Original Article

A retrospective analysis of risk factors in recurrent hemoptysis patients with non-bronchial systematic artery feeding

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Background: Hemoptysis is a symptom of a life-threatening condition. Bronchial artery embolization (BAE) is recommended to control hemoptysis. However, non-bronchial systematic arteries (NBSAs) can be culprit vessels, particularly in recurrent hemoptysis patients after embolization, according to recent studies. Therefore, the purpose of the present study was to retrospectively assess the risk factors of recurrent hemoptysis patients with NBSA feeding after interventional embolization.

Methods: Between January 2014 and December 2017, a total of 545 patients underwent interventional embolization for hemoptysis. A total of 93 patients who were confirmed to have NBSA feeding and underwent embolization were enrolled. Patients' demographic characteristics, clinical information, laboratory tests, imaging findings, and embolization outcomes were reviewed. The Kaplan-Meier method and logistic regression analysis were performed for recurrence-free survival rates and risk factors associated with rebleeding, respectively.

Results: Clinical success was achieved in 40.9% (9/22) of patients who underwent embolization prior to computed tomography (CT) bronchial arteriography (BA), and in 98.6% (70/71) of patients who underwent CTBA first. The median follow-up duration was 511 days (range, 1–1,539 days). CTBA performed after the first embolization (P<0.001) and elevated pre-embolization C-reactive protein (P<0.05) were associated with hemoptysis recurrence in multivariate regression analyses.

Conclusions: Multidetector CTBA was recommended prior to embolization, as it shows the diagnostic value for detecting NBSA. Elevated pre-embolization C-reactive protein was found to be associated with rebleeding after embolization.

Keywords: Multidetector computed tomography (MDCT); non-bronchial systematic artery (NBSA); embolization; hemoptysis recurrence; C-reactive protein

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Introduction

Patients with acute hemoptysis account for the majority of emergency department presentations due to its possibility of asphyxiation. Bronchoscopy is helpful for respiratory doctors to identify the site of bleeding and controlling symptoms when using a rigid endoscope (1). However, computed tomography (CT) is equally capable of localizing bleeding and is more effective in detecting underlying diseases, such as tumors and bronchiectasis (2). Additionally, CT bronchial arteriography (BA), in particular multidetector CT (MDCT) BA can identify uncommon etiologies that are not easily detected on non-contrast

CT. It has been recommended as an essential modality in assisting with the planning of bronchial artery embolization (BAE), as CTBA can reveal normally located arteries and ectopic bronchial arteries, such as non-bronchial systematic arteries (NBSAs) that are bleeding culprit vessels (3-8), which were most common in chronic lung disease, with bronchiectasis accounting most, followed by tuberculosis and pulmonary aspergillosis.

BAE has been demonstrated to be an effective and safe approach for hemoptysis (9). However, recurrence during long-term follow up is common, with recurrence rates as high as 45% (9-12). Bronchial arteries are responsible for most hemoptysis cases that need embolization or surgical resection, but bleeding owing to NBSA is not rare, which were embolized in the first session in approximately 40–62% patients (8,9). Failure to identify culprit vessels at initial angiography may increase the possibility of recurrent hemoptysis after BAE (13,14), especially in transcatheter embolization without CTBA examination, the clinical success rate of embolization of NBSA in the treatment of hemoptysis was reported as about 60%. However, research on the risk factors related to hemoptysis recurrence after BAE for these patients has been underreported in the literature. Therefore, the aim of the present study was to retrospectively investigate the risk factors of recurrent hemoptysis patients with NBSA feeding after interventional embolization.

We present the following article in according with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/atm-20-5544).

Methods

Study design

From January 2014 to December 2017, a total of 545 hemoptysis patients underwent interventional embolization in our department. Of these, 93 patients who were confirmed as having NBSA by 320-row MDCT and digital subtraction angiography (DSA) were enrolled in the present study. CTBA was performed prior interventional embolization in 71 patients and after embolization in 22 patients. The enrollment details are summarized in *Figure 1*.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The ethical approval was not required in our hospital, because this is a retrospective study, not prospective studies, and the requirement for informed consent was waived.

