Received: 9 June 2022 | Accepted: 23 July 2022

DOI: 10.1111/iwj.13915

ORIGINAL ARTICLE

IWJ WILEY

A treatment protocol for chronic post-pneumonectomy empyema associated with bronchopleural fistula: A single-centre retrospective study

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Funding information
National Natural Science Foundation of China, Grant/Award Number: 82002902

Abstract

Chronic post-pneumonectomy empyema (CPPE) associated with bronchopleural fistula (BPF) is a potentially fatal complication and remains a surgical challenge. This study aims to propose a treatment protocol for managing this severe disease. From July 2009 to June 2021, 47 CPPE with BPF patients were treated in our department. CT scan with 3D reconstruction was used to detect BPF and to evaluate the location and volume of empyema cavity. Different surgical techniques were used to close BPFs according to they sizes. Multiple pedicled muscle flaps were chosen to fill the empyema cavity, and among them, latissimus dorsi (LD) was the mostly used flap. For cases that regional flaps were not suitable, free flaps were used. Patients were followed-up from 7.9 to 102.8 months. Forty-four patients (93.6%) healed after the operation. Closure of BPFs failed in three patients (6.4%), leading to regional infection. These patients were treated by bronchoscopic application of sealants, continuous drainage and antibiotics, and they eventually healed. Total or partial flap loss was not seen in any of the cases. Treatment protocol was proposed based on these results. CT scan with 3D reconstruction is an effective examination to evaluate pleural cavity defect and BPF. Proper technique to close the BPF and right choice of flap to fulfil the empyema cavity are the two most important key points to treat CPPE associated with BPF patients.

KEYWORDS

3-D CT reconstruction, bronchopleural fistula, muscle flap, post-pneumonectomy empyema, thoracic reconstruction

Key Messages

- chornic post-pneumonectomy empyema (CPPE) associated with broncho-pleural fistula (BPF) is a leathal complication and there is a lack of consense on its treatment

Ming Zhu and Yang Yang are the first two authors contributed equally to this work and should be considered co-first authors.

- we proposed a treatment protocol for CPPE and BPF patients by retrospectively analysis of clinical data over the past 10 years
- three dimensional (3D) reconstruction was performed based on CT data before surgery to help the surgeons understand the difficulty of the operation and prepare well for the operation
- different techinques were used to close BPFs depending on their sizes
- multiple flaps were used to extinguish the empyema in plueral cavity, latissimus dorsi flap is the mostly used flap.

1 | INTRODUCTION

Post-pneumonectomy empyema (PPE) associated with bronchopleural fistula (BPF), with an incidence of 1% to 11% after thoracic operations,[1] is a lethal complication and remains a challenge for both thoracic and plastic surgeons. Open-window thoracostomy is often performed as the first-stage operation, and this surgical technique promotes resolution of inflammation; however, BPF is unlikely to heal automatically after the operation.[2] Further surgical steps that aim to close BPF and reconstruct thoracic wall are needed. Although several techniques such as endoscopic treatment, flap reconstruction have been proposed, recurrence of BPF and CPPE is still a big challenge, and there is still a lack of systematic treatment protocol for the secondary treatment steps.

In this study, we proposed a treatment protocol for chronic PPE (CPPE) and BPF patients by retrospectively analysis of clinical data over the past 10 years.

2 | PATIENTS AND METHODS

The study was approved by the Independent Ethics Committee of Zhongshan Hospital, Fudan University (No. Y2018-055).

From July 2009 to June 2021, 47 patients diagnosed as CPPE associated with BPF were admitted to the Plastic and Reconstructive Department of Zhongshan Hospital, Fudan University. Each patient underwent an open-window thoracostomy as a first-stage operation in local hospital. After infection was controlled, a second-stage surgery, which aimed to close BPF and dead cavity, is performed in our department.

2.1 | Three-dimensional reconstruction before surgery

Before the surgeries, all patients underwent thin-layer computed tomography (CT), and presurgical three-dimensional (3D) reconstruction was performed routinely based on CT data. The 3D software, Mimics 21.0 (Materalise, Leuven, Belgium), was used to reconstruct the 3D image of the empyema space and residual bronchial stump. With the help of 3D image, size and location of CPPE and a part of BPFs could be evaluated, neighbouring relationship between vital organs/vessels/nerves and surgical site could be also assessed. Bronchoscopy was also used to confirm the location and size of BPFs pre-operatively, especially for BPFs with a small size. Surgical plan is conducted under the guidance of 3D image, and this allows the surgeons to understand the difficulty of the operation and prepare well for the operation.

