



RISK FACTORS AND FREQUENCY OF AEROSTASIS AND HEMOSTASIS INSUFFICIENCY IN LUNG SURGERY (LITERATURE REVIEW)

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Article history:	Abstract:
Received: October 10 th 2023 Accepted: November 8 th 2023 Published: December 14 th 2023	The article provides a review of the literature on current problems in lung surgery – postoperative prolonged air leakage and bleeding from injured lung tissue. The advantages and disadvantages of various mechanical methods of strengthening lung tissue, as well as physical methods of exposure using local agents with adhesive properties, are highlighted. The various proposed methods of prevention and treatment can be used for both minimally invasive and traditional interventions, however, there are still no universal methods that provide reliable aerostasis, and therefore the search and research of new therapeutic and preventive measures dedicated to solving this issue remains a sought-after area in modern thoracic surgery.

Keywords: aerostasis and hemostasis; современной торакальной хирургии; postoperative complications; applications of synthetic and allomaterial flaps.

The issues of prevention of postoperative complications have always been and remain relevant in surgery. In thoracic surgery, it is known that the leading determinant in the prevention of respiratory disorders and the prevention of infectious complications is the fastest and most complete expansion of the lung in the postoperative period. One of the most important components contributing to this, in addition to effective drainage, restoration of muscle tone and adequate breathing, is reliable aerostasis and hemostasis [1-6].

The lack of stable aerostasis leads to incomplete lung expansion, pneumothorax with the formation of residual cavities, the development of empyema and bronchial fistulas. Along with infection, these complications become the main cause of progressive respiratory and heart failure, leading to fatal outcomes [7-11].

Inconclusive intraoperative aero- and hemostasis, and related complications, sometimes force an increase in the volume of surgery, and a violation of the tightness of the pleural cavity in the early postoperative period in some cases serves as an indication for rethoracotomy and expansion of the volume of surgery due to the remaining lobes of the lung [12-15].

With complete expansion of the lung, adequate drainage of the pleural cavity, air discharge, as a rule, stops on its own within 1-4 days after surgery, without significantly affecting the course of the postoperative period [16-19]. At the same time, a violation of the tightness of the lung suture, the formation of alveolar

fistulas, incomplete expansion of the lung with the formation of a residual pleural cavity significantly increase the risk of prolonged insufficiency of aerostasis when air supply through pleural drains after surgery lasts 5 days or more [20-23].

The long-term air seepage is largely explained by the initial qualitative changes in the lung tissue [24-27]. In conditions of persistent pneumothorax, prerequisites are created for the development of infectious complications, the formation of a persistent residual cavity, which, in turn, may require repeated interventions or prolonged drainage [28-30].

Currently, there are many ways to seal the wound surfaces of the lung: suturing, various options for electrical and infrared coagulation, the use of laser, ultrasound, plasma, treatment of the surgical wound with synthetic and biological adhesives, creation of pleural awnings, application of synthetic and allomaterial flaps. Each of these methods has its own set of advantages and disadvantages, which forces in some cases to use a combination of them [31-35]. Despite the variety of sealing methods, the proportion of complications in the form of prolonged air discharge from a lung wound, according to various authors, ranges from 5.6 to 25% [36].

The number of complications in lung surgery associated with insufficient aerostasis and hemostasis from the wound surfaces of the lung and lines of manual or mechanical suture, as well as with a violation of the tightness of the sutured bronchial stump remains significant and has no noticeable downward trend [37].



The development of aerostasis insufficiency in the postoperative period remains a frequent complication in thoracic surgery and occurs in 5.6-18% of cases [13, 38]. The frequency of postoperative intrapleural bleeding and leakage of the pulmonary parenchyma indicates the relevance of the research topic. These complications lead to an elongation of the postoperative period, repeated surgical interventions, an increase in hospital stay, and lead to an increase in mortality in operated patients.

When performing various operations on the lung parenchyma, the frequency of development and duration of leakage of the lung suture can vary widely depending on the type of resection, the initial somatic status of the patient and the condition of the lung parenchyma [39].