CT technique

CTBA images were achieved with a 320-row, 640-slice multidetector scanner (Aquilion ONEVISION; Toshiba Medical Systems). The scan of the upper part of the subclavian artery to the bilateral renal artery was accepted as the field of view. The scanning parameters were based on the manufacturer's recommendations.

CT imaging analysis

All images were analyzed by two independent radiologists with more than 10 years of experience. If consensus could not be reached, a third radiologist reconciled the contradictions. The characteristics of the culprit vessels in the CTBA included thickening (vessel diameter >2 mm) and enlargement or distortion of the BA or NBSA supplying the lesions. In addition to the above CT manifestations, NBSA features included not accompanying the bronchus, not passing through the hilar, passing through the subpulmonary ligaments or adjacent pleura into the pulmonary parenchyma, and pleural thickening. The CTBA focused on the number, location, and source of culprit vessels.

Interventional embolization procedure

All patients signed an informed consent form before the DSA procedure. The femoral artery or radial artery was punctured by Seldinger technique. All relevant systematic arteries (e.g., intercostal artery, subclavian artery, internal thoracic artery) underwent selective arteriography with 5-F curved catheters (Cobra; Cordis) or a left gastric artery catheter (Cook). A microcatheter (2.9-Fr swan-neck microcatheter; Merit Maestro; or 2.7-Fr Progreat; Terumo) was used for superselection of BA or NBSA, noting the spinal arteries' origin from the BA or intercostal arteries.

The arteries were embolized if any of the following findings were viewed on DSA: (I) contrast agent overflow; (II) parenchymal staining; (III) thickening and tortuous artery; (IV) disorder and roughness of terminal artery; and (V) bronchial-pulmonary artery shunts. Interventional embolization were performed with Embosphere particles (300–500, 500–700, or 700–900 μm in diameter; Biosphere Medical) with or without gelatin sponge granules or strips. Coils or medical glue were used if obvious bronchial-pulmonary artery shunts were present. The injection of embolization materials was terminated when the contrast medium did not clear within three cardiac cycles.

