Cancer Management and Research

Elevate Series

Open Access Full Text Article

REVIEW

Bronchoscopic Closure of Bronchopleural Fistula with Occluder

Mingxi Ma[1,2], Daomin Xie[3], Lihui Zhang[1], Mengli Li[1], Qiu Meng[1,2], Shuanglan Xu[1], Xiqian Xing[1]

[1]Department of Pulmonary and Critical Care Medicine, the Affiliated Hospital of Yunnan Medical University, Key Laboratory of Respiratory Disease Research of Department of Education of Yunnan Province, Kunming, 650021, People's Republic of China; [2]Clinical Medical College of Dali University, Dali, Yunnan, 671000, People's Republic of China; [3]Department of Respiratory Medicine, Qiaojia County People's Hospital, Zhaotong, Yunnan, 654600, People's Republic of China

Correspondence: Xiqian Xing; Shuanglan Xu, Department of Respiratory Medicine, the Affiliated Hospital of Yunnan University, the Second People's Hospital of Yunnan Province, Kunming, Yunnan, 650021, People's Republic of China, Email xingxiqian@ynu.edu.cn; xushuanglan99@163.com

Abstract: Bronchopleural Fistula (BPF) represents one of the gravest complications post-lobectomy. Present treatment strategies encompass a wide array of surgical techniques complemented by essential adjunct therapies. Despite numerous treatment modalities, mortality rates associated with BPF remain disconcertingly high. Advances in bronchoscopic technology have led to the widespread adoption of bronchoscopic interventions, celebrated for their safety, minimal invasiveness, and efficacy. The cornerstone of BPF management involves the use of sealants, metal-covered stents, and occlusion devices, with the success of these occlusions critically dependent on the fistula's dimensions. Particularly for expansive BPFs deemed inappropriate for surgical intervention, metal-covered stents and occlusion devices are frequently favored. This review critically assesses the therapeutic efficacy and clinical utility of metal-covered stents and occlusion devices through a comprehensive analysis of the extant literature. Additionally, it outlines risk stratification and management strategies for BPF, with the intent to furnish novel insights and methodologies for the clinical diagnosis and treatment of this complex condition.

Keywords: bronchopleural fistula, bronchoscopy, interventional pulmonology, pneumonectomy, lung cancer

Introduction

Bronchopleural Fistula (BPF) is an abnormal conduit between the bronchial system and the pleural cavity. The causation of BPF is diverse, stemming from factors such as infection, mechanical injury, chronic obstructive pulmonary disease (COPD), and acute respiratory distress syndrome (ARDS). Predominantly, BPF is seen as a complication post-major thoracic surgeries, especially lung resections in lung cancer treatments.[1–3] The incidence rate of BPF is reported to be between 1.5% and 8.5%.[4–6] Despite its low incidence, BPF can result in catastrophic outcomes, with as much as a 67% mortality rate.[7,8] Clinically, BPF manifests with symptoms including cough, purulent or foul-smelling sputum, hemoptysis, difficulty breathing, and high fever, which may be accompanied by sepsis, respiratory failure, and other severe complications. BPF presents significant therapeutic challenges and serious clinical implications. This review aims to methodically evaluate the efficacy and safety of occlusion devices and metal-covered stents in interventional BPF management. Our objective is to critically analyze extant literature, collate data on the effectiveness of occlusion devices and metal airway stents, and investigate their prospective applications in clinical settings. Furthermore, we will identify the inherent challenges and limitations associated with these treatments and suggest potential resolutions. This paper seeks to furnish clinicians with innovative therapeutic insights, potentially enhancing treatment outcomes and the quality of life for BPF patients.

Progress Report

Airway Stents

Airway stents are geometric entities fashioned from biocompatible medical-grade silicone or nickel-titanium alloys. They are principally utilized in therapeutic interventions for airway stenosis. For the interventional treatment of BPF, metal stents and silicone stents are predominantly employed.

