FVC, FEV₁/FVC and RV).
4- Pre and one month post bronchoscopic arterial blood gases.
5- Pre and one month post bronchoscopic radiological assessment by plain chest X-ray and high resolution CT chest.

Chest X-ray was done for every patient in the first group to recognize the size and site of the bulla. Then high resolution CT chest was done as it is more sensitive than chest X-ray to detect bullae number, size and position and its feeding bronchi, in which BBLVR should be applied. The implication of the bulla on the adjacent lung parenchyma and mediastinum can be also identified, as it may compress the adjacent parenchyma or shift the mediastinum. Also chest X-ray and HRCT were done for patients in the second group to identify evidence of emphysema [8] and to measure the Hounsfield Units of the lung to determine the heterogenicity of emphysema [6] and the most affected site to be injected in the procedure.

6- Pre and one month post bronchoscopic evaluation of dyspnea grade according to Modified Medical Research Council (MMRC) Score [7].
7- Echocardiography for assessment of pulmonary artery pressure before the procedure.
8- Fiberoptic bronchoscopy under local anesthesia and light sedation, in which injection of 10ml of autologous blood, 5ml of tranexamic acid and 10ml of prepared gel foam in the feeding bronchus (first group) and in the most affected four subsegments two in each side (second group).

Inclusion criteria:
- Clinical and CT diagnosis of emphysema [7,8].
- Persistent dyspnea (i.e. Medical Research Council Dyspnoea MRCD score of ≥2) despite of at least 4 weeks of appropriate medical therapy.
- FEV₁/FVC <70% and FEV₁ <50% predicted.
- PaO₂ ≥60mmHg on nasal prong ≤4 liters per minute.
- PaCO₂ ≤60mmHg.
- Age >40 years.
- Absence of clinically significant pulmonary hypertension, defined as a pulmonary systolic pressure >45mmHg.
- Absence of a diagnosis of alpha-1 anti-trypsin deficiency.

Exclusion criteria:
- Associated pulmonary comorbidities.
- Medical conditions associated with high risk bronchoscopy as:
  - Life threatening arrhythmia.
  - Severe hypoxemia not improved on supplemental oxygen.
  - Bleeding tendency that can’t be corrected.
  - Severe airway obstruction (FEV₁ <20% predicted).

BLVR procedure: BLVR was done under local anesthesia (lidocaine spray 10% and lidocaine hydrochloride sterile solution 2%, 50ml each ml contain 20mg), light sedative (midazolam 15mg/3ml) and supplemental oxygen using nasal prong during the procedure. Fiberoptic bronchoscopy (storz) was introduced through nostril or the mouth according to the presence of nasal problems or not. The bronchoscope was advanced to reach the targeted segment of the bronchial tree that was rec-
ognized by high resolution CT chest, then the bronchoscope wedged to the targeted segmental bronchi.

A small diameter catheter (OLYMPUS PR-2B) was introduced through the working channel of the bronchoscope, when its tip appeared about 2-3 cm beyond the tip of bronchoscope, the determinant amount of autologous blood and 5ml tranexamic acid (cyclokapron® 100mg/ml) were injected, and then the the gel piece (Cutanplast® Standard 70 X 50 X 10mm) which is a water insoluble material that was cut into tiny pieces and 10ml of normal saline could be added to the pieces to form the gel foam. Determinant amount of prepared gel foam was injected through the catheter. The bronchoscope was left in wedge position for 1 to 2 minutes till the coagulation process completed. (Normal clotting time 2-9 minutes was accelerated by adding the cyclokapron®), and to prevent regurgitation of the blood and foam. The gel foam led to obstruction of the targeted segment, while the blood trickling on the wall of the bulla leads to shrinkage and fibrosis of the bulla as it coagulated and organized. The bronchoscope was done as rapid as possible without inspection of the rest of the bronchial tree to avoid dyspnea and to minimize hypoxemia. Every patient was followed with chest X-ray after 6 hours of the bronchoscope to determine if there is an early complication of the procedure as pneumothorax, or not.

