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Effects of preserving the bronchial artery on cough after thoracoscopic lobectomy

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Abstract

Background: The purpose of this prospective study was to explore the influence of both preoperative three-dimensional (3D) reconstruction and intraoperative preservation of the bronchial artery (BA) on postoperative cough after thoracoscopic lobectomy.

Methods: A total of 60 patients who had received a combination of thoracoscopic lobectomy and systematic lymph node dissection were included in this study. They were divided into two groups, namely the BA preservation group (Group A), and conventional surgical treatment group (Group B). In group A, we used Exoview software for 3D reconstruction of the BA before the operation and the BA was preserved during the operation. 3D reconstruction of the BA was not performed before surgery in group B. The incidence of postoperative cough, the Mandarin Chinese version of the Leicester cough questionnaire (LCQ-MC), physiological, psychological and social dimensions and total score of the two groups were compared and analyzed.

Results: The scores and total scores of LCQ-MC in group B were lower than those in group A one and two months after surgery. There were significant differences between the two groups in physiological and psychological dimensions and total scores (p < 0.05), but there was no significant difference in social dimension between the two groups (p > 0.05). The incidence of postoperative cough in group A (16.7%) was lower than that in group B (30%), while the difference was not statistically significant (p = 0.222).

Conclusions: Preoperative 3D reconstruction and intraoperative preservation of the BA can reduce the severity of postoperative cough.

KEYWORDS
bronchial artery, postoperative cough, thoracoscopic surgery, three-dimensional reconstruction

INTRODUCTION

Lung cancer is one of the most common malignant tumors in clinical practices. The incidence rate and mortality rate are the highest in both the world and China. Among them, non-small cell lung cancer (NSCLC) is the most common pathological type, accounting for 80%–85% of cases.[1] In recent years, with the continuous development of minimally invasive technology and in-depth popularization of the concept of enhanced recovery after surgery (ERAS), the most widely used surgical methods in clinical practice are thoracoscopic lobectomy and systematic lymph node dissection.[2] Nevertheless, systematic lymph node dissection expands the scope of operation, increases the difficulty of operation, and leads to an increase in postoperative complications.[3] Postoperative cough is a common complication after lung surgery, and the incidence of postoperative cough has previously been reported to be 25%–50%.[4] Cough

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Liuying Pan and Xiaofei Zhou contributed equally to this work.

after pulmonary resection (CAP) affects the rapid recovery of patients after surgery, and has serious adverse effects on the physiological, psychological and social functions of patients.[5,6] CAP has so far not been taken seriously by surgeons and there is no unified conclusion on the causes and mechanism of postoperative cough.

Many risk factors lead to CAP. Among them, systematic lymph node dissection, especially the dissection of subcarinal lymph nodes, is one of the most important risk factors.[7] In a previous study,[8] we also confirmed that subcarinal lymph node dissection is an independent risk factor for CAP. Nevertheless, our study has not further