Received: 10 August 2024
Accepted: 19 November 2024
Published: 21 December 2024

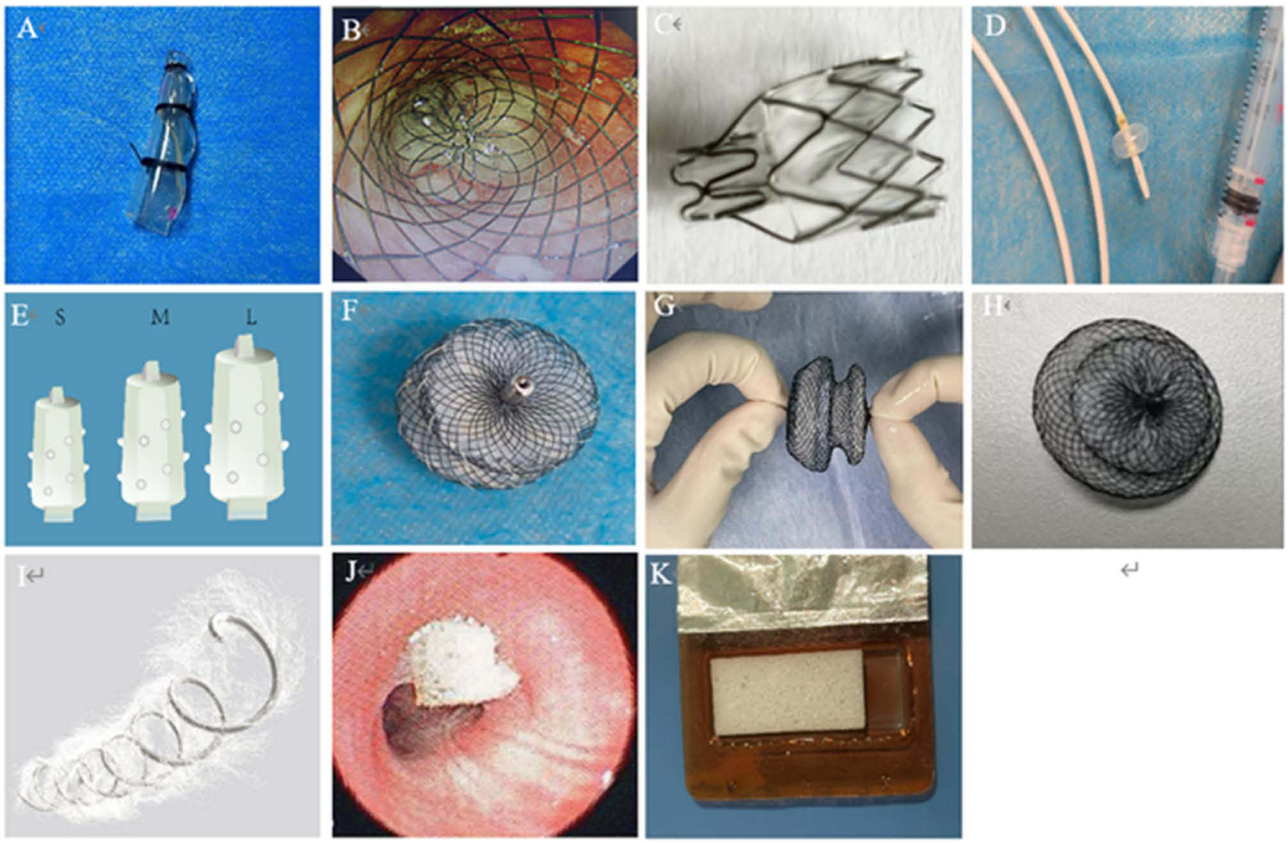

Figure 1 Devices being used for bronchoscopic intervention for BPF. (**A**) Customized Endobronchial Silicone Blocker. (**B**) Metal stent. (**C**) Endobronchial Valve. (**D**) Bronchial balloon. (**E**) Endobronchial Watanabe Spigots. (**F**) Ventricular Septal Defect. (**G**) Atrial Septal Defect. (**H**) Amplatzer Patent Foramen Ovale device. (**I**) Coil. (**J**) Polyvinyl Alcohol sponge. (**K**) Gelatin sponge. (**A**–**I** and **K**) were provided by our research team. (**J**) was reproduced from Battistoni P, Caterino U, Batzella S, Dello Iacono R, Lucantoni G, Galluccio G. The use of polyvinyl alcohol sponge and cyanoacrylate glue in the treatment of large and chronic bronchopleural fistulae following lung cancer resection. Respiration. 2017;94(1):58–61. Copyright 2017 Karger Publishers, Basel, Switzerland.[14]

Customized Endobronchial Silicone Blocker

The Customized Endobronchial Silicone Blocker (CESB) is designed through a meticulous process of manually shaping a silicone stent into a conical form to align seamlessly with the progressively narrowing bronchial contours (Figure 1A). This adaptability provides significant clinical advantages, including the capability to tailor the CESB on-site to accommodate varying bronchial anatomies, even those of large main bronchi. These attributes notably broaden the CESB's clinical applications, making it a versatile option for managing different sizes of bronchial fistulas. Preoperative evaluation with computed tomography scans enables precise identification of the areas requiring intervention, thereby optimizing the placement and efficacy of the CESB. The steps for the bronchoscopic procedure protocol include: (1) Fistula Site Identification: The procedure begins with the direct observation of the fistula through bronchoscopy or by employing a balloon to continuously block sub-segments of the bronchus. This step is crucial for accurately identifying and sealing the fistula, as evidenced by a reduction or cessation in thoracic closed drainage leakage; (2) CESB Sizing: The CESB's size is determined by inflating a balloon within the target bronchus until it is completely occluded. The balloon's volume is then measured, removed, and reinflated externally to the same volume to ascertain the maximum diameter needed for the CESB; (3) CESB Placement: The CESB is placed under bronchoscopic guidance to ensure it fully occludes the bronchial passage, thereby effectively sealing the fistula and preventing any further complications. Mehta and colleagues described the treatment of 14 patients with BPF using CESB via rigid bronchoscopy, with an average fistula diameter of 9.6±3.6 mm. Eleven cases were successfully occluded; however, in the remaining three patients, CESB displacement occurred before the fistula healed, indicating an occlusion failure. The primary causes of failure were large fistula sizes and severe coughing, which led to CESB displacement, necessitating postoperative cough suppression.[9] To prevent migration, medical adhesive can be employed to reinforce the seal, enhance adhesion, and inhibit movement. This method has also been utilized in

treating patients with ARDS and barotrauma, leading to favorable postoperative recovery and substantial improvements in quality of life.[10] Long-term complications associated with CESB include irritative coughing, intolerance, granulomas, hemoptysis, respiratory distress, atelectasis, infections, and displacement.[11,12] For fistulas larger than 8 mm, both previously mentioned cases effectively sealed the fistulas using CESB in conjunction with medical adhesive, significantly ameliorating patient symptoms and markedly reducing the incidence of complications, such as CESB displacement. Reducing the occurrence of postoperative complications can significantly prolong patient lives. Recently, Roy and colleagues successfully employed a novel material, a 3D-engineered silicone stent, for the initial occlusion of a BPF complicated by infection, following the resection of the right lower lobe in a patient with lung squamous carcinoma.[13] The principal benefits of this innovative material include its versatility for almost all types and locations of BPFs, a diminished risk of granulation tissue proliferation, and straightforward removal and insertion, which collectively contribute to a lower complication rate. Further research could expand on assessing the effectiveness of CESB or 3D printing technologies in treating BPFs resulting from benign or malignant causes. Should these trials prove successful, the broader application of these technologies might enhance treatment modalities significantly. The CESB offers a highly effective, adaptable solution for the management of bronchial fistulas. Its on-site customization capability allows for precise tailoring to patient-specific bronchial anatomies, significantly enhancing the therapeutic outcomes. This topic not only highlights innovative methods in managing bronchial fistulas but also provides detailed steps on how to maximize the utility and effectiveness of CESB in clinical practice.

