TREATMENT OF BRONCHIAL FISTULA ASSOCIATED WITH NON-SPECIFIC CHRONIC PLEURAL EMPYEMA (REVIEW)

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https://doi.org/10.35339/ic.8.3.168–176

Abstract
The purpose of the study was to identify the prevalence of allergic rhinitis (AR) symptoms in children of Kharkiv and to establish the dynamics of symptoms since 1998. The study conducted in 2015–2017 is phase IV of the international ISAAC program. 5735 children were interviewed, including 3238 children aged 6–7 years and 2197 children aged 13–14 years. The incidence of non-cold-related sneezing was found in 14.7 % and 16.1 %, respectively; during the past 12 months similar problems with nose breathing were noted in 9.1 % and 9.9 %; accompanied by conjunctivitis – in 3.4 % and 4.8 % of children of 6–7 and 13–14 years, respectively. Most patients had seasonal exacerbations and mild/moderate rhinitis. AR diagnosis was verified in 12.2 % and 11.3 % of children, respectively. Decreasing of AR symptoms prevalence was found in children of all ages. The dynamics of AR symptoms prevalence, "eye" symptoms over the past 20 years show a probable decrease in all indicators, which can be explained by the widespread introduction in medical practice of screening methods for the disease diagnosing, activation of primary and secondary prevention.
Keywords: *children, allergic rhinitis, prevalence, ISAAC.*

Unsatisfactory treatment of tuberculosis, purulent and destructive lung diseases and lung cancer contribute to the development of bronchial fistulae and pleural empyema. Treatment of chronic pleural empyema with unsealed tracheobronchial tree is a complicated task for thoracic surgeons. After lung surgeries, the incidence of bronchopleural complications is 40% and the mortality rate is 5.6% [1]. Pleural empyema usually develops after operative interventions for purulent lung diseases [2, 3]. After resection on the lungs with underlying pleural empyema, bronchial fistula develops in 1.9–13.3% of patients with the mortality rate 20–50% [4–6].

Late diagnosis at the organisation stage, three weeks after the onset of chronic pleural empyema significantly worsens the treatment outcomes [7].

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Treatment outcomes of bronchia fistula associated with chronic pleural empyema are also worsened by continuous contamination of the residual pleural cavity with resistant microbial agents. Therefore, the main objective of surgical treatment is bronchial fistula sealing and obliteration of the residual pleural cavity. Absence of well-defined surgical tactics aimed at solving these two issues accounts for unsatisfactory treatment outcomes [8–10].

Since the incidence of lung cancer is rapidly increasing and this condition is already the second most prevalent oncological disease with a five-year survival rate of 17.8%, the number of complications following surgeries for this condition is also rapidly growing [11–13].

Even the first surgical intervention for lung cancer in the form of pneumonectomy can be complicated by development of pleural empyema. Recently, the number of pneumonectomies has significantly decreased to 7.3% [14].

Leakage of the main bronchus stump is the main source of development of a bronchial fistula and, subsequently, pleural empyema, including a chronic variety. The data of the European Society of Thoracic Surgeons report that bronchial fistula develops in 1.8% of cases after resections on the lungs [15, 16].

Development of bronchial fistulae in the early post-operative period usually results from intra-operative mistakes and inadequate artificial lung ventilation. Later development of fistulae usually has a secondary nature and results from infection processes in the tracheobronchial tree and pleural cavity; bronchial fistulae often develop as a result of a local relapse of the oncological process in the bronchial stump and in the presence of a residual tumour along the suture lines [17].

Single and multiple bronchial fistulae can be distinguished. Late bronchial fistulae usually appear after 8 to 10 weeks. In terms of size, bronchial fistulae are divided into three grades: with a diameter of up to 4 mm (Grade 1), from 5 to 10 mm (Grade 2), more than 10 mm (Grade 3) and complete branching of bronchial stump walls [18].

The main factors contributing to the development of bronchial fistulae and pleural empyema in the post-operative period remain residual pleural cavity, lack of aerostasis, long-lasting drainage of the pleural cavity, leakage of bronchial stump sutures due to ischemia, excessive skeletonization of mediastinum organs, bronchial stump diameter over 25 mm, long bronchial stump, prior chemo- and radiotherapy, massive intraoperative hemotransfusions, severe comorbidity, and immunodeficiency disorders [17, 19–23].

