Transcatheter Arterial Regional Chemoembolization for Lung Malignant Tumor

Fen-Xiang Z and Yu-Jin L*

Department of Interventional Oncology, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, China

Abstract

Transcatheter arterial regional chemoembolization may enhance the local concentration and cytotoxicity of chemotherapeutic drugs and block the blood supply to the tumor, with an expectation to control the tumor, relieve hemoptysis, and prolong survival. This review will introduce the research progression of blood supply to lung cancer, discuss Pulmonary Artery Chemoembolization (PACE) and Bronchial Artery Chemoembolization (BACE) for lung cancer, including their indications and contraindications, operation techniques, efficacy assessments, combined treatments as well as their operating complications and the methods to prevent the adverse event. We will discuss the problems and challenges of percutaneous vascular intervention for lung cancer, such as the uncertainty of blood supply artery for lung cancer, the necessity of high-quality controlled studies, and the best choice for the indications. We hope to explore the direction of transcatheter arterial regional chemoembolization for lung cancer. The aim of this review is to provide a reference for the practice of regional chemoembolization by vascular interventional radiology for lung cancer.

Keywords: Lung cancer; Interventional radiology; Pulmonary artery; Bronchial artery; Chemoembolization

Introduction

A typical malignant tumor that typically develops from bronchial epithelial cells is lung cancer [1]. Non-Small-Cell Lung Cancer (NSCLC) and Small-Cell Lung Cancer (SCLC) are the two common subtypes of lung cancer, with NSCLC being the more prevalent subtype and making up roughly 80% to 85% of all lung cancer cases. On the other hand, SCLC only makes up about 15% to 20% of the remaining cases [2]. Only around 30% of lung cancers with a clinical diagnosis have a chance of receiving radical surgery. Traditional systemic chemotherapy and radiation are effective but limited in treating lung cancer and have several unpleasant side effects that are particularly difficult for older patients. Less than 50% of lung adenocarcinomas have responded satisfactorily to molecularly targeted treatment, which also has a high risk of resistance. Additionally, immunotherapy is currently effective and only useful for a small subset of individuals with lung cancer.

Trans-Pulmonary Artery Chemoembolization (PACE) and Bronchial Artery Chemoembolization (BACE) are two forms of arterial chemoembolization employed in transarterial interventions for lung cancer, targeting the tumor's blood supply arteries. This approach continues until the specific blood supply arteries for the lung cancer are identified.

There is growing proof that the pulmonary artery is not implicated in the blood supply of lung cancer as the findings from multislice spiral CT and DSA technologies [3,4]. The major blood supply artery for lung cancer is the bronchial artery, which is a representation of the body’s circulation. Therefore, BACE progressively replaces PACE for lung cancer. BACE was more frequently reported in the literature. This article reviews the development of PACE and BACE in the treatment of lung cancer.

Blood Supply of Lung Cancer

The discussion on the blood supply to lung cancer involves contrasting research findings that highlight the complexity of this topic. Initially, it was believed that lung cancer receives blood from both the pulmonary and bronchial arteries, necessitating dual-pathway vascular treatment [5]. This view was supported by early studies showing that lung cancers mainly receive blood from the bronchial arteries and other body circulation arteries, with minimal involvement from the pulmonary artery [6].
However, the source of blood supply to lung cancer remains a contentious issue. In a study by Sun et al. [7] using six immunosuppressed dogs, the significance of the bronchial arteries in supplying blood to lung tumors was emphasized. In this study, lung lobes were injected with tissue blocks from canine vaginal infectious tumors, and tumor development was tracked using various imaging techniques. Ten weeks post-injection, it was found that all injection sites developed tumors with a mean diameter of 2.734 cm. Most nodules received blood supply from bronchial arteries, with minimal to no pulmonary arterial blood supply detected. This was evident even in an iodized oil-enhanced CT of the pulmonary arteries, where no iodized oil deposits were observed, indicating that the bronchial arteries are the primary source of blood for these tumor lesions. Conversely, a study by Deng et al. [8] using micro-CT lung and bronchial arteriography on mice with early-stage lung adenocarcinoma presented differing findings. In this study, the majority (84%) of early-stage lung adenocarcinomas received blood supply from densely distributed pulmonary arteries, both internally and externally, while bronchial arteries were not connected to the tumor blood supply. This finding, supported by pathological evidence, suggests a prominent role of the pulmonary arteries in the blood supply to early-stage lung adenocarcinomas. These conflicting findings highlight the complexity and ongoing debate regarding the vascular supply to lung cancer, emphasizing the need for further research to fully understand the intricacies of tumor blood supply in lung cancer.