Metal Stent

Metal stents (Figure 1B), constructed from nickel-titanium alloy, are available in L-shaped, Y-shaped, and I-shaped configurations. L-shaped metal stents are generally employed for upper lobe pulmonary and main bronchial fistulas, as well as for BPFs where lateral airway stent placement is unsuitable.[15] The Y-shaped airway stent, comprising a main tube and two branches, forms an inverted "Y" shape. Encased in a nickel-titanium wire mesh, the entire stent is capable of self-expansion.[16] Following the confirmation of a BPF via clinical symptoms, CT scans, and bronchoscopy, the procedural steps include: Insertion of a tracheal catheter through the mouth into the target bronchus, followed by injection of a contrast agent to visualize the fistula stump; Placement of a metal stent to occlude the target bronchus; bronchoscopic confirmation of the successful occlusion of the target bronchus by the metal stent. Postoperatively, a follow-up CT scan can be conducted to ascertain whether the fistula stump has resolved. Given the significant diversity in the length of the BPF stump, the position of the fistula, and anatomical variations, a personalized approach to selecting the type and size of the stent is essential. The selection of the stent type is determined by both the position and the length of the bronchial stump. For bronchopleural fistulas with a bronchial stump length exceeding 20mm, an articulated, self-expanding, bullet-shaped covered metal stent is utilized. For bronchopleural fistulas with a bronchial stump length between 5mm and 20mm, a Y-shaped, self-expanding, bullet-shaped covered metal stent is employed. When the bronchial stump length is less than 5mm, an L-shaped, self-expandable covered metal stent is employed.[16,17] Han and colleagues described their experience with using customized stents to occlude postoperative BPF in 148 patients undergoing pulmonary resections primarily for lung cancer or tuberculosis. During the follow-up period, 73 patients benefited from the treatment, with stents removed following BPF resolution, typically within three months. Of these patients, 75 died, 52% from infections and 20% from underlying malignancies.[17] Cao and colleagues reported a clinical case in which an airway metal-covered stent failed to occlude a BPF, with continuous bubbling observed postoperatively in the chest drain. The primary cause of failure was ARDS, triggered by preoperative aspiration pneumonia, requiring mechanical ventilation and ultimately leading to death from sepsis induced by empyema.[15] Studies have linked mechanical ventilation to treatment failures in bronchoscopy, and the postoperative use of mechanical ventilation in patients with BPF complicated by ARDS remains controversial.[18] Although Han and colleagues achieved a high success rate in surgeries, severe postoperative complications—including stent displacement, stent occlusion, infections, and bronchial damage—affect patient survival rates as significantly as malignant tumors. For example, during long-term follow-ups, granulation tissue growth may lead to restenosis within the stent, requiring further bronchoscopic interventions to clear obstructed bronchi and ensure stent stability. Consequently, the development of new stent materials is essential to enhance patient tolerance and mitigate the proliferation of granulation tissue. As foreign bodies within the

airway, stents not only stimulate increased mucus secretion but also impair respiratory cilia movement, ultimately complicating phlegm expectoration. Future efforts should focus on establishing more comprehensive and detailed guidelines for post-stent implantation airway management, complemented by suitable pulmonary rehabilitation treatments to enhance the management of compromised lung function.

Occluder

Alongside advancements in modern interventional therapies, a variety of occlusion devices have been deployed to manage respiratory and cardiovascular pathologies, including BPF. Devices including endobronchial valves, endobronchial Watanabe spacers, and Amplatzer occluders have been employed, resulting in some patients achieving therapeutic resolution post-treatment.

Endobronchial Valve

The Endobronchial Valve (EBV) is designed as an umbrella-shaped one-way valve, featuring a nickel-titanium frame encased in a polymer membrane (Figure 1C). Originally designed to treat heterogeneous emphysema, the EBV operates with airflow, effectively restricting air from entering the pleural cavity while facilitating the drainage of distal secretions and controlling local inflammation, thus making it applicable for BPF treatment. The bronchoscopic procedure entails: (1) employing bronchoscopy and balloon occlusion to identify the leaking lobe or segment of the lung; (2) once the EBV is positioned, directing the patient to conduct breathing cycles to check for continuous air leakage in the water-seal bottle. A CT scan should be performed prior to the placement of the EBV to enhance the success rate of the procedure. Following the placement of the EBV, careful monitoring of the patient with a chest drainage tube is essential. The tube may be removed once the patient stabilizes. Should there be no recurrence of symptoms after six weeks, the EBV can be removed via bronchoscopy. Studies comparing the efficacy of EBV with surgical and conservative treatments, such as closed chest drainage, are documented.[19,20] Relative to surgical interventions, EBV exhibits a marginally lower success rate (57% for EBV vs 62.5% for surgery); however, it outperforms conservative treatments (93.3% for EBV vs 67.8% for conservative treatment). Although the long-term outcomes of EBV remain uncertain, it is undeniable that EBV serves as an effective adjunct in the treatment of persistent air leaks, particularly when surgical options are contraindicated or suboptimal. Considering that existing studies are from single centers and limited in scale, future larger-scale research is warranted to further evaluate the efficacy of surgical interventions versus EBV, along with their effects on costs and hospitalization duration. Following EBV implantation, complications including obstructive pneumonia, hemoptysis, displacement, and granulation tissue growth can arise, with pneumothorax resulting from EBV displacement representing one of the most severe complications. Alexander and colleagues reported a case in which an EBV became dislodged due to coughing post-implantation, leading to persistent air leaks; this issue was successfully addressed with autologous blood patch therapy.[21] Consequently, it is recommended to employ combined treatment strategies with EBV and occlusive agents to mitigate the risk of displacement. This approach should include optimizing the selection of customized EBV sizes, adhering strictly to aseptic procedures, preventing and promptly addressing airway infections, and maintaining the cleanliness of the EBV and surrounding tissues to minimize complications. From an economic perspective, the costs associated with EBV surgery and the management of complications are considerable, presenting challenges for both developing and developed countries; thus, the urgent development of new materials is essential.

Bronchial Balloon

Bronchial balloon occlusion is suitable for treating BPF secondary to necrotizing pneumonia and for cases requiring immediate removal of blockages, such as pneumothoraces associated with mechanical ventilation (Figure 1D). Preoperative computed tomography scans facilitate localization, with essential steps including occluding the targeted bronchus through the bronchoscopic working channel under guidance, positioning the fistula at various sites with an inflated balloon, and monitoring for the absence of bubbling in the chest drainage tube during respiratory cycles to indicate successful occlusion. For partially visible fistulas, intrathoracic dye injection confirms complete airway occlusion by the balloon. During the procedure, careful inflation of the balloon is crucial to prevent airway bleeding and damage. Hathorn and colleagues reviewed balloon catheter treatments in six pediatric BPF cases, resulting in four

successes and two failures.[22] The failures were due to persistent air leakage upon balloon deflation, demonstrating that the bronchial balloons are primarily used for temporary occlusion in emergency situations or as a short-term management solution until a suitable occlusive device can be identified, especially in the case of central bronchus laceration. Similarly, complications such as distal bronchial infection, necrosis, and displacement were observed, akin to those associated with other occlusion devices. At present, the clinical application of tracheal balloons is limited, with no definitive conclusions about long-term outcomes, including survival rates, lung function improvement, and cure rates. Furthermore, there is an absence of data on comparative effectiveness with other occlusion devices, and clinical indications require additional clarification.