Table (1): Patient's characteristics and measures before BLVR in the whole study population.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Min.</th>
<th>Max.</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years).</td>
<td>30</td>
<td>40</td>
<td>72</td>
<td>59.6</td>
<td>8.3</td>
<td>62</td>
<td>55-65</td>
</tr>
<tr>
<td>FEV1 (% of predicted).</td>
<td>30</td>
<td>20</td>
<td>48</td>
<td>32.9</td>
<td>8.8</td>
<td>31</td>
<td>26-40</td>
</tr>
<tr>
<td>RV (% of predicted).</td>
<td>30</td>
<td>125</td>
<td>220</td>
<td>156.0</td>
<td>23.2</td>
<td>154</td>
<td>140-170</td>
</tr>
<tr>
<td>6 MWT (m).</td>
<td>30</td>
<td>98</td>
<td>416</td>
<td>275.7</td>
<td>85.3</td>
<td>284</td>
<td>224-350</td>
</tr>
<tr>
<td>MRCD score.</td>
<td>30</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>2-3</td>
</tr>
<tr>
<td>PaO2 (mmHg) on room air.</td>
<td>30</td>
<td>56</td>
<td>78</td>
<td>66.0</td>
<td>6.0</td>
<td>66.5</td>
<td>61-70</td>
</tr>
<tr>
<td>Size of bullae by chest X-ray (cm).</td>
<td>17</td>
<td>3</td>
<td>6</td>
<td>4.3</td>
<td>0.8</td>
<td>4</td>
<td>4-5</td>
</tr>
<tr>
<td>Size of bullae by chest CT (cm).</td>
<td>17</td>
<td>5</td>
<td>10</td>
<td>2.8</td>
<td>0.8</td>
<td>10</td>
<td>9.8-12</td>
</tr>
</tbody>
</table>

Table (2): Outcome measures after BLVR in the whole study population.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Min.</th>
<th>Max.</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (% of predicted).</td>
<td>30</td>
<td>22</td>
<td>68</td>
<td>50.6</td>
<td>15.5</td>
<td>53.5</td>
<td>40-65</td>
</tr>
<tr>
<td>RV (% of predicted).</td>
<td>30</td>
<td>110</td>
<td>220</td>
<td>144.3</td>
<td>22.9</td>
<td>140</td>
<td>130-160</td>
</tr>
<tr>
<td>6 MWT (m).</td>
<td>30</td>
<td>160</td>
<td>477</td>
<td>343.2</td>
<td>83.1</td>
<td>356</td>
<td>300-404</td>
</tr>
<tr>
<td>MRCD score.</td>
<td>30</td>
<td>1</td>
<td>3</td>
<td>2.1</td>
<td>0.4</td>
<td>2</td>
<td>2-2</td>
</tr>
<tr>
<td>PaO2 (mmHg) on room air.</td>
<td>30</td>
<td>60</td>
<td>80</td>
<td>70.9</td>
<td>4.7</td>
<td>72</td>
<td>68-74</td>
</tr>
<tr>
<td>Size of bullae by chest X-ray (cm).</td>
<td>17</td>
<td>2.8</td>
<td>6</td>
<td>4.2</td>
<td>0.8</td>
<td>4</td>
<td>4-5</td>
</tr>
<tr>
<td>Size of bullae by chest CT (cm).</td>
<td>17</td>
<td>6</td>
<td>16</td>
<td>9.1</td>
<td>2.5</td>
<td>8</td>
<td>7.8-10</td>
</tr>
</tbody>
</table>