2.2 | Surgical strategy

In general, the surgical management strategy was selected depending on the size of the BPF, location and volume of empyema space in pleural cavity. A successful surgical technique for BPF with CPPE treatment should meet the following requirements: (a) firmly closure of the BPF and (b) extinguishing of the empyema space in the pleural cavity with a well-vascularised muscle of sufficient volume.

2.2.1 | Closure of the BPF

Different techniques were used to close BPFs depending on their sizes:

1. For a fistula with diameter less than 1.0 mm, bronchoscopic application of sealants, fibrin glue, silver nitrate cautery, or coils was used (group A).
2. For a fistula with diameter from 1 to 3 mm, Neoveil patch (Gunze Co., Tokyo, Japan) was bonded to the fistula by medical anastomotic glue (OB Glue) (group B).
3. For a fistula with diameter from 3 to 5 mm, residual bronchial mucosal and scar tissue around the fistula were carefully raised and sutured, strengthened by Neoveil patch (group C).

FIGURE 1 Study flowchart

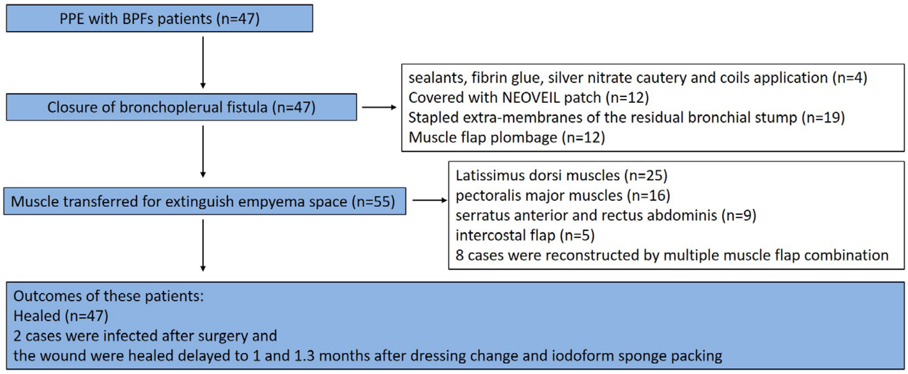

TABLE 1 Patient characteristics

Parameters	Values
Patients diagnosed as having PPE associated with BPF	47
Age (mean ± SD, year)	53.6 ± 11.3
Gender (M/F)	25/22
CPPE allocation (L/R)	29/18
BPF diameter (mean ± SD, mm)	5.5 ± 4.3
Volume of the empyema cavity (mean ± SD, cm^3)	140.3 ± 95.4
Time from initial thoracic surgery to the reconstructive surgery (mean ± SD, month)	6.3 ± 2.4
Days of hospital stay (mean ± SD, d)	25.7 ± 5.3
Days of removing drainage tube (mean ± SD, d)	20.3 ± 11.8
Follow-up (mean ± SD, m)	49.7 ± 32.1

4. For a fistula with diameter more than 5 mm, well-vascularized tissues such as the latissimus dorsi (LD) muscle, pectoralis major (PM) muscle, intercostal muscle were separated and sutured to around the fistula (group D).

2.2.2 | Extinguishing the empyema space in pleural cavity

The empyema space was stuffed with flaps. Briefly, the inner wall of empyema was firstly scratched, then one or more well-vascularized flaps were transferred to cover the repaired fistula and stuff the cavity.

We considered latissimus dorsi (LD) muscle as an optimal choice for extinguishing postoperative empyema if the pedicle was preserved in prior surgeries. If the thoracodorsal vessels have been cut, a retrograde muscle flap supplied by the posterior paraspinal perforating branch could be used, although the volume of the muscle is smaller. Other transferred flap options include pectoralis major (PM) and rectus abdominis (RA) muscle flaps. Serratus anterior (SA) and intercostal muscle were normally used; however, neither of the muscle flaps was large enough to repair the thoracic defect alone in most cases; these muscles were used together in combination with other muscles to increase the volume of flaps.

For patients that volume of regional flaps was not large enough for defect repairing, free anterolateral thigh flap was used. Possible recipient vessels were thoraco-dorsi, internal thoracic, thoraco-acromial, intercostal, and circumflex scapular vessels. In this study, intercostal vessels were used as recipient vessels in all the cases.

