

Bronchial arterial embolization may reduce the risk of severe bleeding in central airway obstruction due to renal cell carcinomas during bronchoscopic procedures

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Abstract

Background: Hemorrhage is a life-threatening complication during bronchoscopic intervention in patients with central airway obstruction (CAO) due to metastatic renal cell carcinoma (RCC). Whether pre-bronchoscopic bronchial arterial embolization (BAE) can reduce the risk of severe bleeding in CAO patients due to metastatic RCC remains unclear.

Methods: A total of 31 CAO patients due to metastatic RCC were included retrospectively and divided into a BAE group (receiving pre-bronchoscopic BAE) and non-BAE group in this study. Based on computed tomography (CT) and bronchoscopic findings, tumor debulking was used to reconstruct the airway during interventional bronchoscopy. The primary outcome was the incidence of severe bleeding during bronchoscopic procedures. Bleeding-related complications, Karnofsky performance score (KPS) and dyspnea score were also analyzed over a 1-month observation period.

Results: There were no significant differences between the two groups in baseline characteristics, including patients' features, tumor morphology under CT scanings, tumor site, and obstruction degree under bronchoscopic examination. Procedure-related bleeding occurred in all 31 patients. Pre-bronchoscopic BAE significantly reduced the incidence of moderate and major bleeding when compared with that in the non-BAE group. The incidence of poor visualization and hypoxia was also reduced significantly in the BAE group. There was no significant difference in KPS and dyspnea score between the BAE and non-BAE groups at 1 month follow up.

Conclusion: Pre-bronchoscopic BAE might be a feasible option to reduce the risk of severe bleeding for CAO patients due to metastatic RCC during bronchoscopic intervention. Interventional bronchoscopy was a safe and effective procedure for CAO due to metastatic RCC.

The reviews of this paper are available via the supplemental material section.

Keywords: bronchial artery embolism, central airway obstruction, interventional bronchoscopy, renal cell carcinoma

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Introduction

Central airway obstruction (CAO) due to primary extra-pulmonary malignancies, ranging from 2% to 50% based on different tumor types, is a serious life-threatening condition.^{1–4} Renal cell carcinoma (RCC), one of the most common malignant neoplasms invading the airway, is characterized by hyper-vascularity in pathology and a higher risk of hemorrhage during treatment.^{5,6} When

RCC invades the central airway, it can cause airway obstruction, impair life quality, and even induce life-threatening problems. Surgery is not preferred due to the location of the lesion, stage of the RCC, and poor general condition of the patients. Additionally, chemotherapy, radiotherapy and molecular-targeted therapy take a long time to resolve the obstruction.⁷ Thus, interventional bronchoscopy, as a palliative modality, is

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used widely to palliate CAO due to metastatic RCC, but how to reduce the risk of bleeding during bronchoscopic procedures is still challenging.

Interventional bronchoscopic procedures include balloon dilation, laser ablation, CO₂ cryosurgery, electrocautery, and implantation of airway stents. Tumor debulking and airway stenting have been used commonly to reconstruct the airway in patients with CAO due to metastatic RCC.^{8–11} However, severe bleeding is still a challenging and life-threatening problem during bronchoscopic intervention. Bronchial artery embolization (BAE) is increasingly considered as a treatment option for patients with recurrent hemoptysis.¹² BAE has also been reported to reduce the incidence of intraoperative severe bleeding in two cases of metastatic RCC prior to interventional bronchoscopy.⁹ However, it is still unclear whether BAE prior to interventional bronchoscopy could reduce the risk of severe bleeding during this palliative treatment.

Given that there are relatively few reports of combining BAE and bronchoscopic intervention in treating CAO due to metastatic RCC, we performed a retrospective study to compare the safety and efficacy of pre-bronchoscopic BAE in CAO patients with metastatic RCC.

Materials and methods

Patients suffering from CAO due to metastatic RCC from January 2014 to October 2019 were included retrospectively. CAO was defined as occlusion of $\geq 50\%$ of the trachea, main-stem bronchi, bronchus intermedius, or a lobar bronchus.¹³ The inclusion criteria were as follows: aged 18 years old or older; CAO due to metastatic RCC confirmed by pathology; appearance of symptoms was caused by airway obstruction and symptoms were expected to be relieved by intervention; tolerance for general anesthesia; normal renal function. Exclusion criteria included multiple organ failure, uncontrolled arrhythmias, and incomplete data in medical file.

