

REVIEW

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Analysis of angiographic findings and short-term recurrence factors in patients presenting with hemoptysis

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Abstract

Objectives: The abnormal anatomical alterations of blood vessels during DSA angiography in patients with hematological disorders were retrospectively examined, and the influencing factors of short-term (≤ 6 months) recurrent hemoptysis were statistically analyzed, and the consistency between admission diagnosis and intraoperative diagnosis was evaluated.

Methods: The intraoperative angiography data of patients who underwent selective bronchial artery embolization for hemoptysis in our hospital from January 2022 to December 2022 were reviewed. They were divided into the observation group and the control group based on whether there was recurrent hemoptysis. The Logistic regression model and forest map were employed to analyze the factors influencing the recurrence rate.

Results: A total of 104 patients were encompassed in this study (12 cases of tuberculosis, 35 cases of infection, 4 cases of lung cancer, 8 cases of bronchiectasis, 22 cases of arteriovenous fistula, 16 cases of aneurysm, and 7 cases of pulmonary hypertension). The coincidence rate of preoperative and intraoperative diagnoses was 73.1%. Pulmonary arteriovenous fistula and aneurysm were the predominant types of diseases that were misdiagnosed. The short-term recurrence rate was 16.3%, mainly attributed to the reopening of responsible vessels related to embolization, angiography leakage, and leaky embolization of specific types of vessels. The recurrence rate of only patients with arteriovenous fistula and aneurysm accounted for 47% of the total recurrence rate. The right bronchial artery, right internal thoracic artery, right thyroid neck trunk, and age were the independent factors influencing the recurrence of hemoptysis ($p < 0.05$).

Conclusions: The main reason for angiographic leakage and embolization leakage in cases of hemoptysis is the lack of understanding of the anatomic variations of the vessels responsible. Careful examination of the specific types and locations of the vessels is the principal approach to reducing secondary operations.

Keywords: Selective bronchial artery embolization, Arteriography, Anatomic variation, Arteriovenous fistula, Aneurysm



Introduction

Hemoptysis constitutes the principal complaint of 15% of patients with lung disorders. Since the introduction of selective bronchial artery embolization into the clinical setting over 50 years ago, it has emerged as a crucial approach for controlling acute hemoptysis, reducing the mortality rate of patients with hemoptysis from 75% in the past to 13–17.8% [1]. 90% of pulmonary hemoptysis stems from bronchial arteries, while the remaining 10% constitutes pulmonary artery hemorrhage or latent hemorrhage [2]. The clinical evaluation as to whether selective bronchial artery embolization should be carried out takes into account the bleeding rate, physiological respiratory reserve, and the self-regulatory ability of the patient's airway [3]. It is a challenging process to determine the pathogenesis of hemoptysis, and approximately 50% of patients have no explicit cause. The common primary diseases in Europe and the United States include tuberculosis, fungal infection, pulmonary inflammation, malignant tumor, bronchiectasis, cystic fibrosis, aneurysm, etc. [4]. In recent years, studies on the classification of bronchial arteries have advanced the understanding of hemoptysis, but this merely accounts for a small branch of the bleeding artery. Angiography and embolization of any accountable vessels, such as systemic circulation-related arteries, arteriovenous fistulas and aneurysms, will lead to secondary surgeries.

Materials and methods

Patient population

This retrospective study was sanctioned by the Institutional Ethics Committee, with informed consent being waived due to its retrospective character. A total of 104 patients with hemoptysis in our hospital were recruited for bronchial artery embolization. The patient underwent multi-row spiral CT angiography as a preoperative assessment, and DSA was employed intraoperatively. The results of intraoperative DSA angiography were reviewed by two interventional physicians in our hospital who have been practicing for over 10 years. When there are inconsistencies, they are resolved through face-to-face discussion. The two radiologists have no access to the patient's information and do not participate in the collection of clinical data.

Contrast methods

All DSA results were obtained through angiography during hemoptysis, encompassing both manual injection and machine injection, with the application of non-ionic positive contrast media. In this study, the responsible vessels implicated in various diseases were statistically analyzed, and the factors influencing recurrence were statistically analyzed by employing the Logistic regression model and forest map. Statistical analysis was conducted using SPSS (version 27.0, IBM).

Methods

All DSA results were obtained through angiography during hemoptysis, encompassing both manual injection and machine injection, with the utilization of non-ionic positive contrast media. Patients were categorized into the observation group (34

cases) and the control group (70 cases) based on whether they experienced recurrent hemoptysis. These cases were analyzed separately or divided into different subgroups in accordance with the primary disease. Logistic regression analysis was conducted on the involved responsible vessels, and forest maps were created. The statistical software employed was SPSS (version 27.0, IBM).