Bronchial artery and pulmonary artery angiography were carried out on lung cancer patients by Xiangsheng et al. [3], who discovered that the bronchial artery served as the sole source of blood supply to lung cancer and that the pulmonary artery was unrelated to the blood supply to either primary or metastatic lung cancer. In a subsequent study, Xiao et al. [9] performed DSA and CT angiography on 32 lung cancer patients, further confirming that the blood supply to lung cancer only originate from the bronchial arteries. This provided a theoretical foundation for BACE in the treatment of lung cancer and supported regional perfusion chemoembolization of lung cancer through the bronchial arteries. Conging et al. [5] collected clinical information from 54 advanced lung cancer cases and then performed bronchial arteriography, pulmonary arteriography, and perfusion chemotherapy. In addition to pulmonary artery wall damage in the tumor location and intense staining of the pulmonary artery surrounding the tumor, bronchial arteriography revealed staining of the tumor arteries. As a result, the two primary blood supply systems for lung cancer are the bronchial artery and pulmonary artery, with the bronchial artery feeding the core component of the tumor and the pulmonary artery serving the peripheral part of the tumor. The effectiveness of dual bronchial arterial and pulmonary arterial chemotherapy in the treatment of advanced lung cancers with multiple and fewer blood supplies was supported by a subsequent study by Yanhao et al. [10], which further investigated the type of bronchial arterial blood supply in lung cancer and its impact on the method and efficacy of vascular infusion. According to research by Jun et al. [4], the kind of lung cancer’s blood supply affects how well bronchial artery perfusion chemotherapy works, and the effect of many lung cancers with different blood supplies is superior. Accordingly, the majority of researchers now accept that the bronchial artery serves as the major blood vessel for lung cancer, with the pulmonary artery serving as a minor blood vessel. According to our findings (Figure 1, 2), the bronchial artery supplies blood to central lung cancer in the majority cases, whereas the pulmonary artery is not. More clinical and fundamental research is required to further validate the likelihood of pulmonary artery blood supply in peripheral lung cancer, especially smaller peripheral lung cancer. We noted that lung metastatic tumor and peripheral lung cancer both have obvious bronchial artery blood supply (Figure 3, 4) and that the pulmonary artery was not involved in the blood supply (Figures 5, 6). BACE performed for them produced satisfactory efficacy.

**PACE for Lung Cancer**

PACE for lung cancer was attempted as early as the 1950s, but it was never widely adopted because of technological and safety concerns [11]. This procedure was once again highlighted after the 1980s since it can successfully slow the progression and spread of lung cancer, increase patient survival time, and enhance the quality of life [12]. Studies have indicated that PACE can slow the growth of tumors in people with locally advanced or metastatic NSCLC, increase patients’ median survival time, relieve their symptoms and improve quality of life.

PACE procedure involves inserting a catheter through the femoral vein into the branch of the pulmonary artery where the lung cancer is located, injecting chemotherapeutic drugs into the lung cancer area, and then embolizing the branch of the pulmonary artery by microspheres or particles to block the blood supply of the lung cancer [13].

The pulmonary artery has a large diameter, is easy to intubate, has less collateral circulation and variation, has lower operational
Male, 54 years old, tumor was found in the right upper lung.

Fen-Xiang Z, et al., Clinics in Oncology - Interventional Oncology

hemoptysis, obstructive pneumonia, dyspnea, and other symptoms. It offers benefits to advanced lung cancer patients with systemic toxicity and adverse effects while preserving the immune system. It reduces combining high drug concentration cytotoxicity in the tumor region with embolization-induced ischemic necrosis [16]. BACE reduces blood flow with particles. This approach achieves dual effects, cutting off the tumor’s blood supply, which will reduce the treatment’s effectiveness and have an impact on lung function.

According to a study by Vogl et al. [15], the local response rate of lung cancer treated via the pulmonary artery route varied from 30% to 80%, the median survival time was between 6 and 18 months, and the one-year survival rate was between 30% and 60%. There aren’t many studies on the PACE method of treating lung cancer in the literature, and there isn’t enough evidence to back up the idea that the pulmonary arteries specifically give blood to lung cancer, which has to be supported by more pertinent research.

BACE for Lung Cancer

The emergence and development of BACE

Based on relevant experimental and clinical studies, BACE involves infusing chemotherapeutic drugs into the lung cancer region via the bronchial artery and simultaneously obstructing blood flow with particles. This approach achieves dual effects, combining high drug concentration cytotoxicity in the tumor region with embolization-induced ischemic necrosis [16]. BACE reduces systemic toxicity and adverse effects while preserving the immune system. It offers benefits to advanced lung cancer patients with hemoptysis, obstructive pneumonia, dyspnea, and other symptoms.

