**Routinary use of fibrin sealants to prevent prolonged air leak in thoracic surgery: our experience**

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**SUMMARY:** Routinary use of fibrin sealants to prevent proloned air leak in thoracic surgery: our experience.


Introduction. Prolonged air leak (PAL) is one of the most common postoperative complications after lung surgery. It is associated with increased significant morbidity, lower quality of life, longer hospital stay and higher hospital costs. Since its great clinical and economic burden, it is important to establish the feasibility and the effectiveness of the routinary preventive use of a fibrin sealant in order to reduce the incidence of prolonged air leaks.

Patients and methods. This is a randomized study on 189 adult patients - 118 men (62.4%) and 71 women (37.6%) aged from 39 to 87 y.o. (mean age 68.3 y.o.) - who underwent lung surgery (lobectomy or bilobectomy) from January 2013 to December 2017, at Department of Thoracic Surgery in “Ospedale Maggiore Carlo Alberto Pizzardi” (Bologna, Italy) and Department of Thoracic Surgery in “Paolo Giaccone” Teaching Hospital (Palermo, Italy). Patients were randomly assigned to the “Glue” arm (90 patients) or the “Control” group (99 patients). We only used stapler or manual suture to achieve aerostasis. In addition, we used a fibrin sealant (“glue”) to cover the suture line on patients in the “Glue” arm. The primary endpoints were incidence of prolonged air leaks, days with chest tube and mean hospital stay.

Results. In the “Glue” arm we experienced only 1 prolonged air leak (1.1%), while in the “Control” group there were 8 leaks (8.1%). Patients kept chest tube for average 4.15 days in the “Glue” arm and 4.45 days in the “Control” group. The mean hospital stay was average 7.4 days for the “Glue” arm, while 9.1 days in the “Control” group.

Conclusions. According to our experience it seems that the routinary preventive use of a fibrin sealant results in a lower incidence of prolonged air leaks, a shorter hospital stay with lower hospital costs, representing a cost-effective, feasible and effective system to decrease morbidity and mortality among surgical patients.

**KEY WORDS:** Prolonged air leak - Pneumothorax - Alveolo-pleural fistula - Fibrin glue - Thoracic surgery - Lung.

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5), lower quality of life (tough post-surgical mobilization, poor pain control), longer hospital stay (1) and therefore higher hospital costs (5). Despite recent methodical and technological improvements (e.g. fissureless technique, use of staplers) literature data report an incidence ranging from 4 to 50% (2, 6). Several preventive efforts (e.g. mechanical or chemical pleurodesis (7-11), staple line buttressing (12), pleural tenting (13), use of fibrin sealants or thrombin patches (14-16), electrocautery or use of laser (17, 18) have been tried with various and sometimes conflicting results (6, 19-21). Since its great clinical and economic burden, in the absence of guidelines, it is important to establish the feasibility and the effectiveness of the routinary preventive use of a fibrin sealant (“glue”) in order to reduce the incidence of prolonged air leaks.

Patients and methods

This is a randomized study on 189 adult patients – 118 men (62.4%) and 71 women (37.6%) aged from 39 to 87 y.o. (mean age 68.3 y.o.) – who underwent lung surgery (lobectomy or bilobectomy) (Table 1) with intraoperative detection of air leakage, from January 2013 to December 2017, at Department of Thoracic Surgery in “Ospedale Maggiore Carlo Alberto Pizzardi” (Bologna, Italy) and Department of Thoracic Surgery in “Paolo Giaccone” Teaching Hospital (Palermo, Italy). The surgical procedures were always performed by the same surgical team with open technique. Before surgery, patients were randomly assigned to the “Glue” arm or the “Control” group. We only used stapler or manual suture to achieve aerostasis. No further aerostatic procedure were carried out (e.g. pleural tenting, patch coverage, chemical pleurodesis). In addition, we used a fibrin sealant (“glue”) to cover the suture line on patients in the “Glue” arm. We used 2-4 ml of a human thrombin (250 IU/mL), human fibrinogen (45.5 mg/mL) and aprotinin-based (1500 KIU/mL) fibrin glue – Tisseel® (Baxter International, Deerfield, USA) – sprayed over the suture line to seal it. No selection bias was made according to age, sex and race. Variables were compared using $\chi^2$ test. A p-value <0.05 was considered statistically significant. The primary endpoints were incidence of prolonged air leaks, days with chest tube and mean hospital stay.

Results

At the end of the trial, the “Glue” arm was homogeneous and composed of 90 patients – 57 men (63.3%) and 33 women (36.7%) – aged from 42 to 87 y.o. (mean age 68.8 y.o.). Their mean forced expiratory volume in one second (FEV$_1$) was 85%. On average, patients underwent single lobectomy procedure - 54 upper lobe (60%) vs 30 lower lobe (33%). In 42 patients the removed lobe was in the left lung (46.7%); 46 in right lung (51.1%). In 4 patients