elucidated the mechanism of the aggravation of postoperative cough by subcarinal lymph node dissection. The mechanism of CAP that is caused by lymph node dissection may include the following three points. First, a residual cavity left after lymph node dissection could result in rapid adaptive lung stretch receptor exposure. In addition, mechanical stimulation that is caused by ambulation and chemical stimulation that is caused by pleural effusion could excite these receptors and lead to cough reflex through vagus nerve conduction. Second, during lymph node dissection, electric scalpel, ultrasonic scalpel and other instruments could damage the vagus nerve
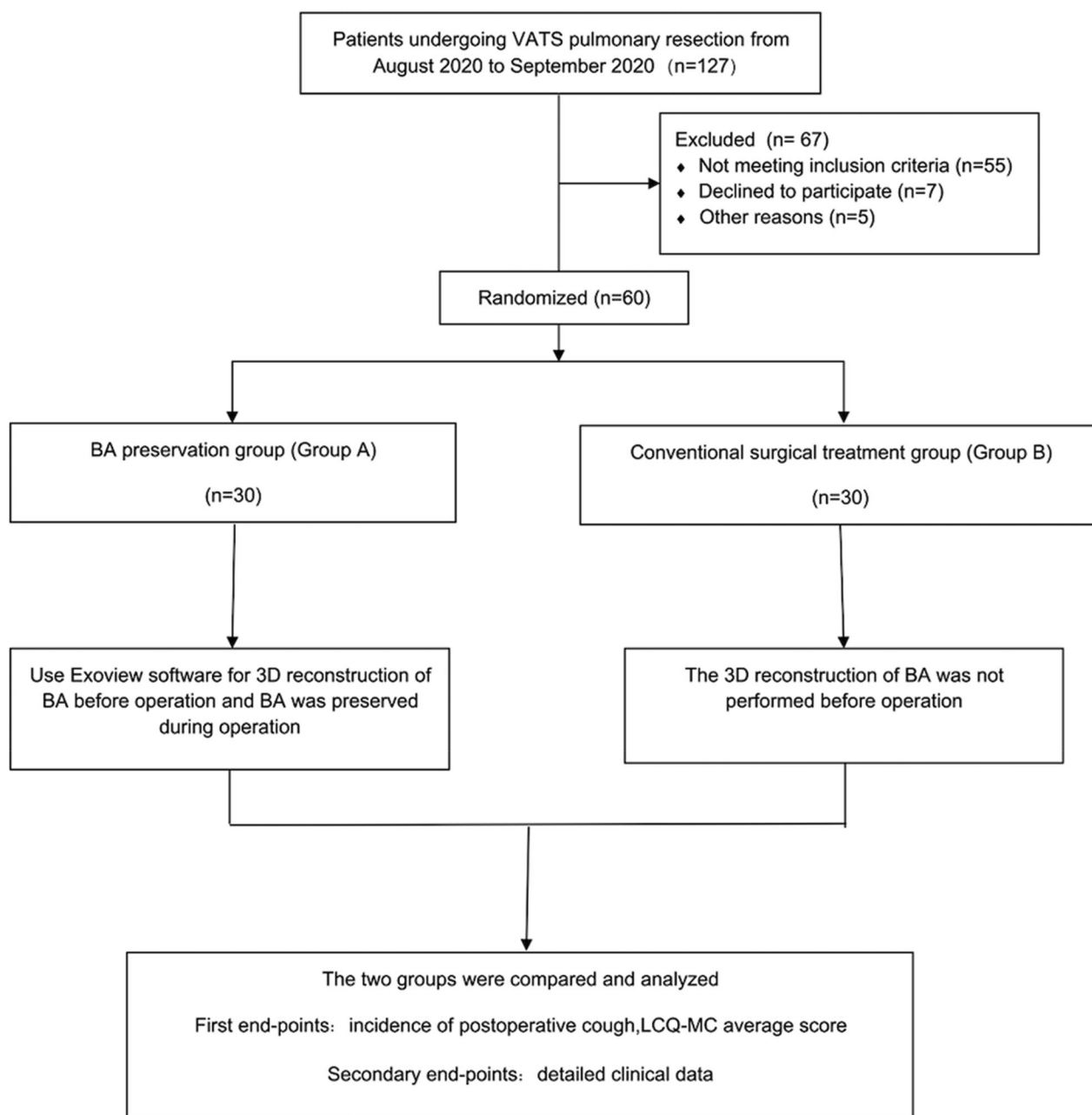

FIGURE 1 Patient flowchart. VATS, video-assisted thoracoscopic surgery; BA, bronchial artery; 3D, three-dimensional; LCQ-MC, the Mandarin Chinese version of the Leicester cough questionnaire

FIGURE 2 Three-dimensional (3D) reconstruction of the bronchial artery (BA) before surgery. (a) The left BA runs behindof the left main bronchus, and the right BA runs under the tracheal bifurcation to the rear of the right upper lobe bronchus. (b) The left BA originates from the right wall of the ascending aorta and runs behind the left main bronchus; the right BA originates from the right wall of the ascending aorta and runs behind the main bronchus and the back of the right superior bronchus. (c) The right BA originates from the right intercostal BA trunk and runs behind the trachea and right main bronchus. (d) The left BA originates from the anterior wall of the ascending aorta and runs above the left main bronchus
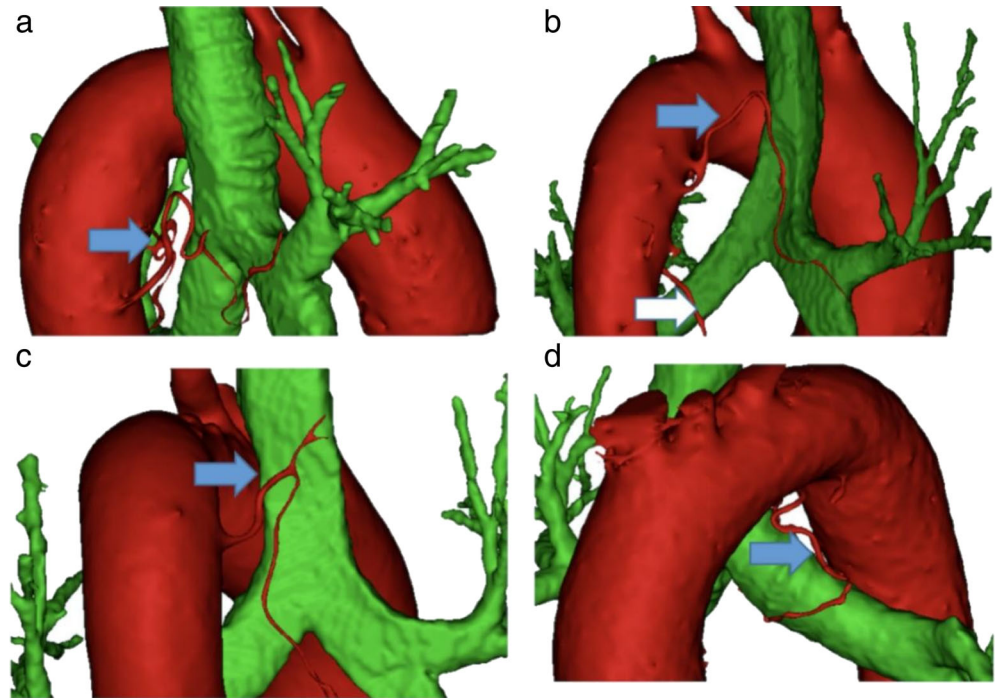
afferent fibers and the trachea wall in corresponding position, thus resulting in increased sensitivity of cough afferent fibers and abnormal excitation of cough receptors in the tracheal wall, and aggravating postoperative cough. Third, lymph node dissection can cause inflammation in the surrounding airway and lung tissues. Inflammatory factors are released through various ways, mainly including bradykinin (BK) and prostaglandin E-2 (PGE2). On this basis, the transient receptor potential channel vanillin subtype 1 (TRPV1) pathway[9] is activated to induce postoperative cough in different ways. During mediastinal lymphadenectomy, especially in subcarinal lymph node dissection, due to improper operation and anatomical variation of the bronchial artery (BA), the BA might be damaged. BA is a part of systemic circulation and is the nutrient vessel of lung. It dominantly supplies blood to the trachea, nerve tissue, esophagus, lymph node, visceral pleura and other organs[10]; there are great differences in the origin, number, branch type and shape of BA among individuals.[11] BA injury can increase intraoperative bleeding, thereby leading to postoperative pulmonary complications. However, research on the relationship between BA injury and postoperative cough is rare.