The development of BACE has involved various phases including perfusion chemotherapy, embolization, combined treatment, and using drug-eluting microspheres.

Stage of infusion chemotherapy: Japanese researchers [17] started using Bronchial Artery Chemotherapy Infusion (BAI) to treat lung cancer as early as the 1970s. Although they had some success, there are still issues with drug diffusion, inadequate doses, and noticeable adverse events.

Embolization stage: Researchers initiated the use of Bronchial Artery Embolization (BAE), coupled with perfusion chemotherapy, for lung cancer treatment. Employing thrombin, gelatin particles, and other agents for arterial embolization proved effective in reducing hemoptysis and tumor size [18].

Stage of drug-loaded microspheres: Yuhua et al. [19] were among the researchers who pioneered the utilization of drug-eluting microspheres in chemoembolization for lung cancer treatment. These polymer microspheres, such as DC Bead, Hypersphere, and CalliSpheres, are known for their dual functionality: They can load chemotherapeutic agents, enabling a gradual and controlled drug release, while simultaneously obstructing blood supply [20].

Stage of combination therapy: To harness the advantages of BACE while mitigating its limitations, researchers are exploring its integration with various therapeutic modalities, such as brachytherapy [21], molecular targeted drug therapy, immunotherapy, and radiation therapy. This synergistic approach has been shown to improve both the survival rates and the quality of life for lung cancer patients [22].

Thanks to technological advancements and medical progress, BACE is widely employed in various lung cancer types and stages, yielding favorable results. It holds particular significance in the management of unresectable lung cancer.

Anatomy and clinical significance of bronchial arteries

Bronchial arteries play a vital role in lung vascular supply, delivering oxygenated blood to bronchial walls, lung parenchyma, pulmonary lymphoid tissues, and the visceral pleura. They contribute to lung defense, metabolism, and gas exchange. Individual anatomical variations in bronchial arteries, such as their number, origin, distribution, and course, exist [23]. Familiarity with bronchial artery anatomy is crucial for recognizing arterial lesions, enabling differential diagnosis, and guiding interventional therapies.

Almeida et al. [24] categorized the anatomical origin of bronchial arteries into two types: Normal (orthotopic) and ectopic, based on their connection to the descending thoracic aorta.

Bronchial arteries of normal origin typically arise from the descending thoracic aorta near the T3-T6 vertebral plane, located 1 cm to 2 cm above and below the tracheal bulge [24]. The right bronchial artery primarily originates from the intercostal bronchial trunk or the aorta, while the left bronchial artery mainly originates from the anterior or lateral wall of the aorta, with its primary source being the thoracic aorta or its branches, including intercostal and subclavian arteries.

Common variants in bronchial artery origins, as classified by Ittrich et al. [25] and Mansur et al. [26], fall into four types: (1) type 1, two left bronchial arteries arise from the descending thoracic aorta and one right bronchial artery originates from the intercostal artery (ICBT); (2) type 2, one right bronchial artery originating...
Figure 3: Female, 66 years old, lung adenocarcinoma treated with molecularly targeted drug therapy (gefitinib) for 2 years after tumor progression with multiple nodal metastases in the right lung. Figures A and B are CT cross-sectional images of the patient, showing Multiple nodules (→) in the right lung. Figure C is a right bronchial arteriogram showing that the right lung tumor (→) is supplied by the right bronchial artery. BACE regimen: pemetrexed 800 mg + carboplatin 300 mg and gelatin sponge particles. Figures D and E show that most of the nodules (→) in the lungs disappeared and shrunk after two courses of BACE, and PR was assessed.
from the intercostal artery and one left bronchial artery from the descending thoracic aorta; (3) type 3, two right bronchial arteries having distinct origins, one from the intercostal artery and the other from the descending thoracic aorta, and two left bronchial arteries both originating from the descending thoracic aorta; (4) type 4, one left bronchial artery originates from the descending thoracic aorta, and two right bronchial arteries have separate origins, one from the intercostal artery and the other from the descending thoracic aorta.