Results

Pathological features and influencing factors of patients

A total of 104 patients presenting with hemoptysis (12 cases of tuberculosis, 35 cases of infection, 4 cases of lung cancer, 8 cases of bronchiectasis, 22 cases of arteriovenous fistula, 16 cases of aneurysm, and 7 cases of pulmonary hypertension) were enrolled in this study (Fig. 1). The average age was 56 ± 16 years (ranging from 15 to 85 years), and the proportion of females was 29% (31/104). The coincidence rate between preoperative diagnosis and discharge diagnosis was 73.1%. Pulmonary arteriovenous fistula and aneurysm were the predominant misdiagnosed diseases, followed by pulmonary hypertension. The success rate of selective bronchial artery embolization was 100%, and no complications such as spinal artery ectopic embolization were observed. The recurrence rate of hemoptysis in the short term (≤ 6 months) after surgery was 16%, mainly attributed to the reopening of responsible vessels related to embolization and the leakage of angiography and embolization of specific types of vessels. Among them, only the recurrence rate of patients with arteriovenous fistula and aneurysm accounted for 47% of the total recurrence rate, which was in accordance with previous studies [5]. The classification of different subgroups based on the primary disease did not have statistical significance for the responsibility-related line Logistic regression. When the primary disease factor analysis was excluded, it was indicated that the right bronchial artery, right internal thoracic artery, right thyroid

Responsible vessel	Primary disease (first hemoptysis/recurrent hemoptysis)						
	Phthisis (n=10/2)	Infection (n=32/3)	Lung cancer (n=4/0)	Bronchiectasis(n=7/1)	Arteriovenous fistula (n=19/3)	Aneurysm (n=11/5)	Pulmonary hypertension (n=4/3)
Left bronchial artery	7 (70%) /1 (50%)	28 (85%) /2 (66%)	3 (75%) /0 (0%)	6 (85%) /1 (100%)	17 (89%) /3 (100%)	7 (63%) /2 (40%)	4 (100%) /2 (66%)
Right bronchial artery	9 (90%) /2 (100%)	27 (84%) /0 (0%)	4 (100%) /0 (0%)	6 (85%) /1 (100%)	17 (89%) /2 (66%)	9 (81%) /2 (40%)	3 (75%) /2 (66%)
Left intercostal artery	0 (0%) /0 (0%)	2 (6%) /0 (0%)	1 (25%) /0 (0%)	0 (0%) / (0%)	1 (11%) /0 (0%)	1 (9%) /0 (0%)	0 (0%) /0 (0%)
Right intercostal artery	0 (0%) /0 (0%)	6 (18%) /1 (33%)	0 (0%) /0 (0%)	1 (14%) / (0%)	5 (26%) /1 (33%)	0 (0%) /0 (0%)	1 (25%) /0 (0%)
Left thyrocervical trunk	2 (20%) /0 (0%)	4 (12%) /0 (0%)	0 (0%) /0 (0%)	1 (14%) /1 (100%)	6 (31%) /0 (0%)	1 (9%) /0 (0%)	0 (0%) /0 (0%)
Right thyroid neck trunk	2 (20%) /0 (0%)	7 (21%) /1 (33%)	1 (25%) /0 (0%)	1 (14%) / (0%)	6 (31%) /1 (33%)	0 (0%) /0 (0%)	1 (25%) /0 (0%)
Left internal thoracic artery	0 (0%) /0 (0%)	13 (9%) /1 (33%)	0 (0%) /0 (0%)	0 (0%) / (0%)	8 (42%) /0 (0%)	2 (18%) /0 (0%)	1 (25%) /0 (0%)
Right internal thoracic artery	2 (20%) /1 (50%)	17 (53%) /1 (33%)	2 (50%) /0 (0%)	1 (14%) / (0%)	9 (47%) /2 (66%)	1 (9%) /0 (0%)	2 (50%) /0 (0%)
Left inferior phrenic artery	6 (60%) /0 (0%)	10 (31%) /1 (33%)	2 (50%) /0 (0%)	3 (42%) /1 (100%)	12 (63%) /1 (33%)	3 (27%) /1(20%)	1 (25%) /0 (0%)
Right inferior phrenic artery	7 (70%) /1 (50%)	7 (21%) /1 (33%)	2 (50%) /0 (0%)	3 (42%) /1 (100%)	11 (57%) /1 (33%)	0 (0%) /2 (40%)	1 (25%) /0 (0%)
Others (subclavian artery, ostocervical trunk, thoracic dorsal artery and vagal artery)	2 (20%) /0 (0%)	9 (28%) /0 (0%)	4 (100%) /0 (0%)	3 (100%) /0 (100%)	15 (78%) /3 (100%)	4 (36%) /0 (0%)	3 (75%) /0 (0%)

Fig. 1 Proportion of patients experiencing first hemoptysis and recurrent hemoptysis involving the accountable vessels. (The primary diseases in patients with hemoptysis exhibit a strong regional correlation. The most prevalent primary diseases in this study encompassed infection, arteriovenous fistula, aneurysm, tuberculosis, bronchiectasis, pulmonary hypertension, and lung cancer.)