Endobronchial Watanabe Spigots

The Endobronchial Watanabe Spigots (EWS), developed by Watanabe and colleagues, feature a unique silicone resin construction and are cork-shaped, serving as silicone bronchial blockers (Figure 1E). EWS come in three sizes: small (5 mm), medium (6 mm), and large (7 mm).[23] Consequently, EWS are particularly effective in sealing larger fistulas, specifically those measuring between 5 and 7 mm. Rapid identification of the affected bronchus during the procedure enhances patient comfort and safety. Consequently, preoperative chest CT scans are essential. Moreover, if feasible, employing bronchial 3D reconstruction or virtual bronchoscopic navigation can significantly aid surgeons in rapidly locating the target bronchus. The specific technical approach involves inflating a balloon under mild or local anesthesia to achieve complete occlusion of the lobar, segmental, and subsegmental bronchi. After occlusion, air leakage is reduced or eliminated through a chest drainage tube to identify the affected airway. Once persistent air leakage has ceased, an EWS is deployed in the affected bronchial segment using forceps. For technically challenging target bronchi, Date and colleagues reported a novel "traction method" for deploying EWS. This method attaches the EWS to the tip of a guidewire, inserts it through the thoracic cavity into the BPF fistula, and employs bronchoscopic forceps to navigate the guidewire to its destination. Subsequently, the surgeon withdraws the guidewire from the surgical field, allowing the EWS to automatically insert into the target bronchus.[24] This innovative technique significantly enhances bronchoscopic interventions for BPF, particularly benefiting patients for whom such interventions are challenging. It prompts the need for improvements in EWS materials to better accommodate complex bronchial anatomical structures, thereby reducing surgical complexity and benefiting a broader patient population. In recent years, the EWS occluder has demonstrated satisfactory outcomes in cases of BPF following esophagectomy,[23] associated with empyema due to pulmonary tuberculosis,[25] after right upper lobectomy,[24] caused by interstitial lung disease,[26] and accompanying empyema secondary to COVID-19 pneumonia.[27] However, identifying the optimal bronchus for EWS placement, determining the most appropriate timing for its insertion and removal, and minimizing complications remain the focus of our ongoing research. The EWS is constructed from a non-absorbable material, which does not facilitate wound healing and poses risks of infection and displacement. Regular follow-up visits and monitoring are crucial to prevent recurrence and manage complications effectively. In a retrospective study by Sasada et al, EWS therapy was administered to 24 patients with pneumothorax that was resistant to surgical intervention. This treatment successfully eliminated or significantly reduced air leakage in 79.2% of the cases. Notably, this group included four patients who were dependent on mechanical ventilation. However, among those with persistent air leaks, twelve patients experienced complications related to the surgery after EWS occlusion. These complications included dislocation, fever, atelectasis, and lung abscesses. Fortunately, all these conditions improved following the removal of the EWS devices.[28] The appropriate application of antitussive medications or the combined use of occlusive agents, such as medical glue, in intervention therapy can stabilize the EWS.[29] Future research should offer more detailed surgical information for clinical reference, improve long-term follow-up regarding survival rates, recurrence rates, and pulmonary function recovery in patients with BPF treated with EWS interventions, and establish management guidelines suitable for these patients.

Amplatzer Devices

Amplatzer Devices (AD) encompass a broad category of devices originally designed for the transcatheter closure of cardiac ventricular septal defects or patent ductus arteriosus. This category primarily includes occluders for Ventricular Septal Defects (VSD) (Figure 1F), Atrial Septal Defects (ASD) (Figure 1G), and Amplatzer Patent Foramen Ovale (PFO)

device (Figure 1H). The diameter of ADs ranges from approximately 4 to 38 mm, and each device consists of a disc formed from a nitinol mesh attached to a central connector. Owing to the properties of nitinol, these devices can be compressed within a catheter. Once deployed in a BPF, an AD will reassume its original shape. The selection of AD size and type is based on the diameter of the bronchial stump and the length of the fistula. The goal is to ensure that the occluder's retention disc fully covers the fistula connection, effectively occluding the bronchial stump. The primary technical approach involves: (1) visualizing the fistula under bronchoscopy and inserting a guidewire via the bronchoscopic working channel; (2) employing a balloon at the guidewire and fistula site to determine if the air leak ceases and to measure the balloon's diameter; (3) positioning an AD slightly larger than the balloon's diameter at the fistula site to assess for air leaks. Case reports have validated the effectiveness and safety of ADs in managing BPF following lung transplantation, lung cancer resections, pulmonary tuberculosis, and infections from pulmonary aspergillosis. ADs not only seal BPF and mitigate air leakage but also incite inflammatory responses, enhancing granulation tissue growth and fistula healing. When the Amplatzer device is chosen with the appropriate size, it can address the majority of air leakage associated with BPF after placement. This immediate effect relies on selecting the correct diameter, which ensures an effective seal of the fistula. This approach has achieved a success rate of up to 95% and is well-regarded by clinical physicians.[30–35] Additionally, the Amplatzer device contributes to controlling pulmonary infections, which are common complications associated with BPF. By effectively preventing further air and fluid leakage, the device minimizes the risk of infections that can develop due to ongoing leakage. The use of ADs to occlude BPF is considered off-label; therefore, it is imperative to thoroughly discuss potential postoperative complications and adverse events with patients or their relatives prior to surgery. This ensures that all parties are well-informed about the risks and expected outcomes associated with the procedure. Major complications of using ADs include device displacement, infection, airway obstruction, and bronchial injury. It is crucial to monitor these risks closely and manage them promptly should they arise to prevent further health complications. Should patients with BPF who have received endoscopic AD treatment exhibit symptoms of airway obstruction, such as a reduced voice or increased difficulty breathing, reconsideration of AD reinstallation may be necessary.[32] This step should be undertaken with careful assessment to ensure it is the most appropriate course of action based on the patient's current condition and overall treatment goals. Bai and colleagues reported three cases in which VSD occluders either partially or completely failed in underweight patients with chronic empyema.[36] Consequently, underweight status or the presence of an infection may contribute to the failure of AD occlusion, potentially resulting in the enlargement of the BPF and displacement of the AD into the thoracic cavity. Postoperatively, it is crucial to provide adequate nutritional support and timely infection control to promote fistula healing. Additionally, to prevent AD displacement, supplementing with appropriate occlusive agents, such as medical glue, injected at the edges of the occluder, can enhance stability. A 17.6-month follow-up study revealed that the survival rate for 30 patients, who underwent AD occlusion following pulmonary resection for BPF, was 45%. The primary causes of death, malignancy recurrence, and sepsis, were unrelated to the BPF.[37] This necessitates the consideration that malignancy and infection are significant factors affecting the postoperative survival rates of BPF patients. In the future, additional long-term follow-up studies are expected to yield crucial insights into the treatment of BPF. Regular imaging and clinical assessments are essential for monitoring recurrence, particularly in the initial months following treatment. These assessments are critical to ensuring timely responses to any changes in the patient's condition. It is recommended that patients with BPF undergo their initial follow-up bronchoscopy four weeks post-surgery, and subsequently at intervals of three to six months, to facilitate early intervention for any postoperative complications or adverse reactions, thus enhancing survival rates. This periodic monitoring allows for immediate adjustments in treatment strategies based on the patient's recovery progress. Furthermore, following successful occlusion, an improvement in patients' lung function is anticipated. Through rehabilitation training and appropriate medication, the lung function of some patients may near pre-surgical levels. This gradual recovery is vital for restoring quality of life and functional ability to patients post-surgery.