In a 128-slice spiral CT angiographic study by Lu et al. [27] of 79 patients, bronchial artery origins were classified as follows: Type 1, featuring one right bronchial artery from the intercostal artery and one left from the descending thoracic aorta, was predominant, occurring in 59.4% of cases. Type 2, with two right bronchial arteries (one each from the intercostal artery and descending thoracic aorta) and one left from the descending thoracic aorta, comprised 17.7%. Type 3, having two bronchial arteries on each side, with each pair comprising one from the intercostal artery and one from the descending thoracic aorta, was observed in 7.6% of cases. Type 4, with one right bronchial artery from the intercostal artery and two left from the descending thoracic aorta, also accounted for 7.6%. Type 5, presenting one right bronchial artery from the intercostal artery without any left bronchial arteries, constituted 7.6%. Type 6, featuring one right bronchial artery from the intercostal artery and three left from the descending thoracic aorta, was noted in 2.5%. Lastly, type 7, with two right bronchial arteries (one from the intercostal artery and one from the descending thoracic aorta) and three left from the descending thoracic aorta, also represented 2.5%. Similarly, Yu et al. [28] analyzed 443 chest CTA images, finding that the most frequent type was one right bronchial artery from the intercostal artery and one left from the descending thoracic aorta, occurring in 53.48% of cases. The second most common type, with two right bronchial arteries (one from each of the intercostal artery and descending thoracic aorta) and one left from the descending thoracic aorta, was observed in 17.55%. Other less prevalent types included variants with differing combinations of right and left bronchial arteries.

Additionally, bronchial arteries with ectopic origins, arising from vessels like the aortic arch and subclavian artery, can be observed. Identification of ectopic bronchial arteries can be based on their proximity to the corresponding bronchus. According to Stoll’s literature [29], seven distinct types of ectopic bronchial artery origins are documented, including the subclavian, thoracic, pericardial diaphragmatic, innominate, thyroid carotid, subphrenic, and abdominal aorta. Mansur et al. [26] research also mentions the rare possibility of bronchial arteries originating from the left gastric artery. These arteries may either have juxtaposed origins or emerge from a common trunk. In summary, bronchial arteries exhibit diverse origins.

The bronchial artery follows a typical dendritic distribution upon entering the hilum and accompanying the bronchus. The right bronchial artery travels along the right anterolateral aspect, crossing the esophagus posteriorly, anteriorly, and from right to left, ultimately reaching the level of the right main bronchus. In contrast, the left lateral bronchial artery directly crosses the left side of the esophagus anteriorly and superiorly or anteriorly and laterally, reaching the level of the left main bronchus. During this course, they come into proximity or intersect with structures such as the chiasmatic arch, thoracic duct, mediastinal lymph nodes, pericardium, and atria.

Throughout all levels of the bronchial tree, bronchial arteries branch into various smaller vessels, including the bronchi, upper lobe, middle lobe (lingual lobe), and lower lobe. These vessels follow the course of the fine bronchi, forming a capillary network that supplies oxygen and nourishment to the bronchial walls. At the alveolar walls, they merge with the alveolar capillary network, contributing to pulmonary circulation. With the exception of the primary bronchi in the mediastinum, the majority of blood transported by bronchial arteries flows directly into the pulmonary circulation without venous return.

The distribution of bronchial arteries extends beyond the bronchi to encompass the lung parenchyma, pulmonary lymph nodes, and the visceral pleura. These arteries give rise to branches supplying structures such as the pulmonary parenchyma, pulmonary hilar region, and pleura. Under normal circumstances, these branches are small, but they can significantly dilate and thicken in pathological conditions like pulmonary hypertension, pulmonary embolism, and pulmonary arteriovenous malformations.

Accurate assessment and utilization of bronchial arteries are essential for transbronchial arterial interventions in lung cancer, hemoptysis, surgery, and lung transplantation, as it involves meticulous identification and treatment of target arteries to maintain therapeutic integrity [7,23]. In summary, bronchial arteries, with their intricate anatomical characteristics and variability, serve as a crucial source of lung blood supply, contributing significantly to clinical diagnosis and treatment. A comprehensive understanding of their anatomy is imperative for effective bronchial arteriography and related therapeutic procedures.

Operating technique

Preoperative assessment of bronchial artery orientation is based on tumor location and enhanced CT or CTA scans, forming the basis for intervention planning. Puncture access is typically established via the femoral or radial artery using the Seldinger or modified Seldinger technique, with a catheter traversing the thoracic aorta to reach the bronchial artery [30]. Various catheters like MIK, Cobra, RLG, SIMON are available options. Coaxial microcatheters usually range from 2.2F to 2.7F, but finer microcatheters can be used when necessary [31]. It is advisable to minimize microcatheter use to prevent bronchial artery spasm and entrapment [31].

Ionic contrast agents have been replaced by non-ionic iodine-containing contrast agents for angiography. Both hand-push and high-pressure syringe angiography can be performed with appropriate saline dilution. Contrast is used to confirm catheter placement and lung cancer blood-supplying arteries, followed by slow injection of chemotherapeutic agents and embolic particles while avoiding hazardous vessels [32]. If necessary, potential blood-supplying collateral branches, such as side branches, vagus bronchial artery, internal mammary artery, lateral thoracic artery, intercostal artery, thyroid neck trunk, and subphrenic artery, should be sought. Larger tumors are more likely to have multiple target arteries supplying them.

