Original Article

The technique of stump closure has no impact on post-pneumonectomy bronchopleural fistula in the non-small cell lung cancer—a cross-sectional study

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Background: Pneumonectomy is a high-risk radical resection procedure, with bronchopleural fistula (BPF) being its most challenging and severe complication. This study aimed to assess the surgical risk factors and the impact of the bronchial stump closure technique on the incidence of the BPF.

Methods: This is a single-center, cross-sectional study of the medical records of 455 post-pneumonectomy patients operated due to non-small cell lung cancer (NSCLC) in 2006–2017. We analyzed the following variables and their influence on the occurrence of the BPF: operation side, surgical techniques (i.e., manual suture or the stapler), stump buttressing, the extension of pneumonectomy, comorbidities, and postoperative complications.

Results: BPF occurred in 7.47% of post-pneumonectomy patients. BPF was more prevalent in right-sided pneumonectomy versus left-sided (10.98% *vs.* 5.32%; P=0.026). The use of a stapler or manual suture was not associated with the incidence of the BPF (7.96% *vs.*7.09%, P=0.72). There were no significant differences in the occurrence of BPF among bronchial stump buttressing with the parietal pleura (P=0.80), intercostal muscle flap (IMF) (P=0.46), and pericardial fat pad (P=0.88). When comparing data from 2006–2012 with those from 2013–2017, we found a steady decrease in the number of performed stump reinforcements, but this was not associated with a higher risk of BPF.

Conclusions: The method used for stump closure, additional tissue buttressing of the bronchial stump and year of the surgery had no significant impact on the occurrence of BPF. Only right-sided pneumonectomy was associated with higher BPF occurrence.

Keywords: Pneumonectomy; bronchopleural fistula (BPF); intercostal muscle flap (IMF); bronchial stump buttressing

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Introduction

Pneumonectomy is a radical procedure associated with significant morbidity and mortality (1,2). However, it is still an effective treatment for over 10% of patients with centrally located non-small cell lung cancer (NSCLC) (3). Since the first pneumonectomy performed by Graham and Singer, the advancements in surgical materials, operating techniques, antibiotics, and perioperative care have decreased the risk of severe complications and improved overall survival and quality of life, even among elderly patients (1,4-7).

Post-pneumonectomy bronchopleural fistula (BPF) remains the most devastating complication in the early postoperative period. It affects 1.5–12.5% of NSCLC patients undergoing pneumonectomy (5,8,9), leading to life-threatening complications, such as respiratory insufficiency, pneumonia, empyema, and sepsis in the remaining lung. Furthermore, 13–67% of individuals who develop BPF after pneumonectomy dies within 30 days after the operation (8-11).

To reduce the occurrence of BPF, several surgical methods may improve bronchial stump vascularization. The main principle of this surgical technique involves making a short and firmly closed bronchial stump (7,10,11). Many surgeons consider it worthwhile to buttress the bronchial stump with well-perfused tissues like an intercostal muscle flap (IMF), parietal pleura, pericardium, and mediastinal fat (12,13). Despite many cases of successful buttressing, the ideal tissue material has still not been identified, and the actual benefit of the bronchial stump coverage after pneumonectomy remains controversial (10).

This cross-sectional study analyzed the surgical solutions and techniques performed in our department over the last decade. Our study aimed to evaluate the surgical factors and techniques that could influence the occurrence of BPF. We also aimed to assess the influence of different buttressing tissues on the frequency of early post-pneumonectomy BPF. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-240/rc).

Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by The Bioethics Committee of the Poznan University of Medical Sciences (No. 948/21). Appropriate consent for analyzing and publishing anonymized data has been obtained.

The follow-up was based on the medical records of our department's database. Out of 3,600 NSCLC patients operated on in our department from 2006–2017, 472 patients underwent pneumonectomy (13.1%). The specific number of pneumonectomies performed in our center per year is presented in *Figure 1*.

According to the Rami-Porta definition (14), we included 455 cases that underwent radical resection (R0) due to NSCLC. Patients who underwent R1 resection were excluded from the study; this resulted in a homogeneous group in terms of the radicality of the procedure and its potential impact on BPF development. We divided patients into two groups for several analyses: those who underwent surgery during 2006–2012 (259 patients) and during 2013–2017 (196 patients). This was related to a radical change in the surgical technique employed in our department. In 2012, we started performing fewer cases of bronchial buttressing with IMF and mediastinal fat. Alongside this, the availability of equipment, including staplers, has also improved.