In recent years, studies on the intervention measures and treatment methods of reducing cough after thoracoscopic lobectomy have mainly focused on drug treatment,[12] traditional Chinese medicine (TCM) treatment,[13] surgery[14] and anesthetic intervention,[15] etc. However, studies on reducing postoperative cough by improving surgery are relatively rare. The purpose of this prospective study was to investigate whether preoperative three-dimensional (3D) reconstruction and intraoperative preservation of the BA can reduce the severity of cough in patients after thoracoscopic lobectomy, so as to

further explore the effective intervention measures of postoperative cough and enrich the concept of ERAS.

METHODS

This study was approved by the ethics committee of the First Affiliated Hospital of Soochow University. In the ClinicalTrials. gov successful registration (NCT04651686), all patients signed the informed consent before operation.

Patient selection

From August 1, 2020 to September 31, 2020, 60 patients with single port thoracoscopic lobectomy and systematic lymph node dissection were enrolled in this prospective study. The Research Unit of the In Patient Department randomized the patients by using sequentially numbered, opaque, sealed envelopes. They were randomly divided into two groups, namely the BA preservation group (Group A) and the conventional surgical treatment group (Group B). Inclusion criteria were as follows: (i) Age ≥ 18 years old, male or female, (ii) no symptoms of cough two weeks before surgery; (iii) lung adenocarcinoma confirmed by pathology, and (iv) single port thoracoscopic lobectomy and systematic lymph node dissection. Exclusion criteria were as follows: (i) Cough caused by respiratory diseases, pharyngitis, rhinitis, etc., before surgery, (ii) pneumonia indicated by chest X-ray or chest computed tomography (CT) in recent months; (iii) conversion of thoracoscopic surgery to thoracotomy, (iv) pulmonary arteriovenous angiography cannot be performed in patients allergic to the contrast medium, and
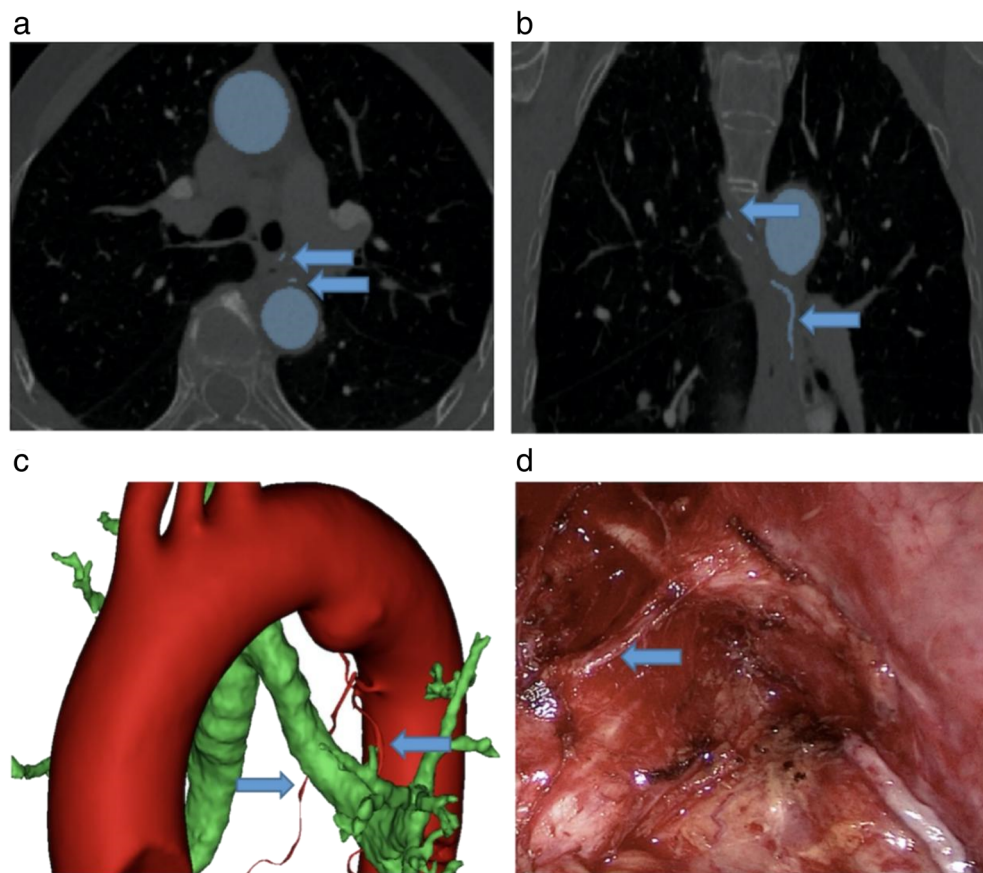
FIGURE 3 Three-dimensional (3D) reconstruction and intraoperative protection of the bronchial artery (BA). (a and b) Chest enhanced CT showed that there were two bronchial arteries (one left and one right). (c) Preoperative 3D reconstruction showed that the left and right bronchial arteries originated from the anterior wall of ascending aorta. (d) During the operation, lymph node dissection under the carina was performed and clearly displayed a left BA