Postoperatively, drains at the flap donor site were removed in sequence after at least 1 week, when the flow rate was less than 30 mL/day. Antibiotic therapy was performed in collaboration with the Department of Infectology. Patients were encouraged to begin movement as soon as possible. The perspective data of this study are presented as a flowchart (Figure 1) (Table 1).

3 | RESULTS

The 47 patients comprised 25 men and 22 women with a mean age of 53.6 ± 11.3 years (range 32-76 years); 61.7% CPPEs were located in the left thoracic cavity (n = 29) and 38.3% in the right thoracic cavity (n = 18). The indications for the thoracic operations that result in CPPE associated with BPF were lung cancer (n = 31), bronchiectasis (n = 9), congenital pulmonary cyst (n = 5), and aspergilloma (n = 2). The mean diameter of the fistulas was 5.5 ± 4.3 mm (range 0.7-15 mm), and the volume of empyema cavity was 140.3 ± 95.4 cm^3 (range 64-302 cm^3), as calculated using the 3D image. BPFs were divided into four groups as described before: 25.5% in group A (n = 12), 42.6% in group B (n = 20), 9.1% in group C (n = 8), and 14.9% in group D (n = 7).

For thoracic reconstruction, single flap was used in 29.8% patients (n = 14) and combined flaps were used in 70.2% patients (n = 33). In single flap group, LD flap was

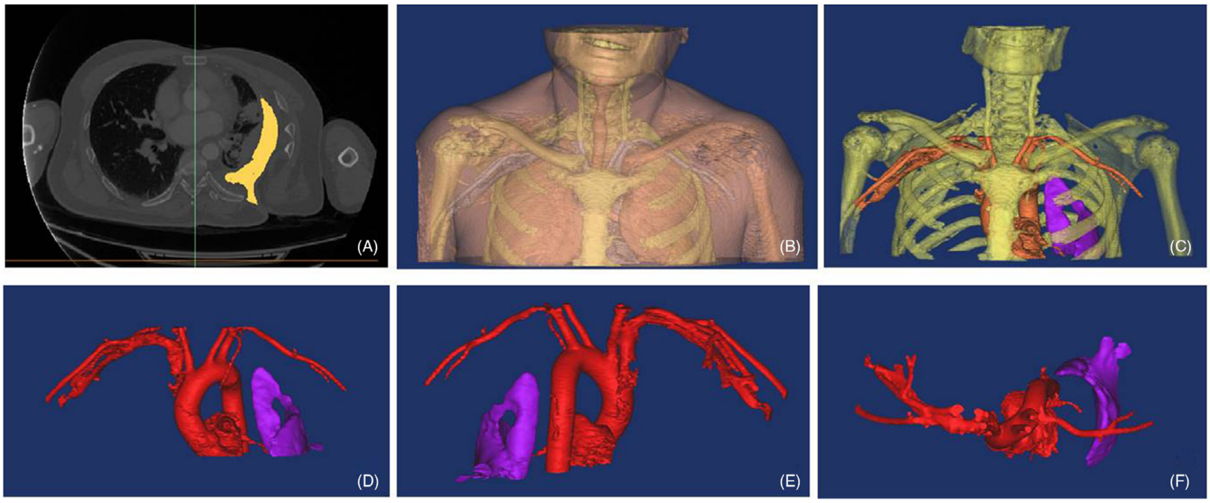

FIGURE 2 Three-dimensional (3D) reconstruction image of post-pneumonectomy empyema with bronchopleural fistula before surgery. (A) Computed tomography (CT) slicer shows the empyema cavity and bronchial fistula (bright yellow part); (B) anterior view of the patient after 3D reconstruction based on CT data; (C) perspective view of the patient: yellow part-bone; red part-angiocarpy; purple part-empyema cavity; (D-F) the relationship between the empyema cavity and important vessels from the anterior, posterior, and superior views