Table (3): Comparison of the outcome measures before and after BLVR in the whole study population.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Pre-BLVR</th>
<th>Post-BLVR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (% of predicted).</td>
<td>30</td>
<td>32.9 (8.8)</td>
<td>50.6 (15.5)</td>
<td>&lt;0.0001¶</td>
</tr>
<tr>
<td>RV (% of predicted).</td>
<td>30</td>
<td>156.0 (23.2)</td>
<td>144.3 (22.9)</td>
<td>&lt;0.0001¶</td>
</tr>
<tr>
<td>6 MWT (m).</td>
<td>30</td>
<td>275.7 (85.3)</td>
<td>343.2 (83.1)</td>
<td>&lt;0.0001¶</td>
</tr>
<tr>
<td>MRCD score.</td>
<td>30</td>
<td>3 (2.3)</td>
<td>2 (2-2)</td>
<td>&lt;0.0001§</td>
</tr>
<tr>
<td>PaO2 (mmHg) on room air.</td>
<td>30</td>
<td>66.0 (6.0)</td>
<td>70.9 (4.7)</td>
<td>&lt;0.0003¶</td>
</tr>
<tr>
<td>Size of bullae by chest X-ray (cm).</td>
<td>17</td>
<td>4.3 (0.8)</td>
<td>4.2 (0.8)</td>
<td>0.083¶</td>
</tr>
<tr>
<td>Size of bullae by chest CT (cm).</td>
<td>17</td>
<td>10.9 (2.8)</td>
<td>9.1 (2.5)</td>
<td>0.0002§</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD) or median (interquartile range).

¶: Paired-samples t-test. §: Wilcoxon signed ranks test.
Bronchoscopic Biological Lung Volume Reduction in Emphysema

Fig. (3): Mean FEV$_1$ before and after BLVR in the whole study population.

Fig. (4): Mean RV before and after BLVR in the whole study population.

Fig. (5): Mean 6 MWT before and after BLVR in the whole study population.

Fig. (6): Mean PaO$_2$ on room air before and after BLVR in the whole study population.

Fig. (7): Mean size of bullae before and after BLVR as estimated with chest X-ray in the emphysematous bullae group.

Fig. (8): Mean size of bullae before and after BLVR as estimated with chest CT in the emphysematous bullae group.
Table (4): Comparison of the outcome measures before and after BLVR in patients with emphysematous bullae or heterogeneous emphysema.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Heterogeneous emphysema (n=13)</th>
<th>Emphysematous bullae (n=17)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 before BLVR (% of predicted)</td>
<td>30.4 (6.9)</td>
<td>34.9 (9.7)</td>
<td></td>
</tr>
<tr>
<td>FEV1 after BLVR (% of predicted)</td>
<td>49.4 (16.0)</td>
<td>51.5 (15.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RV before BLVR (% of predicted)</td>
<td>141.9 (13.6)</td>
<td>167.6 (23.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RV after BLVR (% of predicted)</td>
<td>132.8 (16.4)</td>
<td>153.1 (23.6)</td>
<td></td>
</tr>
</tbody>
</table>

Table (7): Procedure related complications.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of affected patients</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoptysis</td>
<td>16</td>
<td>30</td>
</tr>
<tr>
<td>Cough</td>
<td>22</td>
<td>30</td>
</tr>
<tr>
<td>Low grade fever</td>
<td>7</td>
<td>30</td>
</tr>
<tr>
<td>COPD exacerbation</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
<td>30</td>
</tr>
</tbody>
</table>

Table (5): Prevalence of pulmonary scarring among patients with heterogeneous emphysema.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary scarring</td>
<td>7 (53.8%)</td>
<td>13</td>
</tr>
</tbody>
</table>

Fig. (9): Percentage of pulmonary scarring among patients with heterogeneous emphysema.