Coil

Coils, primarily made of steel or platinum, are considered significant embolic agents (Figure 1I). As a method for occluding BPF, the use of coils in conjunction with occlusive agents such as fibrin glue has the potential to reduce the number of surgical interventions and may successfully close major bronchial stump fistulas. The primary

procedural steps are as follows: (1) After administering general anesthesia, the fistula is located using sequential balloon occlusion or bronchial angiography; (2) the appropriate guidewire size is selected to access the target bronchus, followed by the placement of coils along the guidewire, and concluding with the injection of occlusive agents around the coils. While early cases report success in using coils with occlusive agents such as fibrin glue and medical glue to treat post-pulmonary resection BPF in patients with small BPFs (<5mm), the potential for these agents to dislodge from the coils during activities like coughing, posing a risk of coil displacement, necessitates long-term follow-up.[38,39] Currently, no long-term follow-up studies for coil occlusion of BPF have been reported. Clinicians must ensure diligent case follow-up, enhance patient health education to improve compliance, and prevent complications. Additionally, there is anticipation for the development of new coil materials that offer fewer complications without reliance on occlusive agents. Recently, Baden and colleagues documented a case in which a high-density, large-capacity, detachable coil was successfully employed under bronchoscopy to treat a child with BPF complicated by pulmonary infection.[40] This publication constitutes the first account of coil occlusion in pediatric BPF, introducing a promising alternative for minimally invasive intervention in children with BPF that offers the advantage of minimal pulmonary tissue damage. Furthermore, given the limited extent of coil intervention for BPF and the feasibility of its application under local anesthesia, it may be particularly well-suited for patients at high risk from general anesthesia.

Sponge Material

Bronchoscopic intervention using sponges for BPF represents a minimally invasive technique, involving the placement of a sponge into the fistula through bronchoscopy. This method aims to seal the opening, minimize air leakage, and facilitate healing. This article specifically addresses the use of Polyvinyl Alcohol (PVA) sponges (Figure 1J) [14] and gelatin sponges (Figure 1K). The primary diagnostic and procedural steps include confirming the fistula through thoracic imaging or bronchoscopy and, under intravenous anesthesia, inserting the sponge into the fistula via the bronchoscope to achieve occlusion. PVA sponges, composed of polyvinyl alcohol polymers, are highly hydrophilic and rapidly expand upon absorbing liquid.[14] These sponges can be tailored to the appropriate size to fit the bronchial cavity during use. Battistoni and colleagues utilized PVA sponges with medical glue in the interventional treatment of seven cases of post-pulmonary resection BPF, achieving a success rate of approximately 71%.[14] The predominant cause of failure was the displacement of PVA sponges, resulting in BPF recurrence. Gelatin sponges, being water-soluble hemostatic materials, offer advantages such as high absorbency and affordability. Liu and colleagues described a case in which gelatin sponges combined with autologous blood failed to occlude a BPF following pulmonary resection, primarily because the BPF fistula was too extensive for the occlusive materials to seal effectively.[41] Displacement and large fistulas frequently result in occlusion failures; however, employing combinations of occlusive agents can mitigate such complications. This effect is likely due to the agents inducing local inflammatory responses or granulation tissue proliferation, thereby securing the sponge and reducing the fistula's diameter. This necessitates that patients regularly return to the hospital for bronchoscopic re-evaluation to assess the airway conditions, whether to continue injecting a specified dose of occlusive agents or to remove excess granulation tissue, thus preventing bronchial constriction or obstruction. Consequently, for BPF patients unable to undergo timely follow-up, treatment effectiveness may be compromised, underscoring the importance of enhanced patient health education post-intervention. Recently, Ueda and colleagues developed silk-elastin sponges, a versatile new material usable in various forms including glue, sponges, and sheets, offering extensive potential applications.[42] Histological examinations in animal models have demonstrated that silk-elastin sponges, while obstructing airflow at bronchial remnants, can promote the regeneration of airway epithelium, significantly reducing the risk of airway narrowing or obstruction, thereby expanding the options for interventional BPF treatment. Although sponges serve as a viable material for the interventional treatment of BPF, the long-term outcomes of sponge-based interventions remain underreported, necessitating further comprehensive evaluations through prospective clinical studies. Additionally, the development of novel materials aimed at reducing complications and lowering the mortality rate associated with BPF is anticipated.