All patients were assessed with contrast-enhanced chest computed tomography (CT) prior to treatment. Based on multidisciplinary discussion, pre-bronchoscopy BAE was recommended when patients demonstrated recurrent hemoptysis or strong enhancement on the contrast-enhanced CT.¹⁴ However, pre-bronchoscopy BAE was not

performed because of technical failure ($n=3$) or patient refusal ($n=10$). Technical failure of BAE was defined when corresponding arteries were not identified or BAE was terminated due to patient intolerance.¹⁵ Patients were divided into a BAE group and a non-BAE group based on whether pre-bronchoscopy BAE had been performed.

Pre-bronchoscopic BAE

Selective BAE was carried out based on previous reports.¹² An initial angiographic survey was performed to identify the corresponding arteries. A 5 Fr catheter was inserted to the level of the origin or proximal segment of the bronchial arteries. A 2.8 or 3 Fr micro-catheter was used to catheterize in a super-selective way, through which embolization was performed with polyvinyl alcohol microsphere (BioSphere Medical, Rockland, France). A hot compress to the abdomen and morphine were applied to relieve the pain after BAE.

Interventional bronchoscopy

All patients underwent rigid bronchoscopy (Karl Storz, Tuttlingen, Germany) under general anesthesia 24–48 h after arterial embolization. Heat ablative techniques including laser (Ligenesis, Wuhan, China), argon plasma coagulation (APC, ERBE, Tübingen, Germany), electric snare (Olympus, Tokyo, Japan) were initially used, then cryotherapy (Kooland, Beijing, China) and flexible forceps were used to remove the tumor. APC, laser, high-pressure balloon, cold saline, and hemocoagulase were used to manage bleedings as needed.

Post-bronchoscopy evaluation

Patients were followed up at 1 month post-discharge. Outpatient or telephone follow ups were made by the referring doctors. Karnofsky performance score (KPS) and dyspnea scores were also evaluated at 1 month post discharge.

Assessments

As an intraoperative complication, the severity of bleeding was defined as minor (requirement of a single repeat application of the laser or APC), moderate (prolonged mechanical compression and/or multiple repeat applications of the laser or APC) and major (need for arterial embolization or emergency surgery).¹⁶ Respiratory distress was

defined as worsening oxygenation or dyspnea after the bronchoscopy.¹⁷ Hypoxia was defined as oxygen saturation lower than 90% ,and poor visualization (bronchoscope visual field impairment with blood) was defined as the unclear airway structure, both of which were imperative during bronchoscopic procedures.⁸

Technical success of interventional bronchoscopy was defined as not only reopening the airway lumen to >50% of the normal diameter, but also ensuring a viable area of distal lung.¹⁰ KPS and dyspnea score were applied to estimate the quality of life and the degree of dyspnea. The severity of airway obstruction was determined by the Myer–Cotton stenosis grading system: Grade I, ≤50% luminal stenosis; Grade II, 51–70% luminal stenosis; Grade III, 71–99% luminal stenosis; and Grade IV, no lumen.¹⁸ The bronchoscopic time was recorded.

Statistical analysis

Statistical analysis was performed using SPSS 20.0 software (SSPS Inc., Chicago, IL, USA). Continuous variables are presented as mean ± standard deviation (SD). Categorical variables are presented as numbers and percentages. The relationship between categorical variables was assessed using the Chi-square test. The connection between quantitative variables was evaluated using independent-sample *t* test. Statistical significance was set at $p < 0.05$.

Results

Baseline CT, bronchoscopic characteristics, and patients' features are summarized in Table 1. A total of 31 CAO patients (24 males and 7 females) due to metastatic RCC were included for analysis, with a mean age of 61 ± 10 years (42–87 years); 20 (64.5%) patients had received chemotherapy at hospitalization, 5 (16.1%) had undergone radiotherapy, and 15 (48.4%) had received targeted drugs. In total, 18 patients received pre-bronchoscopic BAE (BAE group) and 13 were in the non-BAE group. Patients did not receive anti-platelet or anticoagulation treatment in this study. Cough was seen in all 31 patients, dyspnea in 21 cases, and hemoptysis in 22 cases. All patients with hemoptysis accepted hemostasis of drugs. CT scanning revealed different morphologies of metastatic RCC, including polypoid shape with narrow or wide basements ($n = 12$, Figure 1A), the branching

