



## REVIEW

# Epidemiology, Etiology and Prevention of Postpneumonectomy Pleural Empyema

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**Background:** Pleural empyema after pneumonectomy still poses a serious postoperative complication. A broncho-pleural fistula is often detected. Despite various therapeutic options developed over the last five decades it remains a major surgical challenge.

**Materials and methods:** A literature search in MEDLINE database was carried out (accessed through PubMed), by using a combination of the following key-words and MeSH terms: pneumonectomy, postoperative, complications, broncho-pleural fistula, empyema, prevention. The following areas of intervention were identified: epidemiology, etiology, prevention.

**Results:** Pleural empyema in a post-pneumonectomy cavity occurs in up to 16% of patients with a mortality of more than 10%. It is associated with broncho-pleural fistula in up to 80% of them, usually in the early postoperative months. Operative mortality could reach 50% in case of broncho-pleural fistula. Unfavourable prognostic factors are: benign disease, COPD, right-sided surgery, neoadjuvant and adjuvant therapy, time of chest tube removal, long bronchial stump and mechanical ventilation. Bronchial stump protection with vascularised flaps is of utmost importance in the prevention of complications.

**Conclusion:** Postpneumonectomy pleural empyema is a common complication with high mortality. The existing evidence confirms the role of bronchopleural fistula prevention in the prevention of life-threatening complications.

## INTRODUCTION

Postoperative pleural empyema is the second most frequent form of empyema, accounting for up to 20% of all pleural empyemas. It occurs usually after surgery of the lungs, esophagus or mediastinum, but it may occur after abdominal, urologic, and pelvic operations as well.<sup>1</sup> The incidence is 1% to 3% after lobectomy and 2% to 12% after pneumonectomy.

Despite various therapeutic options developed during the last five decades, postpneumonectomy pleural empyema (PPE) is still associated with 10%-20% mortality rate, reaching up to 50% in case of broncho-pleural fistula (BPF), with high morbidity and prolonged hospitalization.<sup>2-5</sup>

The aim of this review is to summarize the epidemiology, etiology and prophylaxis data in PPE. The treatment is discussed elsewhere.

## MATERIALS AND METHODS

We performed a literature search in MEDLINE database (accessed through PubMed) by using a combination of the following key words and MeSH terms: pneumonectomy, postoperative, complications, broncho-pleural fistula, empyema, prevention. The search strategy did not include time limits and was performed in May 2016. We included references irrespective of the study design and published in the English language. We excluded references published in abstract form only.

Prevention of complications was covered by 32 papers. Rather than being exhaustive, our objective was to narratively explain the results from the most relevant papers identified in the following areas of intervention:

### 1. Epidemiology

2. Etiology
3. Prevention

#### AREAS OF INTERVENTION

##### **Epidemiology**

The incidence of PPE is 4.4% - 16%.<sup>6</sup> 75% of it occurs within the first 3 months after pneumonectomy<sup>7</sup>, but its occurrence several years after the procedure has been reported as well<sup>8</sup>. In up to 80% of patients, PPE is associated with bronchopleural fistula (BPF).<sup>9</sup>

The range of PPE with BPF incidence is wide - 1.3%-15%. Recently, in a large study, it was reported to be 3.8%.<sup>10</sup>

##### **Etiology**

The role of well known errors in surgical technique as a cause of BPF and PPE, with consequences that become evident from the end of the operation and during the first 24-72 postoperative hours, was not a subject of the analysis. Other factors identified as unfavorable in terms of PPE occurrence are: benign disease and low DLCO (p=0.001), followed by low FEV1 and serum hemoglobin, right-sided operation, completion pneumonectomy, time of chest tube removal and the amount of transfused blood.<sup>11</sup> Immunosuppression and neoadjuvant or adjuvant therapy were also identified as unfavorable prognostic factors.<sup>12,13</sup>

Longer length and absence of coverage of the bronchial stump, as well as the duration of the mechanical ventilation increase the risk of BPF. Although there are some suggestions that stapling of the bronchus is superior to manual suture, such statement is not sufficiently evidence-based.<sup>14</sup>

The postpneumonectomy cavity infection may occur incidentally as result of spillage of secretions from the bronchial tree at the moment of the bronchial cut, or as a result of occult bronchial stump leakage in the immediate postoperative period. These causes could be attributed to surgical technique and have not been specifically addressed in the literature, and therefore were not included in the review.