(v) refusal of patients and their families to be enrolled into the study and followed up (Figure 1).

Preoperative CT examination

All patients underwent pulmonary arteriovenous angiography before the operation. A Toshiba 64 slice spiral CT was used for pulmonary arteriovenous angiography with iodixanol as the contrast agent. Before scanning, the patient was assisted into the supine position, and the contrast medium was injected through the elbow vein with a double cylinder high-pressure syringe at the rate of 5 ml/s and an injection volume of 70–90 ml. Scanning was commenced 4 s after injection of the contrast medium. The scanning range was from the top of the chest to the costophrenic angle and patients were instructed to hold their breath during this period. They were asked to take a deep breath and hold it, and the breath holding time was about 10 s.

Image analysis and 3D reconstruction

The bronchial arteries originate from the aorta and carry oxygenated blood to the lungs as part of the general systemic circulatory system, supplying the trachea, bronchi,

esophagus and posterior mediastinum before entering the lungs through the hilum. Oxygenated blood is widely distributed in the vascular and bronchial walls, lung tissue and visceral pleura.[16,17] In group A, a senior radiologist identified and marked the BA in the venous phase of the CT images, and a thoracic surgeon used Exoview software (independently developed by our team, who have obtained the patent right in the US) to reconstruct the aorta, BA and tracheobronchial region, respectively. The aorta and BA are shown in red, and the trachea in green (Figure 2). 3D reconstruction of the BA was not performed in group B.

Origin and anatomic classification of the bronchial artery

The transverse axis of the descending aorta was divided into four parts: anterior, posterior, left and right walls,[18,19] and the starting position of the left and right bronchial arteries in descending aorta was identified and recorded. The Morita classification method[20] was adopted to classify BA, type I: right BA originated from the right intercostal BA trunk, type II: right BA originated from the thoracic aorta, type III: Common trunk of left and right BA, type IV: left BA originated from thoracic aorta, type V: left BA originated from left intercostal BA, and type VI: left or right BA originated from other arteries.

T A B L E 1 Comparison of general clinical data between group A and group B

| Characteristics	Group A (n = 30)	Group B (n = 30)	c2/Z	p-value
Gender			0.067	0.795
Male	13 (43.3)	14 (46.7)		
Female	17 (56.7)	16 (53.3)		
Age, year	62.50 (52.75–67.25)	64.00 (56.00–69.00)	0.836	<0.0001*
Smoking			0.693	0.405
Yes	8 (26.7)	11 (36.7)		
No	22 (73.3)	19 (63.3)		
Surgical site			0.067	0.796
Left	14 (46.7)	15 (50.0)		
Right	16 (53.3)	15 (50.0)		
Hypertension			0.635	0.426
Yes	10 (33.3)	13 (43.3)		
No	20 (66.7)	17 (56.7)		
Diabetes			0.351	0.554
Yes	2 (6.70)	1 (3.30)		
No	28 (93.3)	29 (96.7)		
Heart disease			0.162	0.688
Yes	6 (20.0)	3 (10.0)		
No	24 (80.0)	27 (90.0)		
Postoperative cough				0.222
Yes	5 (16.7)	9 (30)		
No	25 (83.3)	21 (70)		
Duration of surgery, min	139.50 (123.50–170.50)	153.50 (119.00–175.00)	0.569	0.569
Intraoperative blood loss, ml	50.00 (40.00–100.00)	95.00 (60.00–120.00)	3.232	0.001*
Number of lymph node dissection	5.00 (4.00–6.00)	5.00 (4.75–6.00)	0.302	0.762
Length of hospitalization, days	4.00 (3.00–4.25)	4.00 (3.00–4.25)	−0.466	0.642
Chest tube duration, days	2.00 (2.00–3.00)	2.00 (1.75–3.00)	−0.603	0.546
Postoperative drainage, ml	320.00 (142.50–475.00)	375.00 (135.00–627.50)	0.355	0.723