Furthermore, the bronchial stump closure technique and the extent of lung resection significantly affect the risk of bronchial fistula development [24].

According to other authors, development of the main bronchus stump leakage after lung resection or pneumonectomy occurs in 2.5–13.3% of cases and depends on numerous factors: etiological factor of the primary disease, severity of the general condition due to comorbidities, and method of bronchial stump formation [25–27].

The bronchial fistula development is caused not only by the above factors but also by the fact that extended lymph node dissection has become a standard in lung cancer surgeries [6, 28, 29].

Lack of bronchial stump isolation results in cavity formation near it, which creates favourable conditions for a bronchial fistula formation, mainly due to devascularization of the tracheal bifurcation area and the operational trauma [30].

There are three main objectives in the treatment of patients with bronchial fistulae – sanitation of the pleural cavity, removal of the bronchial fistula and removal of the chest wall defect. Some authors consider that the best technique for the treatment of bronchial fistulae after resection interventions on lungs are open surgeries [31].

Pleural cavity drainage, minimally invasive thoracoscopic techniques, and antibacterial therapy taking into account sensitivity to the microbial spectrum of causative agents do not achieve lung expansion, especially in the presence of a bronchial fistula [32, 33].

Bronchoscopic occlusion of the tracheobronchial tree defect is another widely discussed issue [34, 35].

There is data about spontaneous closure of the bronchial fistula with underlying chronic pleural empyema [36, 37].

The rigid lung and bronchial fistula prevent lung expansion by evacuating air from the pleural cavity, primarily due to the fibrine layers and several small fistulae or one fistula with a large diameter. The only way to achieve lung expansion is to seal the bronchial fistula. However, in the presence of pleural empyema it is reasonable to keep to a phased treatment tactics aimed at sealing the bronchial fistula only after pleural cavity sanitation. Throughout the history of thoracic surgery, many other techniques and devices have been developed to seal the bronchial fistula: different methods of endobronchial occlusion of the main bronchus – silver nitrate, ethanol, cyanoacrylate compounds, lead plugs, cylinder, fibrine and tissue glues, serum albumin, gel foam, autologous thrombi, antibiotics; transcervical occlusion of the bronchus stump, Angeo-Seal, Watanabe spigot, Amplatzer vascular plug, valves used for lung emphysema, devices for closing interatrial septum defects, valves, obturators used in cardiovascular surgery; variations of the transsternal transpericardial occlusion of the main bronchus stump first proposed by L.K. Bogush in 1972. Bronchi with fistulae are detected by bronchoscopy and bronchography. The above methods have many advantages as well as disadvantages [9, 38– 53].

The choice of the method and materials to achieve aerostasis also depends on the size of the bronchial fistula. In case of small fistulae (up to 3–4 mm), videothoracoscopic interventions can be performed using endoscopic methods, such as fistula site coagulation, glue sealing (fibrine glue), cuff link-type bone cyanoacrylate filling, 2–3 mm gelatine spherical obturators (with antibiotics), and closure. A positive aspect is the use of organic materials that dissolve and exclude the possibility of a foreign body remaining in the pleural cavity. These techniques help avoid repeated operations for the resection of bronchial obturators or bronchial link closure. It is not possible to close large defects using the above techniques due to the physical and technical properties of the materials used [54].

One of the wide-spread sealing materials is fibrine glue. Due to its biological structure, it can be injected in the submucosal layer of the bronchial stump without the rejection reaction, especially in case of small fistulae (up to 3 mm). In case of fistulae over 3 mm, it is recommended to use collagen plaster with a fibrine surface [9, 43, 44].

The most common synthetic sealing material is cyanoacrylate glue. It is polymerized on contact with biological fluids and body tissues. The development of an inflammatory response to the foreign agent in the site of its injection in the bronchial stump leads to development of fibrosis and proliferation of the mucous membrane of the bronchus, thus sealing the bronchial fistula [55].

There are disputes about large defects (more than 5 mm) because they must be sealed but also healed. Foam rubber bronchial obturators, spheric or conic, can be applied bronchoscopically in such cases. A foam rubber bronchial obturator can migrate to larger bronchi, which may cause atelectasis in healthy lung segments [56].