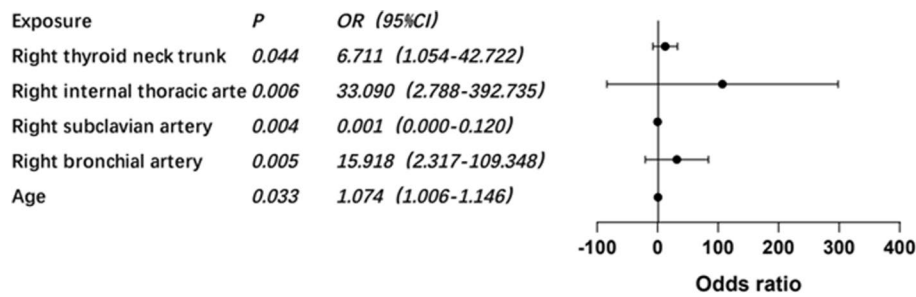


Fig. 2 Analysis of the risk factors associated with the recurrence of hemoptysis. (Logistic regression was conducted to analyze the impact of the patient’s primary disease, gender, age, and involved responsible vessels on hemoptysis recurrence. Subsequently, forest plots were generated. The right thyrojugular artery, right internal thoracic artery, right bronchial artery, and age were identified as independent influencing factors for hemoptysis recurrence in patients ($p < 0.05$). Among these factors, age exhibited the least effect while a negative correlation was observed with the right subclavian artery.)

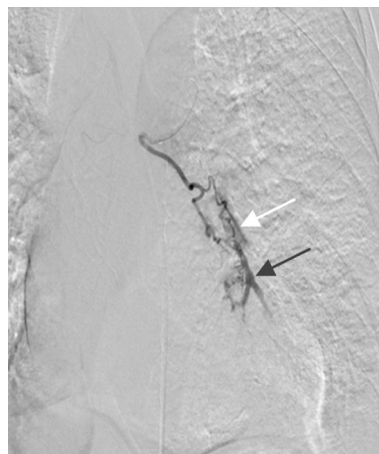


Fig. 3 Hemorrhage outside blood vessels. **A** Patient exhibited extravascular bleeding, and the contrast agent leaked into the bronchioles (indicated by the black arrow) following rupture of the left bronchial artery (indicated by the white arrow.)

neck trunk and age were independent factors influencing the recurrence of hemoptysis ($p < 0.05$) (Fig. 2).

Angiographic findings following anatomical variations of the responsible vessels

The recurrence rate following hemoptysis embolization ranges from 16% to 25% [5], suggesting that nearly one-fifth of patients are overlooked during angiography, and interventional physicians may lack insight into the dynamic changes in imaging during the brief retention of contrast agents in blood vessels. First, it is essential to differentiate between arterial and venous bleeding in patients undergoing selective liability vascular embolization. The most common source of arterial bleeding in pulmonary diseases is the bronchial artery, characterized by a bright red color. Venous hemorrhage manifests as a pulmonary aneurysm with a dark red hue. Second, distinguishing between intravascular and extravascular bleeding is crucial; intravascular bleeding presents as exudative hemorrhage gradually collected within alveoli and coughed up,

resulting in less hemoptysis volume. On the other hand, extravascular arterial wall rupture occasionally leads to a large influx of blood into the bronchioles, causing significant bleeding with low incidence and poor response to drug-based hemostasis (Fig. 3).

Vessels of collateral circulation

In patients presenting with hemoptysis, various arteries such as the bronchial artery, intercostal artery, subclavian artery, internal thoracic artery, thyroid truncus, vertebral artery, truncus costocercus, thoracic dorsal artery, coronary artery, inferior phrenic artery and abdominal parietal artery may be implicated (Fig. 4). Notably, patients with hemoptysis often exhibit diverse degrees of anatomical variation; thus