All patients included in the study underwent chest computed tomography (CT) scan, electrocardiography, pulmonary function tests, and fiberoptic bronchoscopy. The decision of pneumonectomy was based on diagnostic imaging, endoscopy, and several bioptic procedures (transbronchial biopsy and transthoracic needle aspiration biopsy). In addition, pulmonary function tests, diffusing capacity of the lung for carbon monoxide, and capillary blood gas screening were all employed to assess respiratory efficiency. If indicated, echocardiography, and exercise testing were performed. Each operation included complete mediastinal lymphadenectomy. The histopathological examination results were assessed according to the eighth edition of the 2017 TNM classification. The patients operated on before 2017 were reassessed. We have extended the diagnostics to include invasive mediastinal staging in suspected mediastinal node metastases [i.e., mediastinal lymph node >10 mm in diameter on chest CT and/or standardized uptake value maximum >2.5 on positron emission tomography (PET)/CT scan].

The anterolateral thoracotomy was the surgical approach used for all patients. To close the bronchial stump with a stapler, we used the mechanical linear stapler with an adjustable head (length of the sewing line): 55 or 35 mm; height: 4.8 mm; Medtronic, Minneapolis, MN, USA).

Manual suturing was performed via continuous manual suture through the entire length of the stump back and

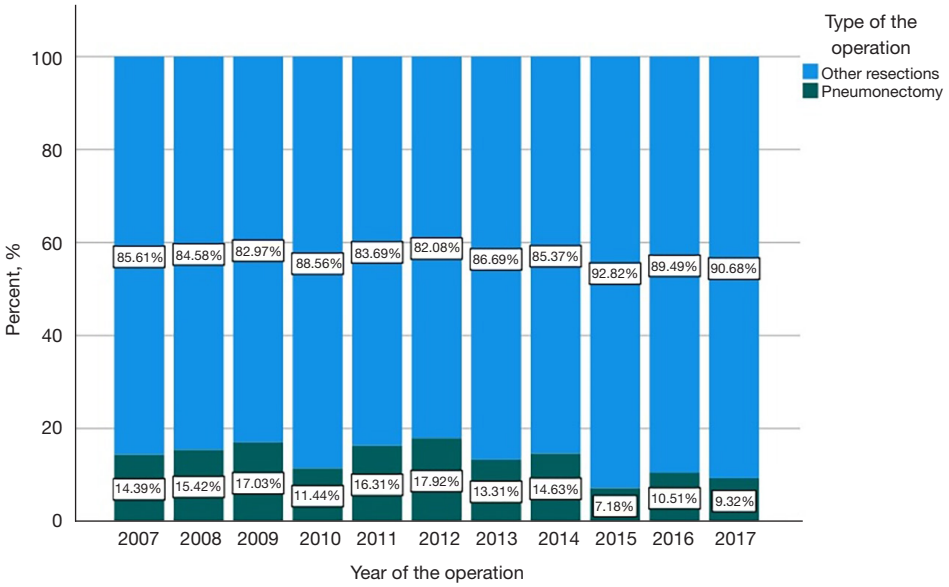

Figure 1 Our department's percentage of pneumonectomies to other anatomical resections in 2007–2017.

forth (double-layer suture). We used an absorbable monofilament suture with a long absorption period (PDS®, Maxonor Monosorb 3/0 suture, Yavo, Bełchatów, Poland).

The diagnosis of BPF was made based on clinical symptoms followed by endoscopy. We analyzed the occurrence of BPF considering the side of the operation, comorbidities, postoperative complications, the use of manual suture *vs.* stapler, stump buttressing, and type of tissue used to cover bronchial stump (IMF, parietal pleura, or pericardium). We also analyzed the influence of extended pneumonectomy on the occurrence of the BPF. Extended pneumonectomy included surgical procedures such as partial resection of the chest wall, diaphragm, left atrium, or superior vena cava, as well as pulmonary artery sleeve resection. This study only included cases of BPF that were diagnosed within 30 days postoperatively.