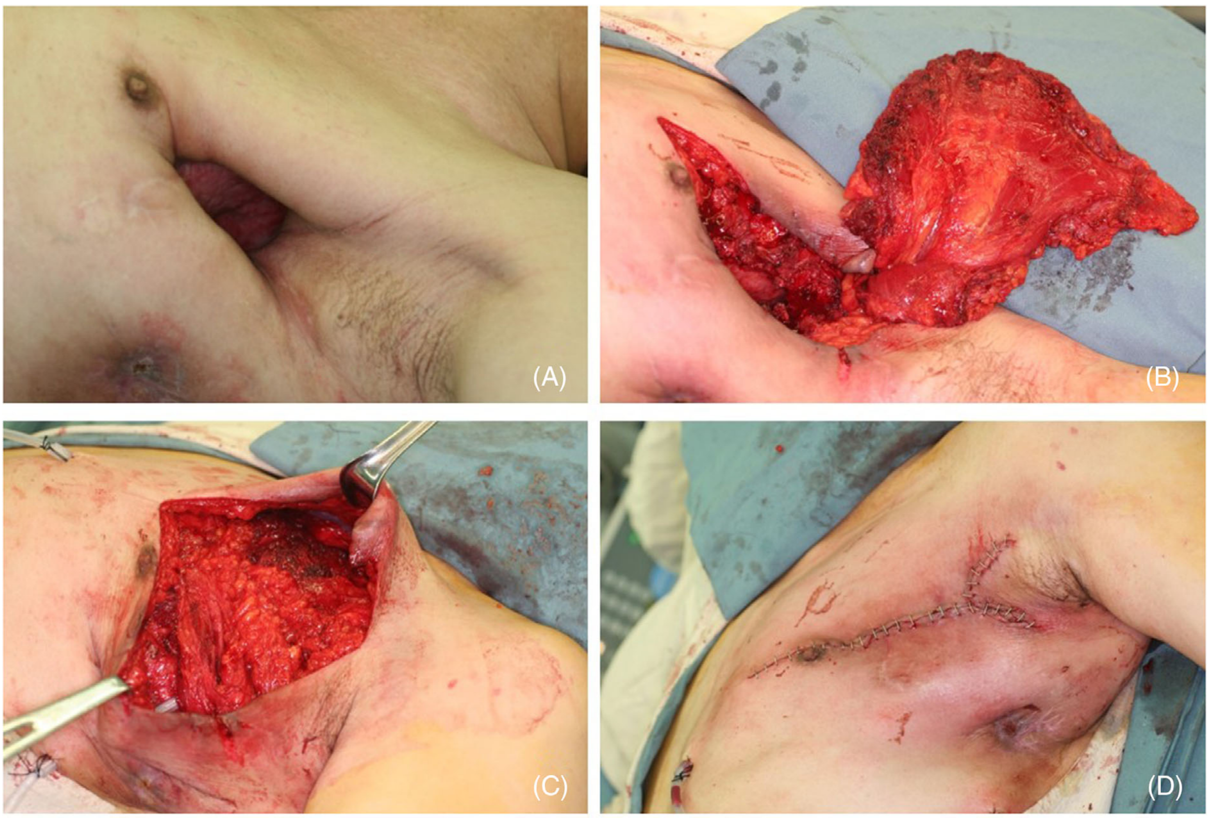

FIGURE 3 Patient diagnosed with chronic post-pneumonectomy empyema associated with bronchopleural fistula was treated by muscle stuffing. (A) preoperative image of the fistula; (B) latissimus dorsi muscle harvesting; (C) the bronchial fistula was closed by sewing the muscles to the fistula and plombage to the cavity; (D) wound closure after drainage tube insertion

used in 21.3% patients (n = 10), while PM flap was used in 8.5% patients (n = 4). In combined flaps group, LD +- RA + intercostal flaps were used in 51.5% patients (n = 24), PM + RA + intercostal flaps were used in 10.6% patients (n = 5), and LD + PM + free ALT flaps were used in 8.5% patients (n = 4).

The average time from initial thoracic surgery to the reconstructive surgery was 6.3 ± 2.4 months (range

FIGURE 4 Images of the patient before and 2 months after surgery. (A) Preoperative image of the patient; (B) the local situation of wound 2 months after surgery; (C) anterior view of the patient, he was in good health during the entire follow-up

3-9 months). The mean length of hospital stay was 25.7 ± 5.3 days (range 13-53 days). Antibiotics were applied after surgery for 7 to 14 days. Drainage tubes were removed when out-put fluid <30 mL/d, and in this study, drainage tubes were removed 20.3 ± 11.8 days (range 9-63 days) after the operation.

Our average follow-up time was 49.7 ± 32.1 months (range 7.9-102.8 months). BPF recurrence occurred in three patients, whose BPFs were all classified into group D, this led to local infections. Since all the BPFs became smaller after the operation (diameter <1 mm), bronchoscopic application of sealants were used to seal the air leakage. One patient received 1 bronchoscopy operation, the other two patients received 3 bronchoscopy operations each, besides antibiotics and continues drainage were applied. Eventually, these three patients recovered at 1, 2.5, and 3 months after the reconstructive surgery. All the patients were in good health during follow-up.