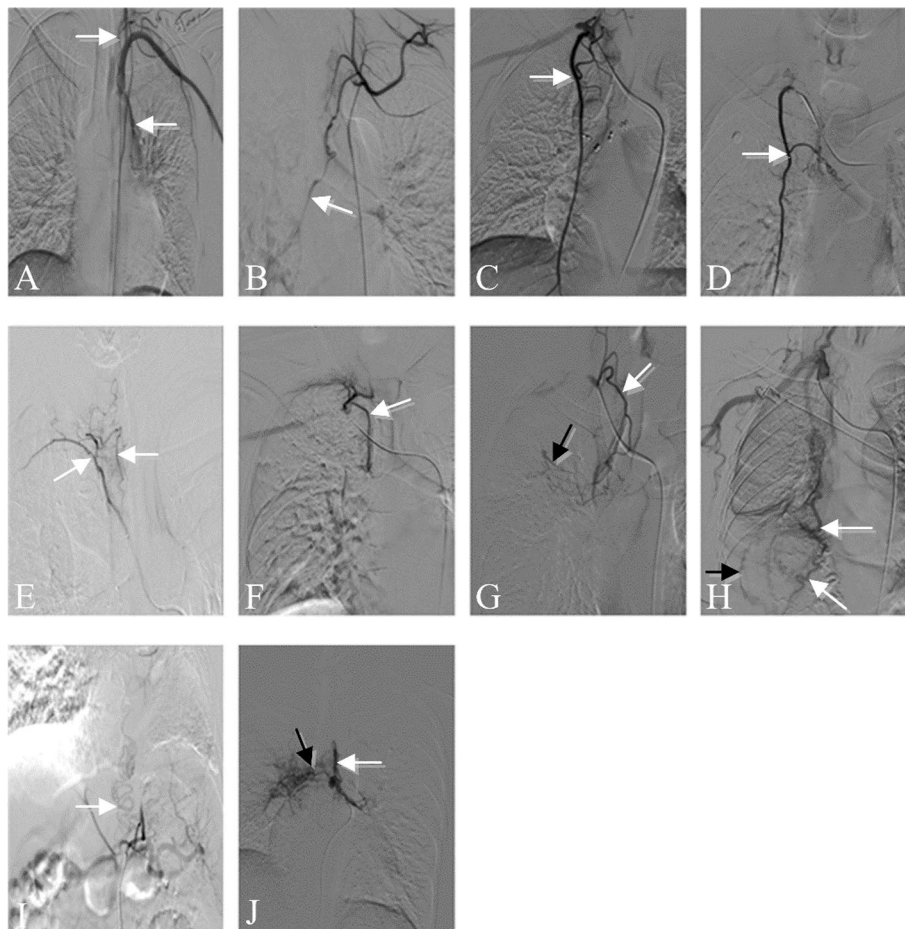


Fig. 4 Common anatomical variations of blood vessels in patients presenting with hemoptysis. **(A)** left thyrocervical trunk vagal bronchial artery; **(B)** left thyrocervical trunk with right bronchial artery vagus; **(C)** right internal thoracic artery vagus cervical trunk with more branches; **(D)** right internal thoracic artery vagobronchial artery; **(E)** right intercostal artery vagus thyrocervical trunk; **(F)** Right vertebral arteria—internal thoracic artery; **(G)** Right vertebral arterion—intercostal artery (white arrow)—pulmonary venous fistula (black arrow); **(H)** Internal thoracic artery—epigastric artery (white arrow)—pulmonary venous fistula (black arrow); **(I)** abdominal trunk vagal bronchial artery; **(J)** Bronchial arterio-pulmonary venous fistula (black arrow), spinal artery (unilateral pulmonary discontinuity) (white arrow)

understanding anatomy is fundamental for vascular intervention. This study found that collateral circulation or vagus arteries primarily developed in the thyroid jugular trunk and subsequently in the internal thoracic artery.

Arteriovenous fistula

Arteriovenous fistula represents the most prevalent type of vascular anatomic variation observed in patients with hemoptysis in this study, encompassing both arterio-venous and arterio-arterial fistulas. Chronic conditions such as recurrent pulmonary infection, lung cancer, pulmonary hypertension, congenital patent ductus arteriosus, and unilateral arterial discontinuity may contribute to the formation of these fistulas. The interventional physician must discern whether it is an arterial or venous fistula based on the direction of blood flow during the limited duration of contrast agent retention. Arteriovenous fistula typically arises from abnormal connections between the bronchial artery or pulmonary artery and the pulmonary vein, with rapid injection and propagation of contrast agent from the pulmonary hilum to the periphery (Fig. 5). In patients with arterio-arterial fistulas, contrast agent propagation occurs from the pulmonary hilum to the peripheral vasculature (Fig. 6). Arteriovenous fistulas can impede oxygen exchange, while arterio-arterial ones are more likely to result in persistent hemoptysis. Notably, in this study, arterio-arterial fistulas were predominantly found in the right lung. Distinguishing between arteriovenous fistula and arterial variations influences embolic agent selection. An arteriovenous fistula denotes an abnormal connection between blood vessels that does not primarily facilitate substance exchange or nutrition; conversely, variable arteries can provide nutritional support for target organs.