Table (6): Comparison of the characteristics and change in outcome measures in patients with emphysematous bullae or heterogeneous emphysema.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Heterogeneous emphysema (n=13)</th>
<th>Emphysematous bullae (n=17)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63.2 (4.5)</td>
<td>56.8 (9.5)</td>
<td>0.024§</td>
</tr>
<tr>
<td>Change in FEV1 (% of predicted)</td>
<td>19.0 (15.0)</td>
<td>16.6 (10.9)</td>
<td>0.613§</td>
</tr>
<tr>
<td>Change in RV (% of predicted)</td>
<td>-9.1 (7.6)</td>
<td>-13.6 (10.1)</td>
<td>0.182§</td>
</tr>
<tr>
<td>Change in RV (m)</td>
<td>38.5 (34.1)</td>
<td>89.8 (63.8)</td>
<td>0.009§</td>
</tr>
<tr>
<td>Change in MRCD score</td>
<td>0 (-1 to 0)</td>
<td>-1 (-1 to 0)</td>
<td>0.333³</td>
</tr>
<tr>
<td>Change in PaO2 (mmHg)</td>
<td>2.5 (1.5)</td>
<td>6.8 (4.0)</td>
<td>0.0005§</td>
</tr>
</tbody>
</table>

Table (8): Selected cases in the study.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Before</th>
<th>After</th>
<th>Before</th>
<th>After</th>
<th>Before</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>35</td>
<td>44</td>
<td>25</td>
<td>46</td>
<td>35</td>
</tr>
<tr>
<td>Case 2</td>
<td>78</td>
<td>80</td>
<td>60</td>
<td>72</td>
<td>78</td>
</tr>
<tr>
<td>Case 3</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Discussion

In both the surgical treatment as well as the endoscopic treatment of emphysema, the therapeutic aim is similar: Diminish pulmonary hyperinflation. BLVR is able to: Reduce respiratory effort and pressure on the diaphragm and chest wall, improve lung elasticity, reduce airway resistance, improve the ventilation/perfusion ratio and there-
fore oxygenation and improve breathing dynamics by reducing dyspnea and increasing tolerance to exercise [9].

This study was conducted on thirty patients chronic obstructive pulmonary disease with emphysematous bullae or heterogeneous emphysema. Chest X-ray and high resolution CT chest were used to detect the site and size of the bullae, and to measure the Hounsfield Units of the lung to determine the heterogenicity of emphysema and the most affected site to be injected in the procedure.

In the present study, results of FEV1% for the whole study population after the procedure showed highly significant rise (from 32.9±8.8 to 50.6±15.5 p-value <0.0001).

In the first group (emphysematous bullae) FEV1% results showed highly significant values (from 34.9±9.7 to 51.5±15.5, p-value <0.0001) 16.6% which agreed with the results achieved by Sherif M. et al., [10] who used autologous blood (10ml) and gel foam (10ml) injection for thirty patients with emphysematous bullae (from 25.9±10.2 to 41.8±9.9, p-value 0.0001) 15.9%. Zaid Zoumot et al., [11] who used autologous blood (240ml) injection for five patients with giant emphysematous bullae (from 36.4±16.8 to 53.7±17.8) 17.3% and Santini M. et al., [12] who used endobronchial valves EBVs insertion in nine patients with giant emphysematous bullae (from 35±9.9 to 52±17, p-value <0.01) 17%. These results were better than the results which obtained by QingTian et al., [13] who used EBVs insertion in five patients with giant emphysematous bullae (from 27.1±11.4 to 32.8±12.0 p-value >0.05) 5.7%, due to presence of collateral ventilation in three of them.

In the second group (heterogeneous emphysema) FEV1% results showed highly significant values (from 30.4±6.9 to 49.4±16.0, p-value 0.0006) 19% which agreed with the results achieved by Criner et al., [14] (high dose group 20ml, not low dose group 10ml) who used 20ml (per site) of hydrogel (fibrinogen and thrombin solutions) injection for twenty two patients with heterogeneous emphysema (upper lope predominant) at eight subsegments four in each side (from 28±7.15 to 50±24.4, p-value 0.003) 22% after six weeks follow-up.