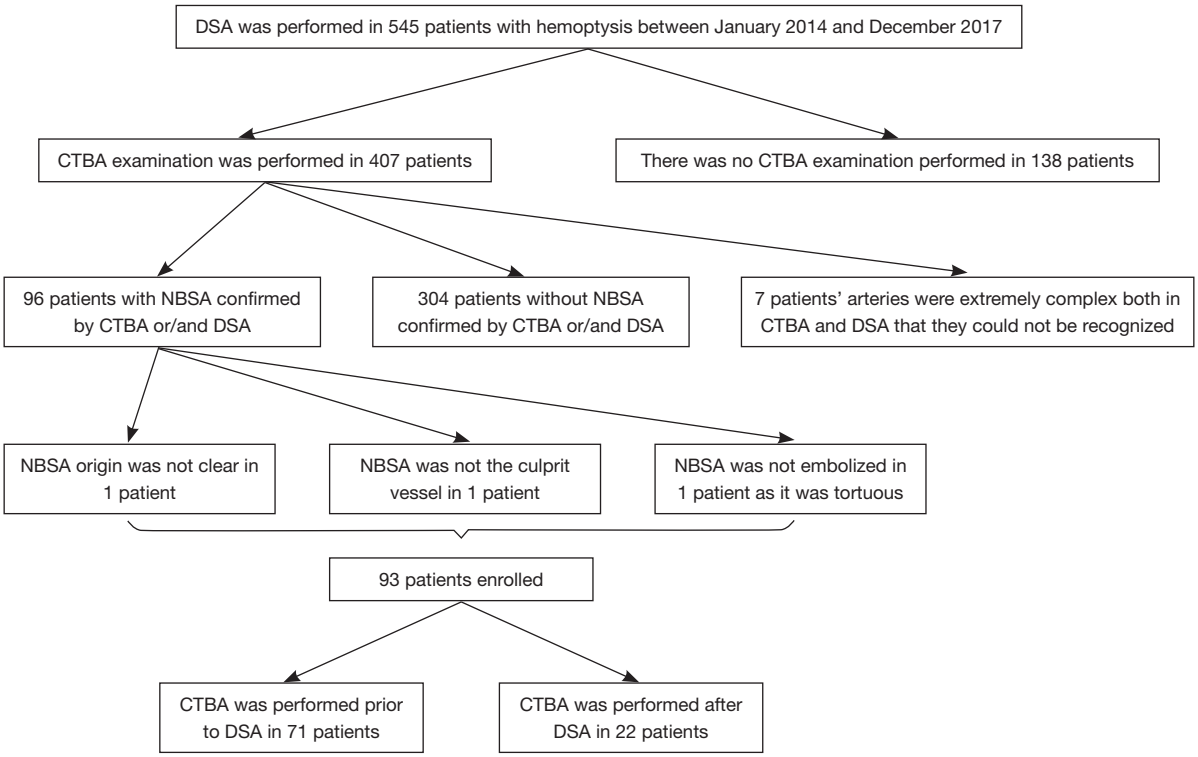

Figure 1 The enrollment details. CTBA, computed tomography bronchial arteriography; DSA, digital subtraction angiography; NBSA, non-bronchial systematic arteries.

Assessment and follow up

The amount of bleeding was defined as severe hemoptysis (≥300 mL/day), moderate hemoptysis (100–300 mL/day), and mild hemoptysis (≤100 mL/day).

The patients was observed for 1 week after the embolization procedure and discharged if there was no hemoptysis recurrence. Repeated embolization or CTBA examination should be performed if recurrent hemoptysis was present within 1 month to determine if there are any missing or recanalization culprit arteries (15).

Clinical success was defined as no hemoptysis within 24 hours after BAE (16,17). Survival and hemoptysis recurrence were retrospectively analyzed after following up the patients by telephone or interviewing the doctors in charge. Follow up was set from the date of first embolization to the terminal point. The recurrence-free time was defined as the time from the first embolization procedure to the second embolization procedure or to the patients' death or last follow-up.

Statistical analysis

Data analysis was performed with SPSS version 17.0 software. The recurrence-free survival likelihood was calculated by the Kaplan-Meier method and log-rank test. Logistic multivariate analysis was used to reveal independent risk factors associated with hemoptysis recurrence. Hazard ratios (HR) with 95% confidence intervals (CI) were calculated. $P<0.05$ was considered statistically significant.

Results

Patient demographics

The demographics of the 93 patients are summarized in *Table 1* (61 males and 32 females, median age: 59 years, range, 15–80 years). The most common comorbidity was hypertension (n=27), followed by diabetes mellitus (n=14). All patients underwent CTBA.

Table 1 Clinical characteristics of hemoptysis patients

Variable	CTBA first (n=71)	Embolization first (n=22)
Mean age (years) ± SD	57.3±11.9	56.5±15.6
Sex (male/female)	49/22	12/10
BMI	21.9±2.6	21.3±1.6
Comorbidities		
Hypertension	22	5
Diabetes mellitus	10	4
Chronic liver disease	10	1
End-stage renal disease	3	0
Use of anticoagulant/antiplatelet agents	3	0
Main cause of hemoptysis		
Bronchiectasis	33	13
Pneumonia	1	0
Tuberculosis	6	0
Silicosis	5	1
Lung cancer	1	3
Pulmonary aspergillosis	6	2
Arteriovenous malformation	13	3
Bronchial pulmonary vessel shunt	5	0
Hemoptysis amount day (mL/day)		
Major (≥200 mL)	9	3
Moderate (100–200 mL)	13	8
Minor (<100 mL)	49	11
Laboratory finding		
White blood cells (10^9/L)	7.9±2.6	8.9±3.2
Platelets (10^3/μL)	214.4±65.5	180.6±58.5
C-reactive protein (mg/L)	20.1±25.7	18.4±23.6
Prothrombin time (seconds)	14.3±1.5	15.0±1.3
Prothrombin time activity (%)	88.2±15.1	79.2±13.0
D-Dimer	8.6±7.5	12.8±7.3

BMI, body mass index; CTBA, computed tomography bronchial arteriography; SD, standard deviation.