Aneurysm

The rupture of aneurysms is fatal, with an autopsy incidence of 0.007%, rupture rate of 87%, probability of involving the main pulmonary artery of 89%, and probability of involving the distal segment of 11% [6]. Aneurysms involving bronchial arteries are rare, and only one case was included in this study. The proportion of true aneurysms and false arteries is roughly equal, and true aneurysms are often secondary to congenital heart diseases (such as abnormal ductus arteriosus, atrial septal defect and ventricular septal defect). Pseudoaneurysms are often secondary to chronic diseases such as infection, malignancy, iatrogenic injury and vasculitis, and have a high risk of rupture and bleeding. If aneurysms secondary to various chronic diseases are not treated in time, they can easily develop into arterial fistula (Fig. 7) [7, 8]. Patients with aneurysms present with persistent hemoptysis of unknown cause, which is affected by the small branch wall of the pulmonary artery at the end, and it is difficult to show superselective pulmonary angiography.

Discussion

Hemoptysis is frequently the result of a combination of various diseases. Clinical biomarkers and imaging findings can effectively aid in diagnosing tuberculosis, lung cancer, pulmonary infection, and bronchiectasis. However, their role in diagnosing arteriovenous fistula, aneurysm, and pulmonary hypertension is limited. Apart from the impact of acquisition time, arteriovenous fistula mainly occurs in the terminal segment of