These results were in agreement with Refaely et al., [15] who used 20ml (per site) of hydrogel (fibrinogen and thrombin solutions) injection for seventeen patients with advanced heterogeneous emphysema at eight subsegments (from 29.6±8.59 to 41.2±16.36, p-value 0.007) 11.6% after three months follow-up due to the nature of heterogeneous emphysema which give results bad than the heterogeneous one. These results were less than the results obtained by Mordechai et al., [16] who used 20ml (per site) of gelfoam (AeriSeal®) injection for twenty patients (ten patients with homogenous type and ten patients with heterogeneous type) at four subsegments two on each site (from 32.7±8.7 to 61.6±30.6, p-value 0.003) 28.9% due to follow-up after three months.

Also agreement with results obtained by Wan et al, [17] who used endobronchial valves insertion in ninety-eight patients (multicenter study, nine centers in seven countries) with heterogeneous emphysema (from 30.1±10.7 to 40.8±26.2%, p-value 0.007) 10.7% but were agreed with the results which obtained from patients managed with EBVs in unilateral manner rather than bilateral (sixty four patients) and lobar exclusion rather than non lobar (70 patients) in the same study (16.3%) after three months follow-up.

In the first group (emphysematous bullae) RV% results showed highly significant values (from 166.7±23.5 to 153.1±23.6, p-value <0.0001) 13% which are agree with the results achieved by Sherif M. et al., [10] (from 128.00±70 to 117.00±4.051, p-value 0.0001) 11%, but less than the result obtained by Santini M. et al., [12] (from 231±32 to 142±33 p-value <0.01) -89% because he used a guided insertion device, and agree with kanoh et al., [18] who used an autologous blood (10ml) and fibrinogen and thrombin solution (3ml) under fluoroscopic guide for LVRT in one case report (from 150% to 110%) 40%.

In the second group (heterogeneous emphysema) RV% results showed highly significant values (from 141.9±13.6 to 132.8±16.4, p-value 0.001)-9.1% which agreed with the results achieved by Criner et al., [14] (from 197.6±29.94 to 187.9±14.5, p-value 0.022)-9.7%, and agree with results obtained by Mordechai et al., [16] (from 218.0±43.3 to 208.9±18.2, p-value 0.036)-10.9%, but the results were less agree with results obtained by Refaely et al., [15] (from 195.3±49.94 to 190.3±6.54 p-value >0.05)-5% after three months follow-up due to the nature of heterogeneous emphysema which give results bad than the heterogeneous one.

These results were agreed with the other which achieved by Ralf Eberhardt et al., [19] who used endobronchial valves EBVs insertion in the first group (eleven patients with heterogeneous emphysema), patients received unilateral valves aiming
for total occlusion of one lobe (from 264.8±46.98 to 255.6±22.0) -9.2% but the results are better than other one obtained from the second group (11 patients with heterogeneous emphysema), valves were placed in two contralobes with incomplete closure (from 269.3±66.89 to 268.2±17.1) -1.1% after one month follow-up in the same study.

These results are in agreement with achieved results of Wan et al., [17] who used the one way valves AS described before and reported that there was decline of RV% after BLVR for -4.9% (from 244.3±60.3 to 239.4±17.4, p-value 0.025).

The results are less than achieved by Venuta et al., [20] who used endobronchial valves EBVs insertion in thirteen patients with heterogeneous emphysema (from 233±75.5 to 207±74 p-value 0.01) 26% after one month follow-up mostly due to it was performed as unilateral BLVR in 11 and bilateral BLVR in 2 patients only (unilateral give better results than bilateral).

These results were agreed with the results achieved by Dirk-Jan et al., [21] who used coils for LVRT in twenty patients with heterogeneous emphysema (from 225±43 to 212.6±9.0, p-value <0.001) –12.4% one month after second treatment, Cardoso et al., [22] who used paclitaxel-eluting stents for LVRT in thirty two patients with homogeneous emphysema RV improvement was –12%.