Statistical analysis

Statistical calculations were performed using the Statistica 12.0 PL software (StatSoft Polska, Kraków, Poland) and StatXact 9.0 (Cytel Inc., Cambridge, MA, USA). Categorical data were analyzed using the χ^2 test. An unpaired *t*-test was used to analyze the data with normal distribution and homogeneous variances. The normality of the distribution was tested using the Shapiro-Wilk test, and the equality of variances was checked with Levene's test. Data that did not follow a Gaussian distribution were analyzed using the Mann-Whitney U test. Statistical significance was set at $P<0.05$. We verified the obtained results by conducting an supplementary Propensity Score Matching Analysis.

Results

The patients' characteristics are illustrated in *Table 1*. There were 41 (9%), 153 (34%), 257 (57%), and 4 (1%) patients diagnosed as having NSCLC stages I, II, III, and IV, respectively. The average postoperative hospital stay for the whole group was 14±13 days. There were 18 (3.96%) in-hospital deaths. The data on comorbidities, surgical technique, complications, and the extent of resection is presented in *Table 2*.

A total of 34 (7.47%) cases of BPF were recorded. Specifically, it occurred in 6.6% and 8.7%of patients in 2006–2012 and 2013–2017, respectively, but no significant differences between these two time periods were found (P=0.90). In the BPF group, 7 people died in hospital, 22 died after discharge, including 7 (20.0%) within 30 days, and another 5 within 90 days after operation. The total 90-day mortality was 12 people (35.3%). There was no association between the in-hospital, 30-day, and 90-day mortality and the method used for stump closure.

BPF was more prevalent after right-sided pneumonectomy than after left-sided [19 (10.98%) *vs.* 15 (5.32%); P=0.026].

In 198 patients (43.5%), the bronchial stump was not

Table 1 Patients after pneumonectomy—the clinical characteristics of the study group

Patient data	Pneumonectomy (n=455)
Age (years)	61 [56–66]
Gender	
Male	337 (74.1)
Female	118 (25.9)
Comorbidities	
COPD	95 (20.9)
Past MI	13 (2.9)
Diabetes	42 (9.2)
Coronary artery disease	11 (2.4)
Arterial hypertension	179 (39.3)
Past stroke	1 (0.2)
NSCLC pathologic stages	
I	41 (9.0)
II	153 (33.6)
III	257 (56.5)
IV	4 (0.9)
Side of the procedure (pneumonectomy)	
Right	173 (38.0)
Left	282 (62.0)
Technique of bronchial stump closure	
Manual suture	251 (55.2)
Stapler	204 (44.8)
Covering tissue used	
Muscle flap	110 (24.2)
Mediastinal fat tissue	112 (24.6)
Parietal pleura	35 (7.7)

Data are presented as median [interquartile range] or n (%). COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; NSCLC, non-small cell lung cancer.

covered with any additional tissue buttressing. In 257 patients (56.5%), the bronchial stump was buttressed with tissues: IMF (42.8%), pericardial fat pad (43.6%), or pleural flap (13.6%). The selection of the tissue buttressing material was an individual decision of the surgeon.

The closure of the bronchial stump with a stapler or manual suture and tissue buttressing was an individual decision of the surgeon. The bronchus was often closed through the manual suture when there was not a sufficient bronchial margin free from neoplastic infiltration. The difference between closing the bronchial stump with a stapler or manual suture was not statistically significant (7.96% *vs.* 7.09%, P=0.72). Bronchial stump buttressing with the parietal pleura, IMF, or pericardium fat pad (5.88%, 9.09%, and 6.36%, respectively; P=0.88) had no significant influence on the frequency of BPF.

When comparing patients operated on from 2006–2012 and those from 2013–2017, we found that the bronchial stump was significantly less frequently buttressed with the IMF (36.7% *vs.* 7.7%; P<0.001) and pericardium fat (29.7% *vs.* 17.6%; P<0.01). The number of cases with parietal pleura buttressing increased in 2013–2017 [14 (10.7%) *vs.* 21 (5.4%); P=0.054], but due of its small sample size, it was not statistically significant. These comparisons are presented in *Table 3*.