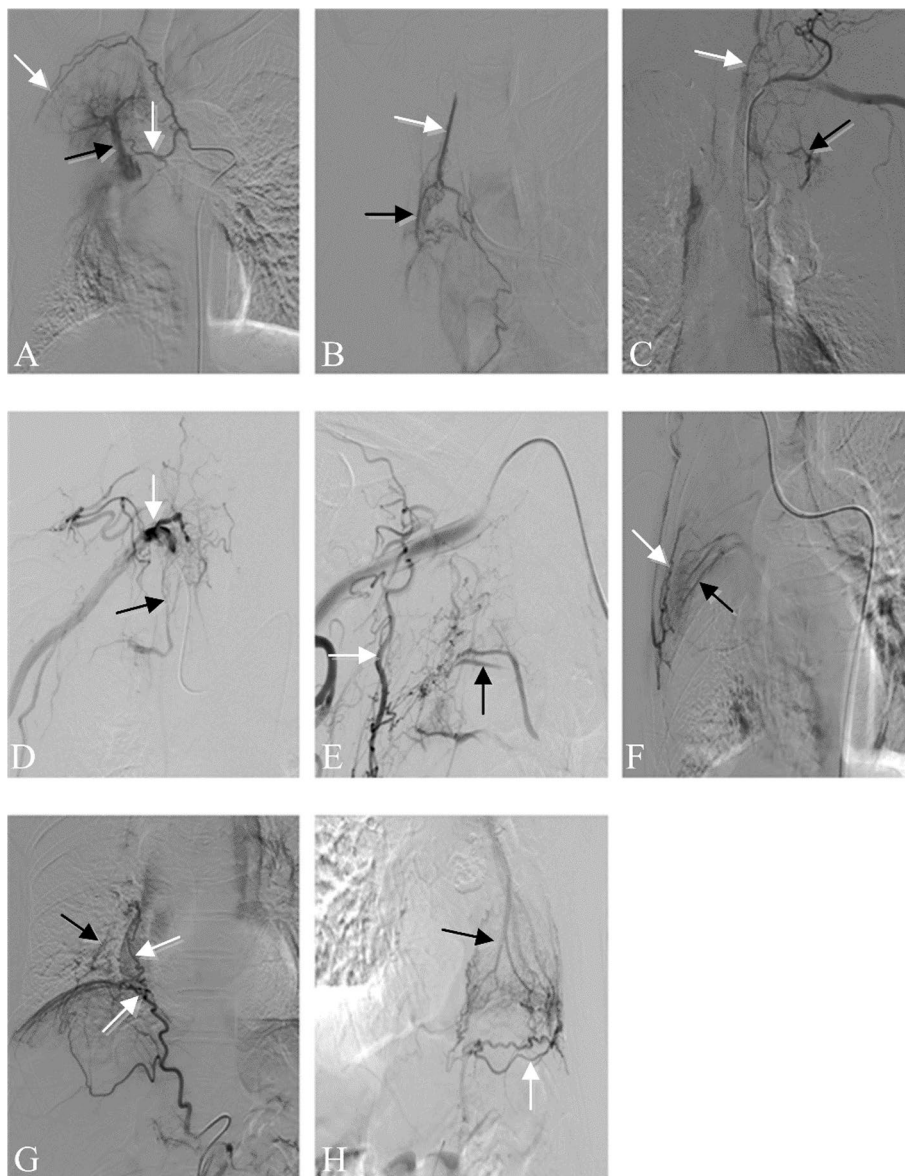


Fig. 5 Arterio-venous fistula. (In this image, the white arrows are arteries and the black arrows are veins. **A** Right bronchial arterio-pulmonary venous fistula; intercostal arterio-pulmonary venous fistula; **B** right internal thoraco-pulmonary venous fistula; **C** left thyrocervical trunk-pulmonary venous fistula; **D** right subclavian artery-pulmonary venous fistula; **E** right costocervical trunk-pulmonary venous fistula; **F** right thoracodorsal arterio-pulmonary venous fistula; **G** right inferior phrenic arterio-bronchial arterio-pulmonary venous fistula; **H** left inferior phrenic arterio-pulmonary venous fistula.)

blood vessels with narrow lumen making superselection difficult and hindering effective contrast agent development. Inflammatory stimulation caused by the primary disease can lead to blood vessel wall contraction and increased pulmonary artery pressure; for patient radiation exposure reduction (hilar angiography) and machine injection pressure safety considerations during angiography often result in unclear tumor display. Arteriovenous fistula, aneurysm, and pulmonary hypertension are commonly secondary to other diseases. This study found that arteriovenous fistula is often accompanied by

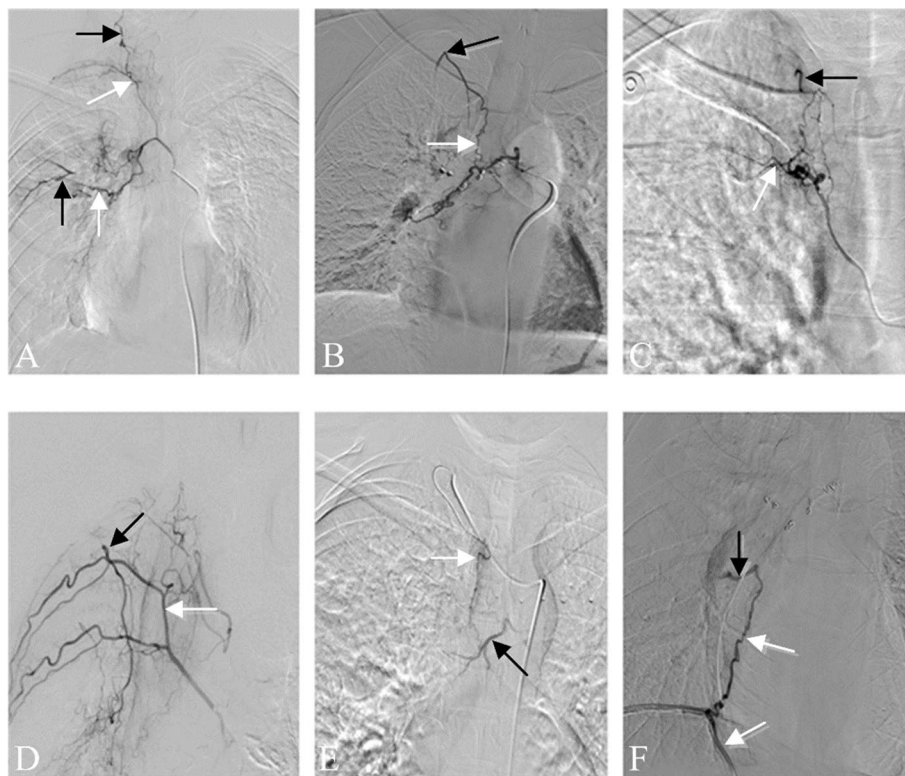


Fig. 6 Artery–arterial fistula. **A** Right bronchial artery (white arrow)—pulmonary artery fistula (black arrow); intercostal artery (white arrow)—vertebral artery fistula (black arrow); **B** right bronchial artery (white arrow)—costocervical trunk fistula (black arrow); **C** right intercostal artery (white arrow)—thyrocervical trunk fistula (black arrow); **D** intercostal artery (white arrow)—costocervical trunk fistula (black arrow); **E** right internal thoracic artery (white arrow)—bronchial artery fistula (black arrow); **F** right inferior phrenic artery—bronchial artery (white arrow)—pulmonary artery fistula (black arrow).