*Statistically significant ($p < 0.05$).
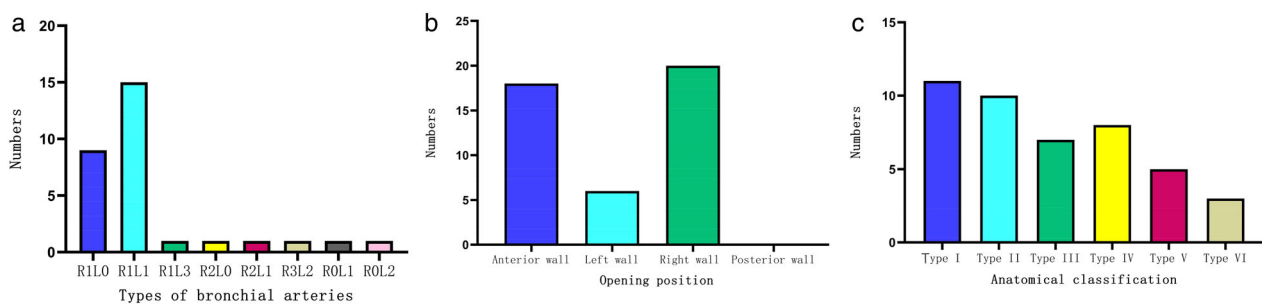
F I G U R E 4 Bronchial artery. (a) Branching types of bronchial arteries. (b) Anatomical types of bronchial arteries. (c) The opening position of bronchial arteries in the aorta

Surgical methods

All patients were given intravenous general anesthesia, double lumen endotracheal intubation, and were positioned on the healthy side in a recumbent position. A surgical incision was made at the fourth or fifth intercostal space (3–5 cm in length) in the anterior axillary line. One lung ventilation was performed on the contralateral side during the operation. Lobectomy and mediastinal lymph node dissection were conducted.[21] In group A, according to the 3D reconstruction image of the BA before surgery, the BA was preserved (Figure 3). A 28F chest tube was inserted into the incision after the operation.

Evaluation of cough severity

The Mandarin Chinese version of the Leicester cough questionnaire (LCQ-MC) was adopted to evaluate the severity of cough from physiological, psychological and social aspects. The questionnaire was completed by professional medical staff of thoracic surgery before surgery, and one and two months after surgery. LCQ-MC is an effective tool to evaluate cough related quality of life.[22] LCQ-MC is composed of physiological, psychological and social dimensions. There are 19 multiple choice questions, including eight physiological items, seven psychological items and four social items. There are seven options for each question (positive score, 1–7 grades. The higher the score, the lighter the cough). The score of each dimension is 1–7, and the total score range is 3–21.[23]