Management of Bronchopleural Fistula

BPF represents a severe complication of pulmonary resection. Factors predictive of BPF include male gender, a history of smoking, diabetes, a positive pulmonary disease history, decreased FEV1, right-sided pulmonary resection, and various postoperative conditions, including pulmonary complications and the use of adjuvant therapy.[43,44] Mazzella and colleagues categorize patients into distinct risk levels based on preoperative assessments, comorbidities, and treatment histories, enabling more effective risk stratification, which includes optimizing comorbid conditions before surgery, minimizing the extent of bronchial dissection during the procedure, and enhancing postoperative monitoring. This grading system facilitates information sharing among physicians, patients, and multidisciplinary teams throughout the surgical decision-making process, thereby mitigating the risk of postoperative BPF.[44] However, the Mazzella grading system was initially described in the context of pneumonectomy, with the majority of researchers advocating for the coverage of the bronchial stump post-pneumonectomy to prevent stump insufficiency. Furthermore, BPF is more prevalent in patients undergoing standard lobectomy or sleeve resection compared to those undergoing pneumonectomy, attributed to the higher frequency of lobectomies and sleeve resections. Managing BPF is complex and varies significantly, necessitating a comprehensive assessment of the patient's medical history, fistula size, and associated complications. Expanding upon the work of Mazzella and colleagues, we have developed individualized treatment plans that categorize fistulas by diameter into large (>10mm), medium (5–10mm), and small (<5mm). BPF can be classified based on the duration and clinical presentation of fistula formation into acute BPF (fistulas that occur within days to weeks post-surgery, trauma, or infection, typically within the first 30 days) and chronic BPF (usually developing weeks to months, or even years, post-surgery, trauma, or infection). BPF management strategies are summarized in Figure 2. This proposal for prospective studies, based on current research findings, recommends conducting multicenter, randomized controlled trials to validate the effectiveness of risk stratification models and to explore the efficacy of new intervention measures. In managing BPF, this thesis underscores the critical need for collaboration among pulmonologists, thoracic surgeons, radiologists, and critical care specialists to enhance patient survival rates and quality of life significantly.

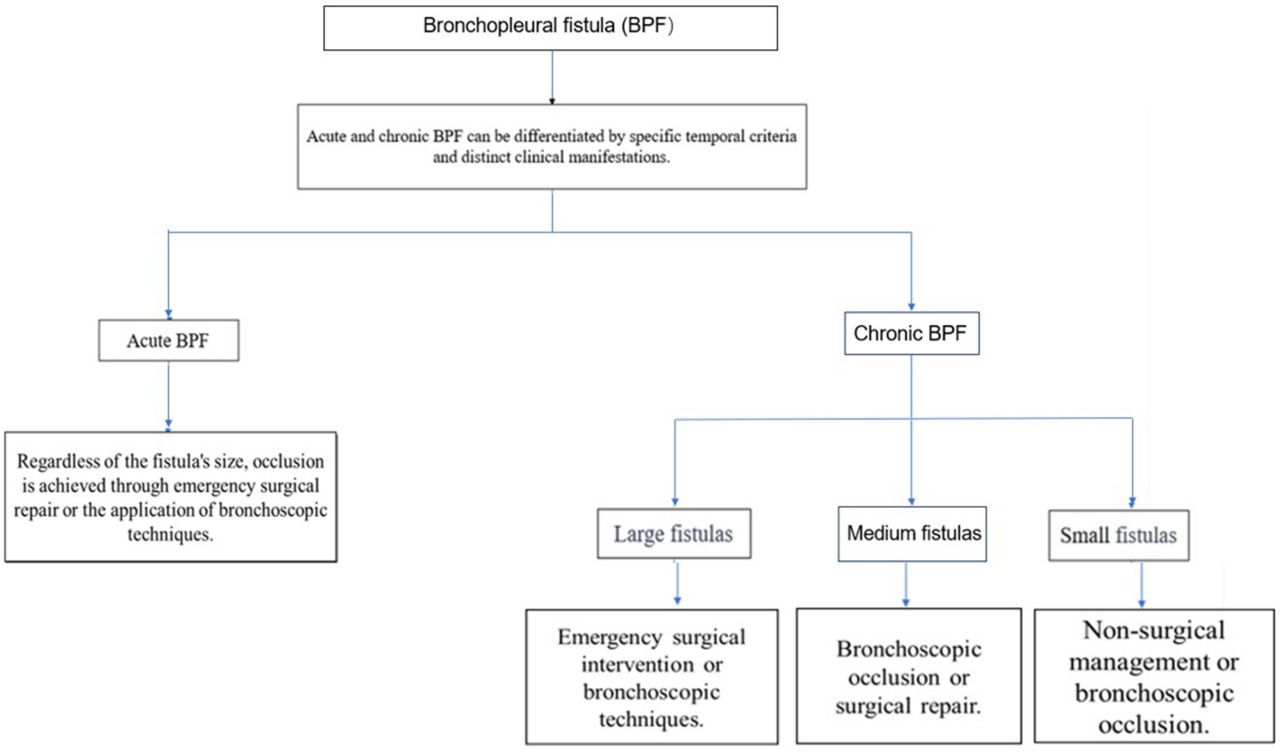

Figure 2 Management of bronchopleural fistula.

A comprehensive follow-up plan for BPF patients is designed to facilitate early identification and management of recurrences or complications, as well as to assess life quality and patient satisfaction following treatment interventions. Initial assessment involves a comprehensive evaluation at patient discharge, which includes logging symptoms and assessing physiological and psychological status. Short-term follow-up entails face-to-face or remote sessions at one week, one month, and three months post-discharge, concentrating on fistula healing, signs of infection, pain management, and the ability to perform basic activities of daily living. Long-term follow-up includes annual evaluations at six months and twelve months post-treatment, and annually thereafter. These evaluations encompass imaging studies (such as CT scans), blood tests, respiratory function tests, and comprehensive assessments of quality of life. Physical Health: Pulmonary function tests are utilized to quantify improvements or declines in respiratory capacity, enabling assessment of a patient's capability to perform daily and higher intensity activities. Mental Health: Evaluation is conducted using standardized mental health scales, including the Hospital Anxiety and Depression Scale (HADS). Quality of Life: Specialized questionnaires such as SF-36 or EQ-5D are employed to assess overall patient well-being. Post-Intervention Strategies: Rehabilitation programs, encompassing physical and respiratory therapies, are designed, alongside psychological counseling and support groups for patients and families, to mitigate the psychological impacts of the disease. Educational Initiatives: Education on nutrition, exercise, and disease self-management is provided. Treatment plans are dynamically adjusted during follow-up, based on patient feedback and regular assessments.