Concerning causative organisms, an increase of mixed infections with 2 or 3 strains of bacteria and an increase of Gram negative bacteria including *Pseudomonas aeruginosa* has been observed and confirmed by other studies, but often with cultures being negative because of the antibiotic treatment. Nevertheless, bacterial culture results were reported as useful in terms of perioperative prophylaxis.<sup>15,16</sup>

##### **Prevention of complications**

##### ***Bronchial suture technique***

The existing evidence does not suggest whether stapling devices are advantageous over the manual bronchial closure, given the incidence of BPF after manual and stapling closure being 0-17% and 0.8±5.4%, respectively.<sup>18-22</sup> Some modifications of the stapling closure, either in form of proximal or distant reinforcement to the stapling line, have been reported to decrease the BPF rate (from 1.9% to 1% with reinforcement of both sides), or to achieve very low BPF rate (0.7% with reinforcement of the proximal side).<sup>23,24</sup>

Despite some clear advantages of mechanical suture (more rapid closure and less probability for contamination of the pleural space), reliable comparison between the two techniques remains difficult, because in the reported series of manual suture of the bronchus, data about the exact way of suture (cartilage-to-membranous, cartilage-to-cartilage or membranous-to-membranous) are usually missing. These uncertainties about the bronchial closure technique underline the need to optimize the bronchial protection irrespectively of the applied suture technique.

##### ***Bronchial suture protection***

There is a broad consensus that bronchial stump protection with vascularised flaps plays an important role in the prevention of complications, especially in patients undergoing a pneumonectomy after chemo- or chemo/radiation therapy and especially for right-sided operations.<sup>25</sup> The most frequently reported flaps are intercostals muscle, pericardium, pericardial fat, diaphragm, omentum, azygos vein or latissimus dorsi.

There are different techniques of the bronchial stump protection. The technique of harvesting and efficacy of the intercostals flap was sufficiently documented quite a long time ago.<sup>26-28</sup> As the need for the flap use is sometimes not clear preoperatively, an alternative to full mobilisation of the flap is mobilisation from the rib only at the level of the rib spreader, thus making intercostals muscle still available in case of the unexpected need for the bronchial stump protection.<sup>29-31</sup> The key point of this quite simple technique is to avoid placement of the rib spreader before harvesting the full flap thickness and preservation of the periosteum. Recently, thoracoscopic and robotic preparation of this kind of flap have been reported as well.<sup>32,33</sup>

No major complications have been reported, except pedicle ossification, usually without major clinical implications.<sup>34,35</sup>

Given the consistent anatomy of thoracodorsal vessels, it is possible to split the latissimus dorsi muscle into separate units, so that the use of lateral split muscle flap has also been described.<sup>36</sup> The harvested muscle flap is rotated anteriorly and is passed through the second or third intercostals space into the pleural cavity. This method seems to be preferred to serratus transposition, because the problem of wing scapula can be avoided.

Diaphragm flap seems to be more frequently used than reported in the literature. Rare reports are in favour of its use as efficient for the bronchial stump reinforcement after pneumonectomy.<sup>37</sup>

Studies comparing muscle flap techniques, although suggesting a smaller operative morbidity with intercostal muscle vs. diaphragmatic flaps, did not confirm a statistical significance of such a difference. In addition, a thick diaphragmatic flap is a suitable option for extended resections with wide pericardiectomy, when compared to only bronchial stump coverage, but the pericardial defect closure is necessary as well.<sup>38</sup>