Diagnosis of postoperative cough

In this study, the visual analog scale (VAS) was applied to evaluate the diagnosis of cough in postoperative patients. VAS is a linear scoring method, with 0–100 mm scale: 0 refers to no cough, and 100 represents the most serious cough. According to their own perception of cough, patients are required to mark the severity of cough on the scale line, and measure the distance from the starting point to the marking point as the score. The higher the score, the more
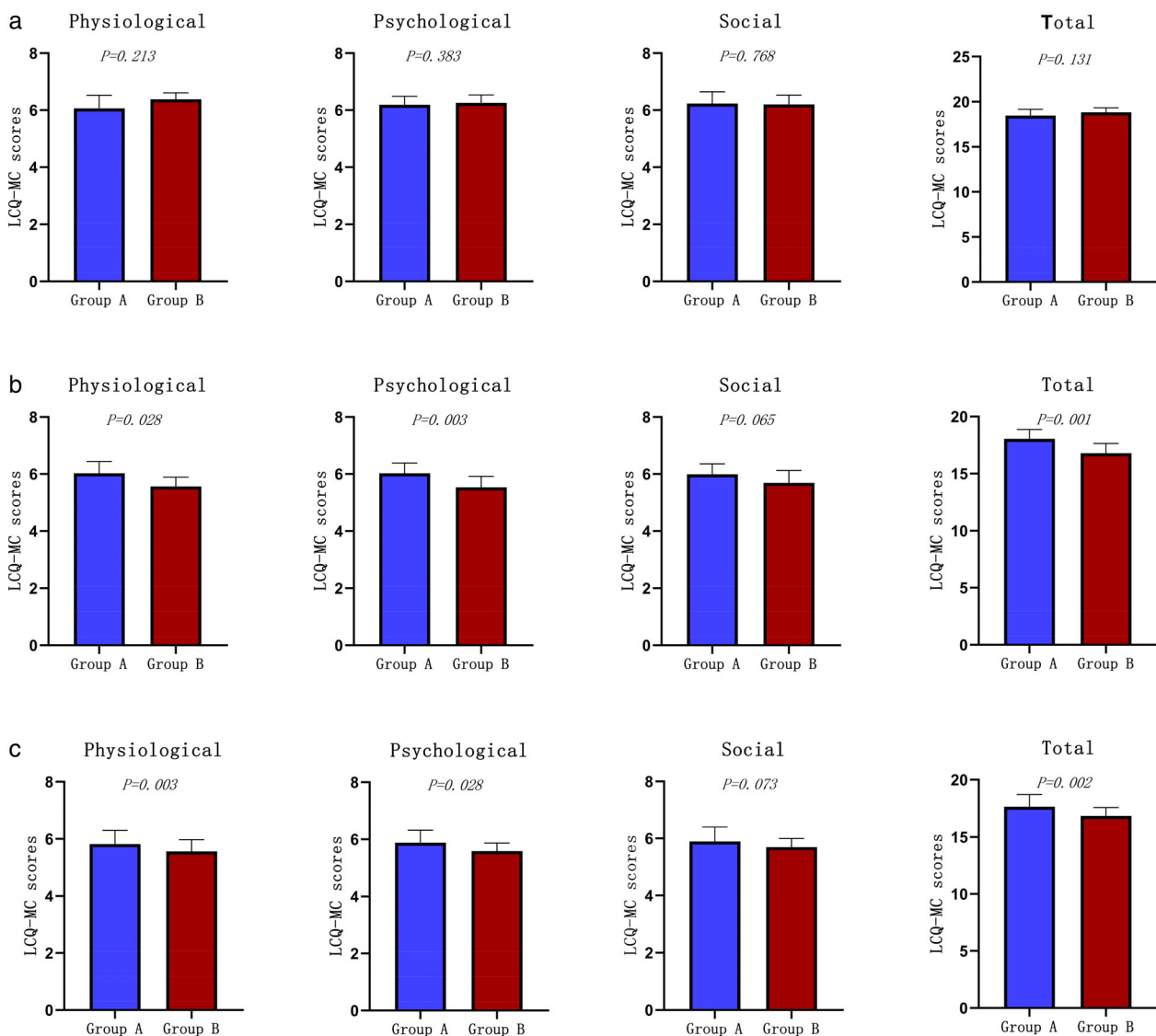

FIGURE 5 Comparison of the mean LCQ-MC score between the two groups before and after surgery in patients. (a) Preoperative, (b) one month, and (c) two months after surgery. LCQ-MC, The Mandarin Chinese version of the Leicester cough questionnaire

TABLE 2 Comparison of the mean LCQ-MC score between the two groups before and after surgery in patients

Variables	LCQ-MC	Group A ($n = 30$)	Group B ($n = 30$)	t	p-value
Preoperative	Physical	6.27 ± 0.39	6.38 ± 0.23	-0.938	0.213
	Psychological	6.18 ± 0.31	6.25 ± 0.29	-0.879	0.383
	Social	6.23 ± 0.42	6.20 ± 0.33	0.297	0.768
	Total	18.58 ± 0.70	18.82 ± 0.49	-1.531	0.131
One month after	Physical	5.82 ± 0.47	5.56 ± 0.41	2.256	0.028*
Operation	Psychological	5.88 ± 0.44	5.59 ± 0.28	3.062	0.003*
	Social	5.89 ± 0.50	5.69 ± 0.30	1.880	0.065
	Total	17.64 ± 1.07	16.84 ± 0.73	3.368	0.001*
Two months after	Physical	5.88 ± 0.44	5.59 ± 0.28	3.062	0.003*
Operation	Psychological	5.82 ± 0.47	5.56 ± 0.41	2.256	0.028*
	Social	6.02 ± 0.67	5.99 ± 0.61	1.650	0.073
	Total	18.03 ± 1.26	17.29 ± 1.73	3.346	0.002*

Abbreviation: LCQ-MC, The Mandarin Chinese version of the Leicester Cough Questionnaire.
*Statistically significant ($p < 0.05$).

serious the cough.[23] When the scale reaches 60 mm, the patient is diagnosed as having a postoperative cough.

Statistical analysis

Data analysis was performed using SPSS 25.0 software. The measurement data in accordance with normal distribution was expressed as mean $\pm$ standard deviation, and the comparison between the two groups was conducted by independent sample t-test. The measurement data that did not conform to normal distribution was represented by Wilcoxon rank sum test, and expressed by median and interquartile distance (M [P25, p75]). Count data was expressed by frequency or percentage, and intergroup comparison was carried out by standard chi square test. The test level was set as 0.05, and $p < 0.05$ was considered statistically significant.