configuration of the tumor adapting the bronchus ($n = 24$, Figure 1B), extrinsic compression ($n = 7$, Figure 1C), and atelectasis ($n = 8$). The endobronchial mass of RCC showed high attenuation (95.1 ± 12.9 Hu) and strong enhancement (60.6 ± 11.4 Hu) in contrast-enhanced CT images. The metastatic RCC exhibited polypoid lesions and thrombus-like lesions that were parallel to the corresponding bronchial branching under bronchoscopic examination. The surface of tumor was relatively smooth, with congestion of the mucous membrane. The locations of tumor base included single (21/31, 67.7%) and multiple (10/31, 32.3%) lesions. Lobar bronchus was the most common site of metastatic RCC in the airway. A total of 87.1% patients had a stenosis of Grade III or IV. There were no significant differences between the two groups in baseline characteristics, including patients' features, tumor morphology under CT scanning, tumor site, and degree of obstruction under bronchoscopic examination (Table 1).

Procedure-related bleeding occurred in all 31 patients (Table 2). In the BAE group, minor bleeding occurred in 12 (66.7%) patients and moderate bleeding in 6 (33.3%) patients; in the non-BAE group, minor bleeding occurred in 3 (23.1%) patients, moderate bleeding in 8 (61.5%) patients, and severe bleeding in 2 (15.4%) patients. Pre-bronchoscopic BAE significantly reduced the rate of moderate and major bleeding compared with those without pre-BAE patients ($X^2 = 5.743$). Pre-bronchoscopic BAE significantly reduced the rate of poor visualization and hypoxia, as compared with those in non-BAE group (both $X^2 = 4.841$). Typical cases of clear visualization and poor visualization are shown in Figure 2A and B. The duration of bronchoscopic therapy was longer in the non-BAE group than that in the BAE group. No respiratory distress and pneumothorax were observed. Complications after BAE, including chest pain (9/18, 50%) and abdominal pain (2/18, 11.1%), were alleviated on the next day after receiving supportive therapies. Fever, shivering, and vomiting occurred in 7/18 (38.9%), 7/18 (38.9%), and 5/18 (27.8%) patients, respectively. Spinal cord injury was not observed in this study.

Follow up

There was no significant difference in KPS (83.9 ± 7.0 versus 83.1 ± 4.8 , $p = 0.06$) and dyspnea score (0.9 ± 0.6 versus 1.2 ± 0.4 , $p = 0.280$) between the BAE and non-BAE groups at 1 month follow up.

Table 1. Baseline characteristics, and CT and bronchoscopic findings (n=31).

	BAE group	Non-BAE group	p value
Male/female	15/3	9/4	0.309
Age (years)	61.6 ± 9.6	61.0 ± 12.4	0.988
Time from diagnosis to first procedure (months)	84.9 ± 95.5	91.3 ± 42.3	0.569
Clinical symptoms			
Dyspnea	12/18 (66.7%)	9/13 (69.2%)	0.597
Hemoptysis	14/18 (77.8%)	8/13 (61.5%)	0.433
Cough	18/18 (100%)	13/13 (100%)	
Dyspnea score	2.4 ± 0.7	3.0 ± 0.8	0.883
KPS	58.3 ± 9.9	56.9 ± 6.3	0.171
Comorbidities			
Chronic bronchitis	5/18 (27.8%)	3/13 (23.1%)	0.552
Hypertension	6/18 (33.3%)	5/13 (38.5%)	0.532
Diabetes	2/18 (11.1%)	1/13 (7.7%)	0.624
Previous therapy			
Chemotherapy	11/18 (61.1%)	9/13 (69.2%)	0.641
Radiotherapy	3/18 (16.7%)	2/13 (15.4%)	0.924
Targeted drugs	10/18 (55.6%)	5/13 (38.5%)	0.347
CT findings			
Polypoid shape	7/18 (38.9%)	5/13 (38.5%)	0.638
Shape adapting the bronchus	14/18 (77.8%)	10/13 (76.9%)	0.642
Extrinsic compression	3/18 (16.7%)	4/13 (30.8%)	0.309
Atelectasis	5/18 (27.8%)	3/13 (23.1%)	0.552
CT number (HU)			
Unenhanced CT	33.1 ± 5.9	36.3 ± 4.6	0.112
Contrast enhanced CT	92.2 ± 13.9	99.2 ± 10.8	0.143
Bronchoscopic location			
Single location	12/18 (66.7%)	9/18 (69.2%)	0.880
Trachea	1/18 (5.6%)	1/13 (7.7%)	0.811
Right intermedius	1/18 (5.6%)	1/13 (7.7%)	0.811
Lobar bronchus	10/18 (55.6%)	7/13 (53.8%)	0.925
Multiple location	6/18 (33.3%)	4/13 (30.8%)	0.880
Trachea and bronchus	3/18 (16.7%)	3/13 (23.1%)	0.656
Multiple lobar bronchus	3/18 (16.7%)	1/13 (7.7%)	0.462
Severity of airway obstruction			
II	1/18 (5.6%)	3/13 (23.1%)	0.186
III	11/18 (61.1%)	6/13 (46.2%)	0.323
IV	6/18 (33.3%)	4/13 (30.8%)	0.597