Table 1 - Patient Characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Glue (n=90)</th>
<th>Control (n=99)</th>
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</thead>
<tbody>
<tr>
<td>Sex (M/F)</td>
<td>57/33</td>
<td>61/38</td>
</tr>
<tr>
<td>Age</td>
<td>42-87 (mean 68.8)</td>
<td>39-84 (mean 67.8)</td>
</tr>
<tr>
<td>FEV$_1$ (mean)</td>
<td>85%</td>
<td>88%</td>
</tr>
<tr>
<td>Procedures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left Upper Lobectomy</td>
<td>25 (27.8%)</td>
<td>24 (24.2%)</td>
</tr>
<tr>
<td>Right Upper Lobectomy</td>
<td>29 (32.2%)</td>
<td>36 (36.4%)</td>
</tr>
<tr>
<td>Left Lower Lobectomy</td>
<td>17 (18.9%)</td>
<td>19 (19.2%)</td>
</tr>
<tr>
<td>Right Lower Lobectomy</td>
<td>13 (14.4%)</td>
<td>12 (12.1%)</td>
</tr>
<tr>
<td>Middle Lobectomy</td>
<td>4 (4.4%)</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Upper Bilobectomy</td>
<td>2 (2.2%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Lower Bilobectomy</td>
<td>0 (0%)</td>
<td>3 (3%)</td>
</tr>
</tbody>
</table>
(4.4%) we removed the medium lobe. Only 2 patients (2.2%) underwent upper bilobectomy procedure. Instead the “Control” group was composed of 99 patients – 61 men (61.6%) and 33 women (38.4%) – aged from 39 to 84 y.o. (mean age 67.8 y.o.). Their mean forced expiratory volume in one second (FEV1) was 88%. On average, patients underwent single lobectomy procedure - 60 upper lobe (60.6%) vs 31 lower lobe (31.3%). In 43 patients the removed lobe was in the left lung (43.4%); 52 in right lung (52.5%). In 4 patients (4.4%) we removed the medium lobe. Only 4 patients (4%) underwent upper or lower bilobectomy procedure. On the later analysis the two groups look quite homogeneous and no gross biases arise. In the “Glue” arm we experienced only 1 prolonged air leak (1.1%), while in the “Control” group there were 8 air leaks (8.1%). This result appears statistically significant (p=0.025). Patients kept chest tube for 4.15 days in the “Glue” arm and 4.45 days in the “Control” group. This outcome appears similar in the two groups, therefore not statistically significant. The mean hospital stay was 7.4 days for the “Glue” arm, while 9.1 days in the “Control” group. It is acknowledged a statistically significant result for this endpoint (p=0.010). In summary, it seems that the routinary use of a fibrin sealant may result in a lower incidence of prolonged air leaks (1.1% vs 8.1%) and a shorter hospital stay (7.4 days vs 9.1 days) with lower costs (Table 2).

Since healthcare charges are increasing ever more, there is a growing pressure to reduce hospital stay thus better controlling costs. Even though it is widely proved that using fibrin sealants is feasible and effective to reduce prolonged air leaks (6, 19, 22), improving financial performance (5); no guideline actually recommends the routinary preventive use of fibrin sealants to reduce the incidence of PAL. This is probably related to the various and sometimes conflicting results conveyed by previous studies, leading to a lack of consensus (6, 14, 20-23). Fibrin sealants act like a real glue, sticking rapidly to the lung tissue, facilitating coagulative cascade and granting both hemostasis and aerostasis, thanks to their capability to promote tissue regeneration. They are easy to use, cost-effective and generally well-tolerated. Even though a potential risk of Human Parvovirus B19 blood-borne transmission has been recently demonstrated (24), the use of an autologous fibrin glue (6) would avoid this issue. In fact in this case, fibrin is obtained direct from patient’s blood (although more complicated and expensive). In summary, as pointed out from our study, the use of fibrin sealants is a cost-effective, safe and feasible system for reducing the incidence and complications linked to PAL. According to our experience, the routinary preventive use of a fibrin sealant results in a lower incidence of prolonged air leaks (1.1%), a shorter hospital stay (on average 7.4 days) thus lower costs.

Discussion

Prolonged air leak (PAL) is one of the most common postoperative complications after lung surgery and one of the most challenging burden for hospital institutions. In fact it is associated with increased significant morbidity (cardiac complications, empyema, pneumonia) (4, 5), lower quality of life (tough postsurgical mobilization, poor pain control), longer hospital stay (1) and therefore higher hospital costs (5).

Table 2. PRIMARY ENDPOINTS.

<table>
<thead>
<tr>
<th></th>
<th>Glue</th>
<th>Control</th>
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<tbody>
<tr>
<td>Prolonged Air Leaks</td>
<td>1 (1.1%)</td>
<td>8 (8.1%)</td>
</tr>
<tr>
<td>Days of chest tube (mean)</td>
<td>4.15 days</td>
<td>4.45 days</td>
</tr>
<tr>
<td>Hospital stay (mean)</td>
<td>7.4 days</td>
<td>9.1 days</td>
</tr>
</tbody>
</table>

Conclusions

According to our experience it seems that the routinary preventive use of a fibrin sealant results in a lower incidence of prolonged air leaks, a shorter hospital stay with lower hospital costs. Therefore, it represents a cost-effective, feasible and effective system to decrease morbidity and mortality among surgical patients. Nevertheless further larger scale trials and meta-analysis are needed to get statistically significant conclusions and to recommend the routinary use of fibrin sealants in lung surgery.

Disclaimer

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References