RESULTS

Comparison of general clinical data between the two groups

From August 1, 2020 to September 31, 2020, 60 patients with thoracoscopic lobectomy and systemic lymph node dissection were enrolled in this prospective study, including 30 patients in group A and 30 patients in group B. There were 13 male patients and 17 female patients in group A, with an average age of 62.50 (52.75–67.25), and 14 male patients and 16 female patients, with an average age of 64.00 (56.00–69.00) in group B. The comparison of general clinical data between the two groups was not statistically significant. The average intraoperative blood loss of group A was 50.00 ml (40.00–100.00), and that of group B was 95.00 ml

(60.00–120.00), with statistical significance ($p = 0.001$). The detailed clinical data of the two groups is illustrated in Table 1.

Display of left and right bronchial arteries

3D reconstruction of the BA was performed in 30 patients in group A. Meanwhile, 23 branches of the left BA, 32 branches of the right BA, one branch of the left BA and one branch of the right BA were discovered in 15 cases (62.5%) and 25 cases (78.1%), respectively. The patients with two branches of the BA were left BA (8.33%) and right BA (6.25%). Among them, R1L1 was the most common, accounting for 50% (15/30), followed by R1L0, accounting for 30% (9/30) (see Figure 4(a) for details).

Anatomical classification of left and right bronchial arteries

Right BA was common in type I (25%), followed by type II (22.7%). Left BA was most common in type IV (18.1%), followed by type III (15.9%). Among them, heterotopic BA 3 branches (R2L1) were found, and they all originated from the aortic arch (see Figure 4(b) for details).

Opening position of the bronchial artery in the aorta

The origin of BA in the aortic wall is mainly from the right wall (45.4%), followed by the anterior wall (40.9%) (see Figure 4(c) for details).
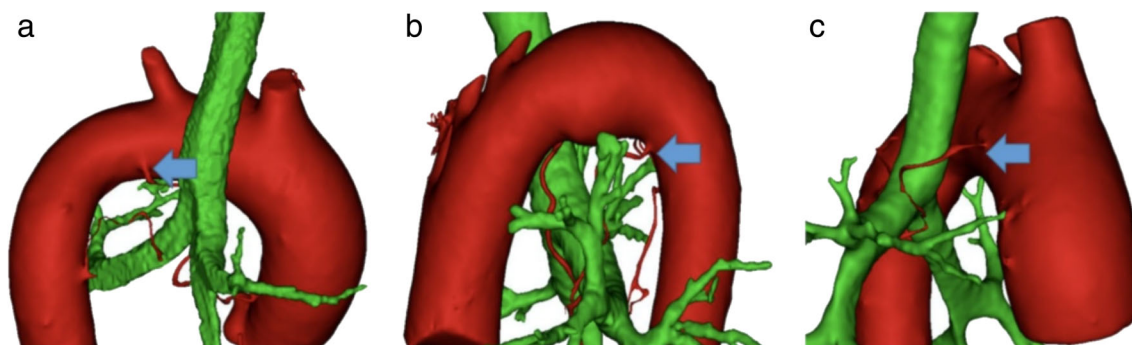
FIGURE 6 Bronchial artery (BA) originating from the aortic arch (indicated by the blue arrow)

Comparison of the incidence of postoperative cough between the two groups

The incidence of postoperative cough was 16.7% (5/30) in group A and 30% (9/30) in group B. The incidence of postoperative cough in group A was lower than that in group B, but the difference was not statistically significant ($p = 0.222$) (Table 1).

Comparison of LCQ-MC scores between the two groups before and after surgery

Compared with group B, there was no significant difference in the scores and total scores of LCQ-MC in three dimensions before surgery ($p > 0.05$) (Figure 5(a)). There was a significant difference in the scores of physiological, psychological and total points in 1 and 2 months after surgery ($p < 0.05$). However, there was no significant difference in the scores of social dimensions between the two groups ($p > 0.05$) (Figure 5(b),(c)), and the specific scores of LCQ-MC is shown in Table 2.

DISCUSSION

CAP is one of the most common complications after thoracoscopic lobectomy. In this study, Exoview software was chosen to reconstruct BAs before surgery, and the lymph nodes under the carina were resected during surgery to protect the BA. LCQ-MC and the VAS cough questionnaire were used to evaluate postoperative cough in patients. The results showed that the preservation of BA can reduce intraoperative bleeding and severity of cough after thoracoscopic lobectomy. The effective intervention measures of postoperative cough promote the rapid recovery of patients after surgery.