The period of development of aerostasis insufficiency depends on the initial state of the lung parenchyma, the method of resection and the method of sealing the seam, the volume of resected tissue, the ratio of the resected lung and the residual pleural cavity, etc. Many authors in their works pay attention to the timing of the occurrence of leakage of the lung seam. In the studies of G. Antanavicius et al. 2009, intraoperatively, a violation of the tightness of the lung suture was recorded in 28-60% of cases [40]. According to A. Brunelli 2004, on the first day of the postoperative period, air discharge through pleural drains remains at 26-48%. On the 2nd and 4th days of the postoperative period, aerostasis insufficiency develops in 22-24% and 8%, respectively [41].

The risk of lung suture failure in patients with interstitial lung diseases after marginal resection was 1.6-30.2 % [42].

A wide range of the frequency of the studied complications can be explained by the initial state of the lung parenchyma, the different somatic status of the patients included in the study, and the different duration of artificial lung ventilation after surgery.

Modern approaches in the prevention of postoperative complications associated with insufficiency of aero- and hemostasis in the literature are based on the use of new technologies for strengthening the bronchial suture. Nevertheless, the literature data on the effectiveness of the use of various flaps are largely contradictory. Along with the use of traditional materials, an active search and development of bio-based materials is underway [43].

Existing devices for hemostasis and aerostasis are coagulators, mechanical clippers, which are ineffective in the presence of an extensive bleeding surface, as well as near large vessels and vital organs.

In this regard, the development of new biocompatible materials and the creation of specialized

biomedical products from them is becoming a leading area of research and production at the present time.

Technologies are being sought for the creation of bio-artificial materials and organs, which are a system of materials of artificial or biological origin, including cells of tissue organs, or stimulating the regeneration of the corresponding cells in the implantation zone. The most in demand are resorbable materials with high biocompatibility.

The implants being developed in surgery, from filaments, meshes to the most complex organ replacement devices, are aimed at creating biologically compatible materials for surgery. They can be divided into groups depending on the type of materials used: the body's own biological tissues, blood preparations and its fractions, animal tissue processing products, preparations based on natural and artificial polymers.

To date, adhesive coatings have been widely used in surgical practice [44, 45]. Their use is associated with the need to have special equipment in the operating room, and operating surgeons and staff must know the technique of mixing its components. The rapid polymerization of the prepared preparation and the occurrence of an adhesive process in the application area explain the restrained attitude of surgeons to the widespread introduction of such adhesive compositions in abdominal and thoracic surgery [46].

One of the directions of the search for remedies for local hemostasis was the use of collagen and gelatin. Gelatin sponges are produced abroad under the names "Spongostan", "Gelfoam", etc. [47]. The experience of using such drugs has shown mixed effectiveness, especially in cases of blood clotting disorders, as well as the danger of renewed bleeding. In addition, biological films have an antigenic property, stimulate tissue reaction and lead to increased adhesion processes. With massive, profuse bleeding, it shifts and "washes away" from the wound surface. The drug does not adhere well to an uneven wound surface due to the rigidity of collagen fibers.

Thus, hemostatic films and substances used in clinical practice have limited use due to insufficient effectiveness and unidirectional effects. Many of these coatings are made of biological materials (animal or plant origin), which causes their high antigenicity, as well as destruction during thermal sterilization.

To perform the most complex surgical interventions on the lungs, heart and mediastinal organs, biocompatible effective coatings for hemostasis and aerostasis are required. A literature search on search sites (Medline, PubMed) revealed only 20 publications over the past 20 years devoted to the problem of aerostasis in lung surgery. Most of the studies relate to the application of physical methods and



are dated 10 years ago. According to recent publications, this issue is still open [48-51].

The problem of using new materials in various fields of medicine, in addition to fundamental issues related to the study of the interaction of material with body tissues, is of great interest for practical medicine. These studies are carried out at the intersection of medicine, chemistry of high molecular weight compounds, biotechnology, biophysics, molecular and cellular biology and include the following interrelated tasks:

- development of new materials, methods of their modification and processing into specialized biomedical products;
- study of the mechanism of interaction of biomaterials with blood and tissues;
- assessment of the physico-chemical and biomedical properties of biomaterials and products made from them;
- experimental and clinical research and application of new materials and products.