bronchiectasis while aneurysms are frequently associated with tuberculosis. Pulmonary hypertension is almost always secondary to congenital heart disease (ventricular septal defect, patent ductus arteriosus, and patent foramen ovale), congenital unilateral pulmonary discontinuity or numerous arteriovenous fistulas along with some aneurysms. With multi-slice spiral CT emergence has come increased recognition of involved bronchial artery opening locations from 45% to 97%. The ectopic bronchial artery's blood supply may originate from systemic circulation arteries such as the descending aorta, thyroid truncus subclavian artery internal thoracic artery costal truncus thoracic dorsal artery inferior phrenic artery gastric artery coronary arteries [9]. Understanding and classification of bronchial arteries continue to evolve; recent studies classify their opening locations into 5 categories comprising 13 types [10]. Besides abnormal blood supply probabilities these arteries themselves have high likelihoods of thickening and tortuous bleeding; this study discovered that arteriovenous fistulas can occur at any location among these arteries' openings [9, 11]. The preoperative imaging diagnosis revealed that the average diameter of the involved artery in patients with hemoptysis was 2.8 ± 1.2 mm, with an average of 2.75 ± 1.73 involved arteries and an average of 1.44 ± 0.58 and 1.35 ± 0.54 involved left and right bronchial arteries, respectively [5, 10, 12]. The recurrence of hemoptysis after selective bronchial artery embolization can be

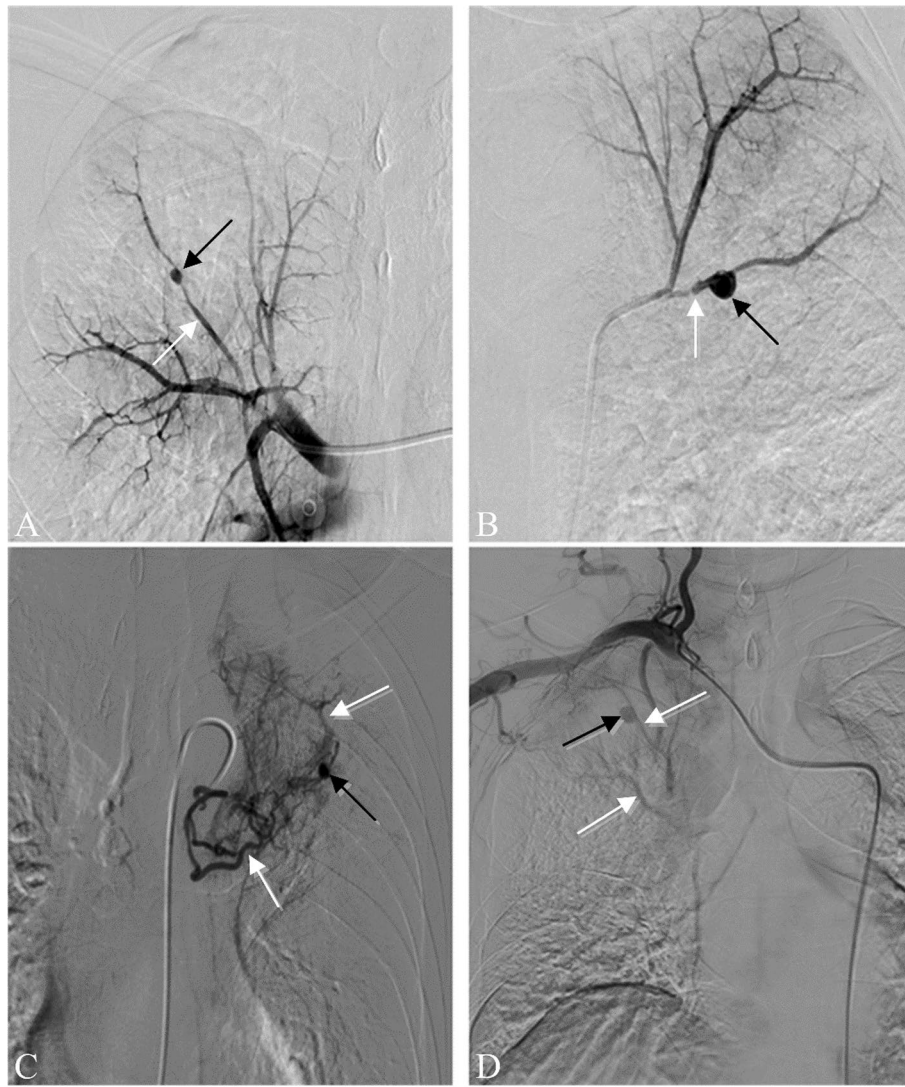


Fig. 7 Aneurysm. **A** Pulmonary aneurysm in the anterior upper lobe of the right lung (black arrow); **B** pulmonary aneurysm in the anterior segment of the left superior lobe (black arrow); **C** left bronchial arterio-pulmonary venous fistula (white arrow); aneurysm of the anterior bronchial segment of the left superior lobe (black arrow); **D** right subclavian artery-pulmonary venous fistula (white arrow); costocervical trunk aneurysm (black arrow)