The total number of BPF cases did not differ significantly between the two study periods. However, the percentage of bronchial stumps covered via manual suture steadily diminished from 2006–2012 compared to 2013–2017 (66.78% *vs.* 33.22%, P<0.001), whereas the number of staplers used increased (28.96% *vs.* 64.29%, P<0.001).

Propensity Score Matching results comparing right and left pneumonectomy did not differ from those obtained in the initial analysis. There are available in Supplementary Material (Appendix 1) and Table S1.

Discussion

Despite advances in surgical techniques, post-pneumonectomy BPF is still a severe, and challenging complication for every thoracic surgeon (15). BPF is associated with several risk factors, such as the side of the pneumonectomy (9), neoadjuvant chemotherapy (12), diabetes mellitus (12), or residual tumor in the bronchial stump (12). Here, we analyzed factors related to BPF among individuals with NSCLC who underwent pneumonectomy. We found that the occurrence of BPF was more prevalent after right-sided pneumonectomy. Anatomical qualities seem to play a pivotal role in this phenomenon. Firstly, the right bronchus is wider, shorter, and more vertical than the left leading to a more frequent placement of inflammatory material in the bronchial stump (16). Secondly, the smaller mass of surrounding mediastinal tissue that could buttress the bronchial stump also promotes BPF formation (17).

Table 2 Significance of factors that could influence the incidence of BPF among patients after pneumonectomy

Feature	Developed bronchopleural fistula (n=34)	Did not develop bronchopleural fistula (n=421)	P value*
General characteristics			
Males	27 (79.4)	310 (73.6)	0.46
Age (years)	62.0 (58.2–66.0)	61.0 (56.0–66.0)	0.54
Comorbidities			
Diabetes	3 (8.8)	39 (9.3)	0.93
COPD	8 (23.5)	87 (20.7)	0.69
Past MI	2 (5.9)	11 (2.6)	0.27
Coronary artery disease	0	11 (2.6)	0.34
Arterial hypertension	16 (47.1)	163 (38.7)	0.34
Past stroke	0	1 (0.2)	0.78
Side			
Left pneumonectomy	15 (44.2)	267(63.4)	0.026
Right pneumonectomy	19 (55.8)	154 (36.6)	
Surgical technique			
Year of surgery			
2006–2012	17 (50.0)	242 (57.5)	0.4
2013–2017	17 (50.0)	179 (42.5)	
Extended pneumonectomy	10 (29.4)	132 (31.4)	0.81
Manual suture	21 (61.8)	268 (63.7)	0.83
Stapler	16 (47.1)	185 (43.9)	0.73
Tissue buttressing	18 (52.9)	219 (52.0)	0.9
Without tissue buttressing	16 (47.1)	202 (48.0)	
Pleural flap	3 (8.8)	32 (7.6)	0.80
Pericardial fat pad	8 (23.5)	104 (24.7)	0.88
Intercostal muscle flap	10 (29.4)	100 (23.8)	0.46
Complications			
Cardiac arrhythmia	13 (38.2)	144 (34.2)	0.63
Hemorrhage requiring intervention	0	16 (3.8)	0.25
Hematoma requiring intervention	0 (0.0)	13 (3.1)	0.30
Postoperative wound infection	1 (2.9)	5 (1.2)	0.39
Acute kidney injury	0	6 (1.4)	0.48
Chylothorax	0	1 (0.2)	0.78

Data are presented as median (interquartile range) or n (%). *, statistically significant (P<0.05). BPF, bronchopleural fistula; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction.

Table 3 Comparison of the number of BPF cases and bronchial stump buttressing tissues in the pneumonectomies performed in 2006–2012 and 2013–2017

Buttressing and tissue material	2006–2012	2013–2017	P value*
All			
Covered	175 (67.6)	84 (32.4)	<0.001
Uncovered	62 (31.7)	134 (68.4)	
Type of tissue			
Parietal pleura	14 (5.4)	21 (10.7)	0.054
IMF	95 (36.7)	15 (7.7)	<0.001
Pericardium fat pad	77 (29.7)	35 (17.6)	<0.010
BPF	17 (6.6)	17 (8.7)	0.970

Data are expressed as number (%). *, statistically significant (P<0.05). BPF, bronchopleural fistula; IMF, intercostal muscle flap.