The results of 6 MWT for the whole study population after the procedure showed highly significant rise (from 275.7±85.3 to 343.2±83.1, p-value <0.0001).

In the first group(emphysematous bullae) 6 MWT results showed highly significant values (from 235.4±83.0 to 325.1±96.1, p-value <0.0001) +89.7m which agreed with the results achieved by Zaid Zoumot et al., [11] who used autologous blood (240ml) injection for five patients with giant emphysematous bullae +88m±69.9. and with results obtained by William McNulty et al., [23] who used autologous blood (240ml) injection for six patients with giant emphysematous bullae (from 274±209.5 to 374±216)+100m.

The obtained results in this study are more than the achieved results by Sherif M. et al., [10] (from 231.33±31.675 to 271.17±40.888 p-value 0.0001) +39.84m, but less than the results obtained by Santini M. et al., [12] (from 156±92 to 291±93 p-value <0.01) +135m because he used a guided insertion device.

In the second group (heterogeneous emphysema) 6 MWT results showed highly significant values (from 328.5±55.5 to 366.9±57.5, p-value 0.002) +38.4m, these results match with the results that achieved by Criner et al., [14] in (low dose group 10ml, not high dose group 20ml) who used 10ml (per site) of hydrogel (fibrinogen and thrombin solutions) injection for twenty eight patients with heterogeneous emphysema (upper lobe predominant) at eight subsegments four in each side (from 349.9±97.67 to 390.1±40.8, p-value <0.001) +40.2 mafter six weeks follow-up, but better than the results of the other group, 22 patients with 20ml injection per site (from 291.4±83.87 to 283.5±70.7, p-value 0.660) 7.9m.

These results were agreed with the results achieved by Refaely et al., [15] (from 293.1±68.09 to 277.7±71.9, p-value >0.05) –15.4m after three months follow-up due to the nature of homogeneous emphysema which give results bad than the heterogeneous one.

These results were agreed with the results achieved by Anthony P. et al., [24] who used endobronchial valves insertion in twenty patients with heterogeneous emphysema (from 251.6±100.2 to 306.3±112.3, p-value 0.012) +54.7m after one month follow-up, and by Douglas E. et al., [25] who used endobronchial valves insertion in a multicenter trial for treatment of thirty patients with heterogeneous upper lobe-predominant emphysema, (from 334±110 to 360±113) +26m after six months follow-up, and by Wan et al., [17] who used endobronchial valves insertion in ninety-eight patients (multicenter study, nine centers in seven countries) with heterogeneous emphysema (from 303±118 to 326±55.3, p-value <0.001) +23m.

The results were less agreed with that achieved by Venuta et al., [20] (from 223±170 to 375±150, p-value 0.005) 152m after one month follow-up mostly due to it was performed as unilateral BLVR in 11 and bilateral BLVR in 2 patients only (unilateral give better results than bilateral).

These results were agree with results achieved by Ralf Eberhardt et al., [19] either in unilateral group (from 305.4±68.7 to 321.1±18.2) +15.7m or bilateral group (from 293.2±85.9 to 284.7±27.8) –8.5m after one month follow-up.

These results were less agree the results achieved by Dirk-Jan et al., [21] (from 338±112 to 407.8±64.2, p-value .006) 69.8m one month after second treatment.

The results of MMRC dyspnea score for the whole study population after the procedure showed highly significant value (from 3 (2-3) to 2 (2-2), p-value <0.0001).
In the first group (emphysematous bullae) MMRC dyspnea score results showed highly significant values (from 3 (3-3) to 2 (2-2), p-value 0.001) which agreed with the results achieved by Sherif M. et al., [10] (from 2.77±0.430 (2-3) to 1.50±0.509 (1-2), p-value 0.0001) after two weeks follow-up.