BAE group, patients receiving pre-bronchoscopic bronchial artery embolization; CT, computed tomography; HU, Hounsfield units; KPS, Karnofsky performance score; Non-BAE group, patients without pre-bronchoscopic bronchial artery embolization.

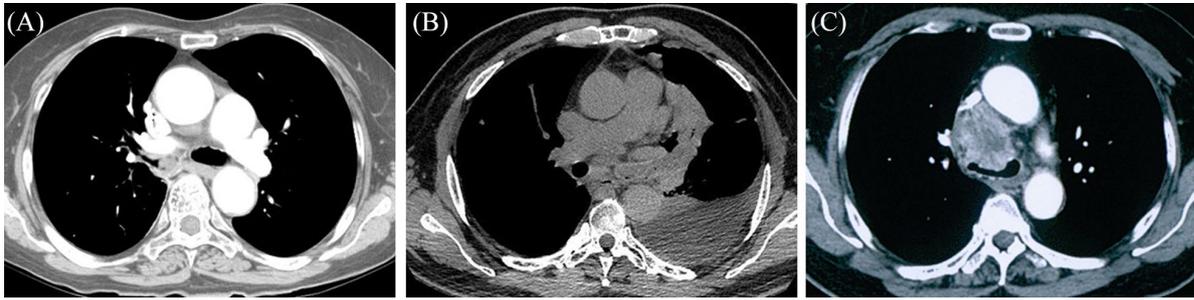


Figure 1. CT images of metastatic RCC. (A) Contrast-enhanced CT shows an enhancing endobronchial polypoid lesion in the right main bronchus. Attenuation of this mass was measured as 98 HU. (B) The branching configuration of the tumor adapted the left main bronchus; and (C) Enlarged mediastinal lymph node compressed the carina and right main bronchus. CT, computed tomography; HU, Hounsfield units; RCC renal cell carcinoma.

Table 2. The complications, effects, and procedure duration between BAE and non-BAE group.

	BAE group (%)	Non-BAE group (%)	<i>p</i> value
Moderate and major bleeding	6/18 (33.3)	10/13 (76.9)	0.029
Significant hypoxia	2/18 (11.1)	6/13 (46.2)	0.028
Poor visualization	2/18 (11.1)	6/13 (46.2)	0.028
Bronchoscopic duration (min)	40.2 ± 10.7	51.2 ± 12.3	0.012
KPS after IB	85.0 ± 7.1	83.0 ± 4.8	0.074
Dyspnea score after IB	0.9 ± 0.6	1.2 ± 0.4	0.758
Cough after IB	2/18(88.9)	3/13(76.9)	0.371
Hemoptysis after IB	2/18 (11.1)	4/13(30.7)	0.179
Technical success	17/18 (94.4)	11/13 (84.6)	0.361

Cough and hemoptysis relieved after the bronchoscopic therapy in all patients. Dyspnea score decreased and the KPS increased significantly after treatment ($p < 10^{-3}$). There were no statistical differences in dyspnea and KPS scores between the two groups. There was also no significant difference in technical success between BAE and no-BAE groups ($\chi^2=0.834$) (Table 2). BAE group, patients receiving pre-bronchoscopic bronchial artery embolization; CT, computed tomography; non-BAE group, patients without pre-bronchoscopic bronchial artery embolization; IB, interventional bronchoscopy; KPS, Karnofsky performance score.