CTBA findings

A total of 151 NBSA and 240 BA were identified in 93 patients. Two patients had single NBSA without bronchial arteries. After retrospectively analyzing the CT findings, the most frequently involved foci was the right lung. The common origins of NBSA were the internal mammary arteries (n=58, 38.4%), followed by the intercostal arteries (n=42, 27.8%) and subclavian arteries (n=37, 24.5%). The CTBA findings of these arteries are summarized in *Table 2*.

Table 2 CTBA and DSA findings of bronchial and non-bronchial systematic arteries

CTBA and DSA findings	CTBA first (n=71)	Embolization first (n=22)
Bronchial artery (n=240)	187	53
Right	101	25
Left	86	28
Bronchial pulmonary vessel shunt (n=71)	53	18
Non-bronchial systematic artery (n=151)	106	45
Location		
Right	69	11
Left	37	34
Origin		
Intercostal artery	30	12
Internal mammary artery	40	18
Subclavian artery	29	8
Lateral thoracic artery	0	5
Esophageal common artery	2	0
Thyrocervical trunk	2	0
Inferior phrenic artery	2	0
Cephalic artery	1	0
Brachiocephalic trunk	0	1
Left circumflex branch	0	1

CTBA, computed tomography bronchial arteriography; DSA, digital subtraction angiography.

BAE outcomes

Clinical success was achieved in 40.9% (9/22) of patients who underwent embolization prior to CTBA, and 98.6% (70/71) in patients who underwent CTBA first. The median follow-up duration was 511 days (range, 1–1,539 days). There were no major complications or embolization-related deaths. The estimated hemoptysis-free survival rates in the two groups at 1, 2, and 3 years were 80.3% versus 31.8%, 40.8% versus 18.2%, 11.3% versus 0%, respectively.

The Kaplan-Meier survival curves and log–rank tests were performed to evaluate the risk factors that influenced the recurrence-free period. There were four factors associated with short recurrence-free time after embolization: embolization first (P<0.001), elevated pre-embolization C-reactive protein (P=0.001), prothrombin time above the normal range (P=0.029), and decreased prothrombin time activity (P=0.010) (*Figures 2-5*). Multivariate regression analysis identified embolization first (HR: 32.778, 95% CI: 7.049–152.411, P<0.001) and elevated pre-embolization C-reactive protein (HR: 3.618, 95% CI: 1.050–12.470, P=0.042) as independent risk factors for hemoptysis recurrence after embolization (*Table 3*).

Discussion

The present study showed the necessity for hemoptysis patients to undergo CTBA and to correct coagulation abnormalities before embolization to prevent hemoptysis recurring after a short period of time. Moreover, an elevated C-reactive protein level prior to first embolization was found to significantly affect rebleeding.

BAE is recommended for hemoptysis patients, with a recurrence-free procedure success rate of approximately 90% (18). Previous studies have reported the recurrent hemoptysis rate to be approximately 10–30% (18). In the present study, the incidence of rebleeding was 31.2%

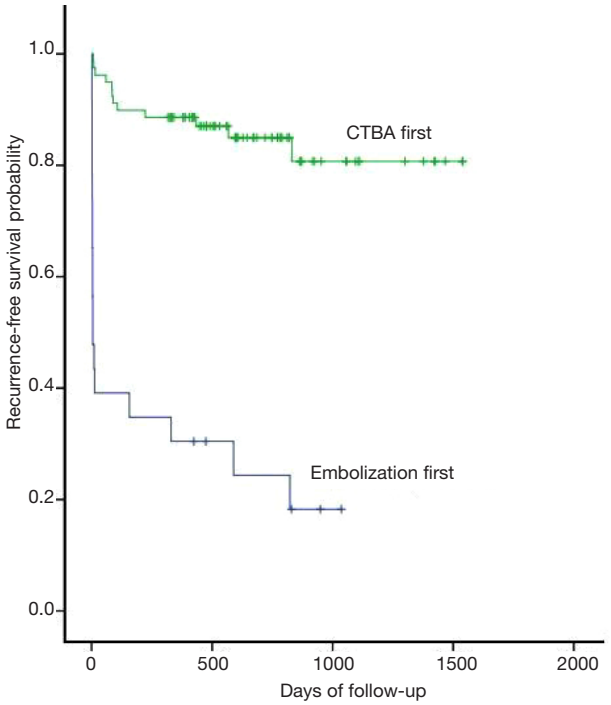

Figure 2 Recurrence-free survival curves of patients who underwent CTBA first or embolization first. P<0.001. CTBA, computed tomography bronchial arteriography.