Conclusion

Occluder interventions showed a high success rate in sealing fistulas effectively, which is pivotal in preventing the severe complications associated with BPF, such as persistent air leaks and infections. The application of these devices facilitated prompt restoration of lung function and improved overall patient well-being, underlining their importance as a therapeutic option in the clinical setting. Future studies should focus on comparing different types of occluders, establishing standardized protocols for their use, and expanding the evidence base to solidify their role in the management of bronchopleural fistula. This will ultimately contribute to the refinement of treatment strategies and enhance patient care in respiratory medicine. This review comprehensively synthesizes research findings on occluders interventions for BPF, discusses the clinical implications of these findings, and proposes directions for future research. It provides a detailed and integrated summary that encapsulates the current discourse on this treatment modality.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study was supported by Famous Doctors of High-level Talent Training Support Program of Yunnan Province (No. YNWR-MY-2020-013), Yunnan Provincial Innovation Team for Respiratory and Pulmonary Circulation Diseases (No. 202405AS350018).

Disclosure

The authors declare no competing interests in this work.

References

1. Li Z, Mao G, Gui Q, Xu C. Bronchoplasty for treating the whole lung atelectasis caused by endobronchial tuberculosis in main bronchus. *J Thorac Dis*. 2018;10(7):4000–4005. doi:10.21037/jtd.2018.06.126
2. Hanada S, Uruga H, Takaya H, et al. Nebulized liposomal amphotericin b for treating aspergillus empyema with bronchopleural fistula. *Am J Respir Crit Care Med*. 2014;189(5):607–608. doi:10.1164/rccm.201311-2086LE
3. Okuda M, Go T, Yokomise H. Risk factor of bronchopleural fistula after general thoracic surgery: review article. *Gen Thorac Cardiovasc Surg*. 2017;65(12):679–685. doi:10.1007/s11748-017-0846-1

4. Mammana M, Marulli G, Zuin A, et al. Postpneumonectomy bronchopleural fistula: analysis of risk factors and the role of bronchial stump coverage. *Surg Today*. 2020;50(2):114–122. doi:10.1007/s00595-019-01871-0
5. Sonobe M, Nakagawa M, Ichinose M, Ikegami N, Nagasawa M, Shindo T. Analysis of risk factors in bronchopleural fistula after pulmonary resection for primary lung cancer. *Eur J Cardiothorac Surg*. 2000;18(5):519–523. doi:10.1016/S1010-7940(00)00541-8
6. Pforr A, Pages PB, Baste JM, et al. A predictive score for bronchopleural fistula established using the French database epithor. *Ann Thorac Surg*. 2016;101(1):287–293. doi:10.1016/j.athoracsur.2015.06.026
7. Uramoto H, Hanagiri T. The development of bronchopleural fistula in lung cancer patients after major surgery: 31 years of experience with 19 cases. *Anticancer Res*. 2011;31(2):619–624.
8. Sirbu H, Busch T, Aleksic I, Schreiner W, Oster O, Dalichau H. Bronchopleural fistula in the surgery of non-small cell lung cancer: incidence, risk factors, and management. *Ann Thorac Cardiovasc Surg*. 2001;7(6):330–336.
9. Mehta RM, Singla A, Bhat RS, Godara R, Lokanath C, Cutaia M. An innovative solution for prolonged air leaks: the customized endobronchial silicone blocker. *J Bronchol Interventional Pulmonol*. 2018;25(2):111–117. doi:10.1097/LBR.0000000000000459
10. Bansal S, Furtado A, Kalpakam H, Loknath C, Mehta RM. A customized multimodality approach for prolonged air leaks (PAL) in mechanically ventilated patients. *Respir Case Rep*. 2023;11(7):e01173. doi:10.1002/rcr2.1173
11. Zakaluzny S. Complications of tracheobronchial airway stents. Otolaryngology. *Head and Neck Surg*. 2003;128(4):478–488. doi:10.1016/S0194-5998(03)00002-0
12. Nashef SAM, Dromer C, Velly JF, Labrousse L, Couraud L. Expanding wire stents in bengin tracheobronchial disease: indications and complications. *Ann Thorac Surg*. 1992;54(5):937–940. doi:10.1016/0003-4975(92)90653-L
13. Roy P, Héluain V, Leyx P, et al. A 3D-engineered silicone stent to treat a refractory bronchopleural fistula. *ERJ Open Res*. 2023;9(2):00670–02022. doi:10.1183/23120541.00670-2022
14. Battistoni P, Caterino U, Batzella S, Dello Iacono R, Lucantoni G, Galluccio G. The use of polyvinyl alcohol sponge and cyanoacrylate glue in the treatment of large and chronic bronchopleural fistulae following lung cancer resection. *Respiration*. 2017;94(1):58–61. doi:10.1159/000477350
15. Cao M, Zhu Q, Wang W, Zhang T, Jiang M, Zang Q. Clinical application of fully covered self-expandable metal stents in the treatment of bronchial fistula. *Thorac Cardiovasc Surg*. 2015;64(06):533–539. doi:10.1055/s-0034-1396681
16. Wu G, Li ZM, Han XW, et al. Right bronchopleural fistula treated with a novel, Y-shaped, single-plugged, covered, metallic airway stent. *Acta Radiol*. 2013;54(6):656–660. doi:10.1177/0284185113481596
17. Han X, Yin M, Li L, et al. Customized airway stenting for bronchopleural fistula after pulmonary resection by interventional technique: single-center study of 148 consecutive patients. *Surg Endosc*. 2018;32(10):4116–4124. doi:10.1007/s00464-018-6152-x
18. Grotberg JC, Hyzy RC, De Cardenas J, Co IN. Bronchopleural fistula in the mechanically ventilated patient: a concise review. *Crit Care Med*. 2021;49(2):292–301. doi:10.1097/CCM.0000000000004771
19. Hance JM, Martin JT, Mullett TW. Endobronchial valves in the treatment of persistent air leaks. *Ann Thorac Surg*. 2015;100(5):1780–1786. doi:10.1016/j.athoracsur.2015.05.073
20. Tchkonia D, Vacharadze K, Mskhaladze T. The efficacy of endobronchial valve therapy in complex treatment of broncho-pleural fistulas. *Georgian Med News*. 2020;306:73–76.
21. Alexander ES, Healey TT, Martin DW, Dupuy DE. Use of endobronchial valves for the treatment of bronchopleural fistulas after thermal ablation of lung neoplasms. *J Vasc Interv Radiol*. 2012;23(9):1236–1240. doi:10.1016/j.jvir.2012.06.009
22. Hathorn C, Armitage N, Wensley D, Seear M. Bronchial balloon occlusion in children with complex pulmonary air leaks. *Arch Dischildhood*. 2013;98(2):136–140. doi:10.1136/archdischild-2012-302529
23. Uchida S, Igaki H, Izumo T, Tachimori Y. Effective treatment of empyema with bronchopleural fistula after esophagectomy by endobronchial embolization using endobronchial Watanabe Spigots. *Int J Surg Case Rep*. 2017;33:1–3. doi:10.1016/j.ijscr.2016.11.025
24. Date N, Komatsu T, Fujinaga T. A novel technique for Endobronchial Watanabe Spigot placement for bronchopleural fistula: a traction method. *Eur J Cardiothorac Surg*. 2021;60(5):1237–1238. doi:10.1093/ejcts/ezab332
25. Dalar L, Kosar F, Eryuksel E, Karasulu L, Altin S. Endobronchial Watanabe spigot embolisation in the treatment of bronchopleural fistula due to tuberculous empyema in intensive care unit. *Ann Thorac Cardiovasc Surg*. 2013;19(2):140–143. doi:10.5761/atcs.cr.11.01760
26. Hayama M, Sato S, Shiroyama T, Nishida T, Nishihara T, Okamoto N. Endoscopic bronchial occlusion with silicone spigots under virtual bronchoscopic navigation. *Respir Case Rep*. 2016;4(4):e00157. doi:10.1002/rcr2.157
27. Nakano T, Kawada M, Minami K, Kaneda H. Successful endobronchial occlusion in empyema with broncho-pleural fistula secondary to COVID-19 pneumonia: a case report and literature review. *Respir Case Rep*. 2021;9(7):e00785. doi:10.1002/rcr2.785
28. Sasada S, Tamura K, Shu CY, et al. Clinical evaluation of endoscopic bronchial occlusion with silicone spigots for the management of persistent pulmonary air leaks. *Intern Med*. 2011;50(11):1169–1173. doi:10.2169/internalmedicine.50.5016
29. Kaminuma Y, Tanahashi M, Suzuki E, Yoshii N, Niwa H. Extensive bronchial occlusion with N-butyl-2-cyanoacrylate for bronchopleural fistula and a destroyed lung. *Respir Case Rep*. 2020;8(1):e00500. doi:10.1002/rcr2.500
30. Motus IY, Bazhenov AV, Basyrov RT, Tsvirenko AS. Endoscopic closure of a bronchopleural fistula after pneumonectomy with the Amplatzer occluder: a step forward? *Interact Cardiovasc Thorac Surg*. 2019;ivz241. doi:10.1093/icvts/ivz241
31. Krumpolcova M, Durand M, Rossi-Blancher M, et al. Endobronchial closure of bronchopleural fistula with amplatzer PFO Device. *Thorac Cardiovasc Surg*. 2012;60(05):366–368. doi:10.1055/s-0031-1280005
32. López AG, Luján RG, Gafas ADP, et al. First use of Amplatzer device for bronchopleural fistula after lung transplantation. *Thorax*. 2017;72(7):668–670. doi:10.1136/thoraxjnl-2016-209543
33. Pasley T, Ruygrok PN, Kang N, O'Carroll M, Kolbe J, Morrice D. Closure of a broncho-pleural fistula using an atrial septal defect occluder. *Heart Lung & Circulation*. 2014;23(3):e92–e95. doi:10.1016/j.hlc.2013.10.092
34. Cheyney SR, Herrera L, Zul Jiwani A. Management of recurrent bronchopleural fistula secondary to aspergilloma using atrial septal defect closure device. *CHEST*. 2023;164(4):A5357–A5358. doi:10.1016/j.chest.2023.07.3476
35. Bashenow AV, Motus IY, Tsvirenko AS, Medvinskiy ID, Dovbnya SA, Dotsenko IA. Right main bronchus para-occluder fistula closure with a septal defect occluder. *Asian Cardiovasc Thorac Ann*. 2019;27(6):505–508. doi:10.1177/0218492319854240
36. Bai Y, Li Y, Chi J, Guo S. Endobronchial closure of the bronchopleural fistula with the ventricular septal defect occluder: a case series. *BMC Pulm Med*. 2021;21(1):313. doi:10.1186/s12890-021-01676-3