Pericardial flap is used less frequently. It can be prepared by incising the pericardium in a way to avoid a pericardiophrenic bundle, rotating and placing it over the suture line or around bronchial anastomosis.<sup>39,40</sup> Pericardial fat pad graft is a very suitable solution, but not always available, especially in thin individuals or after previous lung resection, if a complete pneumonectomy is anticipated. The viability of this flap is based on thin pericardial branches of the internal mammary artery.<sup>41</sup>

The omentum has been reported as very useful for the bronchial suture protection<sup>42,43</sup>, with a very low rate of failure, like in 35 patients with a high risk of fistula after right pneumonectomy and in two patients with an acute bronchial fistula, with only one patient with treatment failure<sup>44</sup>. The omentum produces angiogenic factors and has anti-inflammatory and immunological effects as well.<sup>45</sup> The prevention of infections is based on lymphocytosis and other immunocompetent elements which leads to decreases bacterial burden. The main disadvantage of the omental transposition, the extension of the surgery into the abdomen, usually in patient not fit for major surgery, can be overcome by recently proposed transdiaphragmatic harvesting, thus avoiding a laparotomy. The experience on 43 patients at high risk for pneumonectomy confirmed this method

as safe and efficient.<sup>42</sup>

Although not frequently cited in the literature, azygos vein flap has been also reported as effective for the bronchial stump coverage.<sup>46,47</sup> Recently, a pedicled internal mammary artery flap has also been shown as suitable for the bronchial stump reinforcement.<sup>48</sup>

## CONCLUSIONS

Postpneumonectomy pleural empyema occurs in up to 16% of operated patients, being associated with BPF in up to 80% of them, usually in the early postoperative months. Operative mortality after PPE is 10-20%, reaching up to 50% in case of bronchopleural fistula. Unfavourable prognostic factors of PPE are: benign disease, COPD, right-sided operation, neoadjuvant and adjuvant therapy, time of the chest tube removal, long bronchial stump and mechanical ventilation. Bronchial stump protection with vascularised flaps is of utmost importance in the prevention of complications. The most frequently reported flaps are intercostals muscle, pericardium, pericardial fat, diaphragm, omentum, azygos vein or latissimus dorsi.

Despite the evident progress in the field of technology, bronchial suture tools and techniques, preoperative and postoperative care, postpneumonectomy pleural empyema, either with or without bronchopleural fistula, remains a major surgical challenge. The existing evidence clearly confirms the role of bronchopleural fistula prevention in the prevention of life-threatening complications.

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## Эпидемиология, этиология и профилактика постпульмонэктомической эмпиемы плевры

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**Введение:** Эмпиема плевры после пневмонэктомии все ещё является серьёзным послеоперационным осложнением. Бронхоплевральный свищ устанавливается часто. Несмотря на разнообразие вариантов лечения, которые были разработаны в течение последних пяти десятилетий, он продолжает оставаться серьёзной хирургической проблемой.

**Материалы и методы:** Обзор литературы был проведён в базе данных Medline (доступ к которой осуществляется через PubMed) с использованием комбинации следующих ключевых слов и терминов MeSH: пневмонэктомия, послеоперационный, осложнения, бронхоплевральный свищ, эмпиема, профилактика. Были определены следующие области поиска: эпидемиология, этиология, профилактика.

**Результаты:** Эмпиема плевры в постпневмонэктомической полости наблюдалась у 16% пациентов со смертностью более 10%. Она связана с бронхоплевральным свищом более чем у 80% из них, как правило, в первые послеоперационные месяцы. Хирургическая смертность может достигать 50% в случаях бронхоплеврального свища. Неблагоприятными прогностическими факторами являются: доброкачественное заболевание, ХОБЛ, правосторонняя хирургия, неоадьювантная и адьювантная терапия, время удаления торакального дренажа, длинная культя бронха и искусственная вентиляция лёгких. Закрывание культи бронха с использованием васкуляризированной ткани имеет первостепенное значение для предотвращения осложнений.

**Выводы:** Постпульмонэктомическая эмпиема плевры является распространённым осложнением с высокой смертностью. Имеющиеся данные подтверждают роль профилактики бронхоплеврального свища в профилактике опасных для жизни осложнений.