Indications and contraindications

Indications: BACE presents a crucial therapeutic option for patients with advanced lung cancer who are unsuitable for current standard treatments. In the literature, BACE is primarily applied to patients with intrathoracic tumors, specifically stage IIIb or more advanced NSCLC and SCLC that are inoperable. In cases of extrapulmonary metastases, BACE can be combined with other
treatments to manage intrapulmonary lesions. Possible indications including:

1. Failure, progression, or recurrence of stage IIIb or more advanced NSCLC and SCLC after standard treatments (radiotherapy, targeted therapy, immunotherapy).
2. Patients unable to tolerate or declining standard treatments.
4. Adjuvant therapy following surgical resection recurrence.
5. Emergency management for complications like hemoptysis.
7. Lung cancer in conjunction with airway stenosis or pulmonary atelectasis [33].

While the lung cancer diagnostic and treatment guidelines suggest that patients with stage IV NSCLC [34] and an Eastern Cooperative Oncology Group (ECOG) physical status score >2 may not typically benefit from systemic chemotherapy, considering that BACE mainly local efficacy with minimal systemic side effects, it is advisable to actively assess the potential of BACE while implementing optimal supportive care. By judiciously reducing the chemotherapy agent dosage, it remains possible to effectively manage the tumor, alleviate symptoms, enhance the quality of life, and capitalize on the benefits of BACE.

**Contraindications:** Before considering BACE for lung cancer treatment, it is essential to rule out the following contraindications or relative contraindications:

1. Blood analysis indicated WBC <3.0 × 10⁹/L, Neutrophils <1.5 × 10⁹/L, RBC <2.0 × 10¹²/L, Hb<80 g/L, and Platelets <50 × 10⁹/L.
2. Severe bleeding tendency and coagulation dysfunction, not correctable within a short timeframe (prothrombin time >18 s, prothrombin activity <40%).
3. Severe pulmonary fibrosis, pulmonary hypertension, or reduced pulmonary circulation due to various reasons.
4. Infectious or radiation-related inflammation around the lesion, uncontrolled skin infection at the puncture site, systemic infection, and fever >38.5°C.
5. Severe hepatic, renal, cardiac, pulmonary, and cerebral insufficiency, severe anemia, dehydration, and significant nutritional metabolism disturbances that cannot be corrected or improved within a short period.
6. Uncontrolled malignant pleural or pericardial effusion.
7. Patients with extensive metastatic tumors and an expected survival of less than 3 months.
8. Allergy to iodine-containing contrast agents, inability to lie supine, inability to cooperate with puncture, intubation, and contrast procedures, and patients with a history of psychosis.
9. Intraoperative imaging reveals an inability to achieve super-selective cannulation to completely avoid spinal arteries and other hazardous vessels.
10. Inability to achieve selective bronchial artery cannulation following preoperative assessment, especially after descending thoracic aortic overlay stent implantation.

**Principles of drug selection**

The individualized treatment plan is determined based on the patient’s tumor pathology, treatment history, therapeutic evaluation,
and laboratory test results. Selection of chemotherapy agents considers factors such as tumor type, cell growth pattern, drug mechanism, pharmacokinetics, and combines two to three agents with complementary mechanisms and anti-tumor properties. For arterial regional perfusion chemotherapy, which achieves a localized high drug concentration, concentration-dependent, cell-cycle nonspecific drugs are preferred to maximize cytotoxic effects. The use of cell-cycle specific drugs is minimized when possible [15,35,36].

The primary regimen for lung cancer medication involves systemic chemotherapy, which encompasses course duration and dosage. In accordance with the 2023 National Health and Health Commission's guidelines for primary lung cancer diagnosis and treatment, there are recommendations for first, second, and third-line drug treatments for advanced lung cancer [34].

For advanced NSCLC, the initial drug options primarily consist of platinum-based two-drug combinations. These combinations include cisplatin or carboplatin (with recent use of nedaplatin) combined with vincristine, gemcitabine, paclitaxel, docetaxel, pemetrexed (for non-squamous histology), paclitaxel liposome, and albumin-bound paclitaxel. Drug dosages are generally calculated based on body surface area, with carboplatin calculated at an AUC of 5-6. A typical treatment cycle spans 21 days, usually comprising 4-6 cycles. Vincristine and gemcitabine may also require dosing on day 8 and can be administered intravenously based on the clinical context following BAI/BACE.

In the treatment of lung adenocarcinoma, the first-line recommendation involves cisplatin (or carboplatin, nedaplatin) in combination with pemetrexed. The second-line option is cisplatin (or carboplatin, nedaplatin) combined with docetaxel or albumin-bound paclitaxel.