The development of new biocompatible materials and the creation of specialized biomedical products from them is becoming a leading area of research and production at the present time.

The requirements for the biological properties of materials and products that are intended for contact with blood can be formulated as follows: hemocompatible medical devices should not have toxic, allergic and inflammatory effects; activate enzyme systems; have a negative effect on protein and shaped elements of blood, as well as organs and tissues; cause an antigenic and carcinogenic response and abnormalities in the metabolic system; provoke the development of infection and disrupt the electrolytic balance; change their medical and technical properties in the process of undesirable calcification and (or) biodegradation [52]. Indicators of the lack of hemocompatibility of medical materials and products are the appearance of blood clots and thromboembolism induced by their surface.

A special and significant problem is the need to create biodegradable materials and capable of imitating the properties of biological structures. Research on such materials is most relevant and in demand at the present time. This is the use of genetic, cellular and tissue engineering technologies for the development of bio-artificial (hybrid) organs and tissues, cloning organs and tissues from the patient's own stem cells in vitro.

Materials intended for contact with the environment of a living organism and used for the manufacture of medical devices and devices are called "biomaterials", among them:

- compatible with a living organism are materials that, when implanted into the body, staying in it for a

long time, do not cause negative reactions (silicone, Teflon, polycarbonates, polyglycolides and polylactides, polyethylene, titanium, etc.);

- having antithrombogenic properties are materials suitable for long-term contact with blood and used for the manufacture of vascular prostheses of heart valves, etc.

- adsorbents are materials used in the construction of artificial organ devices (kidneys, lungs, hearts) currently used (activated carbon, zirconium, ion exchange resins, etc.);

- oxygen-carrying substances are a class of substances such as fluorinated hydrocarbons used to dissolve oxygen in high concentrations, as well as systems based on capsule coatings of animal and human blood erythrocytes or chemical binding of high-molecular substances with erythrocyte heme;

- dialysis-diffusion film materials (necessary for the production of dialysis films that selectively remove urea, creatinine and other metabolic products from the body);

- fibrous materials are microporous materials with high metabolic efficiency used in the structures of artificial organs, for example, vinyl acetate fibers (artificial kidney), silicone capillaries of artificial lungs;

- microencapsulation materials are necessary for the manufacture of microcapsules with a diameter of the order of microns for drug delivery systems, oxygen carriers;

- elastic materials resistant to abrasion, designed to create artificial bones and joints, heart valves. These materials must have a set of mechanical and physical properties that ensure their safety during long-term operation under mechanical loads;

- bioclues for connecting living tissues (necessary for connecting fragments of the intestine, blood vessels, bile ducts, etc.; such substances must be instantaneous, stable in a liquid aggressive environment of the body, do not produce heat and substances of a toxic nature);

- composite materials, including those for reusable use, can be created by varying combinations of polymers of a single homological series, as well as synthetic materials with metals, biopolymers with synthetic polymers or metals. This makes it possible to obtain materials with fundamentally new functional properties.

In the expanded interpretation of biocompatibility, it should be understood not only the mutual "coexistence" of two substances (artificial and natural), but also that artificial material should perform the functions of living matter. At the same time, it is quite obvious that the biocompatibility of a particular material or implantable element is determined not only by its chemical and supramolecular structure, but also



by the shape, topography of the surface, and specifics of interaction with surrounding tissues.

Thus, the requirements for biomaterials are diverse and multifaceted. Therefore, in each individual case, it is necessary to consider the specific content embedded in the concept of biocompatibility in relation to the intended purpose of each individual material.

The logical way to achieve reliable aerostasis and hemostasis – one of the main conditions for a successful outcome of surgical intervention in thoracic surgery - is to seal the line.

To do this, various methods of strengthening the wound surfaces of the lung are used in clinical practice: the use of laser, plasma, ultrasound, electrical coagulation, treatment of the surgical wound with synthetic and biological glue, applications of adhesive collagen plates and synthetic materials.

In this regard, the development of new, more physiological adhesive compositions was constantly continued. Biological adhesives based on fibrinogen were studied, one of the main advantages of which was that such glue was not a foreign agent and resorbed without the formation of toxic products [53-54].