categorized into short-term and long-term recurrence, corresponding to two distinct time peaks. The first peak (≤ 6 months) is primarily attributed to systemic circulation artery involvement or thrombus leakage, resulting in a recurrence rate of 16%, with 70% occurring within 1 month post-embolization; arteriovenous fistula and aneurysm accounted for 64% of these cases, highlighting the significance of interventional physicians' familiarity with anatomical variations to reduce missed angiography and embolization rates as well as the need for subsequent operations due to unfamiliarity with responsible vessel anatomy. The second peak (1–2 years) is mainly associated with collateral circulation formation and disease progression leading to long-term recurrence at a rate of 45.5% in women and 35.6% in men; recurrent cycles were observed at approximately 34.8 ± 6.46 months in women and 25.5 ± 10.9 months in men [12]. Continuous

lung tissue erosion by tuberculosis bacteria or cancer, poor control over lung infections, or persistent elevated pulmonary artery pressure due to congenital heart disease are identified as primary causes contributing to long-term recurrence [13, 14]. Preoperative imaging using multi-slice spiral CT aids in determining the number and location of bronchial arteries but has limited impact on non-aortic vascular indications; however, it should not overlook arteriovenous fistulas which play a crucial role in hemoptysis evaluation [14, 15]. In the embolization of the responsible artery, appropriate embolic agents are typically selected based on vessel diameter. Smaller embolic agents can reach the distal end of the blood vessel, resulting in effective embolization, while larger-diameter particles are chosen for arteriovenous fistula to prevent ectopic embolization [16]. Aneurysms pose a life-threatening risk and should be actively treated regardless of their size [17]. Identifying bronchial aneurysms and pulmonary aneurysms is exceptionally challenging and demands extensive clinical experience. DSA angiography serves as the gold standard for determining the responsible artery in cases of hemoptysis. Insufficient injection pressure during manual contrast agent administration is a primary reason for unsuccessful identification of the responsible artery. Intraoperative pressure from manual contrast agent injection cannot be measured, with machine injection pressure usually below 25 mmHg. According to guidelines from the European Society of Cardiology and Respiratory Society, pulmonary hypertension is diagnosed when mean pulmonary arterial pressure exceeds 20 mmHg [18, 19], often associated with chronic conditions such as infection, inflammation, and lung cancer. Inflammatory factors stimulate muscle fibers and new capillaries leading to increased pulmonary artery pressure. Additionally, systemic circulation pressure is approximately six times that of pulmonary artery pressure. When systemic arterio-pulmonary arteriovenous fistula occurs, regurgitation of blood into the pulmonary artery leads to hypoperfusion obscuring true vascular status. Therefore, routine machine injection pressures at 25 mmHg may not effectively reveal changes in pulmonary vasculature; however, professional standards discourage increasing injection pressures when no suspected lesions are identified. Selective bronchial artery embolization has limitations; its most serious complication—ectopic spinal cord embolization—has an incidence rate of 0.19% [20, 21]. While this procedure can immediately halt bleeding, it has limited impact on restricting abnormal blood flow supply due to continuous occurrence of underlying diseases leading to collateral circulation formation—especially evident in patients with congenital heart disease- or lung disease-induced pulmonary hypertension. Previous studies have indicated that delayed embolization and presence of aspergillus are independent risk factors for recurrent hemoptysis [22]. This study identifies right bronchial artery along with right internal thoracic artery and right thyrocervical trunk as independent risk factors for recurrent hemoptysis ($p < 0.05$), emphasizing thorough examination these arteries could reduce recurrence probability among patients requiring secondary surgery.

The study has several limitations. First, it is a single-center study with a smaller sample size of relapsed patients compared to real-world scenarios. The identification of responsible vessels relies on the expertise of interventional doctors and lacks diagnostic evidence such as pathology. Second, the analysis focused on short-term recurrence factors of hemoptysis without reaching a conclusion regarding the extent of supplementary embolization for responsible vessels, leading to a lack of controlled studies on

embolization efficacy. There exists an inter-group difference between primary disease and patients with short-term recurrent hemoptysis, necessitating additional data for conclusive findings. We aim to conduct prospective studies with larger samples in the near future.

Conclusion

Utilizing ultra-selective angiography, standardized surgical procedures, and a comprehensive understanding of vascular anatomy by interventional physicians can significantly decrease the likelihood of missed angiography, missed embolization, and secondary surgery, particularly for the right thyrojugular artery, right internal thoracic artery, and right bronchial artery.

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Author contribution

W.A. and H.L.S. wrote the main manuscript text and Y.W.C. prepared all figures. All authors reviewed the manuscript.

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Data availability

No data sets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the ethics committee of the First Hospital of Lanzhou University.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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