Occluders that were initially developed for the closure of interatrial and interventricular septa are also used for the treatment of bronchial fistulae. This technique is believed to have almost no side effects and is indicated to patients who require artificial lung ventilation and extracorporeal membrane oxygenation (ECMO) [39, 40, 42, 57].

Occlusion of the bronchus with a fistula using a foam rubber obturator is effective in 65.7–80% of cases [58, 59].

The effectiveness of bronchoscopic setting of the endobronchial valve is 91.7%. This method does not guarantee complete sealing of the bronchial fistula. The main complication of the blocking the bronchus with a valve is the valve migration to the adjacent bronchi with development of lung atelectasis [60, 61].

The closure of large defects is a more complex problem than the closure of small ones. Traumatic approaches to the stump of the leaking bronchus, thoracotomy and sternotomy involve a number of risks in the post-operative period. The positive outcome of bronchial fistula closure in open surgeries is observed in 80–5% of cases. These surgeries are usually complemented with reinforcing the bronchial stump with different tissue flaps. When repeated closure of the bronchial stump is not possible, the tissue flap is attached directly to the fistula area. The flaps are usually taken from the broadest muscle of the back, greater pectoral muscle, intercostal muscles, greater omentum on the feeding vascular pedicle, or free tissue flaps. According to different authors, the sealing of the bronchial stump was achieved in 75% and complete obliteration of the residual pleural cavity was achieved in 95% of patients [62–73].

It is not recommended to use pericardial flaps because the exposure of the mediastinum becomes a portal of entry on contact with infected pleural cavity [74].

High risks of mediastinum organ infection during surgeries involving purulent inflammation in the residual pleural cavity dictate the need to perform transpericardial sealing of the bronchial stump [73].

Most methods aim to prevent the occurrence of the main bronchus stump leakage and subsequent formation of bronchial fistulae. The main aim of preventive measures is to strengthen the stump with different biological materials, such as larger omentum, muscles, pleura, pericardium; fibrine-collagen plates are also used as the final stage of bronchial stump treatment [5, 29, 75].

There is an ongoing discussion about the method of bronchial stump closure. Should it be manual or hardware-assisted? The most common method is the bronchial stump treatment with its suturing through all layers using Suit's method. Another rather wide-spread method is wedged bronchus and bifurcation resection with transversal trachea closure using Sprengler's technique. All these open methods are widely spread, but, taking into account the bronchial stump leakage due to the uneven compression of bronchial tissues, the penetration of foreign agents in the bronchial lumen ruins the conditions for initial healing of the bronchial stump suture line. A combination of manual stump treatment with the use of an appliance for suturing the root of the lung rendered this stage of the operative treatment safer, which is confirmed by data from different studies indicating decreased formation of bronchial fistulae as compared to isolated uses of individual methods of tracheobronchial tree sealing [76, 77].

Another disputable question concerns the reasonability of supporting the bronchial stump suture line with muscle or tissue flaps on the vascular pedicle [20, 78, 79].

Some authors report an increased risk of bronchial fistula development after resections on lungs using additional methods for bronchial stump suture line sealing, thus indicating the ways to prevent the bronchial stump leakage: prevention of bronchus mucous membrane traumatization, tension-free closure of the bronchial stump, prevention of excessive skeletonization, precise approximation of stump edges "mucous to mucous" [24, 80].

Removal of the bronchial fistula does not guarantee recovery from chronic pleural empyema, and the tactics for the treatment of the residual cavity is controversial in such cases [81].

Resection of purulent and necrotic masses is the only way to treat pleural suppuration. Transcutaneous drainages with evacuation of the purulent content and sanitation of the pleural cavity help restore the evacuation function of the draining bronchus [82].

In 1961, J. Ambruzini proposed transsternal occlusion of the main bronchus stump, and in 1964 L.K. Bogush and Yu.L. Semenenkov modified the proposed method by exposing the pericardium widely along the anterior, superior and posterior side, repeatedly treating and dissecting the pulmonary artery stump, which made it possible to manipulate in the aortocaval space – Ambruzini space [47].

However, the above surgery is quite traumatic and complex, which makes it impossible to perform outside of a thoracic surgery department.