The origin, branch type, number and shape of BA were different among different individuals.[16,17] In this study, 30 patients in group A underwent preoperative 3D reconstruction of BA, and a total of 55 bronchial arteries were displayed, including 32 branches of right BA and 23 branches

of left BA. Among the branching types of BA, R1L1 was the most common, accounting for 50.0% (15/30), which is consistent with previous studies.[11] The results of this study revealed that the number of right BA (32) was more than that of left BA (23), and the reasons were analyzed. First, it may be related to the increase of right lung volume and the delivery of large amount of blood from right BA to trachea, pulmonary airway, lymph node and pleura.[17] Second, the difference of technical parameters of CT scanning, such as the concentration of contrast medium, scanning delay time and reconstruction interval, is also one of the reasons why the number of right BA was more than that of left BA in our study. Morita et al.[20] discussed the anatomical relationship between BA and esophagus, and tracheobronchial in patients with thoracoscopic esophageal cancer. They proposed a 3D anatomical model of BA. In this study, the Morita classification method was adopted to anatomize BA. It was clear that the common type of right BA was type I and II, and left BA was type IV. In addition, three ectopic bronchial arteries, including one right BA and two left BAs originating from the aortic arch, were discovered (Figure 6). Previous studies[24] have shown that ectopic bronchial arteries originate from the subclavian artery, internal thoracic artery, pericardial phrenic artery and even the coronary artery, which may be due to the small sample size in this study group. In our study, we observed that the opening position of the BA on aorta was more common in the anterior and right walls, a similar finding to previous reports.[18] In this study, the average intraoperative blood loss of group A was 50.00 ml (40.00–100.00), and that of group B was 95.00 ml (60.00–120.00). The difference between the two groups was statistically significant ($p = 0.001$). Through 3D reconstruction before surgery, the origin, branch number and deviation of BA was shown stereoscopically and intuitively, which is helpful in reducing injury to the BA during surgery, reduces intraoperative bleeding, and avoids the visual field being affected.

The BA is the nutrient vessel of lung tissue, which provides a blood supply to the trachea, bronchus, regional lymph nodes and pleura, and also participates in the blood supply of lung cancer. In this study, 30 patients in group A underwent 3D reconstruction of the BA before operation,

and the BA was preserved during lymph node dissection under the carina. There were five patients with postoperative cough in group A, and the incidence of postoperative cough was 16.7 (5/30), while that in group B was 30% (9/30). The incidence of postoperative cough in group A was lower than that in group B, but the difference was not statistically significant. Therefore, injury to the BA may also be one of the risk factors of CAP, and the occurrence of postoperative cough can be reduced by intraoperative protection of the BA. One of the causes of CAP is the inflammatory reaction in the surrounding airway and lung tissues. Inflammatory factors are released through various ways, mainly including bradykinin (BK) and prostaglandin E-2 (PGE2). On this basis, the transient receptor potential channel vanillin subtype 1 (TRPV1) pathway is activated to induce postoperative cough.[9] During lobectomy, the BA might be injured by accident. Injury of the BA could lead to ischemia of the bronchial wall that is supplied by it, thereby resulting in blood supply interruption from the supplied airway wall, causing ischemic necrosis of airway wall mucosa, and leading to the accumulation of inflammatory cells and triggering an inflammatory reaction,[25] which could excite the cough receptor, thus aggravating a postoperative cough. Wada et al.[26] reported that preoperative 3D CT angiography (3D-CTA) of the BA could clearly show the anatomical structure of the BA, help protect the BA and reduce intraoperative bleeding and postoperative pulmonary complications. In this study, all patients in the group A underwent 3D reconstruction of the BA before surgery, so as to avoid damaging it to a greater extent, thereby alleviating the severity of postoperative cough.

LCQ-MC was used to assess cough severity, intensity, frequency, and impact on quality of life.[23] Lin et al.[7] and Xie et al.[13] reported that the questionnaire could effectively, simply and reliably assess the severity of cough in patients with lung cancer after thoracoscopic surgery. This study proved that the LCQ-MC scale can be used to evaluate the cough of patients with pulmonary disease after surgery. In this study, two professional medical staff of thoracic surgery guided patients to fill in the questionnaire before and after surgery, and compared the scores of the two groups. We confirmed that there was no significant difference in the scores of LCQ-MC items between the two groups before surgery. After one and two months following surgery, the scores and total scores of LCQ-MC in group A were lower than those in group B. In terms of physiological and psychological dimensions and total scores, the differences between the two groups were statistically significant ($p < 0.05$), while in social dimension, there was no significant difference between the two groups ($p > 0.05$). Through preoperative 3D reconstruction of BA and intraoperative preservation, the severity of postoperative cough can be reduced. It can improve the quality of life of patients who have undergone pulmonary surgery, and further promote the practice of the rapid recovery concept in lung surgery.

There are also some limitations in our study. First, this is a prospective, single center study with a small sample size. In the results, there may be deviation that needs to be supported by a multicenter and larger sample prospective study. Second, the diameter of the BA is small, and its imaging is affected by CT scanning technology, contrast agent injection technology, heart and large vessel pulsation, and there may be some errors in the anatomical type and number. Third, the mechanism of preservation of BA to reduce the severity of CAP is not clear, and further studies to determine this are needed.

In conclusion, persistent postoperative cough has been the cause of psychological and physiological problems to patients which has seriously affected their quality of life. This study suggested that the anatomical type of BA is complex, and its origin, number and shape vary greatly. Preoperative 3D reconstruction and intraoperative preservation of BA can reduce intraoperative bleeding, and reduce the severity of postoperative cough.

CONFLICT OF INTEREST
No potential conflicts of interest were disclosed.

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