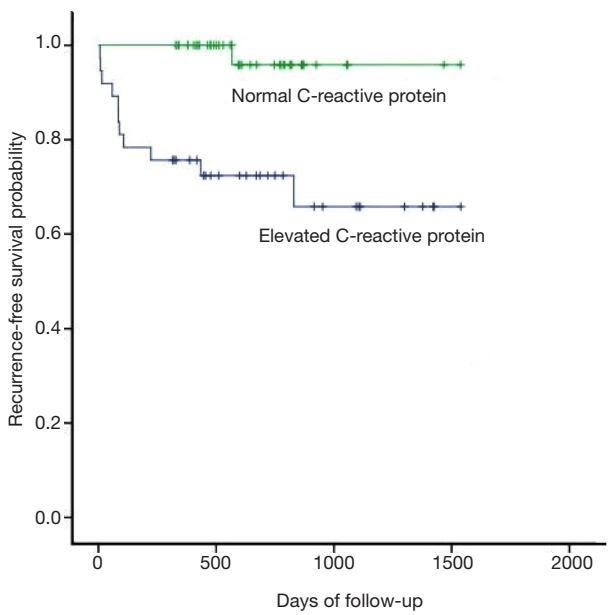

Figure 3 Recurrence-free survival curves of patients who had normal or elevated C-reactive protein. P=0.001.

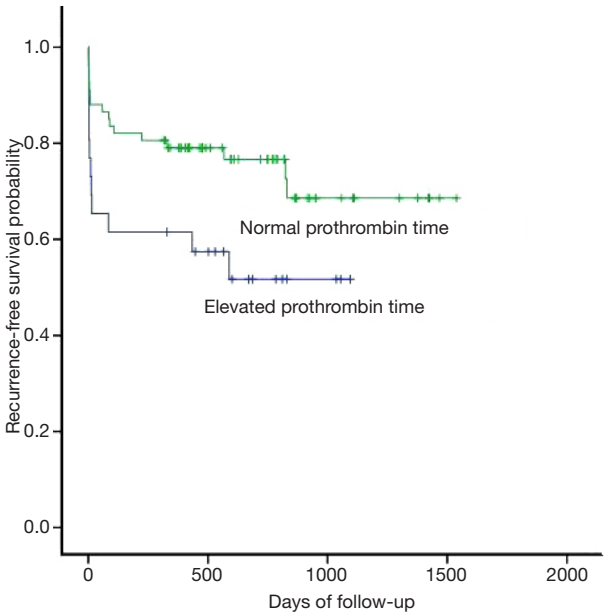

Figure 4 Recurrence-free survival curves of patients who had normal or elevated prothrombin time. P=0.029.

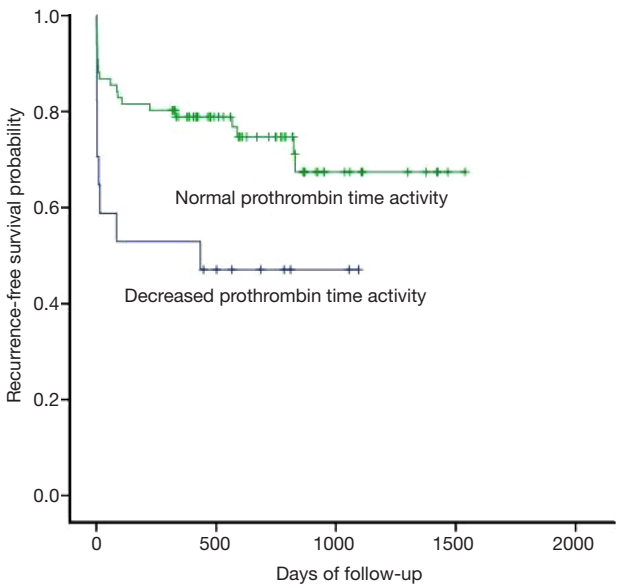

Figure 5 Recurrence-free survival curves of patients who had normal or decreased prothrombin time activity. P=0.010.