Lymph node dissection in extended pneumonectomy is difficult during the mobilization of the trachea and main bronchi due to the adhesive process, which becomes one of the main features in case of chronic pleural empyema. An indication to transsternal occlusion remains the length of the bronchial stump of at least 20 mm. However, L.K. Bogush believes that a 15 mm long bronchial stump is enough to perform this operation. Another disputable issue concerning the phases of transsternal main bronchus stump occlusion is the need to dissect the distal stump of the resected bronchus. Rejecting to resect the distal part of the bronchial stump, electrocoagulation of the mucous membrane is often opted for with closure from the mediastinal side. The authors separated the proximal and distal bronchial stumps with a pericardial flap and a muscle flap following Ginsberg in order to prevent bronchial stump recanalization. The advantages of transsternal occlusion include reduced relapse rates and duration of the in-patient stay [47, 83].

Since open transsternal surgeries are rather traumatic, thoracic surgeons are constantly searching for techniques allowing the closure of a bronchial fistula with a diameter of 2 to 10 mm and sealing of the pleural cavity. A two-component mushroom-shaped adhesive filling is used to fill the defect thoracoscopically from the side of the pleural cavity with the "cap" and the bronchoscopically from the side of the tracheobronchial tree with the "stem". The components of the filling are made of oxidized 100% cellulose impregnated with chlorhexidine solution and fibrine glue. Considering that tissues have homogeneous structure and composition, the bronchial fistula junctions on both sides stick together well and form a single complex that seals the fistula. The material of the filling prevents topical inflammation and development of the infection process due to the use of antiseptic solutions. It is good that no foreign bodies remain in the bronchial and pleural cavity after healing, tissue regeneration improves, and the fistula heals faster [84].

However, the removal of the bronchopleural fistula does not guarantee recovery from chronic pleural empyema. Another important issue in the treatment of pleural empyema remains the obliteration of the residual pleural cavity.

The history of residual pleural cavity obliteration dates back to the early 20th century. Different authors described the transposition of skeletal muscles to the pleural cavity, the use of a muscle flap on the feeding vascular pedicle, and a strand of the larger omentum and other tissue flaps to obliterate the residual pleural cavity [85–91].

There is a discussion about the use of different agents for obliteration, such as glycerine, fibrine with antibiotics taking into account the microbial sensitivity of the pathogenic flora, foam polymer compounds, and foam gel based on acrylic acids. Most of them were used historically [92].

Biological materials mostly used for the obliteration of the residual pleural cavity include the broadest muscle of the back, greater pectoral muscle, serratus anterior. Serratus anterior and rhomboid muscle are used less frequently [93–95].

Clinical trials indicate effective obliteration of the residual pleural cavity with muscles on the vascular pedicle with no pleural empyema relapses and a 5% mortality rate [96].

Thoracoplasty is another technique for the obliteration of the residual pleural cavity. There are many modifications of thoracoplasty, for example extrapleural subperiosteal thora-coplasty, intrapleural thoracoplasty using Schede's method, and thoracoplasty using Andrews' method [95, 97].

Foreign authors point to the effectiveness of thoracoplasty for obliteration of the residual pleural cavity in 77% of patients [95].

Other authors report a 11.7% mortality rate after thoracoplasty with the rhomboid muscle and serratus anterior [98].

There are no clear indications to thoracoplasty. Total thoracoplasties involve a large number of post-operative complications, pleural empyema relapses, a high mortality rate, and a high percentage of functional failures as compared with traditional and minimally invasive methods for the sanitation and obliteration of the residual pleural cavity [99].

Conclusions

The search for the optimal method of bronchial fistula sealing associated with non-specific chronic pleural empyema motivates thoracic surgeons to conduct further research aimed to improve the outcomes of traditional and minimally invasive surgical treatment. The literature contains many controversial opinions on using particular treatment methods, their phases and optimal terms. Upon analysing the above data it can be concluded that nowadays there is no single tactics for the surgical treatment of non-specific chronic pleural empyema, which motivates its creation.

Declarations

Statement of Ethics

The authors have no ethical conflicts to disclosure.

Consent for publication

All authors give their consent to publication.

Disclosure Statement

Authors have nothing to disclosure.

Funding Sources

There are no external sources of funding

Data Transparency

The data can be requested from the authors.

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Received: 18-Jun-2021
Accepted: 06-Sep-2021