4 | CLINICAL CASE

A 54-year-old man undergone left upper lobectomy for a metastatic pulmonary tumour originating in the liver, delayed empyema occurred 3 years after pulmonary lobectomy. The first-stage surgery, open-window thoracostomy, was performed in a local hospital. In this surgery, second and third ribs in the left anterior chest were removed. When the patient was in better condition, he was transferred into our department. The bacterial culture from the thoracic wound showed methicillin-resistant *Staphylococcus epidermidis*, which was treated with vancomycin. CT scan with 3D reconstruction image before surgery showed the empyema cavity was large, located on the upper thoracic cavity (Figure 2). Bronchoscopy showed a 5-mm-diameter BPF located in left bronchus. The curative surgery was performed with an alteration of the vertical muscle-sparing incision, preserving the LD muscle. After debridement, the bronchial fistula was closed by sewing the muscles to the fistula and plombage to the cavity (Figure 3). Continuous ablution with vancomycin via the thoracic tube was performed for five days. Postoperative infection was not exacerbated, and the patient was discharged from the hospital 2 weeks after surgery. The 3D CT scan showed that the muscle flap engrafted to the cavity completely filled the space at 1.5-year follow-up (Figure 4).

5 | DISCUSSION

PPE, mostly caused by BPF, occurs in 1% to 11% of patients after thoracic operations.[1] This complication is difficult to manage and would increase the mortality rates as high as 50%.[3] Various techniques have been attempted in the last decades; among them, Clagett procedure and Pairolero's modification are the most classic surgical plans.[4] Clagett presented a two-stage procedure for managing PPE: open pleural drainage and granulation tissue formation, followed by obliteration of the pleural cavity with an antibiotic solution during chest wall closure.[5] However, in Clagett's method, high recurrent rate of dead space and BPF remains an issue. To reduce the recurrence rate, Pairolero modified the Clagett method by transferring the intrathoracic muscle to reinforce the BPF and obliterate the empyema cavity.[6] Recently, the development of endoscopic technique and novel medical materials application has reformed the treatment of CPPE with BPF. However, none of the research has proposed a surgical protocol to treat this complication both considering the classic operations and the novel techniques.

In this study, thin-layer CT scan with 3D reconstruction image was obtained from each patient before the operation. We did this for the following reasons: (a) dead space is commonly in a complex 3D shape in the thoracic wall, which could easily be detected by 3D CT reconstruction. This makes the surgeon obliterate the defect more accurately, thus avoids dead space residue and decreases the recurrence rate of CPPE[7]; (b) comparing with two-dimensional view provided by CT scan, 3D CT reconstruction provides a more accurate view of the relationship between the empyema cavity and surrounding important organs and structures,[8] moreover the volume of the dead space could be calculated; (c) combing the results of bronchoscopy and 3D reconstruction, location and size of BPF could be easily observed and calculated, choices of BPF closure could be made accordingly. 3D reconstruction images help surgeons observe the operative site prudently and make a better surgical plan. It is considered as the first step for CPPE and BPF treatment protocol.

The second step in this protocol was closing BPF. As noted, BPF is presented in as many as 80% of patients with PPE and increases the mortality rate considerably,[9] firmly closing BPF is extremely important. In this study, techniques for BPF closure depend on fistula size[10]: (a) for small fistula with a diameter less than 1 mm, endoscopic treatment is very effective; although in some cases, multiple attempts might be taken; (b) for fistula with a diameter from 1 to 3 mm, since BPF is likely to reoccur after endoscopic treatment, patch is used. It not only seals the air leak, but also promotes growth of bronchial mucosa. In this study, BPFs in group B were all successfully treated with this technique; (c) for fistula with a diameter from 3 to 5 mm, residual bronchial stump flaps were turned over and sutured, the repair was reinforced by patch and muscle flap, surgeons should avoid devascularization of the proximal bronchus in this step because it could lead to failure of the repair and recurrence of BPF[11]; (d) for fistula with a diameter larger than 5 mm, normally there was no bronchial stump long enough left, besides the blood supply for a long random flap is not reliable, so traditional muscle flaps reconstruction technique was used to seal the air-leakage. Although BPFs recurrence were seen in three patients in group D, size of fistulas significantly decreased, subsequent endoscopic treatment successfully seals the air-leakage. In this study, 93.6% BPFs healed after treating under the guidance of this protocol, and we believe this category system and treatment protocol are worth promoting.