For squamous lung cancer, the first-line regimen consists of cisplatin (or carboplatin, nedaplatin) combined with docetaxel or albumin-bound paclitaxel. Due to the local irritation and severe cough associated with gemcitabine, it is advised to use it cautiously or administer it slowly after further dilution. In the second-line setting, cisplatin (or carboplatin, nedaplatin) in combination with vincristine and other agents is recommended.

In the case of SCLC, the first-line treatment recommendation includes cisplatin or carboplatin in combination with etoposide. For those who experience recurrence or progression within 6 months after the initial chemotherapy, topotecan, irinotecan, gemcitabine, vincristine, temozolomide, or paclitaxel may be considered in the second-line setting. Patients experiencing recurrence or progression after 6 months can opt for the initial treatment protocol.

Selection of embolic agents

Prior to embolization, panoramic Digital Subtraction Angiography (DSA) is essential for assessing vascular anatomy to prevent inadvertent access to non-target vessels [37]. Microcatheter super-selective cannulation provides precise guidance for
directing the embolic agent into the intended vessel. Embolization enhances therapeutic efficacy by obstructing tumor blood supply, leading to ischemic necrosis, hemostasis, and delayed washout of chemotherapeutic agents. The choice of embolic agents, such as gelatin sponge particles, blank microspheres, or drug-eluting microspheres, depends on the purpose of embolization and available materials. It is recommended to use embolic agents with a diameter exceeding 300 micrometers, while liquid embolic agents like ethyl iodine oil and anhydrous ethanol should be avoided or used cautiously.

A study demonstrated that microspheres offer comparable efficacy and safety to Polyvinyl Alcohol (PVA) and can serve as an alternative to PVA [38]. When selecting embolic agents, factors to consider include embolic efficacy, biocompatibility, particle size, as well as tumor and vascular characteristics and therapeutic goals [39,40]. When employing drug-eluting microspheres, attention must be given to the choice of drug and dosage. Regardless of the chosen embolic agent, it is crucial to prioritize safety, proper catheter insertion, and standardized panoramic angiographic assessment [41].

**Evaluation of efficacy**

The short-term evaluation of BACE for lung cancer relies on standard assessments such as RECIST or mRECIST, classifying responses as Complete Response (CR), Partial Response (PR), Stable Disease (SD), Progressive Disease (PD), Overall Response Rate (ORR), and Disease Control Rate (DCR). Additionally, changes in tumor markers, physical condition, lung cancer symptom grading, quality of life, and adverse event monitoring are considered. Long-term efficacy is typically evaluated through Progression-Free Survival (PFS) and Overall Survival (OS). Treatment strategies are adjusted based on the assessment results throughout the diagnostic and treatment process.

In 2008, a randomized controlled trial conducted by Huang et al. [42], 127 patients were divided into three groups: Bronchial arterial infusion chemotherapy, systemic intravenous chemotherapy, and sequential therapy. The results indicated that the bronchial arterial infusion chemotherapy group (59.22% effective) and the sequential treatment group (69.05% effective) achieved significantly higher primary lesion efficacy (complete remission + partial remission) compared to the systemic intravenous chemotherapy group (30.23% effective). Furthermore, the sequential treatment group demonstrated significant control of extrapulmonary metastasis when compared to bronchial arterial infusion chemotherapy alone (complete remission + partial remission: 60.00% vs. 18.19%, P<0.05), highlighting clinical significance.

In another study by Cao et al. [43], 178 cases were examined. The observation group, which received both BACE and systemic chemotherapy, outperformed the control group (chemotherapy alone) with an Overall Effective Rate (ORR) and Disease Control Rate (DCR) of 73.40% and 93.62%, respectively, compared to 58.33% and 84.52% for the control group (P<0.05). The observation group also showed a higher rate of hemoptysis remission (75.00% vs. 41.51% in the control group) and a lower incidence of serious adverse reactions (9.57% vs. 20.24% in the control group). During the follow-up period, the observation group exhibited significantly lower mortality and recurrence rates compared to the control group.

In a study conducted by Shang et al. [20], 36 lung cancer patients at different stages were treated with BACE, yielding an effective rate of 72.2%, a one-year survival rate of 75.4%, and a two-year survival rate of 52.1%. In 2022 a retrospective analysis by Japanese scholars, Hori et al. [44], which included 98 patients with progressive or recurrent lung cancer, the treatment achieved an impressive overall response rate of 97.9%. Among these patients, 24.2% exhibited partial remission, while 72.6% maintained stable disease, with only a 2.1% rate of disease progression. The median survival time was 11.4 months, accompanied by one-year and two-year survival rates of 45.2% and 35.6%, respectively. Notably, in the subgroup of patients with adenocarcinoma (51 patients), the median survival time reached 18.6 months, a significant improvement compared to patients with squamous carcinoma (29 patients), whose median survival was 9.4 months. These findings underscore the promising potential of this treatment regimen for lung cancer, particularly in patients with adenocarcinoma.