In the second group (heterogeneous emphysema) MMRC dyspnea score results showed significant values (from 3 (2-3) to 2 (2-2), p-value 0.031), these results agree with the results achieved by Criner et al., [14] either in low dose or high dose group (from 2.5±0.59 to 0.9±0.68, p-value <0.001) and (from 2.6±0.67 to –0.6±0.96, p-value 0.020) respectively after six weeks follow-up, and by Mordechai et al., [16] 2012 which show significant improvement of MMRC dyspnea score (-1, –1, p-value 0.011 after three months follow-up. And by Refaely et al., [18] who found that from 2.7 ±0.48 to –0.6±0.61, p-value >0.05 after three months follow-up due to the nature of homogeneous emphysema which give results bad than the heterogeneous one.

These results were agreed with the results achieved by Anthony P. et al., [24] from 3 (2-5) to 2 (1-5), p-value 0.006) after one month follow-up, also with the results achieved by Ralf Eberhardt et al., [19] in the first group who received unilateral valves aiming for total occlusion of one lobe (from 2.64±1.03 to –1.1 ±1.1) but the results are better than the results obtained from the second group who received valves which placed in two contralateral lobes with incomplete closure (from 3.09 ±0.94 to 0.0±1.0).

The results of PaO2 for the whole study population after the procedure showed highly significant value (from 66.0±6.0 to 70.9±4.7, p-value <0.0001).

In the first group (emphysematous bullae) PaO2 results showed highly significant values (from 62.7±5.1 to 69.5±5.0, p-value <0.0001) which agreed with the results achieved by Sherif M. et al., [10] (from 60.40±9.361 to 71.37±8.369, p-value 0.0001) after two weeks follow-up, but more than the results obtained by Santini M. et al., [12] (from 57±7.9 to 58±6.4).

In the second group (heterogeneous emphysema) PaO2 results showed highly significant values (from 70.2±4.3 to 72.7±3.7, p-value 0.0001), these results agree with the results achieved by Douglas E. et al., [25] who used endobronchial valves insertion in a multicenter trial for treatment of thirty patients with heterogeneous upper lobe-predominant emphysema, (from 70.6±4.2 to 72.9±9.0) after one month follow-up, but more than the results obtained by Venuta et al., [20] from 77±22.5 to 71±22, p-value 0.57) after one month follow-up.

As regard the size of the bullae in the first group, the results achieved in this study showed that there is non-significant changes in bullae size in CXR (from 4.3±0.8 to 4.2±0.8, p-value 0.083) but showed highly significant reduction in the mean size of the bullae in HRCT (from 10.9±2.8 to 9.1±2.5, p-value 0.0002) which agreed with the results achieved by Sherif M. et al., [10] (from 4±0.3 to 3.5±0.4, p-value 0.231) for CXR and (from 10±3 to 8±2, p-value 0.01) for HRCT.

The results were less than achieved by Zaid-Zoumot et al., [11] who used autologous blood (240ml) injection for five patients with giant emphysematous bullae and showed decreased in the size in all patients 100% due to high dose of injected blood for only five patients, Santini M. et al., [12] who used endobronchial valves EBVs insertion in nine patients with giant emphysematous bullae showed that there is a reduction in the size of bullae in eight patients because he used a guided insertion device, also these results are low regarding the achieved results in the case reported by kanoh et al., [18] in which the bulla size decreased from 12cm to 3cm after BBLVR as the injection was done under fluoroscopic guidance.

As regard the scar formation in the second group, the results achieved in this study showed that there is Pulmonary scarring as HRCT finding in 7 patients (53.8%), which compatible with the results achieved Refaely et al., [18] who showed 60% of patients with pulmonary scarring after three months follow-up, Criner et al., [14] who showed in low dose group that 57% of patients had pulmonary scarring, but less than the high dose group which showed 68% of patients had scarring after six weeks follow-up, also Anthony et al., [24] who showed 43% of patients had pulmonary atelectasis after endobronchial valves insertion in twenty patients with heterogeneous emphysema after one month follow-up.