Moreover, a more extensive lymphadenectomy is usually performed on the right side (18). Finally, the right bronchus is supplied only by one bronchial artery, whereas two arteries supply the left bronchus (19). Among other surgical factors, leaving a short bronchial stump is crucial in decreasing the risk of BPF formation (20).

We did not find a significant difference between using a stapler or the manual suturing on the incidence of BPF. However, our results show that the more frequent stapler use was not associated with a significant reduction in the incidence of BPF. In contemporary thoracic surgery, staplers seem to be the preferred closure method (20). Staplers decrease contamination of the operation field, reduce the time required for closure, and enable safe vessel preparation. However, the thickened bronchial tissues could make efficient staplers use difficult (20). A disadvantage of some types of staplers is their excessive compression of the bronchial tissues. which may increase the formation of BPF (21). Nevertheless, the superiority of stapler over manual sutures in preventing BPF remains controversial (12). Several studies have reported a lower incidence of BPF after stapler closure compared to manual suturing (11,22,23), while others report a similar incidence between both techniques (24). Beyond the scope of this paper, in recent years, video-assisted thoracic surgery (VATS) pneumonectomy has been performed in selected cases (25), which requires the use of staplers in most situations (26).

Our analysis reveals that the incidence of BPF was not related to the type of tissue used for buttressing the bronchial stump; It is also worth highlighting that limiting the number of cases with IMF and mediastinal fat coverage did not have an adverse effect on BPF incidence over the last decade. Some studies found that bronchial stump coverage could reduce the risk of BPF (10,27), but there is no consensus regarding the superiority of any specific tissue material. The literature describes the advantages of several types of autologous tissue buttressing, such as with IMF (28), pleura (27), pericardial fat pad (13,29), or diaphragm (28). A recent study by Caushi *et al.* reported no significant differences between buttressed and non-buttressed bronchial stumps in the occurrence of BPF (30). Some studies consider IMF as a durable and blood supply-adequate material for bronchial buttressing (27,28). However, some authors described its tendency for calcification over time and unreliable vascularization (31-33). Moreover, the improper harvesting could potentially cause the iatrogenic ischemia of the IMF (28,29). An interesting fact that is not so widely described in the literature is the possible adverse effect of the IMF covering. According to Deschamps *et al.*, prophylactic reinforcement of the bronchial stump was associated with an increased incidence of BPF on univariate analysis (22). In our department, we have gained experiences in buttressing the bronchial stump. Piwkowski *et al.* (34) used indocyanine green fluorescence (ICG-FL), which allowed to intraoperatively observe any distal ischemic sections of the IMF directly covering the bronchial stump. Supporting the bronchial stump with such a poorly perfused muscle could potentially increase the occurrence of BPF. This experience caused us to lessen the use of IMF in buttressing bronchial stumps at our institution from 2013–2017 (Skrzypczak, unpublished data). These observations are supported by the study of Kawamoto *et al.*, which used both ICG-FL and thermography to assess

the blood supply of the IMF (35). They found that the IMF had reduced ICG-FL intensity and temperature at the tip, despite the similar techniques of surgical preparation. Nevertheless, none of the buttressing methods completely protected against the development of BPF (15).

Moreover, not all of these materials were reliably compared during the properly design studies. In this regard, the IMF was tested a few times in a randomized trial (36). In a randomized trial, Sfyridis *et al.* reported a lower incidence of BPF in the IMF group among 68 diabetic patients who underwent pneumonectomy (36). That difference was significant in the univariate analysis, but the use of the IMF was not significantly associated with reducing the development of BPF when adjusted for covariates.

Our study broadens the scope for further, more detailed research into the possibilities of intraoperatively reducing the risk of BPF. Our analysis involves a multi-year observation of a large group of patients after pneumonectomy. In the future, a multi-center study with the randomized use of buttressing tissues could provide a comprehensive answer to the legitimacy and actual advantages of different buttressing tissues.