Table 3 Multivariate regression analysis of risk factors associated with recurrent hemoptysis after embolization in the computed tomography bronchial arteriography-first group

Variables	Hazard ratio (95% CI)	P value
Embolization first	32.778 (7.049–152.411)	0.000
Elevated pre-embolization C-reactive protein	3.618 (1.050–12.470)	0.042
Elevated prothrombin time	0.289 (0.038–2.272)	0.238
Decreased prothrombin time activity	8.118 (0.818–80.537)	0.074

CI, confidence interval.

(n=29), which is higher than that of previous studies (18-20). The higher incidence may be associated with etiology, from immediately controlled, such as bronchiectasis, to easily recurrent, such as pulmonary tuberculosis and aspergillosis (19,20). The common origins of NBSA were the internal mammary arteries (n=58, 38.4%), followed by the intercostal arteries (n=42, 27.8%) and subclavian arteries (n=37, 24.5%), which is similar to previous literature (5,9,21,22). Those NBSA can be easily missed by inexperienced radiologists when performing selective angiography, which may be another reason for the lower incidence of NBSA as culprit vessels reported in previous studies (18-20).

At present, the introduction of NBSA is mainly based on the DSA, which is considered a rare culprit vessel in hemoptysis patients; therefore, missing NBSA in embolization treatment is common and may cause hemoptysis recurrence in a short period of time (5,23-25). With improvements in MDCT technology, CTBA is more frequently used in hemoptysis patients. It has an important role in detecting NBSA as culprit vessels prior to embolization; in the present study, it demonstrated a short rebleeding time after embolization. DSA is less sensitive to NBSA and ectopic BA, and depends on the interventional radiologists' experience. Therefore, CTBA performed before embolization/DSA can detect more culprit vessels and guide interventional radiologists to embolism, and then decrease the possibility of hemoptysis recurrence, especially 320-row MDCT compared with 64-row and 256-row MDCT, according to previous studies (26-36).

Among the laboratory data retrospectively analyzed, elevated C-reactive protein above the normal upper limit prior to the first embolization revealed active inflammation, and was approved as a significant risk factor for rebleeding after treatment. Clinically, a higher C-reactive protein level indicates more severe inflammation (37). CRP level is apparently always greater than it is in case of viral or aseptic meningitis. This distinction is not true with infection elsewhere, for instance, in the respiratory tract. The CRP level reflects activity of the disease and in severe cases, high levels are always seen. The suppressive effect of some preparations of CRP on platelet aggregation, activation, and release reactions is now known to have been due to a coisolating low-molecular-weight material which contaminated these preparations (37). Therefore, hemoptysis patients with lung inflammation are at high risk of hemoptysis recurrence after initial treatment. Unfortunately, we did not analyze the C-reactive protein level at follow up after embolization, thus statistical significance as a risk factor could not be determined, which is a limitation of the present study.

The present study was also limited by its retrospective nature and small sample size. Successful identification and embolization of the bleeding arteries depend on the experience of the interventional radiologists, which may bias the results.

In conclusion, the results revealed that MDCT is a valuable method for identifying NBSA that are easily missed on conventional DSA. We recommend the routine use of high-quality CTBA and the correction of coagulation abnormalities before embolization. Hemoptysis patients with an elevated C-reactive protein level, who are prone to recurrence in a short period of time, should be closely monitored.

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Footnote

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Data Sharing Statement: Available at http://dx.doi.org/10.21037/atm-20-5544

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm-20-5544). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The ethical approval was not required in our hospital, because this is a retrospective study, not prospective studies, and the requirement for informed consent was waived.

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