In this study all patients were discharged from the hospital in the same or the second day of BBLVR treatment. No serious adverse events were observed in any patient during or after BBLVR therapy. Adverse events were minor and transient, and most of them were likely attributable to the bronchoscopic procedure. They included haemoptysis in sixteen patients from the injected blood which persist for one or two days, irritating cough in twenty two patients, low grade fever in seven
patients, one patient (58 years old with GOLD stage 3 airflow obstruction and had emphysematous bulla occupying anterior segment of the right upper lobe) developed mild COPD exacerbation after 2 weeks of the procedure and treated in outpatient chest clinic, no reported cases complicated by pneumothorax and no mortality.

This agree with the multicenteric studies done by Criner et al., [14] and Refaeley et al., [15] in which there were no deaths or serious medical complications during the study.

The achieved results were agreed with the results obtained by Venuta et al., [20] who observed complications in 3 patients (23% of the patients), complicated by pneumothorax and one patient had pneumonia. Patients with complications need hospitalization till stabilization of the condition, Mordechai et al., [16] who stated that there were two deaths during follow-up period. One occurred in a 76-year-old male patient with GOLD stage IV airflow obstruction and advanced homogeneous emphysema who developed a tension pneumothorax immediately post treatment attributed to either catheter trauma or barotrauma. The patient was intubated and stabilized, but subsequently developed nosocomial sepsis and died on study day 9. The second death, on study day 32, was due to pancreatic cancer that was not detected at screening. The remaining events included three COPD exacerbations, one upper respiratory tract infection and two pneumonias.

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العلاج البيولوجي لتقليل حجم الرئة بواسطة المنظار الشعبي لمرضى الانتفاخ الرئوي

هـدف هذا البحث إلى تقييم مدى أمان وفعالية إجراء العلاج البيولوجي لتقليل حجم الرئة بواسطة المنظار الشعبي باستخدام الدم الذاتي والرغوة الهلامية في علاج مرضى الانتفاخ الرئوي.

ومن أجل تحقيق ذلك تم إجراء هذا البحث على ثلاثين مريضاً تم تشخيصهم بممرض السدة الرئوية المزمنة (الانتفاخ الرئوي) داخل قسم الصدر بمستشفى الحسن وسجع خلال العام وقد تم تقسيم المرضى إلى مجموعتين: مريضاً وسجعة مريضاً مرضى ذوي انتفاخ رئوي. وقد تم ذلك بواسطة المريض على بعد الفحوصات اللازمة لعمل البحث.

وقد تم عمل اشعة مقطعية عالية التفاوت قبل وبعد البحث. وتم إجراء منظار شعبي تحت المشرد الموضعي حيث تم حقن عشرة مليلاتر من الدم الذاتي وخمسة مليلاتر من حمض البرانيدامين وعشرة مليلاتر الرغوة الهلامية في العلاج الهوائي المغذى للفقاعات التنافخية (المجموعة الأولى) وفي دون القطعات الأربع الأكثر تضرراً بكلا الجانبين (المجموعة الثانية).

وقد أظهرت التحليل تحسن سرعة تدفق الهواء الزفير في الثانية الأولى وصعوبة اختبار المشي لمدة 6 دقائق وضغط الأكسجين في الدم الشرياني بعد العلاج لكل مريض من الدراسة.

وقد خصص البحث إلى أن العلاج البيولوجي لتقليل حجم الرئة بواسطة المنظار الشعبي باستخدام الدم الذاتي والرغوة الهلامية في علاج الانتفاخ الرئوي المتقدم خاصة النوع الغير متئاسي من هو إجراء يتمتع بالأمان وأظهر تغييرات معنوية على مستوى فيتخار وталوق التنفس وغازات الدم الشرياني واختبار المشي.