Experimental studies of the possibilities of plasma surgical installations in lung surgery have shown that it is possible to obtain highly effective aero- and hemostasis on the wound surfaces of the lung, which is achieved by coagulation of blood vessels, welding of small bronchi, and formation of a durable coagulation film [55]. The effect of plasma flows on lung tissue leads to its superficial thermal damage and reversible circulatory disorders in the lung parenchyma adjacent to necrosis. During the healing process of the "plasma wound", coagulation necrosis undergoes gradual replacement with scar tissue, which ends by the 30th day, and there is no rejection of the thermal scab.

The peculiarity of reparative processes is the development of aseptic inflammation with minor neutrophil infiltration at the border of necrotic tissue and intact tissue. Plasma exposure makes it possible to provide aerostasis in large areas of the lung, does not lead to deformation of the remaining part of the lung, does not prevent the expansion of the lung in the postoperative period, does not require preliminary preparation of the wound surface, has a pronounced sterilizing effect. At the same time, the strength of the coagulation film created is such that it allows suturing the lung tissue without fear of their eruption [56].

The most promising means of biological hemostasis are fibrin polymers. Their main advantage is that they consist entirely of biological components of blood and, when applied to the damaged area, mimic the physiological mechanism of hemostasis [57]. However, fibrin compositions are usually two-component and are applied to tissues using injection

needles, sprayers, and catheters. Moreover, double-needle applicators are used, which creates certain difficulties when using them in thoracic surgery.

An analysis of the literature data on the problem of combating postoperative bleeding and, in particular, using hemostatic implants and surgical adhesives showed their three main areas of research, their advantages and disadvantages. One of the directions is the creation of biological multicomponent fibrin adhesives based on blood components, the other is biochemical two-component adhesives containing natural materials and chemical crosslinking additives, and the third is synthetic adhesives – most often single-component cyanoacrylate adhesives, which are most widespread in this group of adhesives [58].

To date, the most common materials used as hemostatic implants include: thrombin, absorbent gelatin, microfibrillar collagen, oxidized cellulose [59].

In addition to the local hemostatic effect of implants, when they are used, an undesirable allergic reaction and infection are also observed. For example, thrombin, along with its effective hemostatic property, has a risk of inducing allergic reactions in hypersensitized patients, absorbent gelatin is able to absorb and retain whole blood during hemostasis and undergo degradation in the body for 4-6 weeks, the gelatin sponge increases in volume when used, which can provoke compression complications [60-61].

Oxidized cellulose is an interesting material for use in medicine due to its ability to degrade in the body, antibacterial properties [62]. There are 2 types of oxidized cellulose: regenerated (ROC) and unregenerated (UROC). A comparative study revealed a higher hemostatic effect of UROC, the same pH levels in the body environment and bactericidal action. The results of a clinical study of the use of UROC (Traumastem TAF, India) in thoracic surgery for extended lung resection revealed a decrease in the time to achieve hemostasis (2-6 minutes) due to the high density of the implant surface and the presence of free carboxyl groups [63].

The antibacterial effect is achieved by reducing the pH in the wound area due to cellulose biodegradation. This mechanism presumably works among gram-positive and gram-negative bacteria. UROC has the ability to accelerate biochemical processes, thereby significantly reducing the time of wound healing.

Recent studies have shown that the hemostatic effect of oxidized cellulose is due to the activation of internal coagulation mechanisms and platelets [64].

The previous generation of adhesive pharmacological agents (synthetic adhesives of the MK series, Surtsizhel, Spongostane, Gelfoum, Aviten, Tissuflais) was insufficiently effective in operations on



the lungs and mediastinal organs. Fibrin glue is much better, but it was also often washed out not only by blood, but also by air flow during lung depletion [65]. It became obvious that for the effective use of fibrin glue, a coating is necessary, which, in addition to hemostatic properties, has an adhesive ability and can be tightly fixed on the surface of the lung.

The adhesive compositions used today contain esters of 2-cyanoacrylic acid (ethyl, n-butyl, 2-octyl) as an adhesive component. Polymerizing in the presence of moisture at human body temperature, these adhesives glue body tissues within 2-5 minutes [63].