In another study by Xu [45], the efficacy and safety of BACE with drug-eluting beads were examined in patients with SCLC refractory to or ineligible for standard treatment (STRI-SCLC). Clinical data from 28 patients treated with BACE between January and December 2019 were retrospectively analyzed. After a 20.5-month follow-up, an impressive 77.8% of patients achieved disease control within three months. The PFS was 5.0 months, and the median OS was 9.5 months. These results affirm the satisfactory efficacy of BACE in tumor remission, hemoptysis control, and survival, all with a high safety profile.

A comprehensive review of the literature supports transarterial therapy as a viable treatment option for lung cancer, particularly in combination with other modalities or for advanced disease. This approach offers the advantage of minimizing normal tissue damage while enhancing tumor therapy. Although widely acknowledged in the academic community, further evidence-based medical research is essential to substantiate this concept.
Combination therapy

The comprehensive management of lung cancer can be significantly enhanced through the synergistic utilization of BACE in combination with surgical procedures, radiotherapy, particle implantation, and target-free therapy. Jiang Sen’s retrospective analysis of 51 cases of arterial interventions for lung cancer [46], has demonstrated that lung cancer often exhibits polyarteritis involvement within the circulatory system. This observation suggests that lung tumors may receive nutrition from multiple arteries, making it challenging for single-artery interventions to completely disrupt tumor blood supply. This inadequacy can result in suboptimal treatment outcomes or recurrence. Hence, to address the multifaceted vascular supply of lung cancer, a multifaceted, multi-tiered intervention approach is warranted, aiming to more effectively impede tumor growth and metastasis.

Furthermore, the incorporation of BACE with radiation therapy yields several benefits. This combination leads to reduced tumor volume, heightened precision and sensitivity in radiation therapy, diminished tumor cell adaptability to hypoxia, and amplified radiation therapy efficacy [47,48]. Additionally, BACE contributes to reducing the required radiation therapy dose and frequency, thereby mitigating harm to normal tissues [22,49].

The integration of BACE with 125I particle interstitial implantation radiotherapy offers a comprehensive strategy for combating lung cancer [50]. BACE facilitates the conditions necessary for 125I particle interstitial implantation radiotherapy, thereby augmenting local control rates through the inhibition of tumor blood supply and growth. The combination of these approaches collectively enhances therapeutic outcomes and extends the time to disease progression [51].

Finally, the combination of BACE with targeted drugs serves to obstruct tumor blood flow, reduce tumor cell resistance, and establish a localized, high-concentration chemotherapy environment. This combination strengthens the effectiveness of targeted therapy, promotes tumor cell apoptosis, and concurrently reduces the required dosage and frequency of targeted drugs, thus mitigating systemic toxicities [52].

The combined use of BACE and immunotherapy offers distinct advantages. This approach enables localized high-concentration chemotherapy, triggers the release of antigens and inflammatory factors from tumor cells, activates the immune system, enhances immunotherapy efficacy, reduces the required dosage and frequency of immune checkpoint inhibitors, and mitigates immune-related adverse reactions [53,54].

BACE serves as a neoadjuvant therapy that provides an opportunity for curative surgical intervention in lung cancer cases. In a retrospective study by Zhu et al. [55], it was demonstrated that for unresectable stage III squamous carcinoma, two cycles of BAI (Bronchial Artery Chemoembolization) resulted in 22.2% of patients regressing to a lower stage, with 52.8% becoming eligible for surgical resection in subsequent stages of the disease. The median survival in the BAI group was 25 months, significantly surpassing that of patients not receiving BAI treatment. These findings underscore the potential of BACE to revolutionize treatment strategies, particularly in inoperable locally advanced (stage III) squamous cell lung cancer, thereby enhancing their quality of life when compared to transvenous chemotherapy.

Furthermore, BACE is an invaluable treatment for postoperative lung cancer recurrence (Figure 7). In cases of postoperative recurrence of lung adenocarcinoma without driver gene mutations, and where tumor progression persists after adjuvant chemotherapy, BACE therapy achieved Partial Response (PR).

The integration of BACE with radiation therapy, targeted therapy, immunotherapy, and surgery enhances the overall treatment effectiveness while minimizing treatment-related side effects. BACE, as a key component of comprehensive treatment, holds promise for improving clinical outcomes in lung cancer patients [13].