The authors acknowledge several limitations of this cross-sectional study. We did not perform regression analysis. In our study, right-sided pneumonectomy was the only variable associated with an incidence of BPF. Therefore, we could not implement a decent regression model. Moreover, we only described the population of patients after R0 procedures because we aimed to analyze the most homogeneous research group. Furthermore, our paper is a single-center study. However, the analysis was performed entirely in a high-volume clinical center by an experienced team performing ~400 anatomical lung resections per year. All pneumonectomies in our department were performed and supervised by three experienced surgeons, who performed operations in a similar, previously planned method. Lastly, to the best of our knowledge, our findings are based on a multi-year observation of one of the largest pneumonectomy groups analyzed in the literature.

Conclusions

Right-sided pneumonectomy was significantly associated with higher occurrence of BPF among individuals with NSCLC. Neither the mechanical stapler nor the manual suture influenced the occurrence of BPF. None of the tissue types used for buttressing the bronchial stump were related to the incidence of BPF. Limiting the implementation of IMF and pericardium fat coverage did not increase the occurrence of BPF at our department over the study period.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-240/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-240/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-240/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Bioethics Committee of the Poznan University of Medical Sciences (No. 948/21). Appropriate consent for analyzing and publishing anonymized data has been obtained.

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Appendix 1

We performed a propensity score matching analysis. We used the R-programming language (version 3.6.1.; Vienna, R Project) and R package for propensity score matching called MatchIt. We set the method of propensity score matching as "nearest". We matched individuals who underwent right *vs.* left pneumonectomy and adjusted matching for common risks of BPF: sex, age, suffering from diabetes, chronic obstructive pulmonary disease, and/or coronary artery disease. The matched subset was used to compare the population who underwent right *vs.* left pneumonectomy.

We matched n=158 individuals who underwent right pneumonectomy and n=158 who underwent left pneumonectomy. Then we performed a further univariate analysis in these groups, comparing tissue buttressing, stapler or manual suture closure, the most critical complications, and their potential influence on the bronchopleural fistula occurrence. Categorical data were analyzed using the χ^2 test. An unpaired *t*-test was used to analyze the data with normal distribution and homogeneous variances. The normality of the distribution was tested using the Shapiro-Wilk test, and the equality of variances was checked with Levene's test. Data that did not follow a Gaussian distribution were analyzed using the Mann-Whitney U test. Statistical significance was set at $P<0.05$. The results were not statistically significant. The results are presented in *Table S1*.

Table S1 The table presents the propensity score-matched data results performed in the right *vs.* left pneumonectomy group. The patients from these groups are divided into those who developed the bronchopleural fistula and who did not develop the bronchopleural fistula

Features	Developed bronchopleural fistula, n=27 (100%)	Did not develop bronchopleural fistula, n=289 (100%)	P value
Males	21 (77.8%)	218 (75.4%)	0.786
Age (years)	61.0 (55.0-66.0)	60.0 (56.0-65.0)	0.728
Diabetes	2 (7.4%)	29 (10.0%)	>0.99
Chronic obstructive pulmonary disease	6 (22.2%)	55 (19.0%)	0.688
Past myocardial infarction	0	3 (1.03%)	>0.99
Coronary artery disease	0	1 (0.3 %)	>0.99
Arterial hypertension	14 (51.9%)	114 (39.4%)	0.209
Past stroke	0	1 (0.3%)	>0.99
Operation years: 2006–2012	10 (37.0%)	110 (38.1%)	0.916
Operation years: 2013–2017	17 (62.7%)	179 (61.9%)	0.916
Extended pneumonectomy	8 (29.6%)	86 (29.8%)	0.989
Manual suture	15 (55.6%)	166 (57.4%)	0.85
Stapler	15 (55.6%)	153 (52.9%)	0.795
Tissue buttressing	13 (48.1%)	129 (44.6%)	0.726
Pleural flap	3 (11.1%)	25 (8.7%)	0.720
Pericardial fat pad	7 (25.9%)	61 (21.1%)	0.56
Intercostal muscle flap	6 (22.2%)	56 (19.4%)	0.722
Cardiac arrhythmia	13 (48.1%)	101(35%)	0.172
Hemorrhage requiring intervention	0	11 (3.8%)	0.608
Postoperative wound infection	1 (3.7%)	4 (1.38%)	0.68
Acute kidney injury	0	6 (2.08%)	>0.99