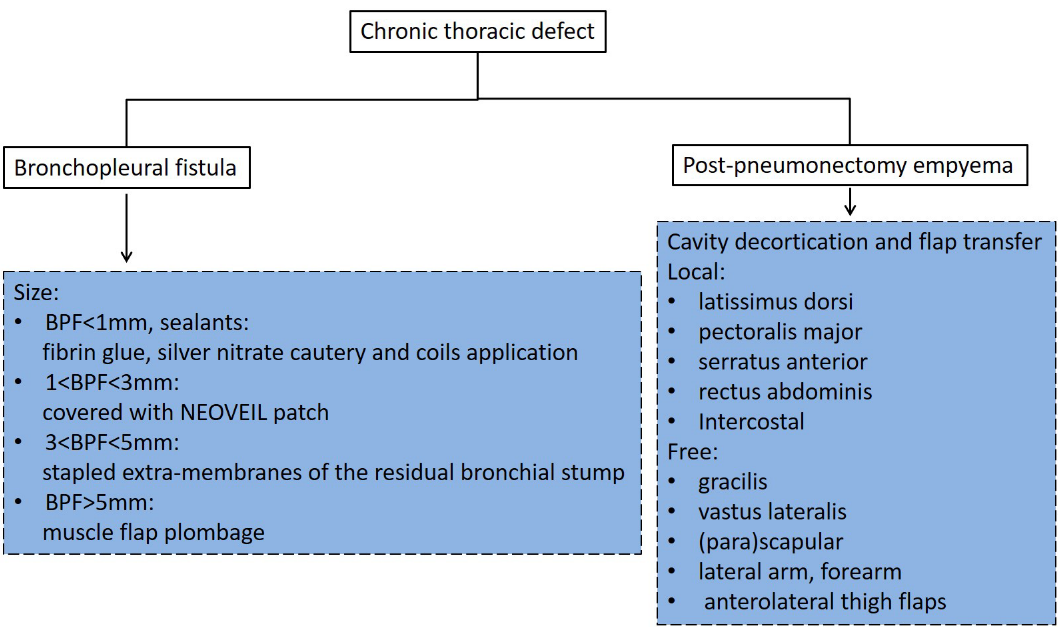

FIGURE 5 Treatment protocol for CPPE associated with BPF

The final step of this protocol is obliteration of the post-pneumonectomy dead space with well vascularized-tissue. As the LD muscle provides the reconstructive surgeon with a well-vascularised tissue with a pliable pedicle and good volume,[12] it became the standard procedure in our department. Other local regional flap options include intercostal, pectoralis major, LD, serratus anterior, and rectus abdominis muscle flaps as well as the omental flap and fasciocutaneous perforator flaps.[13] Occasionally, single flap could not provide sufficient volume and combined flaps are used. Serratus anterior and intercostal muscle are relatively small, and they are usually used as supplement flaps to increase the volume of flaps. If local regional flaps are not suitable, free flaps should be used, which include the free anterolateral thigh flaps, gracilis, LD, and vastus lateralis muscle flaps and the (para)scapular, lateral arm flaps.[14] Among them, ALT is the mostly used flap since it is easy to harvest and has sufficient volume with stable blood supply system. Possible recipient vessels are the thoraco-dorsi, internal thoracic, thoraco-acromial, intercostal, and circumflex scapular vessels and the azygos vein.[15] Among them, internal thoracic vessels are the mostly used recipient vessel, since these vessels are stable with proper calibres for anastomosis. Based on the results of this study, we proposed the treatment protocol for CPPE associated with BPF (Figure 5).

6 | CONCLUSION

Proper technique to close the BPF and right choice of flap to obliterate the empyema cavity are the key points to treat CPPE associated with BPF patients. CT scan with 3D reconstruction provides a clearer image to help surgeons evaluate thoracic cavity and BPF. We believe our treatment protocol for CPPE associated with BPF could be a helpful clinical option.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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How to cite this article: Zhu M, Yang Y, Shi Y, Zhang Y, Liu J, Lu N. A treatment protocol for chronic post-pneumonectomy empyema associated with bronchopleural fistula: A single-centre retrospective study. *Int Wound J*. 2023;20(3):725-731. doi:10.1111/iwj.13915