Hemostasis when using hydrophobic cyanocrylate adhesives is carried out by forming an adhesive film on the wound surface.

At the same time, a number of disadvantages were noted for cyanocrylate adhesive compositions:

- high curing rate of the adhesive film;
- low mechanical strength;
- low resistance to biological environments;
- slow germination of connective tissue.

At the same time, cyanocrylate adhesives are characterized by general and local toxicity and cause necrotic changes in the application area. Due to the rapid glazing of such adhesives on the surface of wounds and weak connection with tissues, there are known observations of early rejection of the adhesive plate with the resumption of life-threatening bleeding. As already mentioned, the most significant drawback is an acute inflammatory tissue reaction. In the first day after gluing the soft tissue around the adhesive film, an acute segmental nuclear reaction occurs with a noticeable vascular component and varying degrees of severity in different tissues.

The use of chemical compounds based on alpha-cyanoacrylates in medical practice has made a significant contribution to the development of the newest surgical technologies. They have taken a prominent place in the global market, surpassed the commercial success of biological sealants based on fibrin and collagen [66].

Currently, there is a search for more advanced modifications of synthetic adhesive compositions, which requires extensive morphological, toxicological, experimental and clinical studies to create bio-adhesives of new modifications devoid of the above disadvantages.

Thus, the use of synthetic adhesive compositions in surgical interventions has not lost its relevance to the present time. There is a constant need to search for new adhesive compositions that are convenient to use and devoid of the disadvantages described above. This determines the relevance of the development of new methods for the application of adhesive compositions.

One of the directions of the search for local hemostasis was the use of hemostatic collagen and gelatin sponges. Gelatin sponges are produced abroad under the names "Spongostan", "Gelfoam", etc. In Russia, a gelatin sponge with gentamicin included in its composition, Gemacept, has been developed. The experience of using such drugs has shown mixed effectiveness, especially in cases of blood clotting disorders, as well as the danger of renewed bleeding. In addition, biological films have an antigenic property, enhance the tissue reaction and lead to increased adhesion processes [67].

In recent years, combined hemostatic collagen preparations have appeared, the most effective of which turned out to be Tachocomb. The basis of the "Tachocomb" is a combination of a collagen plate with fibrin glue components dispersed on it (human fibrinogen, bovine thrombin). Like fibrin glue, the drug accelerates blood clotting in the application area, provides plastic closure of the wound surface, and allows for hemostasis in case of damage to the liver and spleen. However, its effectiveness is manifested only with moderate parenchymal bleeding. With massive, mixed bleeding, it is "washed off" from the wound surface. The drug does not adhere well to an uneven wound surface due to the rigidity of collagen fibers.

The hemostatic capabilities of such biological agents of hemostasis as dry thrombin, hemostatic sponge, collagen, cellulose are limited due to poor fixation to the wound surface [68-71]. The use of infrared coagulation is limited by the small coverage of the coagulating surface and the occurrence of tissue necrosis of the boundary zone.

The long-term use of cellulose as a dressing material is experiencing a new period of application of its derivatives, which, depending on the type and degree of polymerization, can be widely used in surgery as an independent active principle as a bioinert non-toxic biodegradable implant with certain physico-chemical and therapeutic properties.

CONCLUSION. Reliable intraoperative aero- and hemostasis is an important condition for the uncomplicated course of the postoperative period. However, traditional methods of sealing the lung are not effective enough, and the primary failure of the "pulmonary stump" remains the most common of the early complications.

The experience of using various methods of aero- and hemostasis in lung surgery shows that each of them has certain disadvantages that limit its use. At the same time, many studies conducted in this area are limited to comparing only two of the many methods of additional sealing of the lung seam. There are no algorithms in which the choice of the resection method and the choice



of the additional sealing method would be rationally combined.

The search and development of effective multifunctional means of aerostasis and hemostasis continues, and the available analogues are ineffective and can cause a number of complications in the postoperative period.

Thus, the study and introduction into biomedical practice of new materials for aeroheostasis in thoracic surgery is an urgent and highly demanded area, the success of which will contribute to progress in many areas of medicine and ultimately improve the quality of treatment and human life.

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