Prevention and management of complications

While BACE offers numerous advantages over traditional systemic chemotherapy, such as localized efficacy, improved quality of life, and reduced systemic toxicity, as well as a decreased incidence of common side effects like nausea, vomiting, myelosuppression, and fever, it is imperative to remain vigilant regarding potential severe complications. These complications may rare but grave issues such as spinal cord injury, acute cerebral infarction, acute tracheoesophageal injury and esophagitis, and mediastinal fistula.

Spinal cord injury resulting in paraplegia stands out as an infrequent yet serious complication [56]. To prevent such an outcome, angiography should be conducted using nonionic contrast with appropriate dilution, with meticulous attention to the visualization of intercostal arterial trunks or spinal arteries through microcatheter super selective cannulation. Prior to initiating perfusion chemotherapy, lidocaine should be injected into the target artery to monitor signs of spinal anesthesia. Continuous monitoring of the patient’s limb sensation, muscle strength, and urinary and fecal status during and after drug perfusion and embolization is crucial. In the event of spinal cord injury, immediate cessation of treatment is necessary, followed by active symptomatic management, including the administration of high-dose glucocorticoids, mannitol for dehydration, and vasodilators [57].

Acute cerebral infarction, which can result from the anastomosis of bronchial arteries with intracranial arteries through vessels like intercostal, subclavian, and vertebral arteries, poses a potential risk when embolic agents enter the cranial region. A documented case report presented two instances of cerebral infarction following BACE [58]. Hence, meticulous pre-embolization imaging to assess transportation pathways and the judicious selection of embolic agents are paramount to prevent over-embolization or ectopic embolization.

Tracheoesophageal injury and acute esophagitis have been rarely documented [59]. Identifying esophageal artery branches during imaging is imperative, and super-selective intubation should be conducted to avoid them prior to drug instillation and embolization. Active symptomatic management is necessary in the event of such complications, potentially requiring fasting. The formation of an esophageal bronchial fistula, a serious complication, may result from anticancer drug infiltration into the esophageal wall, causing tissue damage and ulceration. Symptoms typically involve a sudden increase in choking cough, relieved by swallowing solid food. Primary treatment involves esophageal laminar stent sealing. Preventative measures encompass thorough pre-imaging, stringent control of drug concentration and infusion rate, and vigilant symptom monitoring [60].
Bleeding complications may arise from various sources, including puncture site bleeding, hematoma, and pseudoaneurysm [57]. Arterial injuries can occur due to a lack of timely fluoroscopy and rough handling during the procedure, leading to complications such as bleeding from renal artery injury, thoracic aortic endometrial tear, bronchial artery dissecting aneurysm, rupture hemorrhage [61].

In the central type of lung cancers and giant lung cancers, the extensive lesion area and rapid tumor necrosis after BACE can lead to the formation of cavities and infections, with insufficient time for adjacent bronchial arteries or pulmonary arteries to repair, resulting in hemorrhage. Preventive measures include reducing drug dosage and diminuer embolization intensity for large lung cancer lesions and administering treatment gradually. In cases of hemoptyysis, contrast CT or CTA scans can identify the bleeding source, enabling necessary embolization and stent overlay treatments.

Additionally, BACE may entail complications such as infection, allergy, liver and kidney function abnormalities, and cardiac arrhythmia. Vigilant symptom monitoring and appropriate precautions are essential during BACE procedures to minimize these potential complications [62].

Prospects

Percutaneous vascular interventions are new approaches for lung cancer, but their application faces several challenges that warrant exploration and advancement.

The existing literature primarily comprises single-center retrospective summaries, lacking controlled studies alongside systemic chemotherapy and demonstrating low research quality. A pressing need exists for high-quality Randomized Controlled Trials (RCTs) to assess the impact of vascular interventions on lung cancer patients’ survival and quality of life. Additionally, investigating the synergy of vascular intervention with other therapies, such as radiotherapy and targeted immunotherapy, is crucial to offer precise clinical evidence.

The source of blood supply in lung cancer remains a subject of debate. While bronchial artery and other systemic circulation artery is recognized as the primary blood supply artery for central type of lung cancers and larger peripheral lung cancers, the presence of pulmonary artery blood supply to lung cancer remains unclear. BACE presents a viable option, particularly for lung cancer patients who do not meet the current managements. Nevertheless, the BACE technique lacks strong evidence-based support and has not been sufficiently compared to systemic chemotherapy, radiation therapy, molecularly-targeted therapy, or immunotherapy. As a result, it has yet to be integrated into lung cancer diagnostic and therapeutic guidelines. Consequently, experts in this field should establish a consensus to streamline the transvascular intervention process for lung cancer, offering a standardized technique that improves efficacy and reduces adverse event. This will facilitate the wider adoption of vascular interventions in lung cancer.

References

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