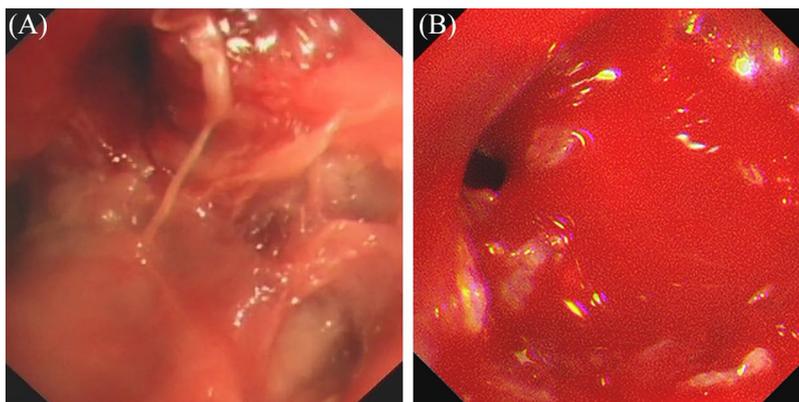


Figure 2. Visualization of metastatic RCC during the intervention. (A) Clear visualization after tumor ablation in a patient receiving pre-BAE and (B) Poor visualization after tumor ablation in a patient without pre-BAE. BAE, bronchial arterial embolization; RCC, renal cell carcinoma.

Discussion

In this retrospective study, we found that pre-bronchoscopic BAE reduced the risk of moderate and major bleeding and bronchoscopic duration in CAO patients due to metastatic RCC. In addition, we also found that pre-bronchoscopic BAE could reduce the occurrence of significant poor visualization and hypoxia in these patients.

Based on previous reports, hyper-vascularity in pathology and a higher risk of hemorrhage were characteristics of CAO due to metastatic RCC.^{5,8,9,19} Sakumoto *et al.* found that bleeding was the most serious complication when CAO patients due to metastatic RCC received bronchoscopic treatment.²⁰ In another report, blood transfusion was required for severe bleeding due to metastases from RCC.²¹ Thus, severe bleeding was still a great challenge when CAO patients, due to metastatic RCC, received bronchoscopic treatment. In pathophysiology, the airways and lungs receive dual blood supply from both the bronchial arteries and the pulmonary arteries.^{22,23} The bronchial artery has been considered the major feeding vessel to pulmonary metastasis, and the blood supply can increase proportionately the number of metastatic sites from middle to inner zones of the lung.^{24,25} Therefore, in theory, BAE could be considered as a potential modality to reduce blood supply when resecting CAO due to metastatic RCC. Suyama *et al.* reported significantly less bleeding during the bronchoscopic therapy in two patients with endobronchial RCC by adopting pre-bronchoscopic BAE.⁹ However, few studies have made a comparison to explore the efficacy of pre-bronchoscopic BAE in reducing bleeding during the bronchoscopic therapy. In this study, pre-bronchoscopic BAE significantly reduced the incidence of moderate and major bleeding when compared with non-BAE. BAE led to a much faster, and technically simpler, ablation during bronchoscopic procedures. In addition, BAE also decreased hypoxia and poor visualization caused by massive bleeding during bronchoscopic treatments. Thus, pre-bronchoscopic BAE could be performed selectively on patients at high risk of bleeding during bronchoscopic treatment, such as patients with CAO due to metastatic RCC.

In previous studies, airway stenting was used to reconstruct the compromised airway due to RCC during interventional bronchoscopy procedures.^{8,14,16,26} Airway stents were effective at alleviating symptoms when patients exhibited a

mixed endobronchial and extrinsic CAO. However, we found that airway lesions were located mainly at lobar bronchus, and extrinsic compression was less common based on CT scanning and bronchoscopic examinations in this study compared with previous reports.^{8,14,20} Depending on these features, we used ablative procedures in the study, which were widely adopted in interventional bronchoscopic procedures for CAO patients, including laser ablation and CO₂ cryosurgery.^{27–31} Bronchoscopic tumor ablation is a valuable option for inoperable CAO due to metastatic RCC. These techniques may be more effective and convenient when severe bleeding is reduced by pre-bronchoscopic BAE.

This study has some limitations. Firstly, patients were not divided randomly into two groups. Secondly, this was a small retrospective single-center report. Furthermore, a prospective randomized control study is needed to confirm our preliminary findings in a large number of patients.

In conclusion, pre-bronchoscopic BAE might be an option to reduce the degree of bleeding in CAO patients due to metastatic RCC. Debulking techniques were also a preferred therapeutic option based on lesion characteristics.

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Author contributions

MT and NZ were involved in conception and design, collection and assembly of data, data analysis and interpretation, and manuscript writing. HW, HM, HG, and ZW were involved in collection and assembly of data and review. NZ approved the final version of the manuscript.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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Supplemental material

The reviews of this paper are available via the supplemental material section.

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