37. Fruchter O, El Raouf BA, Abdel-Rahman N, Saute M, Bruckheimer E, Kramer MR. Efficacy of bronchoscopic closure of a bronchopleural fistula with amplatzer devices: long-term follow-up. *Respiration*. 2014;87(3):227–233. doi:10.1159/000357074
38. Sivrikoz CM, Kaya T, Tulay CM, İ A, Bilir A, Döner E. Effective approach for the treatment of bronchopleural fistula: application of endovascular metallic ring-shaped coil in combination with fibrin glue. *Ann Thorac Surg*. 2007;83(6):2199–2201. doi:10.1016/j.athoracsur.2007.01.005
39. Clemson LA, Walser E, Gill A, Lynch JE, Zwischenberger JB. Transthoracic closure of a postpneumonectomy bronchopleural fistula with coils and cyanoacrylate. *Ann Thorac Surg*. 2006;82(5):1924–1926. doi:10.1016/j.athoracsur.2006.01.069
40. Baden W, Hofbeck M, Warmann SW, Schaefer JF, Sieverding L. Interventional closure of a bronchopleural fistula in a 2 year old child with detachable coils. *BMC Pediatr*. 2022;22(1):250. doi:10.1186/s12887-022-03298-y
41. Liu Z, Mao J, Su M, et al. New treatment of bronchopleural fistula following surgical resection of the dorsal segment of the left lower lobe: a case report. *Thoracic Cancer*. 2021;12(3):382–386. doi:10.1111/1759-7714.13734
42. Ueda Y, Somamoto S, Kawabata S, et al. Development of a novel material to promote wound healing at bronchial defects. *Ann Thorac Surg*. 2023;116(2):239–245. doi:10.1016/j.athoracsur.2022.06.026
43. Management of air leaks post-surgical lung resection -PMC. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6712254/. Accessed July 9, 2024.
44. Mazzella A, Bertolaccini L, Sedda G, et al. Pneumonectomy and broncho-pleural fistula: predicting factors and stratification of the risk. *Updates Surg*. 2022;74(4):1471–1478. doi:10.1007/s13304-022-01290-w